THE OCULOMOTOR SYSTEM AS A MODEL FOR THE STUDY OF NEURONAL INTERACTION PROCESSES

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ABSTRACT

Identified neurons that control eye movements offer an excellent experimental target for the study of information coding and neuronal interaction processes within the central nervous system. Here are presented some preliminary results of the motoneuron behaviour during steady eye fixation, obtained by regression and analysis of variance techniques. A flexible information system intended for the systematic acquisition and analysis of simultaneous records of neuronal activity and both eyes angular position in a great amount of cells, oriented to the definition of mathematical models, is also briefly outlined.

A promishing new approach to the study of information coding and neuronal interaction processes within the central nervous system has appeared recently due to a major factor: the improvement in the techniques for recording the activity of functional identified neurons in alert behaving animals. A further improvement has been obtained with the application of these techniques to systems such as the neurons that control eye movements, where the output and some of the inputs are easily measured under very different experimental situations. (see 4, 6 and 7).

Nevertheless, even restricted to such a class of systems, complexities arise from: i) The wide repertory of natural eye movements (pursuit, saccadic, vergence, vestibular), and ii) The qualitatively different behaviour that can be observed from the activity records of neurons involved in the oculomotor control system. Both difficulties have forced the questions that are the main concerns of this communication: Do similar dynamical properties of eye movements, regardless of their origin, correspond to equal coding principles ? and, can the differences observed in oculomotor neuronal activities be explained by an adequate selection of the individual parameters of a common mathematical model ?.

To cover these objectives a system was developed for the automatic and simultaneous recording of neuronal activity, angular position of the eyes and selected experimental inputs. Experiments were carried out in alert cats. Animals were previously implanted with silver ball electrodes to record their electrooculogram (both in the horizontal and vertical planes) and also with a holding system to restrain their heads during recording sessions. Recordings were carried out with glass micropipettes in selected areas of the brain stem through a transcerebellar approach. A more detailed account of the experimental set has been published elsewhere (1).

The activity of insolated motor or premotor neurons was recorded during spontaneous and vestibular or visual induced eye movements in the alert behaving animal. Only eye movements related neurons were recorded. To further improve the reliability of the results, only identified neurons were considered for analysis.

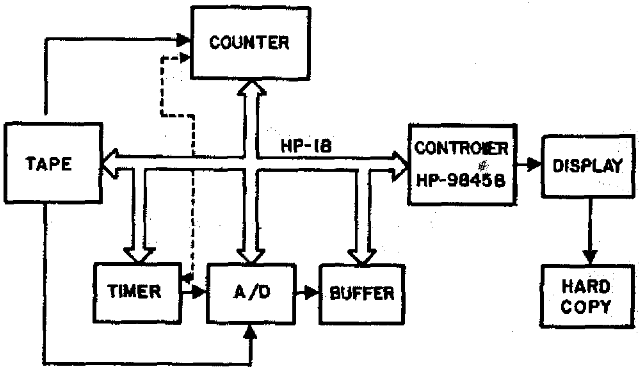

Fig. 1. Block diagram of the acquisition, processing and graphic display system of the experimental data stored in a 4-channel magnetic tape. See text for details.

Neuronal identification was achieved by antidromic activation of their somas from their axonal projections. Activation was carried out by chronically implanted stimulating electrodes located in neuronal projection sites: abducens nerve, oculomotor nucleus, anterior vermis of the cerebellum, etc. (1, 8). The records of unitary activity, eye movements and head position were stored in a 4-channels tape recorder.

For the acquisition, graphic display and processing of the recorded data, a system controlled by a HP9845B computer and a set of programs were implemented (see block diagram in figure 1.). Unit activity of the registered neurons was converted into a point process by filtering, window discrimination and measuring the interspike interval sequence. The operation is performed by a computer-controlled counter that transfer to the computer, in a high speed mode, the intervals between neuron action potentials; so that, no lost of information is guaranteed under the shortest expected intervals with the fastest play-back magnetic tape speed. Analog data (angular position in both eyes and experimental variables) were connected to high speed A/D converters, where sampling is provided by a computer-controlled timer, that also synchronize the counter operation in order to get exact temporal correspondence between the different data channels. Digitized analog data

