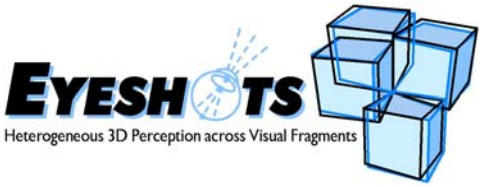

Project no.: FP7-ICT-217077
Project full title: Heterogeneous 3-D Perception across Visual Fragments
Project Acronym: EYESHOTS
Deliverable no: D5.1 update
Title of the deliverable: Report on neural discharges in the medial parieto-occipital cortex.

Date of Delivery:	28 February 2011	
Organization name of lead contractor for this deliverable:	UNIBO	
Author(s):	P. Fattori, C. Galletti, R. Breveglieri, K. Hadjidimitrakis, A. Bosco	
Participant(s):	UNIBO, WWU, UJI, UG	
Workpackage contributing to the deliverable:	WP5	
Nature:	Report	
Version:	1.1	
Total number of pages:	24	
Responsible person:	Patrizia Fattori	
Revised by:	F. Hamker	
Start date of project:	1 March 2008	**Duration:** 36 months

Project Co-funded by the European Commission within the Seventh Framework Programme		
Dissemination Level		
PU	Public	**X**
PP	Restricted to other program participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

Abstract:
Interacting in the peripersonal space requires coordinated arm and eye movements to visual targets in depth. In primates, the medial parieto-occipital cortex represents a crucial node in the process of visual-to-motor signal transformations. Area V6A is a key region engaged in the control of these processes because it jointly processes visual information, eye position and arm movement related signals (Galletti et al., 2003). Using single neuron recordings in behaving macaques, we studied the neural signals related to depth encoding in a task that required the monkeys to perform eye movements and arm movements directed at visual targets located at different distances in peripersonal space. The majority of neurons were modulated by both version and vergence angle, i.e., by the location of the foveated target in depth. There was not a bias for a particular sector of the peripersonal space: the spatial fragments are sampled in the same way, with the same definition, across the entire reachable space. These data suggest that depth signals are implemented functionally in V6A to direct eye movements and arm movements in the 3D space. This modulation, in an area primarily involved in visuo-motor transformation for reaching, together with attentional-related signals already shown to be present in V6A, may form a neural basis for linking eye movements and arm movements across fragments.

Contents

1- Executive summary and relation to previous work in EYESHOTS

This deliverable summarizes and updates the research performed by the Neurophysiology Laboratory of UNIBO with regard to WP5 of the EYESHOTS project. These results have been achieved in collaboration with UG, UJI and WWU. These data are the basis of joint papers already published in International peer reviewed Journals, in Conference Proceedings and Book Chapters.

An intensive neurophysiological work has been done to investigate the neuronal coding of action performance and the attentional modulation in the medial parieto-occipital cortex. Two main findings were found: 1) Preference for gaze positions in peripersonal space. With a task specifically designed to test a wide range of fixation distances, extending from the peripersonal (reachable) to the extrapersonal (non reachable) space, it has been found that neurons in V6A a) respond during gaze shifts in 3D space, b) encode the depth of fixation, and c) preferentially represent gaze positions within reaching distance (Hadjidimitrakis et al., 2010). UNIBO has proposed that the neural modulations strongly biased towards the near space can be used to control reach-to-grasp movements in depth. In fact, the fixation of a target requires a saccadic eye movement that "captures" the target and brings it onto the fovea. The perisaccadic activity found in V6A encodes the saccadic event towards that particular location in 3D space. This signal could be also used to modulate the activity of arm reaching neurons. Note that the information about eye position during the period around saccade is critical for the motor centers that control the hand, because the retinal coordinates of the target change with the saccade. In this context, early fixation activity could constitute a fixation-for-reaching signal that brings to the arm reaching neurons the new retinal coordinates of the target to be grasped. 2) Attentional modulations of neural activity. We measured the influence on V6A neural activity of covert shifts of attention, induced in absence of any effector movement, neither the eyes nor the arm. It has been found that covert shifts of attention without any concurrent shift of the direction of gaze modulate the activity of many V6A neurons (Galletti et al., 2010). We suggested that this attentional modulation is helpful in the spatial encoding of action planning and execution. It could allow V6A cells to select the goal of reaching during movement

preparation, as well as to maintain encoded, and possibly update, the spatial coordinates of objects to be reached out during movement execution.

This update of Deliverable 5.1 reports the study of the neural correlates of multisensory representation of 3D space through active ocular and arm movements. Single neurons were recorded in the medial parieto-occipital cortex when the monkeys performed eye movements and reaching movements in depth. Targets were located in a isovergent and isoversion 3x3 grid. We investigated whether the depth influences the reach-related discharges in the medial parieto-occipital cortex. We show that V6A is able to coordinate eye- and arm-actions in the 3D space as well as to link, in a more general way, perception to action. All these data have been shared with other partners in EYESHOTS and have been embodied in the humanoid robot implemented in WP4.

2- Introduction

Primate lifestyle requires frequent relocations in space and coordinated movements of eyes and hands to interact with objects. For this behaviour, a reliable visual percept of three-dimensional (3D) space needs to be constructed and integrated in a movement plan involving several effectors. The posterior parietal cortex (PPC) plays a pivotal role in these processes. Humans with lesions in PPC show deficits in perceiving the spatial relationship between objects and their own body, and perform inaccurate reaching movements (Critchley, 1953; Perenin and Vighetto, 1988; Karnath, 1997). In addition, damages to PPC affect specifically the depth component of visually-guided reaching movements (Baylis and Baylis, 2001; Danckert et al., 2009). Psychophysical studies suggested that, in order to reach objects in depth, the vergence angle information is critical (Mon-Williams and Dijkerman, 1999; Henriques et al., 2003). Vergence has been tightly related to the fixation distance (Foley, 1980), which, together with the retinal disparity signal that specifies the distance of an object from the fixation plane, encode object location in 3D space (Pouget and Sejnowski, 1994).

To reach an object in 3D space is an action that can be performed with 2 effectors: the eye and the hand. Neuronal coding of eye and arm movements in depth has been studied so far only in a small number of works. In his pioneering studies in the 80's, Sakata explored the influence of eye-position signals on neuronal discharges by varying the position of the fixation target (Sakata et al., 1980). They explored eye position effects not only in the frontal plane, but also in depth, and found that many neurons in area 7a had selectivity for the depth of fixation. Later on, another area of inferior parietal lobule, area LIP, has been shown to carry on signals related to retinal disparity and fixation distance (Gnadt and Mays, 1995; Genovesio and Ferraina, 2004). Very recently, we have reported that the majority of neurons of the medial parieto-occipital area V6A were modulated by both version and vergence angle of the eyes during fixation, i.e., by the location of the foveated target in the 3D space (see Deliverable D5.1). The population activity of these neurons displayed a preference for near, peripersonal space in a time interval around the saccade preceding fixation, and during fixation as well (Hadjidimitrakis et al., 2010).

As for the neuronal encoding of reaching, it has been intensively studied in the 2D space, with reaches performed on a frontal plane. In some of these studies (Fattori et al., 2001; 2005; Bosco et al., 2010) the hand started from a position out-of the target plane, though targets were always located in a 2D space. The encoding of reaching movements in 3D space has been investigated only recently (Bhattacharyya et al., 2009; Ferraina et al., 2009). One of these 2 works demonstrated that in the posterior parietal area PE, the neural activity is monotonically tuned to the distance of reaching to targets from the body, and the reach-related activity is more sensitive to the position of the hand rather than the vergence angle of the eyes (Ferraina et al., 2009). The other work

demonstrated the influence of horizontal disparity and fixation depth on the activity of neurons in area MIP during the delay period before the reaching movement is executed (Bhattacharyya et al., 2009).

No functional study has been so far performed to study the influence of reaching in depth on the activity of medial parieto-occipital cortex, which is known to be involved in encoding reaching actions.

2.1 Aim of the study

Here, we investigate whether neurons are modulated by reaching in depth at earlier stages of the dorsal visual stream, that is in the medial parieto-occipital area V6A located in the anterior bank of the parieto-occipital sulcus (Galletti et al., 1999). Previous studies demonstrated that V6A contains visually responsive neurons (Galletti et al., 1996, 1999) as well as neurons influenced by the direction of gaze in a two-dimensional (2D) space (Galletti et al., 1995; Nakamura et al., 1999). Subsequent researches reported that many V6A cells that receive somatosensory input from the upper limbs (Breveglieri et al., 2002), and are strongly modulated by active arm movements (Galletti et al., 1997; Fattori et al., 2001). Arm movement-related neurons encode the direction of reaches (Fattori et al., 2005) as well as more distal aspects of prehension, like hand orientation (Fattori et al., 2009) and grip formation (Fattori et al., 2010). All these studies were performed with stationary targets occupying different positions on a frontal plane.

The present work was designed to address the issue of the tuning in depth of reach-related discharges in the medial parieto-occipital cortex. The main findings of this research was that the activity of neurons in V6A is modulated a) by the direction of arm movements in 3D space, and b) by the depth of reaching.

