Instituto Juan March
de Estudios e Investigaciones

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CENTRO DE REUNIONES
INTERNACIONALES SOBRE BIOLOGÍA

Workshop on

Principles of Neural Integration

Organized by

C. D. Gilbert, G. Gasic and C. Acuña

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The lectures summarized in this publication were presented by their authors at a workshop held on the 22nd through the 24th of September 1997, at the Instituto Juan March.

Depósito legal: M. 41.257/1997
Impresión: Ediciones Peninsular. Tomelloso, 27. 28026 Madrid.

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INTRODUCTION

C. D. Gilbert and G. Gasic

Studies on the cellular basis of perception and behavior have revealed fundamental new ideas concerning how information is encoded by the nervous system. It is now possible to establish links between the activity of individual neurons and of neuronal ensembles to complex behaviors. There is still considerable debate, however, concerning the conceptual framework by which one should establish such linkage, and the symposium on Principles of Neural Integration was designed to frame the debate on several key issues.

The information carried by neurons can be expressed as a "rate code", in which all that counts is the number of action potentials per unit time, or as a temporal code, in which stimulus information is represented by the precise pattern of impulses over time. The timing of impulses for one neuron may reflect synchronization within an ensemble of cells participating in a larger network. The relative contributions of rate and temporal codes can be measured by using information theory, where the amount of information carried different components of cells' responses to a range of stimuli can be quantified. One argument for the need for temporal codes is to deal with the problem of how to link the components common to particular objects and to segment components belonging to different objects. It is argued, alternatively, that the linkage operation is reflected in changes in the firing rates of cells, whose response depends not only on the characteristics of local features but also upon the global characteristics of contours and surfaces within which those features are embedded. The issue of how one can identify multiple objects within a scene, may be dealt with by attentional mechanisms, where the scene can be dealt with one object at a time.

Another important issue is how sensory information is linked to motor output, and how extrapersonal space is represented. Two model systems that have provided important information on these issues are the superior colliculus and the parietal cortex. Attention has played an important role in this analysis, and has been considered along with intention as playing an important modulatory role.

A third issue explored in the symposium is the role of dynamic changes in cortical circuits and receptive field properties. Parallel studies in human psychophysics and cortical receptive field properties have demonstrated the role of context in shaping the perception of stimulus attributes, the role of experience or perceptual learning, and the role of visuospatial attention. These influences are seen throughout the cortical visual pathway, from the primary visual cortex to parietal cortex and to visual areas in the temporal lobe. The circuitry underlying these different forms of plasticity include lateral interactions within individual areas and feedback connections from higher to lower order areas.

The highest order aspects of memory and perception have become much more accessible to study, and there are a number of elements in the higher order properties of cells that are characteristic of cortical areas. Complex representations of object identity and of the local environment are represented in the temporal cortex and hippocampus. The interaction between high order areas allow for the storage of this information, and interactions between high and lower order sensory areas give the earlier stages much more complex properties that traditionally believed. Exploring the interaction between memory systems in the limbic areas and the higher order sensory areas in the temporal lobe is one of the greatest challenges in the field of neural systems. The joining together of behavioral analysis, responses of individual neurons and of neuronal ensembles, and mathematical models, is providing a groundwork for understanding the brain mechanisms of even the most complex percepts and behaviors.

Session 1: Neural codes

Chairperson: Carlos Acuña

Information Representation and Processing by Neurons in the Primate Brain

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The level at which information is exchanged between the computing elements of the brain is at the level of neuronal activity, for it is by the firing of neurons that information is conveyed to other neurons. This means that to understand brain computation, we must understand how information is represented by single neurons and by populations of neurons, and what information is represented in different brain areas. Analysis of the way in which each brain area transforms the information it receives then provides a foundation on which to build computational models of how the brain solves difficult problems such as vision (see e.g. Wallis and Rolls, 1997) and memory (see e.g. Rolls, 1996), and also provides the data against which models of brain function must be tested (Rolls and Treves, 1997).

Analysis of the information in the spike trains of neurons.

A number of laboratories have developed information theoretic approaches to the analysis of what is represented by neuronal firing, and how it is represented (e.g. Richmond, Hertz and Optican; Bialek; Rolls, Treves and Panzeri; see e.g. Rolls and Treves, 1997; Treves and Panzeri, 1995; Panzeri and Treves, 1996). We have shown for example that much of the information in the responses of single neurons in the temporal visual cortex about which visual stimulus has been seen is contained in the firing rate of the neurons, and that much of the information is available in periods of the firing as short as 50 or even 20 ms (Tovee, Rolls, Treves and Bellis, 1993; Tovee and Rolls, 1995; Rolls and Tovee, 1994). An analysis has also been developed of how information about a single stimulus is related to the firing rate of visual (Rolls, Treves, Tovee and Panzeri, 1997) and olfactory (Rolls, Critchley and Treves, 1996) neuron to that stimulus. The information theoretic approach has been developed for application to the activity of the responses of many neurons to the same stimulus, and it has been shown that the information rises approximately linearly with the number of neurons in the population. This means that the encoding is distributed, and that the number of stimuli that can be encoded increases exponentially with the number of neurons in the population (see Rolls, Treves and Tovee, 1997; Abbott, Rolls and Tovee, 1996). This property is seen even with neurally plausible, dot product, decoding. The implication is that the code can be read off from this part of the visual system (and we have shown also from populations of neurons in the hippocampus and secondary olfactory cortex) just by measuring the firing rates of small populations of neurons. Other laboratories have developed analysis techniques which show that in at least some parts of the cortex, some additional information is available if the relative time of firing of different neurons is taken into account.

The firing rate distribution of neurons under natural conditions of stimulation is frequently somewhat similar to an exponential distribution, with many low firing rates, some higher firing rates, and a few very high firing rates (Rolls and Tovee, 1995; Rolls, Treves, Tovee and Panzeri, 1997). We have shown in more recent work that the responses of inferior temporal cortex neurons to natural visual stimulation (presented using a video recording) have a similar distribution. Although for some neurons the firing rate distribution resembles an exponential distribution, often there are too few very low rates for a good fit, and it is shown for the majority of the neurons that the exponential distribution in not statistically a good fit. To understand how the actual distribution could arise, we have developed a simple model in which the firing rate reflects, at any given time, the amount of current entering the cell soma according to a threshold-linear activation function, and the activation arises from a large number of small independent sources (the inputs from each synapse to the neuron). With two main sources of variability in the inputs to the model, slow reflecting for example the changing stimuli, and fast including noise effects producing variability in the response to a given stimulus, close fits to the actual distributions were produced by the model. We were also able to show that the efficiency of the representation, measured by the ratio of the rate of transmitted information to the maximal possible rate (with the same sparseness of neuronal firing), is moderately high, in the order of 0.5 - 0.7. This finding was supported by an analysis of data obtained when one stimulus at a time was presented using a large set of 65 natural images. The model may account for the firing rate distributions of neurons in many parts of the brain during natural stimulation (Treves, Panzeri, Rolls, Booth and Wakeman, submitted).

Modelling the computations performed by populations of biologically realistic neurons with connectivity realistic for a given brain area.

To help develop and test theories of how individual parts of the brain operate, quantitative data on the neuronal microconnectivity of the area, on the properties of its neurons including their synaptic modifiability, and on the normal responses of neurons in that area, must be combined. Such models have been produced (see Rolls and Treves, 1997) for example for the hippocampus (Rolls, 1996) and for visual invariant object recognition (Wallis and Rolls, 1997). To analyse how the system would work in real time (its dynamics), the biophysical properties of the neurons must be incorporated into the model. This has enabled the conclusion to be reached for example that an autoassociation network which could implement part of a memory system in the hippocampus could recall a memory from a partial cue in as little as two time constants of its synaptic connections, that is in perhaps 30 - 50 ms (Simmen, Rolls and Treves, 1996; Treves, Rolls and Simmen, 1997; Rolls and Treves, 1997).

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THE IMPORTANCE OF PRECISE TIMING IN CORTICAL INFORMATION PROCESSING.

