Results

We successfully recorded the activity of 35 MST neurons, 32 DLPN neurons, and 20 P cells in the VPFL, all of which represent different stages of processing, from sensory input to motor output for ocular following. To investigate the relationship between the neuronal activity and eye movement or retinal slip under single (Local Fitting) or multiple (Global Fitting) stimulus conditions, we used Eq. (1) to quantitatively analyze the temporal firing patterns during the ocular following responses in the preferred directions.

The relationship between the neuronal activity and eye movement

The relationship between the neuronal activity and eye movement shown in Fig. 2 illustrates how, using Local Fitting, our models added the components of eye movement to account for a P cell firing rate. The traces represent an observed simple spike activity of a P cell in the VPFL to a downward ramp at 80 deg/s (thin line) and a reconstructed P cell firing frequency pattern (thick line) derived from the eye movement with estimated coefficients. The C.D. was 0.86 indicating that the simple linear-regression model satisfactorily represented the complex time-course of P cell firing. The temporal patterns of the components decomposed into the acceleration (dotted line), velocity (broken line), and position (dashed line) parameters of Eq. (1), which revealed the relative contribution of each

component. Although the acceleration coefficient (a) was small, its component was predominant in the initial phase of the response as shown in this figure, and its velocity component was dominant in most of the rest of the response. After the initial phase, the acceleration component decreased and the position component increased. The position component, however, had a reversed sign relative to the direction of the movements. These results correspond with those of previous studies (Shidara et al. 1993; Gomi et al. 1998) and are characteristic of all the data in present study.

The traces in Fig. 3 summarize the results of using Local (A) and Global Fitting (B) of eye movements to reconstruct the firing patterns of the same P cell as in Fig. 2 at the five different speeds. In Figs. 3A and B, each pair of traces shows the firing patterns aligned on the onset of the ramp motion. Within each pair, the thick trace (labeled reconstruction) shows the reconstructed firing patterns from eye acceleration, velocity, and position using Local (Fig. 3A) and Global Fitting (Fig. 3B). The thin trace in each pair (labeled observed data) shows the observed firing patterns, which are the same data in Fig. 3A and B at the same stimulus speed. In Fig. 3A, the reconstructed firing patterns using Local Fitting were very close to the observed data within each pair, and the C.D.s were distributed between 0.87 to 0.94 (mean value, 0.91), indicating good reconstruction at each of the five stimulus speeds. In addition, in Fig. 3B, the reconstructed firing patterns using Global Fitting were also very close to the observed data in all the pairs, and the C.D. was calculated at 0.89, again indicating good reconstruction at

each of the five stimulus speeds using only a single set of parameters. These results indicate a linear relationship between P cell firing and the ocular responses through the multiple stimulus speeds.

When the C.D.s were calculated for the residual errors of the 20 P cells, the linear-regression model (Eq. 1) for eye movement was inapplicable for only a small number of P cell firing patterns (unshaded areas of Figs. 3C and D; 15/100 and 3/20, respectively; C.D. < 0.7), indicating that this model accounted for the different neuronal responses to movements of the visual scene under multiple stimulus conditions.

The traces in the Fig. 4 summarize the results of using Local (A) and Global (B) Fitting of eye movements to reconstruct the firing patterns of an MST neuron. As shown in Fig. 4A, the C.D.s were distributed between 0.41 to 0.79 (mean value, 0.65), indicating that the firing patterns at lower stimulus speeds were satisfactorily reconstructed, although the firing patterns at higher stimulus speeds were not. In Fig. 4B, the traces in each pair show that the MST firing patterns were not adequately reconstructed using Global Fitting. The C.D. was calculated at 0.58, indicating a nonlinear relationship between MST firing and ocular responses through the multiple stimulus speeds.

Using Local Fitting (shaded areas of Fig. 4C), 57% of the data from the MST (99/175) were reconstructed relatively well from eye movements. Using Global Fitting, however, the reconstructed firing patterns were not able to approximate to the observed firing patterns of most MST neurons

(71%, 25/35; unshaded areas of Fig. 4D). The results of the DLPN neurons were similar to those of the MST neurons. Using Local Fitting, 55% of the data from the DLPN (88/160) were reconstructed relatively well from eye movements, while Global Fitting produced C.D.s of 0.7 or higher in a small percentage of the DLPN neurons (31%, 10/32). It is clear from these results that this model for the eye movements accounted for the different neuronal responses of only a small portion of neurons in the MST and DLPN under the multiple stimulus speeds, using a single set of parameters.