3 - Materials and Methods

3.1 General procedures

One male *Macaca fascicularis* monkey has been studied. Experiments were approved by the Bioethical Committee of the University of Bologna and authorised by the Ministry of Health (Permit N^{o} DM 47/2008-B, 6/4/2008). Experiments were performed in accordance with National laws on care and use of laboratory animals, with the European Community Council Directive of 24th November 1986(86/609/EEC). All procedures used have been approved and supervised by the Central Veterinary Service of the University of Bologna.

A head restraint system and a recording cylinder were surgically implanted in asepsis under general anesthesia (sodium thiopenthal, 8 mg/kg/h, *i.v.*) following the procedures reported in Galletti et al. (1995). Adequate measures were taken to minimize pain or discomfort. A full program of postoperative analgesia (ketorolac trometazyn, 1mg/kg *i.m.* immediately after surgery, and 1.6 mg/kg *i.m.* on the following days) and antibiotic care [(Ritardomicina ® (benzatinic benzylpenicillin plus dihydrostreptomycin plus streptomycin)] 1-1.5 ml/10kg every 5-6 days) followed the surgery.

Single cell activity was recorded extracellularly from the medial parieto-occipital area V6A (Galletti et al., 1996, 1999). We performed single microelectrode penetrations using home-made glass-coated metal microelectrodes with a tip impedance of 0.8-2 MOhms at 1 KHz, and multiple electrode penetrations using a 5 channel multielectrode recording system (Mini Matrix, Thomas

Recording, GMbH, Giessen, Germany). The latter electrodes were quartz-platinum/tungsten fibers with an impedance of 0.5-2 MOhm at 1 kHz (Thomas Recording). Electrode signals were amplified (gain 10,000) and filtered (bandpass between 0.5 and 5 kHz). Action potentials in each channel were isolated with a dual time-amplitude window discriminator (DDIS-1, Bak electronics, Mount Airy, MD, USA) or with a waveform discriminator (Multi Spike Detector, Alpha Omega Engineering, Nazareth, Israel). Spikes were sampled at 100 KHz. Location of area V6A was identified on functional grounds during recordings (Galletti et al., 1999), and later confirmed following the cytoarchitectonic criteria of Luppino et al. (2005). Signals from both eyes were recorded simultaneously with an infrared oculometer (ISCAN Inc., Woburn, MA, USA) at a sampling rate of 100 Hz.

3.2 Behavioural task

The monkey sat in a primate chair with the head restrained and faced a horizontal panel located at the level of its eyes (Fig. 1, left). Nine light emitting diodes (LEDs) mounted on the panel at different distances from the eyes were used as fixation and reaching targets. The target LEDs were arranged in three rows, one central, along the sagittal midline and two lateral, at isoversion -15° and +15°. Along each row, LEDs were located in iso-vergent positions at 18°, 13° and 8°. Figure 1 sketches the spatial arrangements of the targets.

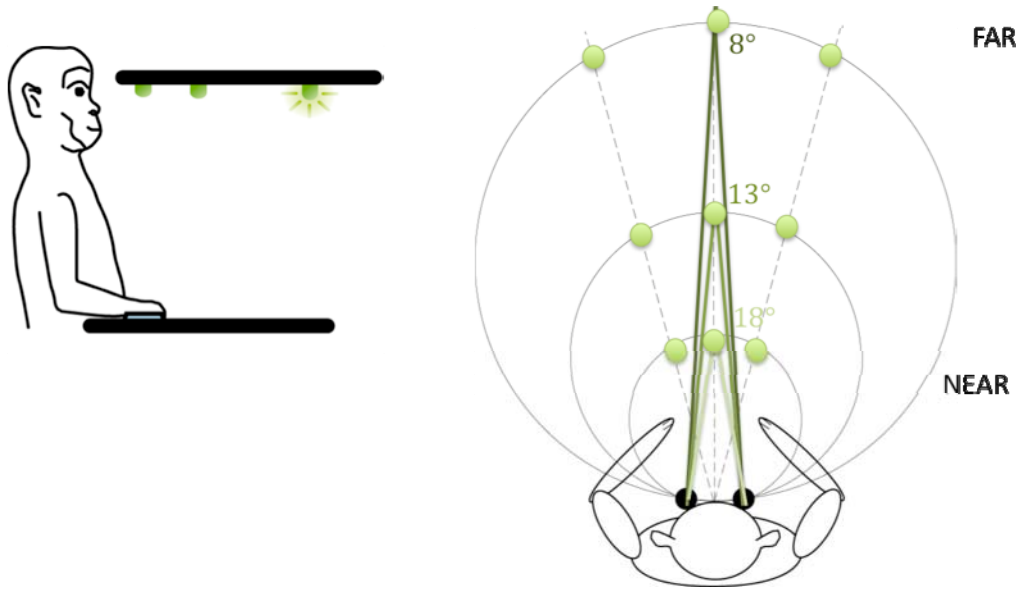

Fig. 1 lateral view (left) and top view (right) of the reach-in-depth apparatus. Each green dot represents the target of a reaching movement. Vergence: 18-13-8°; version: -15-0-15°.

LEDs were lighted in random order, trial by trial. Eye movements were a combination of conjugate (version) and disconjugate (vergence) movements. Because the monkey was free to look anywhere at the beginning of the task, the initial eye position varied from trial to trial. During fixation, eye position was controlled by an electronic window (2^ox2^o) centered on each LED. Stimulus presentation and animal's behavior, including eye position signals, were monitored in real time with the use of custom software written in Labview (National Instruments, Austin, TX, USA) as previously described (Kutz et al., 2005).

Before each recording session, the monkey was required to perform a calibration task that allowed us to calibrate the signals from each eye seperately. In this task, the monkey fixated in sequence ten LEDs that were mounted on a frontoparallel panel at a distance of 15 cm from the eyes. For each eye, signals to be used for calibration were extracted during fixation of five LEDs, one central aligned with the eye's primary position and four peripheral placed at an angle of +/- 15° both in the horizontal and vertical axis. From the two individual calibrated eye position signals we derived the mean of the two eyes (the conjugate or version signal), and the difference between the two eyes (the disconjugate or vergence signal).

The time sequence of the reach-in depth task is sketched in figure 2. The monkey sat in a primate chair in front of the reach-in-depth device and pressed the start button placed near its belly, outside its field of view. After a delay, one of the target lit-up green (and the monkey had to perform a saccadic eye movement towards the target and to adjust its vergence in order to see clearly the target light). After a variable fixation period, the fixation target turned red. This was the go signal for the monkey to release the start button and perform a reaching movement toward the fixated target. The monkey had to push the target, and to keep its hand on it until the fixation LED switched off. Then, the monkey was required to release the target and perform a backward movement toward the start button to be rewarded.

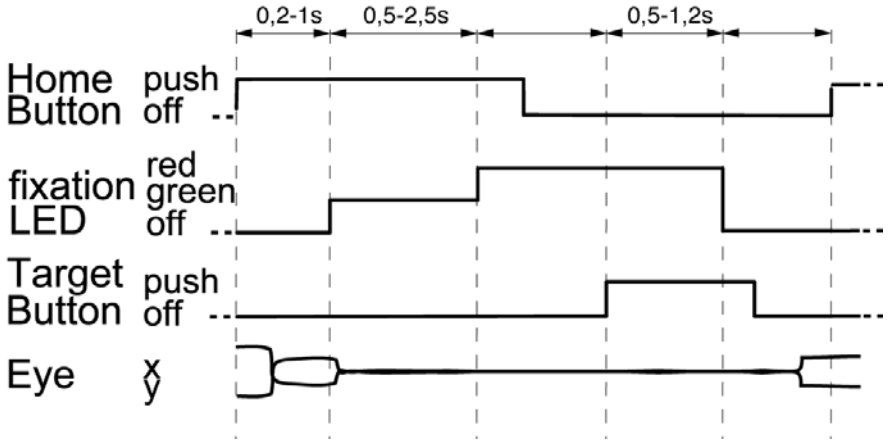

Figure 2: timing sequence of the reach-in-depth task**.**

Each recorded neuron was studied also in a fixation-in-depth task, where the monkey fixated in the same 9 positions of the panel used for the reaching-in-depth panel, but was not required to reach any target. In the fixation trials, the same time sequence as in the reaching trials was used. The change in color of the LED from green to red in fixation trials cued to the animal to release the home button to receive liquid reward without performing any reaching movement. During the tasks, the monkey was fixating the target LED from its lit up until its switching off (reaching task) or changing in color (fixation task). If fixation was broken during this interval, trials were interrupted on-line and discarded.

3.3 Data analysis

We analysed the discharges of neurons tested in both reaching and fixation tasks by comparing different time epochs during the tasks. A total of 111 neurons were studied. The time epochs were defined as follows: FREE: from the beginning of the trial to the light up of the LED. PERISACCADIC: from 50 ms before saccade onset to 50 ms after saccade offset. EARLY FIX: from 50 ms after saccade offset to 550 ms after saccade offset. LATE FIX: from 550 ms after

saccade offset to the lit up of red LED. FIX: EARLY FIX + LATE FIX, i.e. from 50 ms after saccade offset to the light up of red LED. All these task periods are common to both tasks.

