The context dependence of network response properties in V1 of primates and cats.

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By

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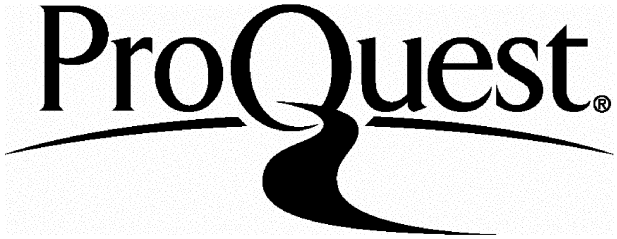

Abstract.

In the mammalian visual system, stimulus context was investigated with respect to the ways it influenced neuronal mean response magnitude (the average number of spikes fired per second), response temporal structure (the timing of spikes with respect to one another), and the extent to which distributed neurones fired spikes synchronous due to synaptic interaction between them. Neurones were presented with bipartite grating stimuli, in which the spatio-temporal relationship between the grating activating the excitatory receptive field and that presented to the surrounding visual space could be varied systematically. Simultaneous extracellular recordings were made of the responses of up to four single neurones separated by 750-1000μm, in the lateral geniculate nucleus (LGN) of the thalamus in the cat, or the primary visual cortex (V1) of non-human primates or cats.

Changing context systematically influenced the activity of groups of cells. The responses of 83% of primate V1 cells to discontinuous stimuli, in which the centre/surround orientation difference was greater than 45°, contained stronger oscillations at frequencies below 80Hz, than responses to continuous stimuli. Many cat and primate V1 neurones exhibited elevated response magnitudes to such stimuli. In primate V1, the strength of a cell's oscillatory discharge was dependent on stimulus configuration rather than response magnitude. In the LGN and V1, cell pairs with different orientation preferences fired synchronised responses when stimulated by specific discontinuous grating configurations.

Stimulus specific synchronised LGN input, and reciprocal excitatory and inhibitory cortico-cortical connections could generate these properties of cells, and the network in which they exist. A model is proposed to account for the function significance of contour discontinuities in generating coherent neural representations of objects in the visual world. It involves response synchronisation in horizontal, feedforward and feedback interactions, within and between the LGN, V1, V2 and V4.

Contents

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Tables.

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1. **Preamble.**

The central nervous system is a highly interconnected body of neural centres concerned with processing information relevant to external and intrinsic events necessary to an organisms survival. External events are processed by the visual system, beginning at the retina, this being the first place where the visual world impinges upon the us. From the retina, information is passed to the thalamus and then to visual cortical centres. Conclusions drawn from early research in the visual system (Hubel and Wiesel, 1962, 1965) emphasised this feedforward aspect of information processing. A hierarchical architecture was proposed in which signals were passed from neural centres directly connected to the retina such as the lateral geniculate nucleus in a serial chain to others in the cerebral cortex, where the role of each subsequent stage was to process the progressively more complicated information passed to it. Recent evidence however suggests that paths of information flow, are not as simple as was first supposed, and in fact there is much feedback connectivity between 'higher' cortical and 'lower' sub-cortical and cortical centres (Van Essen et al, 1985). A feature of the system as a whole is that as information progresses from 'low' to 'high' centres, it is processed by cells that are sensitive to a larger areas of a visual scene. The neurones in these centres have other properties that emphasise different aspects of the visual world, such as form, motion and colour. Thus presence of feedback influences should mean that at a given in point in the system, the activity of a neurone is not simply the result of stimulation by the attribute to which it is sensitive, but is also in part due to the form, motion and colour properties of the visual scene around this optimal stimulus. Sensitivity to the context of a stimulus should be a feature of neural activity. These influences on activity come about because cells communication with others through synaptic mechanisms. The firing of an action potential by one cell, changes the propensity of another to fire an action potential. Action potentials represent aspects of a visual scene, however, how they do this is still a critical point of debate (e.g. Barlow, 1972, Shadlen and Newsome, 1994, and Singer and Gray, 1995). The debate centres on whether cells behave as integrators of network activity and represent the visual world with changes in firing rate. Or alternatively sense coincidences in their input from other cells and respond with distinct temporal patterns of output that are synchronised with those of other cells.

This thesis is concerned with an investigation of these modes of processing and the influence that stimulus context has upon them. The historical background of these ideas will be covered in following chapters, from early and recent philosophical proposals to experiments in the early part of this century which revealed some of the basic features of the CNS, such as functional modularity and synaptic connectivity. The feedforward and feedback connectivity between the LGN and primary visual cortex is typical of the network of connections between cells in many centres in the brain and therefore provides a good model for the investigation. Details of the anatomical characteristics of this network, the visual sensitivity of cells and ideas concerning the code used by these cells, representing visual stimuli, will be discussed in detail. The results section will report the outcomes of experiments that were designed to investigate network codes and the influence of context upon them. A discussion will then examine the implications of the results reported, for what we know about how the visual system functions, in the context of previous work done by others. This will be done in attempt to at least partially answer the question, which is, is visual experience an emergent product of a distributed network ?

2. Introduction.

Historical perspective.

Early ideas.

There has been a long history of debate concerning visual perception, cognition and all matters related to the mind (Grüsser and Landis, 1991) ever since Greek philosophers such as Pythagoras and Homer thought about them. These early philosophers believed in a material body controlled by a transmaterial pneuma, and concepts such as the transmigration of the soul and reincarnation. Plato (427-347 BC) was one of the first people to consider where in the body this soul might reside, in his work entitled 'Timaios'. He divided the soul into three parts the third of which was located in the brain, this part was the divine, immortal, and human-specific component. This immortal soul dealt with 'higher' sensations, its actions were seen as expressions of will. The other parts, rational and mortal, dealt with emotions and various drives and were located in the thorax and abdomen. Central to the beliefs of Plato and his peers such as Empedocles, Diogenes, Pythagoras and Alcmaeon, with regard to vision was the idea that pneuma was emitted from the eyes for the purpose of vision. This pneuma interacted with light to form a 'cone of vision' which actually touched objects in order that they should be seen, this is known as the 'extramission theory of vision'. Early anatomical observations of the central nervous system were made by Alcmaeon of Croton (530-470 BC), he, having observed that brain lesions lead to impairment in perception and cognition, considered the brain to be the 'hegemonikon' of the soul. Alcmaeon discovered the optic nerve and chiasm and proposed that the brain and eyes were reciprocally connected through these, and that pneuma formed the medium inside the channels.

Aristotle (384-322 BC) had a slightly different view from this group, he believed in the tripartite soul and proposed that it guided and organised living organisms. His soul was structured hierarchically according to the type of organism in which it existed. All living things contained a vegetative soul, only organisms such as animals and man contained an animal soul, and only man possessed the rational component, that was

capable of thought. Aristotle attributed perception to the sensitive animal soul, though he rejected the idea that perception and cognition are related to brain function. His view was that the information from sense systems is integrated by the common sense of the hegemonikon, and this extracted the general properties of objects. For Aristotle, the brain was a distilling device for making 'ether', the essential spirit of life. This was made from respired pneuma and energy gained from food. His physical experiments lead him to suppose that the convoluted shape of the cortical mantle was a cooling device for this process.

By the Middle Ages thoughts on brain function had started to be based on the use of the ventricles. These had been discovered in 300 BC by Herophilos and Erasistratos. The view put forward in the fourth century AD by the Christian Bishop Nemesios of Emesa was that two lateral ventricles of the brain were central to perception and cognition. They were thought to contain the soul's multi-modal power of integration that was necessary for the perception of objects. These ventricles were thought to contain the ether that Aristotle had postulated, only now it became known as spiritus animalis ('anima', latin for soul). Anima in the ventricles was said to be the medium for the soul. Further investigations took place in the Arab nations between 800 and 1200 AD, these scientist also believed in the role of ventricles, among the most important pioneers were Costa ben Luca (864-923) and Alhazen (965-1040). Alhazen made detailed drawings of the anatomy of the eye, and much later thought with regard to brain function drew on the findings of this Arabic group.

Albertus Magnus (1198-1280) was one early scientist to recognise the importance of the cortex. He divided brain tissue into three components, the first being the velum, or as we know it today, the cortex, then there was the medulla or white matter, Albertus included last in his classification the ventricles. He then went on to develop a complicated theory of perception and cognition involving all three components. This theory also involved the use of certain rare spirits, analogous to Aristotle's 'ether'. Further theories espousing the use of these special liquids for the mediation of mental processes were still being put forward at the end of the nineteenth century. As late as 1897, Franz Liedig published his view that the seat of mental processes was not the spongy nerve tissue found in the brain but in fact the fluid surrounding it.

In Renaissance times the ventricles were still pre-eminent in theories of brain function, Leonardo da Vinci, famous for many things, investigated the anatomy of the central nervous system and theorised on its function. He believed the retina sent the visual image down the optic nerve, through the optic chiasm and into the ventricles. When inside it was then projected onto the walls. He even calculated, based on his observations of the bovine nervous system, that there should be enough room for a significant amount of magnification of the retinal image. Aside from this view da Vinci did believe that the representation of the visual image was achieved by the formation of a physiological material image that maintained the geometrical order of the original input. Leonardo also believed that each object hitting the retina possessed ten properties that could be perceived by the visual system, light, dark, colour, shape, size, position, distance, nearness, movement and rest. These are views which are relevant to modern studies of the visual system.

Modern Ideas.

Western philosophy and thinking on mental processes has its roots in Greek philosophy and Judaeo-Christian religion and these movements have in great part been influenced by ancient cultures. It is only in the last few hundred years, since developments in optical instruments such as microscopes, that theories have been based on observations from nature (Russell, 1945). A treatise that dealt with vision was that written by John Locke, in his Essay on Human Understanding published in 1690, he writes about vision,

The most comprehensive of all our senses, conveying to our minds the ideas of light and colour, which are peculiar only to that sense; and also the far different ideas of space, figure and motion.

At this time a great source of debate that both John Locke and a philosopher named George Berkeley entered into, was whether or not elementary abilities in vision are dependent upon learning or are based predominantly upon innate neuronal

mechanisms. A question central to this problem at the time was proposed by William Molyneux to John Locke in a letter of 1693. Basically Molyneux asked the question, if a man, blind from birth, had tactile experience of a sphere and cube of the same size, were he suddenly to become sighted, would he immediately know by sight which was the cube and which the sphere ? Both Locke and Berkeley supposed that the subject would not be able to perform the task, many observations of subjects then and since have demonstrated this point. Such elementary visual tasks are impaired by prolonged blindness from birth.

George Berkeley, made early anatomical observations of the retina and its optical functionality, he set out some theories on vision in *An Essay Towards a New Theory of Vision.* Here he describes his ideas on perspective within the visual field and also how the inverted picture on the surface of the retina generates what we sense. He discusses the cognitive aspects of vision and touch and the problem set by Molyneux, his view was that objects of sight and of touch make up two sets of ideas which are widely different from one another, and that vision needs a frame of reference which is based on tactile experience. His view of vision follows from his observations of the flat picture on the surface of the retina, and is shown in the following quote,

All that is properly by the visive faculty amounts to no more than colours, with their variations and different properties of light and shade.

He feels that other aspects of vision such as form, size, and motion which we take for granted when we open our eyes are actually generated by referring to tactile experience, rather than being generated by mechanisms intrinsic to the visual system.

David Hume developed the empirical philosophies of Locke and Berkeley, into a more rational set of ideas. In a section entitled *Scepticism with Regard to the Senses*, in his book *Treatise on Human Nature* published in 1739, he dealt with issues that relate to perception and what can be perceived. He discussed whether an object exists while it is not being perceived. in general his thoughts on vision are related to the time scales on which the senses operate. His view of the mind is given as follows,

.... we may observe, that what we call a mind, is nothing but a heap or collection of different perceptions, united together by certain relations, and supposed though falsely, to be endowed with a perfect simplicity and identity.

The certain relations that Hume mentions are causal relations, Hume believed that we can never say that there is a connection between two perceptions, as we can never properly perceive their cause, however based on spatio-temporal relations which he believes we can sometimes infer, we infer causation. Hume's view of how we perceive our world is empirical, we can only perceive what we *are* perceiving, the rest of our world is based on experience, however this experience must not be based on a view that events cause other events, but rather it must be framed in terms of one events propensity to follow or be simultaneous with another.

A set of ideas that are more directly relevant to the subject of this thesis are those published by Bertrand Russell in 1921 in a book entitled *Analysis of Mind.* This book contains a series of lectures given shortly before the book was published, a number of these deal with issues that relate to visual perception. In these lectures he discusses perception with reference to both physiology and psychology. Russell defines perception in the following way,

Adhering for the moment to the standpoint of physics we may define a 'perception' of an object as the appearance of that object from a place where there is a brain (or, in lower animals, some suitable nervous structure), with sense organs and nerves forming part of the intervening medium.

Later Russell discusses the nature of sensations, and establishes that they are events which have physical causes and mental effects. He suggests that mental phenomena may be explicable in terms of the peculiarities of nervous tissue. In one passage he alludes to the temporal characteristics of sensation,

We are at all times during or waking life receiving a variety of impressions which are aspects of a variety of things. We have to consider what binds together two simultaneous sensations in one person, or more generally, any two occurrences which form part of one experience.

A further set of ideas that Russell uses to discuss cognition and perception were formulated by Richard Semon in his book *Die Mnemischen Empfindungen.* In this book Semon sets out his mnemic principles, there are two, the first being the 'Law of Engraphy', which is,

All simultaneous excitements in an organism form a connected simultaneous excitement-complex, which as such works engraphically, i.e. leaves behind a connected engram-complex, which in so far, forms a whole.

The second mnemic principle, called the 'Law of Ekphory' is as follows,

The partial return of the energetic situation which formerly worked engraphically operated ekorphically on a simultaneous engram complex.

It follows from these two laws that a stimulus that has an excitatory effect, effects a system in such a way that another stimulus with similar attributes to the first, may regenerate the mechanism by which the first stimulus was processed. Russell defines the state of the system before the original stimulus as the 'primary indifference state', and that after as the 'secondary indifference state'. The difference in the system, that is the result of the transition between these states can be qualitatively described as the engram. In terms of the present discussion we might consider an engram to be a set of connections between neurones in the primary visual cortex, this application however appears to generate certain problems. These engrams it is suggested give rise to mnemic phenomena, which have their roots in experience, a mnemic phenomenon can only occur if the particular aspect of a system under investigation is in its secondary indifference state. This characteristic of engrams, thus causes problems when we try to apply them to function of the primary visual cortex, a system that is continuously in flux, and can never be in it's secondary indifference state for long. As David Hume

says, in a section entitled Scepticism with Regard to the Senses in his book of 1739, Treatise on Human nature, concerning the senses,

they give us no notion of continued existence because they cannot operate beyond the extent in which they really operate.

At first sight it might seem that Semon's ideas are more applicable to the maturation of an embryonic nervous system, that develops in a use dependent manner, or to higher cortical areas, where function depends upon unconscious shaping and maturation of their signal processing properties, or to centres of the brain concerned with memory and learning, where mechanisms such as 'long-term potentiation' lend themselves very well to being considered as engraphic. However it is possible to consider the primary visual cortex as functioning in two ways with reference to these ideas. Firstly the high degree of convergent and divergent connections which have been observed in many recent anatomical studies might be the substrate for engrams. Each cell would be part of a multitude of overlapping and interacting engrams, and as a consequence, in it's function the cortex would behave ekorphically. Alternatively the cortex could be considered to be in continuous flux between primary and secondary indifference states, engrams would not be hard wired as in the situation above. The high degree of divergent and convergent connectivity, while obeying a few basic rules, would be a 'free form' substrate for the formation of engrams in a stimulus dependent manner. There would be a multitude of transient engrams, which rather than operating within the spatial constraints of hard-wired anatomy, would function within temporal constraints. These temporal constraints would then be governed by the electrotonic characteristics of the cells involved, which would themselves be under the control of the stimulus.

Historical experimental investigations.

Concurrent with philosophical investigations of the nature of the central nervous system in the last few hundred years have been investigations of the anatomy of the brain. Investigation has focused at all levels from the cellular right up to characterisation of the shape of the cortical mantle.

The first developments in neuro-anatomy came shortly after Hume published his ideas, in the early 1780's several anatomists were making the first descriptions of the gross anatomy of the human brain. Alexander Monroe published a book in 1783, that showed the major subdivisions of the brain, and also depicted the cortex as a uniform grey strip as distinct from the white matter. At about the same time an Italian anatomist named Francesco Genari also described the gross structure of the brain but he also made more detailed observations of the substructure of the cortex, and found that there was a white layer that divided the cortical grey matter in two and ran parallel to the surface of the cortex. He also observed that this layer was most prominent in posterior areas of cortex, he suggested that it might have some particular and important function. This stripe later became called the Stria of Genari.

Luigi Galvani in 1791, discovered animal electricity, this was the first indication of the essentially electrical nature of central nervous system function. Continued exploration of the central nervous system yielded further insights, in the 1860's, discoveries suggested that particular areas of the brain performed particular functions. Among these early discoveries were those by British neurologist John Hughlings Jackson, he observed a recurring epileptic seizure in one of his patients which when started, spread systematically through the body in the same way each time it occurred. From this he inferred that there might be a systematic organisation of the brain, with areas of tissue that are in close proximity controlling movement in limbs that are also in close proximity. These observations were supported by early physiological experiments carried out by two Germans, Fritsch and Hitzig. They electrically stimulated different areas of the frontal lobe and observed movements in different limbs on the other side of the body from the hemisphere of the brain that they were studying. They had thus found areas of the cortex with specialised functions, the control of limb movements, and also that each side of the body is controlled by the contralateral hemisphere of the brain.

Other work being carried out in the middle of the nineteenth century focused on the cellular mechanisms by which the brain functions. German anatomist Rudolf Virchow recognised that cells in the brain could be divided into two groups, the first being

neurones and the second, a larger group of cells called neuroglia, a name that means 'nerve glue', these cells were called this because they appeared to surround the neurones, fill the spaces between them and generally hold the neurones in place. There are two main types of glial cells, astrocytes, which are star shaped and oligodendrocytes.

One early work which focused on vision was by a German scientist named Ernst Mach, who in 1864 devised a mathematical description of the transformation of the retinal image into a perceptual image, In his treatise which dealt with the mathematical characteristics of the analysis of a visual scene. He proposed that the spatial light distributions within the visual field and on the retinal surface are respectively processed by retinal and cerebral neuronal mechanisms. The spatial light distribution i(x,y) on the retina as well as the first and second order derivatives of this distribution constitute the essential signals used for spatial perception and object recognition. He asserted that the second spatial derivative is used in the perception of object contours that separate one object from another.

The first reports of the discovery of a cortical centre which might perform the manipulations on the retinal image that Mach proposed were made by the Briton David Ferrier. In work on monkeys he electrically stimulated different areas of cortex with an alternating current. Eventually he found one, which, when stimulated, caused the animal to move it's eyes. Shortly afterwards he removed the area of brain, located in the angular gyrus of the parietal lobe, and found that his subjects were unable locate objects and pick them up. From much anecdotal evidence he reported that he had found the area of cortex which dealt with visual function at the Royal Society of London in 1875. This finding however was hotly contested at the time by a German named Hermann Munk who had done a similar set of experiments and found that in fact the occipital lobe was responsible for visual function, not the parietal lobe. Munk found that lesioning the occipital lobe on one side of the brain resulted in hemianopsia, blindness in one half of the visual field, and that removal of both lobes resulted in complete blindness. He also suggested that each lobe was connected to both eyes. This opened up a controversy not only because of Ferrier's previous observations, but also because Ferrier reported that when he lesioned the occipital

lobe he did not observe the blindness that Munk had done. This was later attributed to the fact that Ferrier had probably not removed the occipital lobe as thoroughly as Munk, he had left enough of the peripheral field, so that subjects could exploit greater eye movements to perform basic visually guided tasks. It has been suggested that in Ferrier's original experiments in the angular gyrus, what he had actually removed was a centre responsible for visually guided movements. After a number of further experiments later in the 19th century it became generally accepted that the primary visual centre was located in the occipital lobe.

The next step in the investigation of visual function involved the discovery that the visual world is mapped systematically onto the surface of the occipital lobe. This study was initiated by a Swede named Henchen in 1892, who collected together the autopsy reports from people with brain damage, that had lead to impairments in vision. From his data he confirmed Munk's findings and also attempted to map the visual field onto the cortical surface. However his data was limited, it was not until the Russo-Japanese war in 1904 that sufficient data was available to deal with this issue properly. The investigation was carried out by a physician in the Japanese army called Tatsuji Inouye, and facilitated by the rifle that the Russian Army used, it fired bullets with a very high muzzle velocity, which meant that a bullet could enter and leave the skull without shattering it or killing the victim (Glickstein and Whitteridge, 1987). Inouye had 29 patients that had been shot through the occipital lobe, and these people had the visual deficits commensurate with this. Inouye then mapped the areas of the visual field that each of his patients could not see, and reconstructed the trajectory of the bullet relative to the visual cortex from the entry and exit wounds. This allowed him to construct a clear and reasonably precise map of how the visual world is mapped onto the cortical surface of the occipital lobe. He showed a number of things which we would recognise today, firstly that the central visual field is mapped onto the posterior region of the occipital lobe, and that a disproportionate large amount of cortical surface is devoted to processing information from the central visual field.

At about this time there was a great deal of debate about whether the nervous system consisted of enormous numbers of discrete neurones or whether it was in fact a continuous network of tissue, this latter idea being known as the 'reticular theory'.

Central contributors to this debate were two great European neuroanatomists, Santiago Ramon y Cajal and Camillo Golgi. Golgi was a passionate proponent of the reticular theory, whereas Cajal felt that neurones were discrete elements within the nervous system. Cajal went onto to show this using a technique that Golgi had developed, the Golgi silver impregnation process. Both men were later to win the Nobel Prize for their work.

Cajal in 1911 and Brodmann in 1905 initiated the first examination of the distribution of cells as a function of depth within the striate cortex. As a result of this work, both proposed lamination schemes for the distribution of cells throughout the depth of the cortex. However prior to Cajal's lamination scheme other cytoarchitectonic observations of cellular anatomy, lead him to suggest the presence of functional systems within the striate cortex. In a report made in 1898 he discusses "isodynamic groups of neurones that could be activated by elementary sensory impressions." These observations are possibly the first that relate to the columnar organisation of the cortex. A form of organisation which has been demonstrated using modern physiological recording techniques to extend through the full depth of the cortex. Where cells exhibiting particular properties are grouped in anatomically distinct modules that are distributed tangentially to the cortical surface. Cajal's subsequent scheme of cortical lamination was based on differences in morphology that could be observed between cells at different depths within the cortex using the Golgi staining technique. This scheme involved 9 layers, each layer containing cells with a different morphology, particularly relevant to this design was the size and shape of each cell body. Some layers contained large pyramid shaped soma, while others consisted of cells with spherical cell bodies. Using the Nissl staining technique Brodmann's scheme was based on observations of the distribution of total cell populations, it consisted of a cortex with six basic lamina, these have since been further subdivided, but these basic schemes still hold.

Other cytoarchitectonic observations of the central nervous system by Brodmann were of a more global nature. After early reports by Theodore Meynert (1833-1892) and Paul Flechsig (1847-1929), based on Flechsig's observations of the development of myelination, and separate work by Meynert, it was pointed out that there were

correlations between structure and function in some areas of the cortical mantle. Brodmann (1909) proposed a scheme that divided the entire cortical surface into discrete areas on such grounds. His cytoarchitectonic maps are still used today, and it was on the basis of these findings that the mammalian primary visual cortex was denoted area 17.

Shortly after this time several discoveries were made that yielded insight into the function of individual neurones. The first was by Charles Sherrington (1891) who conducted detailed physiological and anatomical experiments on the mechanisms that mediate spinal cord reflexes. This work lead Sherrington to define a pathway that would be responsible for a reflex, in which information could ever travel in one direction. He proposed that an interneuron was involved somewhere in the pathway making it discontinuous. Sherrington proposed that there should be a structure in his pathway, known as the synapses, that allows transmission of information between neurones in a unidirectional manner. At this point however he had not observed the function or morphology of a synapse, but he had functionally defined it. Thus after the anatomical reports of Cajal and the insights by Sherrington into how these discrete entities might communicate, the central concepts on which modern neurophysiology is based had been established. The first person to integrate these disparate concepts was Wilhelm von Waldeyer in 1891, today his theories are generally known as the 'neurone doctrine'. He attributed the function of the CNS to the properties of the neurones within it, this became one of the guiding principles on which studies of the central nervous system were based until recently. One of the first people to publish work on the connectivity of neurones, through synapses was the Viennese physiologist, Sigmund Exner who published a book in 1894. He developed a theory of neural networks and went on to suggest ways in which assemblies of connected neurones might analyse aspects of a visual stimulus such as motion. Visual neuroscience has developed into a reductionist science, in which the physics and chemistry of the central nervous system are studied. Perception and cognition are viewed as biological phenomena. We attempt to find out what tasks the brain is carrying out, and how these come to have a meaning for the organism whose nervous system is being studied.

Recent literature review.

The neural representation of a point in visual space expands as the information contained within it is conveyed from photoreceptors in the retina up to the cortex. A point can be said to be represented by a single rod or cone in the retina, such a neurone has a diameter of only a few microns. However in primate cortex, using information about receptive field size the area of tissue processing a point in the visual field, at 5° eccentricity is approximately 0.18 mm^2 (Van Essen et al, 1984). There is, as a consequence a vastly increased population of cells in the cortex that process any point in visual space. This in turn has important implications for the behaviour of cells at other points in the network which receive feedforward and feedback projections. Divergence is a basic feature of network connectivity in the visual system. Such population expansion provides a substrate for the formation of engram complexes proposed by Semon and Russell, a process which is investigated here. The features of this expansion and how it comes about, in terms of the morphology of individual cells will be discussed below.

The Retina.

The process that occurs in the retina is known as visual transduction. When photons of light pass into the eye and hit the retinal surface, they are converted into electrical signals that the nervous system uses to process information. Visual transduction in the cat and monkey occurs in two types of photoreceptor, rods and cones. These are distributed over the retina, which is dominated by its population of cones, these are either sensitive to long (red), medium (green) or short (blue) wavelength light, making monkeys sensitive to colour in the visual scene, this is not a property of feline retinas however, which are sensitive only to medium wavelengths. Photoreceptor output is then further processed by horizontal, bipolar and amacrine cell networks until it manifests itself in the spatially restricted photic sensitivity of ganglion cells (Hartline, 1940). These cells represent changes in contrast in a visual scene, OFF cells respond to dark spots flashed on a bright background, or the off phase of a bright spot of light on flashed dark background. ON cells have the opposite functionality, responding to

the on phase of a bright spot flashed on a dark background, or the off phase of a dark spot on a bright background (Kuffler, 1953). The area of visual space in which a spot can activate a cell is a small, circular, highly circumscribed zone, this is the receptive field centre. The magnitude of the centre response is reduced when an antagonistic zone surrounding this, is activated by a stimulus that is larger than the centre. A typical ganglion cell receptive field is depicted in figure *1*. Detailed physiological investigation of ganglion cells with visual stimuli has shown that they can be classified into several groups according to their response properties.

In the cat retinal ganglion cells have been categorised as α, β and γ on the basis of their morphologies (Boycott and Wässle, 1974), subsequently these morphological classes were shown to have correlates in the categorisation based on receptive field properties, with Y, X and W cells (Cleland et al, 1975, Piechl and Wässle,1979 and Saito, 1983). A similar relationship is believed to be the case in the primate retina where cells with P type receptive fields have cat β-type morphology, cells with M type receptive fields have cat α-type morphologies (Perry and Cowey, 1981). In the cat α-type ganglion cells have relatively large soma, thick axons and spatially extensive dendritic fields (~200μm in diameter at 1 mm from the area centralis), β-type ganglion cells have smaller soma, thinner axons and dendritic fields covering a smaller area at a given eccentricity, they are ~50μm in diameter 1 mm from the area centralis (AC), a part of the retina with the highest density of cells, and capable of sampling the visual field with the highest acuity. The diameters of these dendritic fields increase as a function of eccentricity, so that 10 mm from the AC α-cell fields are 600-800μm across and β-cell fields are ~120μm in diameter. γ-type ganglion cells were found to have the smallest somas and thinnest axons, these cells did however have sparse dendritic fields covering a large area, approximate 400-500μm in diameter, at an eccentricity 1mm from the AC.

Enroth-Cugell and Robson, 1966, determined two physiologically distinctive types of receptive field exhibited by retinal ganglion cells in the cat. The first type were denoted X cells, characteristically they had small receptive fields, fired in a tonic

Figure 1.

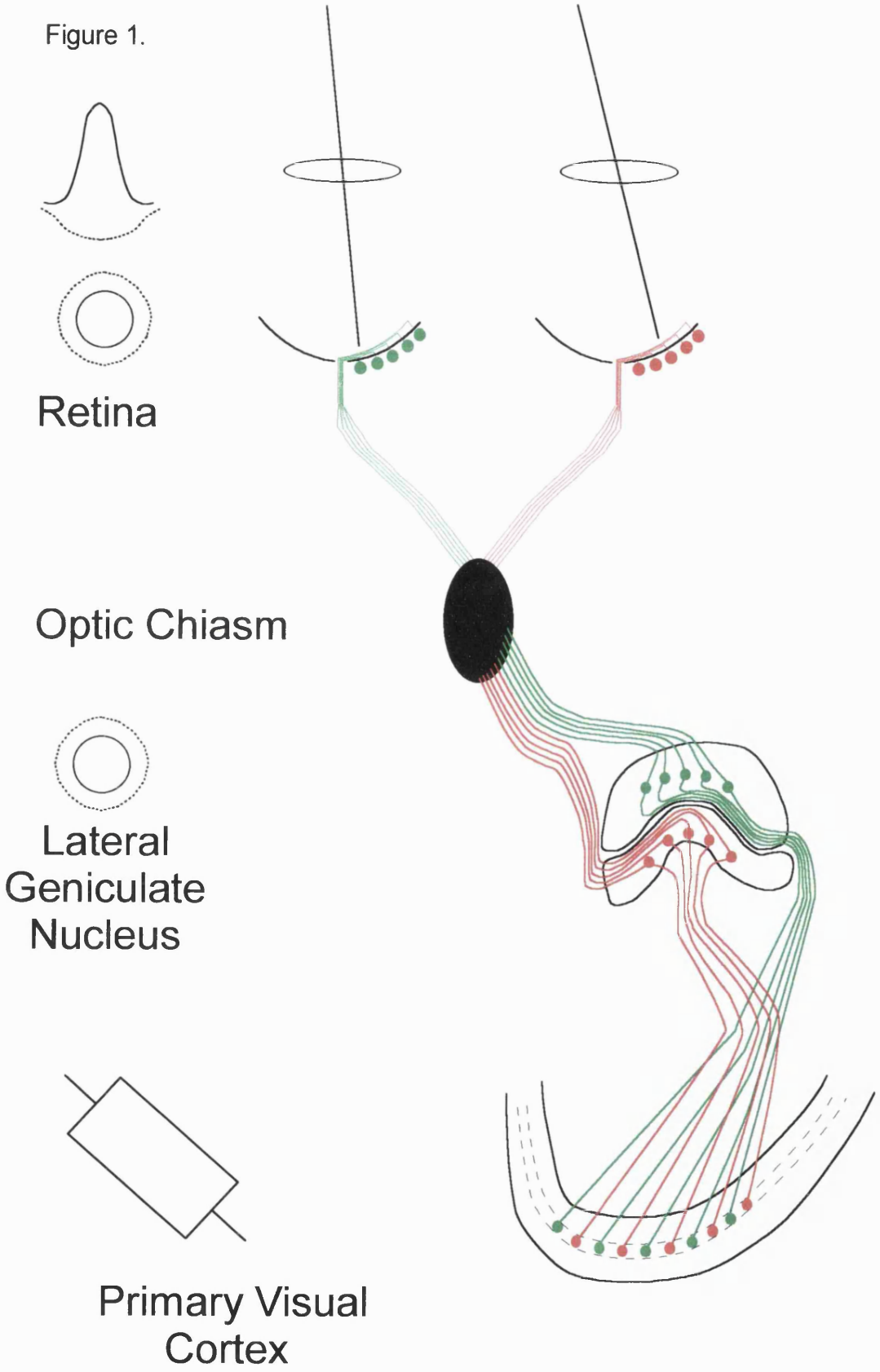

Retina
Optic Chiasm
Lateral
Geniculate
Nucleus
Primary Visual
Cortex

Figure 1.

A schematic diagram of the mammalian visual system, feature retinal output to layer IV of Primary Visual Cortex via the Lateral Geniculate Nucleus. Spatial information from the retina is preserved in a retinotopically distributed termination pattern in the cortex from LGN relay cells. Also featured are typical spatial distributions of photic sensitivity (receptive fields) encountered at each point.

manner when stimulated (Cleland et al, 1971), were insensitive to fast moving stimuli and exhibited linear spatial summation. The second type they denoted Y cells, these had larger receptive fields, responded with a phasic firing pattern, responded vigorously to fast moving stimuli and exhibited non-linear spatial summation. The diameter of both types of receptive field centre increases as a function of eccentricity. In the centre of the area centralis X cells are 0.2° in diameter, while at 25° eccentricity they are 0.4° wide. Y cells are bigger for a given eccentricity, in the middle of the AC they are 0.6° across while at 25° they are 1.4° in diameter (Linsenmeier et al, 1982). The remaining cell type is characterised by having axons with slower conduction velocities and having subtly different receptive field properties from those exhibited by X and Y cells, these cells were denoted W cells (Rodieck, 1967 and Stone and Fukada, 1974). W cells are not necessarily characterised by the centre-surround organisation that is detected in the receptive fields of X\Y cells. As a group these cells exhibit more heterogeneous properties. W cells can either exhibit linear or non-linear spatial summation, phasic or tonic responses can be evoked from them, some respond to both the ON and the OFF of a flashed stimulus. These cells have been said to account for approximately half of all those ganglion cells in the retina, with X cells making another 45% and Y cells the remaining proportion.

The spatial characteristics of the concentric centre-surround receptive fields exhibited by cells with X and Y type receptive fields have been investigated in quantitatively (Rodieck, 1965). Experimental investigation of ganglion cell receptive fields with small bar stimuli showed that the centre and surround interact antagonistically and linearly. It was proposed that retinal centre-surround organisation could be described by a sensitivity profile which was a difference of two gaussian distributions. A spatially extensive negative one of low amplitude that described the surround, and a smaller more focused centre of higher amplitude that described the centre, this is schematically represented in figure *1*. Later work (Hochstein and Shapley, 1976) using a spatio-temporally modulated stimulus, consisting of a series of sinusoidal gratings, showed that X and Y cells respond differently to such a stimulus. X cells with their linear spatial summation respond with a modulated discharge at the frequency of the stimulus, whereas Y cells respond with an unmodulated increase in mean firing rate. This response mode exhibited by Y cells was denoted, non-linear. A model was

developed in which Y cell receptive fields consist of a linearly summating gaussian centre with relatively low spatial resolution, and a series of superimposed non-linearly summing gaussian subunits, that generate the antagonistic surround. An interesting non-linear characteristic of retinal ganglion cells with Y type receptive fields is that they are sensitive to stimuli that are presented to areas of visual space surrounding the receptive field so far described. This response property is known as the 'shift effect', cells can fire when the receptive field is occluded and the periphery is stimulated (McIlwain, 1964).

Macaque monkeys have a visual system sensitive to a similar range of spatial frequencies (DeValois et al, 1982) as human, cells are also sensitive to colour. Investigation of primate retinal cells has shown that they have properties that are not well developed in the cat. The classification of primate retinal ganglion cells has little in common with X, Y and W type cells in the cat. A major difference between the cat and the primate was that because the primate retina is dominated by cone photoreceptors, some retinal ganglion cells have properties consistent with analysis of colour in a visual scene. Early work in the primate retina (Gouras, 1968, 1969) showed that two types of responses could be evoked by stimulating a ganglion cell with a flashed spot. *Tonic* cells were found to respond to the entire duration of a flash, whereas *phasic* cells only responded to the onset of a flashed stimulus. Tonic cells were also characterised by colour sensitivity, they had centre-surround fields in which there was often spectral and sometimes spatial antagonism between the two regions. Phasic cells on the other hand were not sensitive to the colour of their stimuli and were characterised by broad-band spectral sensitivity profiles. Tonic cells were more common near the fovea, whereas phasic cells were more often encountered in the periphery. Further investigation revealed three types based on their responses to visual stimuli (Demonasterio and Gouras, 1975). Some cells were found to be colour opponent, others had broadband spectral sensitivity and yet other had non-concentric receptive fields. Colour opponent cells were characterised by responding tonically and having centre-surround receptive fields, the centres of which were found to receive input from one type of cone (sensitive to long, medium or short wavelength light), while the surround received input from either one or two types. Broadband cells

responded phasically to flashed stimuli, the fields exhibited by such cells reflect inputs received from cones tuned to similar wavelengths.

Recording S potentials in the LGN, that are thought to originate from retinal afferents has shown that there are two physiologically defined groups of cells in the retina, based on their sensitivity to luminance contrast (Kaplan and Shapley, 1984). These groups project to anatomically distinct sights in the LGN. The cells that projected to the magnocellular layers of the LGN, M cells, were found to be 8-10 times more sensitive to stimulus contrast than those that projected to the parvocellular layers, the P cells. There are further differences between M and P populations. The receptive fields of M cells have radii that are 2-3 times greater than those of P cells at a given eccentricity. However it is thought that this does not mean that P cells are capable of resolving stimuli with finer acuity, because the higher contrast sensitivity of M cells makes up for the fact that they have larger fields. It is reported that in the primate retina 80% of cells are P cells and 10% are M cells (Perry et al, 1984). Thus in the cat the basis for functional grouping is the spatial summation properties of cells, whereas in the primate it is contrast and colour sensitivity. It will be seen in the next section that in both visual systems these functional properties will be conveyed to the next node in the network, the dorsal lateral geniculate nucleus.

The lateral geniculate nucleus.

A feature of the input from the retina to the LGN is that it is retinotopically ordered, that is, neighbouring ganglion cells in the retina send axons to LGN that terminate at neighbouring points, and the spatial structure of the retinal image is conserved within the network. Within the feline LGN each retinal afferent axon gives rise to a focused terminal arbour (Sur et al, 1987). Thus when systematic investigations are made to determine which part of the LGN contains cells that are sensitive to neighbouring points in visual space, it is found that visual space is mapped clearly over the horizontal planes of the LGN (Sanderson, 1971). This is represented schematically in figure *1*. Also evident in figure *1*, is the separation of input and output paths from either eye on their way to the cortex. In both the primate and cat retinal ganglion cells

terminate in eye specific layers, with some receiving input from the contralateral eye, and others input from the ipsilateral eye. In the monkey visual system this separation of LGN layers exists along with the topographic separation of populations of cells on the basis of their functional properties

Within the LGN there are thought to be two types of postsynaptic targets, the largest group, accounting for 75% of the total population are known as relay cells, they send axons up to the cortex (Guillery, 1966 and Freidlander et al, 1979, 1981), while the remaining group do not project out of the LGN, they are thought to have an inhibitory function (Fitzpatrick et al, 1984) because they contain the inhibitory neuro-transmitter, GABA. Cells in the feline LGN have receptive fields that reflect those of their retinal afferents, a given population has functional properties making it suited to perform a particular role in processing visual information (Shapley and Hochstein, 1975, Derrington and Fuchs, 1979, So and Shapley, 1979 and Freidlander et al, 1981). X and Y cells both have low pass spatial frequency tuning profiles, however X cells have a strong cut-off at the lowest frequencies. In comparison to Y cells, this makes X cells specialised for processing higher spatial frequencies. These cells are sensitive to frequencies up to 3 cpd, however they have low temporal resolution, their responses decrease as the frequency of stimulus modulation increases. It has been suggested that these might specialise in the analysis of form and pattern in a visual scene. They also exhibit linear spatial summation, this can be assessed using sinusoidally modulated grating presented with variable spatial phase. X cells exhibit a null point for one phase value, where they do not respond, excitatory influences derived from one part of the grating on the receptive field are exactly balanced by inhibitory ones from another part of the field. Y cells characteristically have larger receptive fields and hence exhibit peak spatial tuning to lower spatial frequencies. Their spatial summation is non-linear, they do not exhibit a null-point, when stimulated with a phase-reversing grating they respond with a tonic increase in firing rate which can be modulated at twice the reversal frequency. Y cells fire in a transient manner when stimulated and are capable of following fast moving stimuli. The α-ganglion cell that project to Y cells are spread more evenly throughout the retina, so unlike X cells which are present in largest proportions in the AC, Y cells are distributed evenly over the visual field.

The LGN is not simply a relay point for the retinal signal on its way to the cortex. It exists within a network of feedforward and feedback projections, and as a consequence the properties of cells are manipulated by a number of non-retinal influences. Firstly the excitatory transfer of retinal information to relay cells is shaped by feedforward inhibitory interactions that originate from intrinsic inhibitory cells. Other inhibitory cells in the neighbouring perigeniculate nucleus (Lo and Sherman, 1994, Ahlsen et al, 1985 and Houser et al, 1980) mediate feedback inhibition after having received input from relay cell axons. Both these circuits are themselves subject to feedback from the cortex (Guillery, 1967, Hollander, 1970, Updyke, 1975). Cortico-geniculate axons make excitatory synapses on PGN cells, and LGN relay cells and intrinsic interneurons (Baughman and Gilbert, 1980 and Fonnum et al, 1981 and Guillery, 1969, Weber et al, 1989, and Montero, 1991). Cortico-geniculate axons have been shown to have influences on the stimulus specificity of LGN cell responses (Murphy and Sillito, 1987 and Sillito et al, 1993) and the ways in which they operate as networks (Sillito et al, 1994). LGN relay cells characteristically exhibit length tuned receptive fields. This means that when they are presented with bar stimuli, which are usually used to probe the structure of cortical receptive fields, at parafoveal eccentricities, they respond most strongly to bars shorter than 1° in length, when longer bars are used, response magnitudes are typically reduced by 70% (Cleland et al, 1983 and Jones and Sillito, 1991). This has been reported to be due the antagonistic surround, which has its origins in the receptive field properties of retinal afferents and is further enhanced by feedforward inhibition in the LGN and also by contacts made on intrinsic interneurons by cortico-geniculate layer VI cells (Murphy and Sillito, 1987 and Jones and Sillito, 1994). Such response suppression is also observed when cells are stimulated with large field of sinusoidal gratings (Sillito et al, 1993), stimuli to which layer VI cells respond optimally.

The perigeniculate nucleus is a zone of the reticular nucleus which exists within the network of afferent and efferent connections between the LGN and cortex and receives input from both. PGN cells themselves are thought to have an inhibitory function, intracellular recording (Ahlsen et al, 1985) has indicated that there are inhibitory connections originating from this centre in the LGN, and on the basis of

other recordings a mechanism has been postulated in which PGN cells inhibit the intrinsic interneurons of the LGN. It is thought that there are also interconnections between PGN cells themselves (Ahlsen and Lindstrom, 1982). These observations, and those discussed above, led to the suggestion that the cortico-geniculate pathway and the PGN play a role in gating visual signals. Studies using electrical stimulation of the optic tract or visual cortex, have shown that feedback inhibition in the LGN, brought about by IPSPs generated by the PGN axons as a result of their cortico-geniculate excitatory input (by virtue of their latencies) are decreased in amplitude. Disynaptic feedforward inhibition present in the pathway between ganglion and relay cells was also decreased by stimulation of the cortex. These observations demonstrated that the feedback inhibitory pathway from the PGN can suppress the feedforward inhibitory pathway by inhibiting intrinsic interneurons, in the LGN. The receptive fields of PGN cells are significantly larger than those of the LGN (Wrobel and Tarnecki, 1984), and when stimulated by bar stimuli they do not exhibit the length tuning that characterise geniculate X and Y cells (Jones and Sillito, 1994). When presented with flashing stimuli they respond with mixed ON\OFF discharges (Dubin and Cleland, 1977) and can follow stimuli that are temporally modulated. Most PGN cells receive input from both A laminae in the LGN and so respond to stimulation of either eye.

Cells in the LGN and PGN and their afferent and feedback inputs are then subject to a range of other influences which have modulatory effects on their responses. These arrive from centres such as the basal forebrain, the parabigemminal nucleus, the locus coerulus and the dorsal raphe nucleus. Acetylcholine is a modulatory neurotransmitter that has an influence in the LGN. It brings about transitions from sleeping states to states of arousal. These state changes occur with concomitant changes in the firing patterns of cells. Cells go from rhythmic bursting states at frequencies below 12 Hz (Hirsch et al, 1983 and Leresche et al, 1991), to states where they fire single spikes (McCormick and Prince, 1987 and McCormick, 1991, Rogawski and Aghajanian, 1980). This latter state has been associated with visual function during arousal periods, and is thought to facilitate faithful transmission of visual information to LGN cells (Coenen and Vendrik, 1972) and up to the cortex (Livingstone and Hubel, 1981). Application of ACh to individual cells responding to visual stimuli has also been

reported to increase the signal-to-noise ratio of their responses when they are in single spike mode (Sillito et al, 1983).

As was the case in the cat, cells in the six layers of the primate LGN reflect the receptive field properties of their retinal ganglion cell afferents, this is particularly evident in their chromatic and contrast sensitivity. In the parvocellular layers there are two sub-types of receptive field, both of which have subregions which are tuned to the wavelength of stimulus light (Wiesel and Hubel, 1966 and Derrington and Lennie, 1984). The first group of cells are chromatically opponent exhibit a centre surround organisation in which each zone is tuned to a different wavelength of light. Thus a centre might be sensitive to long wavelengths (red light) while the surround is sensitive to medium wavelength (green light). The other class of P cell are sensitive to wavelength but have no surrounds. Cells in the ventral M laminae of the LGN also exhibit ON or OFF receptive fields, some have antagonistic surrounds and some do not. However compared to parvocellular cells, M cells are only weakly sensitive to the wavelength of a stimulus. They characteristically have higher contrast sensitivity than P cells, equivalent to the contrast sensitivity of X and Y cells in the cat LGN. A common feature of the receptive fields of M and P cells in the primate cells is linearity of spatial summation. All receptive field of P cells and 75% of those displayed by M cells exhibit linear spatial summation (Shapley et al, 1981, Kaplan and Shapley, 1982 and Derrington and Lennie, 1984).

The reports reviewed so far present a picture of network connectivity and function, of which complex paths of feedforward and feedback interaction are a striking feature, and an important implication of this, is the level of control that the cortex has over the information that it receives from the retina. Operating within this network are streams of information, exemplified by cells with X, Y and W, and M and P type receptive fields, that have their origins in retinal afferent output and emphasis subtly different aspects of the visual environment.

The thalamo-cortical projection.

A significant visual input to area 17 comes via the axons of LGN relay cells. The way these cells terminate with the cortex has been shown to be dependent on the type of receptive field exhibited by the cell, X or Y. Most analysis of the axon arborisations of relay cells in the cortex uses anatomical staining techniques which rely on the characteristic differences in the structural morphology of the axons of X and Y cells (Y axons are thickest), and differences in the latency of thalamo-cortical action potential transmission following antidromic stimulation in the cortex (Y cell axons are faster than X cell axons). Studies using horse-radish-peroxidase (HRP) staining techniques have shown that X and Y cells both terminate in layer IV of area 17 and have characteristic arborisation and termination patterns (Ferster and LeVay, 1978 and Humphrey et al, 1985a, b). Another characteristic of the thalamo-cortical projection is that both types of relay cell also invariably send axon collaterals in layer VI, though this input is not as anatomically large as that to layer IV. The axons of Y relay cells provide input to layer IV which is widely spatially distributed, single axons project to an area up to 2 mm square. Although extensive these arborisations are not distributed evenly, axon collaterals are observed to terminate in patches, whose size and spacing are reported to correspond to the dimensions of an ocular dominance column. The axonal arborisation of X relay cells is smaller than that of Y cells, distributed in a much more spatially restricted fashion, in one patch, between 0.6 and 0.9 mm^2 in size. The lateral extent of these arborisations being about 500 microns, rarely extending outside a single ocular dominance column. The axons of X and Y relay cells terminate throughout the depth of layer IV and some cells have been found to penetrate up to 200μm into layer III.

The morphological characteristics of the thalamo-cortical projection demonstrate that cortical connectivity is at the same time very convergent and divergent a given cell receives many thousands of synapses from a plethora of different sources, both intra and extra cortical (Symonds et al, 1984a, b). In layer IV of the primary visual cortex synapses from the LGN account for between 6% (Ahmed et al, 1994) and 20% of the total number of excitatory contacts (LeVay and Gilbert, 1976 and Davis and Sterling, 1979). Others come from other sub-cortical areas, while the majority come from the

same cortical area from layer VI (45%) and from within layer IV (28%) (Ahmed et al, 1994). Contacts originating from the LGN have the largest profiles while those from layer VI cells have the smallest. Spiny stellate cells in layer IV have approximately 2000 spines each, on which it is thought they receive the majority of their excitatory connections. These excitatory connections were categorised as asymmetric type 1 (Gray, 1959). LGN afferents make 80% of their asymmetric contacts onto dendritic spines, a further 15% are made onto dendritic shafts (Freund et al, 1985).

Primate V1, like cat V1 is divided broadly into 6 layers (Brodmann, 1909), but the way that the LGN axons terminate is more complex, axons arising from specific layers of the LGN either M or P terminate within different sublaminae of layer IV, that differ in their appearance after Nissl staining (Lund, 1973, Blasdel and Lund, 1983 and Hendrickson et al, 1978). In primate V1, layer IV has been sub-divided, top to bottom, into IVA, IVB, and IVC, which is further sub-divided into IVCα and IVCβ, M cells terminate in layer VI and IVCα, the upper part of layer IVC, while P cells terminate in IVCβ, IVA and the upper part of VI. In layer IVC M and P axons terminate in 1-2 distinct clumps of boutons, those arising from the P stream are 200-300μm in diameter, while M axons terminate in much larger clumps that can be 300-500μm by 600-1200μm. The majority of thalamic terminals are made onto dendritic spines (50-70%), with the remainder found on dendritic shafts (30-50%) and GABA positive somata (Freund et al, 1989). Though the majority of thalamic afferent terminals are found in layer IV, it has been reported that they can also be found at more superficial sites, in layers II\III. Specifically, the termination sites are found to spatially correlate with zones that are rich in cytochrome oxidase. These appear as circumscribed dark blobs when appropriately stained.

The following section will focus on the mechanisms that distribute the retinal signal through the cortical network, and how this input, in these circumstances, manifests itself in the visual sensitivity of cortical cells.

Cortical Pathways.

Cat Primary Visual Cortex.

Interlaminar Projection Patterns.

Layer IV, the thalamic recipient layer, is the point from which visual signals are distributed throughout the primary visual cortex. Within the primary visual cortex, in layer IV and all other layers, a striking feature of projection patterns is connectivity between layers (Kelly and Gilbert, 1975). Morphologically the largest group of cells in layer IV are spiny stellate cells, such cells have *star* shaped dendritic distribution, typically 200-400mm in diameter. In terms of their output characteristics, these cells exhibit a wide range of projection patterns, HRP labelled axons (Martin and Whitteridge, 1984 and Anderson et al, 1994) have been found to terminate within their own dendritic field and to project down to layers V and VI. The main targets of layer IV axons are cells in layers II and III. Outside layer IV pyramidal cells are the major neuronal class in all layers. Pyramidal cells in layers II\III, have basal dendrites that can receive input from deeper layers, and apical dendrites that can project up to layer I. This layer is sparsely populated with what are thought to be GABAergic cells, the ends of other dendritic arborisations and projecting axons. Pyramidal cell axons provide output paths for information conveyed to layers II\III, these axons exhibit a wide variety termination sites (see figure *2*), intrinsic to the primary visual cortex (Gilbert and Wiesel, 1979 and 1983) and in other cortical areas such as 18 and 19 (Symonds and Rosenquist, 1984). Axons project both horizontally and vertically, vertically distributed targets are cells in layer V, where axons synapse on the basal dendrites of cells in that layer. It is also possible that layer VI cells with densely spinuous apical dendrites in layer V could receive input from these cells.

After receiving information from superficial layers, layer V, another that contains a high proportion of pyramidal cells (Gabbot et al, 1987) passes it to the targets of its neuronal population. Layer V pyramidal cells have spined apical dendrites that project up to the cortical surface through the granular and supra-granular layers, where they can branch to receive input. In terms of output, the axonal projections these cells can

Figure 2.

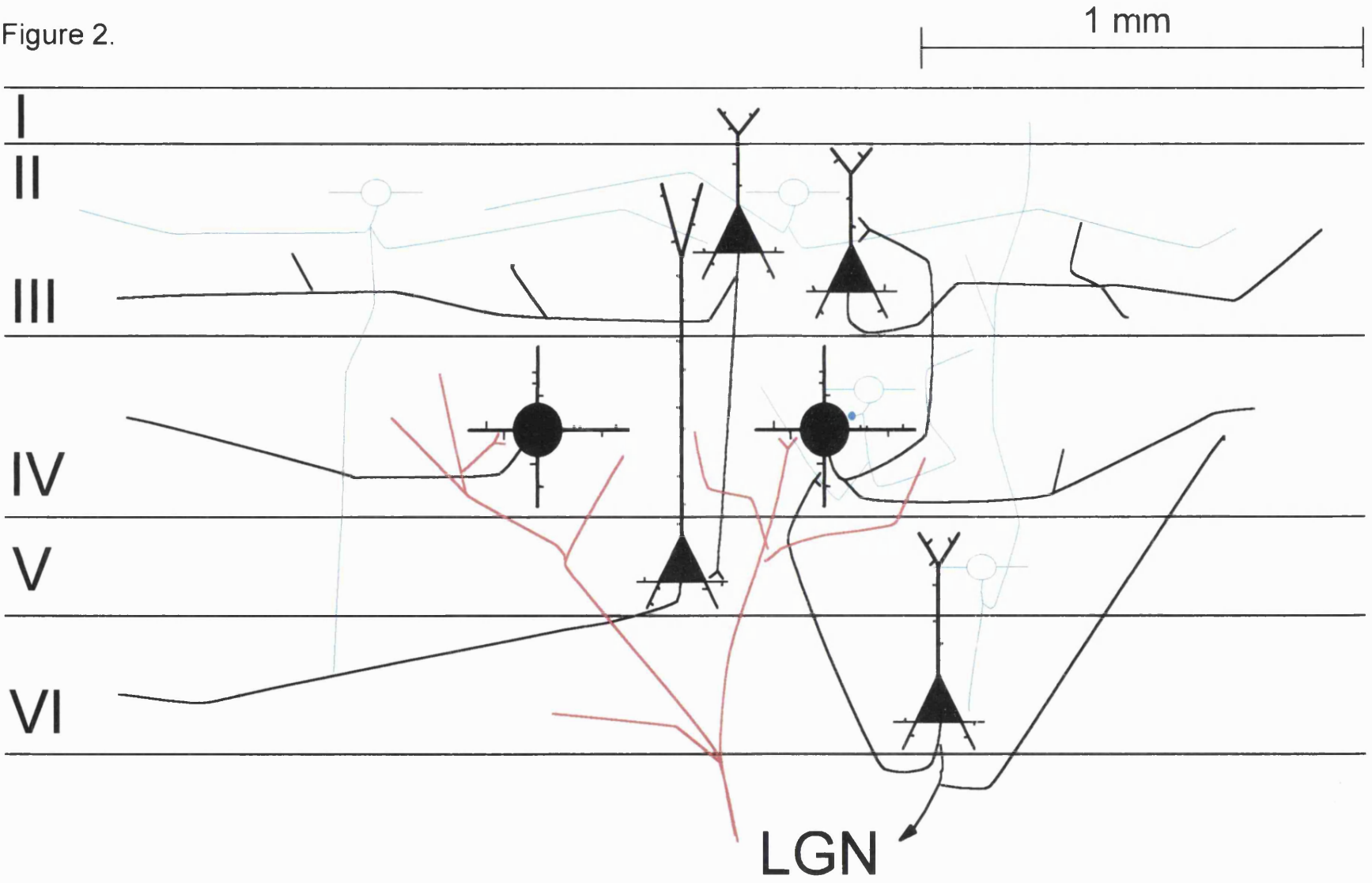


Figure 2.

A schematic representation of the dendritic arbours and axonal projection patterns of cells in the primary visual cortex of the cat. The retino-geniculate pathway is shown in red, excitatory (black) and inhibitory (blue) projection and termination patterns are also featured. The basic pattern of vertical projection is shown, from the layer IV to the superficial layers and then down to the supragranular layers. Horizontal projections are distributed in fields that are several millimetres wide.

be divided into several types, some project locally and arborise within their own basal and apical dendritic trees, while others project sub-cortically to the superior colliculus (Hübener et al, 1990). Many axons have long collaterals, they make the majority of their synapses on spines, within layer V and also down to layer VI.

The vast majority of spiny cells in layer VI also have a pyramidal morphology, they receive input from many sources, and like those in layer V, are another of the main channels of subcortical output for area 17. Their basal dendrites receive a direct excitatory influence from thalamic relay cell axon collaterals that are on their way to layer IV, while apical dendrites receive direct input from layers V and IV, as they pass upwards. Retrograde labelling techniques have been used to visualise the morphology and projections cells in layer VI (Katz, 1987), output targets have been found to correlate with certain other morphological features. Cells sending axons to the two major targets of layer VI, the visual claustrum and the dLGN have different morphologies. Cortico-claustral cells, accounting for 3-6% of the population, have long apical dendrites which project up to layer I and give off short branches in layer V, they have asymmetric basal dendrites which projected horizontally in one direction for up to 1 mm. The axons of these cells gave off collaterals that travelled horizontally within layer VI also for up to 1 mm. In some cases there were periodic clusters separated by 300 microns that entered layer V. Cells projecting to the LGN are found much more often, they form over half of all the cells in layer VI. There are two distinct morphological groups. Type 1 represent 80% of all cortico-geniculate cells, they have radially arranged symmetric basal dendrites, the apical dendrites of these cells coursed upwards generally penetrated layer III, fanning out and branching in layers IV and V, with an increased spine density in layer V. LGN projecting axons give rise to 3-5 collaterals before reaching the white matter, these pass into layer IV where they arborised profusely, collaterals that remained in layer VI were rare. Type 2 cells had radially arranged basal dendrites and poorly developed thin apical dendrites that terminate below layer IV. The axon collaterals of these cells are also restricted, none projected higher than layer V, those that remain in layer VI remain within the basal dendritic arbour. A typical type one cortico-geniculate cell is featured in figure 2, along with all the other main types of cells in the various layers of the cortex.

In figure 2 it can be seen that superimposed on the vertical excitatory connectivity is further connectivity originating from cells that lack spines, they are thought to mediate inhibitory processes. As with excitatory projection there is also significant evidence for inhibitory projections between layers, inter-laminar inhibitory projections are mediated by various morphologically distinct cell types. Inhibitory contacts are found in all layers, and on all parts of cells. Where their distribution has been surveyed, 58% have been found on dendritic shafts, 27% on spines and 15% on cell bodies and axon initial segments (Beaulieu and Somogyi, 1990). Layer IV is characterised by a species of smooth neurone which accounts for about 10 % of it's total population, it is a type of basket cell, called the 'clutch cell' (Somogyi and Soltesz, 1986 and Kisvárday et al, 1985). Morphologically similar to spiny stellate cells, their dendrites reside in a restricted volume of cortical tissue. Clutch cell axons also exhibit spatially restricted output patterns, axons tend to remain within their dendritic field, providing local inhibitory influences to cells receiving the same set of inputs. These cells make 20-30% of their contacts onto the somata of other cells, it is suggested that they provide sections of axon to make inhibitory peri-cellular nets. A minor vertical component of their axon projects down to layers V and VI. In layers II\III and V the most important class of inhibitory cell is the basket cell (large and deep respectively) (Martin et al, 1982, Somogyi et al, 1983 and Kisvárday et al, 1983, 1984, 1987) these like clutch cells, have restricted dendritic fields typically 200-300μm in diameter, the axons of such cells in the superficial layers project vertically down to the infra-granular, and vice versa, to terminate in a restricted arbour of the same dimensions as the dendritic field. Inhibitory cells, like their spiny excitatory counterparts do not simply relay information between cortical laminae, but also distribute it horizontally, within them, this feature of their morphology, and how it relates to this feature of spiny cells, will be discussed below.

Horizontal Projection Patterns.

Many cortical cells project axon collaterals horizontally, to points that are in the same layer, or in a neighbouring one, and that are laterally displaced by several millimetres

from the site of their soma. The thalamic input to layer IV is the first stage in the visual system where a horizontal spread of an afferent projection can be observed. In this respect X relay cell axons are limited and only innervate one patch of cortex 500 microns in diameter (Ferster and LeVay, 1978). However Y cell axons travel up to 2 mm laterally and arborise periodically so that they innervate up to 3 patches of cortex. Horizontally distributed axons are also a feature of the postsynaptic targets of thalamic axons, spiny stellate cells, and their targets, the pyramidal cells of the supragranular and infra-granular layers. Focal extracellular tracer injections, restricted in their vertical and horizontal spread, reveal the patchy projections of cells in the superficial layers, labelled cells are horizontally distributed over the cortex up to 6 mm from the injection site (Luhmann et al, 1986 and 1990, Matsubura et al, 1987 and Gilbert and Wiesel, 1989). Intracellular injection allows reconstruction of individual axons, which have also been found to project over equivalent distances and give out periodic clusters of collaterals approximately every 400-500 microns (Gilbert and Wiesel, 1979 and 1983, Martin and Whitteridge, 1984). Such axonal morphology is seen in all other layers (Gilbert and Wiesel, 1979 and 1983). It means that cells can interact with others, that represent delocalised points in visual space, that is, they have non-overlapping receptive fields. This is evident when fields and their distribution over the visual field are investigated in the context of the gross anatomy of V1. Classical receptive fields 5° from the area centralis typically cover an area of the visual field that is 1-2° square. Systematic mapping of the distribution of visual space over the surface of the cortex has indicated that such dimensions of visual space are represented in area of cortical tissue approximately 0.8-1.0 mm^2 (Tusa et al, 1978). So it is clear that axons that project laterally, further than 1 mm, will interact with cells that are sensitive to points in visual space, that they themselves are not sensitive to.

In layer IV, individual axons of reconstructed cells are reported to project over distances of 2-4 mm, within layer IV and adjacent layers. Axons can give off branches which pass into layer II\III, and then periodically profusely arborise, while traversing laterally for up to 5 mm. In layers II\III further anatomical insights into horizontal connectivity have come from simultaneously reconstructing as many as ten extracellularly injected cells present in the same volume of cortical tissue (Kisvárday and Eysel, 1992). This strategy reveals the true extent of horizontal network

connectivity. Reconstruction of multiple cells labelled after a single injection of tracer has demonstrated the presence of highly interconnected groups of cells distributed over approximately 15 mm^2, thus representing a large area of visual space. Labelled layer III pyramidal cells were observed distributed in several patches, and strikingly there was a high degree of reciprocal connectivity between them, each patch was connected to several others. Each pyramidal cell making an average of 4 synapses on each of it postsynaptic targets. However distributed network connectivity is not just the province of the pyramidal cell, it has also been found to be a striking feature of the projection patterns of large basket cells in the superficial layers. Such cells have axons that project up to 1.5 mm from the soma, and axonal fields with areas up to 6 mm^2 (Kisvárday et al, 1993). These cells make connections to both pyramidal cells and other basket cells with their spatially distributed axons. Approximately five contacts are made to the somata of about 200-300 pyramidal cells and 40-50 other basket cells. This means such cells are in a position to mediate direct inhibitory mechanisms and also indirect excitatory mechanisms, through a disinhibitory path through other distributed large basket cells. Extracellular recording and imaging techniques have been used in conjunction to visual stimuli to probe the relationship between these anatomical projection patterns and specificity for stimulus orientation - a property of cortical cells that will be discussed in a later section (Kisvárday et al, 1994). There is a striking difference here between the projection characteristics of pyramidal and basket cell axons in this domain. Basket cells project to others, in a way which is not dependent on target orientation. While pyramidal cells appear to terminate with much more spatial specificity, many reports conclude that termination occurs at sites where cells have similar orientation preferences (Kisvárday and Eysel, 1992).