As illustrated in Fig. 5, comparing the results of reconstructing the temporal firing patterns from eye movement for the MST and DLPN neurons and for the VPFL P cells revealed distinct differences. In this figure, the C.D.s are displayed for Global Fitting (the abscissa) and for Local Fitting (the ordinate). The filled circles represent VPFL P cells, and are distributed in the right upper quadrant of Fig. 5. It is clear that the temporal firing patterns of the P cells were satisfactorily reconstructed from the components of eye movements using the linear-regression model for both Local and Global Fitting. On the other hand, data points representing the DLPN (open triangles) and MST neurons (open squares) were distributed above the line of slope 1. This indicates that we were able to attain relatively good fittings for one-half of these neurons, using Local Fitting. On the other hand, when we used Global Fitting for the MST and DLPN neurons, the model adequately reproduced the firing patterns for only a small number of the neurons [C.D. $\geq$ 0.8 in 3/35 MST (8.6%) and 1/32 DLPN neurons (3.1%); C.D.

≥ 0.7 in 10/35 MST (33.3%) and 10/32 DLPN neurons (31.3%)]. However, as demonstrated above, Global Fitting was accurate for most of the P cells [C.D. ≥ 0.8 in 9/20 (45%); C.D. ≥ 0.7 in 17/20 P cells (85%)].

Estimated parameters of the model for eye movement

To characterize the global relationship between the neuronal firing patterns and the ocular responses, Global Fitting was applied under multiple stimulus conditions. By applying a threshold level of C.D. ≥ 0.7, we avoided unreliable parameters estimated from data sets with low C.D.s. The significance of each coefficient, determined by the t-test for the null hypothesis, was less than 0.02 in all units except one P cell, indicating that all the components for the units, except in one P cell, were significant in contributing to the firing frequency. The P value for that one P cell was 0.36, so we excluded that result from the following analysis, leaving 16 P cells for further statistical analysis. The mean time delay was 12.7 ± 6.8 (SD) ms for MST neurons and 11.8 ± 3.6 (SD) ms for DLPN neurons. These values were consistent with previous studies of the neural activity in the MST (Kawano et al. 1994) and the DLPN (Kawano et al. 1992) during ocular following. The mean time delay of the VPFL P cells was 7.2 ± 5.3 (SD) ms, which is near the latency period for electrical-stimulation-evoked eye movements (Shidara and Kawano 1993). This satisfies a basic requisite for the firing frequency to represent a motor command.

The coefficients estimated for neurons in each of the three areas (Fig. 6 and Table 1) reiterated the differences in the temporal firing patterns of the VPFL P cells and the neurons in the upstream structures. In Fig. 6, the frequency histograms of the coefficients estimated from the data of the MST neurons (A-C), the DLPN neurons (D-F), and the VPFL P cells (G-I) are shown on the same axis for each coefficient. The means of the acceleration coefficients (Figs. 6A, D, and G) in each of three areas are 0.120 ± 0.075 (SD) (spikes/s)/(deg/s^2) for the MST and DLPN neurons and 0.068 ± 0.039 (spikes/s)/(deg/s^2) for the VPFL P cells. The means of the velocity coefficients (Figs. 6B, E, and H) are 3.93 ± 2.13 (spikes/s)/(deg/s) for the MST neurons, 2.15 ± 0.71 (spikes/s)/(deg/s) for the DLPN neurons, and 2.32 ± 0.94 (spikes/s)/(deg/s) for the VPFL P cells. The means of the position coefficients (Figs. 6C, F, and I) are -21.4 ± 68.6 (spikes/s)/deg for the MST neurons, 5.0 ± 32.8 (spikes/s)/deg for the DLPN neurons, and -12.3 ± 5.6 (spikes/s)/deg for the VPFL P cells. The means of the acceleration coefficients for the MST and DLPN neurons were different from that for the VPFL P cells.

