Instituto Juan March
de Estudios e Investigaciones

77

CENTRO DE REUNIONES
INTERNACIONALES SOBRE BIOLOGÍA

Workshop on

Mechanisms Involved in Visual Perception

Organized by

J. Cudeiro and A. M. Sillito

T. Bonhoeffer
P. Buisseret
J. Cudeiro
J. M. Delgado-García
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The lectures summarized in this publication were presented by their authors at a workshop held on the 23rd through the 25th of February, 1998, at the Instituto Juan March.

Depósito legal: M. 12.767/1998
Impresión: Ediciones Peninsular. Tomelloso, 27. 28026 Madrid.

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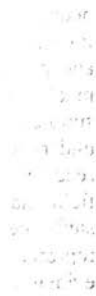
INTRODUCTION

J. Cudeiro and A. M. Sillito



Mechanisms involved in visual perception

Questions regarding the nature and the mechanisms of visual perception have provided one of the strongest focuses for multidisciplinary dialogue in the field of neuroscience. The convergence of the interests of philosopher, theoretician, psychophysicist and neurobiologist in vision tracks back a surprisingly long way in time. It has drawn those with interests in the mechanisms of consciousness into a dialogue with those dissecting subtle interactions in elements of neuronal circuitry in retina, thalamus or cortex. The tensions and synergies following from this have provided a potent stimulus to a dialogue that has constantly questioned ways of thinking about visual mechanisms in particular and brain function in general. In setting up this meeting we sought to bring together a selection of those who hold distinctive and nodal positions in the many components of the dialogue that constitutes the current field of vision research.

Advances in our understanding of the retina are providing a growing insight into the nature of the processes which encode the retinal image and drive the central visual mechanisms. The functional specificity of the filters encoding luminance and chromatic signals in primate retina are being linked with increasing confidence to the circuitry and the properties of these filters associated with visual performance in tasks such as vernier acuity. Despite a wealth of evidence to the contrary, there is still an odd tendency to forget that the lateral geniculate nucleus contributes to the visual mechanism and occasionally it seems some may think the retina provides direct input to the cortex. A convergence of anatomical, pharmacological and functional evidence on the other hand shows the presence of a complex, dynamic and potentially very structured influence on the transfer of visual information through the lateral geniculate nucleus. It is cogent to remember that the retinal synapses on relay cells comprise about 7% of the input whilst corticofugal fibres from layer 6 of the visual cortex comprise 30%. The elegant definition of a third visual channel in primates, linked to konicellular type cells in the lateral geniculate nucleus and cytochrome oxidase rich blobs in the visual cortex shows how easily the edifice on which we attempt to formulate our description of the visual system can change. This "K" channel is driven by broad band luminance contrast signals and the blue-on signal from the retina and appears to be strongly linked to the function of the "blobs" in V1.

The complexity and diversity of cortical visual processing does not allow any simple description with hundreds of anatomically defined pathways and at least ten hierarchical stages in the many parallel streams. However, the insight from non-invasive neuroimaging techniques and increasingly sophisticated visual neurophysiological investigations provide an abundance of pointers to organisational detail in both circuitry and processing hierarchies. Once dismissed, shunting inhibition has re-emerged as a mechanism that may play a strong role in the organisation of the receptive field of simple cells in the primary visual cortex. Both models of the circuitry and recent data underline the complexity of behaviour that emerge from multiple interactions in the recurrent and laterally directed networks. The distinction between classical receptive field and surrounding area of visual space blur when the global context of the image shifts the state of the multiple lateral interactions in the successive horizontal networks representing visual space. In visual cortical area MT there is very thought provoking evidence from innovative work suggesting that the organisation of centre and surround

mechanisms in neurons provides the basis for a computation representing the direction of surface tilt specified by motion. Interestingly the evolution of the timing of responses to image context such as orientation and motion contrast in the primary visual cortex suggest that these effects may well follow from multiple interactions between different levels in the hierarchy of the central visual system.

Whilst it is easy for the neurobiologist to be caught up by slightly parochial ways of thinking about the mechanisms of visual function the interplay with the many observations on the psychophysics of human visual performance and perception provide a rigour that at the very least generates a sense of caution. The need to avoid "inappropriate concepts or theories that generate imaginary mechanisms" is underlined. Illusions and backward masking provide potent questions to mechanism and increasingly a new repertoire of stimuli to dissect the representation of salience in what seems to be mechanism. Whilst avoiding illusory mechanisms for illusory phenomena we should perhaps also pause before setting anatomical boundaries for the presence and absence of consciousness.

Adam M. Sillito
Javier Cudeiro

Session 1: Retinogeniculate processing of the visual information

Chairman: Adam M. Sillito

FUNCTIONAL ARCHITECTURE OF THE MAMMALIAN RETINA

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It is well established that information processing in the mammalian visual system occurs in parallel. In the cortex many highly interconnected areas are involved in visual processing. The projection from the retina to the cortex is organized in parallel routes. In the retina there may well exist as many as 10-20 different ganglion cell types which cover the retina homogeneously with their dendritic fields, and send their axons to the subcortical visual centres. They represent 10-20 specific filters which encode in parallel different aspects of the image projected onto the retina.

Ganglion cells receive specific inputs from bipolar and amacrine cells in the inner plexiform layer (IPL). The IPL is precisely stratified and different ganglion cell types have their dendrites at specific levels within the IPL. The overall subdivision is into ON and OFF layers. Dendrites of OFF-ganglion cells stratify in the outer half of the IPL, those of ON-ganglion cells in the inner half. Within this ON/OFF dichotomy further subdivisions occur. Dendrites of phasic ganglion cells keep a narrow stratification level close to the centre of the IPL, dendrites of tonic ganglion cells stratify more diffusely and are found more towards the outer and inner IPL respectively. This suggests the neurally encoded retinal image is different at different levels of the IPL, depending upon the stratification of various bipolar, amacrine and ganglion cells.

This raises the question as to how specific aspects of the light signal are transferred from the outer to the inner retina. This might be the role of the 9-10 different types of bipolar cells. For colour vision one has to ask, which bipolar cells transfer cone specific signals into the IPL and at what level do their axons terminate. For achromatic tonic and phasic signals or for directional selective responses different sets of bipolar cells are probably involved with axons terminating at different levels within the IPL. Multiple signal pathways from the outer towards the inner retina, imply that parallel processing starts immediately after the cone pedicle, the first synapse of the retina.

These and related questions will be dealt with and the circuitry of the primate retina will be compared with that of the rat and of the cat retina. Since cats and rats, like other mammals are dichromates, this comparison should reveal some details of the circuitry that subserves trichromacy in primates and how this circuitry has evolved from a "standard" mammalian retina.

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Functional Specificity of Luminance and Chromatic Channels in Primate Retina

Barry B. Lee

The primate retina provides an ideal opportunity for a multidisciplinary approach to vision. The physiology of retinal elements can be related on the one hand to retinal synaptic mechanisms and circuitry, and on the other to psychophysical performance, since the old-world primate is now accepted as a suitable model for human vision. Recent physiological and anatomical results have revealed that the primate retina is organised in a very specific and elegant manner, and that luminance and chromatic signals are separated from the very earliest levels of retinal processing.

There exists strong psychophysical evidence for a luminance channel and for red-green and blue-yellow chromatic channels in human vision. The luminance channel has the parasol ganglion cells of the magnocellular pathway as an anatomical substrate (Lee, Martin & Valberg, 1988; Kaiser, Lee, Martin & Valberg, 1990); these cells receive summed input from middle (M) and long-wavelength (L) sensitive cones via diffuse bipolar cells (Boycott & Wässle, 1991). The red-green cone-opponent system has the midget, parvocellular system as a substrate. These cells receive difference signals of the M- and L-cones. Lastly, the blue-yellow chromatic channel has the small bistratified ganglion cell as a substrate (Dacey & Lee, 1994), and receives a signal from the short-wavelength sensitive (S) cone opposed by a combination of M- and L-cone signals. Both these chromatic channels also receive specific bipolar input, so that luminance and chromatic signals become separated at the earliest level, in the outer retina.

Although luminance and chromatic channels revealed in psychophysical flicker experiments (i.e., temporal modulation) have these different pathways as their relevant substrates, for spatial vision the situation is less clear. I shall argue that the

luminance channel which underlies precise spatial vision also has the parasol, magnocellular pathway as a substrate. For Vernier tasks, just a few impulses in a few parasol cells appear adequate to support performance (Lee, Wehrhahn, Westheimer & Kremers, 1995), providing an up-to-date equivalent of earlier suggestions that just an impulse or two from the retina can be detected (Barlow, 1972). Models in which luminance spatial information and chromatic signals are multiplexed through the midget pathway are theoretically plausible but physiologically unrealistic. Although in the cortex recent evidence has been in favor of distributed processing, the signals emanating from the retina have great functional specificity. Luminance and chromatic channels as psychophysical constructs find a direct basis at the retinal level.

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ON THE DYNAMIC TRANSFORMATION OF THE INCOMING VISUAL SIGNAL AT LEVEL OF THE LATERAL GENICULATE NUCLEUS

Javier Cudeiro & Casto Rivadulla.
E.U. Fisioterapia (Univ. De A Coruña) - Unidad Cirugía Experimental (Hosp. Juan Canalejo) A Coruña (Spain).

The lateral geniculate nucleus (LGN) is the major source of visual input to cerebral cortex. Most notable is the discovery that the visual pathways from the retina through LGN comprise at least three parallel neuronal streams that independently analyze different aspects of the visual scene. The best known of these in the cat are the X and Y pathways which course through the A-laminae of the LGN and utilize glutamate as neurotransmitter, operating on both NMDA and non-NMDA receptors.

In recent years we have begun to appreciate in greater depth a very important role of geniculate circuitry, the gating of information from retina to visual cortex. Receptive fields of single cells have been closely studied, and although at first view seem to have properties virtually identical to their inputs, these cells operate as more than just a simple passive relay. Rather, they seem to work as a variable filter, determining what, when and how much retinal information gets passed to visual cortex1.

We have already completed preliminary studies on the "how much" question, showing that the strength of visual information leaving the LGN is critically controlled, amongst other things, by nitric oxide2. Here we present very recent data from our lab addressing the other two problems: a) "what" information, meaning the quality of the signal - we will provide new results extending our previous data3 which suggest a great level of communication between geniculate cells, with information shared over a modest local area, but between radically different cell types, and b) "when", since recent studies have reinforced earlier reports of the context dependency of visual responses, such that the presence of spatially distant stimuli have been shown to influence markedly the responses of visual neurones to "standard" visual stimuli4,5. However, to date the evidence for temporally separate influences is scarce. Here we provide evidence for an elevation of visual responsiveness in cells of the LGN, as a result of electrical, pharmacological and physiological manipulations. These reveal a form of response augmentation dependent upon events up to minutes prior to the presentation of standard visual stimuli. This may be thought of as a form of potentiation which is due to a prior increase in activity in the visual input. We suggest that these effects reflect a general mechanism for the control of visual responsiveness in the context of temporal shifts in the intensity of incoming visual stimulation.

Supported by XUGA and FIS grants.

