Simulated Recruitment of Medial Rectus Motoneurons by Abducens Internuclear Neurons: Synaptic Specificity vs. Intrinsic Motoneuron Properties

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INTRODUCTION

The firing rates of ocular motoneurons (OMNs) in relation to steady-state eye position have been measured in a number of species (reviewed by, e.g., Carpenter 1988). An individual OMN only begins to fire when the position of the eye reaches a threshold value \( \theta \) in the ON direction of the relevant muscle. Above this threshold the firing rate varies linearly with eye position with slope \( K \). Within populations of motoneurons (MNs), \( \theta \) and \( K \) are related: the higher the threshold \( \theta \), the bigger the slope \( K \) (e.g., Van Gisbergen and Van Opstal 1989). Although these properties are well known, their origin is obscure. The projection from abducens internuclear neurons (INNs) to medial rectus MNs (MR-MNs) offers a unique opportunity for studying this problem by virtue of the extensive data available on position-related firing rates for both INNs and MR-MNs (see below).

The three main possibilities for the origin of OMN position-related discharges are as follows.

1) Each member of an OMN pool receives identical afferent input. Differences between the resultant firing rates are caused by differences in the intrinsic properties of the OMNs, for example current threshold for spike initiation (cf. Heckman and Binder 1990). This arrangement has been proposed for skeletal MN pools (Henneman et al. 1965) and termed the “common-drive” mechanism (De Luca and Erim 1994).

2) Differences between the firing rates of OMNs are determined solely by differences in their afferent input to OMNs. The intrinsic properties of OMNs do not vary systematically.

3) Both intrinsic OMN properties and afferent input contribute to differences between OMN firing rates, a combination that has been invoked to explain the effects of stimulating the mesencephalic locomotor region on the discharges of medial gastrocnemius MNs (Tansey and Botterman 1996).

One reason for trying to decide between these possibilities is that the eye position command to OMN pools is the result of outputs from prior stages in oculomotor signal processing, including the neural integrator (Robinson 1989). Characterizing the inputs to the OMN pool therefore helps to characterize the outputs of these prior stages, a step necessary for understanding how they work. For example, many models of oculomotor function treat the eye position command to ocular MN pools as a single, lumped variable that is linearly related to eye position (cf. Dean 1996). This treatment would give cause for concern if the common-drive hypothesis of the origin of OMN firing rates turned out to be incorrect.

Modeling techniques have long proved fruitful for studying the interaction between synaptic drive and intrinsic MN properties for skeletal MN pools (e.g., Rall 1955). The basis for recent studies has been the assumptions that, for steady-
state conditions, 1) an MN fires when the total effective synaptic current $I_s$ entering the cell exceeds its current threshold for spike initiation and 2) above threshold, firing rate is linearly related to $I_s$. These assumptions have been used to construct computer simulations of the firing rates of MN pools in response to synaptic drive from different afferent pathways (Binder et al. 1993; Heckman 1994; Heckman and Binder 1990, 1991, 1993a,b; Powers and Binder 1995a,b; Powers et al. 1992). The present study applies this framework to the responses of MR-MNs to conjugate eye-position-related inputs from INNs. One reason for choosing this system is the evidence suggesting that INNs are the major if not sole source of eye position signals in MR-MNs. INN axons travel rostrally from the abducens nucleus in the medial longitudinal fasciculus to their target MR-MNs in the oculomotor nucleus. Clinical studies of internuclear ophthalmoplegia and experimental studies in monkeys (e.g., Cogan 1970; Evinger et al. 1977; Gamlin et al. 1989b) have shown that interruption or inactivation of this pathway “essentially paralyses the ipsilateral medial rectus except for vergence” (Pola and Robinson 1978, p. 254).