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One of the goals of neurobiological research is to understand how the brain constructs representations of its environment. Knowing the neuronal code of such representations is a prerequisite for any reductionistic explanation of cognitive functions such as perception, memory and learning. At present two hypotheses are pursued: One assumes that perceptual objects are represented by the responses of highly selective, object-specific neurons which are located at the top of hierarchically structured processing systems. The other favours the view that representations are distributed and consist of assemblies of cooperatively interacting neurons. A key feature of assembly coding is that individual neurons can participate at different times in different assemblies which greatly economizes the number of neurones required for the formation of different representations. This, however, requires a versatile mechanism of response selection which allows to associate in a highly flexible way subsets of distributed neuronal responses for further joint processing. Here, it will be proposed that synchronization of responses could serve as mechanism for the dynamic selection and binding of responses because it raises with great precision and without requiring time consuming temporal integration the saliency of responses containing synchronized epochs. Experiments will be reviewed which have been designed to test predictions derived from the synchronization hypothesis. It will be shown that feature selective neurons in the visual cortex can synchronize their discharges if activated by the outlines of the same visual object and that synchronization probability reflects some of the established Gestalt criteria for perceptual grouping. Evidence is further provided, that this synchronization is achieved at least in part by cortico-cortical association projections. The architecture of these connections is shaped during postnatal development by an experience dependent process. Experiments with strabismic animals suggest that cortico-cortical connections are selected according to a correlation rule and that modifications of these connections are reflected by altered synchronization probabilities. It is proposed that these modifications serve the experience dependent generation of new assemblies such as is required for perceptual learning. Data will also be reviewed from awake behaving animals that reveal close correlations between the synchronization of cortical neurons and behaviour. In cats trained to perform a visual discrimination task zero-phase lag synchronization occurs among cortical areas involved in the task (visual, parietal, frontal) during task performance but not while the animal is at rest or consumes the reward. In strabismic cats exposed to stimuli causing interocular rivalry a close correlation exists between the synchronization of neuronal discharges in primary visual cortex and perception. Responses that are perceived exhibit a high degree of synchronicity while responses that are excluded from perception desynchronize. It is proposed that these results are compatible with the hypothesis that temporal relations between distributed neuronal responses play an important role in cortical processing.

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Revealing States of Brain by Single Units Activity

M. Abeles, I. Gat, E. Seidmann and Y. Prut. Dept. of Physiology, and the Center for Neural-Computation, The Hebrew University, Jerusalem
Israel.

Firing properties of neurons are usually evaluated by averaging across many trials, or along prolonged durations. Here we present results obtained by two methods that point to instances at which specific changes occurred in single trials. The precise firing sequences (PFS), and the hidden Markov model (HMM). Parallel recordings from several neurons form the frontal cortex of behaving monkeys were obtained by six metal micro-electrodes and spike sorting hardware. The monkeys were performing tasks of delayed localization in space and solving puzzle boxes. PFSs were detected by looking for excessively repeating sequences of 3 spikes with precision of +/- 1 ms and duration of up to 450 ms. Such PFSs were found in 24 out of 25 recording sessions and 72 out of 77 recorded units took part in one or more PFSs. PFSs were often associated with firing rate modulations but we encountered numerous cases of PFS without any changes of firing rates and vice-versa. PFSs were associated with the monkeys' set in a way that could not be revealed by their responses. The activity of the single units was also analyzed by two types of Hidden Markov Models. Both types revealed clear transitions among quasi-stationary states. The Model properties depends on the concomitant firing rates of several neurons. Although the HMM was based only on firing rates – it revealed changes of cross- correlations between pairs of neurons. The parameters of the underlying Markov model were specific to both stimuli and behavior. On the theoretical level, the PFSs can be explained by simple synfire chains, while the HMM suggests simple attractor neural networks. Both properties are consistent with reverberating synfire chain model. Experimental findings about the relations of precise firing patterns and cross correlations support the latter as the underlying mechanism.

Supported in part by grants from the Israel Academy of Sciences and the Human Frontier Science Program.

Session 2: Sensorimotor transformation

Chairperson: John H.R. Maunsell

The Visuomotor Transformation in Monkey Superior Colliculus. Robert H. Wurtz
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The superior colliculus represents a transition between the visuomotor processing in the cerebral cortex and the generation of specific eye movements in the brainstem. The neurons within the colliculus that are likely to be related to this transition are the type referred to as buildup neurons. They increase their discharge before the onset of saccadic eye movements, but unlike the burst neurons that lie in the same intermediate layers, these neurons show a gradual buildup in their activity as the onset of the saccade approaches. The neurons are also the best candidates to receive inputs from cerebral cortex because they show the earliest change in activity before a saccade. Recent experiments indicate that these neurons might well represent a stage of processing before that related to generating a specific movement.

Although many buildup neurons have a burst of activity that is tied to saccade onset, their buildup of activity is not dependent on saccade generation. For example, their activity can be altered by changing the conditions for movement even before the saccade target is selected. In one experiment, increasing the number of targets, from which the correct target will eventually be selected, reduces the buildup activity. In another experiment, keeping the number of visual stimuli constant, but changing the probability that one will be the target, altered the buildup activity. The modulation in both experiments occurs before any selection of the correct target is made. Thus the buildup activity of these neurons is largely independent of the actual saccade generated.

The fixation neurons at the rostral pole of the SC are most active during periods of fixation, rather than before saccades, but they may represent a rostral extension of the buildup neurons and may reveal an added property of the buildup neurons. We have recently measured the discharge of these neurons when we made small steps in the target location, frequently small enough not to evoke saccades. Each of these neurons in the rostral colliculus had a peak increase in discharge for target steps of a given size into the contralateral visual field. In this respect these rostral fixation neurons are similar to the buildup neurons in the rest of the colliculus in that they increase their discharge with the introduction of an error between where the eye is and where the target is; the size of the error simply ranges from very small in the rostral colliculus (fixation neurons) to progressively larger in the more caudal colliculus (buildup neurons). Furthermore, this error may be used for generation of more than just saccades: neurons that change their discharge with small errors in the rostral colliculus show such a change with the generation of smooth pursuit eye movements as well as small saccades.

The discharge of the buildup neurons can therefore be interpreted as providing an error signal for movement. This error may be used for the generation of saccades, and the burst cells may be a subsequent stage in the processing related specifically to saccade generation. Change in gaze with coordinated eye and head movement and the control of reaching movements might be other outputs using this error signal. Pursuit as well as small saccades can result from small errors. Thus these buildup neurons may provide a generized error signal for movement, and this level of processing in the superior colliculus may precede that devoted exclusively to the generation of saccadic eye movements.

What Is Represented By The Activity Of Neurons Forming The Motor Map(S) Of The Primate Superior Colliculus? Changes In Gaze? Eye Movements? Head Movements? A Research Strategy For Answering A Complicated Question.

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Microstimulation of the primate superior colliculus (SC) produces changes in gaze that may involve coordinated movements of the eyes and head. The latency, velocity, and relative contributions of the eye and head to the stimulation-evoked changes in gaze are remarkably similar to amplitude-matched visually-guided movements. While the results of microstimulation experiments provide compelling evidence that the primate SC is involved in the generation of eye and head movements, they do not inform us about how the movements of the eyes and head are represented by the activity of individual neurons. Two possibilities seem most likely. The activity of cells in the SC could represent a signal of th desired change in gaze - a signal that is subsequently decomposed into separate commands for the control of the eyes and head. Alternatively, one population of cells in the SC could encode the desired change in eye position and a separate population could encode the desired change in head position.

Determining which of these possibilities is true is more complicated than a casual consideration of the problem suggests. Two major factors complicate attempts to answer this question. First, standard correlational methods relating firing rate to movement metrics (direction and amplitude) cannot be use to determine if the discharge of individual cells is related to changes in gaze or to displacements of th eyes or head. Information about the metrics of movements is not coded by the rate of discharge of SC cells. It is the location of the active cells within a motor map, not the rate of discharge, that is the majo determinant of movement direction and amplitude. The second complicating factor is that the movements of the eyes, movements of the head, and changes in gaze are not independent, but highl correlated. Ascertaining whether the activity of a collicular neuron observed on a particular trial is relate to the change in gaze or to the eye or head component of the gaze shift is not a trivial task.

In his dissertation research Ed Freedman examined the discharge of individual collicular neurons during three behavioral conditions which allowed a dissociation of the movements of the eyes, movement of the head, and changes in gaze. An analysis of cellular activity, based upon the location the cell within the active population, indicates that the activity of cells in the caudal SC represents a command for a change in gaze, not a command to move the eyes or to move the head. My talk will describe the analyses that led to this conclusion.

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Coding of Intention and Space in the Posterior Parietal Cortex

To look to or reach to visual stimuli we must transform spatial sensory information into plans to make movements. The posterior pareital cortex (PPC) is ideally placed for this function, since it lies between visual areas, which code spatial locations, and motor areas, which execute movements. The PPC contains several subdivisions which until recently have been regarded as higher order sensory areas. In tasks where monkeys are required to plan either an eye or an arm movement, we have found that different subdivisions of the PPC become engaged depending on the movement the animal plans to make. Area LIP becomes preferentially active when the monkey plans an eye movement and a reach area (RA) nearby becomes preferentially active when the monkey plans a reach. Thus, the "where" pathway of the visual cortex terminates in an anatomical map of intentions within the PPC.

In another series of experiments we have asked what happens when a monkey changes his movement plans, without changing the locus of attention or the spatial destination of the plan. We find that activity shifts from LIP to RA when the monkey changes his plan from an eye to an arm movement, and from RA to LIP when he changes from an eye to an arm movement plan. These shifts all occur prior to the animal performing any movement at all. Interestingly, there is also a greater discharge when a monkey is instructed to change a plan than when he receives the same instruction but it only affirms the previous instruction. Thus PPC activity also appears to play a role in the non-spatial shifting of movement intentions.