In the reaching task, we analysed also three “arm-related” epochs: MOV, from 200 ms before arm movement onset (home button release) to movement end (target button pressing); HOLD, from the end of forward reach (target button pressing) to 200 ms before return movement onset (target button release); RET, from 200 ms before return movement onset (target button release) to movement end (home button pressing).

On this neural population, we performed a 2 ways ANOVA (factor 1 vergence, factor 2 version) and looked for significant effects of factor 1, and/or 2 and/or their interaction ($p<0.05$).

The onset and offset of a saccade were defined as the time point where the version velocity exceeded or dropped below the 15% of the peak velocity, respectively. Trials with eye movements in the wrong direction, anticipatory movements (latency shorter than 100 ms), slow movements (latencies longer than 600 ms), or movements combined with blinks, were rejected.

For the significantly modulated neurons, we calculated 2 indices, able to indicate the selectivity of spatial tuning and its strength: the first was calculated as the percentage discharge difference between best and second best spatial position: $(r_{best}-r_{2nd\ best})*100/r_{best}$. The second, as the best–worst difference: $(r_{best}-r_{worst})*100/r_{best.}$

In the ANOVA significant cells a spike density function (SDF) was calculated (Gaussian kernel, halfwidth 20 ms) for each trial and then averaged over all the trials of a given target position. We found the maximum discharge frequency of the neuron among the behavioral epochs of interest and used it to normalize SDFs. Population SDFs were constructed by averaging the individual SDFs of all the cells with a given activity type (Marzocchi et al., 2008).

A linear regression model was used to relate the activity in the different arm epochs to parameters changing in depth. For each epoch the model was a linear modulation with depth. The following model equation was used: $A\ (X, Y) = a_0+a_1X_i+a_2Y_i$ .The term A represented the neural activity in spikes per second, X and Y were the version and vergence values, respectively, a_1, a_2 the corresponding regression coefficients and a_0 the intercept. The regression coefficients were calculated with the stepwise procedure that left only the significant coefficients in the final model of the data. After being tested for their significance, the coefficients were normalized with their standard deviation. The standarized coefficients allowed a comparison among the independent variables and provided information about their relative influence in the regression equation.

All analyses were performed using custom scripts written in MATLAB (Mathworks, Natick, MA, USA).

4 - Results

We found that a large majority of cells were modulated by ocular and/or reaching movements in 3D. Tables 1 and 2 summarizes these effects and show the incidence of V6A neurons modulated by vergence, version and their interaction.

Table 1: incidence of vergence/version neural modulation in V6A in the fixation task

FIXATION **In depth**	**Vergence and/or** **Version and/or Interaction Effect**	**Vergence only Effect**	**Version only Effect**	**Interaction only Effect**
Perisaccadic epoch	71/111 **64%**	51/111 **46%**	47/111 **42%**	15/111 **13%**
Early Fix epoch	91/111 **82%**	65/111 **58%**	58/111 **52%**	25/111 **22%**
Late Fix epoch	89/111 **80%**	68/111 **61%**	61/111 **55%**	35/111 **31%**
Fix epoch	96/111 **86%**	75/111 **67%**	65/111 **58%**	37/111 **33%**

Table 2: incidence of vergence/version neural modulation in V6A in the reaching task

REACHING **In depth**	**Vergence and/or** **Version and/or Interaction Effect**	**Vergence only Effect**	**Version only Effect**	**Interaction only Effect**
Perisaccadic epoch	67/111 **60%**	46/111 **41%**	37/111 **33%**	21/111 **19%**
Early Fix epoch	91/111 **82%**	60/111 **54%**	57/111 **51%**	27/111 **24%**
Late Fix epoch	95/111 **85%**	77/111 **69%**	53/111 **48%**	39/111 **35%**
Fix epoch	103/111 **93%**	80/111 **72%**	66/111 **59%**	42/111 **38%**
Mov epoch	93/111 **84%**	79/111 **71%**	63/111 **57%**	42/111 **38%**
Hold epoch	92/111 **83%**	76/111 **68%**	57/111 **51%**	39/111 **35%**
Ret epoch	82/111 **74%**	61/111 **55%**	50/111 **45%**	19/111 **17%**

Figures 3-5 show exemplary V6A cells showing vergence and/or version modulations in fixation and/or in arm-movement related periods.

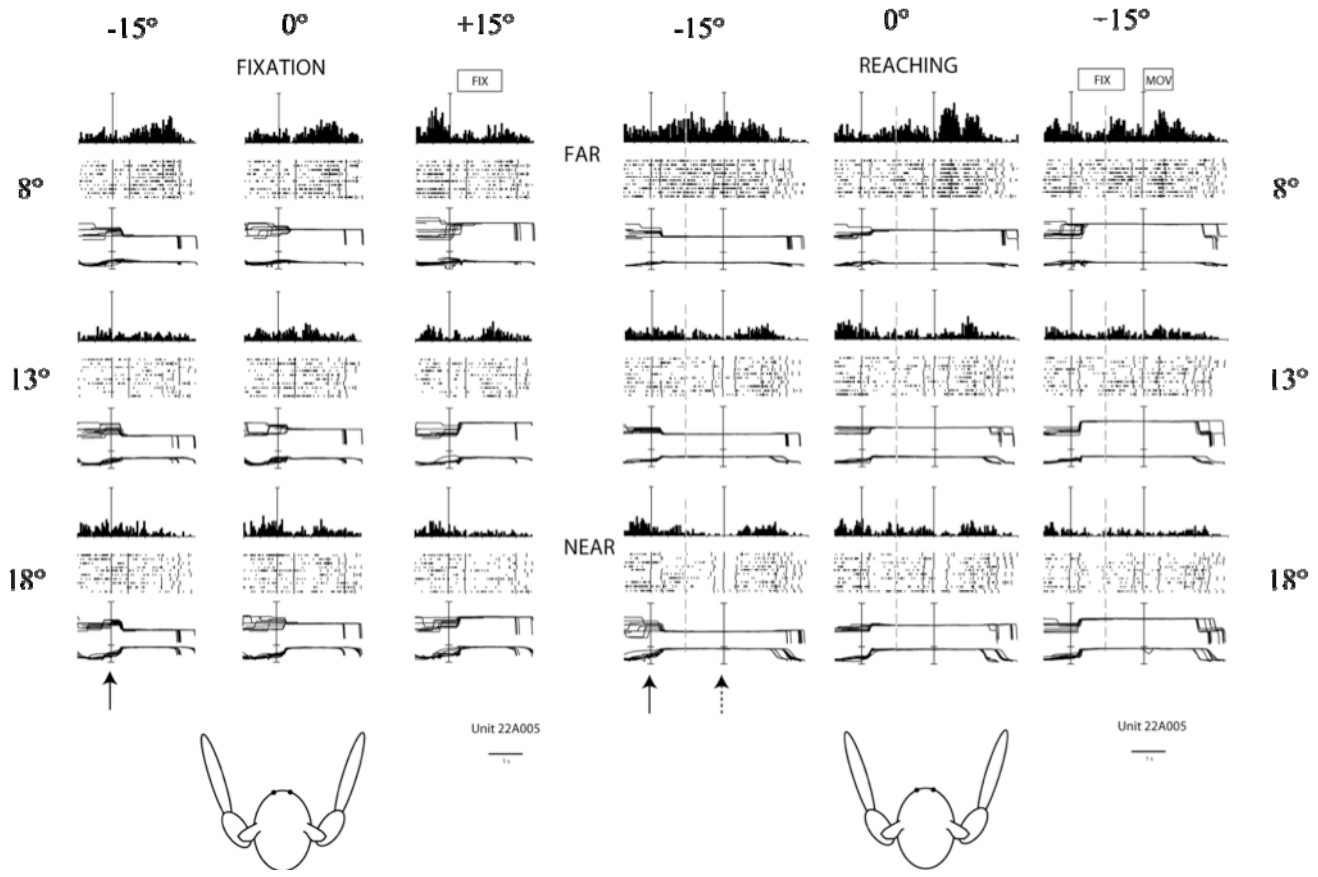

Figure 3: example of a V6A neuron modulated during fixation epochs (both in reaching and in fixation tasks) and in the reaching epochs. Left: neural discharges in the fixation task. Right, neural discharges in the reaching task. Activity is aligned on target presentation for fixation task (arrow) and twice for the reaching task: on target presentation (continuous arrow) and on onset of the forward reaching movement (dashed arrow). Discharges are located according to far (top) and near (bottom) targets. Data in each row are at iso-vergent angles (8° top, 13° center, and 18° bottom). Data in each column are at iso-version angles (-15°, left; 0°, center, +15° right).