Because OMNs are located within the skull, it is technically easier to record movement-related discharges from them than from MNs in the spinal cord (e.g., Robinson 1986). Thus, there are good data for position-related firing rates for both INNs and MR-MNs (Fuchs et al. 1988; Gamlin and Mays 1992; Gamlin et al. 1989a). This advantage was exploited in the present computer simulation by treating the INN and MR-MN pools as the input and output layers of a linear net (Widrow and Stearns 1985). On a given “training trial” the outputs of the simulation were compared with the desired outputs,” i.e., the real firing rates of MR-MNs. The difference between the actual and desired outputs was used as an error signal to change either the input weights from INNs to MR-MNs or properties of the MR-MNs (intrinsic thresholds and gains) so that the simulation produced firing rates closer to those observed experimentally. This is an example of the use of artificial neural nets to estimate the properties needed for real neurons to produce experimentally observed behavior without prejudice toward the issue of how those properties are derived biologically (Churchland and Sejnowski 1992; Dean 1996; Zipser 1992).

The neural net model of INNs and MR-MNs was trained under various constraints to investigate the following questions.

1) For identical INN input to every MR-MN (common drive), how do estimates of intrinsic OMN thresholds and gains from the simulation compare with experimental findings (e.g., Grantyn and Grantyn 1978)?

2) How are these estimates affected when the connecting weights between INNs and MR-MNs are allowed to vary?

Parts of this work have appeared previously in abstract form (Dean 1995).

METHODS

The methods are described in two parts: 1) the modeling of individual MNs and their incorporation into an artificial neural net and 2) the selection of experimental data for INNs and MR-MNs that were used both as input and training data for the net and for comparison with the results of the simulations.

Simulation: individual MNs

The method for calculating the output of an MN given its synaptic inputs and intrinsic properties was taken from Heckman and Binder (1990) and Binder et al. (1993). It is based on a simple neuronal model that neglects dendritic geometry, treats synapses as current sources and not conductance changes, and deals only with steady-state conditions (how far these simplifications apply to OMNs is considered in the discussion). The method assumes that an MN starts to fire, i.e., is recruited, when the rheobase current $I_b$ (current threshold for spike initiation) is exceeded by the effective synaptic current $I_s$.

1) $I_b$ is an intrinsic property of the neuron that derives from the neuron’s voltage threshold for spike initiation $V_t$ and its input resistance $R_i$ (Eq. 1)

$$I_b = \frac{V_t}{R_i}$$  \hspace{1cm} (1)

The $R_i$ itself depends on the specific membrane resistance of the neuron averaged over the relevant membrane area. For skeletal MNal pools, it appears that the −10-fold range in $I_b$ derives mainly from 2- to 3-fold variance in both soma size and membrane resistivity, with a relatively small contribution from voltage threshold (e.g., Gustafsson and Pinter 1984; Heckman and Binder 1990; Pinter et al. 1983).

2) $I_b$ (defined as the total current that reaches the soma) is primarily extrinsic. If each of a set of synapses on a simplified MN (Fig. 1A) has an input firing rate $F_i$ and a weight $w_i$, the total synaptic current delivered to the soma is the sum of the current delivered by each synapse (Eq. 2). The present simulation treats $I_b$ as identical to $I_{TOT}$, i.e., variables such as dendritic geometry that influence current transfer to the soma are neglected (Heckman and Binder 1990, p. 185–186).

$$I_{TOT} = \sum F_i \cdot w_i$$  \hspace{1cm} (2)

Parts of this work have appeared previously in abstract form (Dean 1995).

FIG. 1. A: diagram of model ocular motoneuron (OMN), indicating its intrinsic current threshold $I_b$ and frequency-current ($f-I$) slope $\gamma$. MN receives input from $F_1$, $F_2$, and $F_m$ afferent pathways, each of which fires at $F$, Hz and results through its synaptic weight $w_i$, nA/Hz in a postsynaptic current $F_i \cdot w_i$, nA. B shows how the sum effective synaptic current $I_{TOT}$ (nA) of these currents (Eq. 2) is related to the output firing rate $FR$ (Hz) of the model OMN as a function of $I_b$ and $\gamma$ (Eq. 3).
For $I_{th}$s that are above $I_{th}$, the firing rate $FR$ of the MN is assumed to be linearly related to the difference with slope $\gamma$ (Eq. 3, Fig. 1B).