Optical imaging techniques have been used by a number of groups to investigate the topographic relationship between orientation domains and the horizontal projection patterns of cells in the superficial layers. These layers contain the cells that make the largest horizontal projections and are those in which imaging techniques can quantify the ongoing activity. Investigations that have not specifically highlighted excitatory or inhibitory projections, but have used biocytin injections to visualise the patchy horizontal distribution of all projections from a given point, have indicated the 60% of

labelled patches tend to be distributed in iso-orientation domains (Malach et al, 1993). About 40% of all patches were found at sites where the preferred orientation of cells differed by 45°-90°. These investigators also found that neuronal processes within 400 μm of the injection site crossed freely boundaries between different orientation domains. Cortical connectivity is not simply characterised by strict projections between iso-orientation domains as has been proposed (Gilbert and Wiesel, 1989, Ts'o et al, 1986, Schwarz and Bolz, 1991), a given cell has access to input from orientation domains with the whole range of preferences. The connectivity of a cell depends upon its morphology and on the distance between the presynaptic soma and termination site.

The idea that cells are only connected to others, with similar optimal orientations is not supported by investigation in feline area 18 (Matsubura et al, 1987). Extracellular injection at a cortical site and subsequent determination of the optimal orientation of cells at that site and at others distributed around it, allowed the distribution of transported label to be correlated with distribution of neuronal physiological properties. Labelled cells send axons to points containing cells that exhibit a wide range of preferred orientation from 0° to 90°. Again it was not possible to determine whether the interactions between sites of unlike orientation were excitatory or inhibitory. However as inhibitory cells account for 20 % of the total cortical neuronal population and even if those in area 18 target all orientation domains as they do in area 17, it is still likely that excitatory cells also project in similar ways to the inhibitory population in area 18. This idea however has not been investigated functionally using cross correlation techniques, which might with appropriate stimuli highlight cross-oriented excitatory interactions.

Horizontally distributed networks are a striking feature of cortical connectivity at every level, right from the first synapse that is made by a relay cell axon, to layers V and VI that are implicated in sub-cortical feedback processes. Such networks are anatomical substrates for integrating information from large areas of visual space and multiple neural centres. Such integration can result in excitation, inhibition or disinhibition at a given site. Investigation of the way this integration interacts with

topographically distributed receptive field properties can tell us what strategies the visual network uses to generate visual images.

Primate Primary Visual Cortex.

There are many similarities between the projection patterns seen in the cat, and those encountered when cells in primate V1 are reconstructed, cells in a given layer exhibit similar vertical and horizontal projection patterns. Parallel physiological and anatomical investigations, however show that differences are apparent that allow the system to process the greater diversity of information that comes from the primate retina. These will be discussed below.

Interlaminar Projection Patterns.

Sublayer IVA receives input from IVCß and both receive direct projections from P-type relay cells in the LGN. Layer IVA contains populations of stellate and small pyramidal cells, as well as smooth cells. Spiny cells in this layer have been found to project densely to the lower half of layer IIIB and layer V (Lund and Boothe, 1975, Lund et al, 1993). Below IVA is layer IVB, this receives a vertical M stream projection from IVCα, it contains large stellate cells from which vertical projections cross into layers II\IIIA (Blasdel et al, 1985), as well as down into IVCα, V and VI (Blasdel et al, 1985 and Kisvárday et al, 1989). Having received significant focused inputs from layer IV, pyramidal cells in the superficial layers project reciprocally back to layer IVB and to infra-granular layers V and VI. The infragranular layers also get further input from the superficial layers because they send long vertically oriented apical dendrites to terminate here, particularly in IIIA. Pyramidal cells in IIIB send axon collaterals down to terminate in the upper half of layer V, VA. Cells in layers II\IIIA send their collaterals to terminate in layer VB and below (Lund and Boothe, 1975). Cells in layer V have been reported to make excitatory projection to all layers (Kisvárday et al, 1989). Pyramidal cells in layer VB have axons that terminate in VB and layer VI (Lund and Boothe, 1975 and Blasdel et al, 1985 and Kisvárday et al,

1989). As well as receiving input from layer V, pyramidal cells in layer VI also receive input from descending axons from layers IVCα and IVCβ. Some layer VI cells receive further input from apical dendrites that branch in layer VA and terminate in IVCα, others terminate specifically in layer IVB. The main output targets of cells in layer VI are sub-cortical, centres such as the LGN and the claustrum, however layers V and IVC also receive an intra-cortical projection from layer VI. The modes of projection of these cells have been examined using retrograde labelling techniques, injections of HRP or DiI were made in all layers of the LGN, or just a subset, magnocellular or parvocellular (Fitzpatrick et al, 1994). When both M and P geniculate laminae were injected, retrogradely transported label was found in cortico-geniculate cells that were distributed in two strips, one on the layer VB\VI border and another at the bottom of layer VI above the white matter. These extremities of layer VI, the top and bottom actually contain the fewest cells, but they contain the greatest density of cortico-geniculate cells, in total cortico-geniculate cells were found to account for 13 % of the total layer VI population.

Further features of vertical connectivity are the networks of feedforward and feedback connectivity which exist between V1 and areas in association cortex such as V2, V4 and MT, that place functional emphasis on processing different attributes of the visual scene, form, colour and motion. A feature of V1 is that there is a tendency for input and output paths to be localised in different laminae. Input to V1 is mainly to middle cortical laminae and is focused on neurones with stellate morphology. Information output to V2 is managed by pyramidal cells in layers superficial to the thalamic recipient zone, whereas MT receives input from layers IVB and VI. However while much information is transferred vertically, in tandem with this, axons also make synapses at horizontally distributed sites within V1. The issues that arise from this characteristic of the network are similar to those in the cat visual system, and they will be discussed below.

Horizontal Projection Patterns.

In most layers axons have been shown to traverse in the projection from one layer to another, or within their layer of origin, for up to 2 mm laterally, an axonal field can be up to 4 mm in diameter. It is interesting realise how these projection patterns are related to the spatial distribution of the retinotopically mapped visual field in V1. In the central visual field, around and including the foveal representation, large areas of cortical tissue map small areas of visual space, relative to the representation of space in the periphery, where the area of tissue processing the same visual area is much less. In the primate at an eccentricity of 5°, one square degree of visual space is processed by the cells in 2.62 mm^2 of cortex (Van Essen et al, 1984). Moving 1.41 mm in the cortex is associated with a move of 1° in visual space terms, this value is proportional to the reciprocal of eccentricity, the distance in degrees of visual space from the fovea (Daniel and Whitteridge, 1961). It is evident that the distances which projecting axons of pyramidal cells cover are much larger than the area of visual space that is the province of one parafoveal classical receptive field. A typical receptive field at 5° eccentricity covers an area of visual space of 0.07 $degs^2$ (Van Essen et al, 1984). It is also clear that a given cell will have to process synaptic signals from presynaptic neurones that represent a delocalised area of visual space. This network characteristic suggests that the visual context of a stimulus activating a cell will be a key agent that shapes its response.

Horizontally distributed projections were first encountered in primate primary visual cortex after patterns of degeneration were investigated after spatially restricted lesion had been made in individual layers of cortex (Fisken et al, 1973 and 1975). The presence of horizontally distributed projections was confirmed following focal extracellular tracer injections of HRP restricted to single layers (Rockland and Lund, 1983, Blasdel et al, 1985 and Yoshioka et al, 1994). Intracellular injection of tracer has allowed individual pyramidal cells in the superficial layers to be reconstructed (McGuire et al, 1991). Particularly in layers II\III and IVB projections over 2-4 millimetres have been reported, cells in these layers project within layer IVB for up to 4 mm, though cells in layers II\III also project for up to 2mm within layers II\III. Injections made within layer V give rise to projection that travel horizontally for 1mm

in layer V, some of these enter layer VI and contact sites up to 1.5 mm from their soma of origin (Blasdel et al, 1985 and Kisvárday et al, 1989). As in the cat, laterally spreading axons give off collaterals periodically, approximately every 375-400mm. EM reconstruction of the synaptic connectivity between cells in the superficial layers with others has shown that horizontal connectivity is very sparse, with a cell providing only one synapse to any other (McGuire et al, 1991). 75% of these contacts are made onto the dendritic spines of other pyramidal cells, 5% were found on dendritic shafts of spiny cells, with the remainder on the dendritic shafts of smooth cells.

So far the discussion has focused on the horizontal and vertical components of the projections made by cortical cells. However techniques used in primates that employ extracellular tracer injection do not supply information about whether the cells giving rise to the axons are smooth or spiny. Smooth cells are proposed to have an inhibitory function because they are found to contain GABA an inhibitory neuro-transmitter. On the basis of GABA immunoreactivity and genetic studies it has been reported that all laminae in V1 contain both GABAergic cell bodies and axon terminals. V1 contains one of the highest densities of these when compared with other areas of cortex subserving different sensory functions. Inhibition and the generation of IPSPs, a process in which GABA has been widely implicated must be very important in the function of V1.

It has been reported that at least 15% of cells in V1 contain GABA (Fitzpatrick et al, 1987 and Hendrickson et al, 1994). The highest levels of GABAergic neurones have been found in layer II\III, and in the thalamic recipient zones, layers IVC, IVA and VI. In layers II\III 20% of all cells have been found to be GABAergic. Fitzpatrick et al particularly drew attention to the high levels of terminals in IVC, IVA and III. Extensive studies on the morphology and projection patterns of smooth and sparsely spiny neurones using Golgi impregnation, have highlighted a very wide range structures and terminal distributions (Lund et al, 1987, 1988 and Lund and Yoshioka, 1991). The dendritic fields of smooth cells are generally restricted, they are not found to be wider than 200μm. Populations of these cells, like spiny cells typically exhibit projection patterns that have highly structured laminar specific input/output characteristics. Cells with particular laminar sites have projection patterns that mirror

those of the spiny cells with soma in that layer. A class of smooth cells in layer IVCα and IVCß called the clutch cell (Kisvárday et al, 1986) make 90-95% of their terminals in the same layer as their soma, with an axon terminal field which is 300 by 500μm, similar to the dimensions of their dendritic field. These cells also make minor inputs into layers IVA, IIIB and VI, the same targets as their spiny counterparts, with vertically oriented spatially restricted axons. Smooth cells in layers IVB, IIIB and V exhibit axonal projections that traverse laterally beyond the extent of their dendritic fields, in this respect these cells resemble basket cells in the cat. Axons can terminate in a field which can be up to 1.5 mm in diameter, thus they, like the spiny cells discussed earlier can influence sites that receive visual signals from an area of visual space larger than a classical receptive field. When extracellular injections are made that exclusively label GABAergic pathways in the primary visual cortex, cells are labelled in laterally extensive fields. Injections restricted to the superficial and infragranular layers label fields of cells that are circular and 2-3 mm in diameter in those layers (Kritzer et al, 1992). The distribution of labelled cells within these fields is reported to be even, without any of the clustering that is associated with similar experiments, that non-specifically label cell populations, and primarily delineate the distributions of laterally excitatory connections.

The preceding discussion has focused on the remarkable connectivity that is present both within and between cortical laminae, that mediates both excitatory and inhibitory processes, at near and distant points in visual space. The projection patterns are presented schematically in figure *3*. Shown is a scheme that represents the basic connectivity characteristics of the primate visual system so far discussed, in a section of cortex. In the next section the discussion will focus on the functional manifestations of this complex connectivity, the response properties of all these cells to various kinds visual stimuli.

Figure 3.

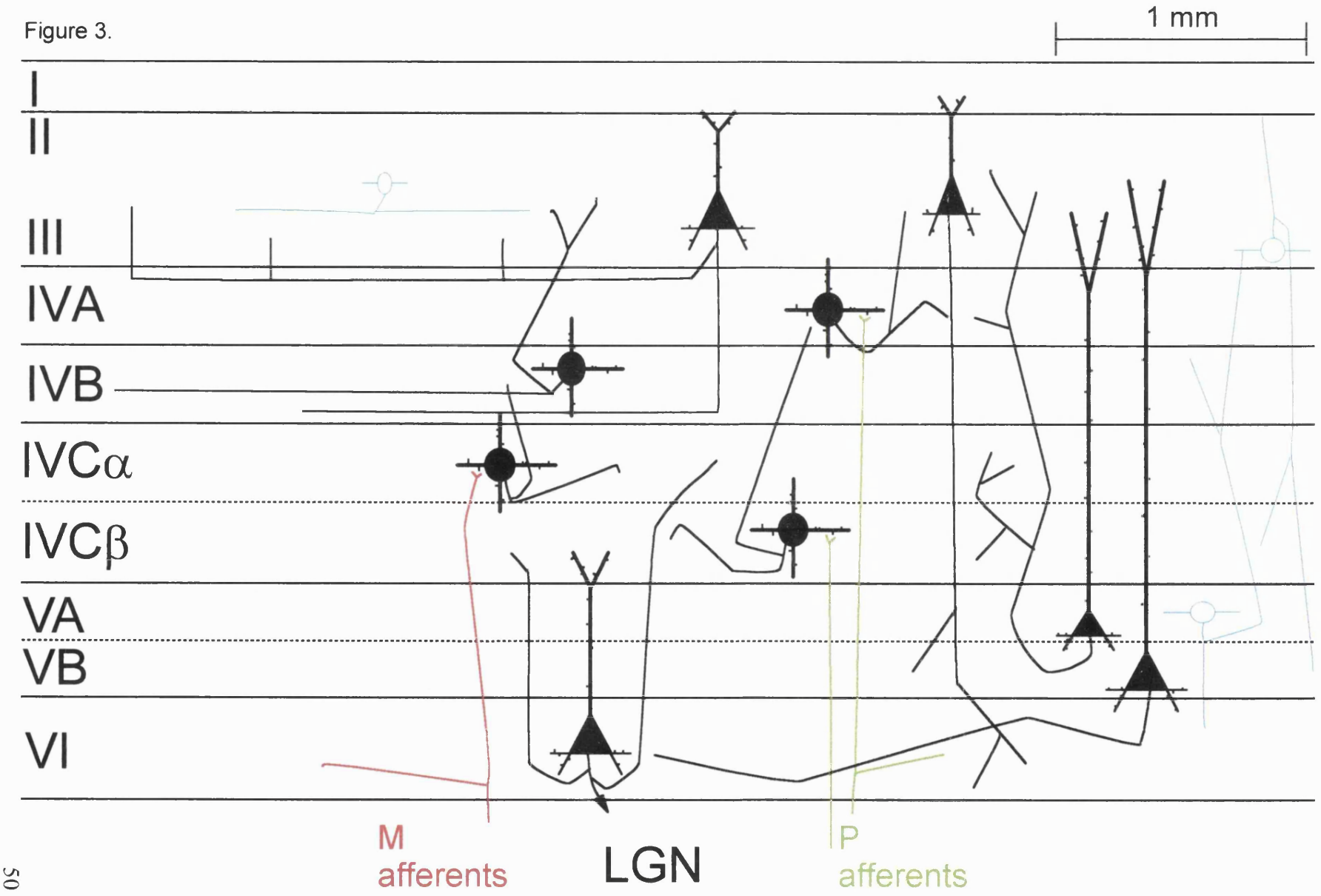

1 mm
I
II
III
IVA
IVB
IVCα
IVCβ
VA
VB
VI
M
afferents
LGN
P
afferents

Figure 3.

A schematic representation of the dendritic arbours and axonal projection patterns of cells in the primary visual cortex of the Primate. Thalamic afferents originating from the Magnocellular layers (M afferents) and the Parvocellular layers are shown in red and green respectively, their input is then relayed vertically and horizontally by spiny stellate and pyramidal cells. Smooth intrinsic cells with inhibitory functions also distribute out put vertically and horizontally, these cells are shown in blue.

The spatial sensitivity of cells primary visual cortex.

Receptive fields in cat V1.

Much investigation into the visual function of cells in the primary visual cortex has taken place in the cat, after the work of Hubel and Wiesel (Hubel and Wiesel, 1962, 1965). Subsequent work in primate species has shown that many of the features of the functionality of the feline visual system are to be found in that of the primate, as well as other features which are thought to mediate the perception of colour in this species.

In the feline visual system, layers of V1 concerned directly with the input from the dLGN have receptive fields which are closest in their functionality to those of X and Y relay cells. Several theories have been proposed to describe the mechanisms that are involved in transforming the centre surround concentric structure of LGN relay cell receptive fields. The original observations concerning the spatial structure of cortical receptive fields, and a model to account for this remarkable thalamo-cortical transformation, were reported in the early 1960's by Hubel and Wiesel. Their serial hierarchical scheme was proposed to have origins in the afferent projections that relay visual information from the retina, through the LGN, and up to primary visual cortex and extrastriate centres. The receptive fields of cells encountered progressively along this path were reported to perform increasingly complicated analysis of a visual scene, using receptive fields of increasing size. Simple fields were posed as the result of systematic synaptic convergence of LGN ON and OFF-centre cells with collinearly aligned receptive field centres on a single cortical cell (Hubel and Wiesel, 1962). This generated a field with subregions that responded to bright stimuli in an ON region and dark stimuli in OFF regions. When a bright or dark stimulus was presented within both, the response represented a linear sum of the excitatory and inhibitory mechanisms driven by that stimulus. It was suggested that this convergent afferent connectivity was responsible for the generation a striking feature of cortical receptive fields, orientation tuning. At the next stage of visual processing, complex cells were said to be the result of structured patterns of termination of iso-oriented simple cells on a postsynaptic cell, generating a complex field, without ON/OFF sub-structure, but exhibiting orientation tuning. Such cells responded to stimuli placed anywhere within the receptive field. In extrastriate visual area 18 it was reported that cells were

sensitive to the length of their stimuli (Hubel and Wiesel, 1965), and thus exhibited a more complicated form of stimulus specificity than their afferents. The serial progression of information through these processing stages was proposed to be the biological substrate for visual perception.

While it has been confirmed that cells with simple fields do reside in cortical laminae that receive direct LGN input in largest numbers and complex cells are encountered most often in laminae which do not receive this input (Gilbert, 1977), other features of Hubel and Wiesel's scheme have been questioned by the results of many subsequent experiments. Attempts to probe this serial network by assessing the response latency of given cell after electrical stimulation of the optic tract or radiation have shown that all cell classes receive a monosynaptic input from fibres in the optic radiation (Bullier and Henry, 1979). If these fibres had origins in the LGN, this means that information is not conveyed serially, but in parallel by cells exhibiting the entire range of spatial substructures. A further finding that supports this idea and has implication for Hubel and Wiesel's scheme is that the majority simple cells exhibit spatial summation like that detected when X LGN cells are stimulated, while complex cells are non-linear in the spatial summation characteristics and resemble Y cells (Movshon et al, 1978). The former cell type responds to a sine wave grating with a modulated firing pattern while the latter responds with a tonic increase in firing rate. The nonlinearity of complex cells cannot be easily explained in terms of the termination of linear simple cells. Hubel and Wiesel's model does not really address how the two channels of information, from X and Y cells projecting to cortex, are mixed at their termination sites. It is difficult to imagine that after being generated in the retina, that they would be mixed to no functional benefit in the cortex. Instead, it has been reported that simple fields are the result of a input from a limited number of either ON or OFF-centre fields (Bishop et al, 1973 and Heggelund, 1981). Subsequent investigations have indicated that spatial structure and the orientation tuning that arises from it are partially derived from intra-cortical inhibitory mechanisms. Inhibitory postsynaptic potential are observed when cells, recorded intra-cellularly are visually stimulated. It is a mixture of excitatory and inhibitory influences that shape the pattern of response of a cell to optimal and non-optimal stimuli (Creutzfeldt et al, 1974 and Ferster, 1986, 1987). Removal of these inhibitory mechanisms with pharmacological blockades

reveals fields whose visual response properties exhibit reduced selectivity for particular spatial and temporal properties of the stimulus (Sillito, 1975 and Tsumoto et al, 1979). Individual cells that have direction selective receptive fields in normal circumstances, loose this property when inhibitory influences are blocked, and many cells exhibit wider orientation tuning profiles. There is however controversy about how inhibitory mechanisms operate to generate orientation tuning, particularly that seen in simple receptive fields. It has been reported that when such cells are intra-cellularly recorded inhibitory potentials have the same tuning profiles as excitatory ones and that these excitatory inputs account for the orientation tuning which is detected (Ferster, 1986). There is however another theory which proposes that inhibition comes about because inhibitory mechanisms are tuned to orientations other the optimal, they thus suppress responses to non-optimal stimuli. This is called the cross-orientation model (Bishop et al, 1971, Blakemore and Tobin, 1972, Blakemore et al, 1970, Sillito et al, 1980 and Morrone et al, 1982). A further problem that exists with the Hubel and Wiesel (Hubel and Wiesel, 1965) scheme is the localisation of cells with receptive fields that were sensitive to stimulus length, in extrastriate cortex. They found cells that responded selectively to short bars presented exclusively to the excitatory field, longer bars which encroached upon zones at one or both ends of the field evoked no response. These end-stopped cells were subsequently detected in the primary visual cortex, they had response properties that, in all other respects, meant that they are classified as simple or complex (Rose, 1977 and Kato et al, 1978). Approximately 50% of all feline cortical cells are end-stopped and these are encountered in the largest numbers in layer II\III and V. This property of cells is a manifestation of sensitivity to spatial context, it and other properties of cells that involve the visual space surrounding the excitatory receptive field will be discussed in detail below.

Receptive fields of primate V1.

Many cells in primate V1 exhibit receptive fields with the same basic characteristics as those exhibited by cells in feline area 17. One of the first studies to examine them was conducted by Hubel and Wiesel in 1968. The receptive fields exhibited by cells

in all layers and were reported to be smaller for a given eccentricity than those encountered in cat visual cortex. As in cat area 17, Hubel and Wiesel classified receptive fields on the basis of the distribution of their ON and OFF zones, and their spatial summation characteristics when mapped with flashing and moving bars, into non-orientation tuned, simple, complex and hypercomplex categories. Cells with simple and non-orientation tuned receptive fields were found in layer IV, and large numbers of cells with complex and hypercomplex receptive fields were found in the superficial layers. Cells with highly direction selectivity or colour sensitivity receptive fields were recorded in clusters.

Subsequent investigations have revealed differences between receptive fields encountered in primate and cat V1. One major difference between the cat and primate visual systems, is the spatio-temporal characteristics of receptive fields analysed when cells in the thalamic recipient zone are recorded. Layer IVC, a layer that receives a strong input from the dLGN, in the primate contains many cells with receptive fields that resemble those encountered in the LGN, they are non-orientation tuned (Blasdel and Fitzpatrick, 1984). These cells reflect the response properties of the M and P type LGN cells that terminate on them. Because the two streams terminate at different levels in IVC, the cells encountered at different level have different contrast sensitivities and centre diameters. Cells with non-orientation tuned fields are also encountered in clusters in layers II\III, these cells are also sensitive to colour (Livingstone and Hubel, 1984, and Ts'o and Gilbert, 1988). The horizontal spatial distribution of these clusters correlate with the positions of cytochrome oxidase rich blobs, these blobs are distributed in mosaic type arrays. Distribution in ordered arrays is a characteristic of neuronal populations that share a common functional property, such as colour sensitivity, optimal orientation, ocular dominance, that they are grouped laterally restricted columns that stretch vertically from the cortical surface to the white matter, Such columns are typically 200-400 μm in diameter. It was the early work of Hubel and Wiesel that led to the discovery (Hubel and Wiesel, 1962) of columnar architectures.

Elsewhere in layer II and upper III Hubel and Wiesel found cells with complex receptive fields (66% of total sample), the rest were hypercomplex, they failed to

record from any simple cells in these laminae. The fields they analysed were mainly binocular, cells outside blobs were found to be very precisely orientation tuned, direction selectivity was not frequently observed in these layers. The spatial frequency tuning of cells in layer II\III, with respect to their locations relative to blobs has been investigated (Born and Tootell, 1991). Mapping the distribution of 2-deoxyglucose, another indicator of cortical metabolic activity, while the visual field was stimulated with sinusoidally modulated gratings, revealed that single units exhibiting spatial tuning to a specific range frequencies are clustered. The distribution was bimodal with cells tuned to low and high frequencies being anatomically segregated, neurones recorded from inter-blob regions displayed band pass tuning to 3.8 ± 2.0 cpd. While cells inside blobs had a mean preferred spatial frequency of 1.1 ± 0.8 cpd. Histological reconstruction of recording sites showed that at the boundaries between blobs and inter-blobs abrupt changes in mean spatial frequency were apt to occur. Thus colour is extracted from a visual scene with a lower spatial resolution than the features processed by cells insensitive to colour.

Classical simple cells are not detected in any significant numbers until the bottom of layer III and in layer IVA and IVB. In non-blob zones of layers IVA and IVB receptive fields are orientation tuned. Most receptive fields are simple and two-thirds of these are direction selective. These cells are either found to be completely monocular or to have a strong eye preference. In layer V cells with mainly binocular complex and hypercomplex receptive fields are encountered (Hubel and Wiesel, 1968). Cells have low spontaneous activities, and their fields are orientation tuned, and most are reported to be length-tuned (Livingstone and Hubel, 1984). Very few receptive fields had any direction selectivity. Layer VI cells are found with both simple and complex type receptive fields. These sometimes have longer receptive fields, and the length tuning seen in layers above was no longer observed. A striking characteristic of cells within layer VI is their direction selectivity, which has been associated with these cells' targets in area in MT, which utilise direction selectivity.

Studies of the receptive field properties of large numbers of cells in primate V1 have indicated that approximately 85% of all cells are orientation tuned when stimulated with bar or sinusoidal grating stimuli (Schiller et al, 1976 and DeValois et al, 1982a,

b). These studies encounter the greatest numbers of non-orientation tuned cells in IVC and the sharpest tuning in IVB, on average cortical cells typically exhibit a tuning width of about 40°. Cells with simple type receptive fields account for 20-30% of the total in all layers except IVC, where they are 65% of all cells present. Complex cells are found in all layers except IVC, and account for 30-50% of all cells encountered. As in the cat, LGN and cortical cells in the primate have been quantitative shown to exhibit significant levels of length tuning, response suppression is reported to be strongest in the LGN and to range unimodally from zero to 100% in the cortex (Schiller et al, 1976). About one third of all cells are found to be length-tuned and these are concentrated in the superficial layers, in layers V and VI, fewest were recorded, layer IV was found to contain an intermediate number. Another form of response suppression was reported that originated from the side-bands of simple receptive fields, such bands were not encountered around complex receptive fields. Approximately one third of cells have suppressive zones entirely surrounding their excitatory centres, at ends and sides, cells with such properties typically exhibit reduced response levels when stimulated with large areas of sinusoidal gratings (Foster et al, 1985). Direction selectivity is reported for about 25% of cells that are recorded in V1 (Hawken et al, 1988 and Orban 1986), such cells are reported to be most often encountered in layers IVB and VI.

It is clear that cells in the primary visual cortex exhibit highly selective classical receptive fields that are sensitive to a wide range of stimulus attributes simultaneously. These cells also can exhibit an apparent specialisation for one attribute that implicates them in a particular functional pathway, such as perception of colour and form, or perception of motion.

Responses from beyond the classical receptive field.

Appropriate positioning of high contrast bar stimuli in a zone of visual space evokes an action potential response from a cell, the spatio-temporal characteristics of this classical receptive field were discussed above. In this section the subject is zones of visual space surrounding such fields, exclusive stimulation of these is not associated with evocation of a response from a cell that can be detected extracellularly. Rather

stimulation of these zones serves to modulate activity evoked when the classical receptive field is stimulated simultaneously.

The concept that the visual world is mapped retinotopically onto the surface of the cortex was introduced above (Daniel and Whitteridge, 1961 and Van Essen et al, 1984). Anatomical investigations have revealed that cells projected to points at distant sites up to 3-4 mm away. These projection distances are larger than the cortical distances that are associated with the visual space dimensions of the classical receptive field, and so by implication, neuronal activity represents an integrated response to stimuli in an extended area of visual space. Distant termination sites contain cells that have receptive fields which are shifted in visual space. Distant cells also possess differences in other stimulus specificity attributes, these are distributed tangentially to the cortical surface in a systematic fashion. Columnar architecture spatially subdivides cells with common orientation tuning, ocular dominance and other properties, within the retinotopic distribution of sensitivity. Thus a given cell could interact with others that have receptive fields displaced in visual space and tuned to a wide range of different stimulus attributes.

Initially zones surrounding the classical receptive field were found to have inhibitory influences, they were detected at receptive field ends. Subsequent work revealed that cells with simple and complex receptive fields had inhibitory end-zones (Dreher, 1972, Henry, 1977, and Kato et al, 1978). End-zones have the effect of suppressing response magnitude to long bar stimuli. End-zones occupy areas of visual space at the ends of an excitatory response field, that do not respond when mapped with short bars. They can totally overlap the excitatory field, or partially at its longitudinal ends (Sillito, 1977), meaning that the optimal bar for a length-tuned cell is the same length as, or slightly shorter than, the length of the excitatory response field. Length-tuning that brings about a response reduction greater than 40%, for long bar stimuli, is reported to be encountered in all layers of the cortex from approximately 50% of cells tested. The greatest numbers are encountered in the superficial layers where 56% and 13% of cells have length-tuned simple and complex fields respectively, and in layer V where cells with length-tuned fields account for 70% of the total population. In other layers 70% of cells are typically non-length-tuned. Cells without end-zones are

reported to exhibit summation to a length equivalent to the length of the classical receptive field (except special complex cells), stimulation with bars longer than this does not generate a further response increase. In the feline visual system at parafoveal eccentricities, length tuned cells are typically optimally stimulated by bars shorter than 3°, increasing the length of a bar stimulus reduces the responses of cells by between 40-100%. The strongest inhibitory influences mapped with bar stimuli have been shown to arise from a zone lying precisely along the orientation axis of the cell. Investigations of the stimulus specificity of inhibitory end-zones have shown that they exhibit similar tuning to the cells to which they provide inhibitory input (Orban et al, 1979a, b). The orientation tuning of end-zone inhibition is studied by artificially elevating the spontaneous discharge of cells with a conditioning stimulus, and then probing the response properties of the surround with stimuli moving with different orientations in different directions. End-zones are found to be tuned to the same orientation as the excitatory centre, rotation of an end-zone stimulus through 90° removes the suppressive influence on the cell. The orientation tuning width measured from the end-zone was approximately equivalent to the width of a single cell. Inhibitory end-zones have been shown to have a much larger spatial extent than the excitatory field of the cell and to overlap the excitatory field (Creutzfeldt et al, 1974 and Orban et al, 1979). Systematic mapping in cat V1 shows that end-stopped simple and complex cells have excitatory fields that were between 1.4-1.6° long. The end-zones influencing simple cells are on average 1.9° long and 5.4° wide, while those that suppress complex cell responses are 3° long and 6.1° wide. Pharmacological elevation of the spontaneous discharge of an end-stopped cortical cell has shown that stimulation of the receptive fields with a long bar, strongly suppresses discharge while the stimulus is over the field, indicating strong postsynaptic inhibitory influences on the cell (Sillito, 1977 and Sillito and Versiani, 1977). The orientation tuning exhibited by end-zones and the effect of their stimulation on an artificially elevated discharges indicates that they have presynaptic origin in the cortex. However the length tuning that is observed in the cortex is thought not to be a purely cortical phenomenon, but rather it has its origins in the interaction between the cortex and LGN. The majority of LGN cells are themselves strongly length tuned (Jones and Sillito, 1991), this property is thought to be generated by synaptic interactions

between afferent, intrinsic and cortico-thalamic feedback (Murphy and Sillito, 1987) features of the network at the level of the LGN.

Though most reports place a functional emphasis on the observation that long bars evoke suppressed responses from cells with end-zones, interestingly, under certain specific conditions stimulation of end-zones can have a detectably excitatory influence on a cell. This is the case when a length-tuned cell is stimulated with a long bar, broken by a gap located over the excitatory field, which is as long as a bar that would elicit a maximal excitatory response, were it presented in isolation (Sillito, 1977).

As well as having inhibitory zones at the ends of the receptive fields, cortical cells have also been reported to have inhibitory zones on the sides of their receptive field, along the direction axis (Hubel and Wiesel, 1962, Henry et al, 1969, Blakemore and Tobin, 1972, Bishop et al, 1973, and Maffei and Fiorentini, 1976). Recent attempts to investigate zones surrounding the classical receptive field have indicated that cells in cat primary visual cortex can have both side and end inhibitory zones, only one type, or neither (DeAngelis et al, 1994 and Li and Li, 1994). Cells that are subject to inhibitory influences originating at the sides and ends of their classical field account for 48-63% of sampled populations. Cells receiving exclusively inhibition from side-bands account for 13-24% while cells that are only subject to end-zone inhibitory influences account for 10-17% of a sample. Cells with neither type of suppressive zone accounted for 17% of those tested. Where no inhibitory influences are detected in a side-band or end-zone region, responses were often found to increase when a grating stimulus was extended beyond the boundary of the classical receptive field. Initial attempts to measure inhibitory side-bands in simple cells showed that they can be 10° wide and centred over the excitatory centre (Bishop et al, 1973). Subsequent work has shown that facilitatory and suppressive end-zones and side-bands are of equivalent size and can stretch up to 20° in the surround, they are typically between 2 and 8 times longer or wider than the classical receptive field that they surround (Li and Li, 1994).

There have been a range of different results reported concerning the tuning properties of side-bands. Early investigations reported that these zones were insensitive to

stimulus orientation (Bishop et al, 1973 and Orban et al, 1979). However more recent studies have indicated that side-bands like end-zones exhibit tuning to the same orientation as the excitatory field they surround (DeAngelis et al, 1994 and Li and Li, 1994). Quantitative analysis of response magnitude modulation brought about by the influence of these surround zones has taken place using bipartite stimuli, stimuli containing two spatially segregated but conjoined gratings presented with independently variable attributes, one presented to the excitatory receptive field the other to the surround. Analysis using an optimally oriented grating in the centre and one presented with a range of orientation in the surround has indicated that the tuning band width of the surround is wider than that of the centre. If a cell had inhibitory end-zones and/or side-bands, they were most influential when stimulated with a grating that was the same orientation as that in the centre. Surround stimulation with orthogonally oriented gratings was associated with response levels equivalent to those evoked by centre stimulation alone. When the spatial frequency tuning of a surround has been investigated, the optimal frequency of the inhibitory surround zone is the same as that for the receptive field, but the band width is greater by as much as 6 times (DeAngelis et al, 1994). Similar experiments carried out in primate V1 (Born and Tootell, 1991) have focused on side-band inhibition and have used metabolic activity indicators and single-unit activity to probe the properties of neurones in superficial inter-blob zones. Excitatory receptive field structures were defined using bar stimuli and then tested with gratings of different widths. Side-stopped cells accounted for 70% of cells in the superficial layers, side bands were mapped systematically, in some cases they were found to partially overlap the excitatory centre and to extend up to 6° into the surround. Side-stopping was quantitatively defined as a response to a laterally extended grating less than 50% of the response to grating of optimal width and spatial frequency. Interestingly end-stopping was only detected in 21% of the same sample. As in the previous study the orientation tuning of this inhibition was investigated, it was found to be maximal and the cell's preferred orientation.

The tuning properties of even more peripheral zones have also been functionally mapped with a conditioning stimulus/mask paradigm (Nelson and Frost, 1978). The spatial distribution of the excitatory receptive field, it's end-zones and side-bands were

determined, these were then simultaneously stimulated with a conditioning stimuli and covered by an opaque mask approximately 5° in diameter (polarising filters were used to facilitate this dual stimulus strategy). A surround stimulus was then used to stimulate the surround exclusively. Many cells were found to be subject to inhibitory influences driven from the surround, variations in the orientation of the surround grating indicated that these influences were again orientation tuned, and in most cases the effect was found to be maximal within 15° of the receptive field optimal orientation. This inhibition was found to be significantly reduced if the surround stimulus was rotated through 90°, but this did not completely remove it. It was suggested that these effects might have a role to play in sharpening the tuning of cortical cells.

For some cells stimulation of the surround produced excitation. Facilitation from beyond the classical receptive field was explored in simple cells in the cat striate cortex (Nelson and Frost, 1985). Excitatory receptive fields and inhibitory flanks were again masked, except for a small area in their centres which was used to generate an activated discharge using a small optimally oriented bar. Surrounds were then stimulated with large concentric patches of grating whose orientation could be varied. In many cases the authors found remote inhibition of the activated discharge could be generated by passage of the surround grating. However in about 20% of the sample the authors reported that they observed excitation from points remote from the receptive field. This excitation was observed to exceed the activated discharge control level, in a few cases by as much as 30%. By masking the surround at both ends of the receptive field mask, it was determined that the peripheral excitatory input was coming from sites on the surround that were co-axially aligned and co-oriented with the cells classical receptive field.

There is thus evidence for both excitation and inhibition that can be activated from visual space around the classical receptive field. In the following pages the implications that these influences might have on visual function will be discussed. For instance the effect that stimulus context has on detection thresholds for certain stimulus parameters such as orientation and contrast has been a focus of much attention in human visual psychophysics. It has been shown that the surrounding

spatial context of a stimulus can effect it's perceived orientation (Westheimer, 1976). Lines of a particular orientation can cause the orientation of a fixation stimuli to tilt. Extracellular recordings from the feline visual cortex during stimulation with such a paradigm have indicated that Westheimer's observations correlate with the properties of single units at the level of the primary visual cortex (Gilbert and Wiesel, 1990). In this investigation the receptive fields of single units were mapped and then stimulated with a bar, while their surrounds were being stimulated by assemblies of other bars, at no time did these other bars encroach upon the receptive a field, and when presented in isolation they did not generate any response. The surround bars had a range of orientation specific effects on responses to a centred optimal stimulus, ranging from inhibition to facilitation. Surround facilitatory effects were seen most often close to the optimal orientation, while surrounds containing orthogonally oriented bars generally provoked inhibitory effects. Surround stimulation also had the effect of broadening the orientation tuning curves of some cells, and according to the authors, actually changing the optimal orientation of the cell. Shifts in orientation could be repulsive or attractive, i.e. away or towards the surround orientation, the mean shift for the 30% of the sample that exhibited this effect, was 11°.

In other psychophysical experiments it has been shown that the context of a stimulus can effect detectability of target element. This effect is known as 'pop-out', target stimuli appear distinct from their surroundings when there is a contrast in their attributes (Treisman and Gelade, 1980, Bergen and Julesz, 1983 and Cannon and Fullenkamp, 1991). When there is an orientation difference between a test target and it's spatial context, supplied by surrounding features, the target is more easily detected than when the surrounding context is iso-oriented. Again these observation have been found to correlate with the behaviour of a set of neurones recorded from V1 of an alert monkey (Knierim and Van Essen, 1992). When the excitatory receptive field of a single cell was stimulated with a bar, and surrounded by other bars that did not encroach upon its field, there was observed to be a differential effect on the response of the cell as compared to the responses to centre stimulation alone. 90% of cells were suppressed when an iso-oriented surround field was presented, the average decrease in response relative to the centre stimulus alone was 34% for the whole sample. However the evoked response from 32% of the sample was found to increase from

this level, if the surrounding bars were oriented orthogonally to the central target rather than being iso-oriented with it. The average increase in response was found to be 28%, and was detected in 80% of cases, for only one centre stimulus orientation. When a surround stimulus was used that contained bars displayed at a random range of orientations, response suppression was detected relative to the response evoked by an isolated centre stimulus, this was equivalent to that generated by an aligned surround field. Similar findings have been reported using texture defined checkerboards to evoke magnetic and electric responses that were recorded non-invasively from human observer using scalp electrodes (Bach and Merigan, 1992, Lamme et al, 1992 and Regan and He, 1995). Large changes in activity were detected approximately 100 ms after a stimulus transition from a large field of parallel lines to a checkerboard composed of segments containing orthogonally oriented lines. It was suggested that these effects had their origins in activity in the striate cortex of human subjects.

Single cells in primary visual cortex of an awake monkey, have been further implicated in processes of figure-ground separation (Lamme, 1995). When stimulated with texture elements (dots or line segments) that were either presented with the same orientation and direction of motion as their surround, or as figures, by virtue of orientation and direction differences, the vast majority of cells were found to respond most strongly to texture elements as figures. Typically when an area of texture appeared as a figure because of differences in the orientation or motion of its elements a cells response was found to increase by about 50%. In addition to this it was reported that this response enhancement was highly specific to situations when the receptive field was 'inside' the figure (at any position within), if the receptive field was 'outside' the figure, no matter how close the figure was, there was no response elevation. These cells were not implicated in edge-contour or orientation-contrast detection, that in anyway depended on the stimulus specificity of the cells receptive field, but in signalling the presence and position of an entire figure, in an 'intelligent' way, with reference to a large area of the visual scene.

Another level of investigation that addresses the interaction of stimulus context and networks of horizontal connections, is the study of global activity in the visual cortex.

Such strategies, with the use of the right stimuli, can bring together insights gained from anatomical and physiological analysis and psychophysics, to tell us about the integrated activity of chunks of cortex millimetres wide. These techniques use signals like membrane potential, metabolic activity, blood oxygen level and population potentials to highlight small global activity changes generated by focal central stimuli and surround stimuli. Changes in neuronal membrane potential in superficial layer neurones that are the result of visual stimuli, have been optically imaged with voltage sensitive dyes and a 6 mm square array of photo-diodes (Grinvald et al, 1994). Stimuli used were focal patches of grating covering 1° of the visual field or surround gratings lacking the focal centre. Results from central stimulation of an area of cortex showed that there is an extensive spatially distributed area of elevated electrical activity. Single unit recordings were made in order to determine whether the elevated activity detected by the periphery of the photo-diode array was due to action potential signals in response to direct stimulation of receptive fields of cells near the periphery or to postsynaptic sub-threshold activity. Such recordings showed that single units at 12 peripheral sites were not driven to respond by the centre stimulus, thus the observed effects were postsynaptic. Again it was found that the presence of a surround influenced the magnitude of the response to the centre and the orientation of this surround was critical. Optical imaging results for centre alone, surround alone, iso-oriented surround and centre and orthogonal surround and centre were obtained. The magnitude of the centre response when an iso-oriented centre and surround were simultaneously presented was found to 39% less than their linear sum generated from results obtained when centre and surround were presented separately. The mean results demonstrate the effect of making the surround orthogonal to the centre, for an iso-oriented stimulus the mean suppression compared to the linear sum was 21%, however when the centre and sum were orthogonal the mean suppression was only 14%. Thus in terms of global activity distributed over the cortex, stimuli involving a systematic orientation contrast between centre and surround generate a larger global response than spatially coherent stimuli. The speed of the spread of activity in range of experiments was found to be between 0.09 and 0.25 $msec^{-1}$. The authors made three suggestions of pathways for this spread of activity, the first being non-myelinated long range projection intrinsic to V1, secondly, polysynaptic pathways involving intrinsic myelinated axons and lastly, feedback from higher areas of association cortex.

All these observations show that the surround of a classical receptive field influences a cell's response to simulations of natural stimuli. A wide range of surround effects have been isolated, many inhibitory, others facilitatory. These have been found to depend on stimulus parameters such as orientation and spatial frequency. Where surround stimuli facilitate responses to centre stimuli, possible mechanisms might be directly excitatory or dis-inhibitory in nature. Inhibitory effects could be mediated directly by inhibitory interneurons or via surround driven excitatory mechanisms that provide input to local inhibitory circuits. Interactions between different points in visual space indicate that these surround effects might be mediated by the long horizontal projections of excitatory and inhibitory cells in the cortex, or feedback from higher visual areas. Inputs that mediate surround mechanisms appear to be sub-threshold, since the degree to which surround stimuli can drive a cell in isolation is very limited, they mainly influence a cell's response to more optimal stimuli. Appropriate spatially distributed stimuli can modulate the response of the classical receptive field, thus it is important to consider the classically defined receptive field in the context of visual response specificity that surround it. These observations have the implication that in order to properly describe the stimulus specificity of a cell, in a way that is relevant to human vision, stimuli must be used that contain a contextual component. Classical analysis using bar stimuli, has succeeded in describing the excitatory centre, however such stimuli do not simulate the challenges of the natural environment. Cortical cells at a given point in visual space 'see' features in context, surrounded by other features, they do not see bright bars set in a fields of neutral contrast. In this investigation contextual stimuli were used to stimulate large areas of the visual field, while anatomically distributed cells with spatially distributed fields were recorded simultaneously. In the section below the discussion will focus on how these visual responses are made by interacting networks of cells.

Integrated network properties of the visual cortex.

So far the discussion of the visual system has focused on a number of key anatomical characteristics of the visual cortex, in particular the horizontal projections made by many cells, and the classical receptive fields and effects of spatial context on neuronal responses that emerge from the interaction of these, and the retino-geniculate input. The visual responses of a cell is thus the product of input from an extensive network, distributed both vertically across thalamic and cortical centres and horizontally within each of these. Neurophysiology has focused on the number of spikes a cell fires to a given stimulus as the cardinal indicator of the behaviour of single neurones and of the network in which they exist. In investigations of the visual system spike numbers are measured in epochs of time that correspond to the duration of presentation a stimulus. Analytical paradigms generally preserve the times when spikes are fired relative to stimulus onset. This is important as it allows the temporal distribution of spikes in the stimulation epoch to be studied. Epochs are divided into what are called bins of equal duration, some fraction of the stimulus duration, the number of spikes in each bin is displayed as a peri-stimulus time histogram. Such a strategy reveals how the number of spikes fired by a cell is modulated in time, because it might be the case that some bins will contain more spikes than others. Cells can fire tonically, at a constant rate over time, generating a PSTH in which all bins contain approximately the same number of spikes, or phasically, so that the rate is higher at one point during the recorded epoch, and bins representing this point contain more spikes than bins at other points. The capacity of a cell to fire tonically or phasically is conferred both by the spatial relationship between a stimulus and the receptive field it stimulates and also by the intrinsic properties of the cell being recorded. Analysis of spike numbers generates a response magnitude, which can be analysed in terms of the absolute number spikes fired to a given stimulus or as mean firing rate (the number of spikes fired during stimulation for one second). Both techniques average out any phasic characteristics of the response. Alternatively if information is required which takes account of the phasic characteristics of a spike train, then response magnitude can be quantified in terms of peak firing rate or using fourier transform techniques to quantify response modulation. A key feature of all these techniques is that they convey information about how many spikes a cell fires in time, relative to stimulus onset and offset.

How many spikes a cell fires has been proposed to be a property of neurones that is key to the generation of visual percepts (Swadlen and Newsome, 1994). This theory proposes that objects in a visual scene or auditory signal are represented by changes in the response magnitudes of large distributed population of cells. However it has been proposed that this strategy is not capable of segmenting nearby features that are parts of different objects and binding features that are part of the same object (von der Malsburg, 1981), to deal with these problems another theory has been proposed (von der Malsburg and Schneider, 1986, and von der Malsburg and Buhmann, 1992). This theory proposes that local feature segmentation and object binding to generate coherent visual or auditory percepts, is achieved by generating temporally tagged segments. These segments are bound by synchronisation of distributed temporally tagged populations to generate objects.

Epochs of synchronised oscillation embody a temporal code which is used generate anatomically distributed but distinct neuronal assemblies with functional significance (Singer, 1993), this has become known as the Temporal Correlation Hypothesis (Singer and Gray, 1995). In the primary visual cortex such coding, it is proposed, means that neighbouring populations of cells representing different stimuli are functionally segregated, while more distributed groups representing different features of the same object are functionally bound together. This study has used the visual cortex as network system to investigate these ideas and their impact on the ways in which individual cells are involved in *in vivo* neural networks. This has been done to explicitly describe some of the mechanisms that underlie visual perception. Stimuli have been employed with variable contextual properties to evoke responses from distributed populations of single neurones. These responses have been analysed for the stimulus dependence of their magnitude and temporal properties and the ways in which they synchronise and desynchronise with responses of other simultaneously active cells.

The temporal structure of visual responses.

An important feature of the temporal correlation hypothesis that allows the activity of population of cells to be grouped and segregated unambiguously is temporal

patterning of brain activity, this patterning can take the form of periodic modulation of activity. Oscillating changes in brain activity (during epochs of several hundreds of milliseconds) are explicitly implicated in cognitive function in the Temporal Correlation Hypothesis. Grouping and segregation are said to occur because of similarities and differences between the frequencies and phases of these changes within the network. Experimentally these oscillation are studied by recording EEG, local field potentials, multi-unit activity, and single unit activity. Though oscillation can be detected at a whole range of frequencies in the central nervous system, up to 300 Hz in rapid bursts of action potentials, those below 90 Hz are thought to have functional significance for behaviour, cognition and perception. Delta, theta and alpha band oscillations all occur between 0 and 10 Hz and are associated with sleep and low-arousal behaviours, however oscillations above 10 Hz have been proposed to relevant to cognitive function, such as vision. These oscillations take place in a restricted range of frequencies, called the gamma band, from 30-80 Hz.

Gamma frequency oscillations are detected at various sites in the central nervous system in human subjects. They have been reported to be specifically associated with visual stimulation (Freeman and Van Dijk, 1987, Lutzenberger et al, 1995, and Tallon et al, 1995), auditory stimulation (Joliot et al, 1994) and somatic perception (Desmedt and Tomberg, 1994). In the cat and monkey central nervous system gamma oscillation have been detected in visual centres, and others, such as sensorimotor cortex (Murthy and Fetz, 1992) and the hippocampus (Whittington et al, 1995). The following discussion will focus on the presence and reported functional relevance of oscillation in the visual system. Here, they have been reported to be a property of cells in the lateral geniculate nucleus (Ghose and Freeman, 1992), and of cells in primary visual cortex (Gray and Singer, 1989 and Gray et al, 1990, but also see Ghose and Freeman, 1992 and Young et al, 1992) and extrastriate cortical areas (Brosch et al, 1995). In the visual system one hypothesis has been that these oscillations appear in visual responses in a stimulus dependent fashion, though there have been conflicting reports in both the cat and the monkey suggesting that, this is not the case.

Where gamma oscillations in visual responses have been reported to be stimulus dependent, reports have focused cortical visual area 17 (Eckhorn et al, 1988, Gray and

Singer, 1989, Gray et al, 1990, Livingstone, 1991 and Eckhorn et al, 1993). Visually stimulating with bars of varying orientation and direction of motion, local field potential (LFP), multi-unit (MUA) and single unit activity has been recorded. Oscillations have been detected in the vast majority of LFP recordings, in 50% of MUA recordings and when the responses of single units have been investigated, 30% cells have been found to respond in an oscillatory fashion when visually stimulated.

Quantitative measurement of temporal properties has been achieved by calculation of power spectra and by fitting damped sine waves, called gabor functions to the results of auto-correlating single cell and multi-unit and local field potential activity. The stimulus tuning of the oscillatory components in each of these signals has then been compared to the tuning properties of the cells indicated from response magnitude measurements. Oscillatory responses are reported to be generally strongest for optimal oriented stimuli, a cell's propensity to oscillate decreases around this optimal generating a tuning curve (Gray and Singer, 1989). Tuning curves based on oscillatory power are reported to be similar to those obtained from responses magnitude measurements, strongest oscillations are found within responses to stimuli within 30° of the optimal orientation of a cell. Moving stimuli evoke strongest oscillatory responses from cells, binocular stimulation also has a facilitatory effect. Oscillation amplitude has been reported to increase when a bar stimulus is increased in length within the excitatory receptive field centre (Gray et al, 1990). When patches of grating are used it has been reported that oscillations in each type of recorded activity are stronger in responses to stimuli that are larger than the receptive field centre, and that are associated with lower firing rates in many cases (Bauer et al, 1995). Oscillation frequency has also been found to vary systematically, frequency increases when the velocity of stimuli is increased. When more complex, conflicting stimuli are presented to cell, such as an optimally oriented bar simultaneously moving with an orthogonal bar (forming a cross in the centre of a receptive field) the amplitude of the oscillation has been reported to be reduced in 76% of cases (Gray et al, 1990). Other analysis of the temporal characteristics of oscillations when they occur in visual responses, has shown that a number of their properties are very variable from one stimulus epoch to the next (Gray and Singer, 1989 and Ghose and Freeman, 1992). On repeated presentation of a stimulus, the frequency of the oscillation in a response was never the

same twice. Causing broad-band power increases for a range of frequencies when multiple response spike trains are analysed together for their oscillatory content.

The reports reviewed so far have been restricted to investigations of the feline visual system, however these observations are paralleled by those in anaesthetised primate V1 (Eckhorn et al, 1993), and MT of the awake monkey (Kreiter and Singer, 1992 and 1996). In the latter study, the activity of cell groups, indicated by MUA, was found contain periods of oscillatory discharge of short duration, typically less than 300 ms. Of the sites investigated 58% were found to respond to moving bar stimuli with significant oscillatory discharge, judged using the Gabor fitting technique, however little attempt was made to quantitatively assess the stimulus specificity of these discharges. All oscillations were at a frequency between 30 and 60 Hz, and on average occurred at 46 Hz. Power in gamma frequency range is also detected in the responses of 60% MT cells when they respond to texture fields with variable levels of motion coherence (Bair et al, 1994). However this power was not found to be due to oscillatory discharges, but burst firing followed by a refractory period of 10-20ms, which precluded further bursts. Gamma band power was not found to be dependent on the level of motion coherence in the MT receptive field or to choices made by a primate during a discrimination task using this stimuli. A study (Eckhorn et al, 1993) of V1 reported that cells in this area exhibit strongest oscillation in a frequency band between 60 and 90 Hz, with a dominant range between 70 and 80 Hz. Three types of recording were made simultaneously at a given site, the local field potential, multi-unit activity, and the pattern of response of single cells. Oscillations were found in all three signals, but were stronger (2-3 times stronger than in cat area 17) and more regularly encountered in population activity (70-90% of recording sites). Oscillations found in periods of spontaneous discharge were weak and were characterised by frequencies between 0 and 25 Hz. Oscillatory discharges from single cells, have been detected V1 of anaesthetised squirrel monkeys (Livingstone, 1991). Again oscillations were associated with visual responses, and these were found to occur at a higher frequency range than in the cat, between 50 and 90 Hz. Periods of oscillation were reported to last for 40 to 100 ms, a shorter period of time than in other studies. Half the recorded sample from layers IVCα and IVB and 20% of cells recorded from layer II\III were found to oscillate.

Other experiments in both the cat and monkey have yielded results which disagree with key aspects of the discussion on oscillatory discharges, so far. Firstly some groups have been unable to detected rhythmic oscillation in the gamma frequency range. Recording of various types of activity in primate V1 and other areas associated with visual function has indicated that visual stimulation is not associated with specific increases in oscillatory power in LFPs, in the gamma frequency range (Young et al, 1992). Rather, stimulation brings about a more global increase at all frequencies between 0 and 100 Hz, in fact it was reported after auto-correlation analysis of MUA activity that visual stimulation increased oscillatory power between 12 and 13 Hz, and this only in 10% of cases. In this report, and in another (Ghose and Freeman, 1992) based on work in the feline visual system, it was reported that a cell's propensity to oscillate did not correlate with coherent features in visual stimuli. Significant oscillations in the gamma range, were detected in the responses of approximately 40% of cells in a sample recorded from cat primary visual cortex. When the oscillatory characteristics in responses to coherent patches of grating and to flashed bar stimuli were compared, responses to the latter stimuli were more likely to contain oscillations, it was concluded that oscillation were not a feature responses to optimal stimuli. In investigations in the LGN (Ghose and Freeman, 1992), 50% of LGN cells were found to fire action potentials in an oscillatory fashion. These gamma oscillations were found to be an order of magnitude stronger than those detected in the cortex and were found to be suppressed by visual stimulation, an inverse firing rate dependence. This lead the authors to propose a model in which cortical oscillatory phenomenon were the result of geniculate input, and that such mechanisms might not be involved in processing visual information but might serve functions in attentional or developmental processes.

The observation that oscillations can be detected in the responses of single cells and simultaneously in the pooled activity of larger number of cells, has initiated an investigation of the temporal characteristics of a single cells involvement with population activity. Local network oscillations were detected in LFP and MUA recordings (Eckhorn and Obermueller, 1993), made simultaneously with the same electrode as single-unit visual response recordings. Three modes of interaction were

detected between single unit activity and population signals. The first was a 'rhythmic' state when individual cells exhibited an oscillatory firing pattern that was synchronised with the oscillatory activity present in MUA and LFP recordings. The second mode was denoted a 'lock-in' state, in which the single unit did not exhibit an oscillatory discharge at the same frequency as the population activity, but each of its spikes was phase-locked to the periodic activity in the MUA and LFP signals. There was also reported to be a third condition in which the temporal characteristics of a single cell's firing pattern had no structured temporal relationship with any local oscillatory activity. It was reported that the firing pattern of a cell could move from one state to another dynamically, and that a transition from rhythmic to lock-in was associated with a change from optimal to sub-optimal stimulation.

The dynamic properties of a cell's postsynaptic response, and its operation within distributed networks during visual stimulation, are thought to be factors that bring about oscillations in neuronal responses. They have been studied using direct physiological techniques and by modelling naturally occurring neuronal environments. In literature there are basically two kind of observation, in the first, oscillations are provided by neurones that have membrane channel properties that make them intrinsic pace-maker neurones (Llinas et al, 1991, and Silva et al, 1991, Nunez et al, 1992 and Amitai, 1995, Gray and McCormick, 1996), the other theory is that oscillations are the result of interactions between excitatory and inhibitory cells (Lytton and Sejnowski, 1991). Following sections will focus on influential investigations that have demonstrated the function significance of synchrony amongst populations of cells and oscillatory discharges within spike trains.

Temporal response correlations and network interconnectivity.

The structural features of the visual network, and the spatio-temporal stimulus sensitivity of cells that operate within this network were discussed above. Latterly the focus has been on ideas concerning the code that individual cells use to communicate within the network, and how this is modulated by the spatio-temporal features of a stimulus. Originally this was thought to be a rate code, in which the number of spikes

fired by a cell was a primary functional feature of a response. Recently however an oscillation code has been proposed as a key feature of network operation. It is thought that within the network the code operates engraphically, and that network interconnection, dynamic organisation and information transfer between single units form the basis for brain function. Developments in the last 20 years have allowed limited insights to be gained into the network connectivity, of living, functioning cells. The most influential and widely used technique for this type of investigation of synchronised neuronal processes *in vivo* is temporal correlation analysis.

Correlation analysis is a technique developed in the late 1960s, its key assumption is that if a pair of cells synaptically interact in some way then their there will be some consistent temporal relationship between a subset of each ones spikes. Implementation of cross-correlation analysis allows us to examine the functional connectivity of the central nervous system *in vivo* using physiological recording techniques. This technique is very applicable to the visual system, where the functional connections between cells can be viewed while they are being visually stimulated, the dependence of temporal interaction between connectivity on features of a visual stimuli can be assessed. The first significant papers setting out the theories of this technique were published by Gerstein, Perkel and Moore in 1967 and 1972. They worked on simple systems such as the Aplysia, and computer generated connectivity models. Cross-correlation analysis takes place on simultaneously recorded spike trains obtained from two neurones. The times of occurrence, before and after, of spikes in one train are subtracted from the time of each spike in a reference train. For each reference spike this process yields a series of intervals, negative (before) and positive (after), that form a complete description of the reference spike's temporal relationship with spikes fired by the other cell. These intervals can then be plotted in a binned histogram. It is peaks and troughs within this histogram that can provide information about response synchronisation and network connectivity.

Peaks can have wide variety of shapes and latencies from the origin of the cross-correlogram, thus peaks do not simply indicate that there is an anatomical interaction between two cells they also provide information on the nature of that interaction.

Commonly detected peaks and their associated schemes of anatomical connectivity are depicted in figure *4*. Broadly speaking there are two modes of excitatory connectivity which are have been reported theoretically and in practical experimental situations. In the first case (a) in figure *4* both recorded cells receive synaptic drive from a common source and thus fire at the same times (on the millisecond timescale). When the responses of these cells are correlated they generate a peak which straddles the central bin. The second mode of excitatory connectivity that is less commonly observed is a direct monosynaptic connection, where one recorded neurone projects directly to, and synapse on, another recorded neurone. Peaks indicative of this are temporally compact, due to direct causation of spikes, they are displaced to the left or right of the central bin. Which side of the origin the peak is, depends on which cell was postsynaptic, which presynaptic, and which train was used as reference during the calculation. Peaks are separated from the origin of the cross-correlogram by a latency which corresponds to the time it takes to convert an action potential at the axon hillock of one cell to an action potential at the axon hillock of another. Thus a total monosynaptic latency is composed of packets of time for each of the steps involved in this process, time for an action potential to travel down its axon, to invade the presynaptic bouton and initiate vesicle release, time taken for neurotransmitter to cross the synaptic cleft and interact with the postsynaptic receptor, time to generate an EPSP and transfer it to the soma to be integrated with other simultaneous inputs and yield a supra-firing-threshold result. A disynaptic interaction would be associated with a longer latency, and possibly a smaller peak, because a smaller of subset of each recorded cell's spikes were correlated. All these processes occur during inhibitory interactions, however in these cases the postsynaptic potential does not evoke an action potential from the postsynaptic cell but rather a period of silence. Such interactions are characterised by a trough in the cross-correlogram that again is displaced from the origin. Modelling experiments have shown that detection of inhibitory interactions using cross-correlation techniques is difficult (Aertsen and Gerstein, 1985). This model revealed an asymmetry in the sensitivity of temporal correlation techniques to inhibitory connectivity as compared to excitatory interactions. Cross-correlation was found to be an order of magnitude more sensitive to excitatory connections. This problem was attributed to the variability of the spontaneous activity of neurones, it was shown that inhibitory connections of

equivalent strength to those that are excitatory and are detected frequently, require higher levels of spontaneous activity from the participating cells to be detected themselves. It was shown in the simulation that for an inhibitory connection to be detected, the level of spontaneous activity needed to be at least 10 times greater. This is because insertion of an inhibitory event, into the spike train with a frequency of 10 Hz (i.e. 1 spike every 100 ms), lasting 10 ms, perturbs the stochastic nature of the spike distribution far less than insertion of a similar event in a spike train with a frequency of 150 Hz (i.e. 1 spike every 6.7 ms). Whereas the insertion of two synchronised spikes with a co-ordinated temporal interaction into two spike trains is detectable in a cross-correlogram whatever the firing frequency of the cells involved. Thus physiologically observable inhibitory connections have to be very strong in order to be detected. Detection of inhibitory common input connections should in theory be less susceptible to low firing rates of the recorded cells, as this mode of connectivity reduces the stochastic nature of the temporal distribution of spikes in both trains. A common source of IPSPs causes the recorded cells to synchronise their silent periods, and thus limits the distribution of spikes in both trains to periods when there is no common inhibitory influence. The result is a temporally diffuse synchronisation of the cells firing patterns, which results in a broad centrally located peak similar to that which might be generated by excitatory common input, but as this mechanism does not act directly on spike formation it is broader. The width of the peak would be related to the frequency of incoming common IPSPs, with higher frequencies being associated with narrow peaks. In practise when using cross-correlation to investigate the functional connectivity of cells in a network it is possible to imagine that a pair of cells would interact in more than one of these ways. Two recorded cells could not only receive a common input but also are directly connected. The resulting peak might contain contributions from the temporal structure constraints applied to the spike trains by both modes of connectivity, and thus it would contain characteristics of peaks that are the result of purely one interaction or another. In this situation it is the relative strengths and temporal interactions of the two inputs, the result of their morphological characteristics which determines the final shape of the peak. Factors such as the relative firing frequencies of the input neurones, the state of modulatory influences and the relative spatial arrangements of the synapses are all important in

Figure 4.