The neuron shown in figure 3 was sensitive to vergence, both in the eye-related epochs (FIX) and in the arm-related epochs (MOV), showing a congruent preference for the 2 effectors (eye, hand) landing on the farthest targets. Note that fixation and reaching of near positions did not significantly modulate cell's activity. In other cells, the neural activity was influenced by depth in only one of the 2 effectors. The example reported in figure 4 is a cell sensitive only to eye displacements. In particular, the cell was sensitive to vergence (with a preference for high vergence angles) and to version (with a preference for fixations to the right) in both fixation and reaching tasks. Note that the reach-related activity was not present for any of the reached positions (see epoch MOV).

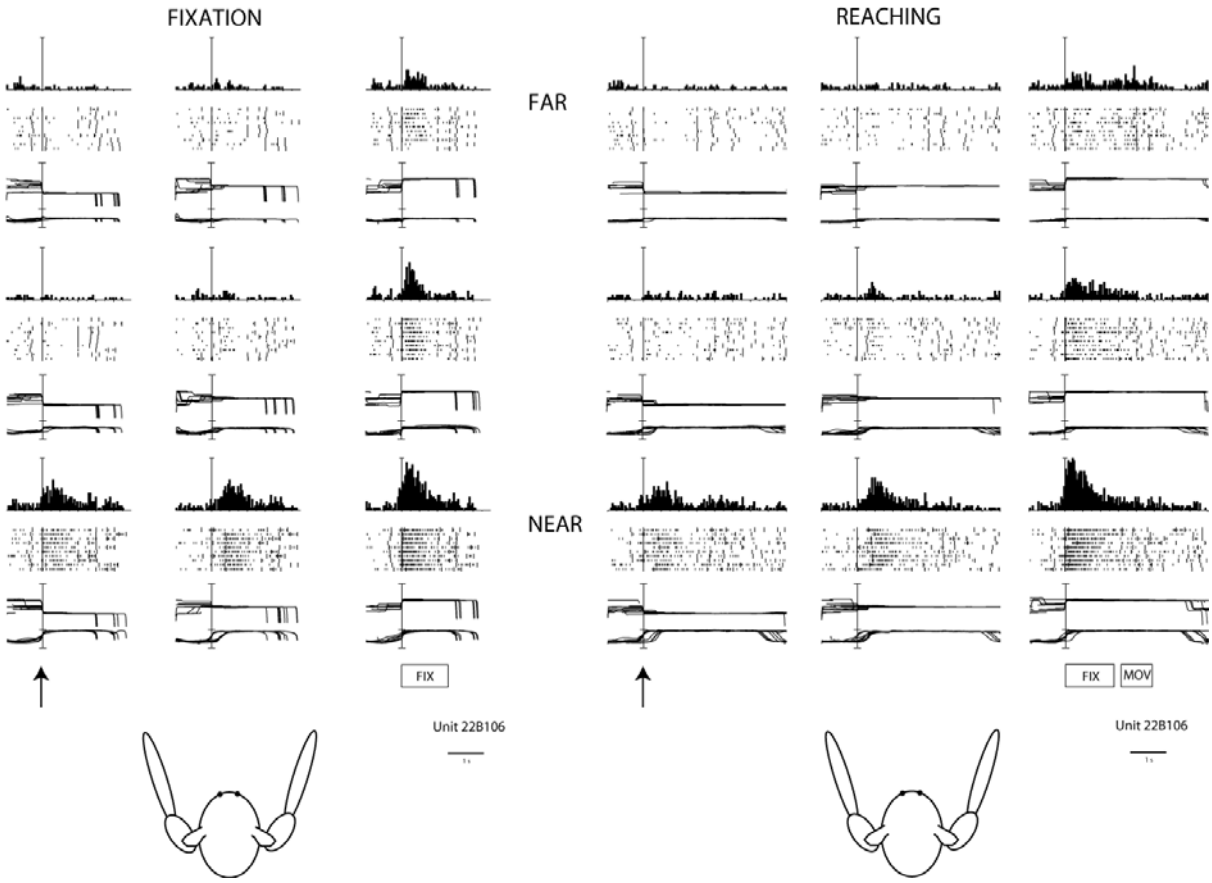

Figure 4: example of a V6A neuron sensitive to fixations in the near space and not sensitive to the depth of the reaching movements. Activity is aligned on target presentation (arrow) for both tasks. All conventions are as in Fig. 3.

In the cell reported in figure 5, the discharge was present only in the reaching task, in HOLD and RET periods. The reaching discharge was modulated in depth, with a strong preference for farthest targets. No discharges were evoked during fixation in both tasks for all the target positions we tested. This means that this cell, contrary to the cell shown in figure 4, did not receive vergence/version information, but only postural (proprioceptive) or motor-related signals from the performing arm.

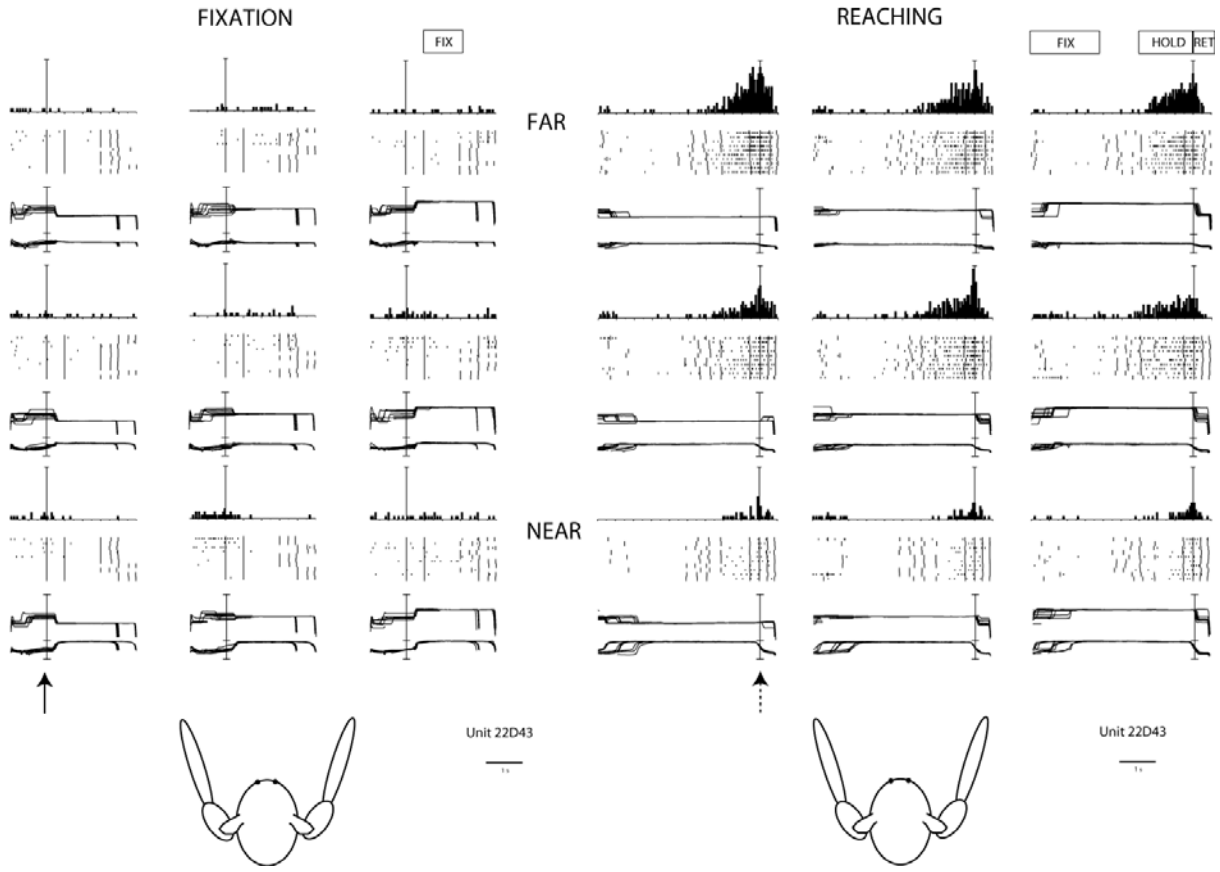

Figure 5: neuron not sensitive to eye positions nor eye movements in depth, but sensitive to postural information and motor/related information. Activity is aligned on target presentation for fixation task (continuous arrow) and on onset of return movement for the reaching task (dashed arrow). All conventions as in Fig. 3.

4 .1 Effect of depth on arm movement/position-related neural activity

In this Deliverable, we will focus on the neural activity during arm movement/position-related epochs, that is during the execution of reaching movements toward and from targets located in a 3D space (MOV and RET) and during hand holding in these spatial locations (HOLD).

Since the neuronal encoding of reaching has been intensively studied by many laboratories in 2D space (frontal plane at fixed distance from the animal), we focused the present analysis on the reach-related modulations occurring in depth. We found that 57% of V6A neurons were modulated by depth in the epoch MOV (63/111), 51% in HOLD (57/111) and 44% in RET (49/111). This means that several cells were influenced by depth in more than one arm-related epoch, as shown in the example of figure 6. This cell showed a strong influence of depth on most of the time epochs we analysed. It was modulated by the saccade that brought the object on the fovea, during the fixation period (FIX), and during arm reaching related epochs (MOV, HOLD, RET). The cell shown in figure 6 had a coherent tuning of activity during fixation, reaching, hold, and return with increasing discharges for targets located in the far, left part of the space. It is worthwhile to note that during fixation, where no arm activity occurred, the neural modulations must be ascribed to the changes of vergence and version, particularly to the vergence, with a clear preference for low vergence angles. This is particularly evident by comparing the discharges during MOV to targets far away (upper

row) and to targets near the monkey (lower row) in each iso-version line (for example, the top left with the bottom left responses during MOV, and also during HOLD).