$$FR = \gamma \cdot (I_{th} - I_{th})$$

Injected and synaptic currents are equivalent, $\gamma$ corresponds to the slope of what has been termed the f-I relation, where $f$ denotes MN firing rate and $I$ the magnitude of the injected current (Binder et al. 1993). As with spinal MNs (Binder et al. 1993), the current threshold for repetitive firing ($I_{th}$) is "slightly higher" than the $I_{th}$ for OMNs (Grantyn and Grantyn 1978, p. 263) and OMNs do not fire below a minimal firing rate ($f_{min}$) of 10–20 Hz (Fuchs et al. 1988). It is assumed here that the point ($f_{min} , I_{th}$) lies on the line of Eq. 3. If $f_{min} \approx 15$ Hz and $I_{th} \approx 30$ Hz/nA (see below), this assumption puts $I_{th}$ at $\approx 0.5$ nA greater than $I_{th}$, probably in agreement with the remark of Grantyn and Grantyn (1978). The effects of possible nonphysiological low firing rates in the model on the fit between model output and data are considered in the Discussion.

Simulation: neural net

The properties of the simulated individual MNs outlined above are similar to those of model neurons used in linear artificial neural nets (e.g., Anderson 1995). Accordingly, a two-layer artificial neural net was constructed (Fig. 2) with simulated MR-MNs as the output layer and INNs as the input layer. The main features of the net are as follows.

1) As is conventional, the artificial neurons in the input layer do no intrinsic processing but merely convey desired patterns of input to the output layer. In this case the desired patterns are the firing rates of INNs. Thus the method by which these firing patterns are generated from the fixation command $\phi$ need not be specified provided that the actual firing rates of INNs as a function of $\phi$ are known. In fact this relation is not known directly. However, in the properly calibrated system, the fixation command $\phi$ always produces the desired eye position $\phi$ (cf. Dean 1996). It is therefore possible to use the experimentally observed relations of INN firing rates to eye position, which are approximated by Eq. 4. $T_i$ is the threshold at which the $i$th INN begins firing

$$F_i = s_i(\phi - T_i) \text{ for } \phi > T_i$$

and $s_i$ is the slope of the straight line relating firing rate to eye position.

2) All input layer neurons connect to all output layer neurons via weights ($w_{ij}$, etc.), which in the present simulation are constrained to be positive or zero. The activation in the $j$th output neuron $a_j$ produced by a particular input pattern is given by Eq. 5. Because both $F$s and $w$s are positive or zero, so too are the activations. The activation term in Eq. 5 corresponds to the total synaptic current of Eq. 2 and thus, by the assumptions of the model, to $I_{th}$.

$$a_j = \sum F_i w_{ij}$$

3) All the output neurons have a bias term $B_j$ and a gain term $G_j$. Their outputs are calculated from Eq. 6

$$a_j = G_j(a_j + B_j) \text{ for } a_j + B_j > 0$$

$$= 0 \text{ for } a_j + B_j \leq 0$$

$B$ is constrained to be negative or zero, which corresponds to a positive $I_{th}$ in Eq. 3, and $G$ corresponds to the f-I slope $\gamma$ (this dual set of symbols is used to emphasize the distinction between empirically estimated quantities and their counterparts, which are manipulated within the model).

4) To train the network to produce the firing rates displayed by real MR-MNs, these were used as desired outputs of the model (Eq. 7). $t_j$ denotes the actual output of the $j$th MR-MN in response to the fixation command $\phi$ that produces the eye position $\phi$. $\theta_j$ is the firing rate threshold of the $j$th MR-MN and $K_j$ is the slope of its firing rate with respect to eye position. It should be emphasized that these are observed firing rate thresholds and slopes, not the intrinsic properties described above.