To compare components of the P cells with their counterparts in the motor neurons (Keller 1973), we examined the ratios of the coefficients. The mean ratio of the acceleration coefficient to the velocity coefficient (b/a) of the P cells was 50.3 ± 45.1, which was close to that of motor neurons (67.4, Table 1). On the other hand, the mean ratio of the acceleration coefficient to the position coefficient (c/a) was different and had a reversed sign (Table 1).

Likewise, the mean ratios of the coefficients in the MST and DLPN were different from those of the motor neurons and P cells, as the acceleration coefficient tended to be larger than that of the P cells. As was the case with Global Fitting, the results of Local Fitting also demonstrated the relationship between the neuronal firing patterns and the ocular responses. The means of the acceleration coefficients for the data sets of the MST and DLPN neurons were larger than that for the VPFL P cells in the local relationship between the neuronal firing patterns and the ocular responses.

The relationship between neuronal activity and retinal slip

To examine the relationship between retinal slip and firing frequency, we applied the linear-regression model for retinal slip to the temporal firing patterns using Eq. (1). The majority of the data from P cells (88%, 88/100) were satisfactorily reconstructed from retinal slip data using Local Fitting (C.D. $\geq$ 0.7, data not shown). Global Fitting, however, was accurate for only a small percentage of the VPFL P cells [C.D. $\geq$ 0.7 (7/20, 35%)].

The traces in Fig. 7 summarize the results of reconstructing the firing patterns of the same MST neuron as in Fig. 4 from retinal slip data using Local (A and C) and Global Fitting (B and D). As shown in Fig. 7A (Local Fitting), all the reconstructed firing patterns were very close to the observed data within each pair, and their C.D.s were distributed from 0.82 to 0.94 (mean value, 0.85), indicating good reconstruction at each of the five stimulus speeds. On the other hand, as shown in Fig. 7B (Global Fitting),

the reconstructed firing patterns were quite different from the observed data in each of the pairs. The C.D. was calculated at 0.35, indicating failed reconstruction of the five temporal patterns from retinal slip data using a single set of parameters (Fig. 7B). Using Local Fitting, the linear-regression model for retinal slip was applicable to a majority of the data in the MST [shaded area of Fig. 7C; C.D. $\geq$ 0.7 (130/175, 74%)]. As shown in Fig. 7D (Global Fitting), the C.D.s for a small percentage of MST neurons (22%, 8/35) were 0.7 or higher (shaded areas), indicating that most of the MST neurons were not adequately reconstructed from retinal slip data. The results of the DLPN neurons were similar to those of the MST neurons. The majority of the data in the DLPN (71%, 113/160) were satisfactorily reconstructed from retinal slip data using Local Fitting (C.D. $\geq$ 0.7). Using Global Fitting, however, the C.D.s for only a small percentage of DLPN neurons (25%, 8/32) were 0.7 or higher. These results suggest a linear relationship between the neuronal firing patterns and retinal slip only in local conditions (at each stimulus speed).

The results of firing pattern reconstruction from retinal slip data were similar among the MST, DLPN, and VPFL areas: First, the reconstructions from retinal slip data using Local Fitting were successful for much of the data from all three areas, and second, the reconstructions using Global Fitting were unsatisfactory.

Estimated parameters of the model for retinal slip data

To characterize the local relationship between neuronal response and retinal slip, we examined the significance of each coefficient by the t-test for the null hypothesis. The numbers of data sets classified by the P value of the t-test are listed in Table 2 (A-C). In the majority of the data sets for MST and DLPN neurons (73.7%, 129/175 and 80.6%, 129/160, respectively), the null hypothesis for the acceleration component was rejected. However, in one-half of the data sets of the VPFL P cells (49.0%, 49/100), the null hypothesis for the acceleration component was not rejected. These results suggest that the acceleration component is more significant for the firing patterns in the MST and DLPN neurons than for the firing patterns of P cells. On the other hand, the distribution of the P value for the other components (i.e., velocity and positional components) were similar among the three areas, indicating that these components contributed to the firing patterns in a similar manner. By applying a threshold of C.D. $\geq$ 0.7 and the t-test for the null hypothesis, the reliable parameters for 79 data sets of the MST neurons, 70 data sets of the DLPN neurons, and 21 data sets of the VPFL P cells underwent further statistical analysis. The means of the acceleration coefficients for the data sets of the MST and DLPN neurons and the VPFL P cells were 0.032 $\pm$ 0.036 (spikes/s)/(deg/s^2), 0.025 $\pm$ 0.035 (spikes/s)/(deg/s^2), and 0.005 $\pm$ 0.024 (spikes/s)/(deg/s^2), respectively. The means of the velocity coefficients were 3.81 $\pm$ 4.04 (spikes/s)/(deg/s) for the data sets of the MST neurons, 3.27 $\pm$ 3.19 (spikes/s)/(deg/s) for the data sets of the DLPN neurons, and 2.17 $\pm$ 2.18 (spikes/s)/(deg/s) for the data sets of the VPFL P