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CONTROL OF GATING THROUGH THE LGN

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The LGN is not a simple, machine-like relay of retinal information to cortex: it instead performs a dynamic, variable relay that presumably reflects the varying behavioral needs of the visual system. Two aspects of this will be reviewed. First is the appreciation that LGN (and other thalamic) relay cells have a variety of voltage dependent membrane conductances that dramatically alter the way they respond to retinal inputs. Perhaps the most important next to the those underlying the action potential is a voltage dependent Ca^{2+} conductance. This can be activated by depolarization (e.g., from a retinal EPSP) only from a hyperpolarized level (e.g., more negative than about -65mV), because the Ca^{2+} conductance becomes inactive at more depolarized levels. The activation state of this conductance determines whether the relay cell responds in *tonic* or *burst* firing mode to its retinal inputs, and which response mode is operating is of critical importance to the nature of information relayed to cortex. Second is the fact that, while the information relayed through LGN to cortex is retinal in origin, retinal synapses represent only about 7% of inputs to relay cells. The vast majority of inputs derive from intrinsic local GABAergic cells, from visual cortex, and from the brainstem, and they each contribute about 30% of all synapses on relay cells. These nonretinal inputs are modulatory in nature and, among other things, serve to control membrane potential, thereby controlling voltage dependent conductances like the Ca^{2+} conductance described above. An attempt will be made to bring these observations together in a testable hypothesis that addresses how and under what conditions nonretinal inputs influence the relay through the LGN.

Supported by EY03038

Session 2: To the cortical step (circuits, questions and maps)

Chairman: David A. McCormick

Connections of interneurons containing calbindin, calretinin and parvalbumin in the visual cortex (areas V1 and V2) and inferior temporal cortex of macaque monkeys

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Traditionally, cytoarchitectonics, myeloarchitectonics and patterns of long-range connections have been the main basis for subdividing the neocortex into distinct areas and for trying to correlate anatomical characteristics with the functional subdivisions of the cortex. In addition, a variety of chemical markers have been found to show areal- or subareal-specific distributions. Although certain basic features of cortical microcircuits are common to all cortical areas, it is also clear that pyramidal cells located in different areas participate in different synaptic circuits (that is, differences in afferent and efferent connections with other cortical areas or subcortical nuclei), but relatively little is known about differences in the microcircuitry involving pyramidal cells with nonspiny nonpyramidal cells (interneurons) or between interneurons.

It is well-established that many types of cortical interneurons innervate pyramidal cells and that different portions of a pyramidal cell are innervated by different types of interneurons. Clear examples of this differential innervation are represented by the synaptic connections of double bouquet cells, large and small basket cells and chandelier cells. Double bouquet cells innervate the dendritic spines and shafts of the collateral branches and basal dendrites, while basket cells innervate the cell body and proximal dendrites, and chandelier cells the axon initial segments. Immunocytochemical studies in the primate neocortex have shown that the majority of interneurons are GABAergic and that specific subpopulations of these neurons are immunoreactive for the calcium-binding proteins calbindin (CB), calretinin (CR) and parvalbumin (PV). In general, different types of interneurons are stained for these calcium-binding proteins. Among the most characteristic morphological types of neurons immunoreactive (ir) for CB are double bouquet cells, whereas for PV they are chandelier cells and large basket cells, and for CR, bipolar cells, double bouquet cells and Cajal-Retzius cells.

However, very few studies have been made to investigate in detail the possible differences between various cortical areas in the distribution of particular morphological types of interneurons and in the connectivity patterns of interneurons containing CB, CR and PV. The present study was performed to address some of these issues in three well-differentiated cytoarchitectonic areas of the so-called ventral (occipitotemporal) visual pathway of the macaque monkey: the first and second visual areas (V1 and V2) in the occipital lobe and area TE of the inferior temporal cortex. The latter area represents the final stage of this visual pathway and it is thought to be essential for visual object recognition. We

used immunocytochemistry for CB, CR and PV to study mainly the distribution of double bouquet cells and chandelier cells. Furthermore, we used a powerful double immunocytochemical method to explore the connections between CB-ir, CR-ir and PV-ir neurons and to study the connections of these neurons with a subpopulation of pyramidal cells that are immunostained for non-phosphorylated neurofilament protein (NPNFP). These NPNFP-ir pyramidal cells have been shown to be an important component of certain ipsilateral corticocortical visual pathways in the macaque monkey.

The most significant findings of the present study were two-fold. First, the same morphological types of interneurons were identified in all cortical areas examined, but the number and distribution of particular types differed considerably between areas. Second, the number and frequency of CB-ir, CR-ir and PV-ir terminals, which were observed in contact with the cell somata and proximal dendrites of CB-ir, CR-ir and PV-ir interneurons or with NPNFP-ir pyramidal cells, varied depending on the chemical type of interneuron, but the patterns of these connections were similar in the different cortical areas studied. Thus, certain characteristics of intracortical circuits remain similar, whereas others clearly differ in the various areas of the occipitotemporal visual pathway, which might represent regional specializations related to the differential processing of visual stimuli in these areas.

Stewart H. Hendry

The Color Blue: A Third Visual Channel, A Second Color System

Two visual channels, arising from separate populations of retinal ganglion cells, relayed through distinct layers in the lateral geniculate nucleus (LGN) are the basis for all of primate vision. Or so it is said in the great majority of models that seek to explain visual perception. Where and when those channels, the magnocellular (M) and parvocellular (P), converge is open to debate but that they are the source of all input to visual cortex has been an accepted principle. Recent studies have demonstrated, however, the existence of a third geniculostriate population in macaques, analogous to the koniocellular (K) population of prosimians. Composed of six layers, ventral to each of the M and P layers, the K neurons occupy the entire representation of the visual hemifield and are equal in number to the neurons of the M layers. They are the source of geniculocortical innervation of the cytochrome oxidase-rich blobs in V1. and provide to those compartments two very different signals. One is a broad-band, luminance-contrast signal arising from P gamma- and P epsilon-like ganglion cells, relayed through the most ventral pair of K layers and terminating in blobs at mid-layer III. The second is a Blue-ON signal, arising in part from small bistratified ganglion cells and terminating in blobs at deep layer III. A separate Blue-OFF signal appears to be relayed through a group of displaced K cells in P layers 3 and 4 and terminates in a distinct group of blobs. This third channel is a part of the visual system of all primates examined, from prosimians to apes and humans, and may represent the earliest of visual pathways to the cerebral cortex. In Old World primates a major fraction of this K channel appears dedicated to the perception of colors.

IMAGING THE FUNCTIONAL ARCHITECTURE IN ADULT AND DEVELOPING CAT VISUAL CORTEX

Tobias Bonhoeffer *Max-Planck Institute of Neurobiology, München-Martinsried, Germany*

Optical imaging of intrinsic signals is a new technique allowing to study cortical maps *in vivo* with unprecedented ease and resolution. Using this method we have previously shown that orientation preference of cortical neurons in cat primary visual cortex is organized such that "pinwheels" surround numerous "orientation centers" in the orientation maps.

In my talk I will present new experiments in which we measured orientation maps simultaneously with ocular dominance and spatial frequency maps. These data allowed us to study the geometrical relationship between these feature maps and they showed that contour lines for all three maps tended to intersect at right angles. The functional implications of these finding will be discussed within the talk.

I will also present data acquired in combined imaging and tetrode-recording experiments addressing the nature of response properties of single cells at these pinwheel centers. These data clearly show that neurons in pinwheel centers with respect to all parameters tested - in particular with respect to orientation tuning - do not differ from cells in other regions of primary visual cortex. The only difference between pinwheel centers and other locations is that the range of preferred orientations of neighboring cells (the "orientation scatter") is much larger in pinwheel centers than elsewhere in the cortex.

We also investigated the origin of the spatial frequency maps that we imaged in the visual cortex. Tracer injections showed that spatial frequency maps in cat primary visual cortex are at least in part caused by segregation of the terminals from the x- and y-cells in the lateral geniculate nucleus. This indicates that, like in the primate, also in cat visual cortex there is a certain segregation into separate processing streams, in this case for the low and high spatial frequency content of the visual scene.

Finally I will allude to some of our recent developmental studies reassessing the question of the role of visual experience for the development of cortical maps in young animals.

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MAPPING STRUCTURE AND FUNCTION IN PRIMATE VISUAL CORTEX

Primate cerebral cortex contains a complex mosaic of visual areas that occupy all of the occipital lobe plus portions of the temporal and parietal lobes. This talk will review the functional organization of visual cortex in two primate species - macaque monkeys and humans.

In the macaque monkey, evidence for several dozen distinct visual areas has been obtained using a combination of anatomical, physiological, and behavioral approaches. However, numerous uncertainties persist about the precise locations and internal organization of these areas, particularly those in the temporal and parietal lobes. Recent progress in resolving discrepancies among competing partitioning schemes will be discussed.

Information flows through visual cortex via a complex network involving hundreds of anatomically identified pathways. The detailed pattern of connections suggests that visual cortex is organized hierarchically (with at least 10 stages of cortical processing) and also that it can be divided into several processing streams. Each processing stream has a distinctive functional signature in terms of the receptive field characteristics of its constituent neurons. Particular emphasis will be placed on the role of visual areas V2 and V4 in form analysis and pattern recognition, based on studies using a rich repertoire of geometrically defined stimulus shapes and on other studies involving shifts in visual attention to examine dynamic aspects of information flow.

Recently, there has been impressive progress in elucidating the functional organization of human visual cortex using noninvasive neuroimaging techniques (particularly magnetic resonance imaging) that have high spatial resolution. Analysis of such results can be facilitated using a surface-based atlas of human cortex as a common substrate on which to display results from different individuals and different experimental studies. Application of this approach to published studies of visual cortex demonstrates that there are some regions that are largely or exclusively involved in one aspect of visual processing (e.g., form analysis or motion analysis), whereas other regions involve overlapping or close interdigitation of cortex involved in multiple aspects of vision (e.g., both form and color, or both form and motion). The resolution of this approach can be further enhanced using surface-based warping to compensate for individual variability when mapping experimental data from individual subjects onto the atlas. Surface-based warping also provides a powerful approach for objective comparisons of cortical organization in monkeys and humans, despite the large interspecies differences in cerebral size, shape, and internal organization.

Short-term plasticity in thalamo-cortico-thalamic networks

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The thalamus sends information to the neocortex via different thalamocortical pathways, while the neocortex returns information via corticothalamic pathways. One aspect in which these pathways differ is in their temporal dynamics, such as their short-term plasticity. This is the result of differences in pathway excitability due to the characteristics of their synapses, the intrinsic properties of their neurons, and the emergent behavior of their connectivity.

Primary thalamocortical pathways produce strong responses that depress upon repeated activation (i.e.decremental response). The cellular mechanisms responsible for decremental responses include the basic properties of thalamocortical synapses, and circuit dependent properties such as the strong inhibition recruited in neocortex by this pathway. Decremental responses are present during slow-wave-sleep, but are largely reduced during behavioral arousal. Stimulation of secondary thalamocortical pathways produces small responses that are strongly enhanced upon repeated activation at around 10 Hz (i.e. augmenting response). Augmenting is generated in neocortex by the interaction between inhibition, intrinsic membrane properties and synaptic interconnections of layer V pyramidal neurons. Augmenting responses are dynamically modulated by behavioral state; they are blocked during "attentive states". Stimulation of corticothalamic pathways at frequencies above 10 Hz also produces a short-term enhancement in thalamic relay cells. The properties of this enhancement resemble presynaptic facilitation.

In conclusion, thalamo-cortico-thalamic pathways display a wide array of cellular properties that are reflected in their short-term plasticity. These properties may serve to synchronize, amplify and/or filter neural activity in neocortex and thalamus depending on behavioral demands, and thus to adapt each pathway to its specific function.