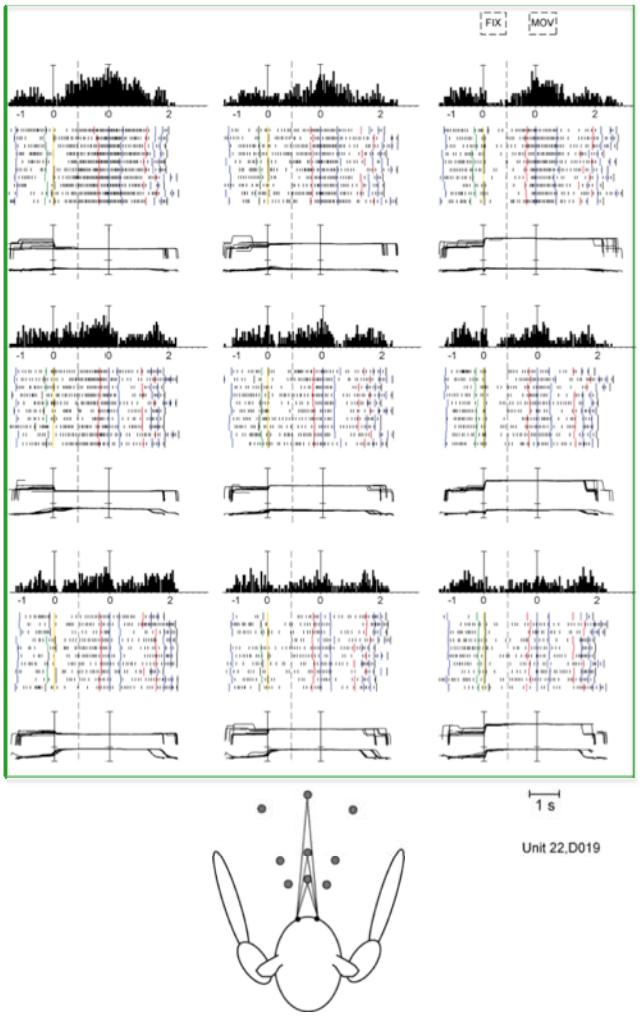

Figure 6 V6A neuron modulated by depth of target locations in all arm reaching related epochs.

The cell shows a spatial tuning, with a clear preference for reaches toward the far targets, especially the left ones. Alignement: saccade onset and reaching onset. All conventions are as in Fig. 3.

4.2 Arm movement epochs

In some cases, the tuning in depth of the neural discharges were confined to one arm reaching-related epoch only.The cell of figure 7, for instance, was modulated by the arm movement in depth only during forward movements (epoch MOV). The cell showed a spatial tuning. Neural activity in this case is enhanced when the monkey performed the reach toward the farthest targets. During fixation epoch, neither vergence nor version significantly modulated this cell.

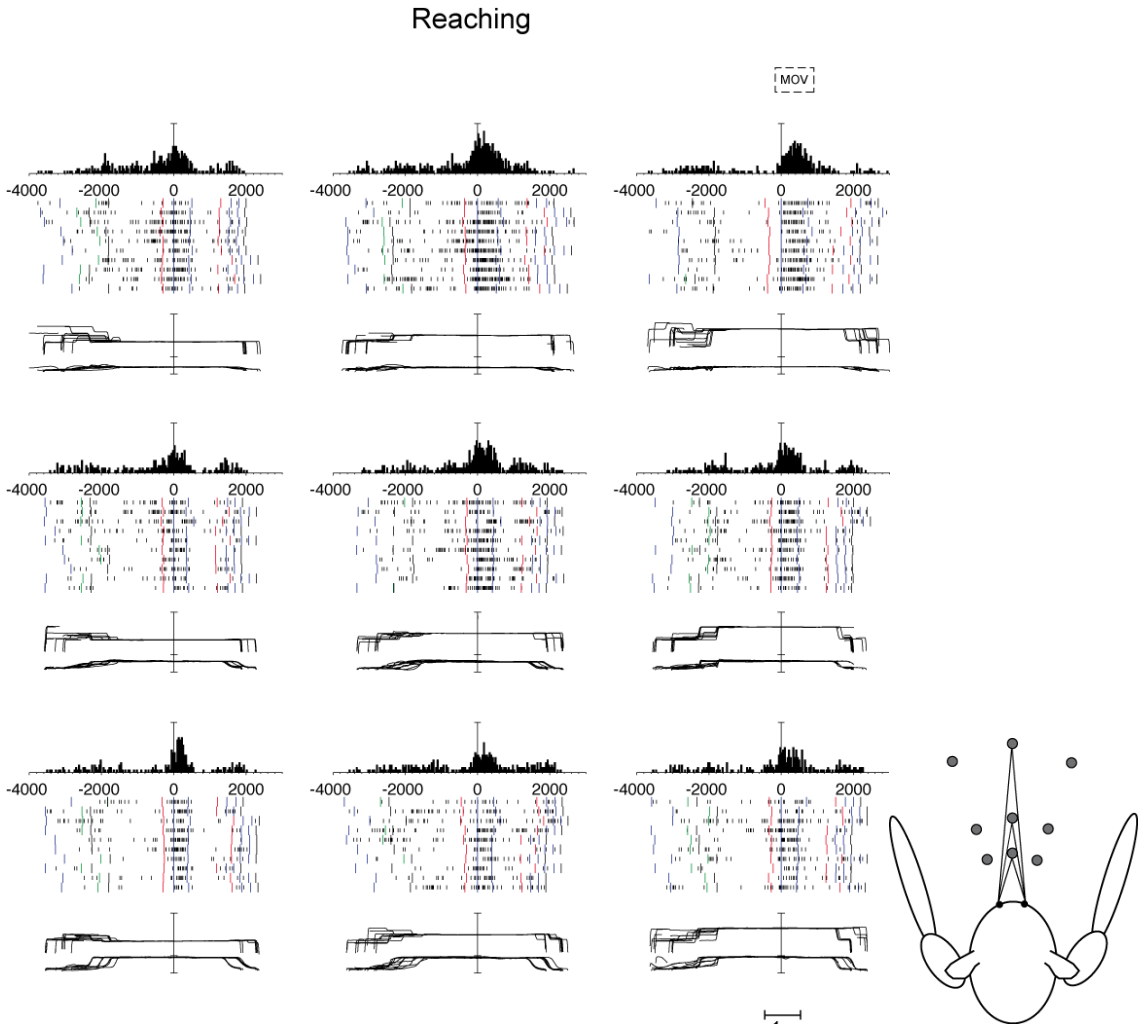

Figure 7. Example of a V6A cell spatially tuned only for forward reaches in depth.

The spatial modulation is specific for the MOV epoch, when the arm reaches its target. Activity is aligned on the onset of the reaching movement. All conventions are as in Fig. 3.

The ability of the entire neural population to discriminate the spatial position of the targets is demonstrated by the population spike density functions (SDFs) shown in the left part of figure 8. When the ranking of SDFs was based on the strength of neural activity (from best to worst activities of single cells), the curves were well apart one from another, with the worst discharge (blue curve) not different from the baseline activity, and the best discharge (violet curve) well above this level. This means that each cell strongly modulated its activity for different depths. In contrast, when the activity was ranked for all cells according to spatial location of the targets (figure 8, center) the 9 curves were superimposed, meaning that the cell population did not show a preference for a certain spatial position. This is also true when the targets were grouped according to their position in depth (Figure 8, right): no preference for a given distance was observed. The ensemble of the plots shown in figure 8 demonstrates that, although the individual cells in V6A were tuned for reaching in depth (as shown in the examples reported in Figures 3, 5, 6, 7), the individual preferences compensated one another without a clear preference for a certain spatial location. In other words, the spatial fragments were sampled in the same way, with the same definition, across the entire reachable space.