The PPC also plays an important role in the representation of space. Many signals converge here for this purpose including visual, auditory, vestibular and somatosensory sensory signals, eye-, head-, and limb-position signals, and efference copy signals. These signals appear to be combined in a systematic manner, using gain field mechanisms, in order to form representations of space. Recent cell recording experiments from our lab indicate separate body- and world-coordinate representations in areas LIP and 7a respectively. Also we have recently found spatial deficits after LIP reversible inactivations which are in at least a head-centered coordinate frame. These include the ability to program sequential saccades to remembered locations, and the selection of targets for eye movements.

Parietal Mechanisms for Visuospatial Attention.

Michael E. Goldberg

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The lateral intraparietal area (LIP) is important in the generation of visuospatial attention and the guidance of eye movements. It has projections to the superior colliculus and from the frontal eye field. It also has reciprocal connections with the inferior temporal cortex This lecture will deal with two aspects of neuronal function in LIP: 1. The nature of the visual response in LIP. 2. The mechanisms by which LIP maintains a spatially accurate representation of the visual world despite eye and head movements.

LIP neurons have visual receptive fields, and give brisk responses to stimuli flashed in those receptive field. However, recent psychological evidence (Yantis and Jonides, 1988) has shown that flashed stimuli evoke attention in human subjects. Since attention enhances the visual response of parietal neurons, it could be that the parietal response to a flashed target is more related to the attentional than to the visual aspects of the target. To distinguish between these alternatives we trained monkeys on a stable target task in which the monkey viewed a circular array of eight symbols on a tangent screen. The symbols were roughly 2 degrees in diameter, and differed in shape and color. The array was positioned so that when the monkey fixated the center of the array at least one of the symbols was in the receptive field of the neuron. When the monkey made a saccade that brought a symbol into the receptive field, LIP neurons did not necessary respond, despite the fact that the retinal receptive field was newly stimulated by the symbol. LIP neurons reliably respond to stimuli brought into their receptive fields when those symbols are salient for the animal. We used two strategies to make stimuli salient. In the first we instructed the animal, before the saccade, that it would have to make a subsequent saccade to the target. In the second we merely flashed the target onto the screen between 500 and 2000 ms before the saccade. In both cases the stimulus evoked a response around the time of the saccade that brought it into the neuron's receptive field.

In the first case the monkey actually makes a saccade to the target that evokes the response. In the second case the monkey could intend to make a saccade to the stimulus which might be canceled elsewhere in the brain. The activity of the parietal neurons could therefore be considered as intention or motor planning. To discount this possibility we trained animals to make identical saccades to gaps in the array, where there was stimulus. Most LIP neurons, as opposed to movement neurons in the frontal eye field, do not reliably respond discharge before such learned saccades. Therefore the response of these neurons must be a visual response to the stimulus, and not related to the intention or planning of a possible saccade. However, the representation of the visual world in LIP is sparse: objects which are not behaviorally salient are not represented.

Parietal neurons have retinotopic receptive fields. When the eye moves, the receptive fields move in space. However, a retinotopic representation is inadequate for the saccadic system: humans and monkeys can make fairly accurate saccades to successively flashed targets, even when there is a dissonance between the retinal location of the target and the saccade necessary to acquire it. Neurons in LIP can compensate for changes in gaze. When a stimulus is flashed in a spatial location that will be brought into a neuron's receptive field by virtue of an impending saccade, LIP neurons will respond to that stimulus, whether or not it is still present, sometimes even before the saccade. The neurons behave as if they predict that the stimulus will enter the receptive field. This predictive response occurs also if the spatial location of the flashed stimulus is brought into the receptive field by a smooth pursuit eye movement or even by the suppression of the vestibulo-ocular reflex during passive head rotation.

Session 3: Cortical plasticity and memory

Chairperson: Wolf Singer

Title: A synaptic view of space and time in visual cortical neurons

Authors: Yves Frégnac, Vincent Bringuier, Frédéric Chavane and Larry Glaeser

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To what extent the potential connectional envelope resulting from the high level of anatomical convergence and divergence of fibers carrying sensory messages from one level of integration to the next can be compared with the classical functional assessment of a receptive field, is an issue which remains largely undetermined at the cortical level. Two constraints in wiring specificity, which may appear contradictory in terms of topological matching, represent two major facets of sensory integration in the thalamo-cortical pathway. One is a funneling mechanism carrying out processing through local feedforward pathways and reentrant short-range connections. Its main role is to establish a retinotopic mapping of the peripheral input onto the cortical structure. The second, mediated by the activation of long-range connections and feedback projections from higher centers, might be required to signal global perceptual coherence across the visual field. Recent functional studies have shown that depending on the visual task to be solved by the visual system (e.g. orientation discrimination vs. orientation contrast detection) these various sets of connections - local, horizontal, feedforward or feedback - could be selected in a differential way in order to generate by their non-linear interplay the appropriate output (orientation selective vs. orientation contrast selective firing; Sillito et al., 1995; review in Frégnac and Bringuier, 1996).

In contrast with extracellular studies of visual receptive fields (RF), the recent development of intracellular techniques *in vivo* (sharp electrode or "blind patch") ideally allow experimenters to go beyond the level of description of the minimal discharge field (MDF), and analyze the relative contribution of feedforward thalamocortical and lateral intracortical connectivity in the functional expression of a synaptic "integration field" (Fregnac and Bringuier, 1996). We will present here data which demonstrate that the spatial sensitivity of visual cortical receptive fields described at the subthreshold level extends over much larger regions of the visual field than those previously established on the basis of the MDF size.

Previous extracellular analysis of visual cortical receptive fields (RFs) based on the evoked firing rate of cortical neurons has revealed the existence of "unresponsive" surround regions by their modulatory effect on the cell's response to a test stimulus presented within the minimal discharge (Li and Li, 1994). Obtaining direct evidence for subthreshold excitatory and inhibitory regions extending beyond the classical RF requires methods for generating, recording, and detecting physiologically identified excitatory and inhibitory post-synaptic potentials (EPSPs and IPSPs). Cells in area 17 of anaesthetized cats were recorded using sharp intracellular or whole-cell patch electrodes while providing pseudo white noise input (small light and dark bars flashed randomly in the visual field every 50ms). After a high pass filtering of the raw membrane potential record, local extrema whose relative amplitudes differ in succession by more than 500 μV were detected, and their dates of occurrence were used to form independent time series regrouping events of a given amplitude and polarity (depolarizing, hyperpolarizing, spike).

Subthreshold receptive field maps were established by applying a modified reverse correlation analysis method (RC) to each time series. The optimization (for each position of the visual field) of the retrograde delays at which averaging of backward correlations with the discretized intracellular signal is done, gives a prediction of the retinal origin of the visual input responsible for the postsynaptic activity of the cell. We found that excitatory and inhibitory receptive regions ranging from 1.5 to 60 times the area of the MDF (5-10° vs. 1°of solid angle for foveal receptive fields). Excitatory profiles were consistent with stimulus-locked waveform averages. Moreover, the RC technique revealed inhibitory regions, undetected using stimulus-locked averaging, which could be either within, surrounding or distinct from the MDF. The better sensitivity of the RC method in certain cases is due to the fact that, although the reverse and forward analysis are mathematically reciprocals of each other, the reverse correlation is applied after detecting individual events using a procedure which acts as a non-linear filter on the recorded membrane potential.

RC method allows in addition to compare RF maps obtained for events of different amplitudes. Amplitude thresholding techniques indicate that the lower the threshold, the larger was the extent of the RF. Subthreshold responses became smaller in terms of amplitude and energy, and showed longer latencies of onset, the futher away the stimulus was from the zone of the MDF eliciting the maximal firing rate. This description of a basin of subthreshold latencies centered on the core of the MDF could explain some of the results obtained by Grinvald and colleagues using optical imaging (Grinvald et al., 1994).

Taking into account the cortical magnification factor of the retinotopic projection onto the plane of the layers in visual cortex, an "apparent speed of propagation" (ASP) was computed as the ratio of the distance in the cortical projection map divided by the difference in response latencies between the central and peripheral loci of stimulation. The calculated ASPs, which ranged in our experiments from 0.02 to 0.95 m/s, is compatible with the conduction velocity along horizontal intracortical axons, which in turn is much slower than that of feedforward X- or Y- thalamocortical axons or of some (but not all) feedback projections from higher order visual cortical areas (Nowak and Bullier, in press).

This work is supported by grants from the Human Frontier Science Program (RG/69-93B)., the GIS Sciences de la Cognition and the CNRS.

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Dynamical Properties of Spatial Visual Processing in Human Observers

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Because of the prominence of orientation-selective receptive fields in the mammalian visual cortex, it is widely thought that there is a mandatory orientation-specific filtering of all visual signals. It is therefore important to be aware of the clear indications that the *position* of targets can be processed with exquisite precision in ways that suggest that there is a mechanism that deals with position as a primitive that is separate and distinguishable from that for orientation. Some evidence for this view is given in Westheimer (1996).

To study the mechanism by which the orientation attribute of borders is developed, several experimental tools can be employed. The simplest and most powerful is the perturbation method where one measures the smallest discernible difference in orientation of a border. In addition, interactions in the domain of orientation can be employed as they are manifest in, for example, orientation contrast effects or the tilt illusion; recognized anisotropies, such as the oblique effect, and masking paradigms can be used as well. During the course of the research one continuously keeps in mind current knowledge of the physiology of the early visual stages in the primate cortex in the hope of relating it to psychophysical findings, and vice versa.