SPATIOTEMPORAL CHARACTERISTICS OF THE RESPONSES TO REPETITIVE STIMULATION IN VISUAL CORTEX STUDIED WITH VOLTAGE-SENSITIVE DYES. Diego Contreras and Rodolfo Llinás. Dep. of Physiology and Neurosciences, NYU Medical Center, 550 First Avenue, New York, NY, 10016.

The role of activation frequency on the spatial distribution of excitation in neocortex was studied *in vitro*, in guinea pig neocortical slices from visual cortex, by means of combined optical recordings with voltage sensitive dyes and intracellular recordings with sharp electrodes. Slices (400 μm thick) were stained with the voltage-sensitive dye RH795 (Molecular Probes) and optical signals monitored with a fast CCD camera (Fujix HRDeltaron 1700) with 128x128 pixels and step resolution of 0.6 ms. Single shocks (1-5 V, 100 μs) to the white matter gave rise to the activation of the overlying cortical column followed by lateral spread of excitation that proceeded mainly through layers VI and I-II of the cortical mantle. Stimulation at 10 Hz did not alter the spatial pattern, although it increased the amplitude of the response in different areas. By contrast, stimulation at 40 Hz restrained the area of excitation to the column directly excited by the stimulating electrode. Intracellular recordings revealed that, during high frequency stimulation, cells within the column of excitation displayed strong temporal summation of EPSPs, while cells located lateral to the column were dominated by powerful inhibition. To determined if the spatial organization is due to dynamic sculpturing by local inhibition, localized injections of bicuculline in the slice were implemented. Blockage of inhibition produced a reorganization of the geometrical patterns of activity distribution that were dependent on the size and concentration of the injections. We conclude that spatiotemporal patterns of coherent activity in the neocortex are dynamically determined by local inhibitory networks.

Supported by NIH-NINDS grant NS13742 and by the Human Frontier Science Program.

Session 3: The cortical step I (mechanisms context and specialization)
Chairman: S. Murray Sherman

Cellular Mechanisms of Contrast Adaptation in the Primary Visual Cortex
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A single variable in a sensory input may extend over a broad range from minimum to maximum values, such as light intensity or contrast in the visual system. In order to maintain a high sensitivity to small changes in the sensory input using neuronal elements that are limited in their discharge frequency, the sensory system may adapt to local, ambient levels of the particular variable in the sensory stimulus (which can also be expressed as afterimages). In the mammalian visual system, neurons at and above the level of the retina are highly sensitive to local contrast and presentation of a sustained level of contrast results in adaptation over a period of tens of seconds or longer. This adaptation to contrast results in an increase in differential sensitivity to small changes in contrast levels. Contrast adaptation occurs largely in the cerebral cortex. It is not prominent at the level of the dorsal lateral geniculate nucleus, but can be prominent in the discharge rate of neurons in the primary visual cortex. Our research has addressed the specific cellular mechanisms of contrast adaptation through the use of intracellular recording techniques in vivo and in vitro.

With in vivo experiments we have replicated the finding of Carandini and Ferster (Science 276: 949-952) demonstrating that contrast adaptation is associated with a hyperpolarization of the membrane potential. Through the use of current and visual stimulation protocols, we demonstrate that this hyperpolarization does contribute significantly to contrast adaptation of action potential discharge.

With in vitro experiments, we have demonstrated that prolonged (30-60 seconds) repetitive stimulation of cortical cells with the intracellular injection of sinewaves results in a prolonged hyperpolarization of the membrane potential. This hyperpolarization is generated in part through the activation of a Na+ - activated K+ current. However, we are also currently investigating the possible contribution of a electrogenic Na+/K+ pump and synaptic depression.

From this work, it is clear that contrast adaptation at the level of the cerebral cortex results in part from decreases in excitability of the postsynaptic neuron owing to a hyperpolarization of the neuron. However, the specific nature of adaptation for features of the adapting stimulus suggest that network mechanisms are also involved.

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An intracellular in vivo reexamination of the Synaptic Integration Field of neurons in Cat primary visual cortex

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Visual receptive fields are classically defined as the region of space (or retina) where presentation of a visual stimulus evokes a change in the firing of the cell (Adrian, 1941, Bishop and Henry, 1972). In contrast with extracellular recordings, *in vivo* intracellular and "blind patch" recording techniques allow the analysis of various types of subthreshold synaptic events and their retinal origin (Creutzfeldt and Ito, 1968, Douglas and Martin, 1991, Ferster and Jagadeesh, 1991, Pei, et al., 1994, Volgushev, et al., 1993). A challenging issue concerns the respective role of feedforward, local recurrent, intracortical "horizontal" and cortico-cortical feedback connectivity in the functional expression of the cortical synaptic integration field (Frégnac and Bringuier, 1996, Stemmler, et al., 1995, Toth, et al., 1996).

The minimal discharge field (MDF) is measured under restricted test conditions (impulsional spot or line of light flashed ON and OFF in the visual field). It tends to reduce the RF substrate to the connectivity provided by the feedforward input arising from the previous stage of synaptic integration (Hubel and Wiesel, 1962). In first-order cortical neurons, the driving dominance of extrinsic input in the functional expression of the MDF (Alonso, et al., 1996) results in an average size of the order of 1-2° of solid angle for RFs centered around the representation of the gaze axis.

Within the minimal discharge field, the gain of the cortical response is controlled through the recurrent action of local excitatory and inhibitory circuits (Douglas, et al., 1995, Sillito, 1984). Two modes of inhibitory control of synaptic excitation are often distinguished - subtractive-hyperpolarizing vs. shunting-divisive - on the basis of the changes they respectively produce in the membrane potential and the input conductance of the cell (Eccles, 1964, Koch and Poggio, 1985). To date reports of small visually-evoked conductance changes have argued against the latter role (Berman, et al., 1991, Douglas, et al., 1988, Ferster and Jagadeesh, 1992, Pei, et al., 1991). In contrast, using whole cell voltage clamp measurements in neurons of the primary visual cortex of the cat, we show that the response to optimally oriented flashed bars can modulate the somatic conductance to more than three fold that of the resting state (Borg-Graham, et al., 1996; Borg-Graham et al, submitted). The early latency of the conductance increase and its apparent reversal potential suggest a dominant contribution by GABAA-mediated synapses. We propose that this shunting inhibition may play a decisive role during the initial stage of the visual cortical processing in setting the balance between opponent ON and OFF responses in different locations of the receptive field (RF).

Although remarkably operational in defining the tiling of retinotopic mapping of the visual space even in remote cortical areas, the MDF output is a poor descriptor of the single cell spatial sensitivity to the external world. If optical imaging techniques have been used to derive the cortical point spread function elicited by a punctual stimulus on the retina (Das and Gilbert, 1995, Grinvald, et al., 1994), the reverse problem, namely identifying what region of retinal space is projecting on the same point in cortex, has not been yet quantitatively tackled. For that purpose in vivo electrophysiological techniques are required: indirect evidence based on extracellular recordings has already been obtained by using dual spatial interaction protocols (review in Li, 1996). They reveal the modulatory effect of conditioning stimuli

shown in the "unresponsive" surround on the cell's firing evoked by a test stimulus presented simultaneously within the MDF. We will summarize here intracellular evidence in primary visual cortex of the Cat, that demonstrates that the subthreshold visual receptive field of neurons extends over much larger regions of the visual field than that established on the basis of spike activity (Frégnac, et al., 1996; Bringuier et al, submitted). Spatial sensitivity measured at the subthreshold level decreases almost linearly from the center to the periphery of the RF. A positive correlation is found between the onset latency of evoked postsynaptic potentials and the relative retinal eccentricity of the visual stimulus from the center of the discharge zone of the recorded cell.

These findings lead us to propose that the spatio-temporal pattern of intracortical activity produced by a focal retinal activation can be visualized from above the cortical surface as a radial wave of activation spreading at constant velocity (axonal conduction) over a radius of 5-10 degrees of solid angle. Reciprocally, when adopting the cortical cell point of view now seen as a receiver rather than an emitting device, functional integration may be described by the summation of intracortical input echoes originating from distant sources in a spatio-temporal coordinate system centered on the center of the discharge field of the postsynaptic cell. Since the delay with which each intracortical source would influence the target cell depends mostly on its distance from the origin of this egocentric coordinate system, precise temporal constraints in time and space can be predicted which optimize the efficacy of the summation process of synaptic responses.

This work was supported by CNRS, AFIRST and GIS Cognisciences grants.

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Spatial and temporal characteristics of network interactions in primate visual cortex.

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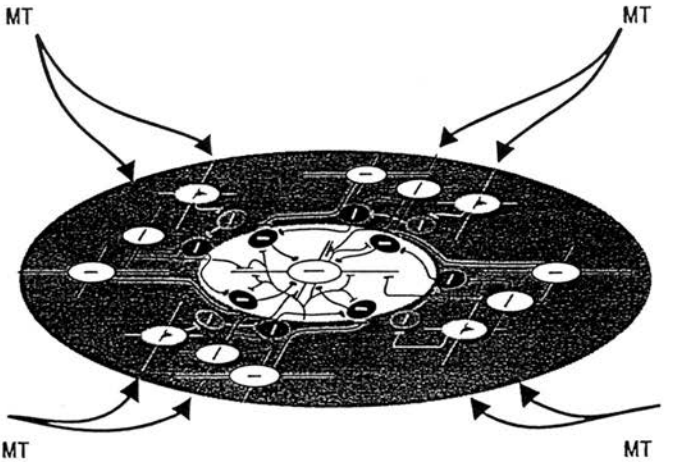
Conventional wisdom tends to describe the functional role of cells in the primary visual cortex (V1) in terms of their focal classical receptive field. However, there is a growing recognition that this level of description is only valid for very simple stimulus situations and that a much richer set of properties subserve system function when more complex stimulus situations engage the cortical circuitry. This is hardly surprising because V1 cells are embedded in a wide ranging network of synaptic connections with extensive feedback inputs from higher visual areas (Rockland and Pandya, 1981) and intrinsic lateral interactions, all of which bring influences from substantive distances outside the classical receptive field. It is worth emphasising that even in the thalamic recipient zone of layer 4 the converging thalamic inputs which seem to link to the classical receptive field (Hubel and Wiesel, 1962, Reid and Alonso, 1995, Ferster et al., 1996) provide only a small part of the synaptic input (2-9%) to layer 4 spiny stellate cells, whilst inputs from layer 6 cells provide something in the region of 45% of the connections (Peters and Payne, 1993; Ahmed et al., 1994; Andersen et al., 1994). Thus although the thalamic afferents relaying the retinal input to the cortex provide the focal input underpinning the CRF, the response of cells is clearly conditional on a range of other influences drawing on the processing occurring at adjacent locations in visual space and the context of the analysis occurring at higher levels in the system (see figure below).



We have examined the influence of stimulus context on the responses of neurons in primate V1 in an attempt to identify elements of the logic of the many processes interacting with the translation of the thalamic input through the system. Our data identified the following patterns of interaction within primate V1. For virtually all cells (and through laminae 2-6) extension of an optimal stimulus configuration for the CRF into surrounding visual space resulted in a marked attenuation of response levels (*94% of the cells in our sample {99/105} showed suppression to stimulation of CRF and surround with a mean reduction in response of 67% +/- 2.07% sem).* This reflected an "and" gate type interaction driving the inhibitory mechanism (cf Sillito 1977, Sillito et al 1995), between processes falling within and without the CRF rather than a simple inhibitory surround. A discontinuity in context between a stimulus centred on the CRF and a surround stimulus, whether producing orientation or direction contrast, disenabled the centre-surround suppressive mechanism and in many cases (65%) resulted in an increased response over that to the inner alone (mean increase 98% +/- 13.36% sem). This increased response could exceed the cell's response to any single stimulus. The effects of orientation and direction contrast were observed, within, on the edge of, and outside the CRF.