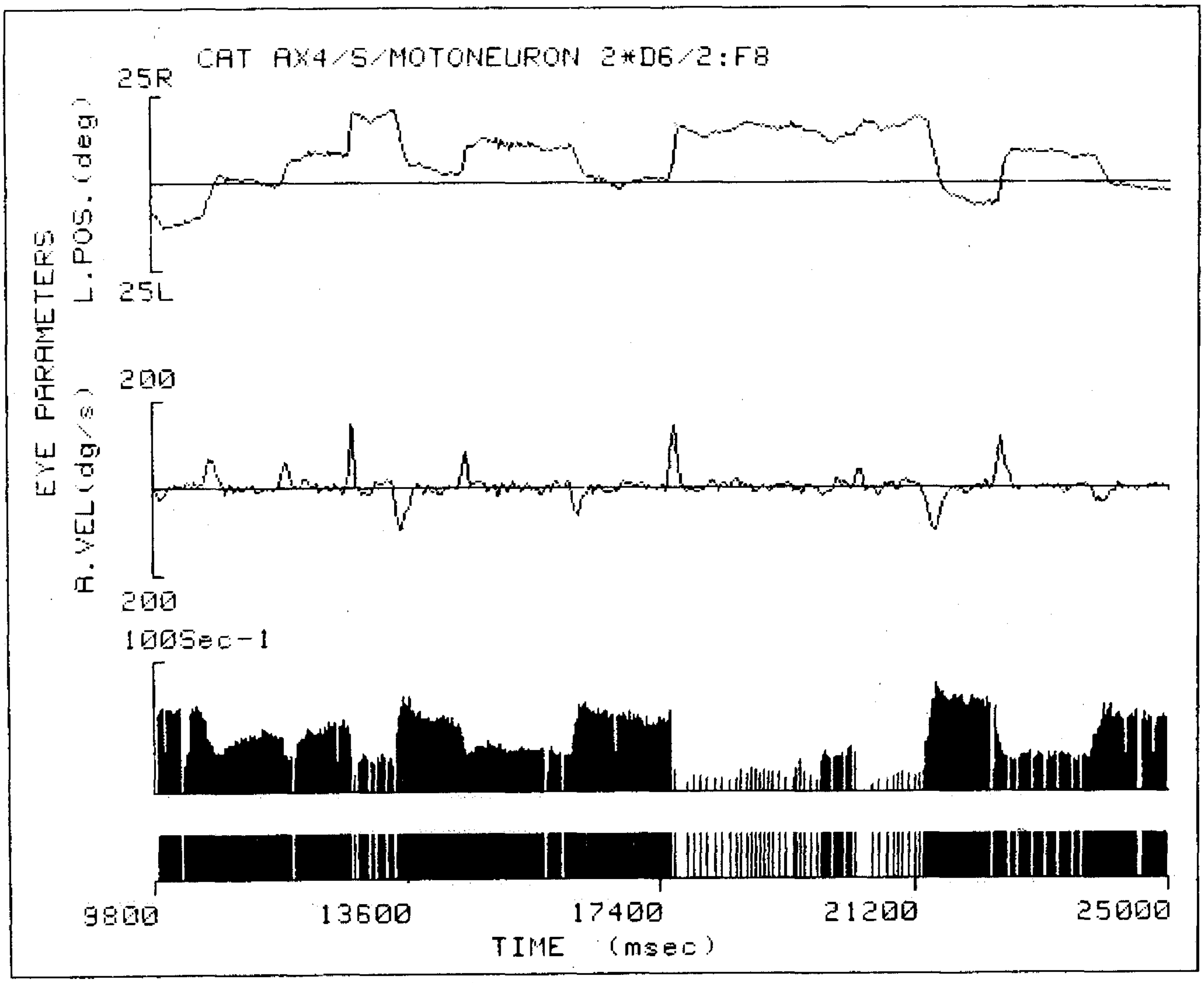

Fig. 2. Activity of an abducens motoneuron (left side) during espontaneous eye movements of the cat. From top to bottom, the angular position of the left eye in the horizontal plane (L.POS.), the velocity of the same eye in the same plane (L.VEL.), the inverse of the interval between spikes (in sec. $^{-1}$) and the spikes record as obtained through a window discriminator from the neuronal records stored on tape are shown. This unit was identified by its antidromic activation from the abducens nerve.

were stored momentarily, after multiplexing, in an auxiliar buffer while the point process is being acquired, and are transferred into the computer, through the system bus, upon complexion of that operation. Finally, data are stored in a flexible disc together with file codes and acquisition variables.