Using these tools, we outlined major aspects of the orientation-elaborating apparatus. It can be addressed not only by explicit lines and edges, but also by a variety of other stimuli, such as single dots moving in a straight line, by stacks of orthogonal lines and by some stimuli without explicit oriented components, such as illusory contours and symmetrical patterns. But using the analytical tools described above, it is found that such stimuli vary considerably in their potency to signal orientation. Lines, edges and symmetrical figures are best, and illusory contours are in fact quite poor.

Interesting results emerge when one measures the combined effect of small line elements. To produce optimum orientation sensitivity, short line segments have to be collinear (within a few arcmins in the fovea), can be up to at least 30 arcmin apart but must be exposed within a few tens of milliseconds. Greater time delays causes active inhibition, not just lack of binding. There are severe limits on the allowable contrast polarity. Masking stimuli must be lines, but they can be of any orientation or contrast or ocularity, and are most effective with a 50msec time delay. Large-field masks cause less impairment than smaller ones confined to the test area.

Orientation sensitivity is poorer when the observer has to distribute attention over a number of stimuli or is uncertain about the time at which the test line is to appear.

Out of this array of findings there is beginning to emerge a view of orientation processing that accepts local processing (likely to be in V1) by a population of related neurons with interaction among them. Distance and time parameters for optimal interaction are of the order of perhaps a degree or less in the fovea, and a few tens of milliseconds. But there are other factors involved, demonstrated by masking and uncertainty phenomena. The current challenge is to partition these among neural circuits at the beginning of the cortical visual stream and those further on, and the interchange of signals between them.

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DYNAMIC PROPERTIES OF ADULT PRIMARY VISUAL CORTEX

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Our ability to interpret visual scenes involves assembling the components of objects into a unified percept and segregating them from background, storing information about earlier visual experiences, and testing our interpretations of the visual world against incoming sensory input. The influences of context, experience and expectation are reflected in the response properties of cells at early stages in the visual pathway. The responses of cells in primary visual cortex (V1) depend not only on the attributes of features lying within the classical receptive field but also on the global characteristics of the contours and surfaces within which these features are embedded. The substrate for lateral interactions includes a plexus of long range horizontal connections within each cortical area which links columns of similar orientation specificity and cells with widely separated receptive fields. The horizontal connections also play a role in the plasticity of receptive field structure and of cortical functional architecture, induced over long time scales by retinal lesions, and over short time scales by patterned visual stimulation. The long term changes are associated with synaptogenesis; the short term changes with an increase in synaptic effectiveness. The lateral interactions observed within V1 may represent the substrate for linkage and segmentation of contours and for fill-in of surfaces. Studies on perceptual learning show specificity for stimulus configuration and spatial position, suggestive of involvement of early visual processes. In area V1 some cells show tuning for the contextual patterns present in the trained stimulus, which may account for the specificity of perceptual learning for the trained configuration. The difference in tuning seen when the animal is actively performing the discrimination task, as compared with the tuning seen under passive fixation, suggests that the cortical changes underlying perceptual learning may be task dependent. Expectation of a stimulus influences one's ability to discriminate its attributes, representing another level of mutability of cortical function. This mutability is seen in V1 as a modulation of contextual influences. The implied mechanism is an interaction between feedforward mechanisms, as represented by intrinsic long-range interactions within V1, and feedback connections from higher order cortical areas. The implication of the effects of training and expectation is that vision is an active process, and that understanding the physiological basis of perception requires doing electrophysiology while the subject is interpreting the visual environment. The dynamics of cortical function persist throughout adulthood, implying a that neurons represent active filters, continually changing their specificities according to the global characteristics of visual scenes, experience and internal representations.

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Abstract for a workshop on "Principles of Neural Integration" at the Instituto Juan March de Estudios e Investigaciones, Mardir, September, 1997

Memory Systems of the Brain

Studies of animals with complex nervous systems, including humans, have provided new insights about how memory is organized in the brain. Neuropsychological analysis of patients with circumscribed memory impairment (amnesia) has led to a distinction between declarative memory, which is dependent on the structures damaged in amnesia, and nondeclarative memory, which is independent of these structures. Declarative memory is severely impaired in amnesia. It refers to information about previously encountered facts and events, the kind of information that is ordinarily available as conscious recollections. Declarative memory includes both episodic (event) memory and semantic (fact) memory, and is typically assessed in tests of recall, recognition, and cued recall.

Nondeclarative memory is spared in amnesia. Nondeclarative memory is a heterogeneous collection of abilities that includes perceptuomotor skills, perceptual and cognitive skills, and conceptual and perceptual priming. Priming refers to an increased facility for identifying words or other perceptual objects, as a result of recent encounters with them. Nondeclarative memory also affords the ability to exhibit shifts in preferences and judgments after exposure to novel material, and the ability to change gradually one's response to the external world as the result of conditioning. These findings provide strong evidence that memory is not a unitary mental function, but a collection of different abilities.

The study of retrograde amnesia, i.e., the loss of memory learned prior to the onset of amnesia, provides additional clues about the foundation and neurological organization of memory. The brain system damaged in amnesia is essential for the formation and storage of declarative memory and for its retrieval during a lengthy period of consolidation and reorganization. As time passes, the role of this system in memory diminishes, and a more permanent memory gradually develops elsewhere, probably in neocortex. These conclusions are supported by quantitative studies of retrograde amnesia in memory-impaired patients and more recently by prospective studies of retrograde amnesia in monkeys and rodents.

Finally, cumulative and systematic work in monkeys has identified structures and connections important for memory function. The findings to date suggest that the hippocampal formation and the closely related perirhinal and parahippocampal cortices comprise the medial temporal lobe memory system. Stereotaxic lesions of the hippocampal region (involving hippocampus proper, dentate gyrus, and the subicular complex) produce only a modest level of memory impairment. A similar level of memory impairment is found after global ischemia, which produces readily detectable damage in the CA1 region of the hippocampus and in the hilar region of the dentate gyrus. Larger lesions that include the entorhinal, parahippocampal, and perirhinal cortices produce more severe memory impairment. Importantly, the perirhinal and parahippocampal cortex, and possibly other cortical areas projecting to entorhinal cortex, do not serve simply as a connecting route to the hippocampus but themselves contribute to memory functions. The amygdala does not appear to be an essential component of this memory system, although it has been implicated in other kinds of cognitive functions, e.g., the formation of associations between a stimulus and its affective component.

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Session 4: Attention

Chairperson: Tom Albright

Neuronal Mechanisms of Visual Attention

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Results from recordings in monkey visual cortex suggest that attentional control arises from the resolution of competitive interactions in the cortex. The competition between neurons representing different stimuli in the environment appears to take place at many processing levels in the extrastriate visual cortex, beginning at least in area V2. At the neural level, competition is evidenced by the inhibitory effects of competing stimuli on neuronal responses. Competition can be biased in favor of one stimulus over another as a result of many different mechanisms, both "top-down" and "bottom-up". At the neural level, top-down bias is evidenced by increased spontaneous firing rates and increased stimulus sensitivity of cells coding the relevant information for the task at hand. Prefrontal cortex may be a particularly important source of top down bias in tasks requiring working memory. Recent results suggest that intrinsic properties of the stimuli themselves, such as relative contrast, can also be a strong source of bottom-up bias. Likewise, stimuli may acquire salience and a competitive advantage as a result of long-term associations with reward.

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FUNCTIONAL ROLE OF THE PULVINAR IN THE MACAQUE

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From the early studies of the primate pulvinar, it is known that the neurons of this nucleus are strongly modulated by attention or intentional activities. I will present an overview of how this modulation occurs on neurons whose activity is related to visual fixation, saccade eye movements, or arm reaching to objects of behavioral interest.

The pulvinar nucleus is reciprocally connected to neocortical areas that process different aspects of behavioral information (e.g.: parietal, frontal or temporal areas). The activity of many pulvinar cells, therefore, is modulated during the performance of a behavioral task, sometimes anticipating the presentation of relevant stimuli. Cortico-pulvinar connections carry information about selective attention and the behavioral state of the animal. Similarly, some pulvinar cells only become active when the animal visually fixates objects of high motivational value, or objects that can be used to guide subsequent behavior. Some of these cells were especially sensitive to movements of visual stimuli towards or away from the head. In fact, neurons in the pulvinar may be truly visual in the sense that they respond to specific visual stimuli and are related to spatially defined visual receptive fields. These visual neurons, however, show spatially selective enhancement of the visual response with attentional use, a property that makes them more similar to the fixation neurons of the parietal cortex.

In general, no passive visual responses have been demonstrated in pulvinar cells, although a reduction in activity can occur with eye movements in the dark. A modulation of the excitability by orbital position of the eye has been described in pulvinar cells, as well as on their target zones on posterior parietal cortex and in area V3A. Nevertheless, pulvinar neurons appear to modulate their activity only when saccadic or arm movements are used as a part of conditional behavior. The responses of different populations of pulvinar cells change before, during or after the onset of eye movements. These changes reflect, however, a participation in mechanisms more complicated than simple codification of the metrics of movement.