The temporal evolution of these effects linked to various configurations of stimulus situations with drifting gratings followed a distinct pattern. Responses to an optimal stimulus restricted to the CRF were not the first to emerge. In virtually all our sample (92%) the earliest responses came in for large stimuli extending beyond the CRF with or without a discontinuity in the stimulus (mean latency 67.7 msecs and 71.5 msecs). The first response to a stimulus restricted to the CRF emerged later with a mean latency of 88.8 msecs but this did not reach its full magnitude until later (mean 111.6msecs) and at this stage patch suppression to larger stimuli emerged. At approximately the same time the enhanced responses linked to orientation or direct contrast appeared (mean 114.2 msecs). It seems that integration over a larger area of visual space generates substantial facilitation within the network and enables the earliest response, detecting the presence of an event and that the "isolation" and representation of its contextual focus and significance follows later.

We believe that these data support the view that a core mechanism in the system centres around the representation of the loci for changes in image properties linked to perceptual salience, where these occur the output of cells underlying them are enhanced and where there is no change the output of the cells is minimised. This process seems to follow a time scale consistent with multiple lateral interactions within the system and the influence of feedback bringing the "context" of higher levels of analysis to bear on local processing. It is commensurate with stimulus representation by a hierarchy of interacting networks rather than "feature" detectors operating in isolation. These conclusions link with observations on surround mechanisms in MT (Xiao, Raiguel, Marcar and Orban 1997)

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The structure and function of the antagonistic surround in area MT/V5.

Guy A Orban.

In this lecture I will review three sets of experiments. A first set of single cell recordings demonstrates that 2/3 of macaque MT/V5 neurons have antagonistic surrounds and that nearly ¾ of these have non-uniform antagonistic surrounds. A second set demonstrates that half the MT/V5 neurons are selective for speed gradient direction, corresponding to the direction of surface tilt specified by motion, and that this selectivity requires a non-uniform surround. A third set of fMRI experiments shows that in humans the homologue of monkey MT/V5 is more active when subject view 3D motion displays (appearing as a set of tilted surfaces) than when they view 2D motion displays (appearing as a fronto-parallel surface). These experiments support the view that in both human and non human primates the antagonistic surround endows cortical neurons with additional processing capacities, important for visual perception.

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The dynamics of recurrent circuits in visual cortex.

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A cardinal feature of the organization of the local (intra-areal) circuits within the neocortex is that individual neurons receive polysynaptic innervation from a number of different sources. Functionally, these sources include not only feedforward excitation and inhibition, but also feedback excitation and inhibition from a number of different neuronal types within a local patch of cortex. Evidence for this combination of feedforward and recurrent organization comes from anatomical and physiological studies in the primary visual cortex (Stratford et al, 1996). Anatomically, the recurrent synapses contribute a very large fraction of the total synapses on the dendritic tree of a given neuron – perhaps over 80% (Ahmed et al, 1994, 1997).

It has yet to be determined what actual fraction of the total inhibitory and excitatory synaptic current is contributed by the feedforward vs. the recurrent pathways, but theoretical estimates indicate that in steady-state the recurrent excitatory synapses might provide at least double the magnitude of the feedforward current (Douglas et al, 1995). The recurrent organization provides for important constraints on the possible circuits and their physiology, because only relatively few recurrent excitatory synapses need be active to produce continuous self re-excitation of the neurons participating in the recurrent circuit.

Traditionally, it is thought that the principal role of the inhibitory neurons is to prevent runaway re-excitation. However, inhibition is not the only factor controlling the magnitude of excitation. Other factors, e.g. depression of excitatory synapses, action potential generation, adaptation of neuronal discharge, may be as important as synaptic inhibition in the local and short-term (ms) control of the 'gain' of the recurrent circuits (Abbott et al, 1997; Douglas et al, 1995). Additional mechanisms, e.g. those involving G-

protein coupled receptor activation (Bowery, 1993; Greene et al, 1994), temporal regulation of synaptic efficacy (Abbott et al, 1997; Markram et al, 1997), and many other transmitter- or voltage-dependent influences on membrane conductances (see Douglas & Martin, 1998), can produce longer duration changes (100ms to seconds) in the gain of the recurrent circuit. Together these mechanisms form part of a rich complex of mechanisms that collectively carry out the computations and ensure the robustness of cortical computations in the face of significant variations in stimulus conditions and brain states.

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Session 4: The cortical step II (external influences on vision

Chairman: Yves Frégnac

"Object Recognition in IT Cortex"

T. Poggio, M.I.T.

Learning is becoming the central problem in trying to understand intelligence and in trying to develop intelligent machines. In this talk I will describe some of our recent efforts in the domain of vision to understand brain mechanisms of learning. I will briefly mention artificial systems that learn to recognize faces and detect specific objects in cluttered scenes: they serve as plausibility proofs of the biological models. I will then describe models of the brain based on the assumption that cortical cells can rapidly learn and become tuned to specific optimal stimuli. Some very recent physiological data from IT cortex in monkeys (from Logothetis' lab) support the learning models we have developed and provide a glimpse of how 3D objects are represented in the visual cortex.

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Role of eye muscle receptors in development of visual cortical cell properties

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From results in the visual system of the cat we know that the «initial» binocularity or orientation selectivity of neurones in the primary visual cortex can be selectively modified by the visual experience that the animals received during a postnatal «critical» period (see Frégnac & Imbert 1984; Hirsch 1985). Moreover, it has been specified that a «normal» visual experience was necessary during that critical period for the development and maintenance of normal orientation selectivity properties by visual cortical cells (Blakemore & Van Sluyters 1975; Buisseret & Imbert 1976; Buisseret et al. 1982).

If it was obvious that vision was necessary, several others indications suggested that «extraretinal» factors should also be involved (see Buisseret 1995).

The paradigm of a short duration of visual experience has been used, in kittens, to study the factors that control the development of orientation selectivity characteristics in visual cortical cells. The conditions of access to their visual environment were modified during the time of the visual experience and the development of orientation selectivity was compared to that of intact animals. The results show that eye movements are necessary with vision, at least during a visual experience after a period of dark rearing, and also, we assumed, during normal development (Buisseret et al., 1978; Gary-Bobo et al., 1986).

How are the central nervous system and the visual cortex informed of the occurrence of eye movements during vision ? The hypothesis of an afferent information from eye muscle receptors has been tested. The results showed that sensory messages from eye muscle receptors, evoked by the eye movements, are an extraretinal factor that must be present with vision during the visual experience (Buisseret and Gary-Bobo, 1979; Trotter et al., 1981). Complementary results have shown that neck muscle inputs were also involved in this developmental process, but to lesser degree (Buisseret 1992). The complete conclusion would be that «gaze proprioception» plays the role of a cofactor of vision in the development of orientation selectivity property of visual cortical cells.

Since abnormal visual inputs containing, for example, information about a single orientation lead to abnormal distribution of preferred orientation in visual cortical cells, favouring the experienced orientation (Blakemore & Cooper 1970; Hirsch & Spinelli 1971), the effects on the distribution of preferred orientation of abnormal muscle inputs, corresponding to a single direction of eye movements, were tested (Buisseret et al. 1988). The results allow to specify that the direction of eye movements influenced the distribution of preferred orientations. By extension, we assume that during the normal development of orientation specificity, eye muscle inputs interact with retinal inputs in such a specific congruent way so as to determine together the encoded orientation by visual cortical cells.

Similarly, it has been shown that EOM sensitivity acts upon cortical binocular integration. Bilateral suppression of EOM afferents «freezes» cortical plasticity for ocular dominance in the kitten in a similar fashion to visual deprivation. Lesions or suppressions must be unilateral to obtain deleterious effects. In such case, unbalanced inflow of proprioceptive information from both eyes is considered the source of effects (Maffei and Bisti, 1976; Trotter et al., 1987; 1990; 1993).

On a behavioural point of view, the presence of movements as a prerequisite for the development of guided behaviour was also ascertained (Held and Hein, 1963).The major role of ocular movements was demonstrated by surgical immobilisation of both or one eye in combination with different visual exposures (Hein et al., 1979; Hein and Diamond, 1983). They also showed that

one source about eye movements was proprioceptive input from the EOMs. Behavioural deficits were also observed in binocular perception following deafferentation of eye muscle proprioception (Graves et al., 1987; Trotter et al 1991).

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ADAPTIVE EYE AND EYELID MOVEMENTS IN RELATION TO VISUAL PERCEPTION

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As a general trend in vertebrate evolution, the oculomotor system was designed from the very beginning to avoid eye movements, that is, to maintain as far as possible the same visual input with the maximum visual acuity. In this sense, all vertebrates have a *vestibulo-ocular reflex* and an *optokinetic reflex*: the first reflex compensates for linear and angular displacements of the head, while the second one compensates for eventual displacements of the visual field, mostly produced by our own movements in the space.

Several species present further developments or adaptations in their oculomotor capabilities. For example, eye *saccades* are fast angular (up to 800 degrees per second) eye movements that allow us to switch from a visual field to another, according to our internal states, that is, in a way no contingent with events occurring in the external world. Another example is *visual pursuit*, that is, the movement that we perform with our eyes following the flight of a little bee across our visual field.

An object of intensive experimental research in nowadays involves the putative plasticity in the oculomotor system during changing conditions for vestibular and visual inputs as, for example, during cancellation of the vestibulo-ocular reflex. Several brain stem and cerebellar structures have been proposed as the site of this sort of motor learning, without any final agreement until present about the place and, more important, about the mechanisms involved. In this sense, evidence will be presented that the oculomotor system is at the same time highly conservative since its appearance more than 500 million years ago, and highly susceptible to minimum manipulation of the internal neural circuitry supporting it.

On the other hand, terrestrial vertebrates are provided with eyelids designed to protect the cornea from an external environment more aggressive than the aquatic one. Surprisingly enough, eyelid movements are rather complex in their kinematic and frequency-domain characteristics, and depend on the sensory modality of the stimulus (puff of air, flash of light, strong sound, etc.), as well as on some internal states (*spontaneous blinks*, *friendly displays*, etc.). Eyelid movements are also produced accompanying eye saccades and slow phases during vestibular and optokinetic reflexes. Finally, one of the most used models of motor learning is the classical conditioning of eyelid responses. In this latter case, conditioned blinks present profiles, kinematics and frequency-domain properties different from those of spontaneous and reflex blinks.

Obviously, eyelids have to move in coordination with the oculomotor system in order to avoid any disturbance of visual perception. However, lids contract every few seconds in order to moist the cornea, and are also involved in the expression of internal emotional states. For this reason, and as described for eye movements, lid movements have to be coordinated with the visual neural system. In this sense, lid position is related to attentional states and, apparently, are in synchrony with them. On the other hand, and as recently reported, the orbicularis oculi muscle is devoid of proprioception, a fact suggesting a central control of lid

position and velocity. For this reason, the lid motor system is a good experimental model to the study of how new (i.e., learned) motor responses are generated by the central nervous system, step by step, until a complete and well-elaborated motor response is achieved.