cells. The means of the position coefficients were 5.61 ± 13.54 (spikes/s)/deg for the data sets of MST neurons, -8.35 ± 35.57 (spikes/s)/deg for the data sets of the DLPN neurons, and -2.33 ± 32.55 (spikes/s)/deg for the data sets of the VPFL P cells. The means of the acceleration coefficients for the data sets of the MST and DLPN neurons were approximately five-fold greater than those for the data sets of the VPFL P cells; however, the means of the velocity coefficients for the data sets of the MST and DLPN neurons were similar to those for the data sets of the VPFL P cells. Thus, the acceleration component of retinal slip contributed more significantly to the temporal firing patterns in the MST and DLPN areas than it did to P cell firing in the VPFL.

Modeling check

We analyzed the temporal firing patterns of the cells in the MST, DLPN, and VPFL primarily using the model in Eq. (1) which represents the firing patterns by acceleration, velocity, and position of eye movement or retinal slip. However, it is possible that another model with fewer parameters may be more accurate than the model in Eq. (1) for defining temporal firing patterns. That is, it is possible that a parameter included in Eq. (1) may be unnecessary for accurate representation of the temporal firing patterns. We tested whether the firing frequency could be estimated by dropping any of the components, then examined the Cp-statistics values using all potential models including acceleration, velocity, and position.

In the model for eye movement using Local Fitting, the necessity of each component on the right side of Eq. (1) was examined by the t-test for the null hypothesis. The numbers of the data sets classified by the P value of the t-test are listed in Table 2 (D-F). In the majority of the data sets for all three areas [94.3% (165/175) for the MST, 98.1% (157/160) for the DLPN, and 95.0% (95/100) for the VPFL], the null hypothesis for the eye acceleration component was rejected (0.005 > P). The P values for the other components (i.e., eye velocity and positional components) were also small, and the null hypothesis for these components was rejected (0.05 > P). These results indicate that all of the parameters of Eq. 1 (acceleration, velocity, and positional components) for eye movement are necessary for adequate reconstruction.

To determine the best model, we examined the Cp-statistics values for all the data sets (175 for the MST, 160 for the DLPN, and 100 for the VPFL). The Cp-statistics value was low for Eq. (1) in most of the data sets: 82.9% (145/175) for the MST, 86.3% (138/160) for the DLPN, and 79.0% (79/100) for the VPFL. These results are consistent with those of the t-test and indicate that all of the components in Eq. (1) are required to describe the relationship between temporal firing patterns and eye movement.

In the model for retinal slip data using Local Fitting, the Cp-statistics values, were low for Eq. (1) in a majority of the data sets for the MST and DLPN neurons (64.6%, 113/175 and 66.9%, 107/160, respectively). On the other hand, in the VPFL P cells, Eq. (1) was accurate in 21/100 (21.0%) of the

data sets, but the best model was that in which the acceleration component for retinal slip was dropped; it was accurate in 71/100 (71.0%) of the data sets. These results are consistent with those of the t-test and indicate the following: (1) all of the parameters (acceleration, velocity, and positional components) of retinal slip data represented in Eq. (1) are required to describe the relationship between retinal slip and the firing patterns of the MST and DLPN neurons, and (2) whereas the other parameters are required to describe the relationship between retinal slip and the firing patterns of P cells, the acceleration component is not essential for most of the P cells.