A general feature of pulvinar neurons is that they are strongly modulated by different types of stimuli. For example, some pulvinar cells increase their activity to smooth pursuit eye movements when following an object of interest in combination with an arm movement towards the target. Other cells can be modulated similarly by two different behavioral events, for example, saccadic and arm movements aimed at the same target. Cells like these were found in the Lateral and Medial pulvinar nuclei, parietal area 7, and supplementary eye field. Neurons of Lateral, Oral, Medial, and Inferior pulvinar nuclei change their activity before, during or after arm reaching towards objects of interest. However, only about 23% of the pulvinar cells appear to encode the parameters of the arm movement, compared to 76% of those in the posterior parietal cortex (area 5).

Results from pulvinar lesions suggest a participation of this nucleus in visual salience. Reversible inactivation of Pdm (dorsomedial region of Lateral pulvinar) increases eye movement reaction times when attention is switched from the inactivated to the normal visual field. Furthemore, although visual pattern or color discrimination does not appear to activate the pulvinar, pulvinar Lateral chemical deactivation does affect color discrimination if a distractor is present. Lesions of the posterior thalamus in humans, although sometimes difficult to interpret, appear to show alterations of attentional control. Moreover, measurements of regional cerebral flow with PET in humans show pulvinar activation in tasks that require focusing attention or to scrutinize visual patterns. For example, in a recognition task, that involves comparison of stored with actually seen patterns, the left pulvinar is activated together with several cortical areas functionally related to this task.

In general, different types of sensorial stimulus, focal attention and intention modulate pulvinar cells. The pulvinar nucleus, therefore, may be part of a distributed system that links cortical areas at the service of a specific behavioral activity.

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INFLUENCE OF ATTENTION ON NEURAL REPRESENTATIONS IN MONKEY VISUAL CORTEX

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Microelectrode recordings from the visual cerebral cortex of behaving monkeys have shown that responses of individual neurons can depend greatly on which aspect of the scene the animal is attending to (Desimone & Duncan 1995, Maunsell 1995). Accumulating evidence suggests that while the early stages of the visual pathway provide a faithful representation of the retinal image, later stages of processing in visual cortex hold representations that emphasize the viewers' current interest. While enhancement of sensory responses by attention has been found in many areas of the visual cortex, much less is known about whether attention dynamically alters the selectivity or reliability of sensory signals to improve behavioral performance.

We have examined these questions by recording from individual neurons in area V4 of trained monkeys while they performed a delayed match-to-sample task. Fixation was monitored and the animal was required to hold its gaze on a central fixation spot while doing the task. On each trial stimuli were presented simultaneously at two locations: one inside the receptive field and one outside. The animal was instructed to attend to the stimulus in only one location on a given trial. The stimulus inside the receptive field was a temporally-counterphasing patch of grating, the orientation of which was varied from trial to trial. The stimulus outside the receptive field was a uniform patch of color. By presenting different orientations in the receptive field, we obtained two orientation tuning functions for each neuron under conditions of identical visual stimulation, one when the orientation in the receptive field was being attended to, and the other while the animal was attending to the color stimulus, and ignoring the oriented stimulus inside the receptive field.

Most neurons (135/185) had orientation tuning curves in both conditions that were well fit by Gaussian functions. For 73% of these cells, the amplitude of the tuning function was greater when the animal attended to the receptive field stimulus (median +21%, n=135). Attention did not appreciably sharpen the tuning, as measured by the width of the fitted function (median 0.6% narrower). We also found that attention did not significantly alter the function relating the mean rate of firing to its variance (t-test, $p > 0.25$), suggesting that it does not increase the reliability of signals in V4.

Thus, selective attention scales sensory responses in area V4 multiplicatively, without altering the underlying orientation selectivity or the variability of responses.

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Session 5: Segmentation/Object vision

Chairperson: Charles D. Gilbert

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Visual Surface Segmentation and Motion Processing

Several lines of evidence indicate that the interpretation of retinal image motions depends upon the larger spatial and temporal context in which they appear. Formally speaking, this context dependence is a functional necessity, as local retinal image motions bear a non-unique relationship to the object motions that constitute perceptual experience. Contextual manipulations have been largely absent from studies of cortical motion processing, however. As a result, motion processing is generally characterized in terms of the local properties of the retinal stimulus rather than the visual scene structures from which these properties arise. In a series of parallel psychophysical and neurophysiological experiments, we have explored relevant stimulus variables, neural correlates, and underlying mechanisms for the role of context in visual motion processing. The results of our research suggest that surface segmentation processes re-interpret local motion signals to render a scene-based representation of visual motion.

The first-step in this operation is the identification of moving image features that arise from occlusion or changes in illumination (Shimojo et al., 1989; Stoner and Albright, 1993). These "extrinsic" features must be processed differently from "intrinsic" features, which reflect real surface properties. In psychophysical experiments, we have examined the variety of image cues that govern this process of feature classification (e.g. Stoner et al., 1990; Stoner and Albright, 1993; Stoner and Albright, 1996; Stoner and Albright, 1997). These image variables include luminance, chrominance, spatial frequency, binocular disparity, as well as size cues for foreground/ background assignment. Despite the diversity of mechanisms seemingly needed to account for the influence of these varied image parameters, our results point to a common principle: motion perception is impacted inasmuch as these manipulations suggest the presence or absence of depth-from-occlusion. Specifically, we have found that feature classification cues dictate whether a dynamic retinal image is perceived as a single or multiple moving surfaces, and thereby markedly alter perceived direction of motion.

In neurophysiological experiments, we have found that the directional selectivity of many neurons in the middle temporal area (area MT) of primate visual cortex parallels these perceptual phenomena. Thus, the response of an MT neuron to the motion of intrinsic image features is typically larger than that elicited by extrinsic features (Stoner and Albright, 1992). In addition, we have found that manipulations of perceptual feature classification alter the responsivity of MT neurons even when such manipulations occur outside the classical field (Stoner et al., 1997), thus implicating the non-classical surround in these contextual phenomena.

We have also carried out a variety of experiments to identify the type of mechanism that underlies these perceptual and neuronal phenomena. Firstly, by dissociating cues for feature classification from the distribution of Fourier components in a moving pattern, we have ruled out the possibility that the latter provide a plausible low-level explanation for these effects (Stoner and Albright, 1996). Secondly, by dissociating depth-from-occlusion cues from feature similarity, we have demonstrated that the segmentation of dissimilar moving features cannot be accounted for via feature-specific motion channels (Stoner and Albright, 1997). Our results instead implicate neural mechanisms sensitive to image cues for surface segmentation.

The results of these various experiments demonstrate the essential role that contextual manipulations play in understanding the transformation from neuronal representations of local retinal image features to representations of visual scene attributes. This view, moreover, reveals that the integration of information from different visual dimensions, such as luminance, chrominance, binocular disparity, and motion, is a necessary step in the formation of scene-based representations.

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INFEROTEMPORAL COLUMNS AND OBJECT VISION

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Area TE of the monkey inferotemporal cortex represents the final stage of the ventral visual cortical pathway, which is thought to be essential for visual object recognition, that is, recognition of objects from their visual images. The recognition process is flexible, tolerating marked changes in input images due to changes in illumination, viewing angle, and pose of the object. We have studied the functional architecture of TE to find mechanisms underlying the flexible properties of visual object recognition in the primate.

We developed a systematic reduction method to determine the stimulus selectivity of each individual cell: first, many 3-dimensional animal and plant models were presented to find the effective stimuli; and, second, the images of the effective stimuli were simplified step by step to determine the features critical for activation. By appling it to over 300 TE cells, we found that most cells in TE required moderately complex features for their activation. We also found that cells recorded throughout a vertical penetration responded to similar critical features. Such commonly responding cells were limited to a short span of around 400 μ in length in horizontal penetrations. Thus, we have concluded that there is columnar clustering of cells with similar selectivity.

To further study the columnar organization in TE, we used optical imaging. We first determined the critical features for 15 to 25 single cells in several unit-recording sessions, and then intrinsic signals were imaged during visual stimulation with the critical features. The image during stimulation with a critical feature divided by that during stimulation with a control stimulus revealed activation of a small spot covering the electrode penetration from which the critical feature was determined. The averaged diameter of the activation spot was 490 μ. In addition, different but related critical features determined for different cells recorded in the same penetration evoked activation in overlapped regions. Although the activation spots were overlapped, the overlap was partial and they expanded in different directions from the overlapped area. With a series of the same doll face, the activation spot moved gradually in one direction as the face turned from the right profile to the left profile through the front and 45 deg faces. The size of these overall regions was around 1 mm. Thus, we have suggested the presence of a continuous map of the space of complex features. Various kinds of computation may be carried out on this continuous map to realize the flexible properties of object vision in primates.