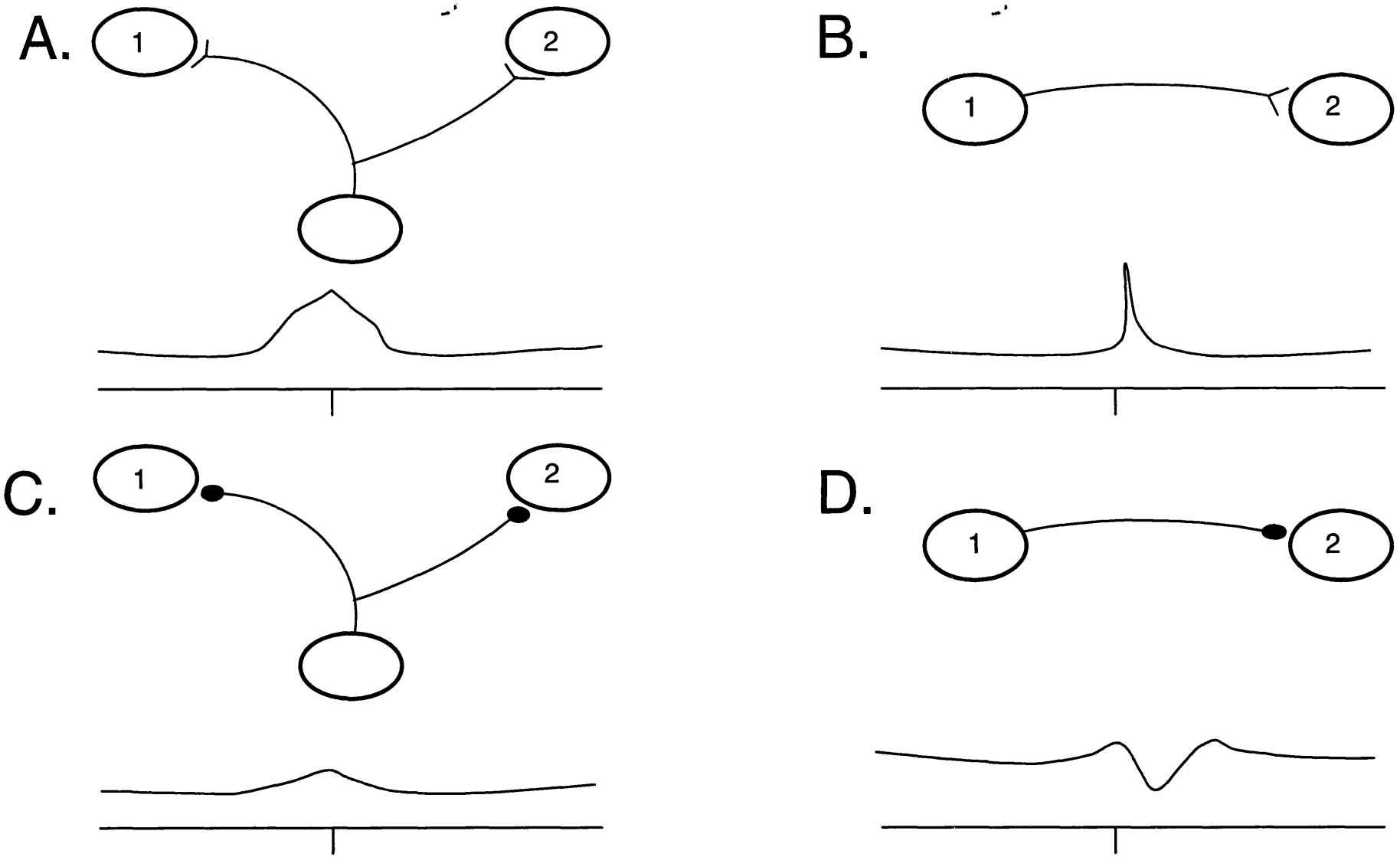


Figure 4.

Featured in this figure are four typical interval distributions that are encountered during cross-correlation analysis, and modes of connectivity between the recorded cells that are said to be the mechanistic substrates for the observed peaks. **a.** shows a symmetrical centre peak which is indicative of a common source of excitatory synaptic input. **b.** shows an offset peak which is taken to indicate that cell 1 provides direct excitatory synaptic input to cell 2. The peak in **c.** is a broader, shallower version of that shown in **a.**, and is thought to indicate common inhibitory synaptic input. In the last panel, (**d**), a displaced trough is shown, this is taken to indicate that cell 1 provides direct inhibitory input to cell 2.

determining an outcome.

The physiological properties of a system that is being studied with cross-correlation techniques are further subject to what are called non-stationarities. Non-stationarities are influences that effect the behaviour of individual cells and consequently the results that are produced using techniques like cross-correlation. Non-stationarities can be changes in the condition of the preparation, this is why during an experiment great care is taken to monitor the vital signs of a preparations condition. Another source of non-stationarity in a cells behaviour is it's interaction with the visual environment, this is manifested in its stimulus specificity. Cells fire responses at high frequencies when perturbed by certain kinds of stimuli and at lower frequencies in response to other stimuli. It is thus clear that the nature of peaks that are detected using cross-correlation techniques might depend on the nature of the stimulus used. A stimulus perturbing a cells environment in one way might result in the detection of a connection with another cell, whereas another stimulus might perturb the environment in another way, the recorded cells would be influenced by a whole different set of interactions. Thus it might be expected that the connectivity that is detected between a pair of cells might exhibit stimulus specificity, it might only be active in certain particular 'visual environments', when the two cells have to function as a 'unit' within the network to perform some particular function. Thus an examination of cross-correlograms generated from the responses of cells to a wide range of visual stimuli is required in order to fully characterise the interactions between them.

This technique has been used in many investigations to a number of experimental ends, initially to test some of the theoretical connectivity patterns that followed from Hubel and Wiesel's early reports, to investigate how the receptive fields of cortical receptive fields are generated from cortico-cortical synaptic interactions, and latterly to investigate the temporal code that the visual system uses to represent spatial distributed visual features amongst population of cells in the network. The literature concerned with each strategy will be reviewed below.

Synchronisation in the visual system.

One early study (Toyama et al, 1981a,b) used vertically separated electrodes and pharmacological manipulations to investigate the anatomical pathways that underlie Hubel and Wiesel's ideas. In this paper, the various interval distributions described above and shown in figure *4* were observed, and the usual connectivity mechanisms inferred. Common synaptic input was detected for neurone pairs (60%) in layer III to V, between pairs of cells with orientation differences as large as 40 degrees and was attributed to LGN input. Approximately 10% of cell pairs recorded from electrodes separated primarily in the vertical domain were found to be connected through direct excitatory projections, in each of these cases the cells involved preferred similar orientations. 12% of cell pairs interacted via a direct inhibitory connection, this form of connectivity was reported to exhibit less restriction in its horizontal distribution than excitatory interactions. Cells in neighbouring orientation columns, with small differences in preferred orientation were reported to interact in this way. The sudden appearance of such troughs in this study was attributed in later reports to the use of glutamate which reduced the variance in the cells firing rates by bringing them constantly closer to their maximum. These authors failed to find specific connections between the cells with receptive field types that was postulated to exist in Hubel and Wiesel's hierarchical model. They concluded that the LGN provides a general photic input to both simple and complex cell and that intra-cortical connectivity is responsible for the generation of other receptive field characteristics such as orientation tuning.

Subsequent experiments (Michalski et al, 1983), involving recordings within a single orientation columns resulted in the detection of peaks indicative of direct excitatory connectivity between 20% of cell pairs in the sample, the interactions between three quarters of these pairs were accompanied by periodic modulations flanking the peak. Interactions which were the result of a common input were detected in 46% of the sampled pairs, such peaks were found to between 10 and 320 ms wide with a mean at about 45 ms. Pairs of cells were also found to exhibit two modes of connectivity simultaneously, in 10% of the total sample, common input and direct excitatory

connectivity, in 4% of the sample common input was combined with an inhibitory connection. Another interacting feature of a few pairs of cells (10%) recorded in this study was that there peaks were distributed on both sides of the origin but that they were 'asymmetric'.

Experiments that have attempted to investigate synaptic interactions between cells in different orientation columns followed from a theory that proposes that long horizontally projecting axons connections (greater than the diameter of a column) that arise from pyramidal cells, link columns of cells with similar preferred orientations (Gilbert and Wiesel, 1979, 1983). Cross-correlation and visual stimulation were used to investigate this idea, with a focus on pyramidal cells of layers II and III of the primary visual cortex separated by significant horizontal distances (Ts'o et al, 1986). Excitatory interactions were detected, of the common input and direct varieties. Of all peaked correlograms, 29% were due to a direct connection, 51% were due to common input, and the remainder were reported to resemble interactions involving both forms of connectivity. Interactions were detected between cells recorded on electrodes separated by up to 2.5 mm. Strong synaptic interactions were only detected between cells similar or identical orientation preferences, when they were stimulated with simple optimally oriented bars. Over the distances tested interactions between iso-oriented cells were detected independently of the interelectrode separation, it was not necessary that the field should overlap. The presence of an interaction was reported to depend more strongly on the cells having a similar orientation preference rather than having other common properties such as similar ocular dominance or length-tuning. Another strategy that was used by this group to explore interactions in the orientation domain, was to stimulate cells differing in preferred orientation with either pairs of bars, one optimally oriented for each or with a single stimulus at a bisecting angle. It was reported that the paradigm using two bars did not generate synchronised activity whereas the bar presented at the bisecting orientation, did. It was concluded on this basis that the cell providing common input was also orientation tuned and thus cortical in origin. These finding provide support for a theory that iso-orientation domains are connected over large anatomical areas and hence over large areas of visual space, however the visual stimuli used might have limited the range of connections that were detectable. Another study (Schwarz and Bolz, 1991), motivated

by this theory, concentrated on the long horizontal connections known to exist anatomically between layers V and VI. These projections had been implicated in the generation of layer VI cell receptive fields, inactivation of parts of layer V with GABA caused small areas of the receptive fields of layer VI cells to be silenced (Bolz et al, 1989). Correlated firing was detected in 31% of the cell pairs tested, and in each of these cases the interaction was attributed to common synaptic input, synchronisation was found between neurones separated by up to 4.2 mm. Strong interactions were generally only seen when the cells receptive fields were collinearly aligned and iso-oriented, and the layer V receptive field lay within in the summation area of the layer VI cell.

Over shorter distances up to 1mm, similar results have been reported (Hata et al, 1991). Common input was detect from 18.5% of sample of 330 pairs, direct excitatory and inhibitory peaks were detected in only 3% of the sample, each. Again connectivity was also reported to be strongly biased towards orientation differences less than 45° at these separations. Inhibitory linkages were more likely to be detected if cells had orientation differences between 30° and 45°. Inhibitory interactions have been investigated explicitly (Hata et al, 1988). Glutamate was used to elevate firing rate and thus the detectability of direct inhibitory connections. Inhibitory connectivity was detected between 10 pairs of cells of the 310 tested. Differences in orientation tuning for each pair were always less than 45°, iso-oriented fields were not found to interact in this way. The results supported previous physiological and psychophysical findings that suggested that inhibitory interactions between cells with different orientations are a feature of cortical function. Cross-correlation of visual responses to bar stimuli reveal that common input synchronisation, and to a much lesser extent direct synaptic interactions, exist between cells closely spaced field and similar preferred orientations.

The cortical classical receptive field, as it appears using bar stimuli, is the result of very specific synaptic interactions, that are reported to be most often detected between cells with certain specific receptive field configurations, when they are stimulated with single simple stimuli. Excitatory interactions, particularly direct ones, are reported to be dependent on the cells have similar preferred orientations. In layers II,

III and IV it is not necessary that they should be sensitive to stimulation of the same point in visual space. Inhibitory connections are most frequently detected between cells with obliquely oriented fields. On average in all the studies discussed so far synchronisation brought about by a common synaptic input is detected at least twice as often as the next most frequently detected interaction, a direct excitatory connection. Possible sources of common input have been reported to be the LGN and the cortex. Where cortical sources have been postulated for common input, a single bar stimulus that excites both cells can generate synchronised responses, while pairs of bars used to optimally stimulate cells with different preferred orientations are not reported to generate synchronised responses (Ts'o et al, 1986). Further analysis of the temporal interactions between the responses of cells to more complex stimuli is discussed below, together with their implication for the ways in which visual percepts are formed.

Oscillatory synchronisation.

Single cells respond to stimuli with oscillating discharges and these oscillations appear in a stimulus dependent fashion within spike trains, so investigators have recorded from groups of simultaneously stimulated cells to learn whether, and under what circumstances, such activity could be synchronised. The results of these experiments have recently led to the proposal of a Temporal Correlation Hypothesis (Singer and Gray, 1995). This is concerned with the strategies that CNS uses to group and segregate activity about the features of our environment. Initial investigations confined analysis to activity recorded within the primary visual cortex of the cat, evoked by stimulation with bright bars. Investigations have undertaken analysis of either multi-unit spike activity (Gray et al, 1989, Engel et al, 1990, Engel et al, 1990, 1991a, 1991b, Kreiter and Singer, 1992, and König et al, 1993, 1995) or the local field potential (LFP) and its underlying multi-unit activity (MUA) (Gray et al, 1992). Recently, analysis of single unit activity been reported, but only from a single site (Gray and Viana Di Prisco, 1995).

Characteristically cells are observed to synchronise their oscillatory firing patterns in a frequency range between 30 and 50 Hz (Gray et al, 1989 and Engel et al, 1990), with on average zero phase lag, though shifts of up to +/- 5 ms are apparent. This synchronisation occurs in multiple epochs throughout a single stimulus presentation, each epochs typically lasts for between 100 and 900 ms (Gray et al, 1992). When oscillating discharges at two sites are cross-correlated, the activity of approximately 50% of site pair generates an oscillating cross-correlogram, that meets the criterion indicating distributed synchronised oscillatory activity (Gray et al, 1989 and Engel et al, 1990). In these investigations non-oscillatory synchronisation was detected from approximately 10-20% of site pairs.

How a pair of sites' propensity to synchronise is influenced by the distance between the sites and the spatial characteristics of their receptive fields has been investigated in primary visual cortex, by recording from sites separated by 0.4-12mm (Gray et al, 1989 and Engel et al, 1990). For separations less than 2 mm where multi-unit receptive fields pairs overlapped in visual space, and where the orientation difference between fields was 22° or less, the visual responses to binocular stimuli of 54% gave rise to oscillatory synchronisation. Synchronisation was non-oscillatory in a further 25% of pairs. Analysis of pairs with receptive field orientation differences of 45-90° revealed that similar proportions of the sample were synchronised in these ways. Oscillatory synchronisation was detected in 50% of the sample of sites with similar orientations that were separated by 2-7mm, but if the orientation difference or separation was increased beyond these ranges oscillatory synchronisation was not frequently detected. Irrespective of orientation difference, increasing site separation strongly reduced the incidence (8-12%) of non-oscillatory synchronisation. Non-oscillatory synchronisation of local field potentials was also dramatically reduced by increases in orientation difference or site separation. However oscillatory synchronised LFPs were typically detected from 75% of the sample irrespective of orientation difference or site separation. Spontaneous LFPs recorded from these sites were not synchronised. Monocular stimulation lead to responses that exhibited oscillatory synchronisation, however interactions had lower amplitudes and decayed more rapidly.

The observations reported above suggest that it is possible that apart from a role in grouping and segregating activity to form functional assemblies, an oscillatory discharge may facilitate response synchronisation over long cortical distances (Engel et al, 1990 and König et al, 1995). The role of the oscillation would not be to provide a temporal code but to make the firing pattern of the cell more predictable, which would facilitate its synchronisation with the firing of other cells. An investigation of this idea (König et al, 1995), concluded that synchronisation could occur from oscillating and stochastic spike trains by reciprocal interactions between sites that were separated by less than 2 mm. However when sites were separated by between 2 and 7 mm, synchronisation was almost always only detected when both sites discharged in an oscillatory fashion. These modes of interaction are also detected between cells in simulated neural networks (Deppisch et al, 1994).

Other investigations demonstrate that oscillatory synchronisation is not confined to sites that are recorded within a single cortical area. Analysis of visual responses recorded from sites in the primary visual cortex of each hemisphere, showed that synchronisation could occur across the vertical meridian of the visual field (Engel et al, 1991a, Eckhorn et al, 1992). Recordings made in the primary visual cortex and extrastriate visual areas, demonstrated that synchrony was occurred between neuronal populations of at different points in the visual system (Engel et al, 1991b, Eckhorn et al, 1992). In all these investigations it was demonstrated that assembly formation was highly dependent on the features of the stimulus. Single bar stimuli were more effective in evoking synchronised oscillatory interactions than more complex stimuli, that were optimal for each site, in each of these situations.

Some recordings made in primates indicate that cells in this visual system also exhibit stimulus specific oscillatory responses, and these are often synchronised. Groups of single V1 cells have been recorded in anaesthetised preparations that exhibit oscillations in their responses to visual stimuli, but not their spontaneous activity. Such oscillation were observed to synchronise, however unlike the situation in the cat, these synchronised oscillations were only detected when the cells had similar orientation preferences (Livingstone, 1991). In area MT of awake monkeys, periods of

population activity discharge can synchronise during periods of simultaneous visual response (Kreiter and Singer, 1992, Kreiter and Singer, 1996). Flanking oscillatory modulation in response cross-correlograms revealed that these oscillatory discharges were synchronised, large central peaks mean that much synchronisation also occurred between stochastically distributed spikes. Interactions were detected between pairs of sites containing cells with different direction preferences, responding to a bar moving in a direction intermediate between them. Presentation of single and dual bar stimuli (Kreiter and Singer, 1994) revealed that, as in the cat, cells specifically synchronised periods of oscillation when stimulated with a single stimulus, rather than two, each of which was optimal for a recording site. However other spectral analysis of MT single units (Bair et al, 1994) responding to moving textures with coherent groups of elements of varying size. has shown that changes in the amplitude spectral power in the gamma range do not correlate with any changes in the spatio-temporal characteristics of the stimulus or with pychophysical discriminatory responses made by the monkey. Gamma frequency power in neuronal discharges was not oscillatory in nature but rather was proposed to be due to burst firing followed by refractory periods of 10-20 ms.

To date it has been shown that synchronised oscillatory population activity is a feature of cortical activity that can be detected readily within a single visual area, where it shows some dependence on relative configurations of the receptive fields of the participating sites, between areas in striate and extrastriate cortex and areas processing different halves of the visual field. The observations the pull all these reports together concern properties of response synchronisation that might help generate coherent visual perceptions of objects in the visual world (Gray et al, 1989, Engel, et al, 1990, Engel et al, 1991a, b). Response synchronisation is highly stimulus dependent. These experiments show that stimuli generate assemblies of neurones that fire synchronised spikes, these assemblies appear to be formed, destroyed and segregated dynamically in stimulus dependent fashion. Grouping and segregation processes amongst populations of cells have been investigated by recording from up to 4 sites simultaneously, sites were separated by 400μm, cell populations at each were found to have different optimal orientations. (Engel et al, 1991c). When stimulated with one bar all sites were found to synchronise their oscillatory responses, regardless of stimulus orientation or

their mutual orientation differences. However when these cells were presented with a conflicting stimulus containing two bars of different orientations, cells at each site did not synchronise their responses with all other sites, but only with one other. Which sites synchronised with which was reported to be dependent on the orientations of the bars in the conflicting stimulus, thus two sites synchronised if their preferred orientations were similar to the orientation of one of the bars. Their activity was segregated temporally from that of the others. Appropriate stimulation groups the activity in the four sites into assemblies that exhibit synchronised responses.

Other experiments have demonstrated how neural synchrony mediated assembly formation works, when stimuli are presented in areas of visual space that are larger than recording site receptive fields. In these experiments the strength of synchronisation between two sites with spatially distinct receptive fields was strongly modulated by the global features of the stimulus (Gray et al, 1989). Pairs of sites with non-overlapping fields, stimulated with one long continuous compound bar stimulus, passing over both fields were strongly synchronised. However if this stimulus was broken into two separate bars by a small gap in the middle, the strength of synchronisation was reduced. It was abolished if the two bars were displayed travelling in opposite directions. It thus appears that it is not only aspects of a visual stimulus that directly excite the classical receptive field which influence whether synchronisation processes generate functional assemblies, but also the spatio-temporal context in which a stimulus is presented. Thus in the light of the discussion above concerning the ways in which stimuli in the surround can effect the firing rate of a cell as it responds to a stimulus presented in the classical field, it suggests that contextual centre/surround interactions are critical to the dynamic formation of functional assemblies using temporal synchrony.

The stimulus selectivity of the oscillatory synchronisation mechanism in forming distinct functional assemblies in the cat primary visual cortex and primate area MT, has lead to proposals about the way the visual system generates percepts from the retinal signal. Functional assemblies are generated from the interactions between the temporal patterning of visual responses to particular stimuli, such as long, straight, coherent, contours (Engel et al, 1991 and Singer, 1993). These ideas about the kind of

stimuli that generate cell assemblies arose from the theories of the Gestalt Psychology movement (Koffka, 1935). The aim of the Gestalt movement was to determine, what it was about the properties of a visual scene that meant they were unselfconsciously perceived in one way and not in another, i.e. groups of features as objects, rather than, just, *many, distributed* features. They suggested that the visual scene was not perceived as a sensation of light, variable in intensity and wavelength over visual space, but as composed of distinct objects distributed in an environment with other objects. They proposed 'Laws of Grouping' in which distributed feature elements are grouped together into a distinct objects, with semantic content greater than the sum of their feature elements, because they meet certain spatial criteria (Wertheimer, 1912). The properties of elements in a stimulus, that were said to bring about grouping, were Proximity, Good Continuation, Similarity and Closure. Elements in a stimulus are grouped into objects because they are in close proximity, elements distributed in linear arrays are grouped into continuous contours because they meet the criterion of Good Continuation. Singer, Gray et al, extended this reasoning on macro-perceptually grouping phenomenon, that is obvious to anybody seeing the stimuli of Wertheimer and Koffka, and applied it to the mechanisms that mediate experimentally demonstrated temporal interactions between responses of small groups of cells in the visual system. When cells respond to a complex feature containing elements with different orientations and directions of motion, distributed over a relative small area of visual space and thus in a restricted volume of cortical tissue, those processing one aspect of a stimulus, are said on the basis of experimental evidence, to separate into a functional assembly which is distinct because the cells involved fire synchronously at a common frequency. Cells in the same volume of tissue but processing some other aspect are distinct because they fire synchronously at a different frequency and phase to other populations. The Temporal Correlation Hypothesis (Singer and Gray, 1995) also proposes that functional assemblies are not just formed during epochs of synchronous oscillatory discharge but are also formed when synchronous discharges have stochastic temporal distributions. Many of the investigations that led to this hypothesis focused specifically on the stimulus specificity of oscillatory synchronisation. Stochastic synchronisation, that generates cross-correlogram peaks without flanking peaks, was discussed in detail above. Such interaction were detected in the course of investigations of anatomical connections between cells. Many cell

pairs that fired synchronously were said to receive common excitatory input. Until recently the stimulus specificity of synchronisation of stochastic discharges (Sillito et al, 1995) received less attention. One of the aims of the work presented was to determine whether these two kinds of synchrony have different stimulus specificities.

3. **Scope of analysis.**

Russell and Semon (Russell, 1921) originally proposed that within the nervous system 'mnemic phenomena' occur. As the system responds to stimuli it undergoes dynamic transitions between 'indifference-states', which can themselves be seen as 'excitement-complexes'. The difference between some equilibrium state and the excitement-complex generated by a stimulus is the 'engram' due to the stimulus. Semon had little idea what the nature of an engram was, his idea was not a result of direct observations of nervous system function. However Russell proposed that physiology would provide grounds for the support of Semon's hypothesis. Early experiments in the nervous system focused on the networks of connections between brain cells, the material substrate for mnemic phenomena. Later physiological experiments provided insights into how cells behave as a result of the connectivity characteristics of the network, and thus provided some insights into what might be the nature of an excitement-complex, at the level of the single neurone. While both these types of investigation continue to illuminate the subtlety of function in the nervous system, in the last decade many investigators have attempted to more fully describe an excitement-complex and determine the nature of an engram, the code used by the nervous system to generate an excitement-complex. It was the aim of the physiological experiments on which this thesis is based, to investigate how a visual stimulus is represented in the activity of populations of cells in the primary visual cortex, so the ideas of Russell and Semon concerning the engraphic operation of the nervous system provide a useful starting point.

The broad aim of this investigation was to examine what strategies individual cells and the network in which they exist use to encode the spatio-temporal characteristics of complex contextual stimuli. Cells were stimulated in a variety of ways with sinusoidal grating stimuli presented in a bipartite fashion centred over a cell's excitatory field, the dimensions of which were determined by presenting circular patches of grating with different diameters. The effect of spatial context was investigated by presenting each cell with up to 200 differently configured stimuli. Centre diameter, orientation and surround orientation were varied to make each configuration of a unique bipartite grating. Single unit visual responses were analysed

to determine the effect changing these stimuli had on the number of spikes fired, the temporal structure of discharges, and the way one response synchronised with other simultaneously recorded ones.

4. **Methods.**

In this study two animal systems were investigated. The data analysis reported below was obtained during recording sessions carried out on seven female monkeys (Macaca Fascicularis) weighing between 6 and 10 Kg, and ten female domestic cats weighing between 2 and 3 Kg. In some cases these preparations were shared with other projects running in the laboratory (e.g. Cudeiro and Sillito, 1996).

Preparation of mammalian models.

Cats.

Experiments were carried out using acute feline preparations, during an experiment these were paralysed and anaesthetised using a gaseous mixture of 70% nitrous oxide, 30% oxygen and halothane. Anaesthesia was induced with a $N_2O\backslash O_2$ and 5% halothane mixture, initially this was delivered into an enclosed cat box, and then through a face mask when the animal had been transferred to the surgery table. During surgery halothane was delivered at a concentration of 2-3%. Before each of the following surgical procedures a local anaesthetic (lignocaine hydrogenchloride and adrenaline acid tartrate) was also administered at each site where an incision was to be made. After each procedure all wound margins were treated by topical application of antibiotic powder (chlortetracycline hydrogenchloride), and then they were sutured. Surgery began with a tracheotomy that allowed a Y-shaped canula to be inserted, this was secured and for the duration of the experiment the animal was artificially respired with a small animal ventilator (SAR-830 from CWE Inc.). Initial indicators of the preparations physiological condition and anaesthetic depth were respiration rate and reflex activity these were closely monitored, subsequently end-tidal carbon dioxide concentration and respiration rate were monitored electronically using equipment manufactured by Hewlett Packard. Carbon dioxide concentration was maintained between 3.8 and 4.2% and respiration rate at 20-30 min^{-1}, deviations from these limits were signalled with alarms, the concentration of halothane was adjusted between 2-3% during surgery to ensure that the preparation was maintained within these limits.

A bilateral cervical sympathectomy was conducted to remove innervation to eye muscles that might cause involuntary eye movements during the experiment. Following this a canula was inserted in the femoral vein, this was subsequently used to deliver drugs to the preparation. Electrodes were then attached to four points on the body, in order that an ECG signal could be obtained and the cardiac pulse rate could be monitored, this was done using equipment manufactured by Hewlett Packard. Body temperature was monitored and controlled to maintain it at 38°C using a thermostatically controlled electric blanket.

After these initial stages of surgery animals were stabilised in a stereotaxic frame with ear, eye and mouth bars. The head was positioned precisely in the centre of the frame by manipulating the positions of the ear bars. Eye and mouth bars were used to prevent rotation around the ear bar axis. This was done so that particular areas of the central nervous system could be localised, using predetermined co-ordinates. When the preparation was stable within the stereotaxic frame, paralysis was initiated, this was achieved using a neuromuscular blocker, supplied through the venous canula, the agent used was gallamine triethiodide (flaxedil). It was delivered as an initial dose of 40 mg Kg^{-1}, and subsequently for maintenance, at a rate of 10 mg $Kg^{-1}h^{-1}$ in 4.3% dextrose saline.

An incision was made in the scalp above an appropriate site depending on whether the aim of the experiment was to recorded from the cortical area V1 or the lateral geniculate nucleus. Subcutaneous tissue was reflected in order to expose the skull. Craniotomy sites were determined using stereotaxic co-ordinates, relative to a zero point defined by the position of two ear bars, if the target was V1 the craniotomy was made on the posterior surface of the skull, near the mid-line, the craniotomy site made when LGN recording was made on the dorsal surface of the skull. Sub-cutaneous tissue was than removed to reveal the skull. A craniotomy was performed using a dental drill, a small aperture was created to reveal the dura, a membrane that covers the cortex, the dura was dissected, so that electrodes could be directly inserted into the tissue. Around this exposed area a cylindrical aluminium chamber was secured using dental acrylic, after electrode insertion this chamber was filled with a agar/cerebro-spinal fluid mixture to protect the underlying cortical tissue, then a layer of wax was

placed on top of this, to prevent fluid leakage and tissue movement. After the chamber had been sited a silver plated electrode was attached to the skull, the scalp incision was then treated with antibiotic powder and sutured around the chamber. The electrode was used to record the electro-encephalogram (EEG) of the animal, the pattern of activity indicated the anaesthetic depth, recordings were made when spindle activity was apparent.

The positions of the area centralis and blind spot were determined by reflecting the tapetum onto a tangential projection screen, using a Keeler pantoscope. It was possible to see these landmarks after dark adapting, they were marked on the screen and used as spatial reference points in later analysis. After this the eyes were washed with 0.9% saline, then they were treated with phenylephrine hydrogenchloride to retract the nictating membranes, pupils were dilated using atropine methonitrate, the corneas were then protected with contact lens. The eyes were focused using 2 mm apertures placed concentrically around the area centralis and a further set of lens, on the stimulation screen 0.57 m away. At regular intervals during the experiment this process was repeated to check that the corneas were clear and healthy.

During sessions of visual stimulation and recording from neurones the preparation was lightly anaesthetised, according to the EEG criterion, the concentration of halothane was reduced to between 0.1 and 0.5%.

Primates.

Experiments were also carried out on acutely prepared primates. Before surgery each experimental animal was given a pre-med injection, of 0.05 mg Kg^{-1} of acerpromazine maleate (manufactured by C-vet). Subsequently atropine sulphate (manufactured by C-vet) administered intra-muscularly at a concentration of 40 mg Kg^{-1}, this was done to ensure a clear respiratory tract. Anaesthetesia was then induced using ketamine (Ketaset), supplied intra-muscularly at a concentration of 10-15 mg Kg^{-1}. Before each surgical incision was made a local anaesthetic was used, this was marcain (bupivacaine hydrogenchloride BP), subsequently wound margins were treated with a

topical application of cicatrin anti-biotic powder (neomysin sulphate BP). The first procedure performed was a tracheotomy, this allowed a Y-shaped canula to be inserted in order to facilitate artificial respiration and the provision of anaesthetic gases in a mixture containing 70% nitrous oxide and 30% oxygen. A small animal ventilator was used to respire the preparation during each experiment (SAR-830 manufactured by CWE Inc.). Next canuli were inserted in both femoral veins, drugs would subsequently be delivered through these.

After these initial procedures the preparation was transferred to a stereotaxic frame for the remainder of the experiment. At this point the preparation was transferred onto a maintenance anaesthetic. The transfer occurred when muscle tone returned as the preparation came round from the ketamine that had been delivered. The maintenance anaesthetic, sufenta forte (sufentanil citrate) (Levitt et al, 1994) was delivered as an initial bolus over a couple of minutes through a venous canula, until cessation of respiration, at this point the ventilation began using the pump, sufentanil was then delivered at a rate of 4 $\mu gKg^{-1}h^{-1}$ continuously throughout the experiment. A neuromuscular blocker was used to prevent movement, the agent used for this purpose was norcuron (vercuronium bromide) (Levitt et al, 1994), again this was supplied through a venous canula, and at a rate of 0.1 mg $Kg^{-1}h^{-1}$. The fluid and nutrition requirements of the animal were managed using the solutions containing the maintenance anaesthetic and paralytic agent. Supplements of lactated ringers (Hartmanns solution) and glucose were supplied in these solutions. To reduce swelling due to cerebral oedema, 0.5 mg Kg^{-1} of a steroid, dexamethasone was administered, antibiotics were also given daily to prevent the development of infection.

Anaesthetic level was adjusted throughout the experiment in accordance with data obtained from various monitors of the preparations condition. ECG electrodes were attached to four points on the preparations torso and limbs. The intersystolic heart rate was monitored, deviations out of the range 120-180 bpm were alarmed, using an electronic monitor manufactured by Hewlett Packard. The state of the preparation was also monitored, using end-tidal CO_2 concentration as a parameter, changes in this value were also alarmed, concentrations between 5-5.5% indicated that the

preparation was stable. EEG was recorded using electrodes that were attached to the scalp, and core body temperature was monitored using a rectal probe attached to a thermostatically controlled electric blanket. Body temperature was maintained between 37.5-38.5°C.

The head was initially secured in the centre of a stereotaxic frame using ear, eye and mouth bars, a head bar was then attached, and the eye bars were removed. This precise head positioning allowed the positions of recording sites to be determined with stereotaxic co-ordinates. This meant that in each experiment cells with receptive fields in similar zones of visual space were recorded. A recording site was prepared by making a craniotomy, 2-3 mm in diameter above the appropriate portion of cortical area V1, over a zone concerned with perception of parafoveal visual space approximately 5° from the fovea, the dura was exposed and a very small aperture was dissected for the insertion of electrodes. A chamber was then secured around the craniotomy with dental acrylic (simplex rapide), after electrode insertion this was filled with agar/CSF and then wax to plug the aperture and maintain a constant cranial pressure and thus minimise brain movement.

Features of the retinal surface were visualised using a reverse ophthalmoscope, this process involved visualising the fovea and the head of the optic nerve separately, by placing a cross-hair over each in turn with the illuminating scope, and then placing a mirror in front of the illuminating beam so that the cross-hair positioned over the landmark was projected back onto the projection screen. Eyes were treated with atropine methonitrate and protected with contact lenses, they were then focused with 2 mm apertures and lenses placed in front of the apertures, on a stimulation screen placed at either 57 or 114 cm.

Electrodes.

Extracellular recordings were made using tungsten-in-glass microelectrodes (Merrill and Ainsworth, 1972), these were manufactured within the laboratory. Tungsten wire (figure *5a*) from Clark Electromedical Instruments, of diameter 125μm was

Figure 5.

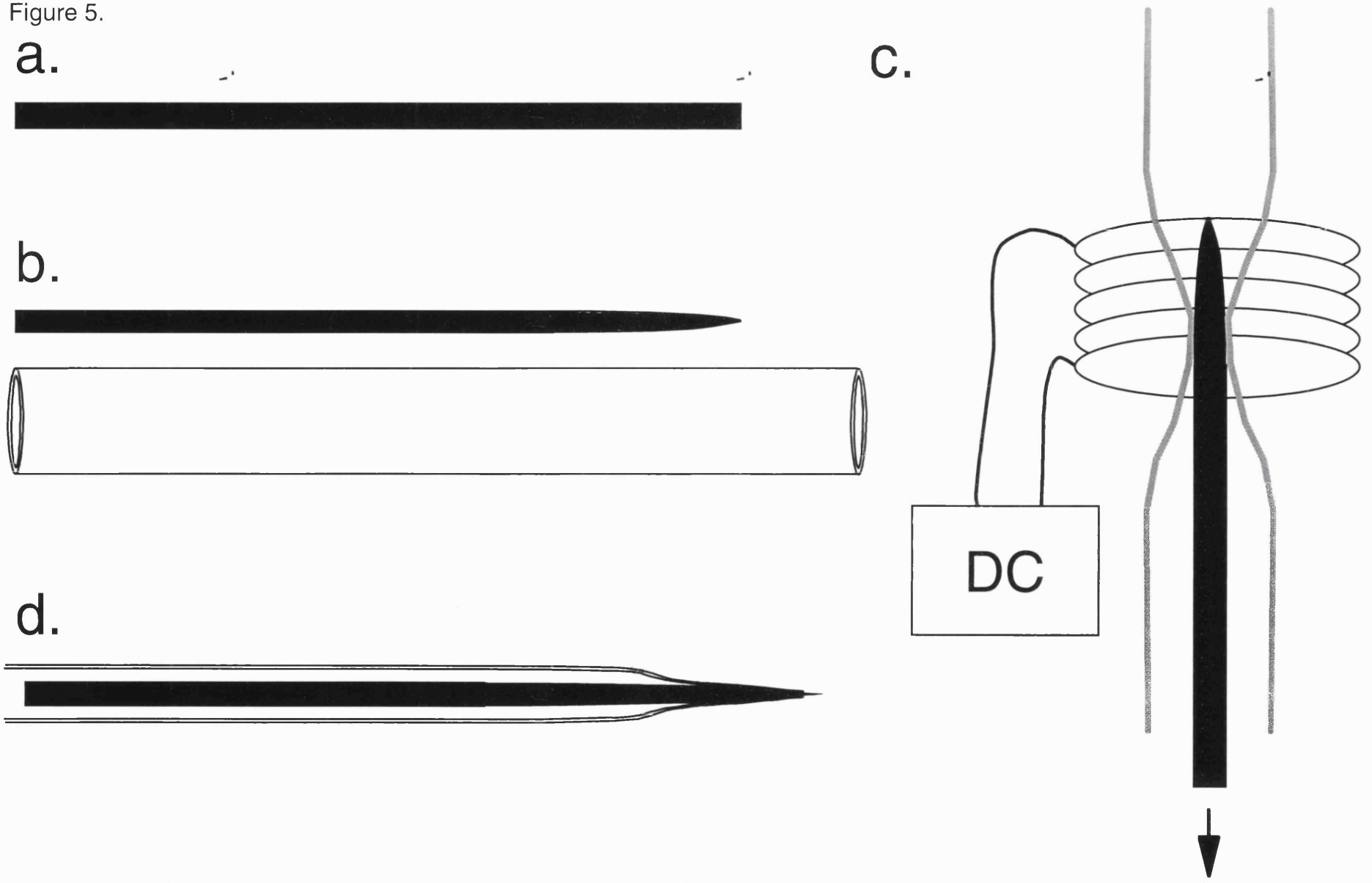


Figure 5.

A diagram of the various of stages in the manufacture of tungsten-in-glass microelectrodes. **a.** An unetched tungsten wire, **b.** a typical etched electrode, and the capillary into which it is inserted. **c.** The process of passing an etched wire inside a capillary through a heated coil to melt an insulating glass coating on to the tungsten surface at the tip. **d.** An insulated tungsten wire which has been exposed at the tip. It is this tip that records from neurones.

electrolytically etched, by repeated immersion in a solution containing $NaNO_2$ (71g\100mls) and KOH (34g\100mls). The resulting sharp point (figure *5b*) was then coated in glass by passing it through a capillary (Clark Electromedical Instruments) and slowly through a heated coil (figure *5c*). The last 8-20μm of the tungsten tip was then exposed by dipping the glass covered tip in molten boric acid. Removing the current from the boric acid caused it to cool, contract and pull the glass coating away from the tungsten tip. This tip could then be etched to the right length and shape electrolytically using a dilute KNO_2 solution, these last two stages, being very delicate, were performed under a microscope (figure *5d*). The next stage of the process involved plating the tip, first with gold, by dipping it in a gold solution, and then applying a current of 0.05μA across the electrode and solution for 5 seconds. A second surface layer of platinum plating is then applied electrolytically by dipping the electrode in a solution containing gelatine and Kolrausch solution (which contains platinum) and applying a current of 0.15-0.25μA for about 10 seconds. This deposited a layer of platinum that is 1-2μm thick on the tungsten tip (figure *6a*), which reduces its impedance. Before plating electrodes can have an impedance of 2-6MΩ at 1kHz, however plating with gold and platinum reduces this to 300-800KΩ. Such an impedance decrease, increases an electrode's ability to detect the spikes fired by individual cells. In these experiments, electrodes with platinum plated tips, between 8 and 12 μm long were generally used, these were inserted in pairs or in triplets. Pairs were made by positioning individual electrodes in a precisely machined perspex holder so that their tips were about 1 mm apart (figure *6b*). To make a triad, three individual electrodes were glued to a central rigid core, a spinal needle was generally used, each electrode tip protruded 4mm from the spinal needle tip, so that this, while providing mechanical support, did not disturb the recording site. The spacing between each electrode tip precisely controlled during triad manufacture (figure 6*c*) by manipulating them under a microscope, using two Leitz manipulators and a Prior manipulator, before being glued in place using quick hardening adhesive. Connections were made with the signal processing system described below using gold plugs crimped onto the other end on the tungsten wire.

Figure 6.

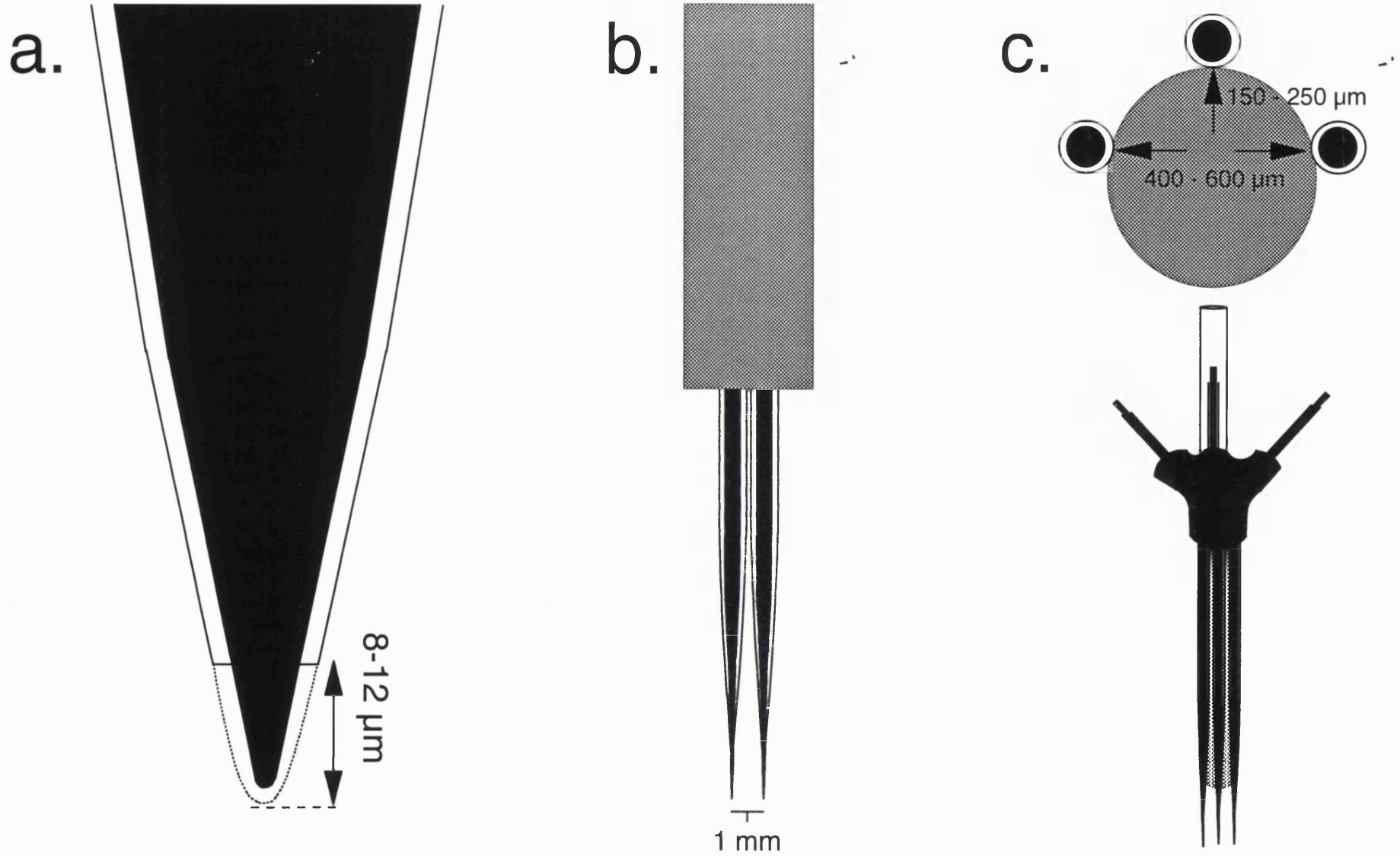


Figure 6.

A diagram showing a close-up of the recording tip of a tungsten-in glass microelectrode (**a**), the uninsulated tungsten tip is plated in gold and platinum to reduce its impedance, a facilitate the recording of cells. In **b** and **c** two configurations of electrodes are featured, a pair where the tips are separated by 1mm and a triad where the separations are smaller. The electrodes were spatially distributed in these ways to facilitate recording simultaneously from nearby and neighbouring orientation columns, to detect connectivity over distances which are associated axon projection in the anatomical literature.

Insertion of the electrodes, with aim of recording in both the lateral geniculate nucleus and the primary visual cortex in both cats and primates, took place with reference to a three dimensional stereotaxic co-ordinate scheme. The zero point for this co-ordinate space was defined as the point at which the axis containing the ear bars met the cranial mid-line, the mid-line was apparent as bony sagital suture on the dorsal surface of the skull. This position as well as all others were recorded using reading taken from vernier scales, in the longitudinal anterior/posterior (AP) axis and medial/lateral (ML) axis, these scales were an integral part of the manipulator used to position the electrode. When attempting to record from the cat LGN, the trajectory of the electrode penetration was tilted in the rostro-caudal direction in order to prevent damage to visual areas in the parietal and occipital lobes. To determine the entry point that was necessary using this trajectory, in order to record from the LGN, a perspex model was used, electrode tips were positioned at a predetermined point within this model that represented the representation of central visual space within the LGN, within 6° of the area centralis. This achieved, the AP and ML values were noted, these values were then transposed onto the cranial surface, it was at this point that a craniotomy was performed and the dura dissected. Typical co-ordinates required were AP=+6.5 mm and ML=+8.5 mm, the electrode was required to proceed below the cortical surface for approximate 5.5 mm before it entered the LGN. Cortical recordings were made by making penetrations that were approximately perpendicular to the surface, and these proceeded up to a depth of typically 2 mm when they entered the white matter. The co-ordinates used to record from a zone containing cells with receptive fields with 6° of the area centralis in the cat were AP=+2 to -6mm and ML=+1.5 to +2.1 mm (Grieve and Sillito, 1991).

During an experiment an electrode or a composite arrangement was positioned in a rigid perspex holder, this was then attached to the electronic stepping microdrive (Digitimer, Scat). This arrangement was then placed directly above the insertion site using a microscope, the microdrive was then advanced to the point where the electrode tips could be seen to enter the cortex. At this point the microdrive counter was set to zero. The microdrive enabled the electrode to be advanced in a highly controllable fashion, in single steps of one micron, or in larger steps, of say fifty microns, at variable pre-set speeds such as ten microns per second. Electrodes were

advanced until they were found to be recording single-unit action potential activity that could be selectively discriminated with the voltage triggers described below. The visual response properties of the discriminated activity were then analysed using the strategies described below.

Histology.

At the end of each penetration made in experiments carried out on both cats and primates, electrolytic lesions were made. This was done in order to provide a reference mark so the laminar position of each recording site could be determined after a subsequent histological reconstruction of the tissue. Each lesion involved passing a negative 3-5 microamp current through the recording tip for 3-5 seconds, this resulted in a heat lesion that would be visible in sections of stained tissue under a microscope.

In the case of cat experiments, on termination of the experiment a large area of skull around the recording site was removed using the dental drill and bone rongeurs, the piece of brain was then dissected out using a scalpel. The brain tissue was then fixed by immersion in 10 % formal saline solution. After fixation it was then placed in a solution of gum sucrose, composed of 1% gum arabic and 30% sucrose by weight. This was done to minimise the chance that ice crystals would be formed during sectioning which took place on a frozen microtome stage. The tissue was cut in sections that were 50 microns thick with this microtome. Once cut, sections were mounted in serial order on gelatine impregnated microscope slides. When dry these slides were then immersed in a 70% alcohol solution before being stained using a 1% solution of neutral red Nissl stain. Each slide was then covered with a slip and allowed to dry. Each section was then examined under a microscope, the staining procedure meant that differences in cell densities between cortical layers (Lund, 1973) and between LGN (Sanderson, 1971) layers were visible, thus the laminar location of a lesion could be determined, using this as a reference point the laminar location of other recording sites could also be determined. This was possible because records were made of the depth from the cortical surface of each recording site as well as the

site where the lesion was made. Sections that contained lesion were drawn using a Wild M8 drawing tube attached to the microscope.

After primate experiments a different set of procedures were used to those discussed above for the cat. This was because it was important to fix the tissue very rapidly to preserve enzyme components of the tissue such as Cytochrome oxidase that indicate the level and spatial distribution of metabolic activity. Primate brain perfusion (Levitt et al, 1994) began with an injection of 1 ml of Heparin (heparin sodium, 5000 units/ml, from Multiparin), after this had been given time to transport, an injection of 5-10 mls of Pentobarbitone (60 mgs/ml). When end-tidal CO_2 had decreased significantly the animal was transferred to a draining grid over a sink. The rib cage was then opened, a small incision was made in the left ventricle and a perfusion needle was inserted. Drainage was facilitated by making an incision in the right atrium of the heart. Next 3-4 litres of solution containing 0.5% Sodium Nitrite and 0.9% saline was delivered through the perfusion needle, following this, 4 litres of 4% paraformaldehyde, then 1 litre of 10% sucrose, both in solution with 0.1M potassium phosphate buffer were delivered. The brain was then removed and was placed in a buffered solution of 30% sucrose, then transferred to a refrigerator. In order to preserve the cytochrome oxidase within sections it was important to section the appropriate block of tissue within 3 days of the perfusion.

Alternate sections were then mounted serially on gelatine impregnated microscope slides, these were then stained using a neutral red Nissl stain as was done for cat tissue. The remaining section were stained in order to visualise an enzyme called Cytochrome Oxidase (Wong-Riley, 1979) within each section. This process began with washing the sections in buffered (0.02M potassium phosphate) 0.9% saline solution for several minutes, the sections were then immersed in a solution containing 20 mg of cytochrome C (Sigma, cat. C-2506), 20 mg of DAB (diaminobenzidine tetrahydrochloride, Sigma, cat. D-5637), and 1.6g of sucrose (BDH, cat. 10274) in 40 ml of 0.1 M potassium phosphate buffer. The sections in the solution were then placed in an oven until dark zones appeared within each section, when they were adjudged to be fully developed, the reaction that brought about the darkening was stopped, this was achieved by rinsing the sections repeatedly in ultra-pure water, changing it every

3 minutes at the start and then every 10 minutes, for about an hour. Sections were then mounted sequentially on microscope slides, allowed to dry, rinsed in alcohol and then xylene, before being cover-slipped.

This process allowed laminar and zonal differences in CO activity to be visualised in dead tissue, and helped the laminar level of recording sites to be determined after reference lesions had been found.

Data Acquisition.

Action potentials fired by a cell during visual stimulation were analysed by the VS system as unitary events. Data was stored as a series of times, each time signifies a moment when a cell fired an action potential. The electrical signals generated by a cell were recorded at the tip of a tungsten-in-glass described in the previous section. These signals passed through a pre-amplifier, before being further amplified with a Digitimer, Neurolog NL106 AC\DC amplifier. This signal was then passed to a Digitimer, Neurolog NL125 filter module, so that only frequencies between 500-10Khz were sampled, a range that contains information about action potential waveforms, this was done using electronic filtering equipment manufactured by Neurolog. From here the analogue signal was passed to a Neurolog voltage trigger module. Neural activity was then visualised with a dual-channel storage oscilloscope manufactured by Tektronix. This visualisation aided separation of spikes from different cells being picked up on the same electrode using the trigger module. Spikes with amplitudes that fell between two adjustable voltage levels were displayed on a second scope or scope channel. The output of each electrode could also be monitored through an audio line. This converted the raw or triggered output of an electrode into a sound.

During visual stimulation, the responses of up to six cells could be recorded. The filtered output of each electrode was then passed to a spike trigger. The discriminated output of each of these triggers, pulses, was then fed into the 1401, a multi-channel analogue to digital converter and digital data buffer. Action potentials were stored as

digital events at specific times, with a resolution of 0.1 ms, with reference to a stimulus start pulse and other reference pulses that described the stimulus. These pulses were produced by a CED model 1708 Picasso Image Generator Controller (Cambridge Electronic Design), which itself provided computer control over all Picasso Image generator (Innisfree) functions, based on a text program that described stimuli, that was generated by the VS software running on the PC. In this way the personal computer was used to specify the characteristics of each visual stimulus to be presented. Such as spatio-temporal configuration, contrast, display duration, and where different stimuli were presented in a pseudo-randomly interleaved sequence. The Picasso image generator then sent instructions to a tektronix 608 oscilloscope that was used to display each stimulus.

Spike times, together with information about the stimulus that generated them, were then sent to the PC by the 1401, to be downloaded to the hard disk for analysis. To a limited extent analysis could be conducted concurrently with data gathering, however due to limited computer power, detailed analysis occurred off-line using a variety of programs. The configuration of the visual stimulation and data processing systems is illustrated in figure *7*.

The visual stimulation system.

Monocular stimulation of cells was accomplished in two ways in this study. Initial investigations of the receptive fields exhibited by cells in the LGN and V1, were carried out using an adapted overhead projector, to project bars and edges at an opaque screen in front of the animal. The spatial extent and position of the receptive field in visual space, relative to the area centralis of the appropriate eye were resolved using bright spots and moving bars. The receptive field types of LGN cells were categorised as either X or Y after analysis of their responses to phase reversing gratings, this is called a null-test and was described above. Cortical fields were mapped to determine their distribution in visual space and their type within the classical scheme (Hubel and Wiesel, 1962) using high contrast bars and edges. The precise and systematic stimulation used to investigate the context dependent response properties of cells, was performed using a system developed by this laboratory and by

Figure 7.

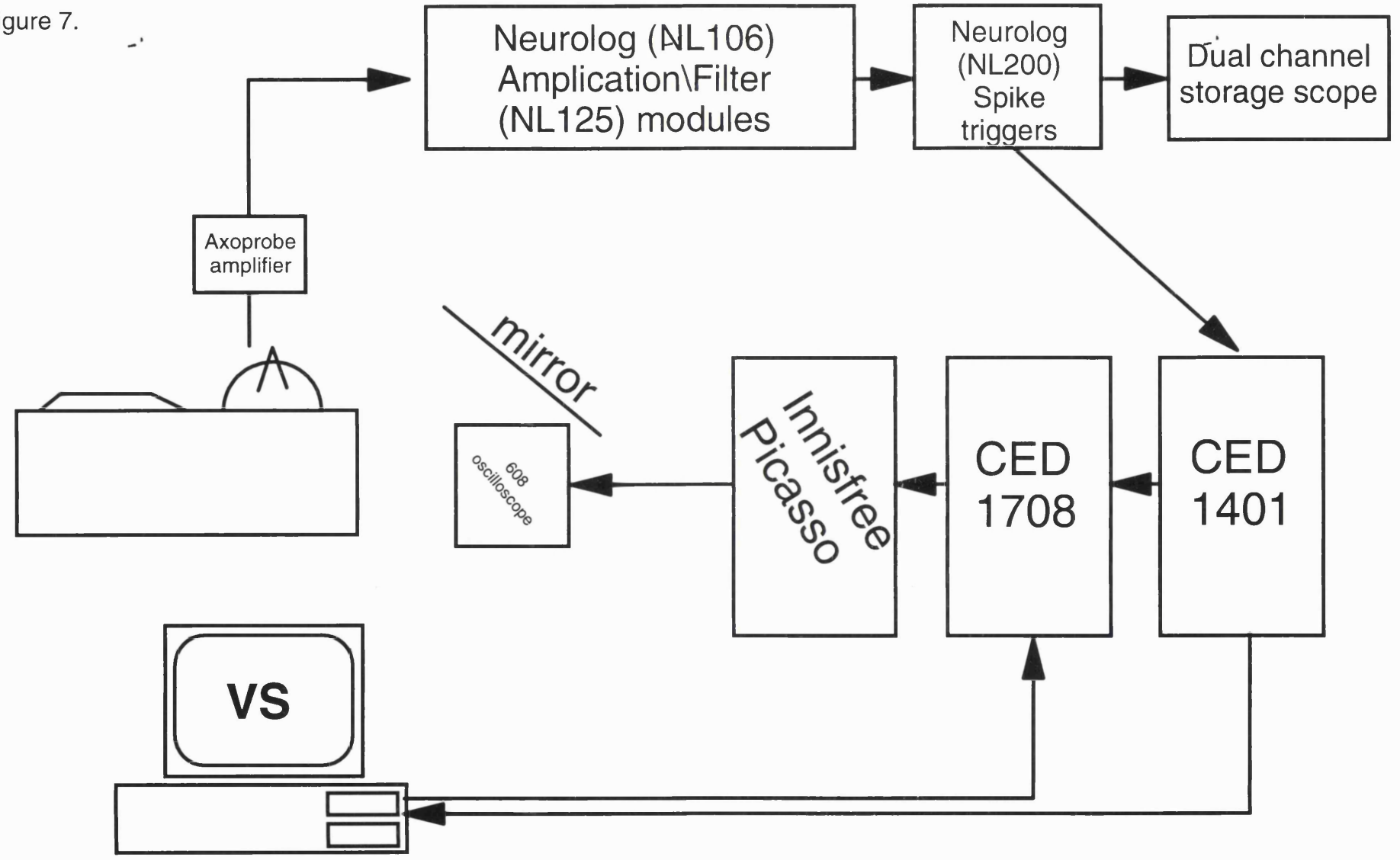

Neurolog (NL106)
Amplication\Filter
(NL125) modules
Neurolog
(NL200)
Spike
triggers
Dual channel
storage scope
Axoprobe
amplifier
mirror
608
oscilloscope
Inisfree
Picasso
CED
1708
CED
1401
VS

Figure 7.

A schematic depiction showing the ways in which the various components that are used to stimulate and record from individual brain cells. Spike discrimination is controlled visually on the scope in the top right, by manipulating electronic filters. Visual stimuli are generated on the lower scope by the Picasso and reflected in the gaze of the preparation which is focused on the reflecting surface. Data is down-loaded to and analysed on the computer in the bottom right, where response action potentials are stored as unitary events at 0.1 ms resolution. The details of the operation of this system are related in the *Methods* section.

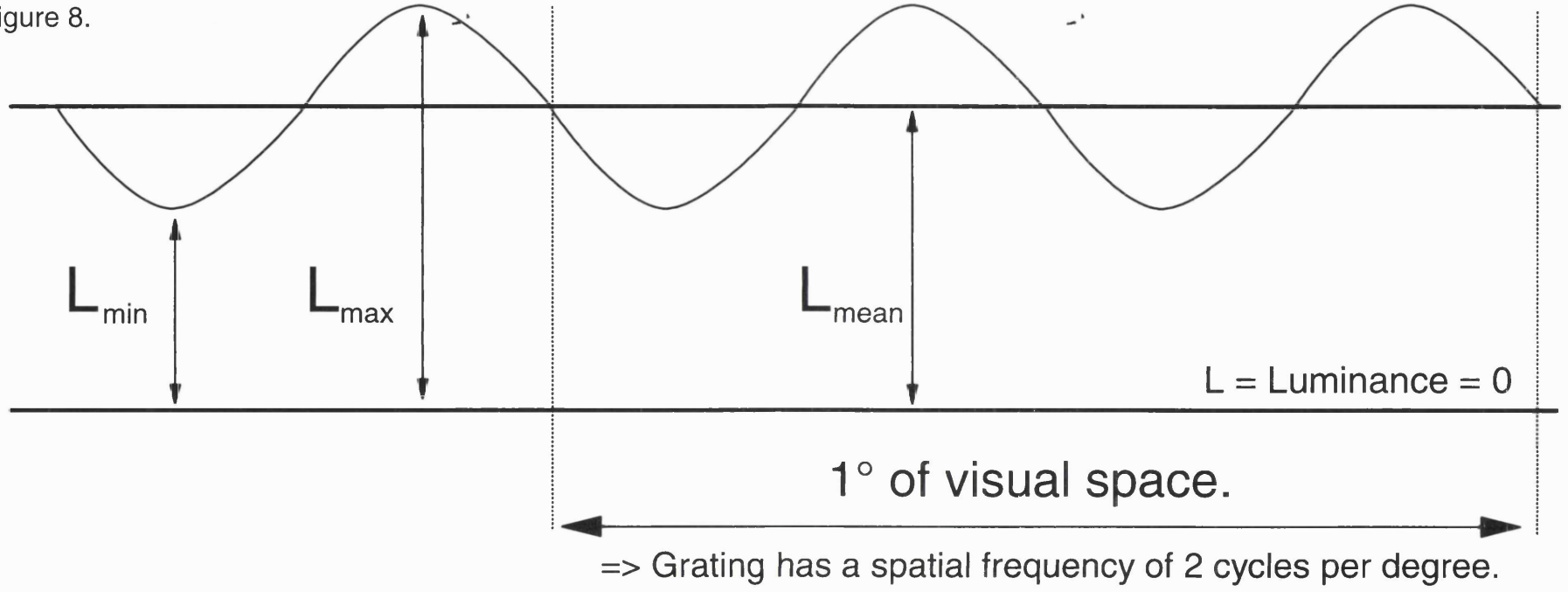
Cambridge Electronic Design. Visual stimuli were programmed using Visual Stimulation, v1.7 software. Stimulus images from the 608 oscilloscope were reflected off an obliquely angled, silver surfaced mirror, placed above the scope, into the animal's field of view. During experiments involving feline preparations the total distance of the scope from the subject's retina was 57.3 cm, meaning that 1 cm on the screen of the 608 was equivalent to 1° of visual space. However when primate experiments were being carried out, this distance was increased to 114 cm, 2cm was equivalent to 1° of visual space, this meant that the visual system could be stimulated at higher spatial frequencies. This was necessary because the spatial resolution of the primate visual system it greater than that of cats. The VS system allowed precise control over the stimulus, with an ability to produce bipartite bars and gratings, as well as simpler stimuli such as edges, spots and bars, whose parameters could be controlled and varied randomly.

If a pair of cells was being recorded, the stimulus selectivity of the one responding most strongly to visual stimulation was used to align the scope in visual space. Centring was accomplished in a number of ways, using smaller and smaller bars swept in the X and Y directions, or small patches of grating, presented at different points on grid distributed in the X and Y dimensions. The centring of the cells being analysed was periodically rechecked throughout a session of data gathering.

Visual stimuli.

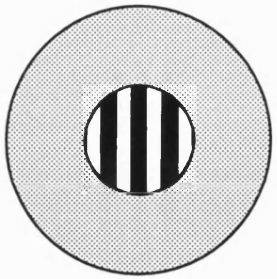
The visual stimuli used to investigate the properties of cells in the primary visual cortices of the cat and monkey were composed of sinusoidal gratings. In figure *8* is a graphical representation of a grating, and what is meant by its spatial frequency. It can be seen that the brightness of the stimulus varies sinusoidally in a direction perpendicular to axes of iso-luminance. In figure *8* the mean contrast of the grating is defined, this was set to 30-50% in all cases. The spatial frequency of the grating is quantified in cycles per degree, i.e. the number of degrees of visual space that it takes the sinusoid to complete a cycle. Each cell in the visual cortex is tuned to a specific frequency, during data collection each cell was stimulated with its optimal spatial

Figure 8.



=> Grating has a spatial frequency of 2 cycles per degree.

A.



B.

C.

D.

Figure 8.