Comparison of desired and actual model outputs for a given eye position $\phi$ yields an error signal $e_j$ for the $j$th MR-MN (Eq. 8). Rules for altering model parameters that used this error signal

$$e_j(\phi) = t_j(\phi) - o_j(\phi)$$

were derived with the use of gradient-descent methods for fully linear nets (cf. Widrow and Stearns 1985), with adjustments for the nonlinearities in the model (Eq. 9–11).

$$\Delta G_j = \lambda_{G} \cdot e_j a_j B_j \text{ for } a_j + B_j \geq 0$$

$$\Delta B_j = \lambda_{B} \cdot e_j G_j \text{ for } a_j + B_j \leq 0$$

$$\Delta w_{ij} = \lambda_{w} \cdot e_j G_j \text{ for } a_j = 0$$

$\lambda_{G}$, $\lambda_{B}$, and $\lambda_{w}$ are learning rate constants whose values were assigned by a two-stage procedure. In the first stage, those parameters required by the overall design of the simulation to be kept constant were assigned learning constants of zero. For example, in the com-

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**Fig. 2.** Diagram of the artificial neural net used in the simulations. The $m$ input units, representing abducens internuclear neurons (INNs), each project to all $n$ output units, representing medial rectus MNs (MR-MNs) via the weights $w_{ij}$ to $w_{mn}$. Firing rates $F_i$ of the INNs in response to the (unknown) fixation command $\phi$ are given as a function of the eye position $\phi$ that results from $\phi$ with the use of the firing rate threshold $T$ and slope $s$ (Eq. 4). Output firing rates $o_i$ of the model MR-MNs in terms of their inputs, bias terms $B_i$, and slopes $G_i$ are given in Eq. 5 and 6. Model outputs can then be compared with real firing rates of MR-MNs to train the neural network to give accurate outputs.
mon-drive condition, \( \lambda_n = 0 \). Second, values of nonzero learning constants were determined by trial and error as those producing rapid learning without instability. The function of the learning rules was to minimize the mean square error \( E_i \) for each MR-MN over the training set of eye positions (Eq. 12)

\[
E_i = \sum s_i^2(\phi)
\]

The values in the training set were chosen at random from the ocular motor range of \( \pm 50^\circ \).

**Data: INNs**

The firing rates of INNs FSK88 and GGM89 with respect to steady-state eye position have been described by Fuchs et al. (1988) and Gamlin et al. (1989a). In both studies, the firing rates of individual INNs could be approximated by Eq. 4, with the values of the slopes \( s_i \) not significantly correlated with the thresholds \( T_i \). The two estimates of the mean value of the slopes were similar \( \{ n = 36, \text{mean value of } s = 4.6 \text{ Hz/deg (Fig. 5 in Fuchs et al. 1988) and } n = 25, \text{mean value of } s = 5.3 \text{ Hz/deg (Table 1 in Gamlin et al. 1989a)} \} \). However, the distributions of thresholds in the two studies were different (Fig. 3). This is reflected in the 13.4° gap between the mean thresholds of the two samples (\(-29.2^\circ \) in Fuchs et al. 1988; \(-15.8^\circ \) in Gamlin et al. 1989a) and in the proportions of neurons with thresholds greater than \(-20^\circ \) (5 of 36 in Fuchs et al. 1988; 16 of 25 in Gamlin et al. 1989a) (\( \chi^2, P < 0.0002 \)).

It is apparent that obtaining a representative sample of the INN population is difficult (possible reasons are considered in the DISCUSSION). In the present simulation, the effects of sampling were investigated by comparing three distributions: Fuchs et al. (1988), Gamlin et al. (1989a), and an artificial distribution with 25 neurons, the thresholds of which were evenly spread between the limits of \(-65^\circ \) and \(+25^\circ \) (giving a lowest threshold neuron of \(-61.5^\circ \) and a highest of \(+21.5^\circ \)) and the slopes of which were fixed at 5 Hz/deg.