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NEURAL RESPONSES IN MONKEY CORTICAL AREA V-1 DURING VISUAL FIXATION.

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Images fade quickly when visual stimuli are stabilized on the retina (Ditchburn and Ginsborg, 1952; Riggs and Ratliff, 1952). During normal vision, eye movements are produced constantly, and we obtain a stable perception even of stationary objects.

In our experiments we have investigated the relationship between bursts of spikes in neurons of area V-1 and eye movements during visual fixation. Previous experiments have shown that in the awake animal, bursts of spikes reflect a more accurate picture of the visual stimulus than single spikes or overall firing rate (Livingstone, Freeman and Hubel, 1996).

Experiments were made in two alert rhesus monkeys. We implanted a recording chamber over V-1 and then recorded extracellular single-unit responses with tungsten electrodes. Eye movements were also monitored and recorded using a monocular scleral eye coil. The receptive field of each unit was mapped while the animals carried out a fixation task. A light or dark stationary bar with optimum dimensions and orientation was then placed over the receptive field.

Our results show that small eye movements during visual fixation are related to the production of spike bursts in V-1 neurons. The average size of eye movements was bigger before a burst as opposed to a single spike, suggesting that the likelihood of spike bursts was enhanced after small eye movements. The delay between the production of small eye movements and the appearance of bursts was found to be about 100 ms or less.

We conclude that involuntary eye movements during fixation, repeatedly moving the retinal images of stationary objects over the receptive fields of visual neurons, cause these neurons to fire, therefore preventing perception from fading. Under these conditions, the perception of the stimulus is best correlated with bursts of spikes in V-1.

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Supported by grant EY00605 from NIH to D. H. H.
S. M.-C. is a fellow of the Real Colegio Complutense, established in cooperation with Harvard University.

NEURAL MECHANISMS OF VISIBILITY AND INVISIBILITY IN THE PRIMATE VISUAL CORTEX. Macknik, S. L. and Livingstone, M. S. *Department of Neurobiology, Harvard Medical School, Boston, Massachusetts 02115.*

An image that has been stabilized on the retina fades from perception (Ditchburn and Ginsborg, 1952; Riggs and Ratliff, 1952). Light falling on the retina, alone, cannot therefore be all that is necessary for a maintained perception of the image. Whatever it is that *is* additionally required for the image to remain visible is moreover provided by eye movements. Eye movements, from the point-of-view of the retina, change the spatial position of the image in time, and so temporal or spatial changes of the image on the retina may account for the effects of eye movements as well as for visibility itself. We investigate these necessary temporal factors of visibility by correlating neural activity with illusions of invisibility: the visual masking illusions.

We first determined, perceptually in humans, the precise timing elements necessary for a masking stimulus to render invisible a target stimulus. These timing conditions were then used to develop new more powerful masking illusions and to determine physiologically, in anesthetized and awake monkeys, the neural correlates of visibility and invisibility in monkey striate cortex.

The results show that in forward masking conditions, when the mask precedes the target, target invisibility is correlated with a decrease in size of the neural transient on-response. Surprisingly, the target's neural on-response did not decrease in backward masking conditions and the target's neural off-response instead was suppressed. This suggests that on-responses within neurons in V-1 cannot by themselves maintain perception and that off-responses in these cells must also be critical to visibility.

It may seem surprising that an off-response would be significant to visibility because the real world is continuously visible and yet it only rarely turns off. It may be, however, that neurons in area V-1 do indeed see the real world turn off due to the action of eye movements, which serve to move the edges of stimuli into and out of their receptive fields several times per second. We therefore propose that it is the transient on and off portions of the neural response that are most significant to producing the visibility of an image and to understanding the neural code at the level of striate cortex.

Ditchburn, R. W. and Ginsborg, B. L. (1952). *Nature* 170, 36-37.
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READING THE CLOCK IN DIFFERENT WAYS - SEPARATION OF THE CORTICAL REPRESENTATIONS OF ATTENTION TO ANGLES AND ATTENTION TO COLOURS.

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The functional and anatomical separation of specific attentional mechanisms requires tasks in which the stimuli are kept constant across the conditions in order to exclude the effects of changes of the physical stimulus. In the present study, this was achieved by presenting subjects with the same set of clocks, while varying the discrimination tasks they had to perform. The change of blood oxygen dependent (BOLD) signal, measured by functional magnetic resonance imaging, was used as a measure of the activity of different cortical areas. The stimulus consisted of clocks with a yellow face and either yellow or white hands showing different times. Subjects were asked to press a button on an optic fibre answer box when the two hands formed an angle of 60° or less (angle discrimination) or when the hands were white (colour discrimination). Eye movements were recorded in separate electrooculography sessions. During the discrimination of angles the superior parietal lobule showed a significantly higher activation than during colour discrimination. Colour discrimination was accompanied by a significant BOLD signal increase in the inferotemporal cortex, particularly the fusiform gyrus. There was no significant difference in eye movements between the different task and control conditions. This implies that the superior parietal activation during angle discrimination represents a selective mechanism for spatial attention, while the inferotemporal activation during colour discrimination represents a modulation specific for attention to colours.

Session 5: The cortical step III (psychophysics, stereopsis, knowledge, and conscious vision)

Chairman: David C. Van Essen

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Circuit Modeling of Visual Cortex

Visual cortical neurons exhibit selectivity along many stimulus dimensions. It is important to understand not only how each of these neural computations is performed, but also how they co-exist within a unified cortical circuit. This talk will summarize the functional requirements for obtaining several selective response properties and will quantitatively explore possible circuit architectures for implementing these requirements. It will be argued that orientation selectivity is best accounted for by a two-stage model in which converging thalmocortical inputs establish broad tuning in layer 4 and intracortical excitatory and inhibitory connections double the selectivity within other cortical layers. This model is then extended to address contrast gain, length tuning, and extra-classical receptive field influences. These and other properties arise from the dynamic balance of cortical excitation and inhibition within the local circuitry.

M.J. Morgan: What does V1 contribute to conscious awareness?

The standard model of visual processing considers vision to consist of a series of data transformations, starting with the optical image in the retina, and ending with a large variety of representations suitable for action, memory and other higher cognitive functions. Within such a scheme, is it useful to ask whether conscious perception is associated with any particular type of representation; and if so, can the neural locus of this representation be identified? The primary visual cortex (V1) represents data in a way that seems especially suitable for textural segmentation, including stereo, but which falls far short of an object-centred representation. For this main reason, Crick & Koch have argued that the retina, the LGN and V1 play no direct role in conscious experience. To support their argument, they point to the fact that the data embodied in the activity of the very large number of monocularly-driven neurones in V1 is not independently accessible to the observer. This argument will be analysed, along the following lines:

(1) Why a stimuli in one eye invisible when there is an appropriate spatial frequency/orientation mask in the other eye? If this is due to pooled gain control at the level of V1, dichoptic masking has no implications for the consciousness debate

(2) Are there separate representations for the two eye's images at the level of learning?

(3) Kolb and Braun argue that the two eyes can produce independent textural segmentations, but that these representations are not available to conscious awareness.

(4) Can independent prism adaptation occur for the two eyes?

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The Neural Determinants of Conscious Vision

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The most fundamental function of the visual brain is to acquire knowledge about the constant, essential, properties of the visual world, in conditions in which the information reaching the brain is never constant from moment to moment. This requires the brain to undertake complex operations on the incoming visual signals, discounting all that is not essential for it to acquire knowledge about the world, selecting that which is important and subjecting the latter to operations that make the brain independent of the continually changing and non-essential information reaching it. One strategy that the brain uses in undertaking this task is that of functional specialisation, through which different essential features, such as motion and colour, are extracted in specialised and geographically distinct visual areas lying outside the primary visual cortex area V1. Our recent psychophysical experiments show that, just as the processing systems for different attributes of vision are separate, so are the final perceptual systems, since different attributes of the visual scene such as colour, form and motion are perceived at different times, with colour leading motion by about 80 ms, thus leading to a perceptual asynchrony in terms of real time. The end-result of the operations in these individual areas is the acquisition of knowledge. But knowledge can only be acquired in the conscious state. A conscious awareness is therefore the corollary of activity in the specialised areas. Recent experiments using imaging and time resolution methods as well as patients blinded by lesions either in V1 or in more extensive parts of the visual cortex show that the activity in one or a small number of visual areas, without involvement of V1, can give rise to both conscious experience and a crude knowledge about the visual world. This leads us to the conclusion that consciousness itself may be modular.

The work of our laboratory is supported by the Wellcome Trust, London.

Imaginary Mechanisms

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It can be hard to know whether a phenomenon is given by a mechanism, or by some kind of default assumption. Thus the Apparent movement (Phi) of an illusory light between alternating lights, has been attributed to a special mechanism - such as the Gestalt psychologists' brain fields - yet Phi might involve no more than *tolerance to gaps* of sequential movement signals.

Filling-in of scotomas is controversial: the brain ignoring regions failing to provide signals (Dennett), or active extrapolation from surrounding retinal pattern (Ramachandran and Gregory).

Inappropriate concepts or theories can generate imaginary mechanisms; so avoiding them requires more than Ockham's Razor. We can easily be misled - even to illusory mechanisms for explaining visual illusions.

POSTERS

CLAUSTRAL AFFERENTS TO THE VISUAL CORTEX

I. GUTIÉRREZ-IBARLUZEA, A. ACERA-OSA, J.L. MENDIZABAL-ZUBIAGA,
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The claustrum is a thin sheet of grey matter located in the basal forebrain near the striatum. It mantains topographical and reciprocal connections with almost all areas of the cerebral cortex in high order mammals. For instance, in cats and monkeys, the dorsocaudal portion of the claustrum contains a single orderly map of the visual field that, in turn, projects back to the visual cortical areas (layer IV). No evidence for such type of connectivity has been reported for rodents or the rabbit. The present study describes the afferences from the claustrum to the visual cortical areas of the rabbit as revealed by means of anterograde tracing methods. Six albino New Zealand rabbits received a unilateral iontophoretic injection of biotinylated dextran amine (BDA) in the dorsointermediate claustrum. The anterogradely labelled axons from the claustrum were observed in the cingulate cortex, areas 24 and 29 a,b and c but specially 29d, and ipsilateral area 17 of the visual cortex. In general, the claustrocortical axons observed in the visual cortex were thiner than those observed in the cingulate cortex, mainly giving small en-passant boutons. However, some boutons were seen at the end of short stalks emerging from the main axon shaft. In area 17, ascending axons with small enlargements were observed in layers VI and specially II-III. In addition to the vertical axons, some horizontal axons that ran tangentially to the white or pia matter were also observed in layers VI and I respectively. Presumptive terminal swellings were found in layers I, II-III and VI–these axon arborizations being less extensive in layers I and VI than in layers II-III. In the ipsilateral visual cortex we also observed some retrogradelly labelled cells in layer VIa, which predominantly presented an inverted morphology (≈70%). On the other hand, layer V pyramidal neurons appeared in the cingulate cortex as retrogradelly labelled from the claustrum.
Thus, we conclude that the claustrum mantains reciprocal connections with the visual and cingulate cortex in rabbits, as occurs in other species (i. e., cats, monkeys) but not in rats. As different from cats and monkeys, the main recipients of claustro-cortical axons to area 17 are layers II-III and VI, instead of layer IV. In light of these connections and those mantained by the cingulate cortex (area 29d) with area 8 (not shown), the claustrum may play an important role in associative functions of the rabbit cortex such as visuomotor integration.