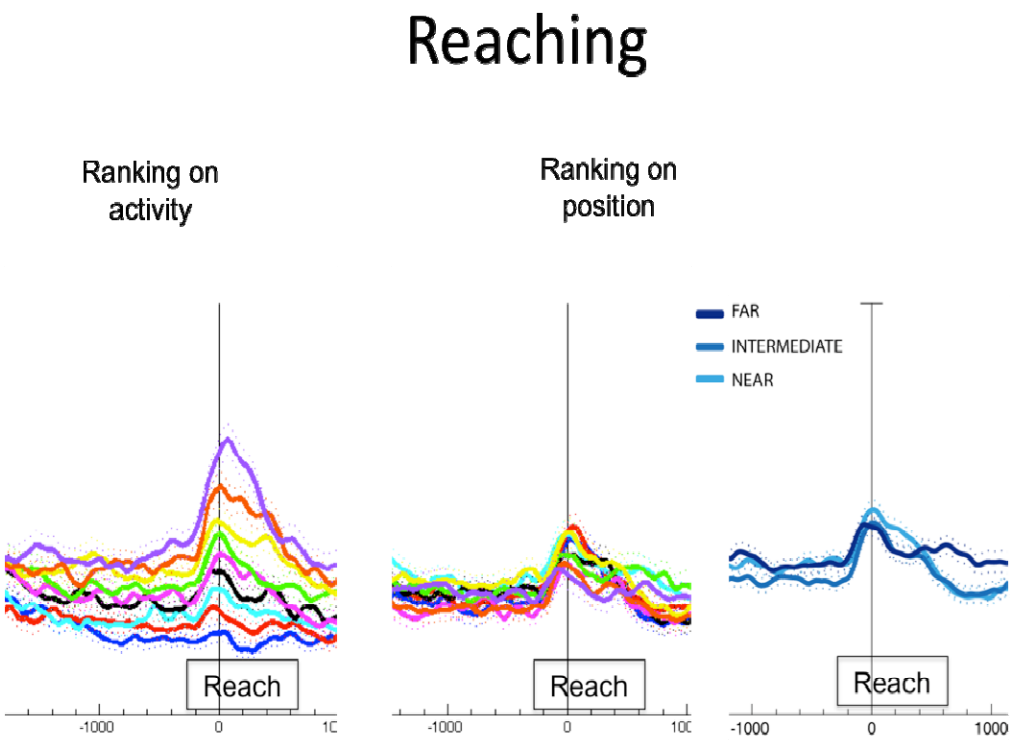

Figure 8. Spatial tuning for reaches in depth at the population level.

Population activity for each target position (different colors) of V6A cells modulated in the MOV epoch. Activity is expressed as averaged normalized SDF (thick colored lines) with variability bands (s.e.m., light lines) and is aligned at movement onset; vertical axis 100% of normalized activity. Rectangles labeled "Reach" indicate the mean duration of MOV epoch. More details are in the text.

Figure 9 shows the population discharges of cells tuned by return reach movements. As observed for forward reach movements, when ranking was based on the strength of neural activity, the SDFs were well apart one from another (Fig. 9, left), whereas when the activity was ranked according to the spatial location of target (Fig. 9, center, right) the curves were almost superimposed. This means, again, that the single cells were able to encode spatial locations, and the whole cell population encoded quite uniformly the 3D extrapersonal space.

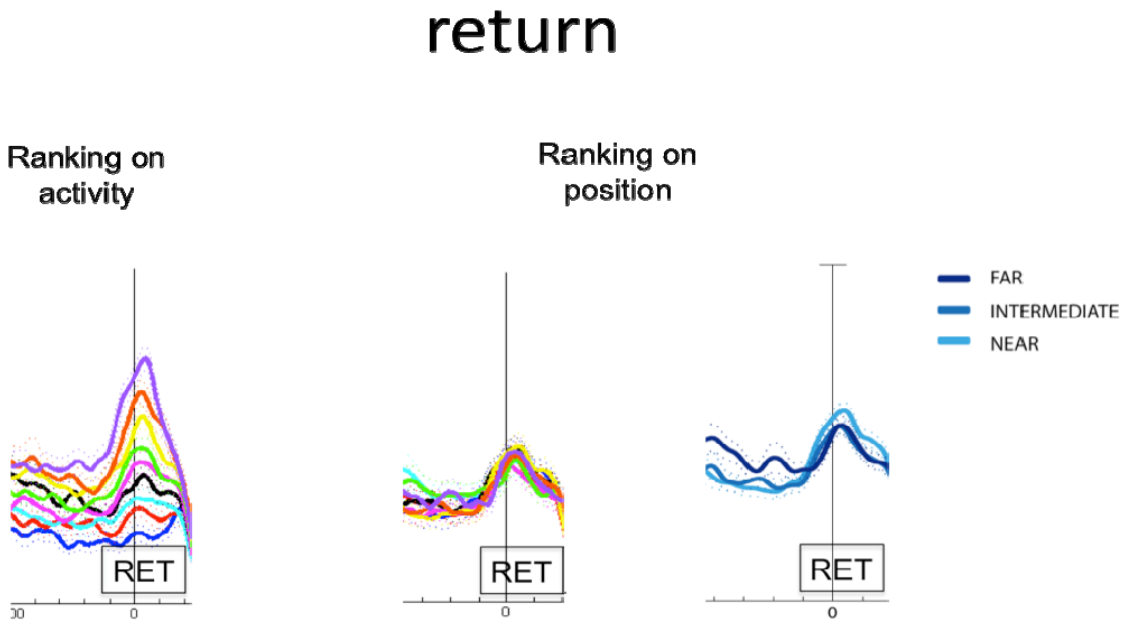

Figure 9. Spatial tuning for return reaches in depth at the population level.

Population activity for each target position (different colors) of V6A cells modulated in the RET epoch. Activity is expressed as averaged normalized SDF (thick colored lines) with variability bands (s.e.m., light lines) and is aligned at return movement onset.; vertical axis 100% of normalized activity. White rectangles: mean duration of RET epoch. All conventions are as in Fig. 8.

4.3 Hold epochs

Fifty-one per cent of V6A neurons (57/111) were modulated by depth in holding time. In this epoch, the monkey was keeping the hand immobile on the targets located in different spatial positions, at different depth in the peripersonal space. Figure 10 shows a cell spatially modulated by depth in HOLD period. This cell displayed the strongest discharges when the hand was held on far and right targets, though it showed quite good discharges also for near and left targets.

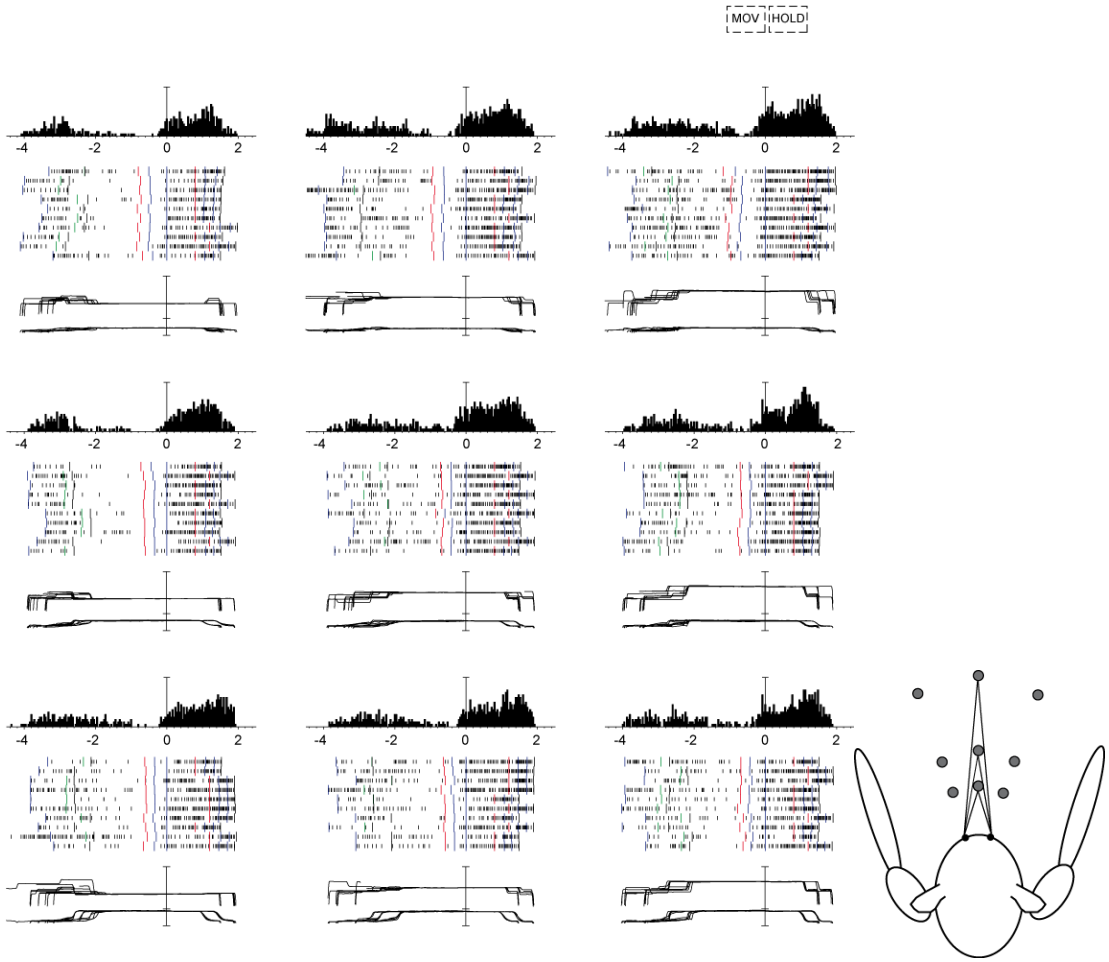

Figure 10 Example of a neuron spatially tuned for HOLD in the 3D space. Activity is aligned on the onset of the hold period. All conventions are as in Fig. 3.