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Objects Representation and Recognition

The visual recognition of an object depends on the process of comparing the appearance of the object with the representations of objects seen in the past. The representations and processes involved should support invariant recognition, that is, the ability to recognize a given object despite the large variability in the object's appearance, caused by changes in viewing direction, illumination, occlusion, and the like.

In this talk I will describe computational schemes for obtaining invariant recognition, and for representing individual objects and object classes. The focus will be on view-based schemes in which objects are represented by a small number of corresponding views. Several stored views of a familiar object can be combined in a way that leads to invariant recognition under a wide range of viewing conditions, including changes in viewing direction and changes of illumination. Views of different objects within a general class can also be used to obtain recognition of a novel object within the class in question. The talk will discuss relevant psychophysical evidence, possible implications to the human visual system, and problems for future theoretical and empirical studies.

On the Physiological Mechanisms of Binocular Rivalry

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Pictures that spontaneously change in appearance, such as depth or figure-ground reversals, have always been thought of as powerful tools for understanding the nature of the perceptual system. For the reason for the perceptual multistability, experienced when viewing such figures, most likely lies in the brain's physical organization; an organization that imposes several constraints on the processing of visual information. Why is it that our visual system fails to lock onto one aspect of an ambiguous figure? What accounts for the spontaneous changes of interpretation? What are the neural events that underlie such changes? Are there neurons in the visual pathways the activity of which reflects the visual awareness of the stimulus?

Addressing directly such questions in invasive, laboratory animal experiments is extremely difficult for two reasons. First, the subject, presumably a monkey, must learn to report subtle configurational changes for one of the handful of known multistable stimuli. Second, individual neurons must be isolated that specifically respond to this stimulus, with the hope that alternate perceptual configurations differentially activate the cell. Fortunately, perceptual bistability can also be elicited by simply presenting a conflict to the two eyes, where the monocular images differ substantially in their spatial organization, color, or direction of motion. Rarely if ever will nonmatching stimuli be binocularly fused into a stable coherent stimulus. Instead each monocular pattern takes its turn at perceptual dominance, only to be overtaken by its competitor after a number of seconds. This phenomenon, known as binocular rivalry, was first noted over two centuries ago (DuTour, 1760) and its phenomenology has been studied extensively over the past three decades in the field of binocular vision (for a review see (Blake, 1989). Does though binocular rivalry has anything in common with the other perceptual ambiguities?

Psychophysical experiments initially suggested a peripheral inhibitory mechanism for rivalry, specifically involving competition between the two monocular pathways. Rivalry has therefore been generally considered a form of interocular, rather than perceptual, competition. In other words, perception of a stimulus was thought to amount to "dominance" of the eye viewing this stimulus. Yet, we have recently shown that the notion of "eye dominance" fails to account for the long periods of perceptual dominance of a stimulus presented alternately to one eye and then to the other (Logothetis et al., 1996). In our experiments the stimulus consisted of two rivalling patterns, a left and a right tilted grating, each presented to one eye, just as in all previous rivalry experiments. In contrast to previous studies, however, our stimuli were exchanged between eyes three times in a second. The subjects were instructed to report exclusive perceptual dominance of each stimulus orientation by holding down buttons on a computer-mouse. The result was unexpected. The temporal dynamics of the rivalry induced by the new stimulus were exactly the same with those measured in conventional rivalry. The two patterns were perceived in alternation at a pace that was entirely independent of their physical alternation between eyes, a finding suggesting indeed a common mechanism between binocular rivalry and other bistable phenomena. How do though neurons in different area respond to their preferred stimulus as the perception of this stimulus is continuously changing?

To examine the neural responses in primary visual cortex and the early extrastriate visual areas we trained monkeys to report the perceived direction or orientation of a stimulus under congruent and dichoptic stimulation conditions. During the behavioral-testing sessions single neurons were isolated in the central representations of MT (Logothetis and Schall, 1989), V4 (Leopold and Logothetis, 1996), and at the border of striate cortex and V2 (V1/V2) (Leopold and Logothetis, 1996). To examine the neural responses of higher visual areas, such as the inferior temporal cortex, we trained the monkeys to discriminate animate objects from simple geometrical patterns, such as gratings or sunbursts.

Our recordings showed that roughly one in three early extrastriate neurons tested modulated its activity in accordance with the perceptual changes. These modulating cells were almost exclusively binocular, and had a higher preponderance in area V4 and MT than V1/V2. In contrast, the activity of the vast majority of studied temporal cortex neurons was found to be contingent upon the perceptual dominance of an effective visual stimulus. Neural representations in these cortical areas appear, therefore, to be very different from those in striate and early extrastriate cortex, reflecting mostly the perceived rather than the retinal stimulus.

These findings make a few new points regarding both binocular rivalry and perception in general. First, the physiological results-just like the psychophysical results described earlier- are incompatible with the hypothesis that phenomenal suppression during binocular rivalry results from a blockade of information emanating from either eye. Eye-specific inhibition would be almost certainly reflected by decreased activity of monocular neurons (Blake, 1989), yet most monocular cells remained entirely unaffected during rivalry suppression. Instead, the highest fraction of perception-related neurons were binocular and encountered in the extrastriate areas V4 (Logothetis and Schall, 1989), and MT (Leopold and Logothetis, 1996).

Second, it is interesting, though perhaps not surprising (given the responses obtained in the anesthetized preparation), that neural activity in visual cortex does not always predict awareness of a visual stimulus. While some neurons appear to modulate their activity in perfect correlation with the animal's changing perception, many others continue firing whether or not the stimulus is perceived.

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POSTERS

GABApositive neurons with AMPA GluR1 and GluR2/3 immunoreactivity in the rat striate cortex

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The co-localization of GABA with AMPA receptor subunits GluR1 or GluR2/3 was analysed in the striate cortex of adult rats by post-embedding immunocytochemistry in semithin sections. Adjacent 1-µm-semithin sections of 4 brains were alternatively incubated with specific antibodies against GABA and the GluR1 and GluR2/3 subunits. The post-embedding immunocytochemistry showed that 38% of GABAergic neurons contained the GluR1 subunit (with most localized to the infragranular layers) and 10% contained the GluR2/3 subunits (with most localized to layers I, II/III and VI). Additionally, all GluR1 and GluR2/3 immunopositive cells in layer I were GABAergic and most GluR1 and GluR2/3 immunopositive cells in the remaining layers were non-GABAergic (72.5% and 98.5% respectively). Previous work has shown GluR1 immunoreactivity in non-pyramidal neurons and GluR2/3 immunoreactivity in pyramidal neurons. However, this study is the first to demonstrate that there are GABAergic neurons co-localized with GluR2/3 AMPA subunits. This small but significant subset of GABAergic neurons could have AMPA receptor channels with a very low Ca^{2+} permeability–because of the GluR2 subnit–and thus be protected against overexcitation. However, no distinction between GluR2 and GluR3 subunits was possible in our study. Further studies are necessary to correlate the presence of distinct subsets of AMPA receptor subunits to the anatomically and chemically well-established GABAergic subtypes of cells.

The full account of this work is (in press) to be published in *NeuroReport* (Gutiérrez-Ibarluzea et al., Vol. **8**, #11; cover date: Monday 28th July, 1997). Supported by the University of the Basque Country, the Regional Government of the Basque Country and the Spanish Government (grant UPV-212.327EB179/96, doctoral grants to I.G-I. and J.L.M.-Z., and grants DGICyT PB92-0463 and FIS 94/1684, respectively).

Neural Correlates of Target Selection in Area MT

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Visual search is a psychophysical paradigm traditionally used to explore the dynamics and mechanisms of focal visual attention. Using this paradigm we have previously shown that both human and rhesus monkeys' search times for targets defined by color/motion conjunctions depend linearly on the number of distractors in a search array. This dependency is commonly accepted as evidence for dynamic and voluntary allocation of focal attention. Now we have explored neurophysiological correlates of focal attention in rhesus monkeys performing such a search task. Specifically, we have recorded responses of directionally selective neurons in area MT of a monkey engaged in a visual search task. The sample, formed by a unique conjunction of color (red or green) and direction of motion (preferred or null direction) of a texture inside a circular aperture, was followed by a search array, composed of eight apertures each containing one of four possible combinations of selected colors and directions. The monkey was required to saccade to the unique target that matched the sample upon detection, or to maintain central fixation on target-absent trials. Responses of more than a third of MT neurons recorded from during the search task, exhibited significant response modulation when the search target was positioned within the receptive field. This modulation was expressed as an enhancement (up to 220% of the estimated baseline) of the neuronal response prior (90-200 ms) to a saccade to the target. The time course of the neuronal response modulation thus paralleled behavioral target detection. The modulation significantly increased discriminability of the target's direction of motion. This finding suggests that attentional modulations of neuronal activity may enhance information processing of sensory targets.

Comparison of the neuronal activity in the SMA and in the ventral cingulate cortex during prehension in the monkey. Geneviève Cadoret, Cognitive Neuroscience Unit, Montreal Neurological Institute; A.M. Smith, Department of Physiology, University of Montreal.