Featured at the top of the figure is the luminance profile of a sinusoidal grating, labelled are the luminance levels at different positions on the grating, the contrast of the grating is given by the equation C = (L*max* - L*min*)\(L*max* + L*min*). Throughout this thesis sinusoidal gratings are depicted as alternating light and dark stripes, due to limitation imposed by the software used to make figures. On the profile are marked dimensions of visual space, the spatial frequency of the grating is 2 cycles per degree of visual space (cpd). Below are shown four of the stimuli that were used during experiments. **a.** is a circular patch of sinusoidal grating surrounded by an area of neutral contrast with a luminance level equivalent to the mean luminance (L*mean*) of the grating, these were presented with a variety of diameters at constant spatial frequency. **b.** this is a bipartite stimuli, a patch surrounded by an orthogonally oriented grating of the same phase and spatial frequency. Many different bipartite stimulus conditions were presented with centre/surround orientation differences that ranged between 0° and 180°. This was achieved by independently varying the orientations of each with respect to a pre-set zero axis, centres and surround orientations had values that ranged between 0° and 90° in steps of 22.5°. **c.** represents a full field stimulus, it is a patch surrounded by a grating of the same orientation, spatial phase and frequency. **d.** A grating presented in the surround only, centre patch is neutral contrast, presented with a range of centre diameters.

frequency. The spatial specificity and contextual sensitivity of a cell's responses was investigated by displaying these gratings in a number of different configurations. The first and most simple stimulus that was used is displayed at the bottom left of figure *8*. A sinusoidal grating was presented as a circle, surrounded by an unmodulated field of the same mean luminance as the grating. These are referred to as 'patch' stimuli in the following discussion of results, they were presented with a range of different diameters and orientations. Context dependent responses were also investigated using stimuli that contained two gratings at different orientations, these stimuli are referred to as a bipartite stimuli. The sinusoidal gratings were simultaneously presented, one in the form of a circular patch, centred over the classical receptive field of one of the cells being recorded, and another immediately surrounding this and covering the rest of the CRT screen. Three examples of such stimuli are shown at the bottom of figure *8*. Bipartite stimuli were presented with different centre grating diameters, the centre and surround gratings were displayed at a pre-set range of different orientations. In the discussion below the case when the centre and surround have the same orientation and are moved in the same direction, is referred as a 'full field' or aligned stimulus, in this situation the stimulus appears as one continuous grating rather than two independent ones. Full field stimuli were the largest used, they were 10° square with CRT screen at 57.3 cm from the retina and a 5° square with the scope at 114 cm. When the orientation or direction of motion was different in the centre and surround, the stimulus will be referred as a discontinuous configuration in the discussion below. Cortical cells do not respond well to flashed stimuli, so in order to evoke a response to these stimuli from a cell, gratings were moved in a direction perpendicular to it's iso-luminance axis, the distance moved was depended on the duration of the stimulus presentation and the temporal frequency of the grating. For instance in a presentation lasting 1 sec, of a grating with a temporal frequency of 5Hz, the distance moved would be equivalent to 5 cycles of the grating. The centre or surround of the stimulus were however was not subject to any translation motion.

These stimuli were specified using the VS software which allowed stimuli to be described using the independent variable fields, each field contained an array of values that described one variable feature of a stimulus, such as centre or surround orientation, or centre diameter. Thus if all three fields were used, and 10 values were

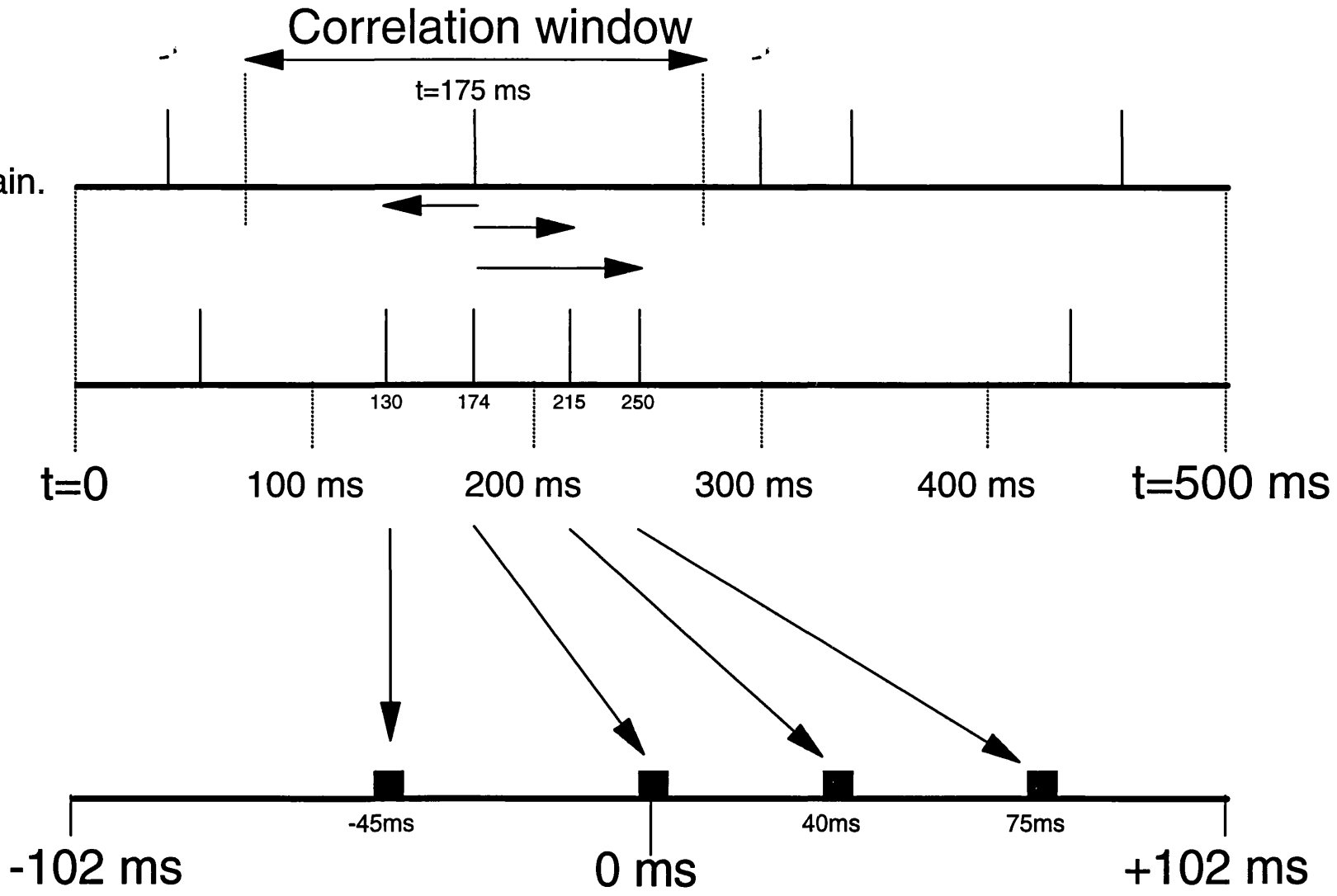
specified for each, then 300 different stimulus conditions were specified, each with a different permutation of 3 independent variable values. These conditions were displayed one after another with a pre-set time interval between them, typically 0.75 seconds, in a pseudo-random fashion. Once all the conditions specified in the variable fields had been displayed, the process could begin again. The responses analysed in the course of this investigation were typically obtained from 3 to 5 presentations of a given stimulus condition.

Data Analysis.

Cross-Correlation.

Cross-correlation analysis was performed on an IBM compatible computer, using a program called Xcorel written by Dr D. West at this Institute. Cross-correlograms are generated by comparing the time of a spike in one train with times of spikes in another train. The interval between two spikes is then plotted in a histogram. This process is shown is schematically depicted in figure *9*. The time after stimulus onset for every spike in the reference train is compared with those times of spikes in another train that fall within a temporal window that corresponds to the width of the histogram. An exact temporal coincidence of two spikes is plotted in the centre of histogram in a bin corresponding to a 0 ms intervals. Where the spike in the reference train occurs after the spike in the other train, a point is placed to the left of the origin, in a bin that corresponds to the negative time interval between the two spikes. In situations where the reference spike occurs before that sampled from the other train, the interval is positive and is binned to the right of the origin. Thus when both trains have been correlated from beginning to end, the resulting histogram depicts the distribution of intervals between all the spikes in the reference train and those in another, that fall within a particular temporal window. It is the peaks that can sometimes be observed in this distribution that enable inferences to be drawn about what influences a pair of cells to fire action potentials when they do. Gerstein and co-workers (Perkel et al, 1967) showed using computer simulations and physiological examples that particular modes of neural connectivity, and functional interaction could be inferred from

Figure 9.



Cross-correlogram (Inter-spike interval distribution).

Figure 9.

A diagrammatic representation of the formation of a cross-correlogram from two spike trains. The two spikes trains were recorded simultaneously in time and represent the action potential response distribution to a visual stimulus lasting 500 ms. The cross-correlation at the bottom is a histogram showing when and how often spikes recorded from cell 2 came before or after a spike in cell 1. Within the cross-correlogram inter-spike intervals from the reference train and the other recorded are distributed in bins. Which bin depends upon the interval between two spikes. As an example a spike that occurred at 175 ms in the reference train is used. It can be seen that when this correlated with spikes in the second train that fall within the correlation window, intervals are distributed on both sides of the correlogram origin. Correlation with a spike that occurred after 130 ms in the second train generates an interval of -45ms, this interval is then placed in a bin on the left of the origin. The results of other correlation calculations between the pairs of spikes can also be seen.

factors which can obscure peaks that are due to neural connectivity. Peaks can occur in cross-correlograms for reasons that are unrelated to any form of synaptic interaction that might co-ordinate neuronal responses. Such peaks are due to pairs of cells firing independently, but in unison to a visual stimulus, the resulting peak is indicative of synchronisation due to a simultaneous stimulus response that is not synaptically synchronised, these peaks thus describe 'stimulus co-ordinated' interactions. Stimulus co-ordinated peaks can be detected and removed by implementing what has been called a 'shift predictor'. In this process one spike train is displaced in time by an amount which corresponds to an integer multiple of the period of one stimulus modulation, the temporally shifted trains are then correlated again. This has the effect, providing the sampling window is smaller than the length of a stimulus modulation, of removing any peaks in the interval distribution histogram (correlogram) which are generated by network connectivity between the recorded cells. This is achieved because the temporal relationship between a set of spikes in two trains, that is the result of connectivity, is specific to their overall position in the spike trains, they are time-locked to the onset of the stimulus display. The key assumption is that pairs of spikes in two trains with connectivity co-ordinated temporal relationships are distributed differently within responses to different modulations of a given stimulus. This relationship can be removed by temporally shifting one train relative to the other, preserving the time-locked characteristics of the two responses. The resulting shift predictor thus only shows peaks which are due to stimulus co-ordination. The result can then be subtracted from the raw correlogram, the difference will then only contain peaks which are indicative of temporal co-ordinated activity due network connectivity. All correlation results are presented as the difference between the raw cross-correlogram and the shift predictor. Calculating shift predictors allowed significance thresholds for peaks to be calculated, based on a Poisson distribution of bin amplitudes around the calculated mean value. Threshold levels were calculated from the standard deviation of the mean amplitude. In all analysis figures showing cross-correlation analysis this threshold was set to indicate that peaks exceeding it were significant deviations from the null hypothesis at the 99.5% level.

The simultaneously recorded responses of pairs of cells to visual stimuli were cross-correlated and inspected in correlograms with bin widths between 0.3 and 15 ms, the

bin size used depended on the temporal characteristics of the interaction and the temporal resolution required for precise analysis. In all analysis figures temporal interactions are shown using bin widths that make them most clearly visible, the size used also reflects the temporal characteristics of any interaction. Some interactions were signified by peaks that were distributed symmetrically over the origin, other were displaced from the central bin by a period of time equivalent to time taken for the initiating action potential to follow the path required to generate an action potential in the second recorded cell. It is likely that smaller latencies reflect a direct monosynaptic path between cells, whereas longer latencies reflect more complex network interactions. The criterion used for the classification of a direct connection was based on the temporal distribution of the bin at a cross-correlogram resolution of 1 ms. For a peak to be attributed to the presence of a direct connection between the two recorded cells, the binned contents of the peak had to be contained within one 1 ms bin. Peaks that were not distributed in this way were adjudged to be due to more complex multiple modes of connectivity between the two cells.

Receptive field configuration groups.

The main focus of this investigation was to examine the influence that context has on the operation of single cells and the networks in which they exist in the early stages of visual processing. The key feature of a context dependent process is its reference to some other piece of information. In the primary visual cortex each cell has a classical receptive field, this is highly circumscribed area of space, if each cell in the cortex is to function in context dependent process then it must refer to other areas of visual space. Using cross-correlation analysis visual response temporal interactions were used to signify reference to this other spatial information, the aim was to determine what that information is and what functional significance it has. It was thus necessary to have a very clear idea about the relative properties of the receptive field at the reference points. Results are presented below, with reference to a classification system of the receptive field configuration of the cell pairs involved in the cross-correlation analysis. Receptive field overlap was determined from the hand mapping data, fields were classified as overlapping if they shared a portion of visual space, where they

were found to be completely delocalised they were classified as non-overlapping. During experiments on primate preparations the relative receptive field distributions of two cells were mapped quantitatively using the VS system. This was done by presenting single small circular patches of grating, typically 0.5° in diameter, at different sites on a square grid separated by 0.5°, this thus generated a map of each cells responses in visual space. Cells were classified as overlapping if both responded to stimulus at one site or two stimuli presented at adjacent sites on the grid, if they did not they were classified as non-overlapping. The preferred orientation of each excitatory receptive field was determined from data obtained after computer controlled visual stimulation with circular grating patches. Group 1 contains cell pairs with overlapping receptive fields and optimal orientation differences less than 30°, cells are overlapping and iso-oriented. Group 2 contains cells with optimal orientation differences greater than 30° and overlapping fields. In group 3 cells have iso-oriented non-overlapping field, while in group 4, fields are non-overlapping and have orientation differences greater than 30°.

Auto-correlation.

In order to investigate the oscillatory characteristics of visual responses, auto-correlograms were calculated for each response. As with the cross-correlograms, the Xcorel program was used for this purpose. Auto-correlograms are calculated by a correlating a cell's response spike train against itself, this process highlights patterns of inter-spike interval that occur with a relatively high probability, in comparison to intervals between spikes in a stochastically poisson distributed spike train (Softky and Koch, 1993). Departure from the stochastic intra-train inter-spike interval distribution was quantitatively assessed by implementing the shift predictor strategy on the responses of a single cell to different presentations of a given stimulus condition. The shift predictor result was subtracted from the raw auto-correlogram, revealing temporal characteristics of distributions of spikes that exist within the entire response with high probability. How significant a range of inter-spike intervals was, with respect to others was quantified using the techniques described in the next section.

Fast Fourier transformation.

A program was written to analyse the oscillatory components within cross and auto-correlograms. It was written in Turbo Pascal, the core of the code that performed the FFT and generated a power spectrum result was taken from Press et al, 1989. The program used the output data, in the form of ASCII files, of the Xcorel program, that was used to calculate correlograms. The input data was either an auto-correlogram, in order to analyse oscillations in a single cell response, or a cross-correlogram, to analyse oscillations when the responses of pair of cells to a given stimulus were correlated. Each correlogram consisted 128 numerical values quantifying the contents 128 2 ms bins, and their associated times. These 128 values corresponded +4ms from the origin to +260ms for the analysis of auto-correlograms. The first 3ms of each auto-correlogram was not spectrally analysed because this period contains a trough due to the refractory period of the cell. For cross-correlograms the 128 values for spectral analysis were extracted symmetrically from either side of the origin. The use of discrete sampling every 2 ms and the division of data into two 64 bin segments yielded a Nyquist limiting frequency of 250 Hz, with a resolution of 4 Hz. The power spectrum of each correlogram therefore consisted of the root mean square amplitude value for frequencies between 0 and 250 Hz, in steps of 4.8 Hz. Because of the limited resolution of this technique, the gamma frequency range in this study went from 28 to 80 Hz. The resulting power spectrum was then used to determine whether there was a significantly oscillating component in the extracellularly recorded spike train. Oscillatory characteristics were analysed in two frequency bands, the first between 12 and 16 Hz, a frequency range that has been reported to have some significance in the primate (Young et al, 1992) and also in the gamma range.

To determine whether the oscillatory components within spike trains, as analysed using auto-correlation techniques, deviate from those that would be present within a completely stochastic distributed spike train, a large set of stochastic spike trains were generated using a computer simulation. These spike trains were also cross-correlated with one another, in order to spectrally analyse the gamma frequency components of

temporal interactions between cells. Stochastic spike trains were generated with a temporal resolution of 1 ms. The probability (P) of a spike being fired in any one millisecond was,

$$P = \lambda / T$$

where λ was the firing rate in Hz of the simulated neuronal response and T was the number of time units in one second. For each time unit in each spike train a random real number between 0.0 and 1.0 was then generated using the random number generator included in Borland Delphi 2.0. If this number n was greater than (1-P) a spike was placed at that time. Stochastic spike trains were generated using this process, that were as far as possible similar to those recorded physiologically, in terms of their duration and firing rate. Typical visual stimuli employed during experiments were composed of five modulations of a grating modulated at a temporal frequency of 3-4 Hz. Each display thus had a duration of 1200-1500 ms, and was typically repeated 10 times, randomly interleaved with displays of other stimulus conditions. So each simulated response was composed of 10 spike trains each with a duration of 1250 ms. The 10 spike trains in each simulated response were then auto-correlated, the 10 auto-correlograms were then added together to generate the raw auto-correlation function of the response. This process was then repeated but with each spike train correlated with the proceeding one. Thus generating a shift predictor, which was then subtracted from the raw function. Stochastic responses were also cross-correlated with one another, to generate a raw function, a shift predictor was calculated by cross-correlating one response shifted by one train with respect to the other, the result was subtracted from the raw function. The power spectrum of these subtracted results were then calculated.

Because one of the aims of this analysis was to investigate the stimulus specificity of oscillatory visual responses and oscillatory synchronisation, it was necessary to develop a technique using this spectral analysis to quantify the strength of any response oscillation, or synchronous oscillation that was independent of changes in response magnitude. The computer simulation was used to generate stochastically distributed response sets at 10 different firing rates between 10 Hz and 100 Hz. This

was done in order to develop and test possible analytical strategies, and to calculate significance thresholds in order that deviation from strictly stochastic processes could be quantified. Each response was auto-correlated in order to investigate the influence of firing rate on spectral analysis measures of oscillation strength. Cross-correlograms were calculated between stochastic simulated responses in order to spectrally analyse temporal interactions between cells.

Simulated responses with firing rate of 10Hz and 100Hz are shown in figures 10-1 and 10-2 respectively. Data obtained from the computer simulation demonstrated that the root mean square amplitude of any particular frequency signal increased with firing rate. One possible measure of the significance of a response or synchronous oscillation could have been the relative RMS amplitudes of that frequency in power spectra extracted from a physiological response and from the stochastic simulation response, where both contained the same number of spikes. However this idea is fraught with problems because although a physiological response can be said to contain a certain number of spikes in a second in response to a given stimulus, these responses are usually temporally modulated, firing rate is not constant throughout the duration of the response. An oscillation could occur within a high or low firing rate epoch within the total response. It was not possible to determine which, in the present investigation. It was also not possible to simulate realistic temporal modulations in firing rate using the computation model. Using this strategy to detect significant levels of synchronous oscillation cross-correlograms is even more of a problem because the cells being cross-correlated might not have the same firing rate, again in this investigation it was not possible to determine whether synchronous spikes within temporally modulated responses occurred during high firing rate or low firing rate epochs for each cell. Because of the difficulty of determining the oscillation strength criterion for significance for a given firing rate, RMS amplitude was not used to measure the significance. A strategy was required that was independent of the number of spikes fired by the cell.

The simulation demonstrated that for a completely stochastic sample of auto-correlograms, RMS power at a given frequency was proportional to firing rate. Auto-correlograms generated from high firing rate spike trains contain higher RMS power

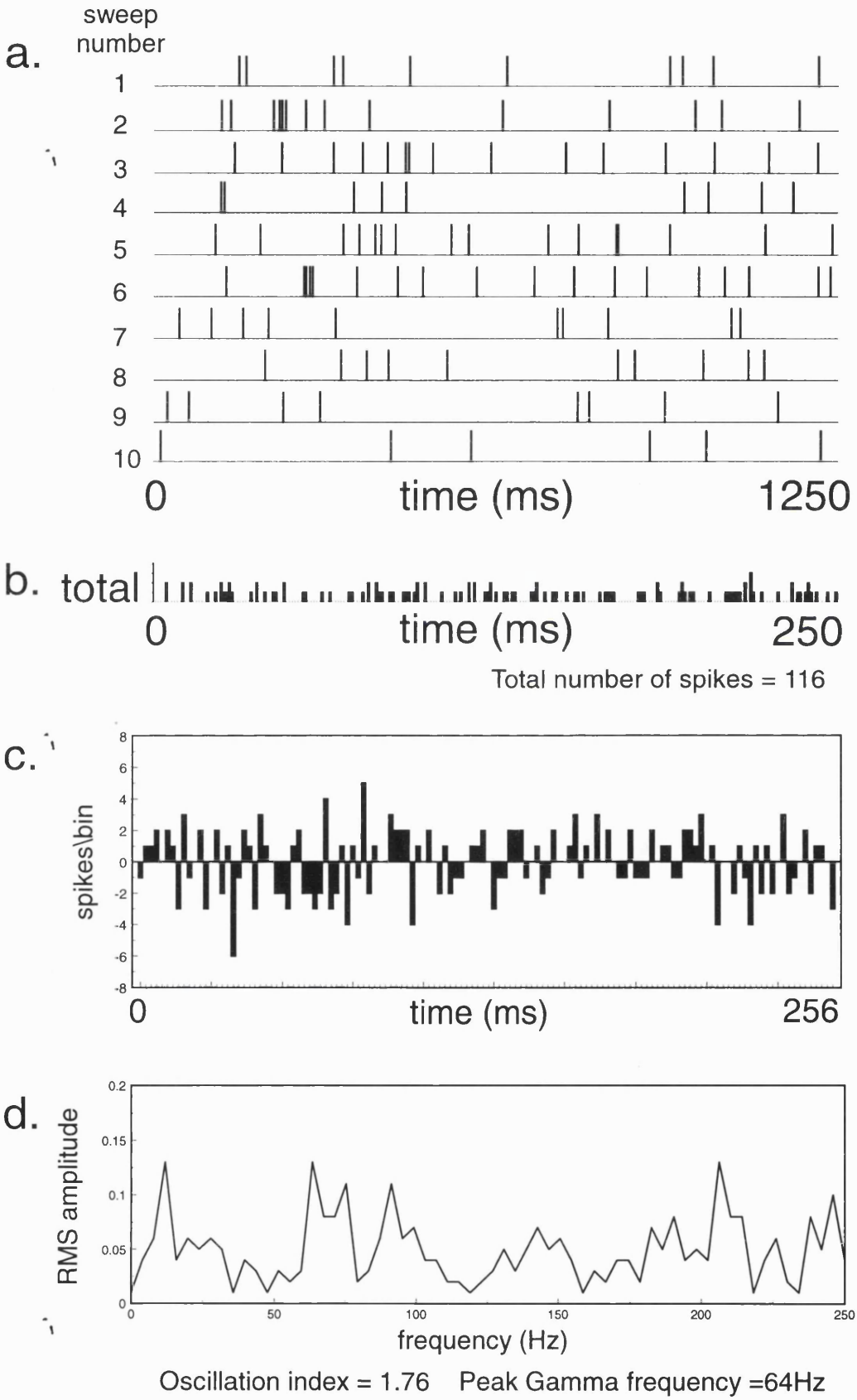
at all frequencies, than do power spectra calculated from auto-correlograms of low firing rate spike trains. For a stochastic response at given firing rate, the RMS amplitude of power at all frequencies is on average equal. These properties of the frequency distribution in correlograms calculated from simulated stochastic spike trains suggested that a ratio of the power in two different frequency bands could be used to indicate whether the power in one band significantly deviated from that which would be present in a stochastically distributed response. As both the ordinate and the denominator have the same relationship to firing rate, the ratio should be independent of firing rate. The aim of this analysis was to determine whether physiological responses contain significant levels of oscillation in the gamma frequency range. In order to do this the ordinate was calculated by finding the most powerful frequency in the gamma range, this was averaged with the power at adjacent frequencies above and below the peak. The mean power of frequencies between 150 and 250 Hz was used as the denominator. The ratio thus provides a measure of the relative strengths of oscillations in a 9.6Hz band in the gamma range and between 150-250 Hz. A value greater than one means that the response spikes are fired in an oscillatory fashion in the gamma range more often than they are between 100-250 Hz.

The next stage in the development of this analysis protocol was to use the simulated spike trains to determine whether the ratio described above is in fact independent of firing rate. The data presented in figures 10-1 and 10-2 for simulated spike trains with firing rates of 10Hz and 100Hz respectively, show that very similar ratios are calculated from very different numbers of stochastically distributed spikes. Figure 10-3 shows the distributions of ratios calculated from 25 different simulated responses fired at 10 Hz (***b***), 100Hz (***c***) and from 250 responses (***a***), 25 from each of 10 response levels between 10 Hz, in steps of 10Hz up to 100Hz. All the distributions are very similar. Plot ***d*** in figure 10-3 shows that the mean ratio calculated from 25 responses at each of the ten firing rates are not significantly different. Thus the ratio is independent of firing rate. The mean ratio for the whole simulated stochastic sample was 1.80 (sd=0.63). A normal distribution with this mean and standard deviation is fitted to the distribution in plot 10-3a. The distribution of ratios calculated from the simulated responses seems well modelled by this normal distribution. The mean value is greater than 1.0 for the stochastic data because the peak value in the gamma

range was chosen to calculate the ordinate. Ratios significantly different from this distribution at the 99.9% level would be greater than 4.08. This calculation provides a ratio value which can be applied to physiologically recorded data to determine whether there are significantly higher levels of gamma oscillations present with in a spike train, than oscillations in the 150-250Hz range.

A further strategy used to detect synchronous oscillations in cross-correlograms was to fit a gabor function (König, 1995). A gabor function is obtained by multiplying a sine function and normal distribution function, the result resembles a symmetrically damped sine wave. This strategy yielded information about the oscillating component of the function, which was indicated by the presence of multiple periodically distributed peaks in the cross-correlogram. The goodness of the fit between a gabor and a correlation function was quantified by χ^2 , a measure of how effectively a given gabor function models the distribution of values within a binned cross-correlation function, a high value of χ^2 indicates that a gabor function is not similar to the correlation function. Thus the fitting process proceeds by sequentially fitting different gabor functions with different parameters, that are adjusted systematically on the basis of the χ^2 value obtained from the previous attempt, until the smallest possible χ^2 value is obtained. This process was carried out by a computationally implemented mathematical strategy called the Marquadt-Levenburg algorithm (Press et al, 1986) using Turbo Pascal. In this investigation it was found that the choice of start parameters was critical in achieving a good fit between the correlation and Gabor function, so nine sets of different start parameters were used. The criterion for a significant fit was adjudged to be a result which generated a χ^2 value which was 15% less than the χ^2 value obtained from fitting a straight line to the correlation function. Where this was achieved the function that yielded the lowest significant value is shown. This was done as a secondary check of significance, in order that the data could be viewed in the context of previous reports that has used this technique as a measure of significance.

Figure 10-1.



Oscillation index = 1.76 Peak Gamma frequency =64Hz

Figure 10-1.

This figure features simulated responses with a firing rate of 10Hz. Ten spike trains with duration of 1250 ms can be seen in part ***a*** of the figure. Part ***b*** shows the averaged response over a period of 250 ms, the duration of a sinusoidal grating modulation with a temporal frequency. The firing rate is not modulated, and spikes are stochastically distributed with respect to one another, in all other respects they resemble physiologically recorded spike trains. Part ***c*** shows the auto-correlogram of the simulated response with shifted correlogram subtracted. Part ***d*** show the power spectrum of this auto correlogram. It has an oscillation index of 1.8. Auto-correlogram bin width is 2 ms.

Figure 10-2.

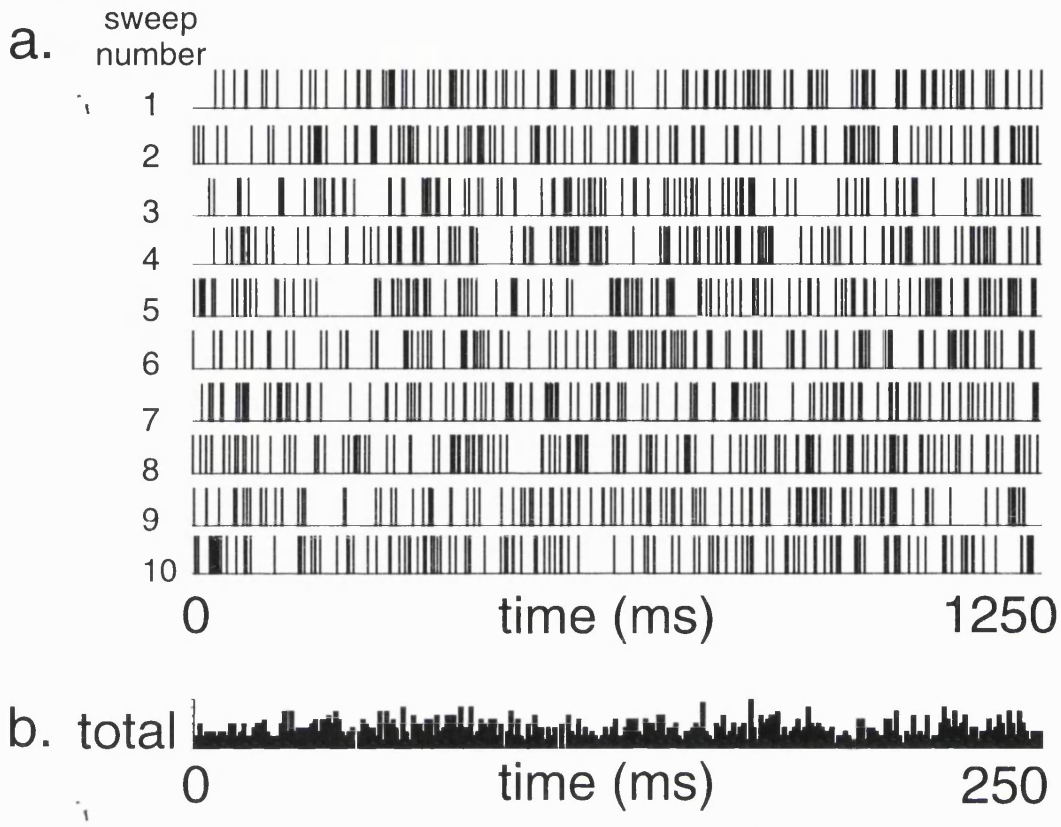
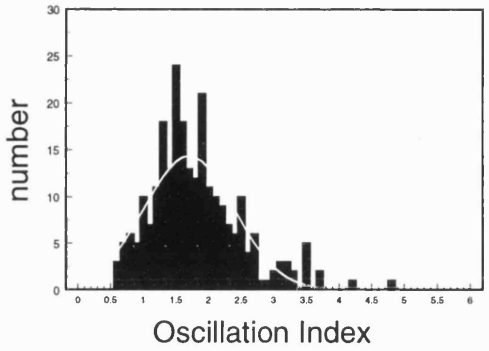

a.
sweep number
1
2
3
4
5
6
7
8
9
10
0
time (ms)
1250
b. total
0
time (ms)
250
Total number of spikes = 1257
c.
spikes\bin
60
40
20
0
-20
-40
-60
2
28
54
80
106
132
158
184
210
236
0
time (ms)
256
d.
RMS amplitude
30
25
20
15
10
5
0
0
50
100
150
200
250
frequency (Hz)
Oscillation index = 1.87 Peak Gamma frequency =60Hz

Figure 10-2.

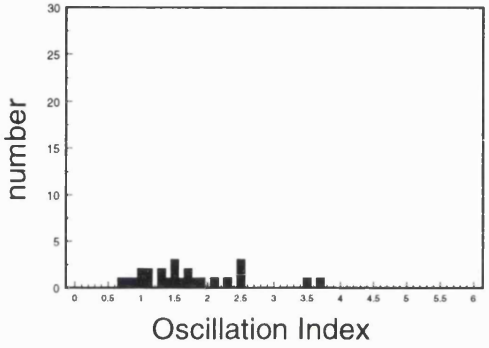
This figure features simulated responses with a firing rate of 100Hz, in all other respects it is the same as figure 10-1. Ten spike trains with duration of 1250 ms can be seen in part ***a*** of the figure. Part ***b*** shows the averaged response over a period of 250 ms, the duration of a sinusoidal grating modulation with a temporal frequency. The firing rate is not modulated, and spikes are stochastically distributed with respect to one another, in all other respects they resemble physiologically recorded spike trains. Part ***c*** shows the auto-correlogram of the simulated response with shifted correlogram subtracted. Part ***d*** show the power spectrum of this auto correlogram. It has an oscillation index of 1.8. Auto-correlogram bin width is 2 ms.

Figure 10-3.

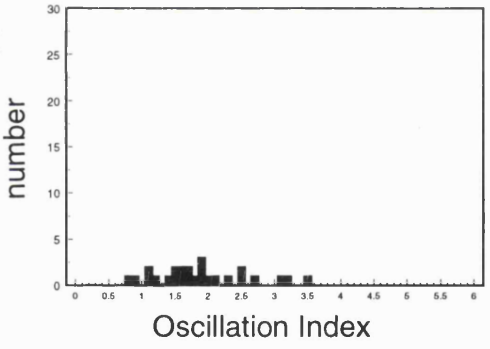
a. all firing rates



b. firing rate=10Hz



c. firing rate=100Hz



d.

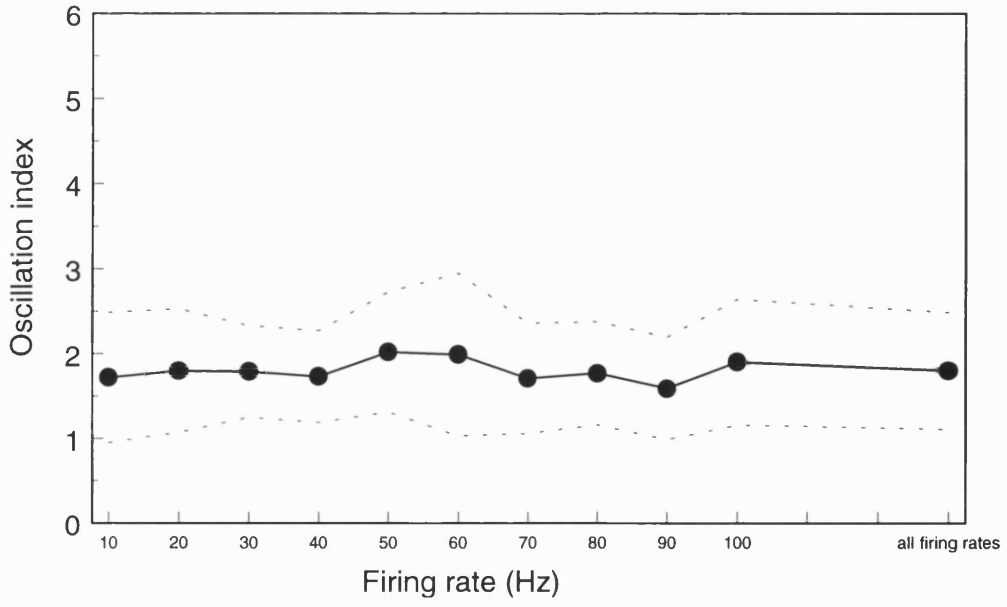


Figure 10-3.

This figure demonstrates that the distributions of ratios calculated from simulated stochastic responses fired at different rates are very similar. Part ***b*** of the figure shows the distribution of ratios calculated from 25 simulated 10 Hz response, ***c*** shows the distribution for responses with firing rates of 100 Hz. Part ***a*** shows the distribution of ratios calculated from simulated stochastic responses at 10 different firing rate between 10Hz and 100Hz. ***d*** is a plot of mean ratio (each as calculated from 25 responses) as a function of firing rate. It can be seen that there are no significant difference between these values. They were pooled in order to calculate the mean ratio and its standard deviation for the entire simulated sample of 250 responses. In part ***a*** a normal distribution with the sample mean and standard deviation has been plotted with sample distribution. The sample and normal distribution have very similar shapes. Based on the assumption that the distribution of ratios obtained from the simulated stochastic sample is normally distributed, a ratio can be calculated which provides a threshold value, such that values larger than it significantly deviate from the stochastic sample distribution with a probability of greater than 99.9%. This value corresponds to the sample mean plus 3.29 times its standard deviation. Ratio values greater than 4.08 significantly differ from the distribution stochastic generated ratios. Thus spike trains that give rise to values greater than 4.08 do not contain spikes, all of which are distributed stochastically with respect to one another. With respect to the relative numbers fired at frequencies in the gamma range and those fired in the range 150-250 Hz, these spike trains contain significantly more spikes that oscillate in the gamma frequency range, than would be the case were spikes in the train completely stochastically distributed.

5. **Results.**

Single unit analysis in primate V1.

Visual responses were recorded from 53 cells in primate V1, 27 cells from cat V1, and from 22 cells in the cat lateral geniculate nucleus. These responses were stored together with a description of the stimulus that generated them, at 0.1 ms resolution. This strategy facilitated quantitative analysis, so that response magnitude to each stimulus could be compared. The high temporal resolution of the data storage system also allowed detailed analysis of the distribution of spikes in time, again with reference to the stimulus that caused the cell to fire spikes. This account of results will initially focus on stimulus specific changes in the temporal distribution of spikes with particular reference to the oscillatory content of responses. Correlation of the stimulus that is associated with specific characteristics of the response will be an important aspect of this report. It will also be important to compare the changes in temporal structure that are observed with changes in the other parameter considered, response magnitude. In a later section context dependent changes in response parameters will be compared as a function of the diameter of optimally oriented stimuli.

Context dependent oscillatory responses.

The responses of 53 cells to optimally oriented patches of sinusoidal gratings of increasing diameter, and to discontinuous bipartite stimuli in the case of 34 of these cells, were recorded from primate V1 and analysed to quantify their mean response magnitude and the extent to which this response had an oscillatory component. Auto-correlograms were calculated for each response spike train and then subjected to FFT analysis to quantify oscillations in the gamma and 12-16 Hz frequency ranges. The quantity used was, what will be referred to as the oscillation index of the response, or alternatively as the oscillation strength. As related in the *Methods* section this value is the ratio of the oscillatory power between 12 and 16 Hz, or in a 10 Hz band around the peak gamma frequency, and the mean power between 100-250 Hz. The responses of 30 cells (57%) were found to meet the criterion necessary to be classified as

oscillating, 27 cells oscillated at a frequency in the gamma range (28-80hz), the responses of 3 further cells were found to contain strongest oscillation in a range between 12 and 16 Hz.

Oscillation indices were calculated from responses of cells to aligned and discontinuous stimulus conditions. For each cell oscillating in the gamma range, a pair of responses, one to each stimulus configuration, were chosen that differed by less than 10% in their mean response magnitudes. This strategy was used, in order to determine whether a cell's changing propensity to oscillate was controlled by changes in the configuration of the stimulus that was used to generate that response, or whether it was due to changes in response magnitude. Thus responses containing approximately the same numbers of spikes but generated by different stimuli were used. Each response was then analysed with the FFT technique to determine it's oscillation index. Data was obtained from 16/18 cells that fulfilled the criteria that were necessary to be included in this analysis. Figure *11* conveys information about the relative average oscillation indices of responses to continuous and discontinuous stimuli of approximately equal mean magnitude. It can be seen in this figure that the oscillation index of a response to a discontinuous stimulus that contains the same number of spikes as a response to a continuous stimulus is 240% greater than the oscillation index of that continuous stimulus response. All eighteen cells in the tested sample individually yielded this positive result.

The above result demonstrates a striking feature of the stimulus specificity of single-unit oscillations and indicates that the context in which a stimulus is presented is a critical factor in shaping that response. Of the total sample, the responses of 16/34 (47%) cells to discontinuous stimuli were found to contain stronger oscillations between 28-80 Hz, than those to spatially continuous full field grating. Responses of 3 cells to discontinuous bipartite stimuli were found to contain strongest oscillations in the 12-16 Hz band, these will be discussed later. In two other cases a reciprocal pattern of response oscillation was detected, in which oscillations between 28-80 Hz in visual responses to contiguous full field gratings were found to be stronger than those present in responses to discontinuous stimuli. Featured in figures *12* and *13* are auto-correlograms and oscillation strength analysis from the responses of two cells

Figure 11.

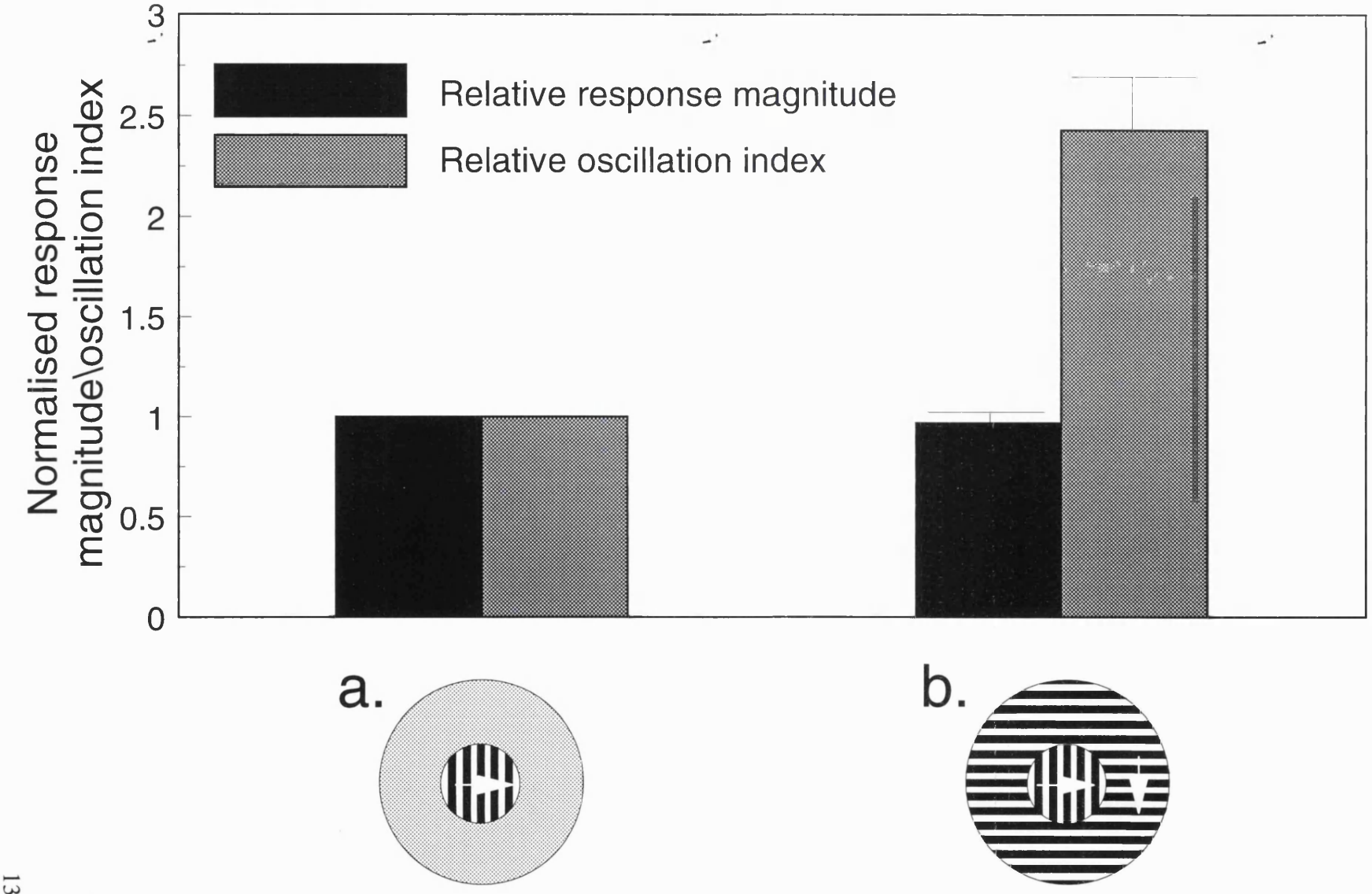

Normalised response magnitude\oscillation index
3
2.5
2
1.5
1
0.5
0
Relative response magnitude
Relative oscillation index
a.
b.

Figure 11.

The relative strengths of oscillations in responses to continuous patch stimuli (**a**) and discontinuous stimuli (**b**) that evoked the same levels of response magnitude from a given cell. Shown is the average result calculated from the responses of 16 cells. Pairs of responses were chosen for each cell that involved optimally oriented stimuli presented to the excitatory classical receptive field, the stimuli differed only in the configuration of the surround. In discontinuous stimuli the orientation difference was either 67.5° or 90°. Responses were chosen for this stimulus specific oscillation analysis that differed by less than 10% in their mean magnitude, this indicated by the dashed line that runs horizontally from left to right on the figure. This shows that the mean response magnitude difference averaged across the whole sample of 16 cells was very small. Each response was generated from five presentations of the stimulus configuration. Continuous patch stimuli had diameters that ranged between 1° and 6°. Discontinuous stimuli that generated the same mean level of response had centre diameter values that ranged between 1° and 3°. In this plot, for both mean response magnitude and oscillation index, values were normalised to those obtained from the continuous patch response. It can be seen that on average the oscillation indices obtained from responses to discontinuous stimuli is 2.4 times stronger than that in the patch response. Error bars depict one Standard Error of Mean.

recorded in the superficial layers of primate V1. Both cells were found to oscillate in the gamma frequency range, the oscillations present in responses to discontinuous stimuli were found in both cases to be significantly stronger than those present in responses to any other form of stimulus that was used. Stimulus *12a* was an optimally oriented grating patch presented exclusively to the excitatory classical receptive field, *12b* was an optimally oriented patch that was 5° in diameter, the stimuli featured in *12c* and *12d* had orthogonal and opposite direction surrounds respectively. It can be seen that the oscillation index that was obtained from the orthogonal discontinuous stimulus condition was 300% greater than that, that was obtained from the responses of the cell to the continuous full field stimulus. The oscillation index obtained from the responses of the cell to bipartite with optimally oriented centre and surround gratings travelling in opposite directions was also larger than that, that was obtained from responses to full field stimuli. A similar pattern of oscillation index stimulus specificity is evident in figure *13,* in this case the oscillation index of the response to the discontinuous response is 330% larger than that that was obtained from the response to the aligned full field stimulus.

During the analysis of response oscillations in the gamma frequency range using FFT analysis between 0 and 250 Hz, it became strikingly obvious that some cells fired trains of action potential at frequencies between 12 and 16 Hz. These oscillations were quantified with a subtly different technique, from those that were detected in the gamma frequency range. Auto-correlograms were calculated with 4 ms bins, so that temporal relationships between spikes could be investigated over a longer epoch, potentially containing an equivalent number of oscillation cycles, as in analysis in the gamma frequency range. This strategy reduced the Nyquist frequency to 125 Hz, the oscillation index for this frequency band was calculated by dividing the mean power in a 4hz band around the peak power between 12 and 16 Hz, by the mean power between 30 and 125 Hz. Figure *14* features these oscillations within responses recorded from a cell in primate V1. These responses contained a strong prolonged oscillation at a frequency of about 12 Hz. The propensity for this cell to respond in an oscillatory fashion exhibits the same stimulus selectivity that was evident for oscillations in the gamma frequency range. Strongest oscillations were detected in responses to spatially restricted grating patches and discontinuous bipartite stimuli.

Figure 12.

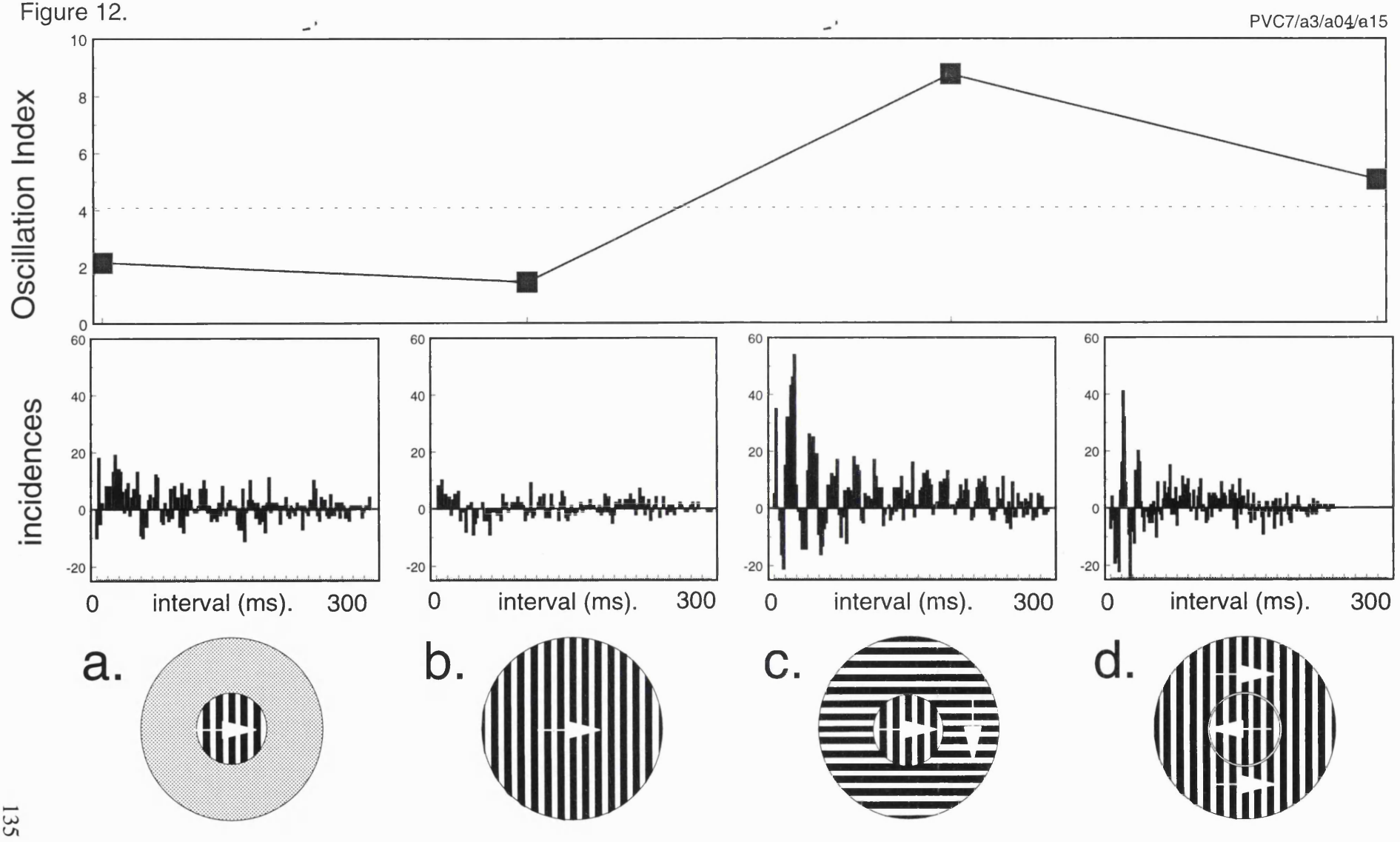

PVC7/a3/a04/a15
Oscillation Index
10
8
6
4
2
0
incidences
60
40
20
0
-20
0
interval (ms).
300
a.
b.
c.
d.

Figure 12.

This figure depicts the oscillations which were detected in auto-correlograms of responses of a single cell recorded in primate V1 to a grating patch of diameter 1.5° and various configurations of a bipartite stimulus with a centre diameter of 1.5°. The stimuli were presented with a contrast level (C) of 0.36. The spatial frequency of the gratings that were used to generate these responses was 2 cycles per degree, they were temporally modulated at a frequency 3Hz. Each presentation of each configuration involved the modulation of five cycles of the grating and thus lasted for 1.66 secs. In total each configuration was displayed 10 times. The first modulation of each display was excluded from analysis, thus the spike trains that were auto-correlated were the result of a response lasting 15 seconds. The top plot shows the oscillation index of the peak gamma frequency oscillation in each stimulus response. A significant oscillation was not detected in the cells response to an optimally oriented aligned full field stimulus, however it can be seen that significant levels of response oscillation were detected in responses to small patches and to various configurations of discontinuous stimuli. Each auto-correlogram is the result of subtracting the temporally shifted result and is plotted using 2 millisecond bins.

Figure 13.

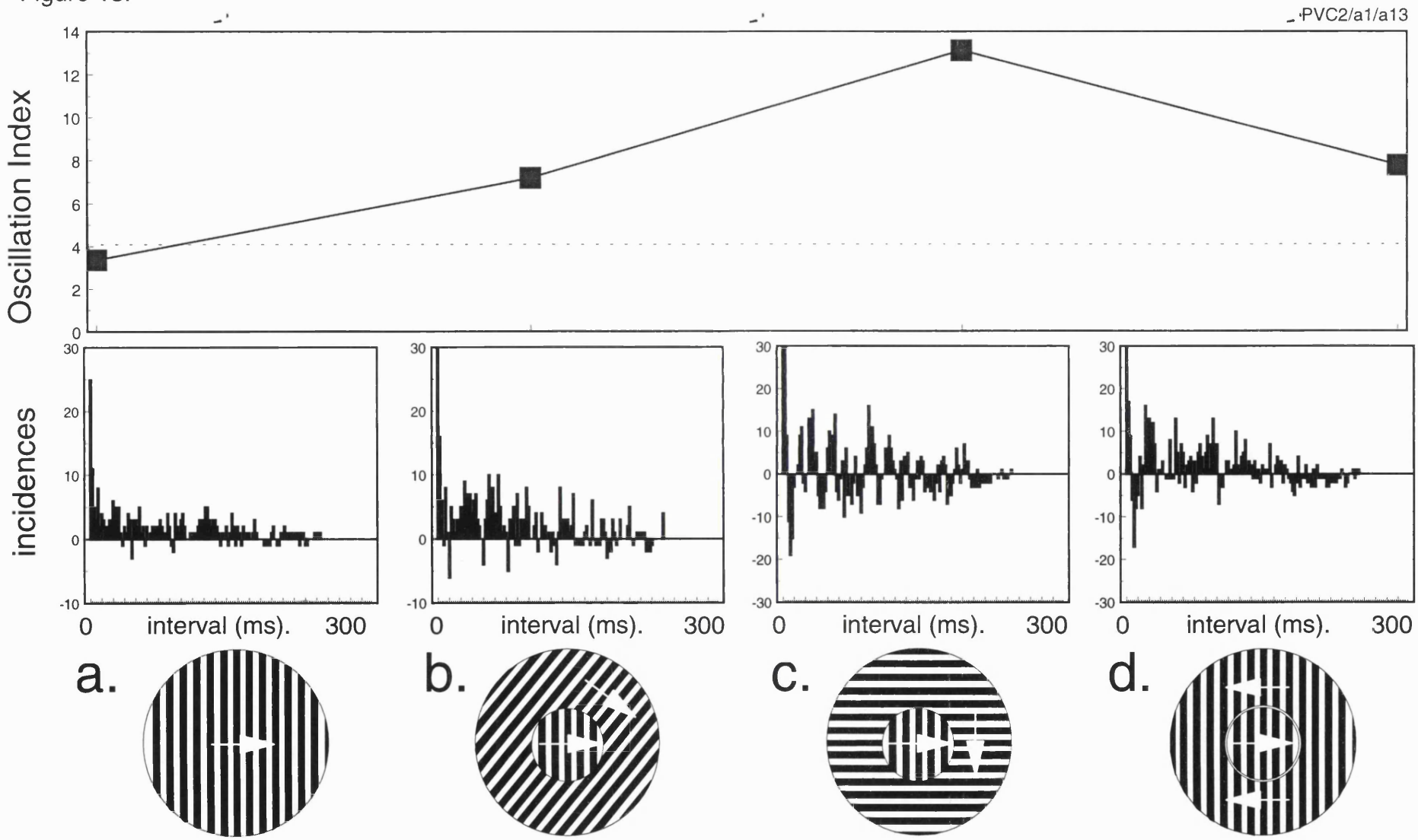

PVC2/a1/a13
Oscillation Index
14
12
10
8
6
4
2
0
incidences
30
20
10
0
-10
-20
-30
0
interval (ms).
300
a.
b.
c.
d.

Figure 13.

This figure depicts the oscillations which were detected in auto-correlograms of responses of a cell to various configurations of a bipartite stimulus with a centre diameter of 3°. The contrast was set at 0.36, spatial frequency was 2 cpd. and each grating was temporally modulated at 4Hz. The top plot shows the oscillation index of the peak gamma frequency oscillation in each stimulus. The oscillation associated with stimulus **a** is very weak, however to the right it can be seen that oscillations associated with discontinuous stimuli **b**, **c** and **d** are much stronger. Strong oscillation are associated with an oblique, orthogonal and opposite direction surround grating. Auto-correlograms are plotted with 2 ms bins.

Figure 14.

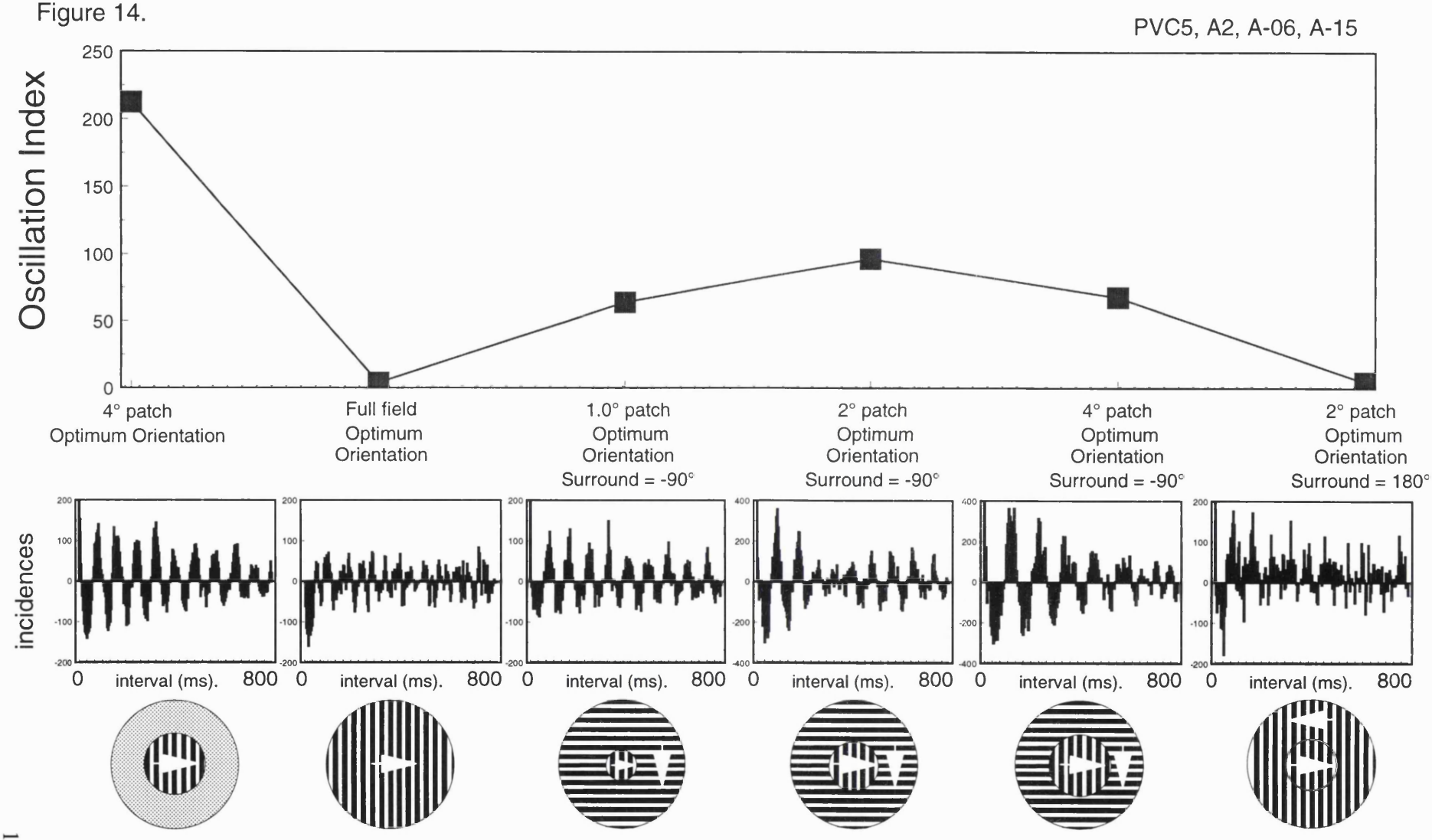

PVC5, A2, A-06, A-15
Oscillation Index
250
200
150
100
50
0
4° patch
Optimum Orientation
Full field
Optimum
Orientation
1.0° patch
Optimum
Orientation
Surround = -90°
2° patch
Optimum
Orientation
Surround = -90°
4° patch
Optimum
Orientation
Surround = -90°
2° patch
Optimum
Orientation
Surround = 180°
incidences
0
interval (ms).
800

Figure 14.

The oscillations detected within visual responses of a cell recorded in primate primary visual cortex to patch and bipartite grating stimuli. The contrast level of the stimuli used to evoke these responses was 0.36, the spatial frequency was 2 cycles pre degree and each grating was temporally modulated at a frequency of 3Hz. The stimuli in terms of these parameters were identical to the ones used to generate the responses in the previous two figures. It can be seen that again oscillations are very strong with in responses to discontinuous stimulus conditions and are notable for their frequencies, between 12 and 16 Hz. Strongest oscillations were detected within responses to a spatially restricted 4° patch and to discontinuous stimuli defined by an orientation disparity (particularly that with a 2° centre). Only weak oscillations were detected within responses to an optimally oriented full field. These stimulus specific changes in oscillation index are apparent in the plot at the top of the figure and in the auto-correlograms are displayed with 4 ms bins with shift predictor subtracted in order to remove the DC signal which could interfere with FFT analysis at this lower frequency range.

Varying centre diameter in bipartite stimuli revealed that it strongly influence the oscillation strength in responses to discontinuous stimuli. Diameters were varied between 0.5° and 4°. 24\34 cells were stimulated with at least two different diameters, on average centres that were 1.67 +\- 0.17° wide generated strongest oscillations. Figure *15* features a cell whose responses oscillated most strongly when the discontinuous stimulus diameter was 1.5°. Larger and smaller centres evoked responses in which the oscillation index associated with each response was significantly reduced. Such cells again demonstrate that the propensity to respond in an oscillatory fashion is not simply dependent on the orientation of the surround grating but also on the diameter of the centre segment.

In contrast to the cells described above, 2/34 (7%) exhibited a strikingly different mode of stimulus specific oscillatory behaviour. These cells oscillated strongly when presented with continuous full field gratings. Figure *16* features the responses of one such cell. Oscillations in the cell's responses to full field gratings are significantly stronger than those associated with discontinuous stimuli. Oscillation indices calculated from responses to continuous stimuli were 300% larger than those to discontinuous stimuli. Exactly the opposite situation to that encountered for the larger group of cells. Both these cells that exhibited this form of specificity oscillated in the gamma frequency range.