The population as a whole (Fig. 11) showed the capacity to encode different spatial locations (ranking on activity; Fig. 11, left), but no preference for a specific depth or position in the 3D space (ranking on position; Fig. 11, center, right), similarly to what observed for reach-related epochs (Figs. 8 and 9). In other words, even for the static positions held on targets, the individual preferences of single neurons compensated one another without a clear preference for a certain spatial location. This means that the spatial fragments were sampled in the same way across the entire reachable space not only during the reaching epochs, but also during the holding time.

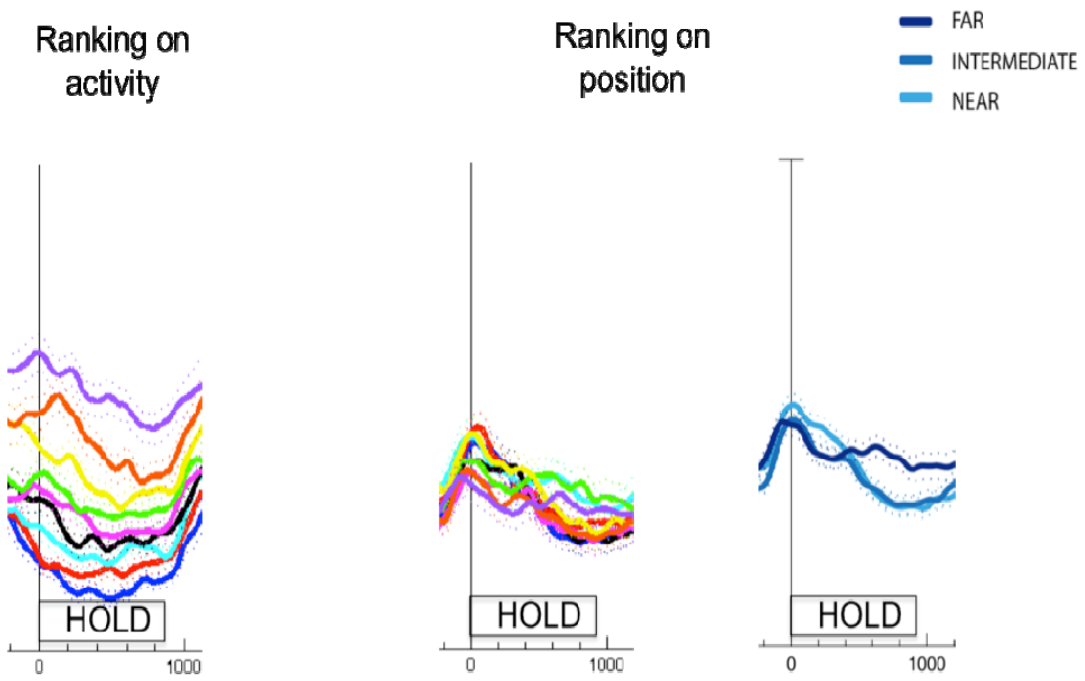

Figure 11 Spatial tuning for HOLD in depth at the population level. Population activity for each target position (different colors) of V6A cells modulated in the HOLD epoch. Activity is aligned at holding time onset; vertical axis 100% of normalized activity. White rectangles: mean duration of HOLD epoch. All conventions are as in Fig. 8.

4.4 Strength and selectivity of depth modulations

To investigate the selectivity and strength of neural modulations for reaching in 3D space, we computed the percentage discharge difference between the best position and the second best, and the percentage discharge difference between the best and the worst position. The first index quantifies the selectivity of reach-related responses in the arm-related epochs in the tested workspace, while the second index quantifies the the strength of the responses. Figure 12 reports these indices, for the cells with a significantly modulated activity in epochs MOV epoch, RET and HOLD epochs.

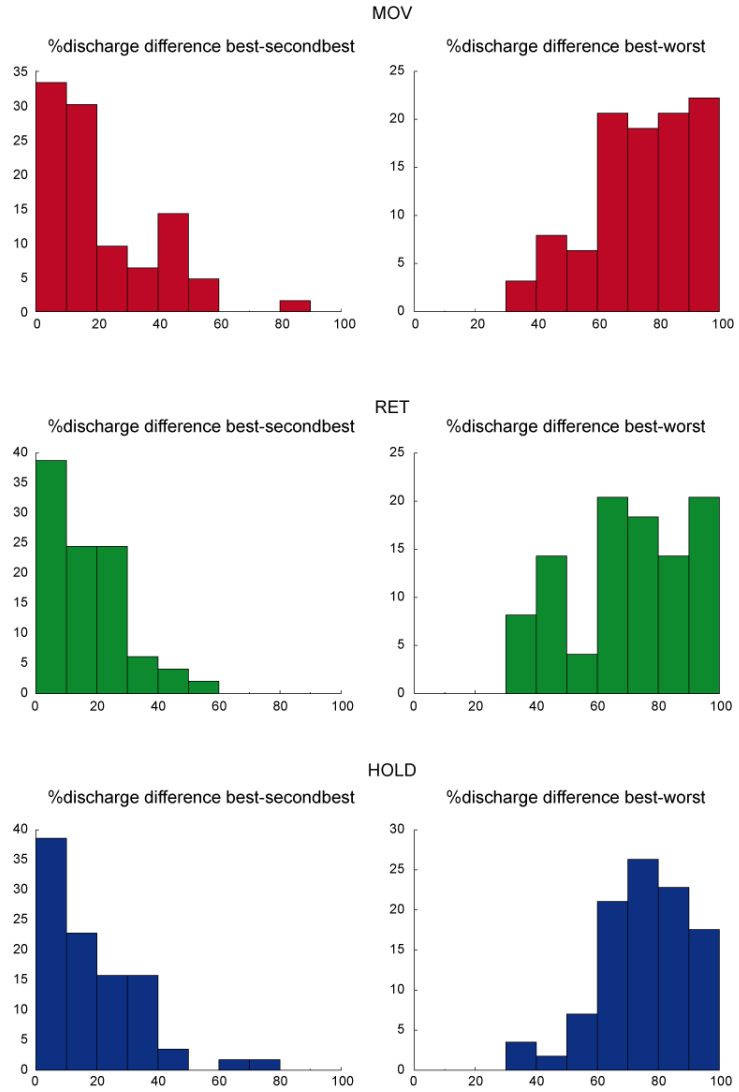

Figure 12. Selectivity and strength of modulation for reaching in depth in area V6A. Frequency distributions of percentage discharge difference between best and second best (left), and best and worst (right) of the cells modulated in MOV (red), RET (green) and HOLD epochs (blue).

The percentage discharge difference between best and second best position showed that more than half of the neurons had a difference between the 2 best positions smaller than 20% in all 3 epochs taken into account (Fig. 12, left). This means that, rather than having cells responding only to reaching in single spatial locations, V6A cells were tipically responsive to discrete regions in the working space.

Data in the right part of figure 12 show that the strength of neuronal modulations for reaching in depth was quite high in all the epochs taken into account: for a third of neurons the best and worst discharges differred more than 80%, with many neurons having a difference close to 100%. These data, that confirm the conclusion obtained from the SDFs shown in Figures 8, 9 and 11, indicate that V6A reaching cells encoded the whole working space by using most of their potential range of discharge.

To measure the magnitude of depth and side effects on the reaching activities of V6A neurons, we applied a multiple linear regression model (see Methods). For this analysis, we used cells that were tuned for depth (vergence) or for side (version) in MOV, or RET, or HOLD (ANOVA, $p<0.05$), as summarized in table 3.

Table 3: effects of depth on neural activity. Number of neurons that significantly fit for the depth of the target in each epoch of analysis.

Fitting for linear regression	**MOV**	**HOLD**	**RET**
Depth	44/63 (*70%*)	39/57 (*68%*)	31/49 (*63%*)
Side	22/79 (*28%*)	27/75 (*36%*)	19/60 (*32%*)

Neural activity correlated linearly with depth in a percentage of cells between 60 and 70% in the different arm-related epochs. Neural activity correlated with side in a percentage of cells about half of that correlating with depth, wtih many cells correlating with both these parameters. For the purpose of studying the modulations of arm-related activity in depth, we will analyze here the regression coefficients of cells correlated with depth, so to find whether there was a tendency of the population to increase the frequency of discharge for nearest targets or for farthest targets.

Figure 13 reports the regression coefficients of all cells whose discharges were linearly correlated with the depth of the target. The distributions for the 3 arm-related epochs were quite similar, with a wider distribution of coefficients for MOV, that is when the arm reached its targets in the peripersonal space. It should be noted that there is a comparable number of negative and positive coefficients in all epochs, signalling a similar presence of far and near space preferences in single V6A cells.