In order to allow the visual inspection of the transferred data and the systematic selection of records in a great amount of cells for further processing, the program enabled the display, upon selection, of the angular position and/or velocity of both eyes with the cellular activity point process. Each partial acquisition can be saved or erased according to its relevance for posterior analysis. It was also possible to select partial segments of a given file using a cursor over the CRT screen and store them with separated codes. Ordinate scales were defined from calibration records of the magnetic tape. Hard-copies of the CRT display can be obtained with a thermal printer. After the presentation of a transferred block, the program automatically continue with a new acquisition.

Figures 2 and 3 show examples of the graphic displays obtained with the program. In both cases, sampling rate was selected to 1/40 msec^{-1} (this rate was used generally during the stage of initial inspection of data, since it allows a convenient 40 sec duration of each acquisition

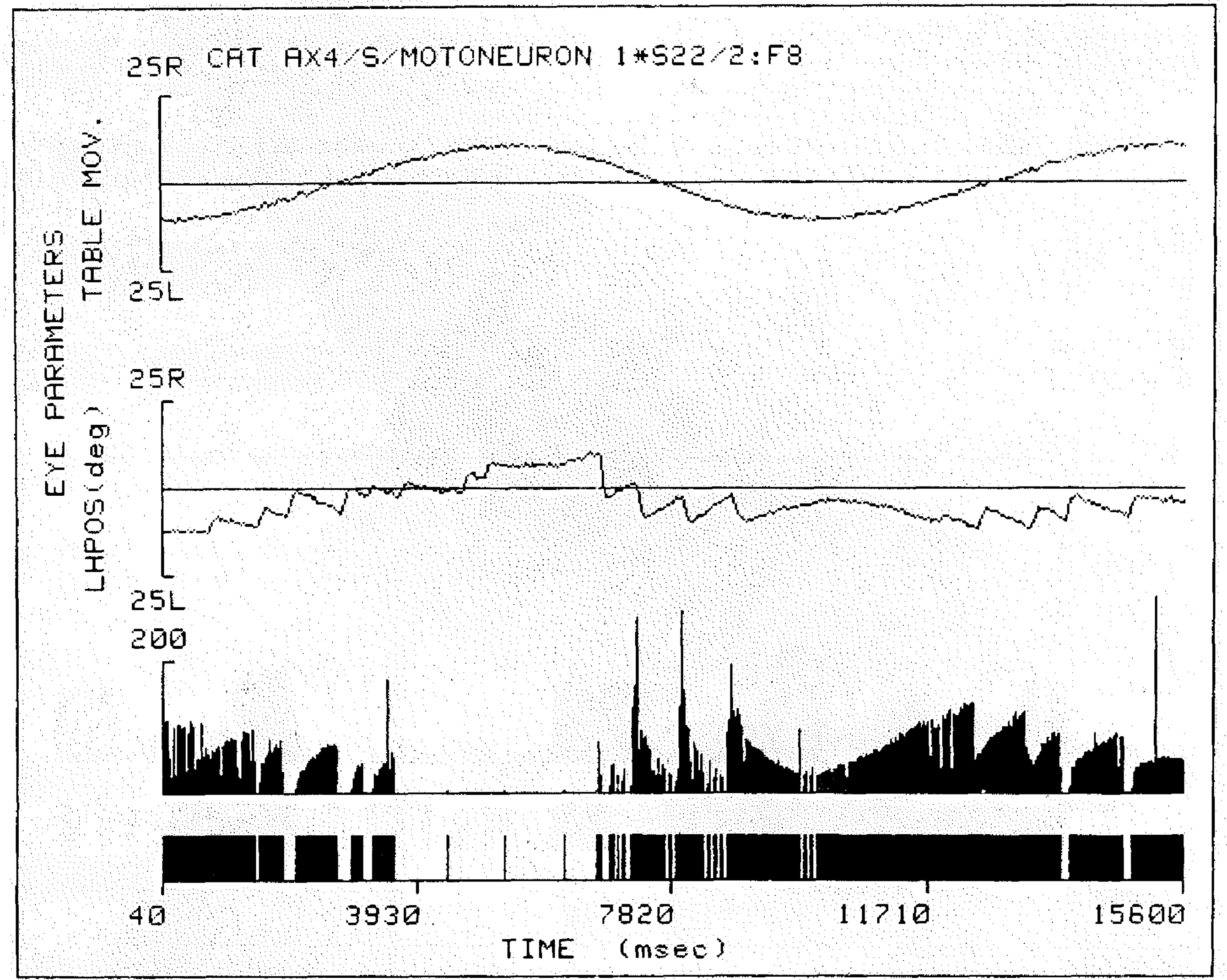

Fig. 3. Activity of an abducens motoneuron (left side) during sinusoidal rotation of the animal. From top to bottom, the instantaneous position of the head (TABLE MOV.), the position of the left eye in the horizontal plane (L. POS.), the inverse of the inter-spike intervals (in sec.$^{-1}$) and the spikes isolated througt a window discriminator from the rough data stored on tape are shown. This unit was identified by its antidromic activation from the left abducens nerve.

block with adequate time resolution for this purpose). The data segments shown in both figures are cursor selected and expanded portions of a 40 sec total duration file. The data presented have not been manipulated in any way to show the clear correlation that exists between the statical and dynamical behaviour of the eyes and motoneuron activity, which has been represented at the bottom of the figures by the inverse of the time intervals between spikes, also included (represented below) as they are obtained after the window discriminator.