No cells stimulated with bipartite gratings were detected in which responses to both continuous and discontinuous contained equivalently strong oscillations . Cells were either characterised by the specificity of the first or the second group, or their responses were not found to contain oscillations in either frequency range. Response oscillation strength was always modulated by the context of the stimulus. This has important implications for network function as it appears using cross-correlation analysis, this will be discussed below.

Figure 15.

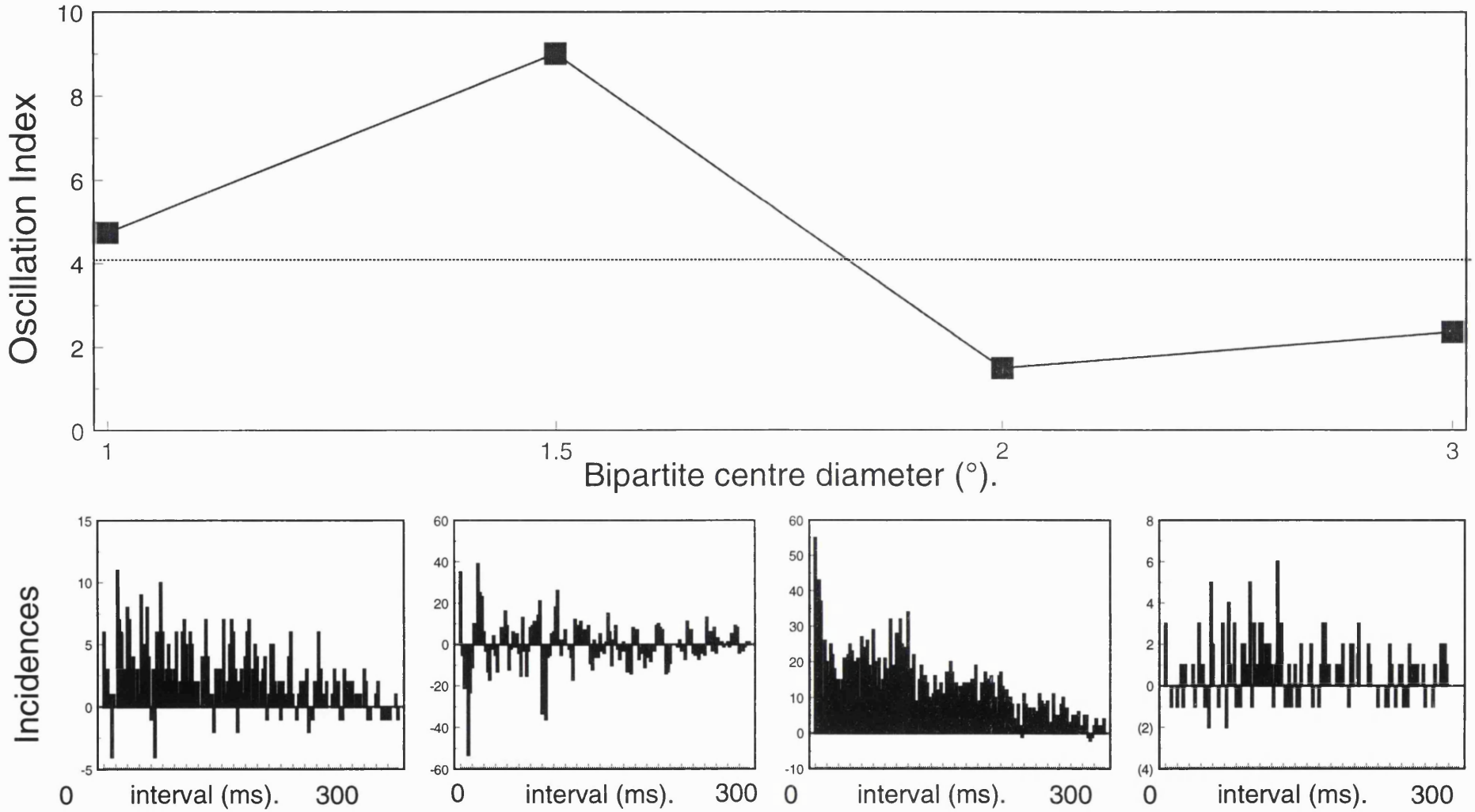

Oscillation Index
10
8
6
4
2
0
1
1.5
2
3
Bipartite centre diameter (°).
Incidences
15
10
5
0
-5
60
40
20
0
-20
-40
-60
60
50
40
30
20
10
0
-10
8
6
4
2
0
(2)
(4)
0
interval (ms).
300

Figure 15.

This figure depicts oscillations that were detected within responses recorded from a single unit in primate primary visual cortex, to discontinuous bipartite gratings as a function of inner patch diameter. The stimulus was centred over the excitatory classical receptive field of the cell, in all these stimuli centre was displayed at the optimal orientation of the cell and the orientation of the surround was 90°. All stimuli were displayed with contrast values of 0.36, the spatial frequency used was 2 cpd, and each grating was modulated at rate of 3 Hz. Auto-correlated responses are shown for centre diameters of 1°, 1.5°, 2° and 3°. It can be seen that the largest oscillation index was detected within the response to the bipartite stimulus with a diameter of 1.5°. The frequency of the oscillation was 44 Hz. In the top plot changes in oscillation index associated with change the bipartite grating diameter. Below this the oscillations within auto-correlograms are depicted with 2 ms bins.

Figure 16.

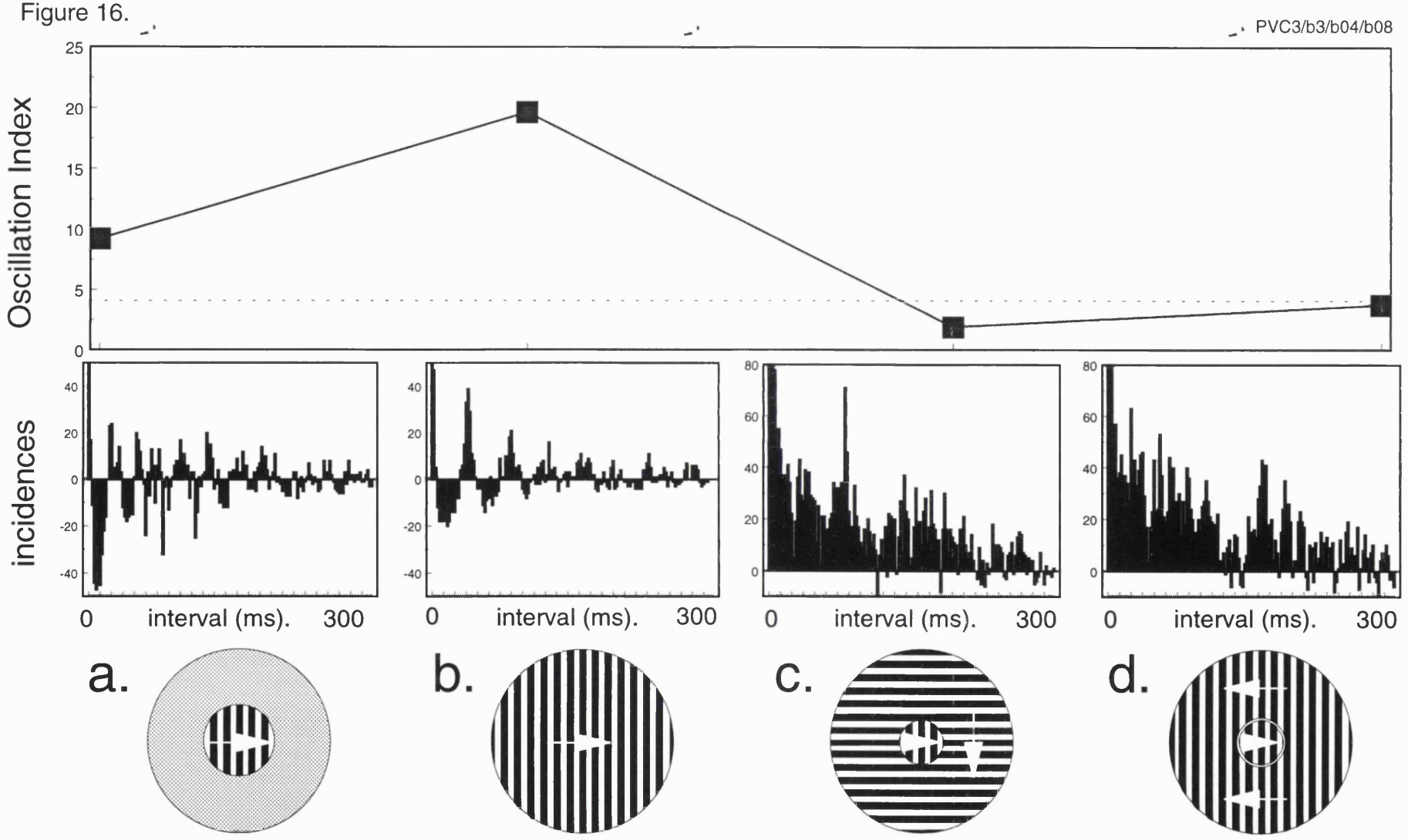

PVC3/b3/b04/b08
Oscillation Index
25
20
15
10
5
0
incidences
40
20
0
-20
-40
80
60
40
20
0
0
interval (ms).
300
a.
b.
c.
d.

Figure 16.

This figure depicts the relative strengths of oscillations detected with in the responses of a cell to patch, full fields and discontinuous bipartite grating stimuli centred over the excitatory classical receptive field of the cell. This cell was recorded in primate primary visual cortex. It can be seen that the propensity of this cell to respond in an oscillatory fashion has an inverse dependence on the characteristics of the stimulus, in comparison to the cells featured in figures *11-15*. This and one other cell exhibited significantly stronger oscillation in response to spatially expansive continuous stimuli. It can be seen that the strongest oscillation was detected in the response to a full field, the addition of a discontinuous surround presented at 90° around an optimally oriented patch evokes a response which does not contain a strong oscillatory component. Auto-correlograms are displayed with 2 ms bins. The bipartite grating centre diameter was 1°. The contrast of all stimuli was 0.36, all gratings were displayed with a spatial frequency of 2 cpd and a temporal frequency of 3Hz.

Context dependent changes in mean response magnitude.

The strength of oscillations was highly dependent on context of the stimulus that evoked the response. Most cells oscillated strongly when presented with discontinuous stimuli. When aligned and discontinuous stimuli evoked equal numbers of spikes from a cell, the oscillation detected in the response to the discontinuous condition was strongest. Strong oscillations are a property of responses to discontinuous stimuli rather than large responses. The stimulus specificity of oscillatory responses was further demonstrated by a smaller group of cells which oscillated specifically when presented with aligned conditions. This section will deal with how stimulus specific changes in response oscillation are related to changes in response magnitude, measured by other criteria to generate a result in terms of mean impulses per second. Changes of this latter type have been reported before (Sillito et al, 1995). Of the total sample analysed in this investigation, 94% (32/34) of cells exhibited patterns of response similar to those in figure *17*. Responses depicted along the line which bisects the origin at 45° are those to stimuli where the centre and surround were aligned, the bipartite stimuli is an aligned full field grating. Responses represented off this line are those to stimuli where the grating in the centre and surround were not aligned. Relatively elevated responses were recorded during presentation of stimuli where this was the case. This was particularly the case when the bipartite stimulus involved an optimally oriented inner segment, and surrounds offset in the orientation domain by between 45°, 67.5° and 90°. However it can also be seen in the upper panel of this figure, that the centre of the stimulus does not necessarily have to be optimally oriented to evoke equivalently elevated responses from a cortical cell. Large responses were also recorded when the inner stimulus was presented orthogonal to the optimum of the cell (defined by presenting the centre grating patch in isolation), provided that the outer stimulus was optimally oriented. The responses in the two panels in figure *17* were recorded from the same cell over the same period of time by interleaving the stimuli and separating them analytically. The only difference between the stimuli that were used to generate the top panel was that they had centre diameters that were smaller than those used to generate the lower panel. In the neuronal sample as a whole, a pattern of responses like that shown at the top was recorded when the bipartite stimulus had a centre diameter that was smaller than the excitatory centre of

Figure 17.

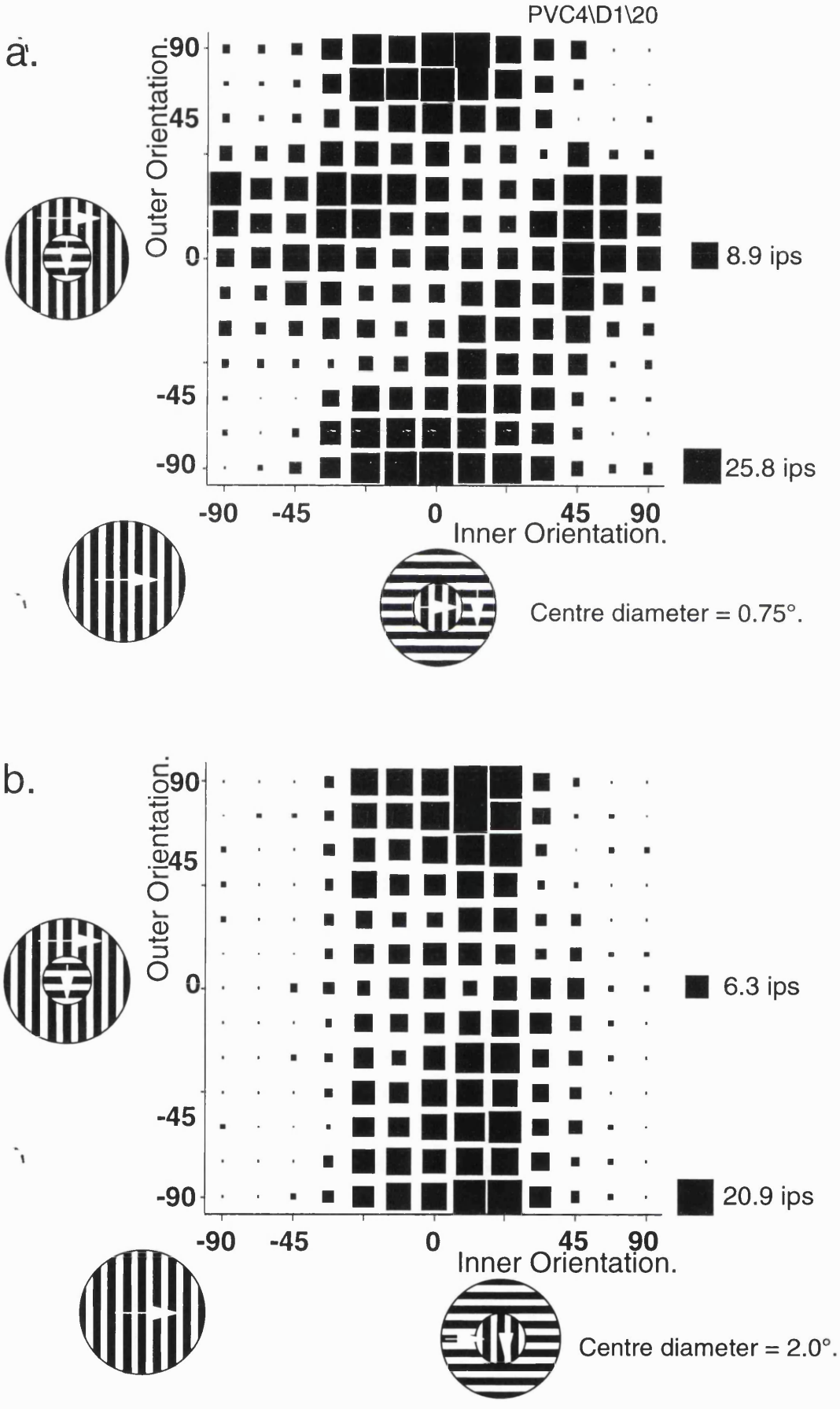

a.
PVC4\D1\20
Outer Orientation.
90
45
0
-45
-90
-90 -45 0 45 90
Inner Orientation.
8.9 ips
25.8 ips
Centre diameter = 0.75°.
b.
Outer Orientation.
90
45
0
-45
-90
-90 -45 0 45 90
Inner Orientation.
6.3 ips
20.9 ips
Centre diameter = 2.0°.

Figure 17.

The responses of an S type cell recorded from layer IV of Primate V1 to bipartite gratings with two different centre diameters. The contrast values of the grating stimuli were 0.36, the spatial frequency was 3 cpd and the gratings were temporally modulated at a frequency of 3Hz. The responses are plotted in the form of a density map in which the size of each square signifies the mean magnitude of the response. Squares are placed in a grid in which each position and square signifies the response to one particular bipartite grating condition with a particular permutation of centre and surround orientation which dependent on the position along the ordinate and abscissa. Two density maps are shown in this figure, each represents the responses to a bipartite stimulus with a different centre diameter. The top map was generated using a stimulus with a 0.75° centre diameter, the lower map was generated by a stimulus with a 2° centre. For each of these maps the mean response magnitude is shown as the upper figure, in terms of impulses (action potentials) per second or IPS, the lower figure beside each map was the largest response evoked by a discontinuous stimulus condition from the cell. It can be seen in the top panel that the cell responds with greatest mean firing rate when it is presented with stimuli that contain centre and surround gratings that are mutually orthogonal. When a larger centre diameter is used the cell fire at the highest rate in response to a stimulus with an optimally oriented centre and an orthogonal surround.

the cell. The lower pattern of response was recorded when the centre was the same size as the excitatory or larger. Thus the response magnitude of a cell, evoked by the bipartite stimuli that were used in the course of this investigation, is dependent on two factors that govern the configuration of the stimuli. The first is the orientation difference between the centre and surround, relative to the optimal orientation of the cell under investigation. The second factor is the dimensions of the segment which directly covers the excitatory classical receptive field of the cell.

For each of the plots shown in figure *17* two values are supplied, in each case the first value was the mean magnitude of the response evoked by an optimally oriented aligned full field grating, the second value was the largest responses evoked by a discontinuous condition, it can be seen that in both panels the lower value associated with discontinuous condition is larger than that above that was associated with the aligned condition. The increases associated with the upper and lower panels are 290% and 332% respectively. For each cell, as well as for the whole sample, a wide range of response increases, relative to the full field response were measured for discontinuous stimuli. Using the full field response of each cell as a firing rate reference, it was possible to quantitatively assess the response magnitude modifications associated with presentation of bipartite stimuli involving inner/outer orientation differences, for stimuli with a range of centre diameters, for each cell. From these data the mean increase in response brought about by presentation of discontinuous conditions could be calculated. A response was adjudged to be significantly elevated if it was at least 10% larger than the cell's response to an optimally oriented full field stimulus. All thirty-two cells were found to exhibit significantly larger responses to discontinuous stimuli, than to aligned full field stimuli. The increase in response in comparison to the full field ranged between 12 and 450% for the sample.

The magnitude of the response elevation brought about by presentation of a discontinuous stimulus showed a degree dependence on the centre diameter. This is evident in figure *17* where responses to bipartite stimuli with different centre diameters are shown. The effect was apparent when cells' responses to discontinuous bipartite conditions, presented with two or more centre diameters, were compared. In

figure *18* a tuning curve shows the responses of a cell to bipartite stimuli as a function of surround orientation, the inner segment of the grating was optimally oriented. The grey bar crossing the plot horizontally indicates the level of response of the cell when a grating patch exclusively stimulated the classical receptive field of the cell, the patch was 2° in diameter. The inner diameter of the bipartite stimulus was 3°, when this was presented with a surround grating displayed at an orientation that was rotated by between 45-90°, elevated responses in comparison to the full field were recorded. This cell is striking because responses evoked by discontinuous stimulus conditions were the largest that were evoked by any visual stimuli from the cell. It can be seen that discontinuous stimulus responses are larger than those to a 2° patch in two cases. This level of response elevation was detected in eleven other cells.

Table 1. Groups of cells stimulated with bipartite gratings, showing context dependent changes in oscillation strength and mean response magnitude.

Group description	Group	n Cells	% of A	% of B
Cells analysed in primate V1	A	53		
Stimulated with bipartite stimuli	B	34	64%	
Elevated IPS* to Discontinuous stimuli	C	32		94%
Total oscillating	D	30	57%	
at 28-80 Hz	E	27	51%	
at 12-16 Hz	F	3	6%	
Group D presented with bipartite stimuli		21	40%	62%
Group E presented with bipartite stimuli		18	34%	53%
Group F presented with bipartite stimuli		3	6%	9%
Elevated OI* to discontinuous stimuli at 28-80Hz		16		47%
Elevated OI* to continuous stimuli at 28-80Hz		2		6%
Elevated OI* to discontinuous stimuli, at 12-16Hz		3		12%
Elevated OI* to continuous stimuli, at 12-16Hz		0		0%

* IPS = impulses fired per second.
OI = oscillation index

In the previous section it was reported that in the largest group of cells (71% of those presented with bipartite stimuli), oscillation strength increases in visual responses were associated with changes in stimulus configuration from continuous to discontinuous. A smaller group (7%) of oscillating cells exhibited changes in oscillation strength, with the opposite stimulus dependency, oscillations were strongest in responses to continuous stimuli. It was demonstrated that for the largest group of 'discontinuity oscillator' cells, that if response magnitudes to continuous and

Figure 18.

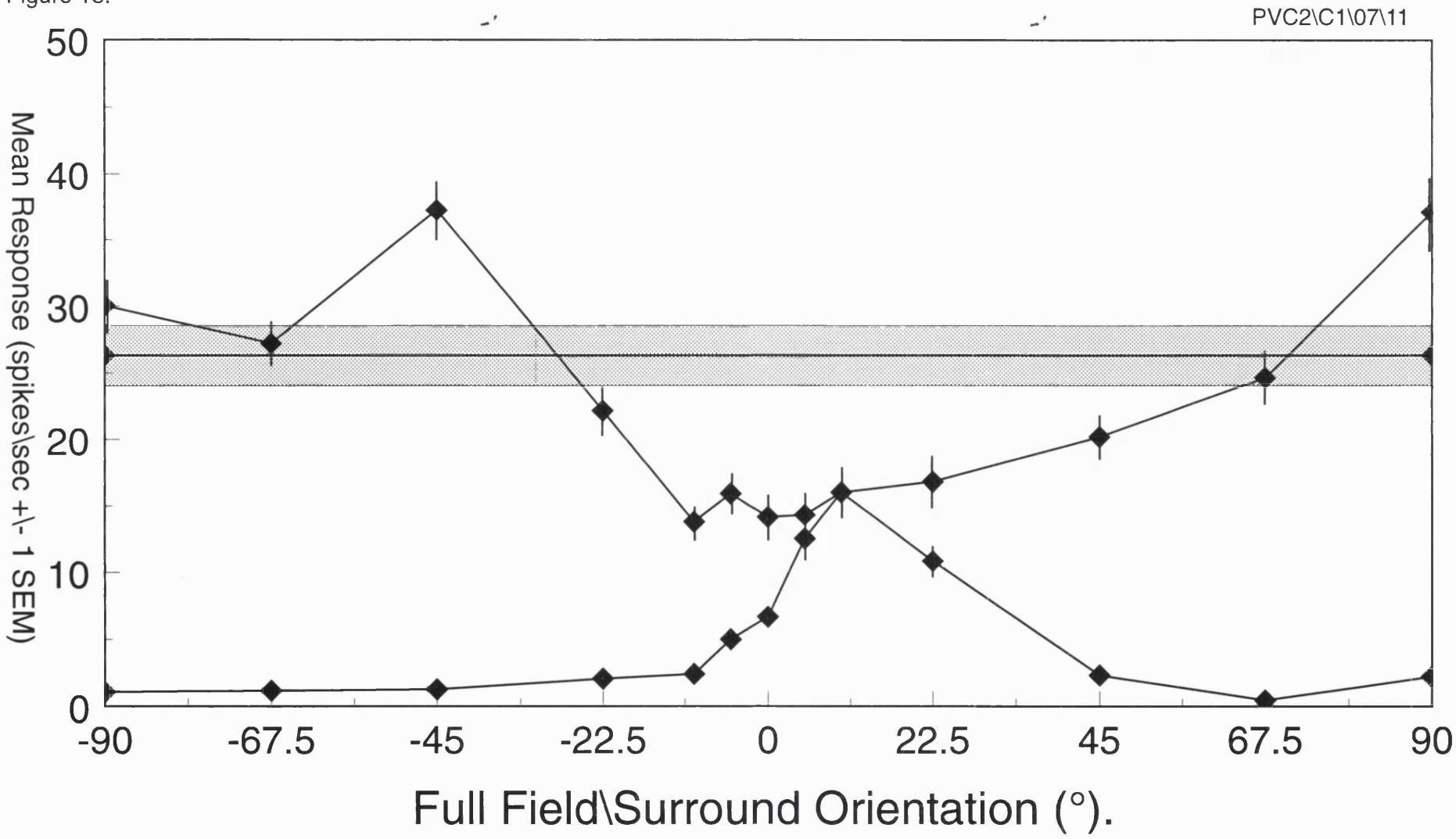

PVC2\C1\07\11
Mean Response (spikes\sec +\- 1 SEM)
50
40
30
20
10
0
-90
-67.5
-45
-22.5
0
22.5
45
67.5
90
Full Field\Surround Orientation (°).

Figure 18.

This figure depicts the surround orientation tuning of context dependent response properties. The field under investigation was centred within a bipartite stimuli, a circular patch of grating of diameter 3° was centred on the cell, the 10° x 10° square surrounding this patch was then stimulated with another grating. Each grating was presented with a contrast value of 0.36, and a spatial frequency of 2cpd, stimuli were modulated at a temporal frequency of 4 Hz. The orientations of each of these gratings could be varied independently and randomly through a specified range of values. Responses to conditions where centre and surround were aligned, are depicted by the lower curve which peaks at an orientation of 0°. The upper curve represents the magnitude of responses evoked from this cell as a function of the orientation of the surround grating presented around an optimally oriented centre grating. It can be seen that as the difference between the centre and surround grating orientation increases then so does the magnitude of the response evoked by it. Also shown in this figure is the magnitude of the response evoked by exclusively stimulating the classical receptive field of the cell with a circular patch of grating with a diameter of 2°. It can be seen that for two configurations of the bipartite condition, the evoked response is larger than simply stimulating the classical receptive field.

discontinuous were approximately equivalent, (this was achieved by selecting responses to patches lacking surrounds, that did not fully suppress the response of the cell), the responses to discontinuous bipartite conditions would consistently contain the strongest oscillations. The stimulus, and in particular the introduction of a non-aligned surround was demonstrated to be a key factor in the generation of oscillations in a response. This point is reinforced if the relationship between mean response magnitude, oscillation strength and stimulus configuration is examined across the two groups of 'continuity oscillating' and 'discontinuity oscillating' cells. All cells in these groups exhibited increased in mean response magnitude (IPS) values when the stimulus configuration were changed from aligned full field to discontinuous, this can be seen in table *1*, above. This has the implication that for the largest group, strongest oscillations were present in some of the largest responses of the cell, however for the smaller group, strongest oscillations were present in the smallest responses. This observation is depicted graphically in figure *19*, shown auto-correlation and oscillation index analysis for two example cells from each of the two oscillating groups. The cell featured in figure *19a* exhibited highest oscillation indices when stimulated with discontinuous bipartite gratings. The cell featured in figure *19b* (one of two in the sample), demonstrates that the two response parameters (response magnitude and oscillation strength) analysed in this investigation diverged in their stimulus specificity's, with regard to aligned versus non-aligned conditions. The cell featured in figure *19b* exhibited the opposite stimulus dependency, the oscillation indices obtained from the responses to continuous stimuli were significantly larger than those calculated from responses to discontinuous stimuli. However it was the case that both cells exhibited highest responses magnitudes when they were stimulated with discontinuous stimulus condition. For one cell the responses that contained the strongest gamma oscillations were also the largest responses it fired, strongest oscillations in the gamma frequency range were detected in the smallest responses fired by the other cell. This is further evidence that a cell's propensity to oscillate is dependent on the spatial features and context of the stimulus, rather than being a dependent mechanisms that control the number of spikes it fires.

Figure 19.

a.
Mean Response
(hz +\- 1 SEM)
Oscillation Index
Incidences
b.
Mean Response
(hz +\- 1 SEM)
Oscillation Index
Incidences

Figure 19.

This figure depicts the two different patterns of stimulus specificity that were exhibited for the propensity of a cell to fire oscillatory responses, from two cells. Stimuli presented to both cells had spatial frequencies of 2 cpd and were modulated with a temporal frequency of 3Hz. The cell featured in panel **a**, only fired in an oscillatory fashion when presented with a discontinuous stimulus with a centre diameter of 1.5°. Whereas the cell featured in figure **b** only fired periodically when stimulated with aligned grating stimuli. However if the responses of both cells are examined from the perspective of response magnitude then both exhibit elevated response magnitudes to discontinuous conditions. Thus this figure dissociate changes in oscillation index from changes in the mean response magnitude of the cell. It demonstrates that changes in oscillation index are stimulus specific, some cells oscillate strongly when presented with discontinuous stimuli, a minority of others oscillate when presented with continuous coherent stimuli. The stimulus specificity of a cell's oscillatory responses is a property of that cell. This figure demonstrates two forms of specificity that were detected in the course of this investigation.

Single unit analysis in cat V1.

Context dependent oscillatory responses.

All the cells in this sample had receptive fields within 6° of the area centralis of the appropriate eye. The population of 27 cells consisted of 12 with S type receptive fields, and 15 with C type. All of these cells were stimulated with bipartite grating stimuli of the kind that is featured figure *7b*. The context dependence of the visual responses of cortical cells was explored with bipartite stimuli by varying the orientation difference between the centre and stimulus. The twenty-seven cells recorded from cat primary visual cortex were analysed for response temporal structure. Again auto-correlograms were calculated for each of a cell's responses, in order that oscillations within them should become apparent. The oscillatory characteristics of each correlogram were quantified using FFT techniques to generate a power spectrum and its associated oscillation index. Of the total sample, 26% (7/27) were found to exhibit visual responses which contained oscillatory components, in the gamma frequency range, between 28 and 80 Hz. As in the primate, the responses of cells were found to exhibit specific changes in oscillation index which correlated with specific changes in the spatial characteristics of the stimulus. Of the 7 cells, the responses of which were found to contain oscillations, the responses of all of these to discontinuous bipartite stimuli, were found to contain oscillations that had larger oscillation indices, than responses to spatially coherent aligned grating stimuli. The mean oscillation index calculated from responses to full field stimuli for these cells was 1.87 +/- 0.28, this was found to be significantly smaller than that calculated for oscillations present in responses to discontinuous bipartite stimulus conditions. The mean maximum oscillation index from responses to discontinuous stimuli was calculated to be 4.2 +/- 0.34. This pattern of response is depicted graphically in figure *20*. It can be seen in this figure that the oscillation index obtained from the response to the discontinuous condition is 3.3 times larger than that obtained from the cell's response to the aligned full field stimulus.

Context dependent changes in mean response magnitude.

From the sample of 27 cells that were tested with bipartite stimuli 48% (13\27), of which 7 had complex type receptive fields and 6 were simple, exhibited elevated responses to stimulus condition where there was an orientation difference between an optimally oriented inner, and the outer grating, in comparison to the full field condition where the centre and surround were aligned. Maximum responses were detected when the surround orientation was rotated to 45° or 90° from the optimal orientation of the cell. A further 22% (6/27) the total population of cells exhibited peak responses when presented with conditions where the centre and surround were aligned. Responses to conditions where the centre and surround were mutually orthogonal, were reduced in comparison to those evoked by the aligned condition. In a further 19% (5/27) of the total population, responses to aligned conditions, and to conditions where there was a centre/surround orientation difference, were roughly similar. This last group of cells contained two cells, the responses of which to discontinuous conditions were found to contain significant levels of oscillation in the gamma frequency range.

Sets of responses that are typical of single-units in each of the first two groups are shown in figure *21*. The cell at the top of the page responded to stimuli in which there was an orientation contrast between centre and surround with elevated responses. The peak response to the discontinuous conditions was 592% larger than that to an optimally orientated aligned full field grating stimuli. It can also be seen that this cell, like that in figure *17,* exhibits relatively elevated responses when the centre was presented at an orthogonal orientation and the surround at an optimal one. Below it can be seen that another cell in the second group responds maximally to aligned conditions at its optimal orientation. Figure *22* features a set of responses from a cell in the first group, its responses are plotted as a function of surround orientation, it can be seen that the largest responses were recorded when the surround was rotated by 45-90°, between these orientations responses are consistently elevated. It can also be seen that this cell responded more strongly to discontinuous contextual stimuli than to a stimulus presented exclusively within its classical receptive field. Shown on this plot is the largest response that could be evoked from the cell by a stimulus that was

Figure 20.

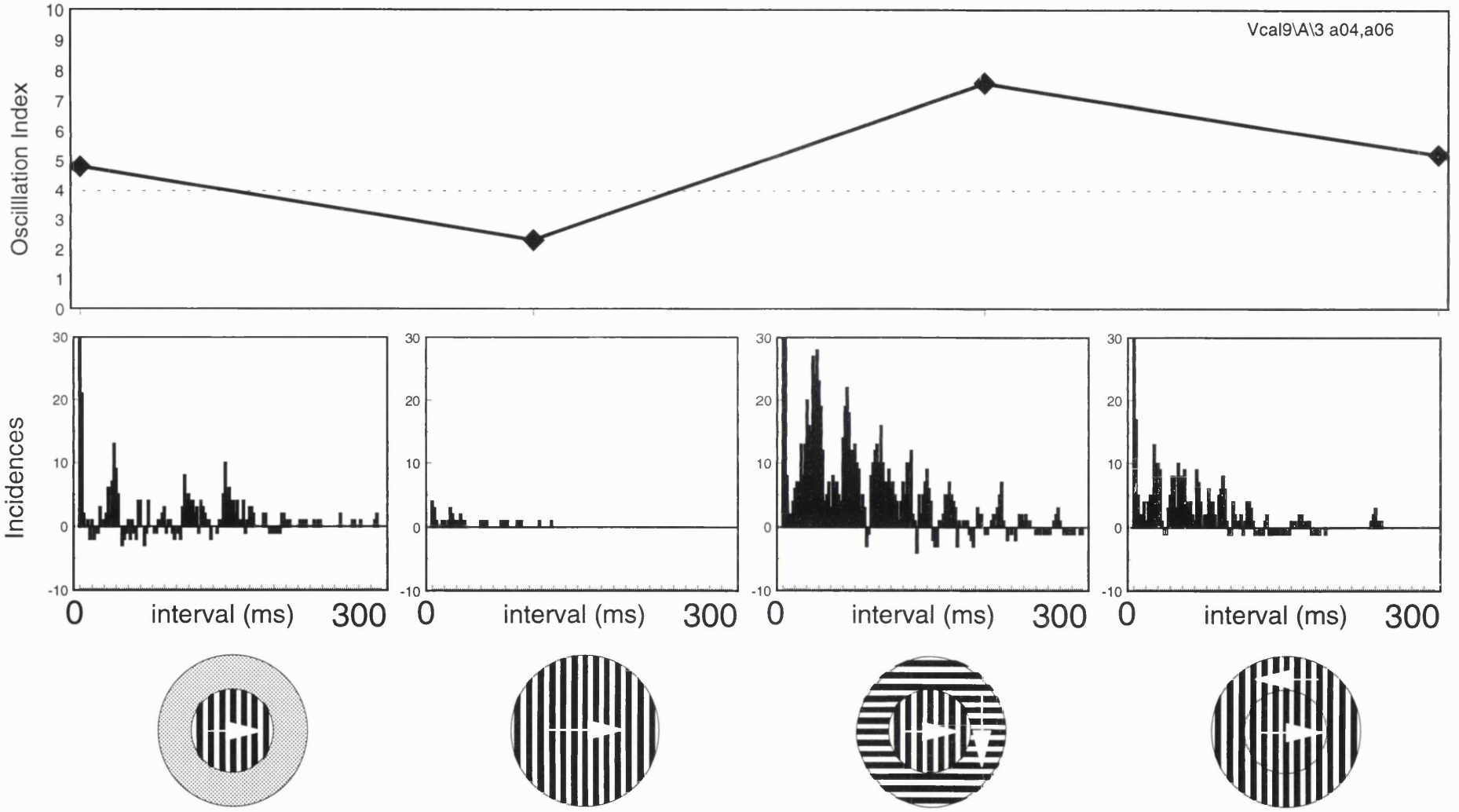

Vcal9\A\3 a04,a06
Oscillation Index
10
9
8
7
6
5
4
3
2
1
0
Incidences
30
20
10
0
-10
0
interval (ms)
300

Figure 20.

This page features oscillations detected with the responses of a cell recorded from the primary visual cortex of the cat. This cell was recorded in layer IV of area 17, it had an S type receptive field. All stimuli were displayed with contrasts of 0.36, spatial frequencies of 0.66 cpd and temporal frequencies of 2Hz. A grating patch of 3° diameter is shown on the far left of the figure, it was centred on the receptive field. Also shown are a full field grating and two discontinuous stimuli with centre diameters of 3°, one defined by an orientation difference the other by opposite directions of motion in the centre and surround. It can be seen that strong oscillations in the gamma range are associated with the patch and discontinuous stimuli. The response to the third stimulus contains an oscillation that is almost four times stronger than that within the response to the full field stimulus. Auto correlograms are displayed with 2 ms bins.

Figure 21.

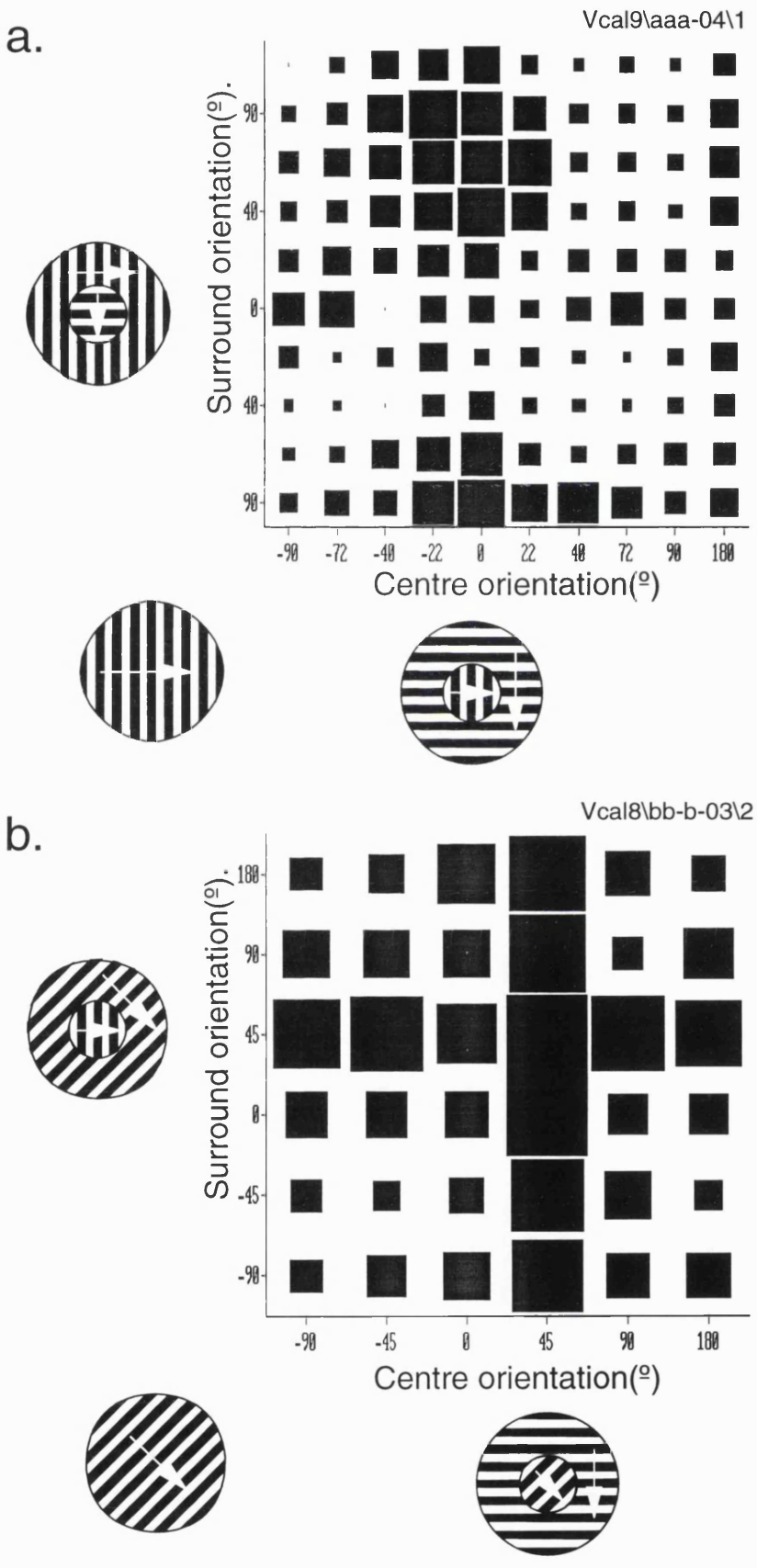

a.
Vcal9\aaa-04\1
Surround orientation(º).
90
40
0
40
90
-90 -72 -40 -22 0 22 40 72 90 180
Centre orientation(º)
b.
Vcal8\bb-b-03\2
Surround orientation(º).
180
90
45
0
-45
-90
-90 -45 0 45 90 180
Centre orientation(º)

Figure 21.

This features to density maps that depict the relative strengths of response to stimuli involving different permutations of centre and surround orientation in a bipartite grating stimulus. **a.** This features a cell that responds most strongly to bipartite stimuli that involve optimal centre orientations and non-optimal surround orientations, maximum responses are recorded from the cell to surround stimuli that are orthogonal to an optimal centre grating. the stimulus gratings had spatial frequencies of 0.66 cpd and temporal frequencies of 2Hz. Peak mean response magnitude was 18.7 Hz. **b.** This cell responds most strongly to a bipartite stimuli in which the centre and surround are aligned and optimal, it does not exhibit elevated responses to stimuli with an orthogonal surround. These bipartite stimuli were displayed with a spatial frequencies 0.75 cpd and were modulated at a temporal frequency of 2 Hz.

Figure 22.

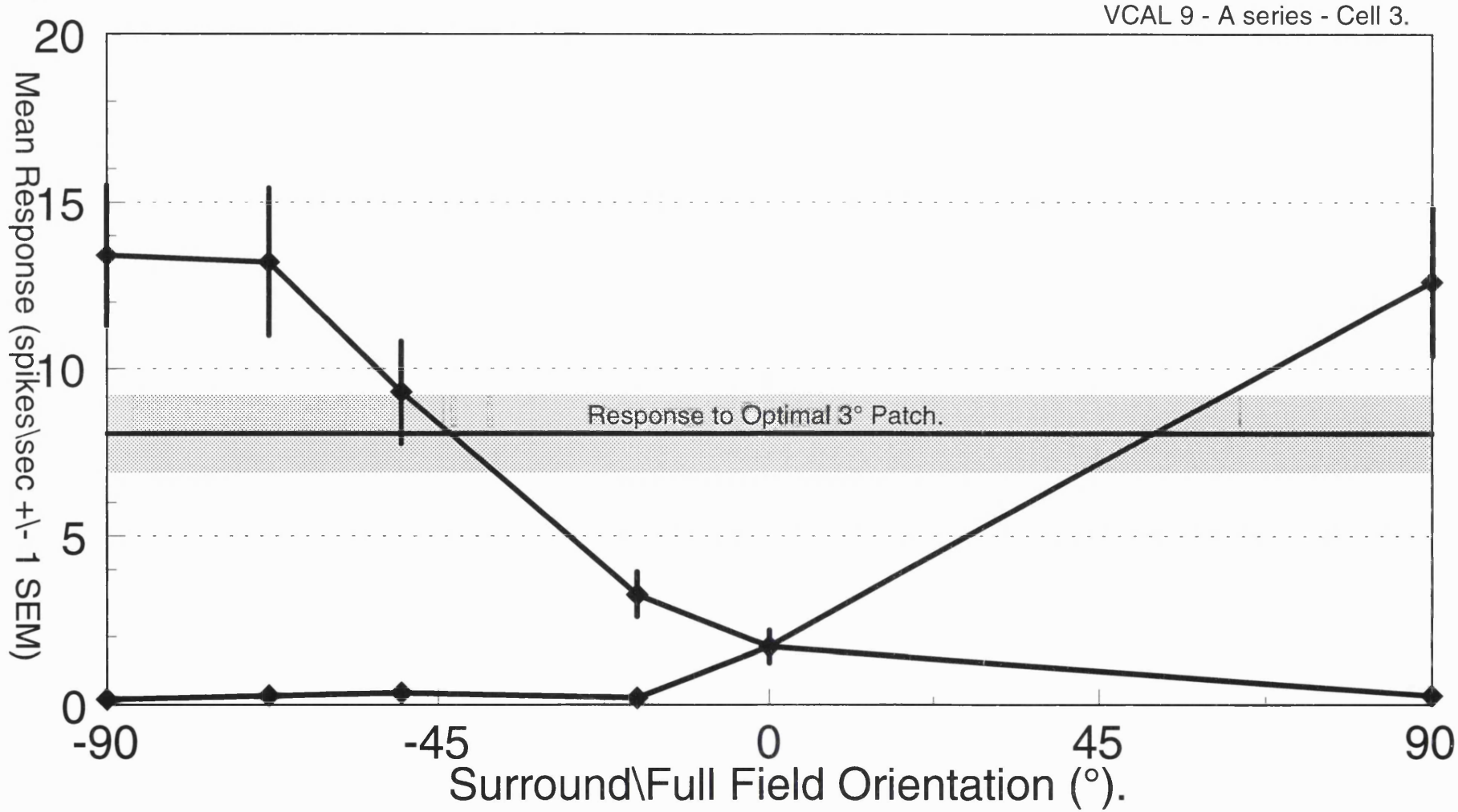

VCAL 9 - A series - Cell 3.
Mean Response (spikes\sec +\- 1 SEM)
20
15
10
5
0
Response to Optimal 3° Patch.
-90
-45
0
45
90
Surround\Full Field Orientation (°).

Figure 22.

A diagram depicting the relative response elevation which is associated with presentation of a spatial discontinuity centred over the receptive field of a proportion of cells recorded from the feline visual cortex. This cell had a simple type receptive field. Responses were generated from bipartite stimuli presented with a spatial frequency of 0.66 cpd, gratings were modulated at a temporal frequency of 2Hz. Responses to aligned bipartite conditions presented at various orientations are shown in the lower curve, the upper curve depicts the change in response magnitude which is associated with increasing the orientation difference between an optimally oriented centre and its surround. The stimulus consisted of an circular grating patch, with a diameter of 3° centred over the receptive field, this was surrounded by another grating, presented at an orientation displayed on the X axis of this graph. As with the cell depicted in figure 18, that was recorded in the primate, the maximum response that could evoked using a discontinuous stimulus was larger than that, that could be evoked by exclusively stimulating the classically defined field (this response level is shown by the grey bar).

presented exclusively within its classical excitatory receptive field. It is clear from this that many of the responses that were evoked by discontinuous stimuli were the largest that could be evoke from the cell. This magnitude of response elevation, associated selectively with discontinuous condition was seen for a further two cells in the sample. For the entire group of cells exhibiting this behaviour responses to non-aligned bipartite stimuli were between 17% and 600% larger than those aligned conditions, the mean increase was 370%.

Responses of cat LGN cells.

The lateral geniculate nucleus is a centre in the thalamus that receives direct input from retinal ganglion cells and makes a direct input into the primary visual cortex. It is the excitatory input from this centre which is thought to generate the structured spatial properties of the cortical classical receptive field. Gamma frequency response oscillations recorded in the cortex have also been proposed to have presynaptic origins in oscillation at the same frequency that are recorded in the responses of LGN cells (Laufer and Verzeano, 1967, Ghose and Freeman, 1992 and Neuenschwander and Singer, 1996). It was the aim of this phase of the analysis to investigate how the temporal structure of thalamic visual responses changes as a function of changes in the spatial context of the stimuli they are presented with. The stimuli that were used to generates the responses analysed in this section were the same as those that were used to evoke responses to cortical cells. In the lateral geniculate nucleus of the cat, changes in response magnitude associated with presentation of stimuli involving differences of centre/surround orientation of bipartite stimuli, relative have been reported (Sillito et al, 1993). Bringing centre and surround stimuli into alignment diminished responses by on average 25% relative to discontinuous stimulus responses. It is the focus of this investigation to quantitatively assess the changes in the temporal structure that might be associated with these different kinds of stimuli. Auto-correlation and FFT analysis was implemented on the responses of 22 cells to aligned and discontinuous bipartite gratings. Of this population 10 cells had X type, and 12 Y type receptive fields as determined with a null-test. Figure *23* features a typical set of responses recorded from a Y cell to aligned and discontinuous grating conditions. For

all cell response magnitude changes consistent with previous reports were observed. However when these responses were analysed for oscillations in the gamma frequency range or at 12-16 Hz a pattern of behaviour similar to that encountered during analysis of cortical responses was not observed. The responses of each cell to between two and five full field gratings, displayed at different orientations, and to five to ten discontinuous stimulus conditions with different orientation differences were analysed for their oscillatory content. Consistently reproducible stimulus specific response oscillations in the gamma frequency range were not detected in the visual responses of the LGN cell population, either to aligned full field or discontinuous gratings. Significant oscillations were also not detected in the 12-16 Hz frequency range. The lack of response oscillations is evident in the typical set of results that are featured in figure *23,* in this changes in gamma oscillation index are plotted for the various stimuli. Shown are auto-correlograms generated from responses to each stimulus, fitted to these are gabor functions. These do not have flanking peaks that would indicate a significant level of oscillation. These correlograms feature a high level of inter-spike intervals between 4 and 15 ms, there is then a negative probability of intervals between 15 and 90-100 ms followed, a stochastic distribution at larger intervals. This was a temporal structure that was often detected from the analysis population, indicating that cells specifically did not fire spikes in the gamma frequency range but rather at much higher frequencies. Some other cells exhibited an unmodulated decrease in bin content as a function of inter-spike interval.

Figure 23.

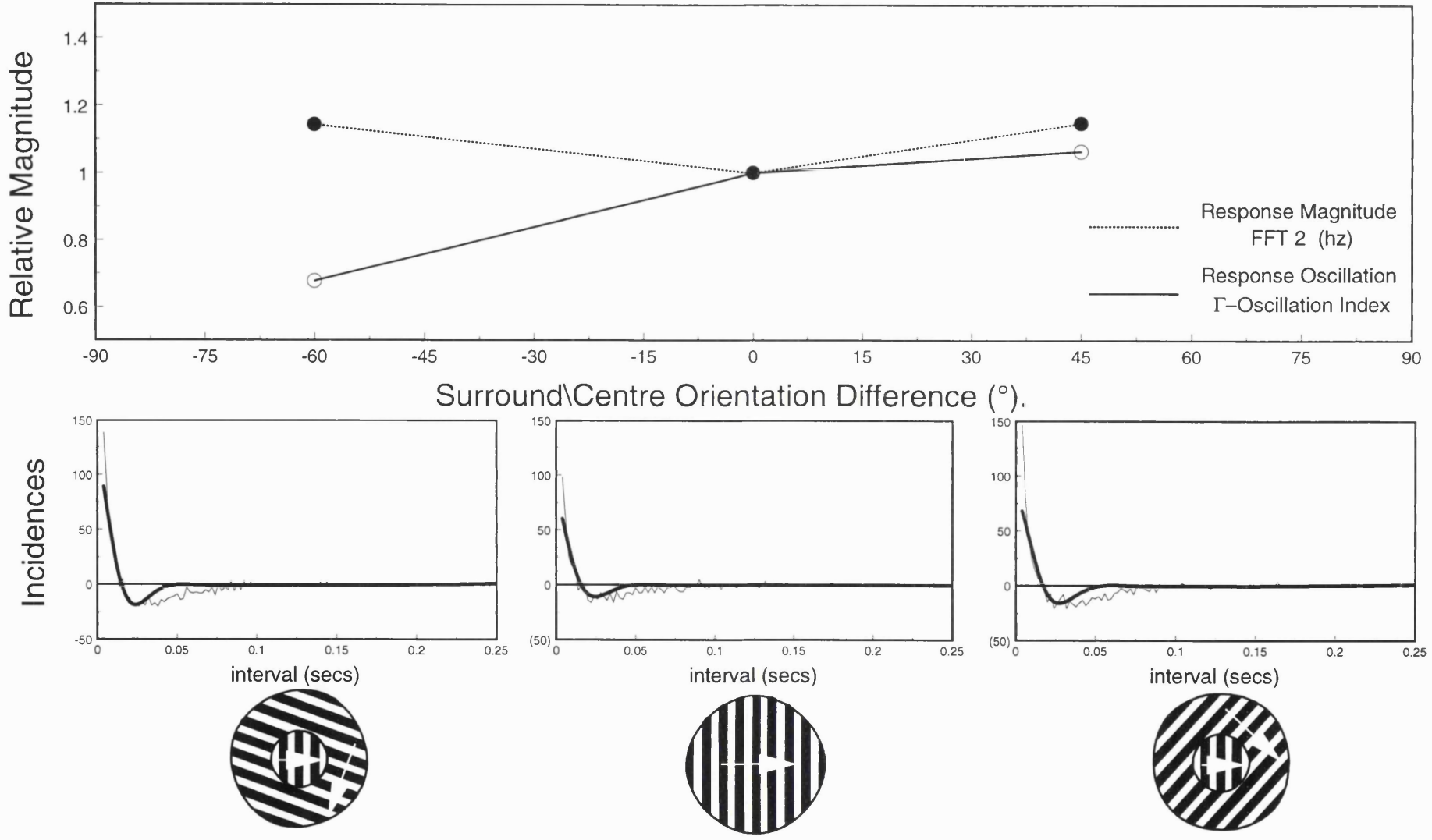

Relative Magnitude
1.4
1.2
1
0.8
0.6
-90
-75
-60
-45
-30
-15
0
15
30
45
60
75
90
Response Magnitude
FFT 2 (hz)
Response Oscillation
Γ–Oscillation Index
Surround\Centre Orientation Difference (°).
Incidences
150
100
50
0
-50
(50)
0.05
0.1
0.15
0.2
0.25
interval (secs)

Figure 23.

Response magnitude and temporal structure changes in responses recorded from a single LGN cell with a Y type receptive field. Stimuli were presented with a spatial frequency of 0.75 cpd and were modulated at a temporal frequency of 2Hz. Shown are changes in response magnitude and oscillation index relative to those values obtained from presentation of an optimally oriented full field. Below this are the auto-correlograms for each response, from which an averaged shift predictor has been subtracted, these are fitted with a gabor function. It can be seen from all plots that gamma oscillations are not present in any of these responses. This was the case for all cells in the sample. Bin size was 2 ms.

Oscillatory responses of primate cortical cells to grating patches.

The aim of this analysis was to determine if there were changes in the oscillatory characteristics of these responses that varied systematically with changes in the diameter of the stimulus, and to see whether these changes paralleled those in firing rate or followed some other pattern.

All cells were stimulated with between 4 and 7 grating patches of different diameters, between 0.5° and 8.0°. As a function of the diameter of a circular sinusoidal grating patch centred on the classical receptive field of the cell, the vast majority of cells were generally characterised by a degree of tuning to patch diameter. The largest responses generated by patches between 0.5° and 2° in diameter, with significant suppression apparent in responses to larger patches of grating. Of a total population of 53 cells recorded from parafoveal V1, all cells were tested with the stimulus paradigm that utilised patches presented with different diameters and orientations. 83% (44\53) of these cells exhibited response suppression when grating stimuli were extended into the surround of their respective receptive fields. A small proportion of cells accounting for 17% (n=9) of cells did not exhibit response suppression, and instead exhibited response summation as a function of patch diameter. These cells were recorded from sites that histological reconstructions indicated were in layers V and VI.

A set of responses from a typical primate cell presented with a range of patches at different diameters and orientations is depicted in figure *24*. In this figure the size of the square is proportional to the magnitude of the response, relative to the largest patch and response to the optimal stimulus. In the bottom panel are responses to stimuli that were composed of patches of neutral contrast surrounded by sinusoidal gratings, covering the remainder of the CRT screen, presented at the same range of orientations and inner rather than outer diameters as in the plot above. Though this cell exhibits suppressed responses as a function of the diameter of the circular grating patch which is centred on its field, it can be seen in the bottom panel of figure 24, that the surround is not simply a source of suppressive influence on a cell's visual

Figure 24.

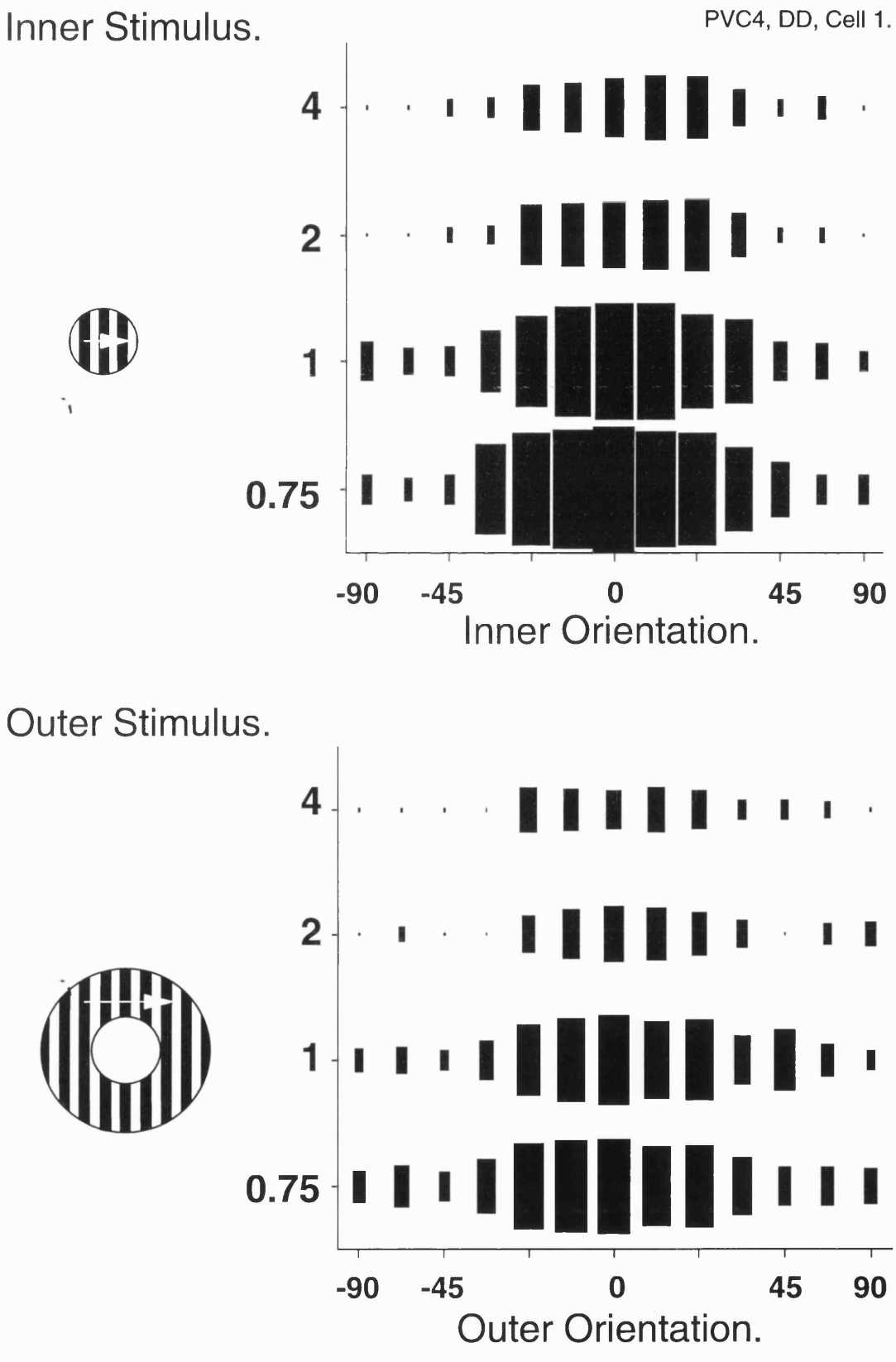

Inner Stimulus.
PVC4, DD, Cell 1.
4
2
1
0.75
-90
-45
0
45
90
Inner Orientation.
Outer Stimulus.
4
2
1
0.75
-90
-45
0
45
90
Outer Orientation.

Figure 24.

This figure contains density maps that show changes in response as a function of the diameter of a centred patch of grating and the inner diameter of a grating presented to the surrounding visual field. All stimuli were presented with a spatial frequency of 2cpd, each grating was modulated at a temporal frequency of 3Hz. **A.** a typical set of responses from an orientation tuned cell with suppressive surround zones. Stimuli larger than 0.75° in diameter encroach upon visual space surrounding the classical receptive field of the cell and evoke a response that is smaller than that to the smallest patch. **B.** This shows responses evoked from a cell by stimulus presented exclusively in the classical receptive surround, it can be seen that as the centre aperture increases in diameter and stimulation occurs at points in visual space more remote from the classical centre. Responses to each aperture diameter are orientation tuned. Largest density blocks correspond to a response level of 55hz.

responses. When the surround is stimulated in the absence of a centre element, an excitatory orientation tuned response can be evoked. Thus in certain circumstances that depend on the spatial configuration of a stimulus cells with fields in the surround of the one being recorded can be a source of excitatory input and inhibitory input.

A range of patch response tuning profiles are shown in figure *25*, generated from the responses of cells to optimally oriented patches of grating presented with the diameters. Shown are two cells that exhibit response suppression and one in which summation was observed, as a function of patch diameter. An averaged patch response profile is shown in figure *26*, this plot is the result of averaging the responses of 39 cells exhibiting surround suppression. Each data point is presented as the proportion of the maximum response for a given cell, generated by a patch, as a function of that patch's increased dimensions over the patch that generated that maximum response, it's degree of extension into the surround. The graph shows that response is reduced by 50% by extending the diameter of a patch 0.85°, extension by 1.25° brings about a 74% decrease. It can also be seen that there are two stages of response suppression as a function extension. When a patch is extended from 0° to 1.5° the rate of response suppression as a function of patch extension into the surround is 17.1 times greater than it is when a patch is extended between 1.5° and 8°. Figure *26* also shows the range of optimal patch dimensions for the entire population of 53 cells are shown, it can be seen that the 40 cells responded optimally to patches with dimension equal to or less than 2°. The mean optimal diameter for a patch calculated using the 39 cells featured in the upper plot, was found to be 1.26° +\- 0.16°. This diameter was found to be consistent with length and width dimensions of each classically mapped receptive field.

In all cases it was found that a cell's propensity to respond in an oscillatory fashion as quantified by the oscillation index of its associated auto-correlogram FFT power spectrum was tuned to the diameter of the circular grating used as a stimulus. This was the case for oscillations in the gamma frequency band and in the 12-16 Hz band.

Figure 25.