Two M.fascicularis monkeys were trained to use the thumb and forefinger to lift and hold an instrumented device within a position window for 1s. This apparatus was equipped to measure the grip and lifting forces exerted by the animal, and the displacement of the object. On blocks of trials the weight and surface texture could be varied, and a force pulse perturbation could be systematically delivred 750 ms after the object entered the window. Two clusters of cells in the medial wall of the frontal lobe were found to be active in relation to the task. One group of cells (n=115) was located in the caudal and medial part of area 6 in the supplementary motor area (SMA) and the other (n=92) was located in the ventral bank of the cingulate sulcus (CMAv) in area 23c. A strong similarity was observed between the SMA and CMAv neurons in their sensorimotor features as well as the modulation of their activity in relation to the prehension task. In both areas, the number of cells with proprioceptive fields was considerably higher than that of cells receiving cutaneous afferents. Most of the neurons were phasic cells, increasing their firing rate < 500ms before the grip force onset. In both areas, the neuronal activity was poorly related to grip forces. No evidence of preparatory responses to the perturbation was found in the cingulate cortex and only 5 cells in the SMA exhibited a preparatory response. These results confirm that the SMA and the CMAv have neurons directly involved in the sensorimotor control of the hand. These neurons seem to be activated in parallel during the prehension task and to be more related to the initiation of the grip rather than to the modulation of the fingers forces. (This research was supported by the MRC of Canada).

Smooth pursuit to a movement flow and associated perceptual judgments

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Smooth pursuit is conventionally regarded as foveal tracking of a small moving target. Here, we show that smooth pursuit can be generated by a moving random-dot pattern even when the possibility of focusing on individual dots is eliminated. Observers were instructed to follow the movement flow of a random-dot pattern (24 x 6 deg), either to the left or to the right. In Experiment 1, we limited dot lifetime (60 ms and 600 ms) in order to prevent observers from using any single dot for continuous tracking. Observers were able to initiate robust smooth pursuit to fast (>5 deg/s), but not to slowly, moving dot patterns. The overall quality of maintained smooth pursuit was comparable to, or under some conditions better than, that observed with a single dot stimulus. The transience of dot life (e.g. 60 ms) virtually excludes the feasibility of using any particular dot continuously. Therefore, the accurate tracking must be based on information extracted across the field. In Experiment 2, we examined smooth pursuit as a function of random dot coherence. On each trial, motion coherence was randomly chosen to be 10, 20, 40, or 80%. At low coherence levels, observers occasionally initiated smooth pursuit in the direction opposite to the coherent motion. Unexpectedly, this tracking in the wrong direction was also observed with stimuli for which observers could make accurate perceptual judgments (e.g., 20-40% coherence). In Experiment 3, observers were asked on each trial to track the stimulus and also to judge its direction of motion. A trial-by-trial comparison verifies that tracking in the wrong direction is uncorrelated with the accuracy of perceptual judgment. In conclusion, smooth pursuit to a movement flow can be produced in the absence of continuously present individual elements whereas this tracking may not entirely depend on the sensory signal processing for direction perception.

Visuotopic Map in Primary Visual Cortex Shows Systematic Distortions that Match Orientation Singularities.

Aniruddha Das & Charles D. Gilbert

The map of orientation columns in primary visual cortex (V1) is known to show a systematic pattern of strong local distortions, with a generally smooth progression of orientation preference interrupted periodically by sharp jumps (fractures) and point singularities. The map of visual space on V1, on the other hand, has been assumed to be locally smooth and isotropic, with only a gradual change in cortical magnification on moving from the centre to the periphery of visual space. Any deviations in smoothness were attributed to random scatter in the positions of receptive fields.

In contrast to the above expectation of smoothness, we find that the map of visual space on cat V1 shows strong and systematic local distortions in register with the inhomogeneities in the map of orientation. By using a combination of optical imaging (of intrinsic signals) and extracellular recording we find that the rate of movement of receptive fields across cortex is largely linearly proportional to the local rate of change of orientation. Thus, pairs of neurons lying on either side of an orientation singularity have essentially non-overlapping receptive fields while neuron pairs lying in regions of cortex where orientation preference changes slowly or remains constant have receptive fields with progressively greater degrees of overlap. Due to this linear proportionality, two-dimensional maps of retinotopic co-ordinates projected on the cortical surface show systematic stretching and compression reflecting the underlying rate of change of orientation preference. Further, the factor of proportionality linking receptive field movement with changes in orientation equals roughly 2 receptive field diameters for each 180-degree shift in orientation; this suggests that the coverage of visual space by receptive fields may not be homogeneous at all orientations.

Our findings of matched systematic distortions in the maps of orientation and visuotopy suggest that the short-range lateral connections underlying local cortical processing in V1 could also display a corresponding range of functional connectivity, from local cortical circuits that connect neurons that are maximally similar to circuits connecting neurons that are maximally dissimilar. Such a range of functional connectivity might reflect the range of visual processing believed to occur in V1.

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ROLE AND MECHANISM OF ACTION OF THE NITRIC OXIDE - cGMP PATHWAY IN THE CONTROL OF HORIZONTAL EYE MOVEMENTS BY PREPOSITUS HYPOGLOSSI NEURONS.

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Motoneurons controlling horizontal eye movements receive both velocity signals and position signals which allow eye displacement and fixation, respectively. The conversion of velocity signals to position signals requires an integration process that takes place, at least in part, in the prepositus hypoglossi (PH) nucleus. This nucleus contains a large number of neurons expressing NO synthase (NOS) and , therefore, are able to produce the intercellular mesenger nitric oxide (NO). The objective of this work was to study the role of NO produced by PH neurons in the control of eye movements in the alert cat, and the possible mechanisms by which NO exerts its action in this sensory-motor system.

Adult cats were prepared for chronic recording of eye movements by the scleral search coil technique and for intracerebral microinjections in the PH nucleus. Experiments were performed in alert conditions during spontaneous eye movements and upon induction of the vestibulo-ocular reflex (VOR). Recordings were obtained before and after local administration of drugs affecting the NO-cGMP pathway and other neurotransmitter systems acting in the PH nucleus.

Local injections of the NOS inhibitors L-NAME and L-NMMA induced a nystagmus with slow phases in a direction contralateral to the injected side, whereas injections of the NOS substrate L-arginine, the NO donors SNP and SNAP and the cGMP analog 8-Br-cGMP resulted in nystagmic eye movements in the opposite direction, suggesting that NO produced by PH neurons, acting by soluble guanylyl cyclase activation, is required for the normal performance of eye movements.

The slow phases elicited by L-NAME, L-NMMA and L-arginine, which affect NOS activity and, therefore, modify endogenous NO levels, were linear and disappeared almost completely when visual input was allowed in light conditions. During VOR, these drugs produced a velocity imbalance similar in magnitude to that measured during spontaneous eye movements, without alteration of the reflex gain. These results suggest that NO produced by neurons in the PH nucleus affects selectively the processing of velocity signals without modifying the integrator function.

On the other hand, the slow phases of the nystagmus induced by administration of NO donors and 8-Br-cGMP were best fitted by an exponential equation. Furthermore, in light conditions, when the nystagmus was attenuated, a loss of eye fixation was evident, indicating an alteration of the position signal. During VOR, these drugs produced the expected velocity imbalance, and no change in the gain of the reflex. These data indicate that exogenous NO was acting on additional guanylyl cyclase-containing structures, which are not physiological targets of the NO synthesized by PH neurons. These additional structures are involved in the integration of velocity signals during spontaneous eye movements, but not during VOR. This is interesting because this is the first time, as far as we know, that integration processes for two types of eye movements have been dissociated pharmacologically, questioning the present hypothesis of a unique integration mechanism for the different velocity signals.

Bicuculline, an inhibitor of GABA A receptors, mimicked the action of NOS blockers when injected in the PH nucleus of alert cats, this is, it produced nystagmic eye movements with linear slow phases directed towards the contralateral side during spontaneous eye movements and velocity imbalance without gain alteration during VOR. Inhibition of AMPA and NMDA glutamatergic receptors or glycinergic receptors resulted in qualitatively different alterations including both velocity and integration function.

The results indicate that i) NO produced by PH neurons modulates via cGMP the generation of the motor signal that control horizontal eye movements, ii) NO produced by PH neurons affects the processing of pure velocity signals, without altering the integrative capacity of the nucleus, by a mechanism involving GABAergic synapses, and iii) The differential alteration of the integrative function during spontaneous eye movements and VOR induced by guanylyl cyclase activation indicates that both processes occur in the same nucleus although by separate mechanisms.

This work was supported by grants 94/ 0388 and 97/2054 from FIS, Spain.

Title: FREQUENCY ANALYSIS OF EEG DURING SPATIAL ATTENTION ON HUMAN SUBJECTS

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In the present study the EEG during spatial selective attention on human subjects was analyzed. We used event-related potentials (ERPs) (averages on time domain) as well as spectral analysis on EEG (averages on frequency domain).
The EEG was recorded on 13 positions of the scalp. The subjects were presented with stimulus in the right and left visual field, attending to the left or the right side in subsequent trials. On the ERPs the voltage amplitudes and latencies of P1, N1 and subsequent components was analyzed. The results showed significant differences between attended and unattended conditions for the latency and for the amplitude. On the frequency analysis of the EEG, the power spectral density of the EEG was computed in the time window after the onset of the stimulus. We detected a supression on alpha band and an increase on the low beta band in attended conditions vs unattended conditions.
These results implies that spatial selective attention produces brain processing changes that can be detected in both, frequency and time domains. It must be remarked that this result has been obtained comparing attended vs. unattended conditions, so the obtained results can be considered as a selective attention effect rather than an arousal effect.