**Data: MR-MNs**

1) The firing rates of a sample of 74 MR-MNs have been described by Gamlin and Mays (1992, their Table 1). As with INNs, their behavior could be approximated by Eq. 4, only in this case the slopes for conjugate eye position \( K_j \) varied with the thresholds \( \theta_j \) as is typical for OMNs (e.g., Van Gisbergen and Van Opstal 1989). The relation between the two is given in Eq. 13, taken from p. 67 of Gamlin and Mays (1992)

\[
K_j = 0.16j + 7.0
\]

The range of thresholds in Table 1 of Gamlin and Mays (1992) is \(-41 \) to \(+4^c\), which is somewhat smaller than the range of \(-60 \) to \(+25^\circ \) given for OMNs in two reviews (Keller 1981; Van Gisbergen and Van Opstal 1989). Possible reasons for this discrepancy are again considered in the DISCUSSION. For the purposes of the simulations, an artificial distribution of MR-MN thresholds was used, identical to that described for INNs. The slope values were assigned from Eq. 13. Because the behavior of any individual MR-MN in the model is independent of the behavior of the other MR-MNs (Fig. 2), this distribution allows the properties of the Gamlin and Mays distribution to be assessed by interpolation.

2) Although the intrinsic properties of primate MR-MNs appear not to have been measured, data are available for OMNs in cat. One set of in vivo measurements was carried out in the cat abducens nucleus by Grantyn and coworkers (Grantyn and Grantyn 1978; Grantyn et al. 1977), \( -6.6 \) to \(+8.3^\circ \) for identified MNs ranging from 1.2 to \(+6.7 \text{ M} \) \( (n = 47) \) (Grantyn and Grantyn 1978, p. 256). \( I_0 \) of OMNs had values roughly consistent with those of the \( R_s \), assuming a threshold depolarization of \( \sim 10 \text{ mV} \) in Eq. 2. Thus a mean \( R_s = 2.3 \text{ M} \) \( \Omega \) corresponded to mean \( I_0 = 4.7 \text{ nA} \) \( (n = 15) \). Neurons with a higher \( R_s \) (3–6 M\( \Omega \)) had a lower average \( I_0 \) (2.2 nA) than neurons with a lower \( R_s \) (1.2–2.9 M\( \Omega \)), which had an average \( I_0 \) of 6.3 nA. This again is consistent with Eq. 2, which suggests that the \( I_0 \) range is similar to the \( R_s \) range of five- to sixfold, i.e., \( \pm1.5 \) to \(+8.3 \text{ nA} \), assuming a depolarization threshold of 10 mV. However, Grantyn and Grantyn (1978) do not explicitly report an \( I_0 \) range. Nelson et al. (1986) obtained an \( I_0 \) range of 1–13 nA from trocheal MNs \( (n = 21) \), \( R_s \) range 1.95–7.17 M\( \Omega \), correlation between \( I_0 \) and \( R_s \) \( (R_s = 0.73) \). This is larger for the \( I_0 \) range that is used here for comparison with the results of the simulations.

Measurement of the steady-state firing rates in cat abducens MNs (Grantyn and Grantyn 1978) produced by injected currents gave a mean value for the \( f-I \) slope \( \gamma = 27 \text{ Hz/nA} \) \( (n = 11) \). Measurement of \( \gamma \) and \( R_s \) in the same cells showed that \( \gamma \) varied with \( R_s \) (Fig. 4) (plotted from Table 2 in Grantyn and Grantyn 1978) with a correlation coefficient of \( r = 0.713 \) \( (P = 0.018; \text{ although it should be noted that the number of data points is small}) \).

\[
\gamma = 4.573R_s + 15.641
\]

**RESULTS**

Simulations were run under two conditions. In the first, the input weights from INNs to MR-MNs (Fig. 2) were held constant \( (\lambda_n = 0, \text{Eq. 11}) \) and the MR-MN variables bias \( B \) and gain \( G \) were allowed to vary. The purpose of this procedure was to identify values of MR-MN \( I_0 \) and \( f-I \) slope necessary for the common-drive hypothesis (cf. INTRODUCTION) to account for the firing rate data. For the second
condition, the variables \( B \) and \( G \) were fixed \((\lambda_B = \lambda_G = 0, \text{Eq. 9 and 10})\) and the weights were allowed to vary (the specific-synapse model) to see what connections between INNs and MR-MNs were consistent with the firing rate data. This section describes the main results of the simulations. Relevant mathematical details are given in the APPENDIX.