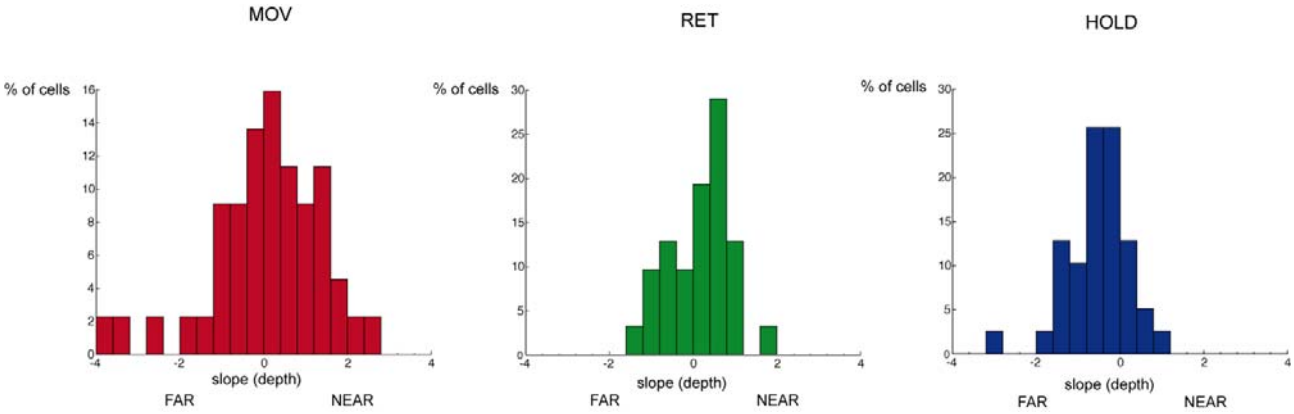

Figure 13. Frequency distribution of the regression coefficients for depth in the 3 arm-related epochs. Negative coefficients: higher activity for far targets. Positive coefficients: higher activity for near targets.

5-Discussion

The present study is the first to provide evidence that neurons of the medial parieto-occipital cortex are sensitive to arm reaching movements in depth. In these experiments, we tried to reproduce the natural situation in which the monkey gazed at the target to be reached out, and then reached the target with an arm movement directed to different locations in the peripersonal space. In the fixation and reaching tasks we restricted the working space of the animal to the horizontal plane extending in depth from the animal's eyes because in that way the elevation of targets remained constant, no matter which were the laterality and the depth of targets. This experimental set up also allowed us to study whether the eye vergence and version influenced the neural discharge.
We found that reaching movements in depth modulate the neural activity in a vast majority of V6A cells, often with strong spatial tuning. Strong modulations were observed either when arm

movements were directed outward, toward visual objects in the field of view (MOV), or inward, toward targets located near the body and outside the field of view (RET). Strong modulations and spatial tuning were also observed during holding time, when the hand remained still on the target and the arm assumed a particular posture in space (HOLD). Most V6A reaching neurons were modulated in more than one arm-related phase of the task.
The present results suggest that V6A is able to encode the peripersonal (reachable) space by encoding direction and depth of arm actions. Together with the data reported by Fattori et al. (2005), according to which V6A reaching neurons are able to finely encode the direction of arm movements for reaching targets located on a frontal plane, present results suggest that V6A reaching neurons encode spatial locations in the 3D reachable space through motor-like signals that could be used to build up and continuously update a map of peripersonal space.
At the population level, in V6A we did not see a particular sector of the workspace preferred with respect to others (see figures 8, 9 and 11). This suggests that the population of V6A spatially-tuned neurons is able to code the entire set of locations we tested. Although the individual cells in V6A are tuned for depth, our data indicate that individual preferences compensate one another without a clear preference for a certain spatial location. In other words, the spatial fragments are sampled in the same way, with the same definition, across the entire reachable space.

5.1 Comparison with other studies of depth in PPC

Modulations of neural activity for effector movements in depth have been reported in other PPC areas. In LIP a third of neurons show a significant effect of vergence on the planning activity for conjugate eye movements, with about 70% of LIP neurons preferring saccades in near space (Genovesio and Ferraina 2004). In area MIP a majority of arm reaching neurons show planning activity influenced by the depth (Bhattacharyya et al., 2009). In V6A itself, the vergence has been shown to powerfully modulate neural activity during fixation as well as in perisaccadic time, when the eye acquires its target in depth (Hadjidimitrakis et al., 2010).
To our knowlegde, no brain imaging studies so far have attempted to study reaching movements in depth. However, two studies have investigeted the role of human medial parieto-occipital cortex in depth. Quinlan and Culham (2007) described a region in the human dorsal parieto-occipital cortex that was more strongly activated when subjects viewed moving or stationary stimuli located in near space than in intermediate or far space. The authors obtained the same result when subjects fixated small LEDs placed at the same range of distances (near and far) and they attributed the evoked activity to the oculomotor near response, most probably to the eyes vergence (Quinlan and Culham, 2007; Culham et al., 2008). A subsequent study from the same group (Gallivan et al., 2009), reported that passive viewing of reachable objects evoked higher activity compared to viewing of objects placed in non reachable space, in the superior part of parieto-occipital cortex (SPOC). The SPOC region, which is also activated during arm reaching movements (Cavina-Pratesi et al., 2010), includes the cortex anterior to the human homologue of V6 (Pitzalis et al., 2006; Cavina-Pratesi et al., 2010) where human V6A is likely located. In Gallivan et al. (2009) subjects were constantly fixating at far locations, so the stronger activation of SPOC by objects located near was not ascribed to the eyes convergence, but to the reachability of targets. The authors suggested that the reachability signal could be extracted in SPOC by the combination of gaze and target depth signals. These data, again, point toward an homologous role of human and monkey medial parieto-occipital cortex in encoding eye and arm actions in the 3D space. Supposing that SPOC contains the human V6A, as suggested, our results would be strongly supported by these imaging data. Conversely, our data support the view that SPOC contains the human V6A, and also support the view of a strong similarity between human and non-human medial parieto-occipital cortex.

5.2 Role of V6A in visuomotor processes

It has been suggested that internal representations of the world and of one's own body are needed to relate ourselves to the external world (Wolpert et al., 1998). These representations would derive from the concurrent computation of sensory inputs and motor outputs. The hypothesis is that we continuously estimate both the configuration of body parts (i.e. joint angles and arm position) and their interaction with the peripersonal space (i.e. contact with objects), and update this representation over time (Kalaska et al., 1983; Kalaska and Crammond, 1992; Johnson and Ferraina, 1996). There is considerable evidence that superior parietal lobule plays a key role in maintaining an internal estimate of both the external world and one's own body (Wolpert et al., 1998; MacDonald and Paus, 2003). We believe that area V6A plays a crucial role in this job.
The convergence on area V6A of both motor signals related to arm movement (from dorsal premotor cortex, Gamberini et al., 2009) and sensory signals (visual and somatosensory inputs, Galletti et al., 1996; Galletti et al., 1999; Breveglieri et al., 2002) suggests a role for this area in monitoring the arm-object interaction. Actually, V6A has visual neurons appropriate to perform the visual control of prehension movements (see Galletti et al., 2003 for a review). We here demonstrate that motor-related signals allow V6A cells to monitor the direction of reaching movements needed to interact with objects in depth in peripersonal space, within and outside the field of view, as well as the position of arm in space. In other words, V6A neurons might participate not only to the analysis of visual space, as previously suggested (Galletti and Fattori, 2002), but also in the online control of arm movement (see Galletti et al., 2003; Fattori et al., 2009; 2010) by elaborating sensory inputs and motor-like outputs that could represent the internal body state for the purpose of sensorimotor integration, as suggested recently by our group within the EYESHOTS project (Bosco et al., 2010).
In this line of thought, the output signals from V6A could continuously adjust the motor command which guides the occurring arm movement, and could continuously update the internal representations of the body (relative positions of the body parts) and the location of target of prehension. In humans, it is well known that the caudal part of superior parietal lobule plays a crucial role in the control of aimed reaching movements (optic ataxia, Perenin and Vighetto, 1988), also in depth (Dankert et al., 2009). Using new tools for anatomical localization of lesions, it was shown that optic ataxia would result from brain damage centred on two foci, one of which is in the medial parieto-occipital cortex (Karnath and Perenin, 2005), almost coincident with SPOC of Culham and coworkers (Culham et al., 2008; Quinlan and Culham, 2007; Gallivan et al., 2009). It seems likely that this cortical region can include a human homologue of area V6A, supporting the view that the medial parieto-occipital cortex is a crucial node in the control of aimed reaching movements in both humans and monkeys.

6- Conclusions

The present study suggests a novel role for the medial posterior parietal area V6A in constructing a 3D representation of the visuomotor world. It is known that V6A contains reach-to-grasp neurons (Galletti et al., 2003; Fattori et al., 2005; 2009; 2010) and cells that encode the two dimensional location of visual targets (Galletti et al., 1995), some of them in spatiotopic coordinates (Galletti et al., 1993). Here we show that many V6A neurons also encode the spatial locations that the animal is reaching out, or has just reached out in the peripersonal space. Taken together, the data of the present study give strong support to the view that V6A plays a key part in the sensory-to-motor transformations that control reach-to-grasp arm movements and in elaborating sensory inputs and motor-like signals that could represent the internal body state for the purpose of sensorimotor integration.

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