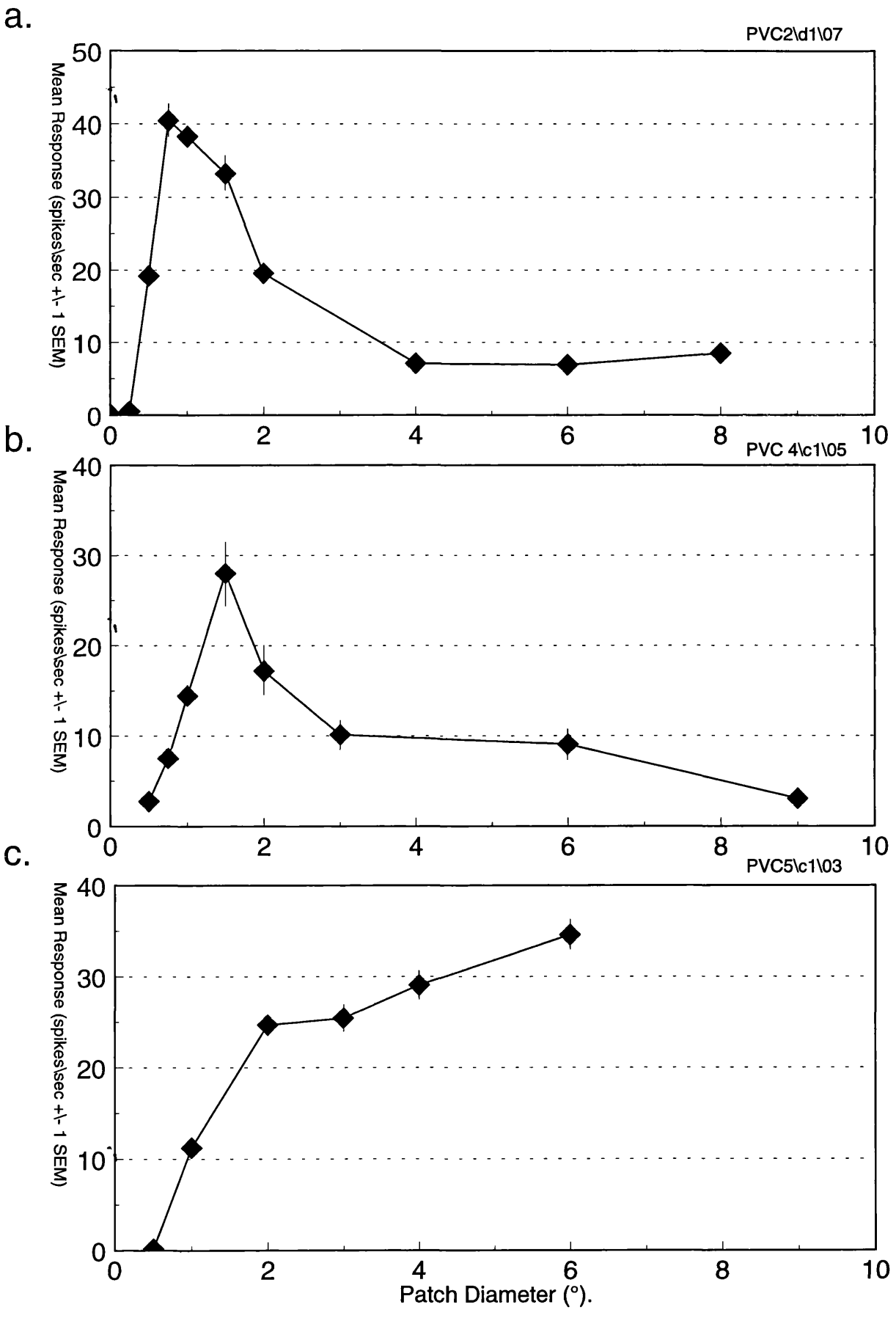

a.
PVC2\d1\07
Mean Response (spikes\sec +\- 1 SEM)
50
40
30
20
10
0
0
2
4
6
8
10
b.
PVC 4\c1\05
Mean Response (spikes\sec +\- 1 SEM)
40
30
20
10
0
0
2
4
6
8
10
c.
PVC5\c1\03
Mean Response (spikes\sec +\- 1 SEM)
40
30
20
10
0
0
2
4
6
8
10
Patch Diameter (°).

Figure 25.

Three typical patch response profiles generated from the responses of cells recorded in primate primary visual cortex to circular patches of sinusoidal grating centred over their receptive fields. All stimuli were presented at the optimal orientation of the cell that was recorded. The upper two (**a** and **b**) represent the behaviour of two cells that had suppressive zones around their classical receptive fields, in the last the surround has a facilitatory influence. Plot **a** shows the responses of a cell with a C type receptive field, stimuli were presented with a spatial frequency of 2 cpd and were modulated at a temporal frequency of 4Hz. Plots **b** and **c** feature cells with S type receptive fields. The stimuli used to generate stimulus b had spatial frequencies of 3 cpd and were modulated at a temporal frequency of 3Hz, the responses in c were generated by presentation of gratings of spatial frequency 1 cpd, they were modulated at a temporal frequency of 3Hz. Error bars indicate +/- one Standard Error of the Mean.

Figure 26.

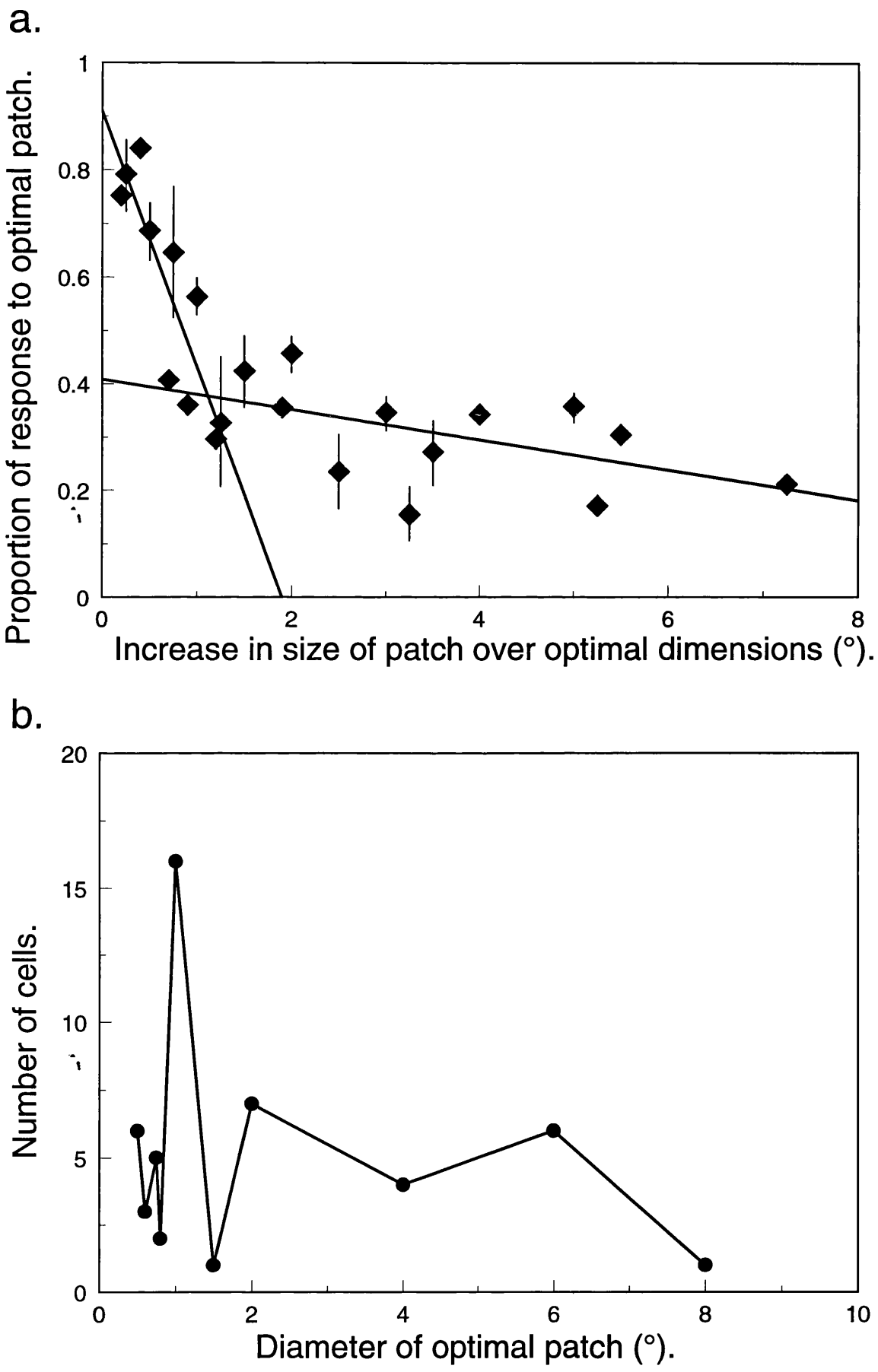

a.
Proportion of response to optimal patch.
1
0.8
0.6
0.4
0.2
0
0
2
4
6
8
Increase in size of patch over optimal dimensions (°).
b.
Number of cells.
20
15
10
5
0
0
2
4
6
8
10
Diameter of optimal patch (°).

Figure 26.

This features an averaged patch suppression profile (**a.**) calculated from the responses of 39 patch suppressed cells, recorded in primate primary visual cortex, to patches of grating with increasing diameters. All stimuli used to generate the responses from which this figure is derived were presented at the optimal orientation and direction of motion of each cell. The spatial and temporal frequencies of these stimuli were very similar to those mentioned for the previous figure. The optimal patch diameter, that which evoked the largest response magnitude, was determined from each cell. The mean pattern of decrease in response magnitude as the diameter was increased beyond this optimal is shown here. Shown are two lines of best fit which delineate a rapid increase when the patch is increased in diameter by up to 1.5°, and a slower rate decrease for patches larger than this. **b.** This plot indicates the range of optimal patch diameters that were exhibited by all the cells that were recorded from V1. Error bars in **a** indicate +/- one Standard Error of the Mean.

Though the propensity of each cell to respond in an oscillatory fashion exhibited an optimal patch diameter, just as was case from analysis of response magnitude, it was the case that the optimal patch judged from oscillation strength, was not necessarily the same as that defined by response magnitude in 37/43 of cases. When oscillation strength was correlated with patch diameter for all the cells in the sample it was evident that there was continuum of diameters that generated the strongest oscillation in the responses recorded from a cell, at one end of this were cells that exhibited strongest oscillations in their responses to the smallest stimuli, while other cells were found to exhibit strongest oscillation in their responses to the largest stimulus presented. Depicted in figure 27 and *28* are the changes in response magnitude and oscillation index recorded from two cells as a function of increasing grating patch diameter. In figure *27* the stimulus that generated the strongest response oscillation was of optimal dimensions, and also generated the largest response magnitude. In figure *28* the cell featured, responded with strongest oscillations to a larger stimulus than in the previous plot, in this case the optimal was 4° in diameter. A stimulus which was larger than the classical receptive field which generates the strongest oscillation. Within the sample of tested cells it was clear that there was a cell's propensity to respond in an oscillatory fashion changed as patch diameter increased, the results of a quantitative investigation of this observation is presented below.

The distribution of optimal patch diameters quantitatively defined using oscillation index for the whole sample of 43 cells is shown in the top plot of figure *29*, it can be seen that the vast majority of cells were tuned to diameters between 1 and 4°. The mean maximum oscillation index for the population of cells is 4.55 +/- 0.388, and this corresponds to a mean optimal patch diameter of 2.362 +/- 0.26°. The lower plot features the averaged tuning curve, it shows that when a cell is presented with a patch that is bigger or smaller than this mean diameter the oscillation index of the response is reduced, examination of the plot indicates that the reduction is similar for smaller and larger, at approximately 2.2. The values for non-optimal patch diameters however were still found to fulfil all the criterion for a significantly oscillatory responses in some cases.

Figure 27.

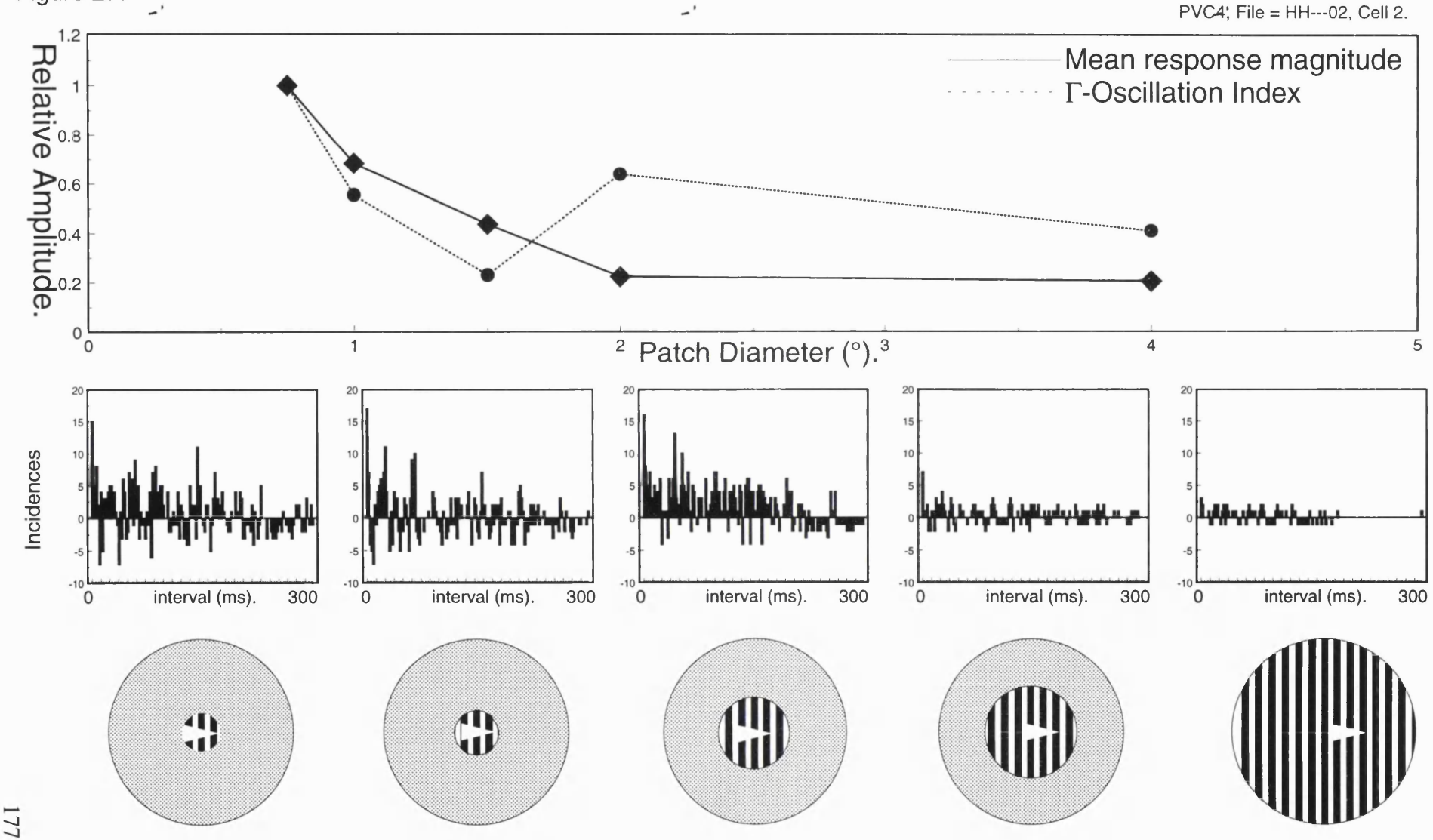

PVC4; File = HH---02, Cell 2.
Mean response magnitude
Γ-Oscillation Index
Relative Amplitude.
Patch Diameter (°).
Incidences
interval (ms).
0
300

Figure 27.

This figure depicts the changes in response magnitude and oscillation strength that were measured from presentation of grating patches displayed with a range of diameters. It can be seen that this cell, recorded in primate V1 exhibits a pattern of mean response which is suppressed as a function of patch diameter. All stimuli were presented at the cell's optimal direction and orientation and had spatial frequencies of 2 cpd and temporal frequencies of 3Hz. Oscillation index, like mean response magnitude was modulated by the diameter of the stimulus. Response magnitude is graphically presented as a proportion of maximum mean response, which was 29hz, changes in oscillation strength were also depicted in this way, the maximum oscillation index was 4.6. Auto-correlograms are plotted with 2ms bins.

Figure 28.

PVC6/EE-02/1/352°.

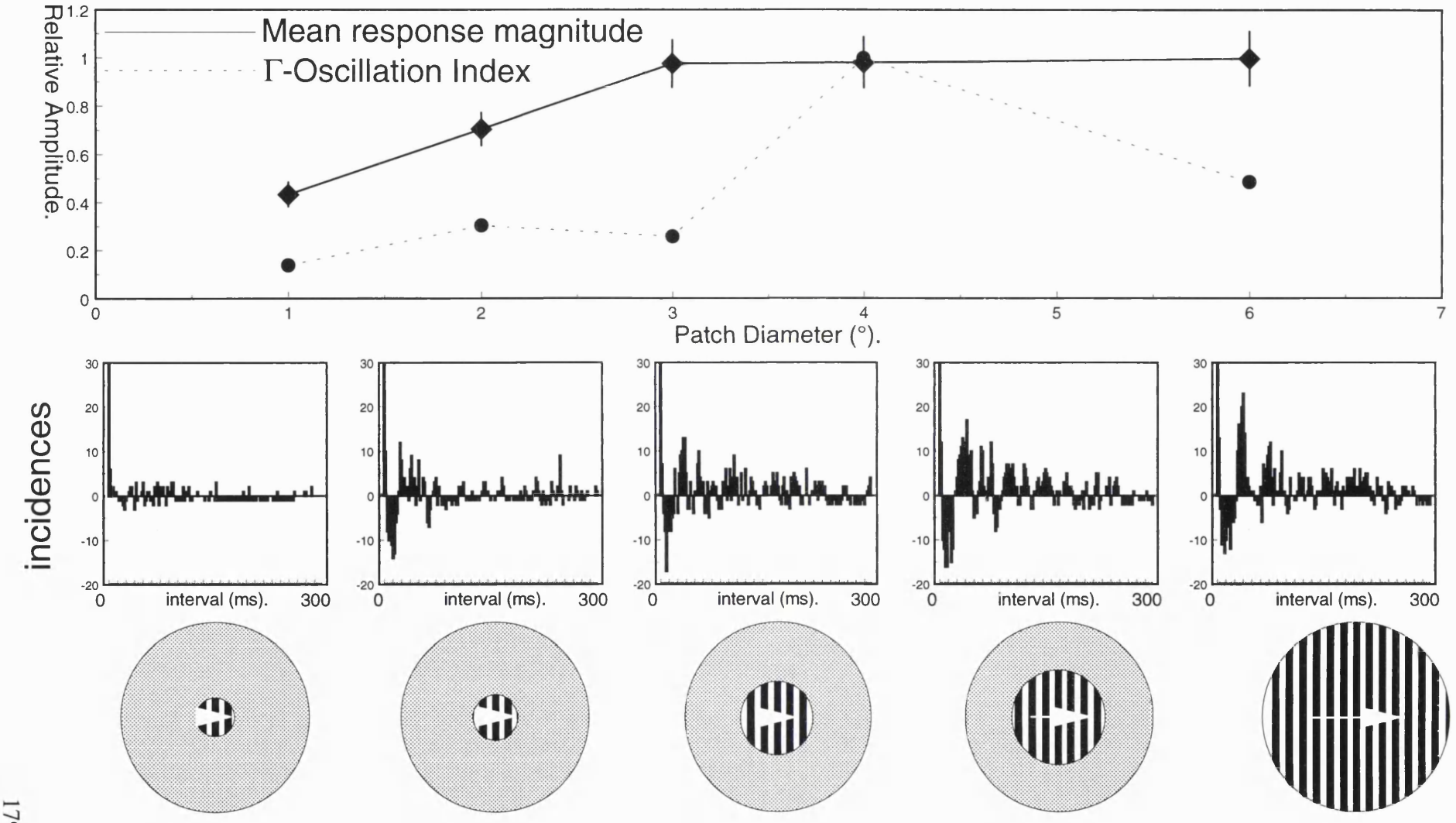


Figure 28.

This figure depicts the changes in response magnitude and oscillation strength that were measured from presentation of grating patches displayed with a range of diameters. The cell was recorded in primate V1. All stimuli were presented at optimal orientation, with spatial frequencies of 1 cpd and with temporal frequencies of 3Hz. Unlike the previous cell, this one did not exhibit suppressed mean response magnitude levels as a function of patch diameter, however it can be seen that when oscillation strength is plotted as a function of patch diameter, the strongest oscillation is not detected in the response to the largest stimulus that was displayed, the optimal stimulus was 4° in diameter. The strength of oscillation is stimulus dependent and has a different tuning profile compared to mean response magnitude. Response magnitude is graphically presented as a proportion of maximum mean response, which was 20hz, changes in oscillation strength were also depicted in this way, the maximum oscillation index was 13.6. Auto-correlograms are plotted with 2ms bins.

Figure 29.

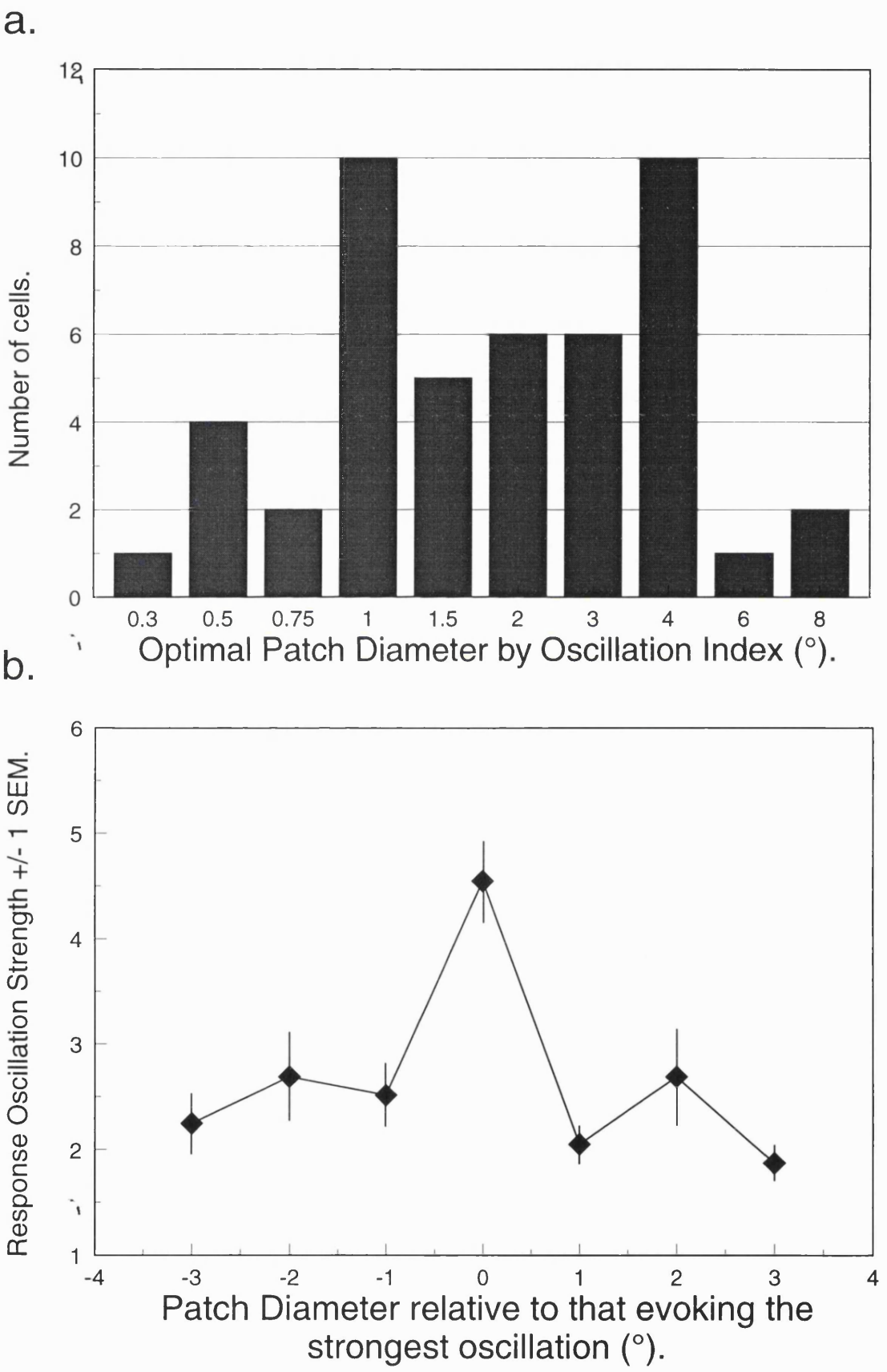

a.
Number of cells.
0
2
4
6
8
10
12
0.3
0.5
0.75
1
1.5
2
3
4
6
8
Optimal Patch Diameter by Oscillation Index (°).
b.
Response Oscillation Strength +/- 1 SEM.
1
2
3
4
5
6
-4
-3
-2
-1
0
1
2
3
4
Patch Diameter relative to that evoking the strongest oscillation (°).

Figure 29.

These plots show the patch tuning characteristics of oscillation indices values exhibited by the sampled population of cells recorded from primate V1. Plot **a** graphically represents the range of optimal patch diameters The mean optimal patch diameter for the population of 43 cells was 2.36+/0.26°. Plot **b** shows the averaged tuning profile for this population of cells, it can be seen that on average a cells propensity to fire a strong oscillatory response is band pass tuned with respect to patch diameter. The mean index of the strongest oscillatory response generated by an optimal patch was calculated to be 4.55+/-0.39.

Of the 43 cells in the sample, twenty-three exhibited strongest oscillations in responses to patches that were larger than those that evoked the largest response magnitude from the cell, indicating that stimulation of the areas immediately surrounding the classical receptive field was necessary to evoke a strongly oscillating response. In 12 cases the patch that evoked the largest response was larger than that evoked the largest oscillation index. Strongest oscillations were detected in the largest response magnitudes of only 8 cells. On average the mean optimal patch diameter defined by response magnitude for the whole population of cells was calculated to be 2.08+/-0.29°, similar to that calculated using oscillation index. However for the largest group in which patches evoking largest response magnitudes were smaller than patches evoking strongest oscillations, the mean optimal diameter from response magnitude was 1.194+/-0.14°, strongest oscillations were detected in a responses to patches with a mean diameter of 2.96+/-0.26°. This indicates that in the majority of cases (23/43 or 53%) the patch that evokes the largest oscillation is significantly larger (approximately 1.8°) than that which evokes the largest mean response. This has the implication, as 80% of the cells in the sample were patch suppressed, subject to response suppressing input when stimulated by grating patches that were larger than the classical receptive field, that suppressive inputs are involved in the mechanisms that bring about response oscillation.

Over the range of stimulus diameters used in this investigation, what is clearly apparent from the sample is the restricted area of visual space, over which a visual stimulus can evoke a strongly oscillating visual response from a cell. A significantly reduced oscillation index is detected when the stimulus is greater than 4° in diameter. This observation has implications for theories that deal with the role of synchronised oscillations and Gestalt perceptual theories, these emphasise the importance of continuous contours in generated temporally tagged networks of cells. The data presented here indicate that visual stimulation with continuous contours, in the form of sinusoidal gratings causes an attenuation in the strength of the oscillatory component of an evoked response, in all but about 10 % of the sample. The observations made so far suggest that networks of temporally tagged cells would instead be generated by spatially restricted gratings, or amongst cells at the ends or edges of a large grating stimuli. It was found that cells exhibit a strongest oscillation

in their responses to a limited range of grating patch diameters. It was found for the population of cells that were found to oscillate in response to such stimuli that the mean optimal diameter was 2.36°, somewhat larger than the mean optimal patch diameter determined from response magnitude measurements. The mean maximum oscillation index present in response to stimulation by a patch of optimal dimensions was calculated to be 4.54, this compares to the mean maximum oscillation index measured from the responses of cells to discontinuous bipartite stimuli, of 5.28.

The distribution oscillation frequencies.

From each auto-correlogram power spectrum three pieces of information were extracted, the oscillation index, amplitude and value of the peak frequency, this last section relates to the last of these parameters, the range of frequencies exhibited by the 45 cells in the sample that were found to oscillate. Figure *30* illustrates the range of different frequencies detected in significantly oscillating visual responses recorded in the primate, in the plot the distribution from responses to patches of grating, and responses to discontinuous bipartite stimuli are shown. It can be seen that in both plots all frequencies in the gamma range in this a plot are represented. However in responses to bipartite stimuli a greater number of oscillation between 36 and 52 Hz were detected.

Figure 30.

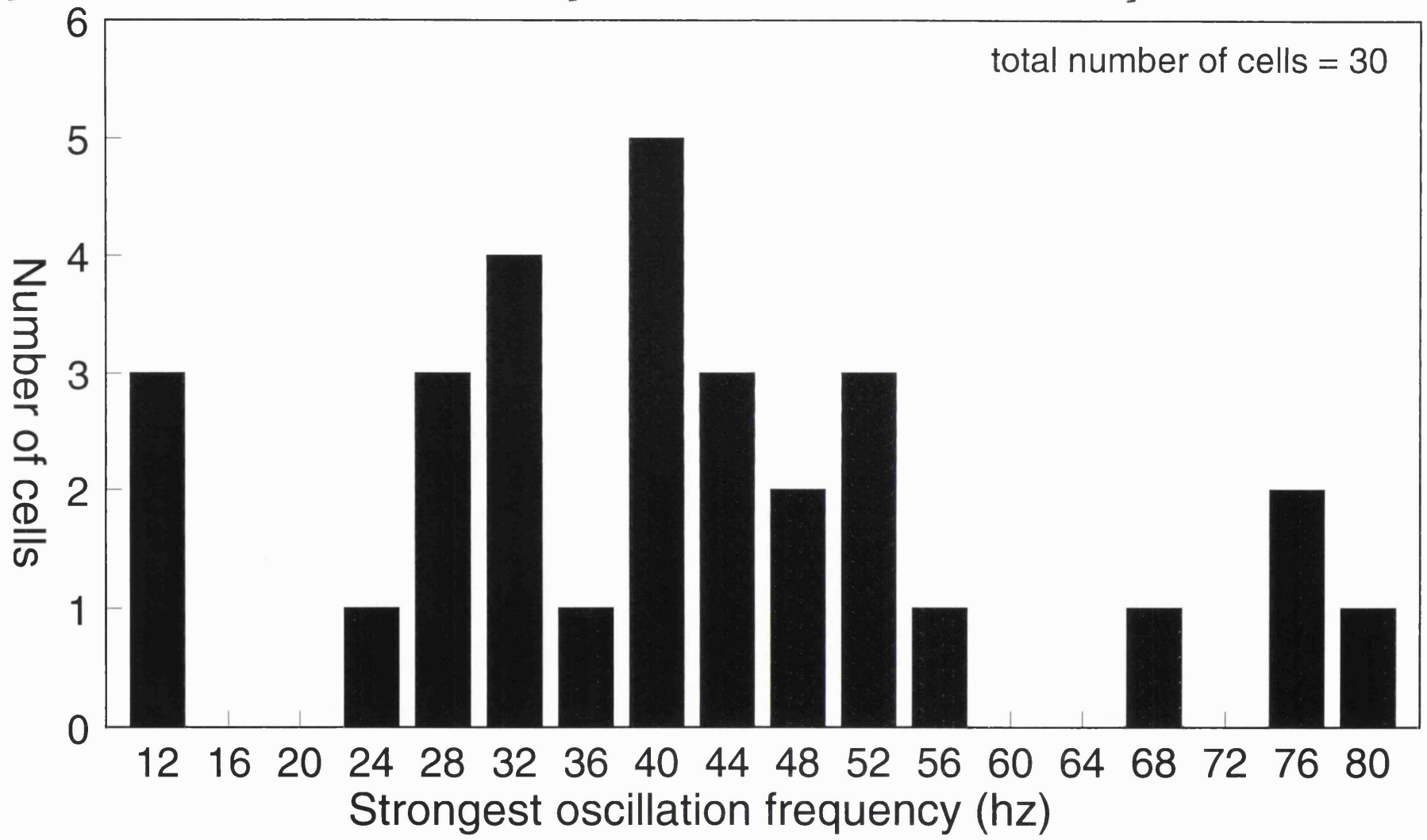

total number of cells = 30
Number of cells
0
1
2
3
4
5
6
12 16 20 24 28 32 36 40 44 48 52 56 60 64 68 72 76 80
Strongest oscillation frequency (hz)

Figure 30.

The distribution of frequency in the gamma range, between 28 an 80 Hz, that were detected for oscillations that were present in the visual responses of a total of 35 cells to continuous patches of gratings of various diameters and to discontinuous bipartite stimuli. It can be seen that in the entire sample of responses, oscillations at all frequencies were detected. Oscillations at the low frequency end of the gamma range were most often detected, both for continuous and discontinuous stimuli.

Cross-correlation analysis.

The single cell data presented above relates many examples where the properties of each cell can be manipulated by changing the orientation and direction of motion of the surround stimulation. This section will examine the data obtained from simultaneously recording the responses of pairs of cells responding to these complex stimuli. A central prediction following the single cell analysis is that the observations made of that activity should reflect the activity of a highly interconnected network of cells. The oscillations detected within the responses of many cells to focally discontinuous stimuli suggest that when the responses of cells pairs simultaneously stimulated in this way should be synchronised. Oscillation have both been proposed to occur because responses are synchronous and to cause cells to fire synchronously by making spike firing more predictable Likely sources of inter-connectivity that could bring about synchronicity are the widely reported networks of horizontally and vertically projecting axons that project within the striate cortex, between cells in these layers and also cells in sub-cortical centres such as the LGN as well as other extrastriate cortical areas such as V2 and MT. Because many of the context dependent of response changes reported here, were dependent on an orientation difference between a grating centred on the classical receptive and another in the surround, it might expected that synaptic interactions between cells with orientation differences of 45-90° would be detected. It would also be predicted that synchronous oscillations should be detected between such cell pairs responding to discontinuous stimuli.

Cortical synchrony in responses to contextual stimuli.

The visual responses of 18 pairs of cells recorded from primate V1, and 15 pairs from cat V1, were analysed using the cross-correlation techniques. Within this sample pairs with receptive field configurations meeting all four of the groups were present. With the exception of 1 pair in the primate and 2 in the cat, which were recorded from the same electrode, cells were recorded on horizontally separated electrodes, separations between 600 and 1100μm. 75% of the pairs recorded in both species were from electrodes separated by 1000-1100μm. Table *2* outlines the distribution between the four receptive field configuration groups of all the pairs recorded from the two mammalian preparations, and the types of interaction which were demonstrated between their responses in cross-correlograms. Of the total sample of 33 cell pairs recorded in the cat and primate, 12 contained cells that were tuned to orientations that differed by greater than 30°, 1 pair was recorded in the primate that contained cells with non-overlapping classical receptive fields that were tuned to orientations that differed by 67.5°. All fifteen recorded in cat V1 were stimulated with patches and bipartite stimuli, generally with a limited range of diameters and centre diameters. In the primate sample the cells in all eighteen pairs were analysed with patch stimuli with a wide range of diameters. Eleven pairs were also stimulated with bipartite stimuli with up to three different centre diameters.

Table 2. Response synchronisation as a function of receptive field configuration.

In cat V1

Pair number	Exp. and Cell numbers	Configuration group	Mono-phasic narrow	Mono-phasic wide	Oscillatory
1	4/b14	1	-	x	-
2	4/b23	1	-	x	-
3	5/a12	1	-	-	-
4	5/b12	1	-	x	-
5	5/c12	1	-	x	-
6	7/c24	1	-	-	-
7	8/a12	1	-	x	-
8	8/b12	1	-	x	-
9	8/c12	1	-	x	-
10	9/a13	2	-	x	-
11	9/a12	1	-	x	-
12	9/a23	2	-	-	-
13	9/b12	1	-	x	-
14	9/b13	2	-	x	-
15	9/b23	2	-	x	-

In primate V1

Pair number	Exp. And cell numbers	Configuration group	Mono-phasic narrow	Mono-phasic wide	Oscillatory
1	2/c12	1	x	-	-
2	2/l12	2	-	x	-
3	3/g12	1	-	-	-
4	3/c12	1	-	-	-
5	4/c12	1	-	x	-
6	4/d12	4	-	x	-
7	4/e12	2	-	x	-
8	4/f12	2	-	x	-
9	4/g12	2	-	x	-
10	4/h12	1	-	x	x
11	5/a23	2	-	x	x
12	5/b23	2	-	x	-
13	5/c13	1	-	x	-
14	6/a13	1	-	x	-
15	6/c13	1	-	x	-
16	6/e12	1	-	x	x
17	7a23	3	-	x	x
18	7b12	2	-	x	x

Analysis of simultaneously recorded responses to visual stimuli revealed cell pairs could exhibit two types of synchronisation. Most often single mono-phasic peaks were apparent in the centre of cross-correlograms. Less frequently cross-correlograms were found to have oscillating profiles, with multiple peaks surrounding a central peak. Gabor functions could be fitted to these distributions, they have been reported to reflect the synchronisation of response oscillations. Both non-oscillatory and oscillatory response synchronisation peaks similar to those reported in many previous investigations were found. Mono-phasic peaks were found to have widths that ranged from 1ms up to 60 ms, the narrowest peaks, 1ms or less, have been proposed to be due exclusively to single monosynaptic connections between cells, the wider peaks, are thought to come about because cells receive common input, it has also been suggested that reciprocal patterns of interactions between populations of cells (Wilson and Bower, 1992, Bush and Douglas, 1991 and Singer, 1993). The temporal distribution of such peaks would thus reflect differences in the time taken for activity in one recorded cell to influence that in others. Cross-correlation of different stimulus responses resulted in peaks that were centred at a range of different positions with respect to the cross-correlogram origin. This interval reflects the average time between an action potential fired by one cell and a synchronised action potential fired by the

other recorded cell. In this analysis intervals ranged between 0 ms and 30 ms. When oscillating cross-correlograms were detected, they typically contained three or more peaks that were distributed symmetrically around the origin of the cross-correlogram. Fitting Gabor functions to these cross-correlation functions provided an accurate way of determining the amplitude and frequency of the oscillation. Synchronised oscillations were detected in the same frequency ranges as the response oscillations that were detected in the previous phase analysis. Pairs of cells were found that synchronised responses oscillating in the gamma frequency range and at 12-16 Hz. Of the three types of synchronisation described above, narrow and wide mono-phasic and oscillatory, it was interesting that different responses of a given pair of cells could generate groups of cross-correlograms that could be distributed amongst the three synchronisation groups. For instance a pair of cells could interact in a way that generated a wide mono-phasic peak during a response to one stimulus, in a response to another stimulus the interaction would be classed as oscillatory after FFT and Gabor analysis.

Each pair of cells was presented with between 150 and 600 separate, spatio-temporally unique visual stimuli. They were presented with a range of different orientations, diameters, and if they were bipartite conditions then centre-surround orientation difference and centre diameter were variable. Typically cell pairs did not exhibited synchronised responses during responses to all the stimuli that were used. Response synchronisation was detected only when the cells involved were responding to a very small number of the stimuli, typically between 1 and 10% of the total number that were used. Thus statistically significant response synchronisation between any given pair of cells showed high degree of specificity for particular stimulus configurations. When detected peaks were correlated with the configurations of the stimuli that evoked the responses from which they were calculated, and with the configuration of the receptive fields of the recorded cells, it was found that stimuli that caused response synchronisation contained features to which each of the cells were tuned. It was the case that synchronisation was not simply specific to certain visual responses but to responses to certain configurations of stimulus.

When recorded cells pairs were in receptive field configuration groups 2 and 4, that is, they had preferred orientation differences greater than 30°, synchronisation between visual responses was not detected when they were stimulated with aligned bipartite gratings, presented at any orientation. Interaction were only detected when the cells involved were stimulated with discontinuous stimuli. These stimuli contained gratings presented at two different orientations, and it was usually the case that the stimuli that evoked interacting responses contained one grating presented at an orientation that was optimal for one of the cells while the other grating was optimal for the other cell. Figure *31* features a temporal interactions between the responses of two cells in group 2, recorded from primate primary visual cortex that demonstrates this point. They had partially overlapping receptive fields and preferred orientations that differed by 45°. The temporal interaction between the responses is signified by a peak (*31d*) that is displaced to right of the origin, and distributed between 2 ms and 8 ms, with a peak amplitude at 5 ms. This interaction was only active between the cells when they were stimulated with certain very specific configurations of a bipartite grating, in this case when the centre grating with a diameter of 1° was presented at an orientation that bisected the angle between the preferred orientations of the cells, and the surround was optimal for the cell with tilted field in the figure. A bipartite grating with centre and surround orientation switched, also activated this interaction, only discontinuous stimuli fulfilling these orientation criteria activated the interaction, no other stimuli did so. It can be seen that none of the aligned stimuli that are shown (*31a-c*) activated the interaction. Stimuli *b* and *c* were presented at the orientations contained within *d* they did not evoke interacting responses, it was necessary that they should be contained with the same stimulus.

Figure *32* features a pair of cells with a receptive field configuration in group 4, the peaks that were generated from the responses of these cells to 8 stimuli are shown in this figure. It can be seen that the cells did not fire in a way which was temporally correlated by neuronal connectivity when stimulated with spatially coherent patches of grating presented at their preferred orientation or at a bisecting angle. However the bipartite stimuli which are featured generated responses which were synchronised in a way that was signalled by a temporally offset peak. The recorded cells had

Figure 31.

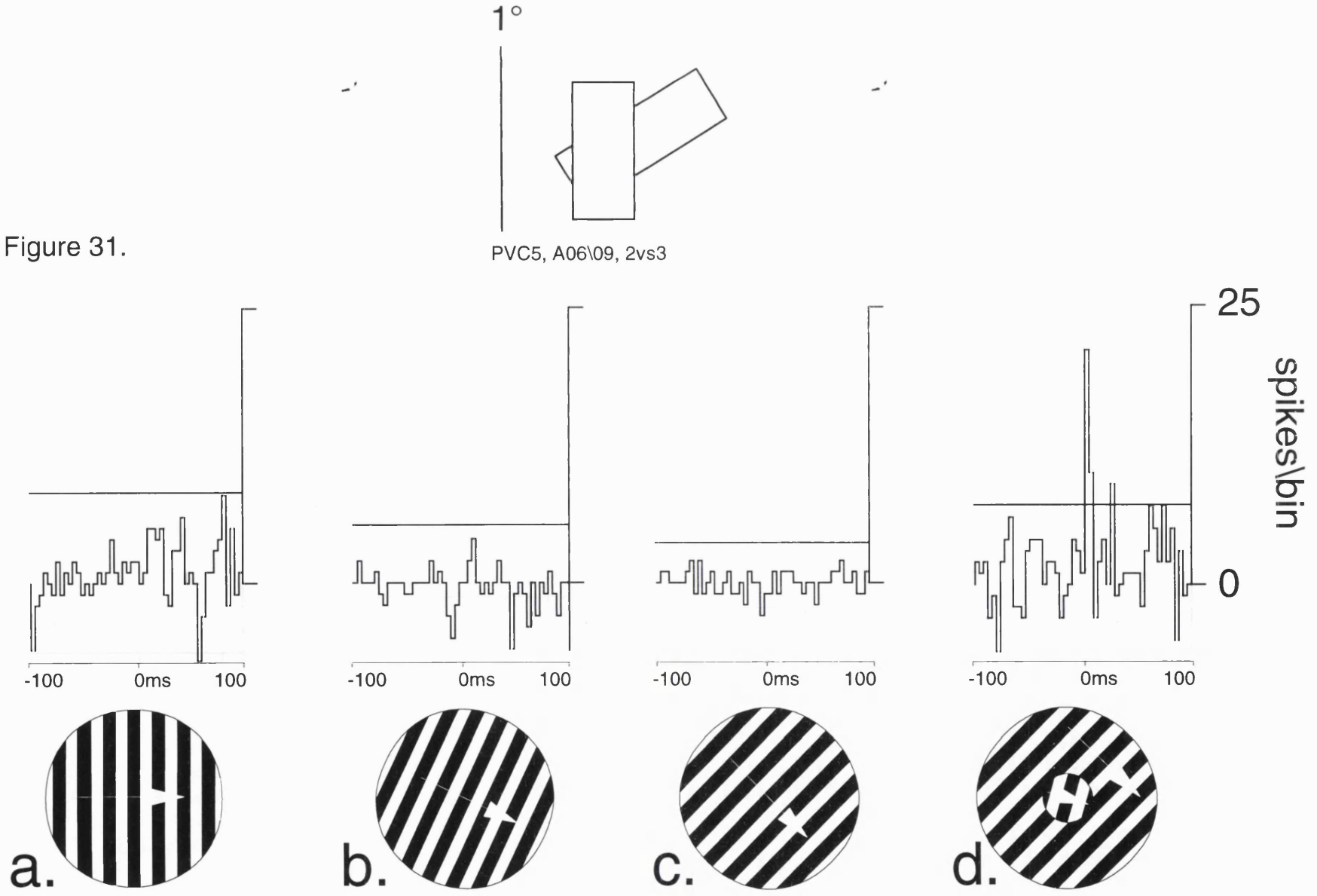


Figure 31.

Cross-correlations obtained from the responses two cells recorded in primate primary visual cortex, to various continuous and bipartite discontinuous stimuli. All stimuli were displayed with spatial frequencies of 2 cpd and temporal modulation frequencies of 3Hz. The centred reference cell was tuned to an orientation of 0°, while the other was tuned to 45°. Cross-correlation of responses to continuous full field gratings presented at optimal (**a.** and **c.**)and bisecting (**b.**) orientations did not generate any peaks. However when the cells were stimulated with specific discontinuous bipartite grating conditions featured in **d.**, a peak was detected which indicated response synchronisation between the cells. This peak indicates a connectivity path between the two cells, the peak is displaced from the correlogram origin by a 4-6 ms latency. Thus synchronised pairs of spikes were temporally separated by this delay. The stimulus that activated this connection contained a 1° centre presented at a bisecting angle with a surround that was optimally oriented for the other cell. This was the largest synchronisation peak that was detected when the responses of these cell were correlated, only discontinuous stimuli were found to evoke such responses. Thus synchronisation was a stimulus dependent phenomenon occurring only for stimulus condition like the one that is shown. Cross-correlograms were calculated with fifty-one bins of 8 ms duration. Those that are shown are the result of a binwise subtraction of the modulation averaged shift predictor from the raw cross-correlogram, thus any significant peaks that are visible are the result of synchronisation between the cells. Each correlogram contains a horizontal line, a peak exceeding this limit is statistically significant at the 99.5% level.

Figure 32.

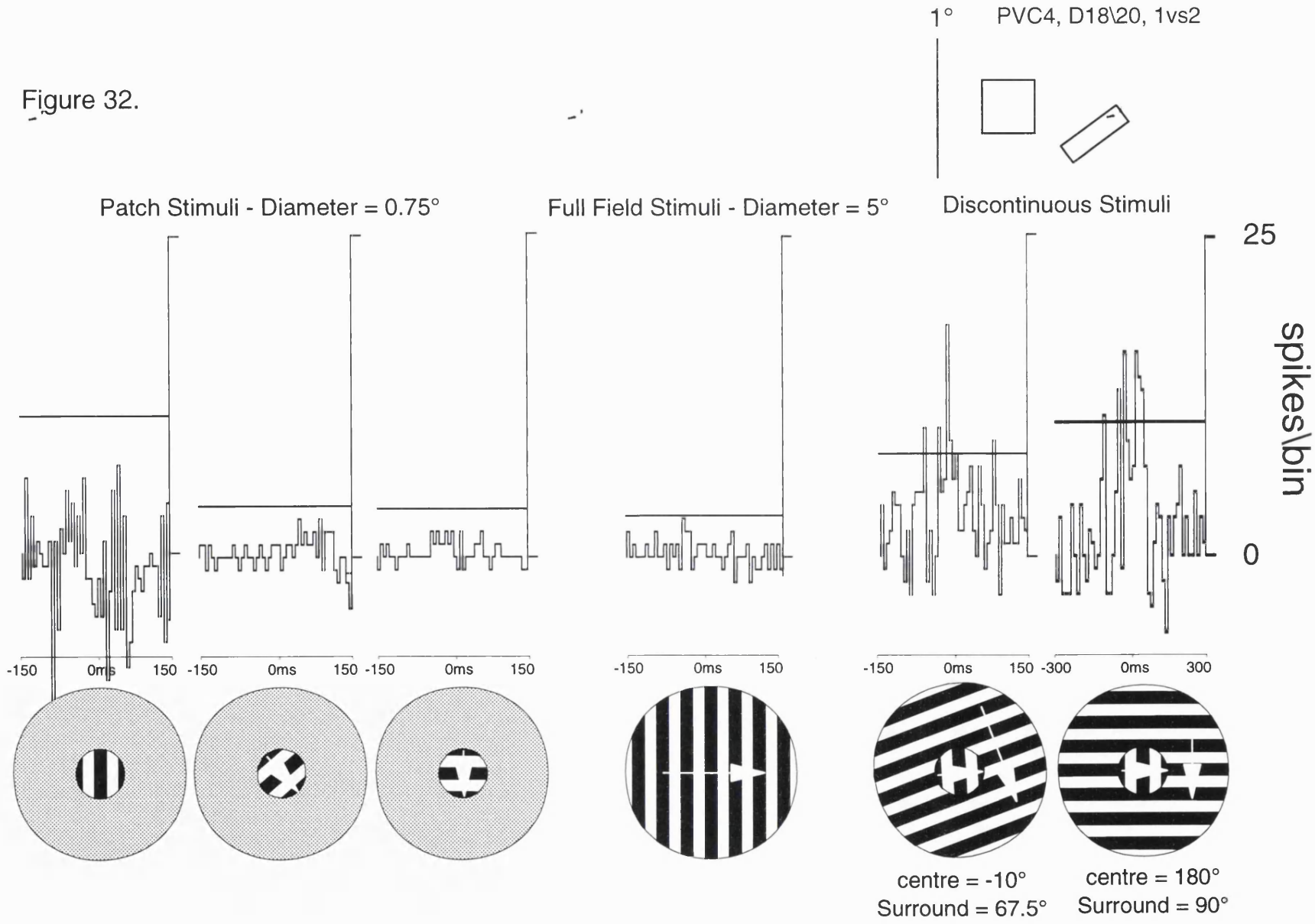

1°
PVC4, D18\20, 1vs2
Patch Stimuli - Diameter = 0.75°
Full Field Stimuli - Diameter = 5°
Discontinuous Stimuli
25
spikes\bin
0
-150
0ms
150
-300
300
centre = -10°
Surround = 67.5°
centre = 180°
Surround = 90°

Figure 32.

Cross-correlograms generated from the responses of a pair of cells recorded from primate V1. Cells were simulated with circular patches of sinusoidal grating of variable diameter and orientations and discontinuous bipartite stimuli All stimuli were presented at a spatial frequencies of 3 cpd and were modulated at a temporal frequency of 3Hz.. Shown are correlograms generated from responses to the smallest and largest patches presented at the optimal orientation for each cell and a bisecting angle. No peaks were detected in these correlograms, nor for any continuos stimuli presented with any diameter or orientation. However when these stimuli were combined into a bipartite grating configuration centred on the left receptive field, cross-correlation revealed a stimulus dependent response synchronisation peaks. In the first, a connectivity path between the cells is the substrate for a peak that is displaced to the right of the origin by 14 ms. When the centre and surround orientations were interchanged a smaller peak was again detected. The cross-correlogram generated from the responses to another discontinuous stimulus, shown here, shows that the responses of these cells to this stimulus are synchronised in a way which generates a significant biphasic peak, distributed on both sides of the origin, both are displaced by 25 to 30 ms. Cross-correlograms are displayed with fifty-one bins of 6 and 12 ms duration. Each cross-correlogram is shown with a line which highlights the significance criteria, at the level of 99.5% for any peak generated from the visual responses of the cells to the stimuli that are shown.

non-overlapping fields, they were spatially distributed such that when they were stimulated with a bipartite grating stimulus with a centre diameter of 0.75°, one was stimulated by the centre patch, the other, by the surround. The two stimulus configurations which are shown on the right in figure *32,* are two of a very limited number that evoked correlated responses from the cells. The cells fired in a correlated manner, very specifically to these stimuli, if the orientations of the centre and surround of each stimulus were changed, or the centre diameter increased, even slightly, no peak was detected in the cross-correlogram of the cell's responses. The stimuli that generated correlated responses are both spatially discontinuous. The inner and outer grating orientations in this stimulus are optimally oriented for the reference and other cell respectively. When stimulated in this way a correlogram peak which was indicative of the cell stimulated by the centre element firing consistently before the surround stimulated cell, there was a constant interval between the synchronised spikes by these cells of approximately 8 ms. It was the case that, as with the cells featured in figure *31,* when the centre and surround orientations in the penultimate stimulus in figure *32* were interchanged the cells were again found to exhibit synchronised responses. The stimulus featured on the furthest right of this figure is the similar to that was previously discussed, however the centre travels in the opposite direction, it can be seen that this stimulus generates a cross-correlogram with two peaks, either side of the central bin and displaced by approximately 25 ms from it, in each case. This distribution of peaks is consistent with reciprocal interactions between the cells with a relatively long latencies.

The neurone pair featured in figure *33* were recorded simultaneously from electrodes that were horizontally separated by 1 mm in layer IV of the primary visual cortex of a cat. They were classified in field configuration group 2, they had overlapping orthogonal receptive fields. When stimulated with the bipartite grating shown, cross-correlation analysis showed that the responses were synchronised, resulting in a peak that was displaced to the right of the origin. No other stimuli were found to evoke responses from this pair of cells that were temporally correlated, thus the functionality of the observed interaction is highly stimulus selective. The stimulus that evoked the correlated responses contained a centre and surround grating which were orthogonal and each was oriented at preferred orientation of one of the cells. The centre was

Figure 33.

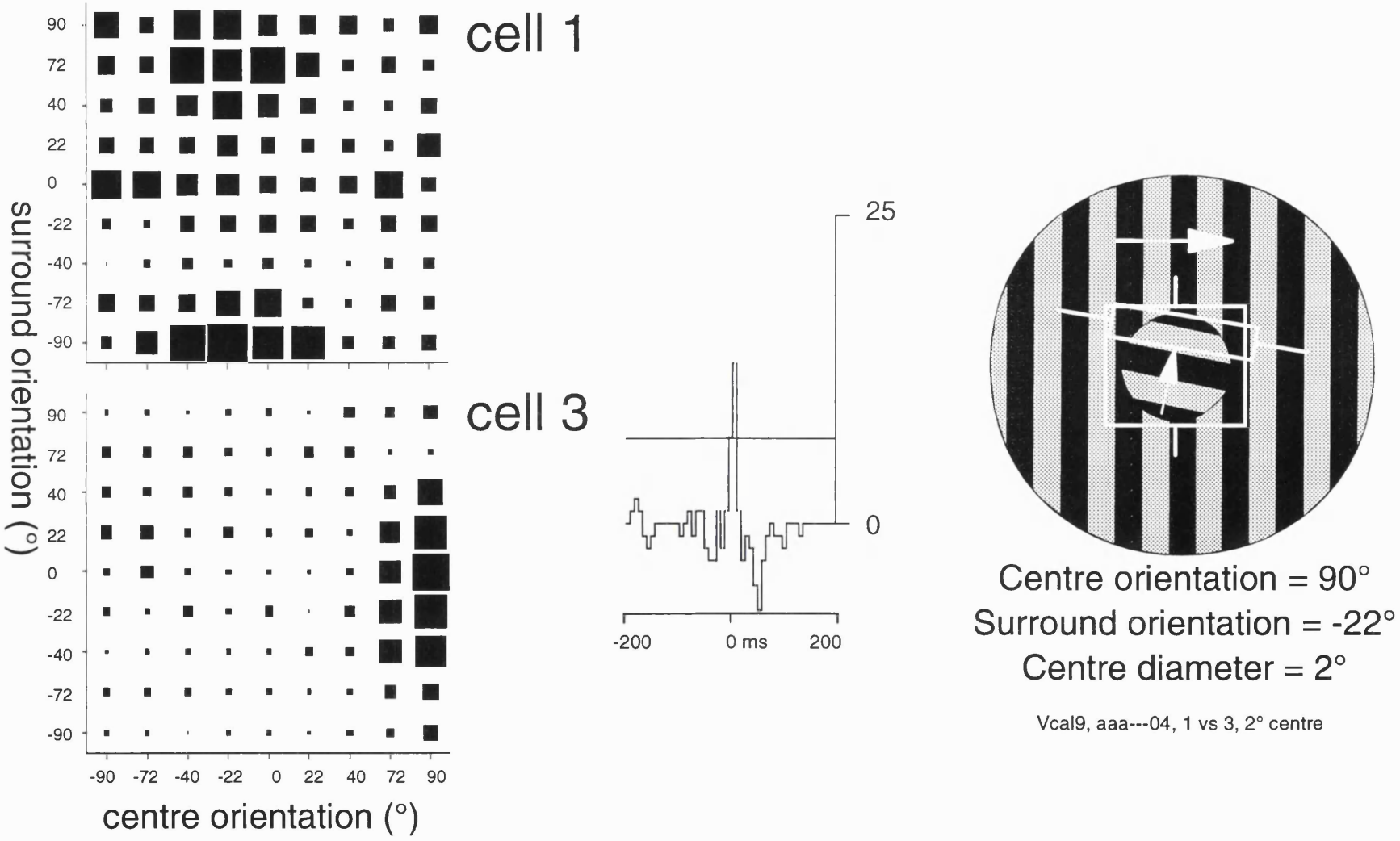

cell 1
cell 3
surround orientation (°)
centre orientation (°)
90
72
40
22
0
-22
-40
-72
-90
25
0
-200
0 ms
200
Centre orientation = 90°
Surround orientation = -22°
Centre diameter = 2°
Vcal9, aaa---04, 1 vs 3, 2° centre

Figure 33.

A cross-correlogram generated from the responses of a pair of cells recorded from electrode that were separated by 1mm, these cells had receptive fields that were orthogonally oriented. All stimuli were presented with a spatial frequency of 0.66 cpd and were modulated at a temporal frequency of 2 Hz. When these cells were stimulated with continuous grating fields presented at all orientation and with diameters ranging from 2° to 10°, cross-correlation analysis of their responses did not reveal peaks indicative of connectivity co-ordinated synchronisation. However when they were stimulated with the discontinuous bipartite sinusoidal grating with a 2° centre synchronisation was apparent. Shown is the condition that generated synchronised responses from the cells, the peak that was displaced to the left of the origin in a temporal zone between 4 and 8 ms. This result as shown as the result of subtracting the modulation averaged shift predictor from the raw correlogram. The peak also exceeds the level that indicate statistical significance at the 99.5% level. The centre and surround are each at an orientation which is optimal for one of the cells. Cross-correlogram is displayed with fifty-one 6 ms bins.

Figure 34.

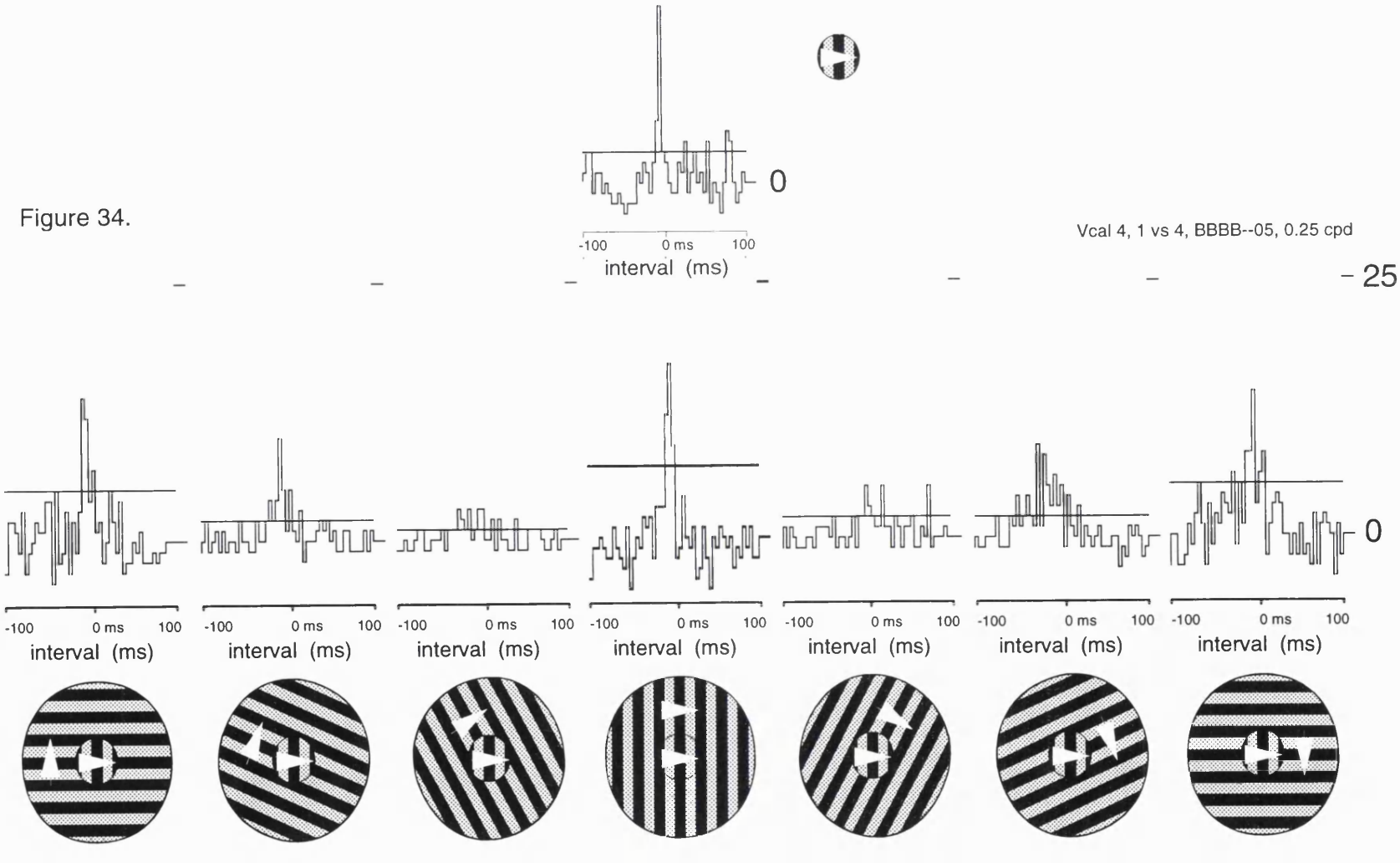

25
0
-100
0 ms
100
interval (ms)
Vcal 4, 1 vs 4, BBBB--05, 0.25 cpd
25
0
-100
0 ms
100
interval (ms)

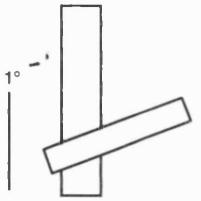
Figure 34.

Cross-correlogram from two S type cells recorded from the same electrode in layer IV of cat V1. The cells were stimulated by a patches of grating and bipartite stimuli with 4° centres. All were displayed with a spatial frequency of 0.25 cpd and a temporal frequency of 2 Hz. This figure depicts stimulus dependent changes in connectivity between two cells tuned to the same orientation as a function of surround orientation. The peaks that were detected were all displaced from the central bin in the same direction by 4-8 ms, they are displayed with 4ms bins. Horizontal lines indicate statistical significance of the observed peak at the 99.5% level. It can be seen that the direct connection is only active when the cells are stimulated with optimally oriented grating patches and discontinuous bipartite gratings with orthogonal surrounds. When the centre-surround orientation difference was less than 90°, but more than 0°, no synchronisation interaction was detected between the cells.

optimal for the reference cell, while the surround was optimal for the other. Figure *34* features another a pair of cell recorded from the cat primary visual cortex that had a group 1 receptive field configuration, their receptive fields shared the same area of visual space and were tuned to the same orientation. Again this figure illustrates the stimulus specificity of temporal interactions between the responses of cells to visual stimuli, 8 of which are shown. It can be seen that these cell exhibit correlated responses to both aligned and discontinuous bipartite condition, however it can be seen that the interaction between the cells is highly dependent on the surround orientation. To bipartite stimuli response synchronisation is detected when the surround is aligned *and* orthogonal with the centre, and non-significant when the surround is presented at oblique orientations. This indicates that as well as input from cells with different orientations contributing to the responses of cells presented with discontinuous stimuli, such responses are also the product of cells with similar orientations. Iso-oriented cells are actively connected when stimulated with optimally oriented spatially coherent stimuli. In the case of the pair of cells that is featured, the connection between them is not active when the surround orientation is oblique.