Supported by the University of the Basque Country, the Regional Basque Governçment and the Spanish Government (grant UPV-212.327-EB179/96, doctoral grants to I.G-I., and J.L.M-Z., and grants DGICyT PB92-0463 and FIS 94/1684, respectively).

A mathematical model for spatial receptive-field organization of dLGN neurons in cat

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Center-surround antagonism of the receptive field is stronger in relay cells on dorsal lateral geniculate nucleus (dLGN) than in retinal ganglion cells. This is at least partly due to inhibition at the geniculate level. Recently Ruksenas *et al.*[1] has studied spatial changes in the dLGN receptive fields by recording action potentials (relay cell response) and S-potentials (input from retinal ganglion cells) in dLGN in anesthetized and paralyzed cats during stimulation with circular flashing spots of varying size. The smallest spots covered only a part of the receptive field center while the largest spots covered both center and surround of the receptive field. For all spot sizes they found the relay cell response to be weaker than the retinal input response. In addition, the difference between retinal input and relay cell response was found to increase with increasing spot diameter up to a diameter that on average was about twice the width of the receptive-field center of the dLGN cell.

In order to use these measurements to gain further understanding of the spatial receptive-field organisation in dLGN in cat, we here derive analytical mathematical formulas for relay cell and ganglion cell response curves during stimulation of circular light spots. The spatial receptive-field function of the ganglion cell is modeled as a difference of Gaussians representing both excitatory and inhibitory connections. In our mathematical scheme we also assume a continuous coupling function between retinal ganglion cells and relay cells. Here we consider two distinct coupling functions, namely (i) a difference of Gaussians and (ii) a sum of an excitatory and an inhibitory square-well function. The limited number of parameters in the mathematical model can be determined by fitting to the experimental ganglion cell and relay cell response curves in Ref.1. With these parameters fixed, the receptive-field functions for the ganglion cells and relay cells (and possibly also the dLGN interneurons) can be predicted. This procedure is illustrated by concrete examples.

[1]O. Ruksenas, I.T. Fjeld, and P.Heggelund, manuscript in preparation.

A computational model of simple receptive fields in layer IV of area 17 in the cat.

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Layer IV of cat area 17 is the main locus where the visual signal originating in the retina and conveyed through the lateral geniculate nucleus, reaches cortex. This layer is composed of densely interconnected excitatory and inhibitory neurones, the discharge of which is transiently increased or suppressed if visual stimuli are presented to the animal in a limited region of visual space called the receptive field (RF) of the neurone. The most frequently encountered RFs in layer IV are the so-called simple RFs, classified as S1, S2 or S3, according to whether ther are made up of one, two or three distinct ON or OFF subregions.

We have been trying to simulate numerically the local dynamics of neuronal activity in layer IV by modelling in a plausible way the cell anatomy and physiology, the time course of synaptic conductances, the intracortical connectivity and the visual excitation coming from thalamo-cortical afferents. Simulations have been carried out with Surf-Hippo, a simulator of networks of biophysical neurones. Our model network represents a region of cortex where the preferred orientation of neurones changes slowly, that is away from a singularity. The circuit is wired according to a simple principle, based on the functional activity-based correlation between cells, which in our case is determined by the degree of overlap and relative sign of RF subregions. This allows to simulate much of the physiology of simple cells in response to stationary bars : (1) the diversity of RF structures within the same network, despite the presence of recurrent excitatory loops (which would *a priori* tend to degrade the selectivity of each cell) ; (2) visuotopy and the similarity between the arrangement of subregions and the thalamo-cortical projection pattern ; (3) excitatory agonist responses and inhibitory antagonist responses ; (4) subfield opponency in the case of S2 simple RFs. In addition, (5) the simulated pharmacological blockade of $GABA_A$ inhibition on a single-cell or in a volume of cortex reveals subthreshold antagonist excitatory responses that are normally masked, and (6) blocking ON geniculate afferents results in the selective disappearance of cortical ON subregions, as has been observed.

In conclusion, this model reinforces the scheme that has started to emerge from the study of orientation selectivity that excitation and inhibition could function as like-to-like and like-to-unlike connectors respectively.

FOS EXPRESSION IN THE RETINA OF *rd/rd* MICE DURING THE LIGHT/DARK CYCLE

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Abstract

An anti-Fos protein antiserum was used to elucidate the diurnal expression of Fos protein in the normal and degenerate *rd/rd* mice retina. We have found that Fos expression is stimulated in cells of both inner nuclear layer (INL) and ganglion cell layer (GCL) at the onset of light period and reaches its maximum after 2 hrs.. After which, the number of stained nuclei decreases along the light/dark cycle until almost no reaction is observed at the end of dark period. This expression pattern was similar in both normal and *rd/rd* mice although degenerate retinas showed a much lower number of stained nuclei. Aged *rd* animals also show Fos expression in GCL and INL in response to light stimuli suggesting that severely degenerate retinas are still able of transducing light stimulus.

Supported by a grant from Spanish DGICYT (PB94-1326) and BIOMED 2 (PL96-2327) to JMG-F.

Synaptically induced increase in [Na+]i and [K+]o can have long-lasting effect on oscillatory activity of abducens motoneurons.

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Abducens motoneurons are known to be responsible for saccadic eyes movement. The bursting activity of these neurons is generated by ionic currents through Na+, Ca2+, delayed rectifier K+-, Ca2+-dependent K+, and NMDA-receptor channels located on the soma and proximal dendrites. Numerous synaptic inputs to abducens motoneurons include AMPA-synapses from trigeminal neurons. We modified a mathematical model of mentioned ionic currents developed by others (Brodin et al. J.Neurophysiol. 1991, 66, 473-484) including the description of dynamic of Na+, Ca2+, and K+ in inter- and extracellular nearmembrane layers. Detail model of kinetic of [Ca2+]i included the Ca2+-induced release of Ca2+ from intracellular stores. This allowed to consider long-lasting effect of activation of excitable Ca2+ and NMDA-receptor channels. We used the obtained model for studies of interaction between AMPA- and NMDA-synaptic inputs. It was shown that beside of modification of intracellular Ca2+ there was a prominent synaptically induced increase in [Na+]i and [K+]o which is enough for modification of oscillatory activity lasting up to hundreds ms.

Intracellular evidence of cortico-cuneate synchronisation during evoked spike-wave seizure activity.

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We investigated the synaptic effects of cortical paroxysmal activity on the cuneate nucleus (CN). Intracellular recordings (micropipettes filled with 2.5 M solution of K-acetate) were made in the CN of cats, anaesthetised (α-chloralose, 60 mg/kg, i.v.) and paralysed (Pavulon, 1 mg/kg.h, i.v.). Cuneo-thalamic neurones were antidromically identified by electrical stimulation of the contralateral medial lemniscus (ML). In addition, the depth-electrocorticogram was recorded through a bipolar electrode placed in the sensorimotor cortex. A set of six stimulating bipolar electrodes were placed in the sensorimotor cortex. Cortical seizures were induced by electrical stimulation (up to 100 Hz) of the sensorimotor cortex.

The electrocorticogram indicated that the paroxysmal activity consisted in spike-wave (SW) complexes at 2-4 Hz and in seizures at higher frequencies (6-20 Hz). Intracellular recordings showed that the seizure activity was transmitted down to the CN, where it induced excitatory effects on local circuit neurones (cells that failed to be antidromically activated by ML stimulation) and various types of responses over cuneo-thalamic neurones. Cuneo-thalamic cells displayed both excitatory and inhibitory responses; the inhibitions followed in most cases by inhibitory-rebound spike bursts. The activity of both types of cuneate neurones was tightly synchronized with the cortical SW complexes.

These results confirm previous extracellular data indicating the powerful effects exerted by corticofugal neurones over the CN through the pyramidal tract, giving rise to a synchronised activity. The cortico-cuneate synchronisation seen in intracellular records appears to be due to a direct depolarisation on the local circuit cells, and to rhythmic hyperpolarisations followed by postinhibitory rebounds on cuneothalamic neurones. The reflection of the paroxysmal activity in the cuneate nucleus could serve to change the responsiveness to somatic stimuli, impairing the flow of information at prethalamic level.

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CONNECTIVITY BETWEEN SIMPLE CELLS AND COMPLEX CELLS IN CAT VISUAL CORTEX

In cat striate cortex, layer II-III complex cells are presumed to be generated from the convergent inputs of layer IV simple cells with similar orientation preference (Hubel and Wiesel, 1962). We have examined the connectivity predicted by this model by using cross-correlation analysis in simultaneous recordings from layer IV simple cells and overlying layer II-III complex cells (n=141; average orientation difference: 30.7 deg.; average receptive field overlap: 77.8%). A positive peak displaced from zero in the correlogram was interpreted as a direct excitatory connection. As expected, excitatory connections were observed only in the direction from the simple to the complex cell (n=40), being strongest when the preferred orientations differed in 22 degrees or less.

Simple and complex cells also appeared to share inputs from a common source (n=33), as indicated by peak centered at zero in the correlogram. These shared inputs were stronger and more frequently found in complex cells deep in layer III, which suggests a thalamic origin (deep layer III: 22/26; superficial II-III: 11/27). To test this idea, we correlated geniculate multiunit activity (layer A) with the activity recorded from pairs of simple and complex cells. In all 7 cases in which the simple-complex cell correlation showed a strong common input, we were able to identify a direct geniculate connection to both the simple cell and the complex cell. However, when the simple-complex cell correlogram indicated excitatory connections with weak or absent common input, only the simple cell appeared to receive a direct geniculate connection (n=8/9). Our results suggest that complex cells in the superficial layers of the cortex, which do not receive layer A input, are strongly driven by layer IV simple cells.

Sponsored by NIH EY05253 grant and The Human Frontier Science Program Organization (LMM).

Synchronization of spontaneous activity in rabbit developing hippocampus.

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Abstract

Bursting is a fundamental hallmark of the immature hippocampal activity *in-vitro*. These bursts or giant depolarizing potentials (GDPs) are GABA and glutamatergic driven events. It has been recently hypothesize a hilar origin for such events sustained by the pacing role of the hyperpolarization-activated current present in the interneurons (Strata,F., Atzori,M., Molnar,M., Ugolini,G., Tempia,F., Cherubini,E. *J Neurosci*, 17, 1435,1997). However, experimental evidences from another group support a CA3 origin since GDPs are recorded in isolated slices of this area (Khazipov,R., Leinekugel,X., Khalilov,I., Gaiarsa,J.L., Ben-Ari,Y. *J Physiol*, 498, 763, 1997). Here, we investigate the origin of GDPs in the hippocampal slices from newborn rabbits. Simultaneous intracellular recordings were performed at CA3, CA1 and the fascia dentata (n=16). We confirm a high correlation degree of the spontaneous GDPs present in both CA3 and CA1 regions (2.92 ± 1.38 GDPs/min). Cross-correlation analysis demonstrated that in statistical terms CA3 area precede CA1 at about 192 ms, although a small population of discharges are recorded first in CA1 (20%). Granule cells (GCs) in the fascia dentata also show GDPs at a frequency significantly lower than CA3/CA1 fields (0.89 ± 0.86 GDPs/min, n=5). Dual recordings in CA3 and fascia dentata show that GDPs in GCs are synchronic with CA3 neurons although there is not any systematic preceding cell. To investigate the origin of GDPs we recorded from isolated CA3, CA1 and fascia dentata areas. GDPs are present in every isolated subfield suggesting that they emerge as a property of the local circuits present throughout the hippocampus.