Key words:

EEG – Frequency analysis – Spatial attention – ERPs – Alpha band – Beta band

CONTOUR DETECTIBIL.TY MAY BE A FUNCTION OF BOTH DIRECT AND MEDIATED CONTEXTUAL INTERACTIONS.

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Psychophysical studies show that contour detectability can be influenced by both *local* (Field, Hayes & Hess, 1993) and *global* characteristics (Kovaks & Julesz, 1993). The results reported here confirm and extend these findings, and suggest that they may both depend upon long-range horizontal collaterals within visual cortex (Gilbert, Das, Ito, Kapadia & Westheimer, 1996). In stimuli with constant local stimulus relations but varying global organization we confirm the effect of closure (Kovaks & Julesz,1993), and also show that detectability increases with increases in the global curvature of contours that are not closed. This suggests that relations between processors that are not themselves directly connected affect figural detectability. Such effects could involve transmission of contextual grouping and/or amplifying signals through cascades of intermediate local contextual interactions (Floreano 1997). Evidence for such mediated interactions comes from a perceptual learning paradigm (Polat & Sagi, 1994). Their results demonstrated that flanking Gabor patches, seperated by as much as 9λ from a central low-contrast target patch, can facilitate the detection of the target. They hypothesize that such effects are mediated via cascades of local interactions. We are currently testing this hypothesis within the contour detection paradigm. Local processors receive direct coordinating input from only a tiny fraction of the set of other processors with which grouping is likely to be useful. Mediated contextual interactions may therefore play a major role in global organization. Studies of global interactions analagous to those reported here could also be carried out using visual evoked potential techniques (Polat & Norcia 1996) and with single unit (e.g. Kapadia, Ito, Gilbert & Westheimer, 1995) and multiple single unit techniques (e.g. Singer 1995).

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Synchronization of spontaneous activity along development in rabbit hippocampal slices.

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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.

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COMPUTATIONAL SIMULATION OF THE PRINCIPAL CUNEATE PROJECTION NEURON

The function of thalamocortical rhythms implied in the regulation of periods of wakefulness and sleep is one of the great unanswered questions in research into the somato-sensory system. Recent *in vivo* electrophysiological studies in cats indicate the possibility that the aforementioned rhythms may control not only the activity of the Thalamus and the Cortex, but also that of the Cuneate Nucleus. In order to explain this, hypotheses have been made at the level of connections between these three regions of the brain, at the level of the internal circuitry of the Cuneate Nucleus itself and at the level of the properties of each of the neurons studied. Experimental confirmation has been hindered by the location and characteristics of the Cuneate Nucleus, which impede electrical signal recordings over long periods of time, and the extraction of slices for the purposes of an *in vitro* study.

As an alternative way, and already in the field of Computational Neuroscience, there exists the possibility resorting to mathematical models and computer simulation. Along these lines, we have proposed the modelling of each one of the neurons of the Cuneate Nucleus, with the aim of finding the circuitry which may explain the experimental data.

The first step consisted of developing a cuneothalamic neuron model. For this we had recourse to the described ionic currents in thalamic neurons, adapting them to our needs. In this way we found that it is possible to replicate the electrical activity observed in *in vivo* recordings, combining a fast sodium current, I_{Na}, a delayed rectifier potassium current, I_K, a low-threshold calcium current, I_T, a high-threshold calcium current, I_L, a calcium-activated potassium current, I_C, and a hyperpolarisation-activated current, I_h. The simulation was carried with *PhasePlane (XPP)* software on a *Sun SparcStation20* workstation. In the Poster we will explain the results obtained by the simulation, accompanied by the experimental recordings.

The functional organization of central nervous system of insects: comparison with vertebrate.

Irina Sinakevitch-Péan

During last years, mostly grace of explosive development of molecular biology methods and gene manipulation, it was discovered that the vertebrate and invertebrate use the similar genes during development of embryo and of tissue-organs. In this communication, I would like to remember the works of Russian morphologist Zawarsin A.A. (1,2), who worked on the adult nervous systems of different order of insects using the methylene blue staining technique. Base on his large experimental materials he formulated the theory of parallelism of tissue functions and structure in the evolution. He showed that the nervous system of highest invertebrate and highest invertebrate do not differ if make comparison by functional structure of nervous system and not on the level of one neuron.

The central nervous system of insect comprises **the brain**, lying in the head above the stomodaeum, and a chain of connected ventral segmental ganglia forming the **ventral nerve cord (VNC)**, lying under the alimentary canal, extending from the mouth to posterior part of the body. Each ganglion of VNC has bilateral symmetry. Zawarzin (1,2) showed that insect ganglia has also dorso-ventral differentiation within ganglia. He characterized five morpho-functional regions in the neuropile of ganglia of dragonfly Aeshna working with methylene blue technique. The latest studies on the structural organization of nervous system confirmed these finding on the locust, cockroaches and bugs (3,4). Two nerve trunks leave symmetrically each ganglion to innervate the corresponding segment of animal body. Each nerve trunk comprises dorsal root that contain axons of motoneurones and ventral root with sensorial neurons. Sensorial neurons have their somata in the periphery of animals and send their axons into the ventral neuropile, that called **ventral sensory neuropile**. The somata of motoneurones lie on the ventral surface of the ganglia, motoneurones send their primary axons out from the ganglion by the dorsal root of nerve trunk. The motoneurones give rise their arborizations on the dorsal part of neuropile, that called **dorsal motorneuropile**. In insect ganglia there are also intraganlionic neurons that serve for integration of information between the sensory and motor neuropile and interganglionic neurons that serves as integration of sensory information between the brain and ventral ganglia. The neurons that send their axons from the brain have their fibers in the dorsal neuropile (**dorsal neuropile of descending fibers**). The neurons that make the interganglionic connections and that send information to the brain send their axons through ventral neuropile (**ventral neuropile of ascending fibers**). The **central neuropile** consists of axons of intra- and inter- ganglionic neurons. There are no strike frontiers between this regions, however the position and morphology of neuron processes in the neuropile can defined the functions of neurons within nervous system. Anatomical organization of VNC of highest insect can be related to that of bird and highest mammalian. However, the comparison should be done according the functional morphological structure of whole nervous system, but not at the level of single neurons. The structure of spinal nervous cord of vertebrate is mirror image of the insect VNC. The motoneurones leave the ganglion via **ventral nerve trunk,** the sensorial neurons send their axons into **the dorsal nerves trunk. Ascending fibers** are in the dorsal part of nerve tube and on the ventral side of tube are **descending fibers.**

The central nervous system is very important organ for life, the damage of CNS can induce the irreversible change in the function of organism and the death. Apparently, during evolution different way of the protection CNS occurred independently: the vertebrate has CNS on the dorsal side protected by skeleton and in insects CNS protected by ventral position. Differentiation of tissue in the evolution determined by interaction and communication with environment that provide the main elementary function of multicellular organism. These general functions are frontier, internal media, reactivity, movement. They stayed the same for each organism in spite of the divergence of evolution. After divergence the multicellular organism developed in parallels in the same environmental conditions , so they use the same or similar mechanisms for receiving, transfer and integration of signals from environment. It is important for theory of parallelism constant comparison of evolution of tissue (as CNS, for ex.) with evolution of function of tissue. Zawarzin A.A. showed that resemblance of architecture of CNS in different order animals determined not only by genetically family, but by the level of development performed by the function of CNS. The highest vertebrate should be compared with the highest invertebrate by function of CNS, as there are more similarities between highest vertebrate and highest invertebrate if compare the functions of CNS, than between lowest invertebrate and highest invertebrate.

The aim of my research is to make connections with old evolutionary works on the CNS together with new molecular biology methods and genetic to understand how the nervous system of highest invertebrate as Drosophila works. Future comparison should be done at the level of brain organizations between highest vertebrate and highest invertebrate.

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2.Zawarzin A.A. (1941)Ocherki po evolutionnoi gistologii nervnoi sistemy. Isbr. tr, 3, Isd. AN USSR, M.-L. 1950 (in Russian);
3.Cvileneva B.A.. (1970) About evolution of ventral nervous system of invertebrate. Leningrad, "Nauka", (in Russian);
4.Plotnikova S.I. (1979)The structure of the central nervous system in insects. Leningrad, "Nauka", (in Russian);

List of Invited Speakers

Workshop on

PRINCIPLES OF NEURAL INTEGRATION

List of Invited Speakers

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PRINCIPLES OF NEURAL INTEGRATION

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The lectures summarized in this publication were presented by their authors at a workshop held on the 22nd through the 24th of September 1997, at the Instituto Juan March.

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