Temporal interactions between the responses of a pair of cells did not always generate peaks which were identical in their temporal distribution, it was the case that the peaks that were displaced from the central bin could move position with respect to that bin to the extent that the responses to one stimulus could generate a peak to the right of the origin, and responses to another subtly different stimulus could generate responses to the left of the origin. This behaviour was detected in the responses of two pairs of cells recorded in the primate and stimulated with bipartite gratings. In figure *35* it is apparent between cells in group 2. It can be seen in this figure that when the responses of these cells were correlated they revealed temporal interaction in three cases. The cells were stimulated with very many stimulus configurations, only these generated peaks. Cross-correlograms are shown that were calculated from the responses to four aligned full field stimuli presented at a range of optimal and bisecting orientations. The correlograms typically represent those for which no significant interaction was detected. Interactions were activated by stimuli *f* and *g* in figure *35,* where it can be seen that interchanging the centre and surround orientation in a bipartite stimulus presented to the cells can radically change the nature in the

Figure 35.



PVC4, G02\04, 1vs2

25

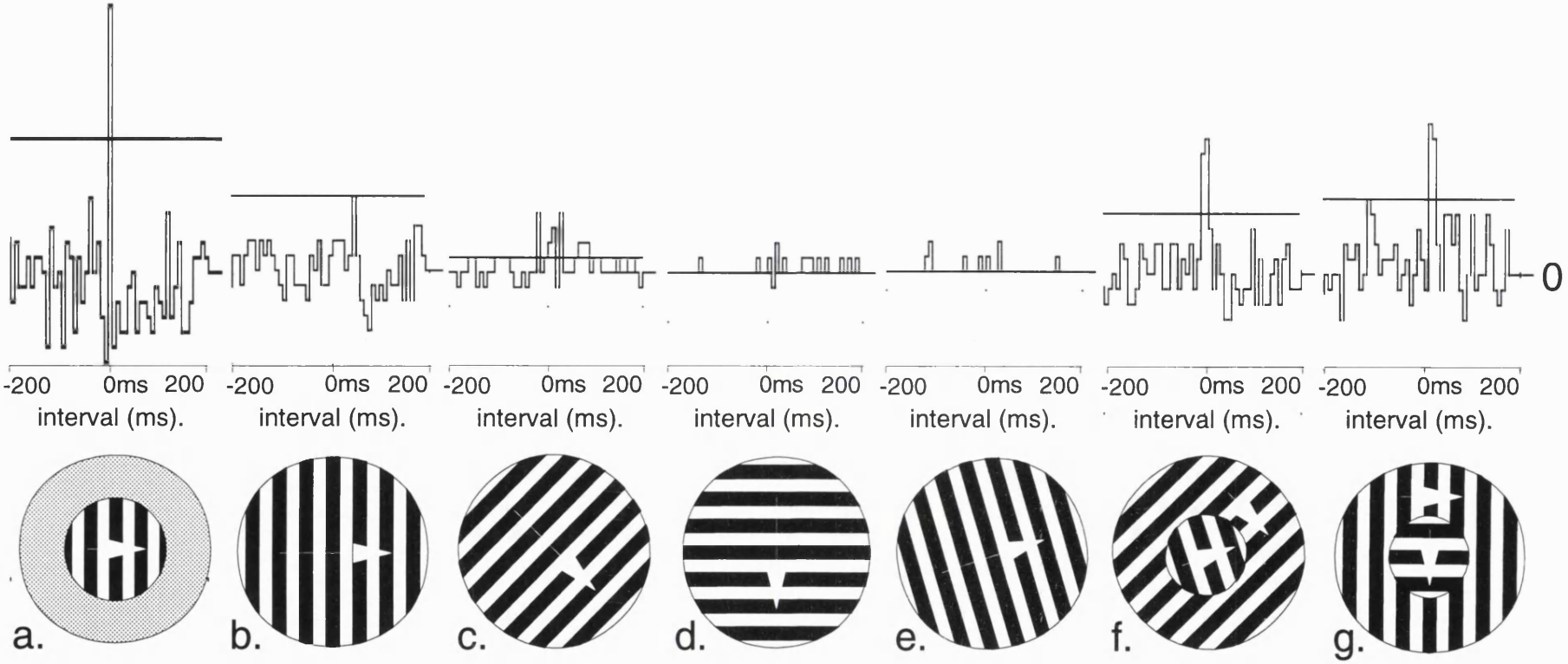


Figure 35.

This page features the non-oscillatory synchronisation between the responses of a pair of cells recorded in primate V1, with a receptive field configuration in group 2, to various configurations of grating stimuli. All of these were presented with a spatial frequency of 2 cpd and a temporal frequency of 3 Hz. **a** features a 2° patch that was optimally oriented for one of the cells, but caused them both to synchronise their responses with no temporal offset. This was the only stimulus orientation which caused this to happen. When another patch was presented at the same orientation, but 5° in diameter (**b**), no synchronisation was detected. **f** and **g** are two other stimuli which activated connectivity between the cells, the correlogram above **f** shows that the cells synchronise their output when stimulated with this bipartite grating, in which the centre is optimal for one cell, while the surround is optimal for the other the peak is distributed over interval between -15 and +3 ms. When they are stimulated with **g** which is similar to **f** in that both stimuli contain orientations which are approximately optimal for the cells involved, however in the case of stimulus **g** the centre and surround orientation have been approximately interchanged with respect to **f**. In **g** it is the centre that is optimal for the titled cell and the surround that is optimal for the cell presented as vertical in the field map. The peak shown in the correlogram associated with **g** was displaced to the right of the origin by 25 ms, as opposed to the left, which was the case for the interaction activated by stimulus **f**. **g** and **f** were the only bipartite conditions to evoke synchronised visual responses from these cells. Correlograms are displayed with 8 ms bins, the horizontal lines indicate statistical significance at the 99.5% level.

interaction. Another interesting feature of the interactions that were detected between the responses of these cells was that when they were stimulated with a small grating patch with a diameter of 2° an interaction signified by a peak distributed symmetrically over the central bin was detected. Three further pairs of cells were found that exhibited interactions that gave rise to both displaced and centrally located peaks.

In the previous section it was related that, using auto-correlation analysis, of the cell sample in the cat 26% were found to oscillate when visually stimulated, in the primate 81% of cells recorded were found to oscillate. Table 2 shows the cell pairs in the entire sample which were found to oscillate synchronously. Oscillatory response synchronisation was not detected between pairs of responses recorded in the cat, of the pairs tested there was only one where oscillating visual responses were recorded from both participating cells. However in the primate there were 5 pairs for which this form of interaction was detected. In total there were 13 pairs in which both cells oscillated, thus these oscillation were not found to synchronise in 8 pairs. Of the remaining 5 pairs there were 2 in which neither cell was found to respond in an oscillatory fashion and 3 in which only one of the cells in each pair oscillated.

Of the five pairs the responses of which generated cross-correlograms that were periodically modulated at a significant level, in four the periodic modulation was in the gamma frequency range, and in one case it was at a frequency between 12-16 Hz. Interestingly it can be seen that all five pairs that exhibited oscillatory synchronisation, also responded synchronously to generate mono-phasic cross-correlation peaks. These two modes of synchronisation were activated by presentation of different stimuli. Synchronised oscillatory interactions occurred between pairs of cells that contained at least one cell, for which large oscillation indices were obtained from the response that was being correlated. The detection of strong oscillations within single responses to certain stimuli correlated with the detection of significant levels of oscillation within cross-correlograms generated from responses simultaneously recorded from other cells that were found to exhibit stimulus specific oscillations. Thus in this investigation though all cells in 13 pairs had the capacity to oscillate stimulus specifically, with the techniques used, only the strongest oscillations were found to

synchronise. Where the cells involved in cross-correlation oscillated to a lesser extent, synchronisation was not detectable. Though these 8 pairs of oscillating cells were not found to exhibit oscillating synchronisation, their cross-correlated responses did generate mono-phasic peaks which were indicative of non-oscillatory synchronisation.

As was the case with the non-oscillatory temporal interactions that were reported in table *2*, the occurrence of oscillating temporal interactions between the responses of pairs of cells was specific to certain pairs of stimulus responses. A pair of cells typically exhibited oscillating synchronous responses to only between 1 and 5% of the grating patch and bipartite stimuli they were presented with. In a previous section of this results report the stimulus specificity of single-unit oscillatory responses were described, the largest group of cells were found to oscillate most strongly when presented with discontinuous bipartite gratings, oscillations were not detected within responses to coherent aligned full field gratings. Oscillatory responses to coherent stimuli was a property only of 7% of the sample. Cross-correlation analysis of pairs of responses revealed that the stimulus specificity of oscillatory synchronisation reflected the stimulus specificity of single-unit response oscillations. Of the cell pairs that were found to exhibit oscillatory synchronisation, 4 were stimulated with both discontinuous and aligned stimuli, in one case only aligned stimuli were used. All the cells in the pairs stimulated with discontinuous stimuli were found to exhibit strongest response oscillation to those stimuli. When the responses of those cells were cross-correlated oscillatory response synchronisation was only generated from responses to discontinuous stimuli, that contained strong oscillations. The stimulus specificity with which oscillatory response synchronisation was detected is related in a number of examples discussed below.

A pair of cells that exhibited non-oscillatory and oscillatory response synchronisation are featured in figures *36*. The featured cross-correlograms are the results of subtracting the shift predictor, averaged over all trials, from the raw function generated from responses to stimuli that are also shown. In figure *36* it can be seen that the temporal interactions illustrated by some of the cross-correlograms are periodic to some stimuli, and non-periodic to others. The pair of cells were recorded from layer IV of primate V1, they had a receptive field configuration which was

Figure 36.

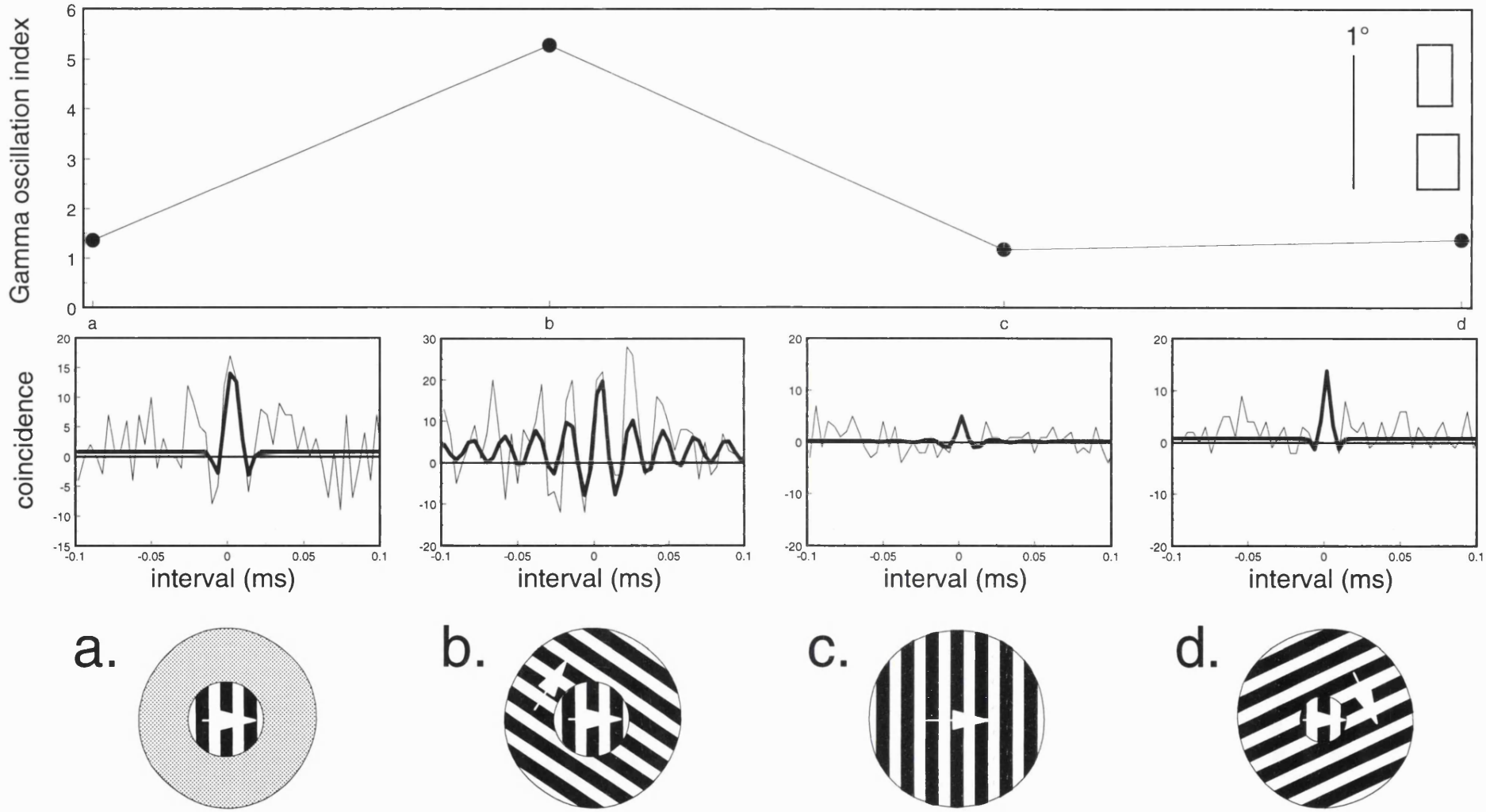

Gamma oscillation index
1°
a
b
c
d
coincidence
interval (ms)
interval (ms)
interval (ms)
interval (ms)
a.
b.
c.
d.

Figure 36.

This illustrates the changes in the strength and nature of the synchronised response epochs, between a pair of cells recorded in primate V1, that were presented with various configurations of sinusoidal grating stimuli. All stimuli were presented with spatial frequencies of 2 cpd and temporal frequencies of 3 Hz. Cross-correlograms are displayed with 4 ms bins, and are the result of subtracting the modulation averaged shift predictor from the raw function. Shown in **a.** is the results obtained from stimulating with an optimally oriented circular patch of grating with a diameter of 1.5°. **b.** shows the result that was obtained from correlating responses of the cells to a discontinuous bipartite grating condition, the centre of which was presented at the same orientation and diameter as patch **a.**, but was surrounded by a grating presented at an orientation of -67.5°. This interaction was found to involve a significant level of oscillation at a frequency of 45 Hz. This is evident in the oscillation index value that was obtained from the cross-correlogram and the fact that this was the only one of the four correlograms to which a significantly oscillating Gabor function could be fitted. The responses of the cells to a 6° full field (**c**), did not correlate to generate a significant peak, however when the cells were stimulated with a bipartite stimulus with a 0.5° centre (**d**), responses correlated to generate a significant non-oscillatory synchronisation peak.

classified in group 3, that is, iso-oriented but non-overlapping. Stimuli that generated these two types of interaction between this pair of cells had characteristics in common, but also some specific differences. Oscillatory cross-correlograms were only detected when the cells were presented with stimuli, that in a previous section, were associated with the evocation of oscillatory response dynamics. It can be seen in figure *36*, that the strongest response synchronisation was detected when the cells were stimulated with spatially restricted, optimally oriented grating patch (*a*) that just covered both fields, or discontinuous bipartite gratings (*b* and *d*). In comparison to these interactions any temporal interaction between the responses of cells to full field stimuli (*c*) was very limited. All the cross-correlation functions are shown with their best-fit gabor function. Stimulus *a* generated a high degree of synchronisation, distributed over the central bin, single side-lobes are also visible around this peak but they are asymmetric, and the gabor fitting program failed to detect them, the oscillation indices extracted from this cross-correlogram was below the limit set for a significant oscillatory component. However when another grating shifted from the cells' preferred orientation by -67.5°, was introduced around *a*, to make the bipartite condition *b*, presentation evoked responses which were temporally related in a way which generated a highly oscillatory cross-correlogram. This is evident in the shape of the best fit gabor function, which has many side-lobes, this function and the oscillation index obtained from this correlogram both met the criterion necessary for the response synchronisation to be considered oscillatory. The frequency of the oscillation within this correlogram was found to be 48 Hz. A typical interaction between responses evoked by a coherent full field stimulus are shown next, there is a small central peak but oscillatory temporal structure was not detected at any significant level within this cross-correlogram. The last correlogram that is shown illustrates that the cells fired anatomically synchronised responses when presented with the discontinuous stimulus with a small centre diameters (in this case 0.5°), this interaction did not meet the criterion necessary to be considered oscillatory, investigation of the temporal structure of the responses used to generate this cross-correlogram showed that neither contained a significant level of periodicity in either frequency range. Comparison of data obtained for each interaction between the responses of this pair of cells, reveals that the strongest oscillation is detected in the cross-correlogram that is generated from the responses to the discontinuous stimuli

that has a centre which is 1.5° in diameter. This observation is paralleled by the observation made in the previous section (see figure *15*) that cells exhibit the highest level of response oscillation when stimulated with bipartite gratings with centre diameters of approximately 1.5°. Examination of the receptive field map also shown in figure *36*, indicates that this dimension precisely covers both fields. Other dimensions can be seen to generate interactions with reduced rhythmical components.

Cross-correlograms with oscillatory components were also calculated from the responses of cells with widely different preferred orientations. A typical pair of cells that exhibited this behaviour is featured in figure *37*, these cells had overlapping orthogonally oriented receptive fields. An extensive examination of the response interactions of these cells to a wide range of patch and bipartite gratings revealed that they, like the previously featured pair, fired synchronised responses selectively to discontinuous stimuli. No interactions are visible in correlograms generated by responses to optimally oriented or bisecting full field stimuli. The figure features a plot which contains the relative indices of the oscillations within cross-correlograms generated from the responses of the cells to various patch and bipartite stimuli that are also shown. It can be seen that oscillations present in cross-correlograms generated from the responses to discontinuous stimuli are quantitatively stronger than those generated from any other type of stimulus, this observation is the same as that, that could be made of the pair of cells featured in figure *36*. However as well as the responses of these cells interacting in a way to generate the correlogram in figure *37c*, to other specific stimuli, the responses were found to generate a cross-correlogram that contained a non-oscillatory interaction in the form of a peak that was temporally offset from the correlogram origin. The nature of the interaction between these cells changed from a non-oscillating to an oscillating interaction in the gamma frequency range apparent in *37c*, as the diameter of the centre increases from 0.5° to 1.5°, at centre diameters larger than this, no interactions is visible. The change in the nature of the interaction parallels the change in the temporal structure of one of the cells. Strong gamma oscillations are selectively present in responses to discontinuous stimuli with 1.5° centres of one of the cells.

Figure 37.

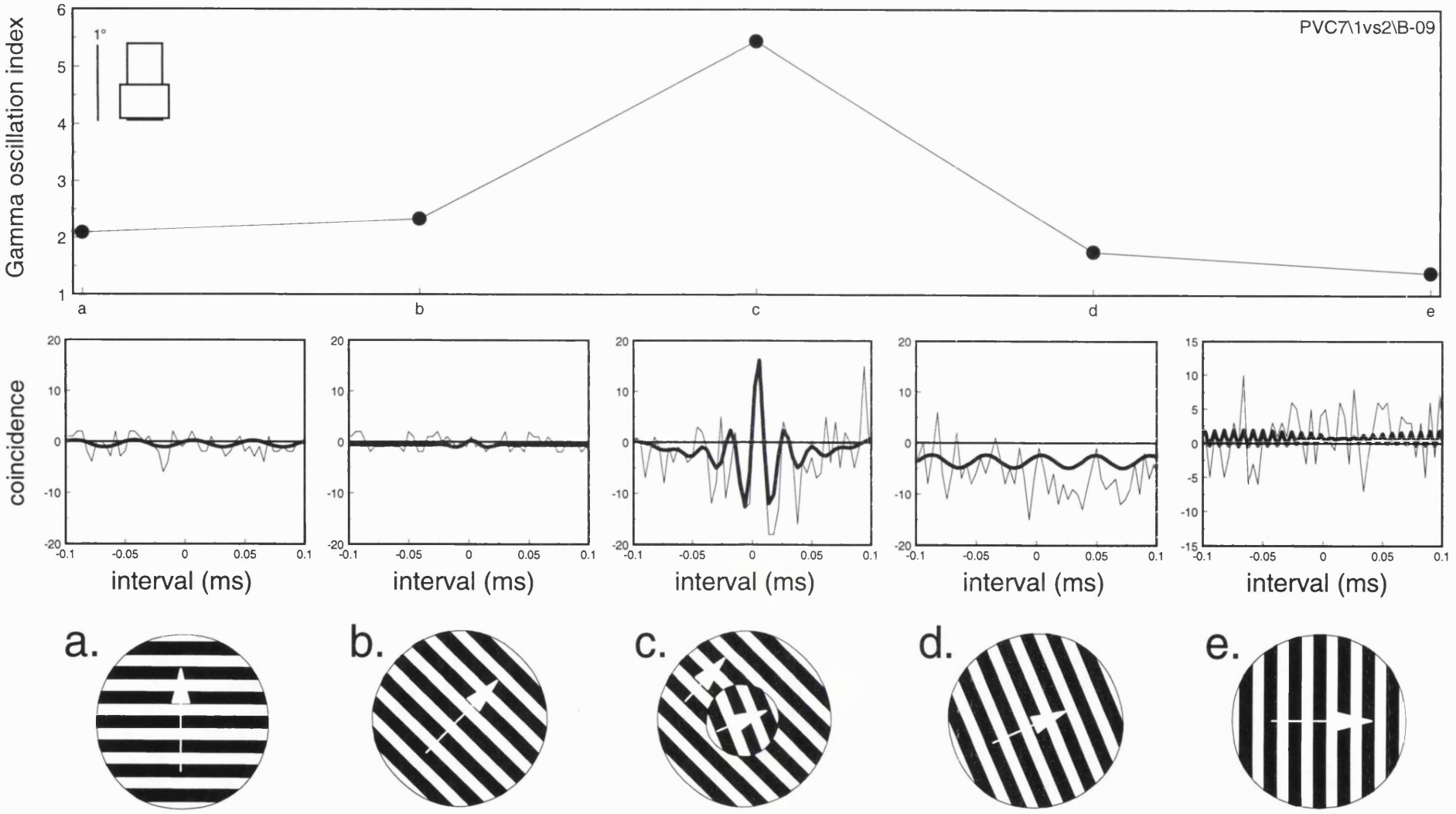

Gamma oscillation index
PVC7\1vs2\B-09
1°
a
b
c
d
e
coincidence
interval (ms)
interval (ms)
interval (ms)
interval (ms)
interval (ms)
a.
b.
c.
d.
e.

Figure 37.

This figure depicts the temporal interactions between the responses of a pair of cells recorded simultaneously in primate V1. All stimuli were displayed with spatial frequencies of 3 cpd and temporal frequencies of 3 Hz. These had receptive fields that overlapped but had mutually orthogonal optimal orientations. The stimuli (**a-e**), the interactions they generate and the strength of the oscillation in the gamma frequency range are shown. It can be seen that the only stimulus that evoked responses that were significantly oscillatory synchronised was stimulus **e**, this was a discontinuous bipartite stimuli, it had a centre diameter of 1.5°, which was oriented to -22.5°, the surround was presented at -45°. Like the cells featured in figure 37, the responses of these cells exhibited non-oscillatory offset synchronisation to specific discontinuous conditions when the centre of the bipartite stimuli were smaller than 1.5°. Continuous full field stimuli, which were 6° in diameter, presented at the optimal orientation of the cells, or at bisecting orientation was ineffective at causing the cells to fire significantly synchronised responses. The interaction generated by stimulus **e**, is fitted with an oscillation gabor function, the frequency of this and the maximum peak in the FFT analysis of this interaction was 44 Hz. Cross-correlograms are displayed with 4 ms bins.

Of the five pairs of cells, the responses of which to certain visual stimuli were found to generate oscillating cross-correlograms, one pair were detected, the responses of which generated cross-correlograms that did not oscillate in the gamma frequency band but instead at a frequency between 12 and 16 Hz. This behaviour is depicted in figure 38, again it was the case that a survey of the response interactions generated by all the stimuli used, indicated that this pattern of correlation was specific to responses to specific discontinuous bipartite grating stimuli. In figure *38* a discontinuous condition is shown together with other aligned conditions presented at optimal and bisecting orientations. It can be seen that stimulus *b* generates the largest oscillatory component in the response cross-correlogram, it is the discontinuous condition. The oscillation present in this correlogram was strongest oscillatory interaction that was detected from the responses of these cells. The stimulus that evoked the responses that generated the oscillating cross-correlogram was a bipartite grating with a 2° centre, it had a centre orientation which bisected the angle between the preferred orientations of the two cells, the surround was optimally oriented for the reference cell. Thus this stimulus is discontinuous but contains orientations which are relevant to the tuning characteristics of the cells under investigation.

Observations made from these cells indicate that oscillations in the gamma frequency range and between 12-16 Hz are consistently found to be stronger in cross-correlograms generated from responses to discontinuous stimuli. In the course of this study significant levels of oscillation were only detected in cross-correlograms generated from responses to spatially expansive continuous stimuli in the case of one pair of cells. The cells had a receptive field configuration classified as group 1, they were iso-oriented and overlapping, neither of the cells were patch suppressed. Cross-correlograms generated from their responses to optimally oriented grating of increasing diameter are shown in figure *39*. In this figure it is apparent that the cells fired strongly synchronised responses when stimulated with the 3° patch. The top plot illustrates the observation that as the diameter of the patch increases the strength of oscillatory component also increases, reaching a maximum when the cells were stimulated with the largest 6° patch. These cells were not stimulated with the range of discontinuous stimuli that were used on the previous pairs so it is not possible to investigate the nature of the temporal interaction between their responses when they

Figure 38.

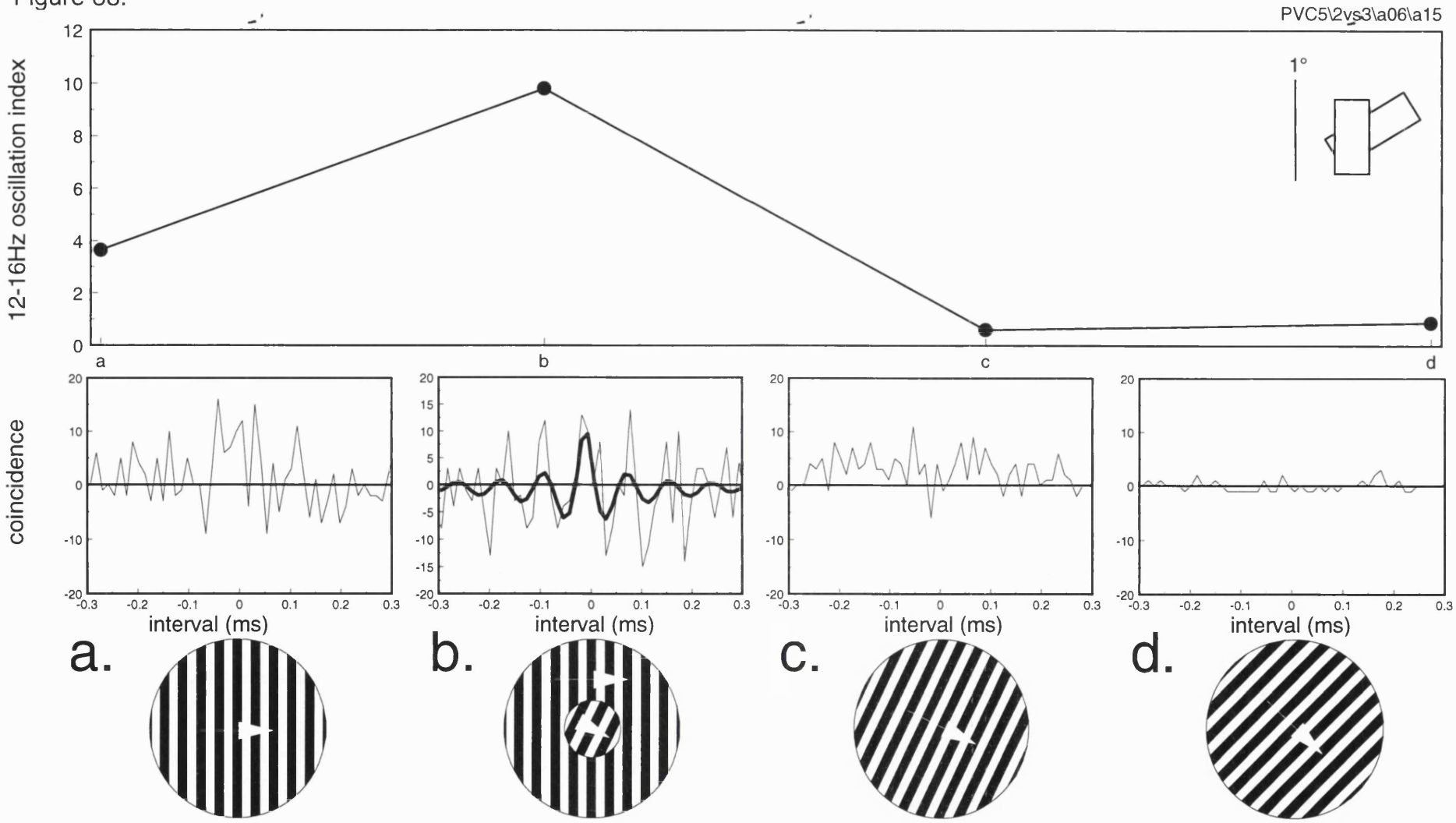

PVC5\2vs3\a06\a15
12-16Hz oscillation index
1°
a
b
c
d
coincidence
interval (ms)
a.
b.
c.
d.

Figure 38.

This figure depicts the temporal interactions between a pair of patch suppressed cells that had overlapping receptive field with an optimal orientation difference of 45°. All stimuli were displayed with spatial frequencies of 2 cpd and temporal frequencies of 3 Hz. These two cells fired synchronised responses to a limited number of stimulus conditions, two of these stimuli are shown (**a** and **b**), a full field grating oriented optimally for the reference cell, and a discontinuous bipartite stimulus. The cross-correlogram generated from the responses to stimulus **b** contains a strong oscillation at a frequency of 12 Hz, this stimulus consisted of a bipartite grating with a centre diameter of 2°, oriented at an angle that bisected the orientations of the cell's fields and a surround that was optimal for the reference cell. This was the strongest oscillation in a cross-correlogram exhibited by this pair of cells, three other discontinuous stimuli evoked such interactions, each had different permutations of optimal and bisecting orientations. Such gratings presented as full field stimuli with diameters of 6°, did not generate significantly oscillatory synchronisation. Cross-correlograms are displayed as the difference between the raw function and the averaged shift predictor, with a bin size of 12 ms.

Figure 39.

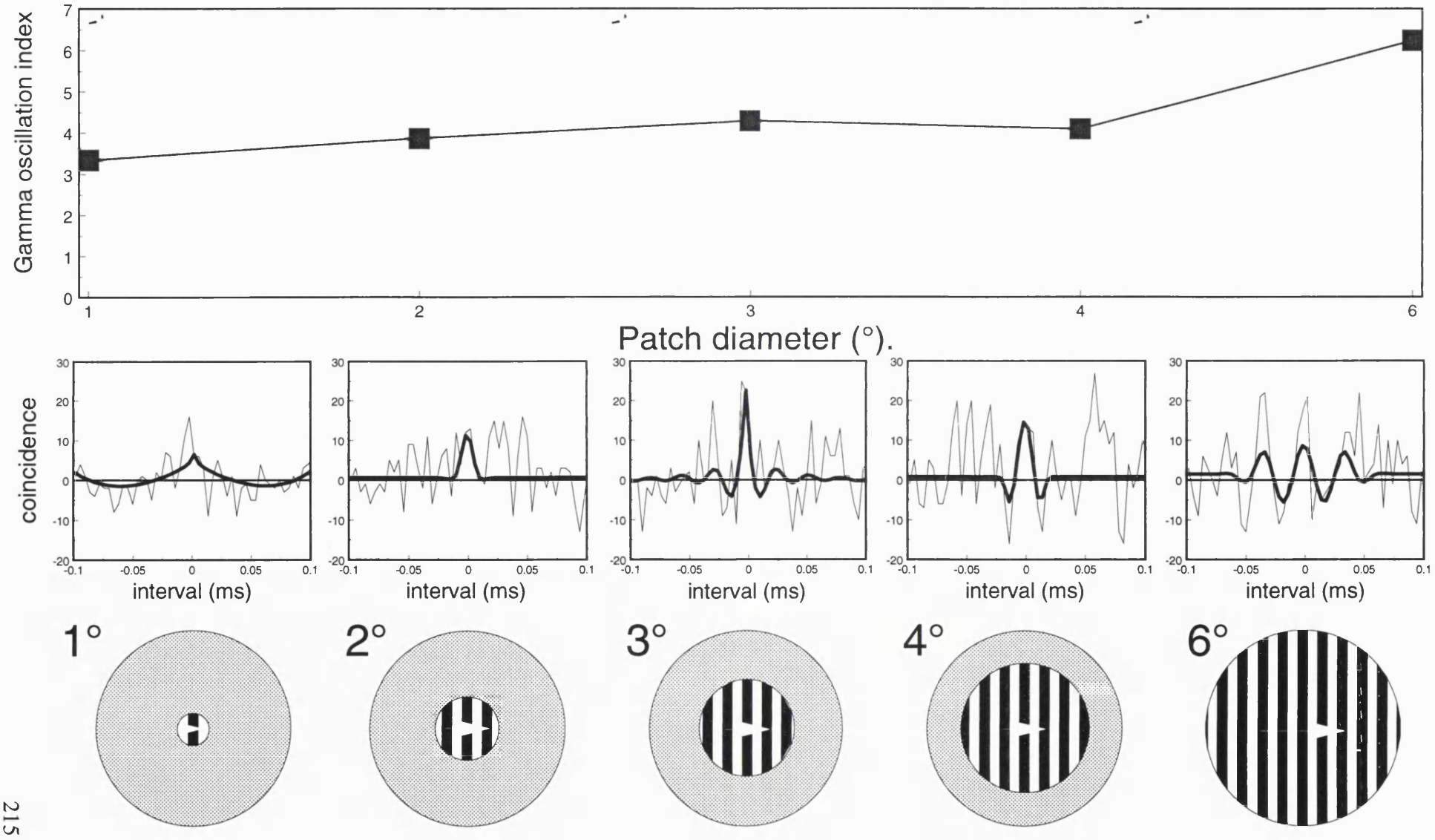

Gamma oscillation index
0
1
2
3
4
5
6
7
1
2
3
4
6
Patch diameter (°).
coincidence
30
20
10
0
-10
-20
-0.1
-0.05
0
0.05
0.1
interval (ms)
1°
2°
3°
4°
6°

Figure 39.

This figure depicts the temporal interactions between the responses of a pair of cells with iso-oriented, overlapping receptive fields, recorded in primate V1. All stimuli were presented with spatial frequencies of 1 cpd and temporal frequencies of 3 Hz. The cells did not exhibit suppressed responses as a function of patch diameter. It can be seen that their responses to various diameters of optimally oriented grating are synchronised. Each interaction is featured with it's best fit gabor function, to indicate an oscillatory component. The gamma frequency component of these increases as a function of patch diameter, this is illustrated by the plot at the top of the page. Cross-correlograms are displayed with 4 ms bins, as the difference between the shift predictor and the raw function.

were stimulated in this way in comparison to interactions generated by continuous stimuli.

The results presented above obtained from implementing cross-correlation techniques on the responses of cortical cells in the cat and primate primary visual cortex, to complex contextual stimuli indicate that there is a high level of response synchronisation when cells are stimulated with particular discontinuous conditions. In a few cases, the synchronisation was oscillatory in nature. In the following section temporal interactions between the responses of LGN cells, will be investigated to continuous and discontinuous bipartite gratings, to investigate the role that these inputs play in the interactions reported above.

Synchrony in the cat dLGN responses to contextual stimuli.

The lateral geniculate nucleus provides the excitatory retinal input to the cortex with axons that spread over areas that several millimetres in diameter. It is thus in a position to provide input to anatomically distributed networks of cortical cells. The lateral geniculate nucleus itself receives input from layer VI cells whose axons terminate in similarly spatially distributed fields. Cortical input has been shown to influence the responses of LGN cells to contextual stimuli (Sillito et al, 1993). Due to this input pairs of cells recorded from sites separated 200-600μm, with receptive field separated by 1-3° cells have been reported to exhibit a capacity to fire anatomically synchronised responses in a highly stimulus specific fashion (Sillito et al, 1994). A pair of cells exhibit response synchronisation when stimulated by a grating presented at an orientation that links their fields with a continuous contour. When this contour is broken with a neutral contrast contour then the response synchronisation is no longer observed, removal of primary visual cortex removes synchronising influences.

As the LGN is a centre from which much cortical input originates, response synchronisation at this level could have important implications for postsynaptic targets in cortical layers III, IV and VI. It is possible that it underlies the response properties of postsynaptic cells in these layers. In earlier sections single cortical cells,

as well as being shown to respond stimulus specifically to continuous contours presented at particular orientations were also shown to exhibit elevated responses to bipartite stimuli where there was a specific orientation disparity between the centre and surround gratings. Stimuli that brought about this response elevation contained an element, either the centre or surround, that was optimally oriented for the cell in question, the other element was rotated by 45-90°. Cortical cells with a whole range of orientation differences were observed to exhibit response synchronisation when they were recorded simultaneously responding to these stimuli. the correlation peaks were most often found to be broad, typically 8-12 ms wide, this diffuse temporal distribution would not be consistent with a simple monosynaptic interaction. The responses of a given pair of cells did not synchronise during presentation of all stimuli but only a small subset, and stimuli within this subset did not always generate responses that were synchronised in the same way, latencies, temporal distributions and oscillatory characteristics varied, from one synchronous response to the next. The complex nature of feedback and feedforward connections between the primary visual cortex and LGN is one candidate for the network that could be the substrate for these interactions with more complex origins. It was thus the aim to investigate whether there was any aspect of the operation of networks of cells in the LGN to discontinuous bipartite stimuli that might underlie the observed contextual response specificity and synchronisation that is seen in the cortex. Thus the responses of thirteen pairs of cells to aligned and discontinuous bipartite stimulus conditions were recorded during four experiments on feline preparation were cross-correlated, to further investigate stimulus specific response synchronisation in this centre. Of the thirteen pairs of cells, the responses of which were investigated using cross-correlation analysis, all consisted of cells with fields which were both ON type or OFF type. Nine of the thirteen were either both X, or both Y type fields, field type was mixed in remaining pairs. Eight pairs were found to exhibit significant highly stimulus specific response synchronisation to particular discontinuous bipartite stimulus conditions, seven of these were matched for both field type and polarity, the remaining pair consisted of one X and one Y type field. A typical example of LGN synchronisation is featured in figure *40*, it can be seen that this pair of cells fired synchronised responses to three of the stimuli that are shown (stimuli *b*, *c* and *d*). The receptive fields were separated by 2° of visual space, their relative position within the bipartite stimulus with a centre

Figure 40.

LGH67\C-07\2vs3

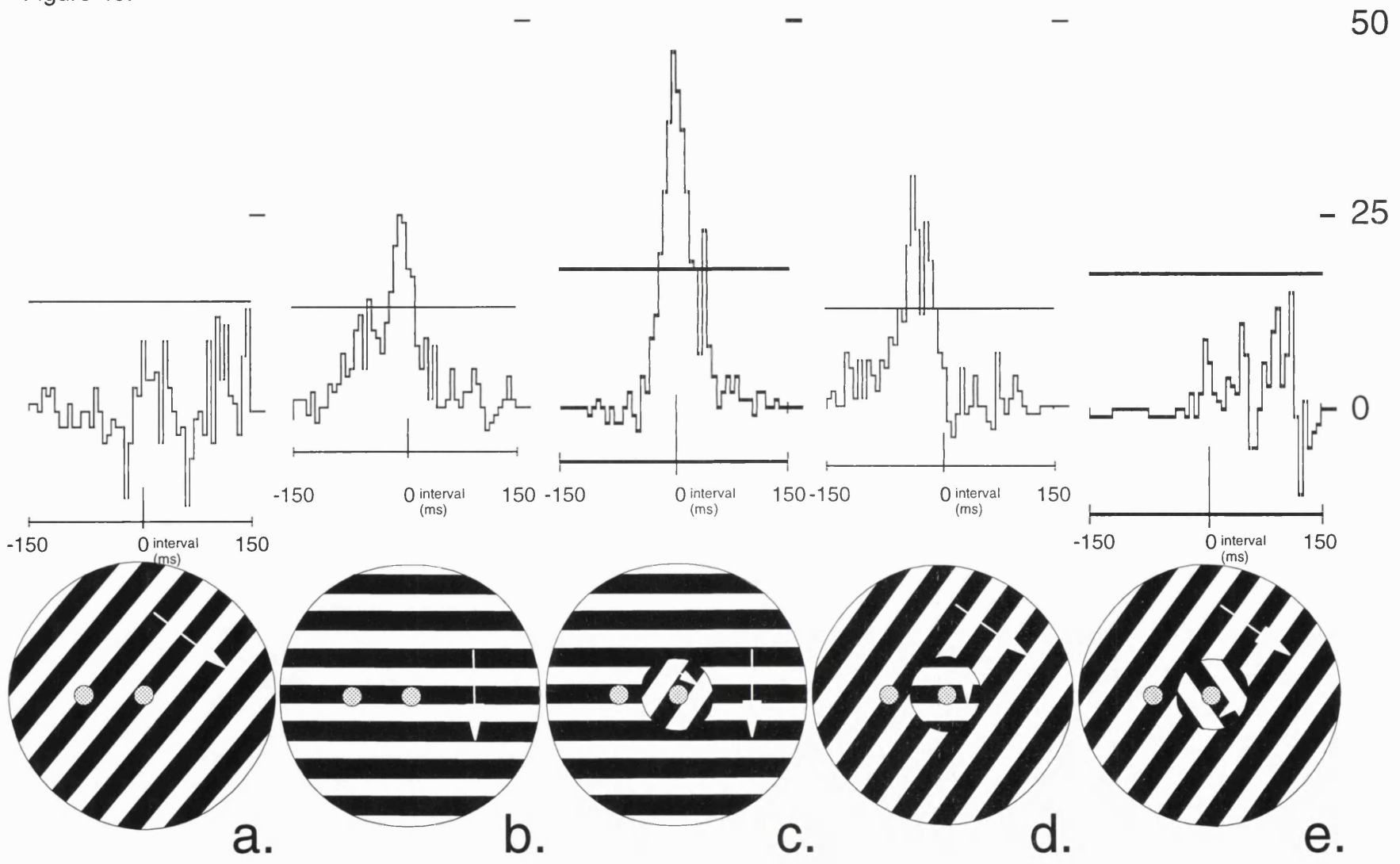


Figure 40.

This figure features cross-correlation analysis of the visual responses of cells recorded in the cat lateral geniculate nucleus to the same kinds of stimuli that were featured in the previous section that dealt with stimulus specific response synchronisation in V1. Shown are the cross-correlation results obtained from the responses of two ON centre cells with X type receptive fields. These fields were separated by 2° of visual space. The cells were stimulated with a bipartite stimulus which had a centre diameter of 3°. All these stimuli were presented with contrast values of 0.25, spatial frequencies of 0.66 cpd, they were modulated at a temporal frequency of 2 Hz. Shown are five cross-correlograms obtained from the responses to five stimuli (**a-e**). Stimulus **a.** was an aligned condition presented at an orientation which did not link the two receptive fields. Stimulus **b.** was an aligned condition presented at the linking orientation, it brings about a significant level of response synchronisation. When this stimulus is then altered by rotating the centre by 45°, making a discontinuous condition, the resulting response synchronisation is signified by a much larger peak. Response synchronisation was also detected when the centre and surround orientation in stimulus **c.** were interchanged to make stimulus **d**. Response synchronisation was only detected when the stimulus contained and a centre and/or surround were presented at the linking orientation. This is highlighted by the cross-correlation that results from analysis of the responses of this pair of cells to stimulus **e.** The cross-correlograms are displayed with fifty-one 6 millisecond bins, and are the result of subtracting the averaged shift predictor from the raw result. Also shown is the 99.5% statistical significance limit for each correlogram.

diameter of 3° are shown in figure *40*. Stimuli *a* and *b* are both aligned conditions of a bipartite grating, it can be seen that *b*, presented at an orientation which links the two fields with a contour, evokes response synchronisation, whereas when the cells are presented with a stimulus that does not link them as in *a*, no response synchronisation was detected. The strongest response synchronisation, signified by the largest peak, however was activated by stimulation of the cells with a discontinuous bipartite grating in which the surround grating was presented at the linking orientation, with the inner segment rotated by 45°, as in stimulus *c*. Response synchronisation, though weaker, was also detected when the centre and surround orientations in stimulus *c* were interchanged, to make stimulus *d*. The stimulus specificity of response synchronisation at the level of the LGN is further highlighted by discontinuous stimulus *e*, where neither the centre nor the surround were presented at the linking orientation, no response synchronisation was detected in the cross-correlogram associated with stimulus *e*. That the stimulus should contain at least one element presented at the linking orientation was a key feature of all the bipartite gratings that brought about response synchronisation. The most critical feature in generating this synchronisation was found to be the surround orientation. Thus cells in the LGN that have receptive fields that are distributed in visual space over a similar range of dimensions to the receptive field distributions that were investigated in the cortex exhibit stimulus specific response synchronisation to the same range of visual stimuli. What is interesting about the interactions in figure *40* that were associated with presentation of stimuli b and c, is that, that which was evoked by the discontinuous condition (*c*) is much stronger than that, that was evoked by the aligned condition (*b*). The peak that was generated from responses to the discontinuous condition had a Y*max* of 46, which was 84% larger than that evident in the cross-correlogram generated by the aligned condition (Y*max*=25). This was the case even though the pair of cells together only fired 11% more spikes to the discontinuous condition than they did to the aligned condition.

As well as peaks indicative response synchronisation being centred over the cross-correlogram origin, it was also the case that the responses of three of the synchronised pairs generated peaks that were displaced from the origin by as much as 180 ms. An example of this is shown in figure *41*. The pair of cells featured in this figure

Figure 41.

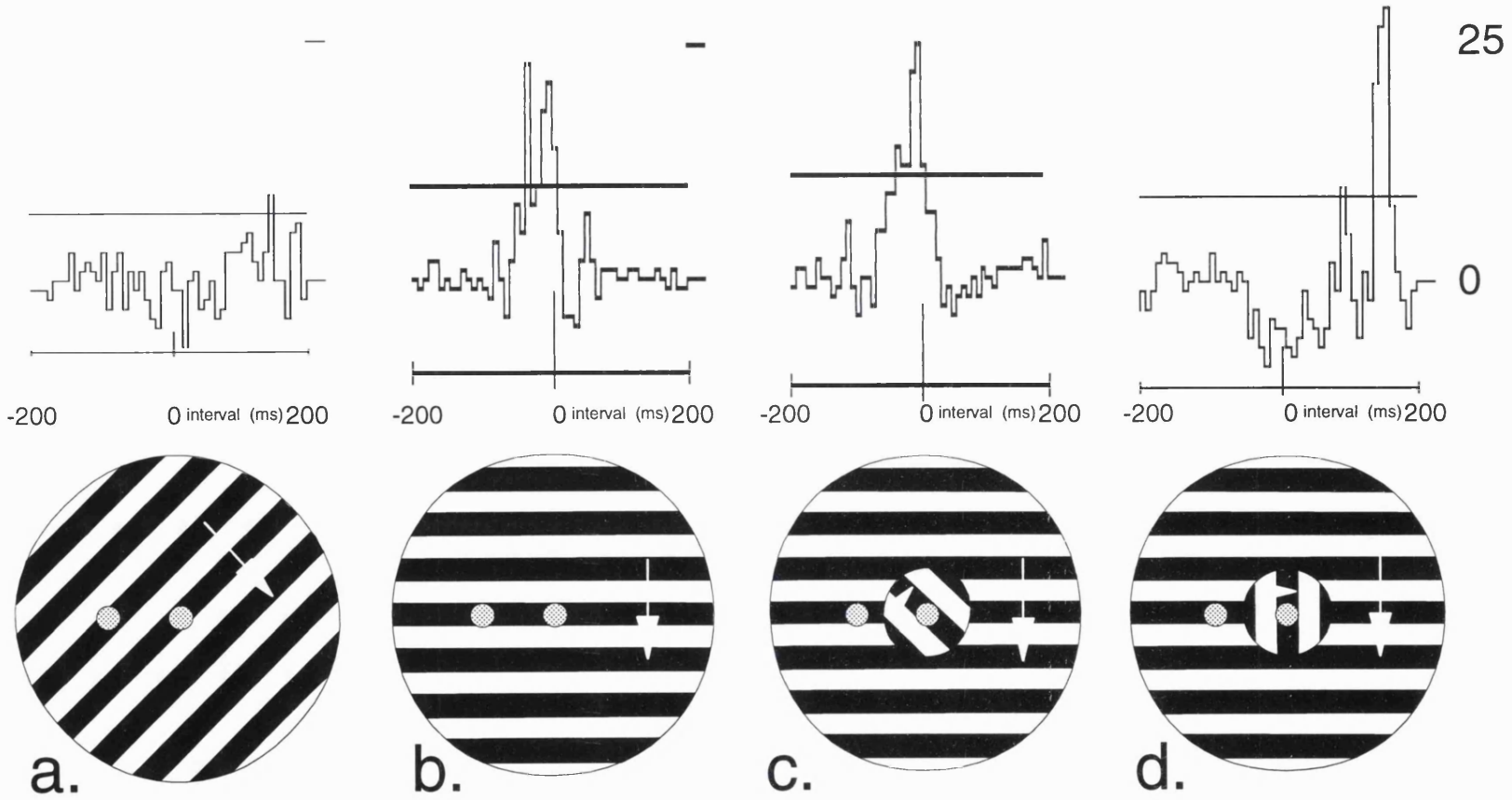


Figure 41.

Cross-correlation analysis of the visual responses that were simultaneously recorded from two cells in the feline lateral geniculate nucleus. The cells both had OFF centre receptive fields. All stimuli were presented with contrast at 0.25, spatial frequencies of 0.66 cpd and temporal frequencies of 2 Hz. Shown are four stimuli (**a-d**) and the cross-correlograms generated from the responses of the cells to these stimuli. Again it can be seen that response synchronisation only comes about when the cells are presented with a grating at their linking orientation. This evident if results **a** and **b** are compared. Again it was the case that the response synchronisation became stronger if the centre was rotated through an angle of 67.5°. It was also the case that for a few stimuli where the centre or surround were optimally oriented and the stimulus itself was discontinuous that peaks of the type associated stimulus **d**. were observed. This peak signifies a connectivity co-ordinated process which generates a cross-correlation peak which is displaced from the origin by 180 ms. In this figure fifty-one 8 ms bins were used, and cross-correlograms are displayed as the difference between the averaged shift predictor and the raw result.

exhibited the same stimulus specific response synchronisation as the pair featured in figure *40,* this is shown in the cross-correlograms that are associated with stimuli *a-c.* Stimulus d however generated a peak that was displaced by 180 ms, the stimulus that generated this interaction again discontinuous and had a surround presented at the linking orientation, this stimulus is similar to stimulus *c* but activated a different form of network interaction. It was not the case that both types of interaction, both central and displaced, were detected between within the same correlogram. It might be the case that the long temporal lag between correlated spikes, that is highlighted by this displaced peak, represents the operation of a highly complex network, which might involve an axonal path passing through several cortical areas before returning to the lateral geniculate nucleus.

There is thus good evidence presented here that indicates that the results that were obtained in the cortex and that were related in earlier sections of this *Results* section have their origins in the functionality of the LGN and its interaction with the cortex. It is clear that cortical cells with spatially offset receptive fields will be getting a *unified* synchronised input from their *separate* thalamic afferents when they are stimulated with bipartite conditions that contain centres and surrounds, one of each of which is optimally oriented for the cells involved. This stimulus specific synchronised output distributed over visual space might be the origin of the context dependent receptive field properties seen in the cortex. It is particularly interesting to note that the synchronisation at the level of the LGN was disproportionately stronger, with reference to the total number of spikes fired by the cell pair under investigation, when the stimulus was discontinuous compared to when it was aligned. These observations will be related to those made in the cortex will be related in further detail in the *Discussion* section below.

6. Discussion.

The first aim of this investigation was to determine how the responses of neurones in the visual system are influenced by the spatio-temporal context of stimuli presented in and around the classical excitatory receptive field, as defined by Hubel and Wiesel (Hubel and Wiesel, 1962, 1965). Theses responses were then used to explore how, and under what circumstances cells exhibited synchronised patterns of discharge. Both these approaches were used in order to understand the strategies that the visual system uses to generate coherent perceptions of objects in the world around us.

Temporal characteristic of responses to contextual stimuli.

Previous reports had indicated that individual spikes were distributed irregularly within a response epoch, with a stochastic, poisson distribution of inter-spike intervals (Softky and Koch, 1993 and Shadlen and Newsome, 1994) while others had shown that particular intervals were more strongly represented than others (Gray and Singer, 1989), and that cells exhibited oscillatory visual responses in a stereo-typed range of frequencies to optimal stimuli.

The novel approach used here, presenting cells with stimuli in a variety of contextual environments, revealed some interesting features of network operation, when it is presented with complex visual stimuli that reflect the spatio-temporal information provided by the natural visual world. Contextual stimuli were used in which the spatio-temporal relationship between the stimulus presented to a cell's excitatory classical receptive field and that presented to surrounding visual space could be varied systematically. The responses of cells to sets of these stimuli were then analysed to detect stimulus specific changes, in mean response magnitude, and in parallel, any deviations from, or changes in the deviation from, stochastic poisson distributions of inter-spike intervals. As a result insights have been gained into the role that spatio-temporal context plays in processing a visual scene, and into codes and strategies that are employed to do this. Cells were recorded in both cat and primate V1, and in the cat dLGN, in all these centres they responded in ways which were strongly influenced by

the contextual characteristics of the stimulus. When the response properties of cortical single-units were investigated with many contextual stimuli, both mean response magnitude and response oscillation index exhibited stereo-typed patterns of stimulus specificity that were characteristic of what might be functional groups.

Results presented in this thesis demonstrate that cells in primate and cat V1 exhibit both types of temporal structure in visual responses. Oscillations were found in responses to specific classes of stimuli.. Multiple (up to 10) response epochs, lasting 1-1.5 seconds generated by multiple presentations of a stimulus with a known configuration, were found to contain trains of spikes oscillating in a single narrow frequency band. In the majority of cases the oscillation was found to be in the gamma frequency range, however a smaller group of cells oscillation were stronger at a frequency of 12-16Hz. This finding thus provides further confirmation that such temporal structures can be detected within epochs of visual response from cells in the primary visual cortex (Gray et al, 1989, Gray et al, 1990 and Engel et al, 1990, Kreiter and Singer, 1992, also see Ghose and Freeman, 1992), and is in contrast to the results of other findings which have proposed that response oscillation is rarely detected (Young et al, 1992) in primate visual cortex. It is interesting to note however that this latter investigation, like the investigation on which this thesis is based, did detect oscillations in a frequency band between 12 and 16 Hz, though only in a tiny proportion of their sample, these were not allotted any functional role.

Temporal analysis of response trains yielded information about the extent to which spikes were, or were not, stochastically (poisson) distributed with respect to each other and how changes in response structure were related to changes in stimulus structure and thus the operation of the underlying network. The magnitude of the departure from a poisson distribution of inter-spike intervals (ISIs) in a visual response was measured in various frequency bands, as a power ratio, that was denoted oscillation index. Oscillations, where they were detected in visual responses in the course of this study, were encountered in a highly stimulus specificity fashion, this is consistent with the results of previous investigations (Gray and Singer, 1989 and Gray et al, 1990). A small group exhibited oscillations within responses to stimuli similar to those reported in these earlier investigations, stimuli that conformed to Gestalt

criteria. However the largest group was characterised by the strong oscillations detected within responses to spatially restricted patches of grating and to discontinuous bipartite gratings, stimuli not consistent with Gestalt criteria and perceptual binding of continuous contours.

The results obtained from oscillation strength analysis, must be seen in the context of response magnitude analysis reported in this thesis and elsewhere (Sillito et al, 1995). Spatial extensive continuous grating fields were associated with relatively suppressed responses, increased mean response magnitudes were evoked by grating stimuli that were spatial restricted to the excitatory classical receptive field, or by contextual stimuli that contain a spatio-temporal discontinuity. For a large proportion of cells, presentation of discontinuous stimuli was associated with increases in mean response and increases in oscillation strength.

In order to determine whether this oscillatory temporal structure was a code that contained more information than mean firing rate, analysis of temporal structure was undertaken on responses containing approximately the same number of spikes. The result of this analysis using 18 cells recorded in primate V1 that exhibited largest oscillation indices to discontinuous stimuli, is shown in figure *11*. In this plot, the mean population response to continuous stimuli, shown on the left, was obtained by presenting patches which were 2-4° in diameter, on the right, and of an equivalent magnitude, the mean population response obtained using explicitly discontinuous stimuli. It can be seen that in responses of the same magnitude obtained during presentation of continuous patches and discontinuous stimuli, the oscillation index obtained from the discontinuous response were on average 2.4 times stronger than that in the response to the patch. Thus of two responses one to a continuous, and one to a discontinuous response, each containing the same number of spikes, the response to the stimulus containing a spatial discontinuity will contain the largest proportion of spikes distributed in epochs oscillating at a single dominant frequency. Thus for this group of cells, oscillation is not dependent on the absolute number of spikes fired by the cell, but on the spatial characteristics of the stimulus, and the mechanisms that generate a cell's response to it. Response temporal structure unambiguous indicates whether the stimulus was contextually discontinuous or continuous. In responses to

discontinuous stimuli, the range of ISIs present is not well modelled by a poisson distribution, rather a particular range of ISI's is more strongly represented. Many responses were found in this investigation were found to oscillate at a frequency between 30 and 60 Hz, thus ISIs between 15 and 33 ms are represented with a greater probability than would be associated with a stochastic poisson distribution. It might be the case that temporal structure provides a code which carries information about stimulus context around the primary visual cortex.

70% (n=24\34) of cells recorded in primate V1, were found to exhibit strongest gamma-range oscillations to discontinuous bipartite stimuli, in which the surround was rotated by 45-90° from an optimally oriented centre, in comparison to a continuous stimulus where both the centre and surround were optimally oriented. These explicitly discontinuous stimuli evoked stronger oscillations within responses than the patch stimuli that were discussed above. Examples of this observation are depicted in figures *12* and *13*. Thus discontinuous stimuli are not only associated with increases in response magnitude, but also with increases in the strength in the oscillatory component of a response. These stimulus specific oscillations were also evident in the responses of cells that oscillations between 12-16 Hz. Figure *14* shows strong oscillations at 12 Hz in responses to discontinuous stimuli, oscillation were not significant in responses to continuous full field stimuli. This cell was consistently found to oscillate at 12 Hz when visual stimulated, significant oscillation in the gamma frequency range were not detected.

The propensity of some cells to oscillate in responses to discontinuous stimuli, exhibited further stimulus specificity, this observation was featured in figure *15*. When oscillations in responses recorded from a single cell, to discontinuous stimuli with different centre diameters were compared, it was the case that strongest oscillations were detected in responses to such stimuli with a limited range of centre diameters. This selectivity was observed in two cells from which responses to bipartite stimuli with a wide range of centre diameters were obtained. In these two cases strongest oscillations were detected within responses to bipartite stimuli that had centre diameters of 1.5°. Such a centre diameter is in the middle of the range of those that were found to generate the largest increases in response magnitude that were

associated with discontinuous bipartite stimuli. A further stimulus specificity was exhibited by oscillatory responses, this was evident when the responses of cells to optimally oriented patches of grating presented with different diameters were analysed. The propensity of a cell's response to oscillate was tuned to a specific patch diameter. In figure *29*, the distribution of optimal diameters is distributed over wider range than the optimal diameter adjudged simply using response magnitude as a criterion. Again this suggests that mean response magnitude and response oscillations were independent of one another. Figure *26* shows the distribution optimal patch diameters adjudged from response magnitude, it can be seen that this is strongly biased towards diameters of around 1°, rather than the 1-4° range determined using oscillation index criterion. This observation again implicates stimulation of the surround (the distribution of which was determined using response magnitude criteria) in the evocation of oscillatory responses. Restricted stimulation of the surround with an optimally orientated grating can evoke an oscillatory response, which can become stronger as the surround orientation is rotated out of alignment with the centre. Hence cells clearly appear to signal spatial context in the temporal structure changes of their responses.

In contrast to the group discussed above, a small minority of cells exhibited a propensity to oscillate that was consistent with previous reports, to stimuli that fulfil 'good continuation' and 'common fate' Gestalt criteria. Like the cells in the larger group, they exhibited a consistent, highly stimulus specific propensity to oscillate, the best example of this specificity is featured in figure *16*. This cell was a member of a group that contained 7% (n=2\34) of the total population, stimulated with bipartite stimuli. Gamma frequency oscillation indices were largest within responses to spatially coherent continuous stimuli, however this cell, like the others that oscillated most strongly to discontinuous stimuli, following response magnitude analysis, exhibited selectivity for spatially restricted patches and discontinuous stimuli. This can be seen, along with data from a cell from the larger oscillating group in figure *19*. The ranges over which the cells change response magnitude, to continuous and discontinuous stimuli, were very similar. Both cells responded with largest number of spikes to discontinuous stimuli, the one on the left oscillated most strongly when stimulated in this way, whereas the cell shown on the right consistently exhibited

strongest oscillations in the smallest responses it fired, to continuous stimuli. Again this suggests that oscillation strength are independent of firing rate.

LGN cells recorded in the cat, responding to the same groups of stimuli that were used in cortical experiments in the cat and primate, and analysed in the same way, were not found to contain oscillations in any of the tested frequency ranges. This observation, however contrasts with results presented in other reports (Ghose and Freeman, 1992, Neuenschwander and Singer, 1996). Where visual responses recorded in the feline LGN were found to contain oscillations that were stronger than those detected in primary visual cortex. Though these investigations did not explore the effect of context changes on the temporal structure of responses, they did use grating stimuli similar to those used in this study, so it is difficult to explain the different results. Oscillations in both the LGN and retina have been proposed to have a functional significance for visual perception (Neuenschwander and Singer, 1996).

The observation that the spatial context of a visual stimulus has an effect on the temporal structure of cortical visual responses is an interesting insight in itself, it however contradicts theories of function in the visual system which propose that oscillations and synchrony are of no functional relevance and that stimulus information is coded by changes in the magnitude of population responses in a given period of time. The observations presented above clearly show that the spatial context of a stimulus is specifically represented by oscillatory responses and network synchrony.

Cells are thought of as either integrators of their presynaptic influences over time courses that approximate their inter-spike intervals (15-100 ms) by proponents of rate coding theories (Shadlen and Newsome, 1994), or as detectors of temporal coincidences in these presynaptic influences over much shorter time courses of (1-5 ms) (Softky, 1995 and König et al, 1996) by those that promote neural synchrony. These two views of the operation of individual cells have important implications for the way that information is represented in the network. If cells are integrators then information is represented in the pooled changes in the firing rate of large population of cells, if however they are coincidence detectors then it is proposed that information

is processed by cells firing synchronously, on the same time scale that they integrate their presynaptic influences. Cross-correlation analysis has revealed monosynaptic connectivity information, and synaptically co-ordinated synchronisation (Ts'o et al, 1986, Hata, 1991 and Singer et al, 1989), between cells in the network. Proponents of the first scheme suggest that this is just 'correlated noise' while proponents of the latter scheme propose that information is contained in correlated spikes. Data obtained for the present investigation, demonstrates that like response oscillation, response synchronisation is stimulus-dependent, it is not noise but contains specific stimulus information. Response synchronisation was not strictly correlated with particular patterns of change in response magnitude, as would be predicted by the rate code hypothesis. Response synchronisation could not be predicted from the size of responses.