Figure 2 is an example of the typical activity of an abducens (left side) motoneuron during spontaneous eye movement of an alert cat. In this case the angular position in the horizontal plane (L.POS.) of the left eye and its corresponding velocity have been selected for representation. Figure 3 shows the activity of the same class of neuron during vestibular stimulation (sinusoidal rotation of the head in the horizontal plane). In this figure it has been selected the table angular position in the horizontal plane (TABLE MOV.) and the angular position in the same plane of the left eye (LHPOS).

One of the analytical procedures implemented with our program was intended for the characterization of the profile of motoneuron discharge rate associated to a saccadic movement followed by a fixation interval. The evaluation of these discharge patterns could provide some insight into the mechanism involved in the integration of information at the motoneuron level of the oculomotor system, since according to our preliminary results (see in figure 4A. some typical profiles during eye fixation intervals) variability during steady fixation does not fit with results published previously. According to Robinson's model (6, 7) motoneuron activity shows a pulse-step increase in the spike rate during saccadic movement in the on direction followed by a constant value which corresponds to the new steady position. As shown in the firing profiles of figure 4 A. a different approach to the interpretation of motoneuronal activity, and corresponding functional system organization, can be intended. Moreover, the adecuate description of those patterns could explain at least, part of the high variation found in the relationship between the angle of fixation and the firing rate during steady fixation. This variation has been hypothetized due to two main contributions: the level of alertness and a dependency on the direction of the previous saccade, i.e. a sort of hysteresis effect (2, 3).

To analyze the temporal evolution of the motoneuron firing patterns it has been used least