Integration of synaptic inputs in cat's visual cortex in response to visual stimulation.

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A number of studies, based on extracellular recording in cortex, have shown that neurons tend to synchronize their activities. In parallel, based on the variability of the interspike intervals observed in trains of action potentials recorded extracellularly, two models of temporal synaptic integration have been proposed: Either the neuron summates randomly occurring EPSPs and IPSPs, or it performs a coincidence detection on synchronously occurring EPSPs. Whether synchronization influences neuronal activity can be determined by studying the membrane potential events preceding visually evoked action potentials.

To characterize these events, we performed *in vivo* intracellular recordings in cat's area 17 (anesthesia: N_2O/O_2 and halothane, or isoflurane). The cells (n = 25) were activated by moving bars with optimal orientation and velocity. We performed spike triggered averages of the membrane potential, to determine what is the membrane potential trajectory preceding visually evoked action potentials.

The averaged membrane potential trajectory preceding an action potential consists of 2 components. A *fast component*, with a mean rise time of 7.7 msec (S. D.: 5.2 msec) and an amplitude of 5.6 ± 2.0 mV, appears to be *directly* responsible for action potential generation. The fast component stands on a *slow component*, with a rise time longer than one second on average, and an amplitude of 7.7 ± 3.8 mV. The slow component does not directly trigger action potentials, and appears to be related to the modulation of the membrane potential by the visual stimulus.

The amplitude of the *fast component* is larger than expected if it was produced by single, isolated EPSPs. This indicates that action potentials are triggered by *coincident* PSPs. This coincidence could result either from a random coincidence, or from a synchronization of neuronal origin in a sub-population of presynaptic neurons. To determine this origin more precisely we performed power spectrum analysis of the membrane potential. Preliminary data indicate that the largest fast components are associated with the presence of a peak in the power spectrum within the gamma frequency range, reflecting large membrane potential fluctuation. This departure from randomness suggests that, in some neurons, action potentials are triggered by PSPs that are synchronized by mechanisms of neuronal origin.

Tittle: Cross-talking between LGN relay cells: a cross-correlation study.

Casto Rivadulla & Javier Cudeiro

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In a classic view of the mammal visual system visual information is transfered from the retina to the cortex by different, parallel, channels (in the cat X / Y/W). Information covering different aspects of visual image is segregated. Avaliable anatomical data show that in the dorsal Lateral Geniculate Nucleus (dLGN) X cells from the retina contact with X cells in the dLGN, and a similar pattern of conectivity is stablised for Y cells, without conection between them. Here we show using cross-correlation analisis the existance of functional conectivity between different cell types.

Experiments were carried out in adult cats, anaesthetized and paralized. We recorded extracellularly pairs of cells in the d LGN, using tungsten electrodes with a horizontal separation between 0.5-2 mm. Cross-correlograms were computed using either visual driven or spontaneous discharge.

We have found positive peaks in 74% of cells recorded with electrodes at 0.5mm, this proportion decreased as distance between electrodes increased (0% at 2 mm). Two different type of peaks were found: 1) Peaks centered at 0, showing a common input. 2) Peaks displaced from 0 (mean 0.56 msc) suggesting a direct excitatory connection.

We provide evidence of local transfer of information between LGN relay cells, including all cell types (X/Y, ON/OFF). It would permit to the system to mix different aspects of the visual world at a very early stage.

FAST SYNAPTIC SIGNALING AND MODULATION OF INTRINSIC CIRCUITS BY NICOTINIC ACETYLCHOLINE AND SEROTONIN $5HT_3$ RECEPTORS IN DEVELOPING VISUAL CORTEX

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From early developmental stages on neuromodulatory projections regulate the excitability of cortical neurons and the plasticity of their interconnections. Fast and slow receptor systems can differentially regulate neuronal activity patterns. Cholinergic and serotonergic fiber systems invade the developing visual cortex several weeks before eye opening; both transmitters have been implicated in plasticity of neocortical circuits. These transmitters have been presumed to act predominantly through second-messenger-coupled receptors, as fast cholinergic or serotonergic neurotransmission has never been observed in neocortex. However, acetylcholine and serotonin also act on ligand-gated ion channels; the nicotinic acetylcholine receptor and the serotonin 5-HT3 receptor, respectively. Here, using whole cell patch clamp techniques and optical recording, in developing ferret visual cortex, we pharmacologically isolated fast, spontaneous and evoked cholinergic and serotonergic synaptic events in pyramidal cells and interneurons of all cortical layers. Whole cell recordings of spontaneous synaptic activity were made from 152 neurons in slices from animals ages postnatal day 8 (P8) to P37. To isolate nicotinic and serotonergic currents, glutamatergic and GABAergic synaptic transmission were blocked by receptor selective antagonists. After P14, 38% of tested cells had spontaneous synaptic events that were suppressed by the nACh receptor antagonist dihydro-beta-erythroidine (100 μM). Serotonergic synaptic currents blocked by the $5\text{-}HT_3$ receptor antagonist ICS 205-930 were found in (20%) of the recorded neurons. The number of cells receiving such inputs increased with the ingrowth of thalamic afferents and the frequencies of the spontaneous events increased at eye opening. Optical recordings of voltage-sensitive dye signals revealed cholinergic and serotonergic response components in all cortical layers.The number of cells receiving such inputs increased with the ingrowth of thalamic afferents and the frequencies of the spontaneous events increased at eye opening. Thus, both acetylcholine and serotonin can mediate fast synaptic transmission in the visual cortex.

Since spontaneous synaptic activity plays a crucial role during the initial setup of cortical circuits the question arises to what extent extrathalamic inputs can pattern this activity. To address this issue we studied the effects of fast, iontropic serotonin and acetylcholine receptors on cortical circuit response properties in slices of ferret primary visual cortex using high speed optical imaging of voltage-sensitive dye signals and whole cell patch clamp recording. Activation of the $5\text{-}HT_3$ receptor or the nicotinic acetylcholine receptor decreased the amplitude and lateral extent of excitation throughout postnatal development with peak effects after eye opening. Serotonin itself had a similar effect, which was largely mediated by the $5\text{-}HT_3$ receptor system. The 5-HT1B receptor on the other hand, which suppresses synaptic responses in rodent cortex, enhanced circuit excitability in the ferret. Patch clamp recordings from single neurons revealed that synaptic responses evoked by white matter stimulation were reduced by $5\text{-}HT_3$ receptor agonists, while the frequency of spontaneous GABAergic synaptic currents was dramatically enhanced. Nicotinic agonists increased both GABAergic and glutamatergic synaptic activity. This indicates that the modulation of spontaneous synaptic activity by fast acting serotonin receptors and acetylcholine receptors is reflected in an inhibition of the circuit response, in line with the notion of background synaptic activity altering the spatiotemporal integration properties of cortical cells by changing their membrane potential and their electrotonic structure. These mechanisms may regulate the response properties of intrinsic circuits both in the adult and developing neocortex. The early onset of these mechanisms suggests a role during initial stages of circuit formation and during subsequent experience- dependent remodeling of cortical connections.

This work was supported by National Institute of Health grant EY07690 (L. C. K.) and a Human Frontier Science Program postdoctoral fellowship (B.R.).

EFFECTS OF ELECTRICAL STIMULATION OF THE LATERAL GENICULATE NUCLEUS ON THE ACTIVITY OF NEURONS OF THE PRIMARY VISUAL CORTEX IN THE RAT.

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The effects of electrical stimulation of the dorsal lateral geniculate nucleus (dLGN), or the optic tract (OT), on the activity of neurons in the primary visual area (area 17) of the rat were studied.

A group of 60 adult Wistar rats were used in this study. Rats were anaesthetized with urethane and placed in a stereotaxic frame. Extracellular recordings were made from 300 spontaneously firing neurons in the area 17 while the dLGN was electrically stimulated. Single monophasic square wave pulses (0.05-0.15 ms duration, 50-250 μA intensity, 0.5 Hz frequency) were applied to the dLGN or the OT using concentric bipolar electrodes. Signals recorded from glass microelectrodes were fed into an amplifier, then to a computer that recorded spike frequencies and interspike intervals.

Stimulation of dLGN produced three types of responses in neurons of area 17. In most of them (185 neurons, 61.6%) dLGN stimulation produced a sequence of excitation and inhibition. In 37 neurons (12.3%) only excitation was found. In the remaining 78 neurons (26.1%) dLGN stimulation produced inhibition. Based on these different responses, neurons were classified into three groups that will be referred below as tipes I, II and III respectively.

Stimulation of the OT produced similar responses on area 17 neurons. Of 48 neurons studied, 16 belonged to type I, 9 to type II and 23 to type III. In 32 neurons it was posible to study the response to both dLGN and OT stimulation. The results were similar regardless of the place of stimulation, although, the latency of the response was longer for OT stimulation.

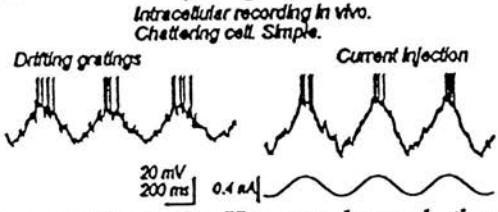
To determine wheter these responses were monosynaptic or polysynaptic in nature, we studied the latency of antidromic responses of geniculate neurons to single pulse stimulation of their terminals in area 17. On the basis of the antidromic latency of the geniculo-cortical neurons (=1.75-2.5 ms), considering the synaptic delay (= 0.5 ms) and the delay between the onset of the excitatory postsynaptic potential and spikes (= 0.8 ms), response latencies of 3 ms or shorter were considered to be monosynaptic inputs from the dLGN. The proportion of monosynaptic responses in type I and II was similar (37% and 44%). On the contrary, most of the type III neurons (74%) showed latencies equal to or shorter than 3 ms.

The laminar distribution of the different types of neurons was determined on the basis of citoarchitectonic criteria. Types I and II were found in all cortical layers and type II in all layers except layer VI. Type I neurons predominated in all layers, followed by types III and II. A similar distribution was found in neurons with latencies shorter than 3 ms.

The results of the present study show that in the rat primary visual area, stimulation of the geniculo-cortical afferents produced three types of response. This multiplicity may involve the participation of two populations of neurons, one of wich is excited (type I and II neurons) and the other inhibited (type III neurons) by dLGN neurons. These results also show that the three types of response are found throughout area 17.

CELLULAR AND NETWORK MECHANISMS GENERATING ADAPTATION TO CONTRAST IN THE VISUAL CORTEX: AN *IN VIVO* AND *IN VITRO* STUDY. M. V. Sanchez-Vives*, L. G. Nowak and D. A. McCormick. Section of Neurobiology. Yale University Medical School. 333 Cedar St. New Haven, CT.

Threshold detectability of a low contrast grating shows a 5x increase after adaptation to a high contrast grating and is associated with decreased action potential discharge of striate cortical neurons, which may result from a hyperpolarization of these cells (e.g. Carandini and Ferster, Soc. Neurosci. Abst. 1996). Here we examined whether or not single visual cortical neurons may hyperpolarize *in vivo* and *in vitro* in response to repetitive activation and the physiological consequences of this hyperpolarization. In order to simulate the modulation produced by drifting gratings in simple cells we used intracellular injection of sinewave currents (see figure).