The influence of stimulus context over mean response magnitudes of single units provides information the synaptic mechanisms that might be operating on a cell to bring about the stimulus specific changes in response temporal structure. Elevated mean response magnitudes were detected when many cells was presented with non-aligned conditions. Peak response increases were recorded when the cell was presented with a bipartite condition that involved an optimally oriented centre grating and a surround that was shifted from the centre orientation by 45-90°. This effect can be seen in figures *17* and *18*, where it is exhibited by primate single units, and in cat V1 in figures *21* and *22*. Response magnitude changes detected in the cortex were much greater than those detected in the LGN, where on average, bringing gratings into alignment brought about a decrease of approximately 25%, this can be seen in figure *23*. In the cortex bringing centre into alignment on average caused a response decrease of 66%. LGN cells were also not found to oscillate, this was a response property only detected in the cortex, suggesting that the mechanisms which causing oscillation are effective only within the cortex.

The influence that surround stimuli have on the responses of cells appears to depend upon the configuration of the centre, and the influence of the centre depends upon the configuration of the surround. Many contextual response properties of cells are not consistent with a cell responding to any one particular feature of the stimulus such as

the centre *or* surround, but rather to the spatial and temporal relationship between them. The key feature of a stimulus that evokes a facilitated mean response magnitude is 'discontinuity'. Discontinuity, explicitly conveyed by an orientation or direction difference between the stimulus presented in the centre and that in the surround, evokes response magnitudes which are greater than those evoked by patches of grating which extend into the surround of the cell. Explicitly defined discontinuities evoked the largest responses that were recorded from 12 cells in the primate population. The mean responses of a cell that exhibited this property are featured in figure *18*. In order to explore the spatial organisation of the processes that generate context dependent changes in response properties, the responses of cells were studied with reference to changing centre diameters in bipartite stimuli. Discontinuous responses were recorded from cells recorded in the primate for centre diameters up to 4° in diameter, stimuli with centres larger than this generated significantly reduced effects and were rarely used. The magnitude of response facilitation and stimulus dependence of the facilitated responses were very dependent on the centre diameter of the bipartite stimulus. The largest increases in discontinuous response magnitudes were recorded when the centre was the same diameter as, or had diameter that was 1° larger than, the patch that evoked the largest response from the cell when patches were presented in isolation. When such patches were used, elevated responses were only detected when an optimal or very near optimal centre was surrounded by an oblique, orthogonal or opposite direction grating. When smaller centre diameters were used, relatively facilitated responses were recorded to bipartite conditions with a much wider range of centre and surround orientation permutations. In figure *17a* a density map is shown of the responses of an alignment suppressed cell to a bipartite stimulus with a small centre diameter of 0.75°. Elevated responses are clustered, notably many of the stimuli involve centre orientations that were non-optimal for the cell under investigation. It can be seen that it responds most strongly to the two directions of motion of two distinct configurations of bipartite paradigm. To the discontinuous configuration that involves an optimally oriented centre and an orthogonal surround, equivalent responses were recorded during presentation of stimuli involving an orthogonal centre and an optimal surround. So the cell is in effect, responding to a classically non-optimal centre with a response level which is more consistent with presentation of an optimal stimulus.

The observations made in this study using contextual bipartite stimuli, the centres of which were configured so that they partially stimulated the inhibitory surround, shows that interactions between the classical receptive field and its inhibitory surround are very complex. Figures *24-26* show, that as a function of centre patch diameter, response magnitude was reduced very rapidly when the centre patches began to encroach upon the surround, on average, stimulation with a grating that was 1° larger than optimal brought about a 50% reduction of neuronal response magnitude, this can be seen in figure *26a*. When an orthogonal grating was introduced around such a surround stimulating centre, the evoked responses, such as those featured in figure *18*, that were often larger (12/34 in the primate), or as large as, responses to stimuli which were restricted exclusively to the classical receptive field. Thus elevated responses to discontinuous stimuli do not just come about because iso-oriented inhibitory end-zones are not active when stimulated with orthogonal surrounds, when such zones *are* notionally active, because bipartite stimulus centres encroach upon them, stimuli that involve large centre/surround orientation contrasts evoke strongly facilitated responses. Some of the strongest facilitation recorded in the course of this investigation required that the inhibitory surround should be partially activated by the centre while the surrounding grating was orthogonal. Elevated responses could come about because surround driven cells excite centre driven cells, or surround driven cell might inhibit cells involved in inhibitory side-bands and end-zones, or the observed neuronal properties might involve both mechanisms. Interaction between excitatory and inhibitory networks appears to be necessary to generate elevated context dependent response magnitudes. For the majority of cells, these strongly facilitated responses contained strong oscillations, and in a very few cases, relatively suppressed responses, contained the strong oscillations. No cells were found in which responses to continuous and discontinuous stimuli contained equivalently strong oscillations. For the majority of cells interaction between excitatory and inhibitory circuits activated by discontinuous stimuli thus also appears to be important in the generation of oscillations within visual responses. This point is reinforced by a point made earlier, that oscillations are strongest in responses to discontinuous stimuli, when compared to oscillations in responses to patches of grating that contained the same number of spikes. One important difference between these stimuli is the extent to

which they activate orientation disparity sensitive centre/surround-excitatory/dis-inhibitory mechanisms. That excitatory and inhibitory influences are activated differentially by different configurations of the stimuli in the surround is apparent from the data presented in figure *24*. Large responses are evoked by exclusive optimally oriented stimulation of the excitatory classical receptive field or exclusive stimulation of its surround, simultaneous stimulation of both, evokes suppressed responses. The cell in figure *24* is patch suppressed, it can be seen that its responses to a surround only with an aperture which is 1° or smaller, are larger than the responses of the cell to patches that are larger than 2°. Five cells recorded in the primary visual cortex of the primate clearly operated in this way.

Apart from orientation disparities between centre and surround stimuli, the other stimulus parameter that was varied and found to influence response magnitude and that could be said to provide an implicitly discontinuous stimulus, was grating patch diameter. Eighty-three percent of cells recorded in layers II-V of primate cortex and 42% of cells recorded in cat visual cortex were found to exhibit increasing suppressed responses when they were presented with patches of increasing diameter. They responded to short segments with larger responses than they did to long stimuli, this form of selectivity is consistent with cortical processing scheme in which the system emphasises discontinuities. The remaining cells in cat and primate V1 exhibited elevated responses to large optimally oriented patches. When presented with bipartite gratings in which the surround grating is sub-optimally oriented, response magnitude was reduced or not significantly changed. Many of these cells were recorded in layer VI. Thus in terms of the context dependence of their response properties there appear to be two populations of cells, based on response magnitude analysis. These properties of layer VI cells has important implication for cells in the LGN, to which many project (Robson, 1983). It has been reported that geniculate responses are length-tuned (Jones and Sillito, 1987 and 1992), and that this is because the cortico-geniculate feedback pathway that originates in layer VI has a suppressive, synchronising influence in the LGN (Murphy and Sillito, 1987 and Sillito et al, 1993, Sillito et al, 1994). Thus context dependent responses properties of cells in the LGN and throughout V1, and the network in which they exist, are not generated at any one

point *de novo*, but come about from complex interactions between the LGN and cortical networks.

This investigation has attempted to demonstrate that discontinuous stimuli drive active mechanisms that impinge upon single neurones, that cause them to respond in an oscillatory fashion, these mechanisms also elevate the number of spikes fired by that cell. The high level of response oscillation was not a consequence of the increased number of spikes fired by the cell. Instead, oscillations are a property of responses to contextual stimuli, that stimulate excitatory receptive fields and their surrounding visual space. Equivalent response magnitudes to patches and discontinuous stimuli, are partially generated by different mechanisms. Those that generate discontinuous responses, it suggested that these are cortico-cortical excitatory/disinhibitory centre/surround interactions, generate response oscillations too. They are not active when an optimally oriented stimulus is restricted to the excitatory receptive field or typically when it has a diameter greater than 4°. Patches with intermediate diameters drive them, and their activity is enhanced further if such patches are surrounded by orthogonally oriented gratings. Hence a given cell can signal the presence of a discontinuity with two dynamic spike train properties, oscillatory structure and/or magnitude.

The discontinuous stimuli that were used in the course of this investigation resemble those that were used in the psychophysical investigations that reported target 'pop-out'. A central idea in this thesis is that the stimulus response properties that were reported above, and that are discussed below are involved in the processes that underlie psychophysical 'pop-out' and the generation visual percepts. These observations reported as a consequence of presenting cells with contextual stimuli, agree with those of several other studies (Knierim and Van Essen, 1992 and Li and Li, 1995). However they disagree with others that emphasise the importance of contextual continuity in generating visual percepts from the responses of single units in V1 (Kapadia et al, 1995). In this latter study workers reported that they recorded facilitated responses relative to those obtained from optimally stimulating classical receptive fields with flashed bar stimulus, when another bar was simultaneously presented in the field's surround. This second bar provided spatial context and was presented at a position

along the orientation axis with variable lateral positions relative to their longitudinal displacement. Facilitation was recorded in 42% (123/291) of their population and on average was associated with a 230% increase in response. When the orientation dependence of this facilitation was tested, in 9/35 (26%) cases facilitation was detected exclusively for aligned surround stimuli, in the remain cases peak facilitation was recorded when the surround was non-aligned. Sixty cells were stimulated with concentric fields of pseudo-randomly oriented bars, twenty-one exhibited inhibition when stimulated in this way, nine of these were facilitated when arrays of aligned optimally oriented bars were introduced. From these results the importance of facilitation recorded during presentation of aligned stimuli was emphasised, it was proposed that it provided support for psychophysical observations that indicate that contextual continuity increases the detectability of target stimuli. However only a limited assessment of the influence orthogonal surround stimuli was attempted, and these workers did not attempt to investigate interaction between the classical field and its side-bands. Therefore their results do not provide a complete depiction of the full range of interactions between centre and surround, as has been attempted in the course of this investigation using moving bipartite gratings. Their use of flashed stimuli would evoke different patterns of response from cells in the visual system, and thus their observations of context effects, effects which are shown in this thesis to be associated with network synchrony, it might be supposed, would be different from those obtained using moving stimuli. The conclusions of their work also contradict other psychophysical observations that suggest that orientation contrasts aid target detection (Bergen and Julesz, 1983, Cannon and Fullenkamp, 1991). Kapadia and colleagues proposed that the results of studies that emphasise the functional importance of orientation contrast can be attributed to reports that indicate that inhibitory surrounds are not active when stimulated with orthogonal features, thus when such stimuli are used they propose that evoked responses equate to the response evoked by exclusively stimulating the classical field. However the data presented in this thesis shows that complex processes are *active*, specifically, when the surround contains a classically non-optimal stimulus. This stimulus activates mechanisms that increase a cell's response in terms of the number of spikes fired, and its propensity to fire the spikes rhythmically. Kapadia et al discount operation of the network, in any other way than between points of iso-orientation, when there is ample data to suggest

that within the network different points in space tuned to different orientations have a capacity to interact, to have wide range of effects on the properties of cells.

Network connectivity underlying contextual response properties.

The context dependent changes in response observed here are not consistent with a model of cortical function in which neuronal responses depend simply on topographically terminated LGN afferents in layer VI of V1 and serial hierarchical pathways beyond. The single cell data presented in this thesis, indicates visual responses are the result of highly dynamic interactions, between thalamic afferents, axons from delocalised cortical sites, and recording sites. It was one of the objects of this investigation to examine the functionality of the cortical network that underlies these responses to discontinuity stimuli. When considering how response changes might come about, there are broadly two mechanisms that operate within a network. One would be for cells to directly excite one another. Alternatively inhibitory cells might provide input to others, the result could then either be inhibitory if the postsynaptic cell was excitatory of dis-inhibitory if it was an inhibitory cell. In the following section it will be the aim to consider how such a network of orientation tuned influences could generate the response characteristics that have been reported.

When the centre of a discontinuous bipartite grating is small and optimally oriented, elevated responses might be the result of input from orthogonally oriented cells in the surround, providing direct excitatory input to the recorded cell, alternatively they may have a disinhibitory influence, by specifically inhibiting cells that are iso-oriented with the subject cell that provide inhibition. Interactions between delocalised cortical sites have been investigated by GABAergically inactivating sites up to 2 mm from recorded cells. This strategy was reported to broaden the orientation tuning exhibited by these cells (Wörgötter and Eysel, 1991, Crook et al, 1991 and Crook and Eysel, 1992). This observation yielded two theories to account for the observation that responses are increased to non-optimal stimuli, in the first it was proposed that inactivation removed inhibitory inputs to cross-oriented cells that function to sharpen an already broadly tuned excitatory input. The second theory was that remote

inactivation released other excitatory synaptic inputs tuned to non-optimal orientations. So, in the literature there are previous reports that might demonstrate the presence of the kind of horizontal connectivity that is suggested to be required to account for the observations reported here. These being that stimuli involving optimal centres and orthogonal surrounds and stimuli involving orthogonal centres and optimal surrounds evoked equivalently facilitated responses. Orthogonal centres in isolation did not generate these levels of response, neither did optimally oriented full fields, however optimally oriented centres *or* surrounds did, this is evident if the responses in figures *17* and *24*, recorded from the same cell, are compared. It seems that when the surround was presented with an optimally oriented grating, it was capable of facilitating or suppressing a cell's response. Precisely what it did depended upon the configuration of centre stimulus. Facilitation was observed if there was no centre stimulus, or orthogonally oriented one. Responses were suppressed when centre and surround were aligned.

What these observations suggest is that the patterns of response that were recorded, were not simply the result of inputs originating from cells in the surround terminating on cells in the centre, but from reciprocal interactions between the cells directly stimulated by the centre, and cells stimulated by the surround. What influence the centre and surround had upon the responses of a cell, was reciprocally conditional upon their spatio-temporal relationship. Interestingly oscillatory response synchronisation, like that detected in this investigation, has been proposed (Singer, 1993) to be the result of reciprocal interactions between population of cells. Reciprocal connectivity has also been implicated in the generation of response oscillations (Singer, 1993). Oscillatory activity is a consequence of response synchrony among populations of cells, it is proposed that a burst of synchronous activity from one group will activate two mechanisms that will cause a silent period in the network. The first of these is recurrent inhibition with a constant latency from a pool of inhibitory cells, and secondly because such a burst, within each cell participating, would activate Ca^{2+}-dependent K^{+} conductances, that are thought to bring about membrane hyperpolarisation, reducing a cell's capacity to fire spikes for a constant period of time after a preceding spike. After this period cells can fire again, repetition of this process will generate rhythmic firing patterns. Reciprocal

interactions have also been shown to bring about synchronisation of random patterns of input in model networks with 'all-to-all' connectivity (Koch and Schuster, 1992). Modelling studies have also demonstrated that interactions between inhibitory and excitatory networks might be necessary for the generation and control of oscillations in the gamma frequency range (Lytton and Sejnowski, 1991 and Wilson and Bower, 1991). Other experiments have shown that when neurones are recorded intra-cellularly, responding to visual stimuli, that gamma frequency oscillations might be due to rhythmic excitatory synaptic input (Bringuier et al, 1992). Alternatively oscillations have been reported to be the result of intrinsic properties of a cell's membrane, cells fire in this way in the absence of depolarising input from others (Gray and McCormick, 1996, Llinas et al, 1991). The level of depolarisation of such cells is reported to control the extent that they oscillate in the gamma frequency range, depolarising current injections and visual stimulation with optimal stimuli, promote the generation of oscillatory discharges. The results of the present investigation of single unit temporal structure stimulus specificity suggest that oscillations also come about as a consequence of synaptic interactions within the network rather than as intrinsic properties of a cell. However it is possible that contextual stimuli drive network mechanisms that influence a cell's intrinsic capacity to oscillate, or the capacity of intrinsically oscillating populations of cells to influence recorded cells. In further defence of the idea that oscillations are the result of reciprocal excitatory/inhibitory distributed network interactions, it was shown that oscillation strength, determined using Fast Fourier transform techniques, was not dependent on the mean firing rate of the cell. Presumably if oscillations were an intrinsic property of a cell it would have been seen to an equivalent extent in responses of the same mean magnitude and thus level of depolarisation, this was not the case. The dependence of oscillation strength on stimulus configuration suggests that networks reciprocally interconnected cells that are responsible for the generation of end-zone and side-bands would be involved.

The function of inhibitory networks has been demonstrated psychophysically (Blakemore et al, 1970). Their influence upon the responses of the excitatory classical receptive field has also been demonstrated physiologically (Creutzfeldt et al, 1974, Sillito, 1975, 1977 and Hata et al, 1988). In the present investigation evidence

obtained by presenting a cell exclusively with optimally oriented patches shows that inhibitory mechanisms also operate as the diameter of the stimulus increases, there is evidence to suggest that this effect has origins in both the LGN and the cortex. When optimally oriented centres that generate suppressed responses from cells are used as components of bipartite stimuli, then it must be assumed that the cells that provide the inhibitory inputs still have the capacity to be active, however the magnitude of the response that is recorded when such a centre is presented with an orthogonal surround, is significantly larger than that which would be recorded if that centre patch was presented in isolation. This is evident in figures *18* and *22* for the primate and cat respectively. Again there are several possible ways that this response increase might come about, firstly figures *40* and *41* show that LGN responses are synchronised to such stimuli, and thus they might be expected to have a greater influence in the cortex, providing synchronised inputs to distributed postsynaptic targets. Figure *23* also indicates that input from LGN cells within the centre of such stimulus would be increased (Sillito et al, 1993). Secondly orthogonally oriented cells in the surround might be provide directly excitatory input which is stronger than the inhibitory influences that originate from iso-oriented cells driven by the larger than optimal centre, or thirdly, orthogonal surround cells might provide inhibitory input to the cells that provide iso-oriented surround inhibition, this mechanism would be disinhibitory nature.

Thus this visual network could operate in a wide variety of ways, at the level of the thalamus and with excitatory, inhibitory and disinhibitory cortical influences when presented with natural images distributed over the visual field. Horizontally vectored cortico-cortical projections are reported as a result of many anatomical studies, many projections specifically traverse horizontally, while other primarily vertical interactions have significant horizontal components, such as input to cortical layer IV from the LGN, and cortico-thalamic feedback originating from layer VI of V1. A feature of such horizontally directed axons is that along their length they give rise to groups of collaterals, thus cells are said to make horizontally and periodically distributed patches of terminals. An important area of debate is how these projection patterns superimpose on the spatial distribution of functional modules such as orientation and hypercolumns. On the one hand reports have indicated that these

projections link volumes of tissue with similar functional properties, other reports indicate that termination patterns are less specific with reference to the distribution of orientation columns. The axonal projections of pyramidal cells in the supra-granular layers have been reported to be span up to 4mm horizontally and to give off periodic clusters of terminal every 800-1000μm. (Gilbert and Wiesel, 1979, 1983 and Martin and Whitteridge, 1984). In the first model of intrinsic connectivity in area 17 of the visual cortex, the proposition is that these patches of terminals connect cells with similar orientation preferences (Gilbert and Wiesel, 1989). However another study in area 18 of the cat visual system (Matsubura et al, 1987) reported the different results, and proposed another model for cortical functional connectivity. Cells were most often found to project to other areas of cortex where cells had orthogonal orientations. This observation was however made without attempting to determine whether a projection was excitatory or inhibitory or whether it terminated on excitatory inhibitory cells. The authors proposed that there results provided an anatomical substrate for a cross-oriented inhibition model, in which basket cells made long projections to terminate on cells with orthogonal orientation preferences, or pyramidal cell made projections to excite interneurons which would provide local inhibition at a cross-oriented site.

More recent investigations in the primary visual cortex of the cat that have attempted to selectively label the projections of non-pyramidal inhibitory (Kisvárday et al, 1994) and excitatory cells (Kisvárday et al, 1995). A typical inhibitory cell was found to make 60% of its terminals at sites where cells were tuned orientation that were shifted by more 30° from its optimal. The impact of these inhibitory projections was found to change with the distance from the recording site, strongest inhibitory targeting of cells with different preferred orientation was found at distances between 300-900μm, at smaller distances and distances up to 1200μm, iso-oriented cells were targeted. Recent investigations into the projection patterns of pyramidal cells in the primary visual cortex have also lead to the conclusion that termination is marginally biased towards sites that are tuned to within 30° of the injection site. However 47% of boutons are made at sites that are tuned to orientations which are shifted by between 30° and 90°, such sites were most often targeted at points that were 400-600 mm. These latter anatomical observations provide some support for the results of this

investigation, in which the functional interactions between cells separated by anatomical distances of 750-1000mm, exhibiting a wide range of relative receptive field positions and orientation preferences have been investigated.

In all cases the observed network interactions between a pair of sites were found to be extremely stimulus specific, significant correlations were detected between the responses of cells to a very small percentage of the stimuli they were presented. Some aspect of each of these stimuli was optimal for each of the cells that were found to be functionally linked during the response. These results suggest that there are paths of interaction between cells which are non-specific with regard to orientation and extend beyond the boundaries of a typical classical receptive field. In responding to a given stimulus a cell recruits inputs from a subset of these. The response to a discontinuous stimulus contains a strong contribution from, detectable using temporal correlation techniques, cells that are tuned to the surround orientation. Where anatomical intra-area projections have been detected between sites that contain cells that have orthogonal preferred orientations (Matsubura et al, 1987, Hata et al, 1988, and Kisvárday et al, 1993, 1994 and 1995), they have been implicated in the generation of cross-orientation inhibition. However pyramidal cells in layer III selectively make 85% of their terminals on dendritic spines, spines are associated with cells that perform excitatory functions in the visual cortex and are present on both stellate and pyramidal cells (Kisvárday et al, 1986, Kisvárday and Eysel, 1991). Pyramidal cells in this layer have been reported to be highly reciprocally interconnected in networks that are spatially distributed over very large cortical areas that can be up to 20 mm^2. Five per cent of pyramidal cell post-synaptic targets were found to be GABAergic cells associated with inhibitory function. A network of this kind would provide a substrate for reciprocal interactions, that were suggested earlier, to be necessary for the generation of contextual responses that are conditionally dependent on the configurations of centre and surround stimuli. Figure *34* shows a pair of cells in which one is driven by the surround, the other by the centre, their responses are synchronised to a discontinuous bipartite grating condition. The responses of both cells to this stimulus are elevated, with respect to their responses to optimally oriented full field gratings. The last cross-correlogram in the figure, depicts a very complex structure, it peaks on both sides of the origin. This indicates that the firing of one cell

was associated with an increased probability of firing of the other, about 15 ms later, *and* vice versa. This observation provides support for the idea that highly interconnected excitatory networks of cells exist in the superficial layers of the primary visual cortex, and extends it, to propose that this network connects cells with a whole range of orientation preferences.

It is possible to determine the anatomical dimensions of the network that is activated by a typical bipartite stimulus to see whether they are consistent with anatomical observations discussed above. Systematic mapping of visual cortex enables the calculation of a magnification factor, the area of cortex that represents a given area of visual space, that is proportional to the eccentricity of that visual space. At a parafoveal eccentricity of 5°, the area of cortex that represents a square degree of visual space is 2.63 mm^2. This means that if the anatomical area is circular, then the centres of discontinuous stimuli with diameters of 1.0°, 1.5° and 2°, activate areas of tissue with radii of 0.8mm, 1.2mm and 1.6mm respectively (Van Essen et al, 1984). Bipartite stimuli with these diameters generated many of the strongest context dependent responses that were recorded. If the observed effects at least partly originate from the horizontal connections between cells in the same layer, as is suggested by the data presented here, then the receptive fields of cells providing the input would have to reside in space adjacent to the boundary between the centre and surround gratings, if they were sited far beyond this zone, they would exhibit suppressed responses because such fields would be stimulated with what approximates a continuous full field grating. The dimensions of the centre stimulated anatomical area are consistent with the unilateral extension of pyramidal cell, and large basket cell axons. The dimensions of centre activated zones indicate that cells providing input to generate elevated responses to discontinuous conditions could reside in a different hypercolumn, they would have non-overlapping receptive fields with potentially any orientation.

Context dependent network synchrony.

The conclusion of this investigation is that interactions exist between cells with a whole range of overlapping and non-overlapping receptive fields, which do not, on the

basis of this sample, preferentially interact with other iso-oriented sites. Synchronised responses was detected between cells with the whole range of orientation differences, from 0° to 90°. The main factor that appeared to determine whether a pair of cells fired synchronised responses or not, was the configuration of the stimulus. Though there is one unifying feature of the data obtained from all the cell pairs and that is, if the orientation difference between the receptive fields was greater than 30°, than aligned coherent full field stimuli never evoked synchronised responses, it was only certain configurations of discontinuous stimuli which were capable of this.

Earlier investigations did not employ contextual stimuli, and only provided limited insights into how the network functions during perception complex visual features. Simple bar stimuli were used in order to detect interactions between cells, reported after anatomical investigations. In such reports conclusions are drawn from the excitatory receptive field properties of cells they find connected without making detailed assessment of the stimuli that bring about the correlated activity. Correlated activity is detected over anatomical distances up to 4 mm, and is typically dependent on the cells having matched receptive field properties such as orientation (Ts'o et al, 1986, Schwarz and Bolz, 1991, Hata et al, 1991). Single spatially coherent long bars, containing information about one orientation, would not be expected to facilitate the detection of synchrony between cells with a wide range of different receptive field configurations. Such stimuli would activate cross-oriented inhibitory inputs, this might explain why the interactions that are discussed have not been reported in the results of these investigations. The same problem would apply if two bars had been used to stimulate both cells optimally, as was the case in one notable investigation (Ts'o et al, 1986). It might be expected that the stimuli used in the course of this investigation would activate cells with a wide range of different preferred orientations as each stimulus contained information about two different orientations, this information was spatially segregated into the centre and surround of the stimulus. In this report it has been shown that, interactions are actually dependent on the characteristics of the stimulus that was used to bring about neuronal activity not the relative orientation preferences of the cells involved.

As well as synaptic interactions between delocalised iso-oriented cortical sites, the data presented here suggests that other mechanisms are involved in generation of visual perceptions. The detection of stimulus specific response synchrony, oscillations within responses of many cells, and modulations in mean response magnitude to contextual stimuli implicates more complex network processes in generating visual percepts. Earlier it was suggested that reciprocal interactions might be necessary for the generation of contextual responses, they have already been implicated in generation of response synchrony (Singer, 1993). Such interactions have been shown to result in synchronisation with zero phase lag. In addition, some synchrony peaks had longer latencies, up to 30ms, and variable, suggesting more complicated anatomical substrate for interactions, possibly a polysynaptic route within the same area or via other visual centres. A feature of network operation which might be critical to the response properties of individual cells is the response synchronisation which was detected at the level of the LGN. In figures *40* and *41* it is shown that cells exhibit strongly synchronised responses selectively to certain configuration of discontinuous bipartite grating, that contained their linking orientation in either the centre or surround that . It has been shown using continuous contours that this occurs because of cortico-thalamic feedback from layer VI of the overlying primary visual cortex (Sillito et al, 1994). Thus the elevated cortical responses that are recorded to discontinuous stimuli in the might have their origins in a high synchronised input from the LGN. This input could temporally prime cortical systems, by depolarising populations of cells synchronously. Facilitating synchronised patterns of output and non-orientation specific cortico-cortical interactions which could further elevate the responses to discontinuous stimuli and cause cells to oscillate. The orientation/neural domains that interact to generate a given response would be selected by the spatio-temporal characteristic of the thalamic input rather than any hard wired characteristics of the cortical network. In this way the visual responses could generate the responses that are recorded dynamically. The dynamic generation of responses was a striking feature of the behaviour of cells encountered in this investigation, presentations were always less for duration's less than 2 seconds, different centre/surround orientation disparities were displayed pseudo-randomly. Thus the results that are reported here are not due to any long term adaptive mechanisms to particular stimulus conditions, as the system would only have time to implement rapid onset strategies lasting very short

times, in response to specific stimulus environments. A schematic depiction of the network that could underlie the neuronal response properties and network interactions that were assessed in the course of this thesis, is shown in figure *42*. In it, it can be seen that cells in layer VI tuned to oblique or orthogonal orientations in layer VI, driven by the centre and surround of a discontinuous bipartite stimuli, that have mutually overlapping termination fields in the lateral geniculate nucleus, provide input to populations of LGN fields underlying these cortical fields to fire synchronised responses. The thalamo-cortical input would thus have two components, synchronised and non-synchronised, cells firing synchronised responses would be those driven by the centre and aligned along the surround contour. The temporal summation benefits associated with a synchronised population input would confer augmented membrane depolarisation on postsynaptic cortical cells that receive it, and would thus render them more labile to reciprocal cortico-cortical influences that are also active due to the synchronised thalamic input. Such influences would originate from cells driven by the centre and surround, with iso-oriented and oblique or orthogonal fields. Other influences that could generate the context dependent response properties reported here, could originate from extra-striate visual areas such as V2 and MT in the primate and area 18 in the cat, where cells that have been recorded have been shown to have larger receptive fields. An observation made as a result of this investigation is that if a particular configuration of centre and surround bring about synchronised responses, the orientations of each can be specifically interchanged and response synchronisation is still detected, but to no other similar stimuli.

This kind of network behaviour would be consistent with the observations made in the LGN in figure *40,* and with involvement of cells sensitive to larger areas of visual space. Interestingly the responses of a limited number of LGN cell pairs were found when correlated to generate peaks that were displaced from the origin by up to 180 ms, a peak of this kind is shown in figure *41* it might be that such a peak might signify the involvement of a complex network of feedforward and feedback connections involving the LGN as well as primary and extrastriate visual areas.

The stimulus specificity reported here and the connectivity of the network that underlies it, shifts the emphasis about what are important features in the visual scene

Figure 42.

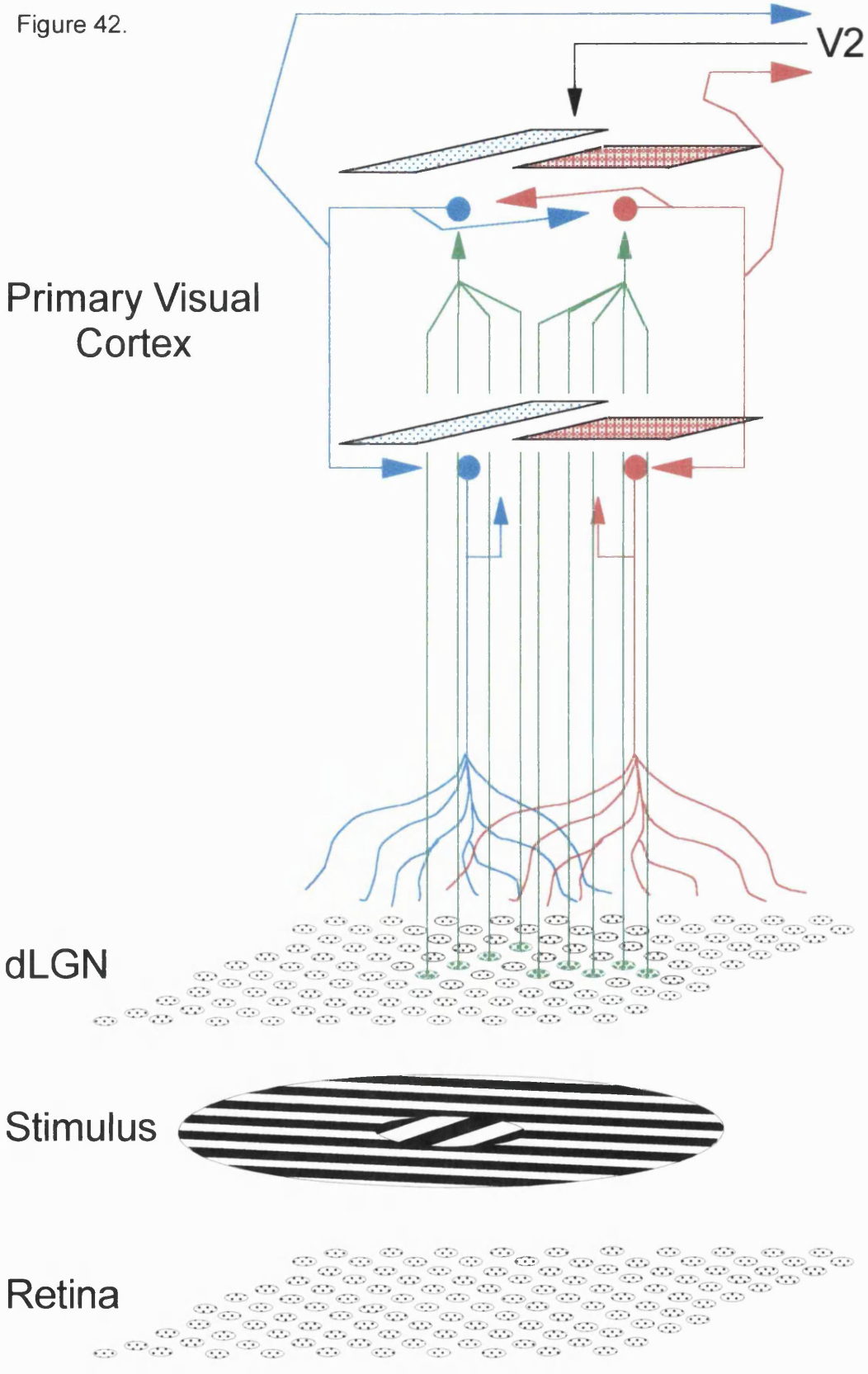


Figure 42.

A summary diagram of anatomical pathway that could underlie the observation made in the course of this investigation regarding the context dependency of visual responses in the cortex. Shown are cells in the retina, dLGN and primary visual cortex and the connections between and within these latter two centres. The feedback to the dLGN originating from layer VI of the cortex causes cells in the LGN that have receptive fields in the centre and surround of a bipartite stimulus to synchronise their output to layer IV of the cortex. Thus cortical cells postsynaptic to this input receive synchronised depolarising influences. This means that the influence of cortical cells driven by the surround on those cells that are driven by the centre, and vice versa, is enhanced because the synchronised input from the LGN temporally locks together epochs of depolarisation in both populations, and thus facilitates the propensity of each population to enhance the activity of the other. Reciprocal excitatory/disinhibitory interaction between cross-oriented cells in the centre and surround evoke oscillations in responses to discontinuous stimuli. This activity is fedforward from the superficial layers of V1 to V2 where it is received by cells sensitive to illusory contours, and is then dynamically fedback to V1, under the guidance of V4 cells sensitive to basic shapes such as stars and squares.

that the cortical system uses to create percepts of the world around us. Based on Hubel and Wiesel's ideas the priority of the primary visual cortex would be to code the orientation and position of line segments in the visual scene using cells' excitatory receptive fields. However data presented here suggests that the classical receptive field interacts with its surround and as a result cells process information about the context of stimuli. It appears that it is the priority of the system to signal the presence of discontinuities and spatially restricted features in the visual scene. A change in the view of the function of cells in the primary visual cortex, of course, has implications for the way in which we imagine they combine their outputs at higher levels in the system. Current thinking on how this is achieved takes as it's starting point the scheme proposed by Hubel and Wiesel. As a way of generating percepts from neuronal output, the Temporal Correlation Hypothesis was proposed in which a scene is segmented into it's constituent parts by the synchronisation of responses of cells responding to these segments (Von der Malsburg, 1981 and Von der Malsburg and Schneider, 1986). Initially analysis using cross-correlation techniques indicated that there was a high incidence of response synchronisation amongst cells tuned to the same orientation responding to optimally oriented bar stimuli (Ts'o et al, 1986, Schwarz and Bolz, 1991). Following this, the observation that the stimulus specific responses of individual cells contain oscillations (Gray and Singer, 1989) led to a search for, and detection of, synchronised oscillations amongst cells (Gray et al, 1989) responding to a common stimulus. The original hypothesis was then developed as a result of these findings, leading to a number of predictions regarding processes of visual feature integration and the involvement of temporal correlation of oscillatory visual responses (Singer and Gray, 1995 and Singer, 1993). It was proposed that cells in columns of like and unlike stimulus specificity would synchronise their oscillatory responses on the millisecond time scale to stimuli that fulfilled certain criteria, these criteria it was suggested should reflect those concerning perceptual grouping proposed by the Gestalt movement in psychology (Koffka, 1935). It was thought that this synchronisation would form unambiguous relations between the visual responses of cells responding to the appropriate type of stimuli, and enhance a salient transfer of information to the next stage of processing.

The experimental detection of oscillating cross-correlograms has been proposed to be a consequence of the fact that cells fire oscillating visual responses in highly synchronised epochs. Cells have been proposed to engage in this form of synchronisation specifically when they are presented with stimuli that fulfil very specific spatial and temporal criterion. It is said that this form of synchronisation is necessary in a distributed neural network because it enables the responses of assemblies of cells performing one task to be separated from those other locally distributed cells that are involved in other processes. The synchronous characteristics of output patterns of cell assemblies responding to specific types of stimuli, mean that they provide more influential input to cells at their termination sites. Conceptually these ideas come together to form the Temporal Correlation Hypothesis, an important feature of this hypothesis, is the stimulus specificity of a network's propensity to fire synchronised oscillatory responses. Experimental investigations have lead to reports that such networks are dynamically generated when the cells within them are stimulated with visual stimuli that fulfil criteria that were originated from the theories of the Gestalt Psychology movement. The basis of Gestalt thinking is that certain groupings and patterns of stimuli acquire a quality to the observer, which is more than the sum of their parts. The Temporal Correlation Hypothesis (Singer and Gray, 1995) proposes that synchronisation occurs to facilitate the generation of perceptual *Gestalten*, an 'object', that is such, because it fulfils certain temporal and spatial criteria. Two delocalised points in visual space acquire a perceptual relationship and become a *Gestalten* because they obey at least some of the Laws of Grouping, such as 'Proximity', 'Common Fate' and 'Good continuation' (Wertheimer, 1912). This view of how visual perception of objects occurs focuses on, for instance the role that three line segments play in the formation of a triangle percept. Logical extension of the hypothesis leads us to suppose that there are three populations of cells, tuned in orientation to each side of the triangle (or any other shape for that matter), the responses of each involved in processing a given edge are synchronised with other cells processing that edge, but also with cells processing the other edges. Within the literature reports have only addressed synchronisation amongst cells responding to the same edge. Experimentally the responses of cells to certain bar stimuli have been found to contain oscillations, it has been shown that when two cells with either longitudinally displaced iso-oriented fields, or obliquely oriented overlapping field are

stimulated by the same bar they synchronise their oscillations, with two different but still optimal bars, the cells do not synchronise (Gray et al, 1989, Engel et al, 1991).

In this investigation the stimuli that were used were not bar stimuli but various configurations of sinusoidal grating, one of the aims was to investigate some of the ideas of the Temporal Correlation Hypothesis. In this study, a stimulus that was considered to fulfil Gestalt criterion was a patch of grating that did not contain an orientation or direction disparity and that extended into the surround zone of the receptive field under consideration, such a stimulus would typically have a diameter of greater than 3°. Response synchronisation was detected between the visual responses of cells to certain very specific stimuli. However the observations presented here depart from the proposition put forward by the Temporal Correlation Hypothesis. These departures and the reasons why they might occur will be discussed in detail below, but basically the main points that come out of the analysis are these :-

a. Response synchronisation that does not involve oscillation was detected far more often than synchronised oscillations, despite that individual cells respond to visual stimuli with oscillating visual responses.

b. In layers II-V, the more superficial of which contain cells which provide input to other visual cortical areas, stimuli that generate both oscillatory and non-oscillatory response synchronisation in the vast majority of cases do not conform to the criterion that originate from Gestalt Psychology.

It has been suggested that response oscillation might play several roles in the Temporal Correlation Hypothesis (TCH). Response oscillation within a response might promote the synchronisation of responses with other neuronal responses, by making the timing of successive spikes more predictable. Alternatively it has been suggested that such a response structure might be a symptom of the fact that cells are firing synchronously (Singer, 1993). It is synchronisation that is the key feature of the TCH, where oscillations are present they can generate a periodic modulation of the cross-correlogram, but only when the visual stimulus conforms to the Gestalt criteria. There are however many investigations that have detected synchronised visual

responses which are not surrounded by periodically modulated flanks, which signify that correlated spikes are within non-oscillatory response epochs. In these cases the correlated spikes within each spike train must be distributed stochastically with respect to other spikes in the train. In this investigation response synchronisation was detected that must have arisen from both oscillating and stochastically distributed spike trains. Synchronisation with origins in stochastic temporal structure was detected significantly more often. Oscillating cross-correlograms were generated from the responses of only five pairs of cells in the cat and primate, in four cases the oscillation in the cross-correlogram was at a frequency of 40-50Hz. Interestingly one pair of cells was found to correlate in a way that generated correlogram that was modulated at a frequency of 12Hz. However it was not the case that these cells only exhibited oscillating temporal interactions between their responses, their responses to other stimuli were sometimes found to generate temporally correlated but without any significant oscillation. Such observations are consistent with recent experiments that have examined the functional interactions between cells as a function of their anatomical separation. It was reported that when cells were separated by distances greater than 2 mm, synchronisation almost always involves oscillation in the cross-correlogram, however over shorter distances it was reported that synchronised spikes could be stochastically distributed with respect to one another (König et al, 1995). Thirty-four percent of pairs separated by less than 2 mm were found to exhibit oscillatory synchronisation, the remainder were not oscillatory. In this study 20% of pairs were not found to significantly interact in any way, 66% of the remaining pairs were found to exhibit response synchronisation in a way that did not generate oscillatory cross-correlograms, 11% of cells interacted to generate both oscillating and non-oscillating correlograms, and 3 % of cells fired synchronised responses that generated exclusively periodic correlograms. In other words there were a limited number of cell pairs that exhibited both modes of response synchronisation. Oscillatory interactions only occurred between the responses of pairs of cells in which at least one of the cells exhibited response oscillation in the strongest range of all those detected. Where strong oscillation were detectable within a response, and a significant interaction was detected, it was oscillatory. However a pair of cells could exhibit significant but weaker stimulus specific response oscillations, but were not found to interact in a significantly oscillatory fashion. It was apparent that this

happened because oscillations were associated with responses to stimuli, which failed to generate any form of temporal interaction between the responses of the cells, yet other stimuli, which failed to evoke oscillatory responses, caused the cells to fire synchronised responses with origins in stochastically distributed spike trains. This suggests that it is not just anatomical separation which influences whether a pair of cells exhibits oscillatory or non-oscillatory response synchronisation, but also the configuration of the visual stimulus. Response synchronisation is promoted by presentation of spatially restricted patches and discontinuous bipartite gratings, in other words by discontinuous features in a visual scene. Thus for the vast majority of sample, neither the propensity for cells to respond with oscillating spike trains nor their propensity to correlate these spike trains or stochastically distributed ones, were consistent with Gestalt criterion, unless a discontinuous grating can itself be considered a Gestalt stimulus. Only 6% of individual units and one pair exhibited properties that were consistent with this scheme. Discontinuous stimuli do not conform to the Gestalt criteria of 'Good Continuation' or 'Common fate'. When cells were found to exhibit response synchronisation to Gestalt stimuli they had receptive field configurations they were either overlapping or non-overlapping, but always iso-oriented, as in other reports (e.g. Gray and Singer, 1989 and Livingstone, 1996). Even so in some cases such cells were found to exhibit stronger interactions to stimuli that did not conform to Gestalt criteria, in contrast to these reports. Within the total sample temporal interactions generated by non-Gestalt stimuli far out-number those that were generated by continuous stimuli. Very specific types of non-Gestalt stimuli caused cells centred within them to fire strongly oscillating spike trains. When such spike trains were correlated, a limited subset of them generated cross-correlograms that oscillated. In all cases it is clear that oscillatory response synchronisation is dependent on the stimulus specificity of a cell to oscillate. If both cells are not oscillating then they can still exhibit stimulus dependent response synchronisation.

In the literature concerned with response synchronisation and network connectivity, there is very little that has been undertaken using the stimuli that were used in the experiments reported in this thesis. Discontinuous stimuli have only been used to study the receptive field properties of individual cells. On this basis, observations presented in this thesis represent additional insights into the functionality of the visual

cortex, functionality that has important implications for the way that the whole system operates. The system responds most strongly when presented with discontinuous features, thalamo-cortical, cortico-cortical and cortico-thalamic circuits underlie this behaviour. The characteristics of the visual scene of the greatest functional significance to the Temporal Correlation Hypothesis are all associated with each part of a stimulus having a set of common properties. One major criterion in the scheme of perceptual grouping proposed by Gestalt psychology is known as 'Good Continuation'. Visual stimulation strategies used in investigations of synchronisation of oscillatory responses have generally only employed high contrast bars to construct stimuli that test the theory that the Gestalt criteria have any functional significance for the system. Where these investigations have explored the effect of discontinuity on the oscillatory characteristics, the discontinuity has been generated by overlapping bars with conflicting orientations. However, such stimuli were found in 75% of cases to reduce the oscillatory content of a response, and 85% of cases to reduce response magnitude compared to presentation of an optimal stimulus alone. The stimuli used in this investigation however have not conflicted over the same point in visual space, disparate orientation information was always spatially segregated, with a centre confined to one area and surrounding it, another grating presented independently. These stimuli unify the observations in this thesis, response synchronisation was brought about by discontinuous stimuli, in which there was a difference of at least 22.5°, in figure *38*, the surround is rotated by 67.5°. In 80 % of cases where oscillatory interactions occurred, the cells also interacted via non-oscillatory response synchronisation. Oscillatory interactions were most often found to occur when a cell was presented with a discontinuous stimulus with a very limited range of centre diameters, that appeared to be around 1.5°, a dimension bigger than the classically defined receptive field of the centred reference cell. Larger and smaller centres were more likely to generate non-oscillatory synchronisation. The questions that will be dealt with in the rest of this discussion will be, what is the functional significance of two modes of response synchronisation, with their subtly different stimulus specificities? Perceptually, what do discontinuous stimuli represent? And how do these ideas fit into the framework of knowledge we have about the receptive field characteristics of cells at various stages of the visual processing stream?

Responses of pair of cells could interact in two ways that appear to have their own distinct stimulus specificity's. A possible functional significance for this observation might be that response synchronisation needs to take place in different time-scales, for certain distinct types discontinuous stimuli. A property of oscillatory response synchronisation is that it places temporal limits on the dynamic generation of networks subserving a particular function. If oscillations are involved in assembly formation by synchronisation, they place temporal limits on cells' capacities to switch assemblies and operate within different networks. The capacity to dynamically generate functional networks is central to the idea behind the TCH, the use of oscillation in the gamma frequency places distinct limits on the systems ability to do this. If response synchronisation comes about from stochastically distributed spike trains, then a given cell can switch between functional networks in the time that it takes to fire a single spike, that is approximately 2-3 ms. If however networks function through epochs of synchronised oscillation then the time taken for a cell to switch between networks is equivalent to the period of that oscillation, which in the gamma frequency range is between 12.5 and 25 ms, a significantly longer period of time. It might be the case that the capacity to form networks over the anatomical distances tested, rapidly from stochastically distributed spike trains might be suited to the processing of a discontinuous stimulus with a small centre, because it's spatio-temporal relationship with the rest of a visual scene, when scaled by size, is more labile, than the relationship between a visual scene and a discontinuous stimulus with a larger centre. A prediction that follows from this then is that if cells are recorded that are separated by less than 1 mm they will exhibit oscillatory response synchronisation when stimulated with discontinuous stimuli with centres that are smaller than 1.5°.

In the next section the discussion will focus on the functional significance of the discontinuous stimulus to the visual system as whole. Everyday experience shows that visual scene is full of such discontinuities. As an image becomes more and more crowded and complex, the number of discontinuities increases. The overwhelming importance of the discontinuity, is indicated by the fact that it evokes a response from the system which is consistent with the two major theories that concern themselves

with how visual percepts are generated from the activity of neurones. The first proposes that objects in a visual scene are neurally represented by changes in the level of activity of the cells participating in a process (Barlow, 1972). In this study, contour discontinuities were found to generate strongly elevated responses from 70 % of cells in the sample. The second theory proposes that information is coded within the temporal relationship of the spike trains of participating a network (Von der Malsburg, 1981). Consistent with this idea it was found that cells stimulated by discontinuous stimuli were found to exhibit temporally correlated responses. A contour discontinuity could be formed in one of two ways, firstly and most simply it could be formed exclusively from the apex of contours of one object, in which case it would be called a 'corner', alternatively it could be formed by intersection of contours from two or more objects. It would then become very important to segment responses to one discontinuity from those to another, in order to separate features in to objects. A third alternative might be that the mechanisms that are described in this thesis are substrates for figure-ground separation, they operate to perceptually separate the centre of a bipartite stimulus from its surround.

The findings of this investigation support the first two requirements of the Temporal Correlation Hypothesis, the first is that cells should exhibit response synchronisation on a millisecond time scale, the second, (as it applies to this investigation in V1 only) that cells in the same and different columns should exhibit temporal correlations in their responses to stimuli. However the last requirement was that the probability that cells should exhibit response synchronisation would be dependent on stimuli fulfilling Gestalt Criteria. In this way it was proposed to bring about the salient transfer of stimulus information to higher visual areas about objects in the visual scene. A synchronised oscillatory output from a distributed population of cells covering a wide area of visual space was proposed reflect the distribution of an object in visual space. However the data presented here indicates that the Gestalt criteria, as they were originally proposed, do not allow for the stimuli that were found to generate response synchronisation most often. Additionally the vast majority of incidences of response synchronisation were non-oscillatory rather than oscillatory in nature. The numbers of individual cells and cell pairs that exhibited behaviour and interactions that were consistent with Gestalt criteria were relatively very limited. Synchrony between

responses to full field continuous stimuli, was only detected between cells with very similar orientations, such cell pairs also exhibited synchrony to discontinuous stimuli. This is demonstrated by the data presented in figures *34* and *36* for the cat and primate respectively. Cells in V1, particularly those in layers II-V, of the cat and primate do not, in general, with the use of response magnitude, oscillation or response synchronisation, to signal exclusively 'Good Continuation' or 'Common Fate'. Instead cells in visual system appear to use mechanistic strategies suggested to have functional significance, such as Population Coding of the Temporal Correlation to saliently signal the presence of discontinuities in the visual scene. Thus going back to the previous example of a triangle, oscillatory temporal correlation would not be detected by cells responding to an edge, but rather those responding to a corner. Cells in V1 use oscillatory response synchronisation to signal points of discontinuity, to other visual areas. On this basis it might be predicted that just as a pair of cells exhibits response synchronisation when they are stimulated with the same focal discontinuity, it might be the case that populations of cells stimulated by different discontinuities might also exhibit response synchronisation. Spatially distinct discontinuities might drive anatomically distinct cells to fire synchronised responses, these discontinuities could then be dynamically perceptually linked. This would make a degree of functional sense perceptually because it would mean that the visual system emphasised corners and line-ends, from these the spatially structure of objects could be built up dynamically. This dynamic representation of visual objects from the use of corners and line ends might come about as a result of interaction between cells in layers II\III in V1 with cells in V2 which receive input from V1. Analysis of the response characteristics of cells in V2 to similarly complex contextual stimuli, to those used in this study, suggests that cells there have receptive field properties that are complimentary to those that have been reported in this study. It has been reported recently that approximately 37% of cells in V2 respond vigorously when they are presented with illusory contours (Peterhans and Von der Heydt, 1989). These are generated by the spatial arrangements of stimuli surrounding the excitatory receptive field of the cell. Such cells do not need to explicitly 'see' a continuous contour, but that they can infer the presence of one, and respond to the illusion, if they are supplied with information about its ends. This is similar to the response property of the cell that was featured in figure *24*, which responded strongly when a stimulus was

presented exclusive in the surround. It might be that this response property in V1 and V2 is the result of a reciprocal feedforward and feedback pathways between the two cortical areas. The response properties that are reported here to be exhibited by cells in V1 would be suitable for the generation of the response properties of cells in V2. The complex system of interconnectivity between these two visual areas, as well as intrinsic V1 connectivity and thalamo-cortical interactions might be responsible for all the observations made in this report. Cells sensitive to illusory contours in V2 might receive converging synchronised inputs from two distinct populations of cells in V1, each of which is stimulated by the discontinuities which must necessarily be at either end of an illusory contour. It has been proposed that the priority stimuli of cells in V1 that provide input to higher visual areas, typically involve spatial and temporal discontinuities. In order to generate a complete percept of a visual scene it would be necessary to form links between cells that were stimulated by certain discontinuities this could be achieved by response synchronisation, in this way they would become perceptually connected and continuous contours would be generated. However if every discontinuity in the visual scene was linked with every other, to generate the responses of many cells in V2, or even only those within a localised area of visual space, it would be difficult to extract the spatial structure of an object from the visual system. There needs to be a strategy that separates 'nonsense' links from links that make perceptual 'sense', this sense could come from areas such as V4 or infero-temporal cortex where cells are selectively sensitive to simple shapes (Tanaka et al, 1991 and Tanaka, 1992). These simple shapes it was suggested could be thought of as 'partial features common to images of several different natural objects', experimentally the receptive fields in this area were larger than those in V1 and V2 and had more complex receptive field properties, commonly responding most strongly to square and star shaped figures. Cells in V1 at points in visual space that were stimulated by discontinuities, and cells in V2 whose response properties were selective for the intervening gap would operate in parallel to extract spatial information from a visual scene. Assemblies of cells would be formed through response synchronisation, these outputs would then target infero-temporal cortex to 'test' the structure of the object that was held with temporally tagged pattern of output, by virtue of the positions in visual space of the receptive fields of the cells participating. This whole process could happen many times, and if response synchronisation was to occur from spike trains

Figure 43.

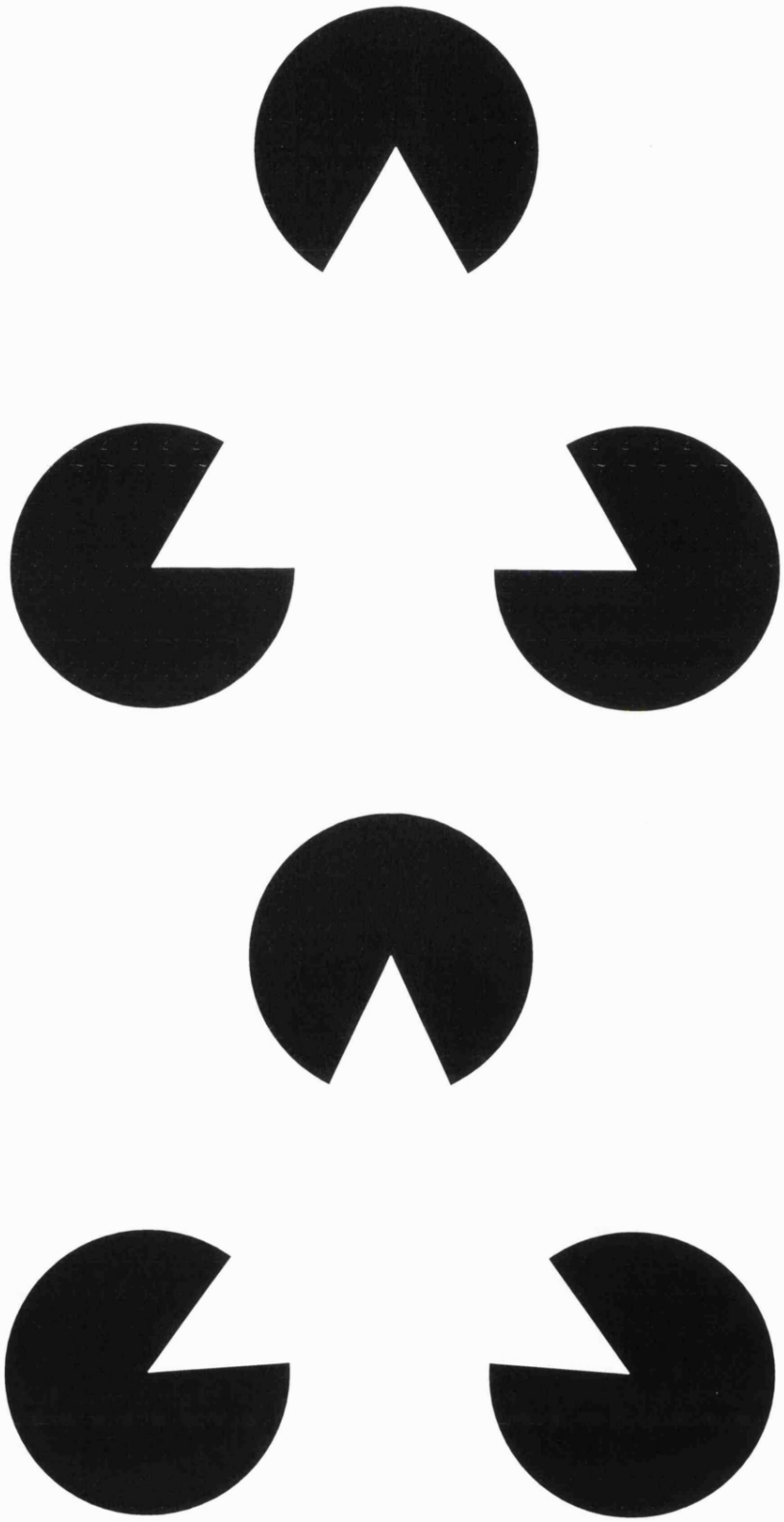


Figure 43.

The Kanizsa Triangle. Broken sectors ('pac-men') provide discontinuity information from which three illusory contours are extracting forming an equilateral triangle that is perceived in a single plane in front of the sectors. If the sectors are broken by a narrower angle then the contour appears curved.

that were structurally stochastic then one iteration of the process could occur very rapidly indeed.

Within the literature there are several reports of perception of illusory contours joining points of spatial discontinuity to generate simple shapes (Prandtl, 1927, Kanizsa, 1955, Gregory, 1972 and Redies, 1984). Several theories so far proposed have been concerned with how and why such perceptual phenomenon occur. It has been reported that when short line segments or points of discontinuity (crosses) are presented, separated by gaps, a bright contour can fill the intervening gap (Prandtl, 1927), it has been proposed that this effect might be due to the pattern of response of an end-stopped cell in the intervening gap (Redies, 1984). Other theories have dealt with the perception of contours that are the result of presenting figures such as the Kanizsa Triangle (Kanizsa, 1955), this is depicted figure *43*. This is an arrangement of broken disk sectors from which can be perceived an illusory triangle. This is possible even though none of the contours that would be needed to classically generate a percept of it, are explicitly included within it. Two paradigms have been proposed that could account for this behaviour of the system (Gregory, 1972). The first explanation is physiological, in which the 'cells in striate cortex are activated by the disc sectors to give the appearance of continuous lines, though only their ends are given by stimulation'. The second explanation in cognitive in nature, in which perception of the triangle comes about from 'object hypotheses', these hypotheses are proposed to be 'selected from sensory data'. Gregory concluded that perception of illusory figures came about as a result of cognitive processes. The data presented as a result of this investigation, demonstrates that cortical networks are indeed activated by the disk sectors. Additionally the model presented here proposes that these cognitive 'object hypothesis' could occur as a result of parallel and co-operative response synchronisation processes in the lateral geniculate nucleus and cortical areas V1, V2 and V4. The model proposed above, in this thesis, combines cognitive and physiological ideas about how perception might occur. Using object hypotheses that are extracted from the responses of a visual system using temporal synchronisation of responses of cells, that are explicitly sensitive to the broken disk sectors and their intervening gaps, via horizontal, feedforward and feedback patterns of connectivity. It is interesting to note that some of the observations reported in this thesis, after

invasive extra-cellular investigations, have been reported recently to be detectable using non-invasive techniques in human subjects who were shown the Kanizsa triangle (Tallon et al, 1995).

Appendix 1. Requirements for the completion of PhD thesis.

A number of methodological changes were suggested during the viva to deal with problems in some of the analytical techniques used to generate the results presented in this thesis. Some of these had serious implications for the results of the analysis. Requirement 18 concerned significance criteria used to quantify the extent to which cells fire oscillatory responses. It was felt that the original criteria were too low and too arbitrary. To alleviate this problem a computer simulation was written in order to calculate more realistic significance limits based on analysis of spike trains generated using the simulation. Two-hundred and fifty spike trains were generated at a range of different firing rates to examine how the spectral power distribution in auto-correlation functions changes as a function of firing rate. The significance measure calculated from the simulated activity was found to be independent of firing rate, but was significantly higher than the original value that had been used. Spike trains with oscillation indices greater than 2.0 were previous said to contain significant levels of oscillatory discharge, based on analysis of the simulated data, responses had to have oscillation indices greater than 4.08. The entire population of sampled neurones was reanalysed using this new criterion. Using this value meant that many fewer cells contained significant oscillatory discharges. Below is a table of data presented in the previous version of the thesis.

Group description	Group	n Cells	% of A	% of B
Cells analysed in primate V1	A	53		
Stimulated with bipartite stimuli	B	34	64%	
Elevated IPS* to Discontinuous stimuli	C	32		94%
Total oscillating	D	43	81%	
at 28-80 Hz	E	35	66%	
at 12-16 Hz	F	8	15%	
Group D presented with bipartite stimuli		30	57%	88%
Group E presented with bipartite stimuli		26	49%	76%
Group F presented with bipartite stimuli		4	8%	12%
Elevated OI* to discontinuous stimuli at 28-80Hz		24		71%
Elevated OI* to continuous stimuli at 28-80Hz		2		6%
Elevated OI* to discontinuous stimuli, at 12-16Hz		4		12%
Elevated OI* to continuous stimuli, at 12-16Hz		0		0%

* IPS = impulses fired per second.
OI = oscillation index

The table above must be compared with *table 1* in the *results* section. The results obtained using the new criteria have been inserted into the text. Using the previous

significance criterion 81% of cells were found to significantly depart from a stochastic distribution of spike times by firing oscillatory discharges. However using the realistic criteria based on the simulation, only 57% of cells were found to respond in an oscillatory fashion, significantly fewer. The previous significance level was set at a low level and this level was arbitrary, as the value was taken from the literature (Ghose and Freeman, 1992), all data based on this value would over estimate the proportion of cells the respond with oscillatory discharges.

In requirement 24, concern was expressed that the distribution of oscillation frequencies detected in the sampled neurone population, depicted in figure 30, differed from distributions published in previous reports. This figure is replaced by another calculated using data obtained using the new criterion for significant oscillations. This distribution is more similar to those that have been previously reported, peaking at frequencies between 40-50 Hz and decreasing at higher and lower frequencies.

In requirement 27, concern was expressed that in figures 31, 32, 34, 35, and 39 cross-correlogram were presented in which certain bins contained significant numbers of events but it was reported that these were not significant in the text of the results section. It was suggested that the significance level for synchrony between two cells using cross-correlation analysis was too low. This was originally calculated from the mean shift predictor calculated from all modulation of the stimulus (30-50). This procedure would minimise the effect on the significance level of firing variability that was seen in the responses of some cells. To deal with this problem the data was reanalysed, significance levels were calculated from averaged shift predictors calculated from fewer shuffles. Cross-correlograms in the original thesis have been replaced by those analysed in this way. For some cells this increased the significance levels for synchrony, removing circumstances were some bins, displaced from the origin, contained significant numbers of events but no discernible synchrony at the origin. This process did not however change the proportion of cells that were found to respond synchronously, generating peaks at the origin of cross-correlograms.

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