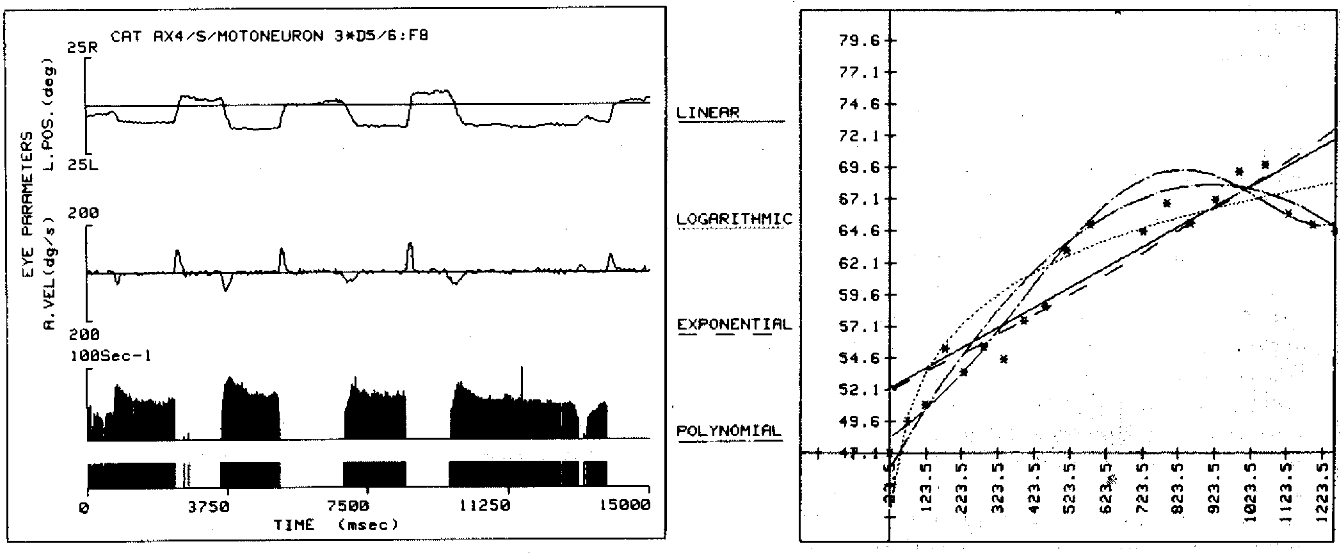

Fig. 4. Examples of the activity of abducens motoneurons during saccadic movements and fixations in alert behaving cat. A) From top to bottom the position of the left eye in the orbit (L.POS.), its velocity (L. VEL.), the inverse of the inter-spikes interval of an abducens motoneuron (left side) and the spike itself isolated from the rough data stored on tape are shown. Note the increasing frequency during saccadic movements in the on direction and the decay during the following fixation. See further explanations in test. B) Linear, logarithmic, exponential and 2^{nd} and 3^{rd} order polynomial regression models least mean square fitted to the second fixation interval of figure 4 A. See text for model significance and selection.

mean square regression techniques, applied to the intervals between action potential and from data segments corresponding to steady eye fixation - states, after the previous eye saccade extintion. This should be considered as a first stage of a more detailed and efficient estimation of the parameters of different probabilistic models of the stochastic point process defined by the motoneuron output. For this purpose the first and second order statistics are at present being estimated in our department.

Different regression models (linear, logarithmic, exponential and polynomial) have been applied to the data (X, Y) matrices defined as follows: Y_1 is the observed time from the first spike to the rth one, Y_2 from the rth spike to the 2rth one, and so on.' X_i was defined as the time scale at mid-points of the Y_i intervals. The parameter r was selected small enough to assume that the firing rate does not change appreciably during any of the Y_i intervals, providing on the other hand adequate efficiency of the estimated model parameters. In all cases the significance of the fitted models was tested by an analysis of variance. It should be kept in mind that significance of a selected regression model does only mean that the model account for a significant portion of the variation observed in the variable along the time. F-statistic was used for rejection of the models, at a 0.01 significance level, and also as a selection criteria of those models proved significant.

In figure 4 A.' four eye fixation intervals, for an identified motoneuron, with different angular position have been included.' Figure 4 B. shows the regression models obtained for the second fixation interval of figure 4 A. The application of analysis of variance to this segment provided the following results: 1) All four models (2nd and 3rd order for polynomial regression) proved to be significant and 2) the highest F value - (54.33; with r = 4 and 19 residual degress of freedom) corresponded to the logarithmic model. The application of the same procedure to a great - amount of fixation intervals provided similar results to those mentioned. However, the coefficients of the models reflect important differences that appear to be related to the fixation angle and previous saccade waveshape. The characterization of this dependences is at present being studied.

SUMMARY

The outlined preliminary results on the firing sequences of ocular motoneurons, in the context of published models, suggest that present experimental approach to the study of the - oculomotor system, could contribute to the advance of present knowledge on the coding principles and neuronal interaction process involved in higher motor functions.

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