The intracellular injection of 2 Hz sinewave currents for 20-30 s generally induced an afterhyperpolarization (AHP) that lasted 10-40 s. During this AHP, the response to low intensity current injections was slightly decreased for 8-12s. However, longer lasting current injections (1-2 min) were also followed by an AHP and sometimes by an ADP (afterdepolarization). Depending on the relative amplitudes of the AHP or ADP the responsiveness of the neuron may be either slightly decreased or increased. Interneurons showed a similar behaviour to the rest of the cells. To test the possibility that PSP barrages may undergo decrement with repetitive activation, we activated barrages of PSPs at 2 Hz (with electrical stimulation in the white matter below layer VI *in vitro*). The repetitive activation of the PSP barrages resulted in an exponential decrease in their peak amplitude with a time constant of 7-11 s. Our results suggest that at least two mechanisms, a slow hyperpolarizing current and synaptic depression, may participate in contrast adaptation. These two mechanisms are currently being examined in detail. Supported by the NIH and NSF.

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Effects of a single-orientation environment on orientation preference maps in cat visual cortex

For many years it has remained controversial whether exposure to contours of a single orientation during the critical period affects orientation selectivity in the visual cortex. Three different paradigms have been employed to address this issue: a) rearing of kittens in stripe-painted cylinders (Blakemore and Cooper, 1970), b) wearing of goggles that contain images of lines of a single orientation (Hirsch and Spinelli, 1970) or c) wearing of strong cylindrical lenses (Freeman and Pettigrew, 1973).

The controversy has centred on two issues. First, the potency of Blakemore's and Cooper's paradigm to modify orientation preference has been questioned (Stryker and Sherk, 1975); single-cell recordings have been criticized for introducing sampling bias. Second, and more importantly, it has remained unclear whether the observed biases in the distribution of preferred orientations entail an active re-specification of cells, i.e. a change in their preferred orientations towards the experienced one, or whether there is a loss of responses of cells whose preferred orientations do not match the experienced one. We determined orientation maps by optical imaging of intrinsic signals in order to address these issues

Ten kittens were reared in the dark from the day of birth. Starting at P14-17, they were placed in cylinders painted with evenly spaced black and white stripes of a single orientation (0°, 45°, 90° or 135°). The animals were exposed to this visual environment binocularly or monocularly for an average of 4 hours a day, until a total exposure of 70 to 100 hours was reached. A titanium chamber was then implanted on the skull, and optical imaging of areas 17 and 18 was performed. After the experiment, the monocularly experienced animals underwent reverse occlusion, and were allowed to recover. They were then exposed to stripes orthogonal to the previously shown ones for another 2 weeks, before a second optical recording experiment was performed.

After the first period of exposure, the experienced orientation was over-represented in all animals but one in terms of cortical surface area compared with any of the other 3 orientations. Of the total area responsive to any of the 4 orientations shown, between 30.5% and 39.0% responded preferentially to the experienced orientation.

Electrophysiological recordings showed that preferences of single neurons matched those predicted from the orientation map; response properties of cells whose preferred orientation matched the experienced one did not seem to differ from those of other neurons.

The overall layout of the orientation maps obtained from the reverse-occluded kittens after the first and second selective exposure remained unchanged, as confirmed by cross-correlation analysis. However, there was now a large non-orientation selective response component, and only a slight over-representation of the orientation experienced last.

In conclusion, rearing in a restricted, single-orientation environment shifts the balance of representation of preferred orientations in cat visual cortex towards the experienced one, without eliminating responses to other orientations altogether.

The fact that, in stripe-reared animals, there do not appear to be visually unresponsive regions of cortex may indicate that responses are re-specified at the single-cell level. But in view of the results from reverse-occluded kittens it is also conceivable that there is a loss of tuning (rather than responsiveness) in regions of cortex where the preferred orientation does not match that prevailing in the environment.

EFFECTS OF SPATIAL CUING ON SHAPE AND COLOR DETECTABILITY ON HUMAN SUBJECTS.

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Abstract:

In the present study the EEG and conductual responses during a discrimination task on spatial selective attention windows were analyzed. We used response time as conductual analysis and event-related potentials (ERPs), average on time domain as psychophysiological analysis.
The EEG was recorded on 13 positions of the scalp. The subjects were presented with stimulus in the right and left visual field. Attention was oriented to the left or the right side using cues. As Posner paradigm there were valid, neutral and invalid trials. Moreover we requested to subjects to do two different tasks: simple discrimination (based in shape of stimulus) and conjunction one (based in shape and color). Response time was acquired for each condition. We detected differences in manual responses between valid, neutral and invalid conditions. On ERPs, the voltage amplitudes and latencies of P1, N1 and subsequent components were analyzed. Also the results showed differences for specific components in conditions mentioned above.

On workshop we will present an explanation about these effects over visual perception implying spatial attention mechanism.

Key words:

Spatial attention – Visual perception – Discrimination task – ERPs – Response time

Discrimination Capacities of Human and Non-human Primates of Oriented Lines.

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Orientation selectivity is a property that depends on processing by cortical visual cells, and first appears in V1. Most of the relevant electrophysiological studies on orientation selectivity have been made using line segments of different lengths, but only a few psychophysical studies on orientation discrimination have used line segments, and there is not a detailed description comparing these psychophysical capabilities of human and non-human primates. Here we present results of psychophysical experiments designed to test the conditions under which monkeys and humans can perform categorizations and true discriminations of oriented lines.

Subjects, monkeys and humans, were placed in a soundproof room facing a monitor at 114 cm from the eyes. The stimulus consists of a stationary line segment. Three different base orientations were used. Comparison lines, ten per base, are presented rotated to the right or to the left with respect to the base line. Humans and monkeys were trained and tested in the orientation discrimination task, a modified 2AFC paradigm. A trial is initiated with presentation of the Fixation Target at the center of the monitor screen. Subjects were required to maintain the right hand on a key lever through a variable Preestimulus Delay until two stimuli (base and comparison) had been presented in a temporal sequence, with a fix Inter Stimulus Interval. Then, they were to indicate the end of the second stimulus by releasing their hand from the key and pressing one of the two switches at their hand reach. Monkeys receive a drop of water as a reward for correct discriminations. Human subjects do not receive a reward for correct discriminations, but a modulation of the masking noise signals the errors. Categorization. Subjects received three independent runs (100 trials per run) each with different base stimuli: 85°, 90°, and 95°. For example, one run in which the base stimulus of 90° was followed by comparison stimuli ranging from 85° to 95° in 1° steps: fixed base task. Discrimination. Subjects received in each run three base stimuli (85°, 90°, 95°) presented pseudo-randomly, followed by the comparison stimuli. Reaction Time (RT) and Movement Time (MT) were obtained, RT as the time elapsed from the end of comparison stimulus till key lever is released. MT goes from key release to pressing one of two switches.

In the fixed base task, the base stimulus was kept fixed through the whole run, only the comparison line changed randomly from trial to trial. Different runs were delivered with different base stimuli (85°, 90°, 95°). Psychometric functions were obtained for subjects discriminations between lines of different orientations by plotting the percent of comparison stimuli identified as orientated to the left of the base stimuli as a function of the orientation of the comparison stimulus. The data was fitted to a sigmoid curve, obtaining the "difference limen" (DL) or minimum angle that elicits 75% of correct responses. Signal Detection Theory analysis was applied, obtaining sensitivities (d'), and criterion used by subjects.

If subjects were discriminating differences in orientation between the two stimuli, they would also be able to discriminate them when the base stimuli changed randomly from trial to trial, in the same run. At each trial, a base (85°, 90° or 95°) and one of the ten corresponding comparisons were selected at random (e.g.: for a base of 90°, comparison stimuli ranged from 85° to 95° in 1° steps). Humans failed to discriminate for the first 20 trials, but then they began to perform correctly. Monkeys must be extensively retrained in order to perform correctly the discrimination task. Subject's performance was clearly decreased at orientations different from 90°. It seemed that, in the fixed base task, subjects were only paying attention to the second stimulus, categorizing it as to one side or the other of the base stimulus.

To test if, in the fixed base task, subjects were paying attention only to the second stimulus and ignoring the first, the base stimulus was removed in separated runs, and only the comparison stimuli were delivered in each trial. The psychometric functions indicate a correct categorization of the stimuli as to the left or to the right with respect to 85°, 90 and 95°. These results indicate that the strategy used was to categorize the second stimulus, paying no attention to the first.

To test that a true discrimination was carried out -i.e.: a trial by trial comparison between the second and the first stimuli during the task- the base stimulus was removed, and only the comparison stimulus was delivered in each trial. Psychometric functions indicate that human subjects were unable to discriminate. These results indicate that this task can only be solved if the two stimuli are being compared during the run.

Conclusions. Humans and monkeys have similar capacities to discriminate orientations. When the base stimulus is kept constant from trial to trial, subjects can signal the orientation of the second stimulus either by comparing both stimuli or by categorizing the orientation of the second stimulus as to one side or the other, ignoring the base stimulus. Subjects choose to categorize the second stimulus. True discrimination is performed when the orientation of the base stimulus is randomly changed from trial to trial. Monkeys have to be extensively retrained in the true discrimination task, until they learn to discriminate correctly and consequently to pay continuous attention to the base stimulus. Performance in the true discrimination task showed higher difference limen (DL) and lower sensitivity (d') than those obtained in the categorization task. The psychophysical data indicated a difference in performance between true discrimination and categorization tasks, and this might have important implications for investigating the neural mechanisms involved in orientation discrimination.

Supported by DGICYT PM96-0027 MEC, Spain. (*) PV is a FPI fellowship. MEC, Spain.

MODULATORY MECHANISMS AT THE MAMMALIAN RETINAL CIRCUITRY INVOLVED IN THE ROD/CONE MEDIATED VISUAL PERCEPTION.

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Purpose. To study the diferent mechanisms implicated in the visual processing at the synaptic terminal of rod bipolar cells (RBCs) that may be involved in the rod-cone circuits at the inner plexiform layer (IPL) of the mammalian retina. **Methods.** Voltage-dependent (potasium and calcium) and ligand-dependent (GABA) induced currents were studied by the patch-clamp technique on enzymatically dissociated RBCs and bipolar cells in retinal slice preparations from the mouse retina. Immunocitochemistry against protein kinase C (PKC) was performed on dissociated RBCs and retinal transverse sections. Image analysis was used to quantify the transport and activation of the PKC in the RBCs upon incubation in several test solutions. **Results.** We demostrate that the RBCs express L-type calcium channels and $GABA_C$ receptors. Both, sustained calcium channels and $GABA_C$ receptors, are located mainly at the axon terminals of RBCs. Upon activation of the calcium dependent PKC by cell depolarization or dopamine, the enzyme is transported to the axon terminal of RBCs where it is supposed to play its functional role. Modulation of GABA induced currents by PKC was tested and an increase in the current amplitude through the $GABA_C$ receptor was observed. **Conclusions.** Modulatory mechanisms mediated by calcium, GABA, PKC and dopamine seem to be implicated in the processing of the visual information at the IPL of the mammalian retina. These mechanisms allow us to propose a model for the segregation of the rod and cone mediated pathways under scotopic or photopic conditions.

LIST OF INVITED SPEAKERS

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The lectures summarized in this publication were presented by their authors at a workshop held on the 23rd through the 25th of February, 1998, at the Instituto Juan March.

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