**Fixed input weights**

An example of the results obtained from simulations under the fixed-weights condition is shown in Fig. 5. In this example, the artificial distribution of INN thresholds (described in METHODS) was used. The weight from each of the \( n = 25 \) INNs to each MR-MN was set at a value of 0.01, corresponding to a synaptic drive of 0.25 nA per Hz of averaged INN firing rates. In this version of the common-drive hypothesis each target MN receives the same synaptic drive irrespective of its intrinsic characteristics.

Figure 5A shows error scores, after training, as a function of MR-MN firing rate threshold \( \theta \). The errors were summed at 5° intervals over an oculomotor range of \( \pm 50° \) (Eq. 12). Figure 5A indicates that the error scores are higher for MNs with low \( \theta \)s, even though the scores were not adjusted to take account of the expected values of the firing rates, which are higher in high-\( \theta \) MR-MNs. Training with fixed weights was seemingly unable to produce a close fit between model and data for MR-MNs with \( \theta \) values less than about \( -25° \).

Figure 5B shows values of the bias variable \( B \) in relation to \( \theta \). The bias term was intended to correspond to intrinsic MR-MN threshold current \( I_R \). Two unrealistic features of the estimated \( I_R \) values are apparent. First, the values for high-\( \theta \) MR-MNs correspond to \( I_R \)s of up to 50 nA. Second, the values drop to 0 nA for MR-MNs with \( \theta \) values of less than about \( -35° \).

Finally, Fig. 5C plots the values of the gain \( G \) against \( \theta \). The gain term was intended to correspond to the slope \( \gamma \) of the straight line relating steady-state MR-MN firing frequency to input current (the \( f-I \) relation). The figure indicates that gain increases with increasing \( \theta \). This is unsurprising given that the slope \( K \) of firing rate versus eye position increases with \( \theta \) for OMNs. However, it is not consistent with the finding that for cat abducens MNs intrinsic gain \( \gamma \) is inversely related to intrinsic threshold \( I_R \) (see METHODS).

Each of the three features of the simulation results illustrated in Fig. 5 indicates a failure of the simulation to reproduce experimental data. The origin of these failures, and their possible remediation by improved choice of model parameter, are described in the next three sections.

**Errors**

One possible cause of the poor fit between the model firing rates and those observed experimentally for low-\( \theta \) MR-
MNs (Fig. 5A) is inappropriate choice of values for the weights connecting simulated INNs to MR-MNs in the model. However, altering the weights by a factor of 10 had no effect on the error curve (not shown). Examination of the model output for a low-θ MR-MN showed the likely root of the problem (Fig. 6A). The output of the model did not vary linearly with eye position, so that a very close match between model and data (see METHODS) for a low-θ MR-MN was precluded. The output of the model varied with eye position in the same manner as the massed INN input (Fig. 6B), and in both cases the nonlinearity reflects the recruitment of new inputs as eye position changes (details in APPENDIX, Errors in common-drive model).

A prediction of this explanation for the errors shown in Fig. 5A is that the shape of the error curve should vary with the distribution of INN firing rate thresholds. Figure 7A shows that this is the case by comparing the error curve for the artificial distribution with the curves from the distributions of Fuchs et al. (1988) and Gamlin et al. (1989a). The total INN firing rate from these distributions (assuming \( n = 25 \) neurons) is shown in Fig. 7A. Because in the Fuchs et al. (1988) distribution many INNs are recruited in the range of \(-40 \) to \(-30^\circ\) (Fig. 3), the slope is more uniform above \(-30^\circ\) than that of the artificial distribution, and the errors of the model are correspondingly reduced. In contrast, in the Gamlin et al. (1989a) distribution most of the recruitment takes place above \(-30^\circ\) (Fig. 3), which contributes toward higher error scores for MR-MNs with firing rate thresholds less than \(-30^\circ\).

**MR-MNs: \( I_{RS} \)**

The unrealistic range of the \( B \) values apparent in Fig. 5B could have resulted from two deficiencies in the model rather than from any inadequacy of the common-drive mechanism.

1) Because of the nonlinearity in the summed INN input, the model’s attempts to find the best fit to the data produced impossible values of bias, i.e., \( B = 0 \) for MR-MNs with low firing rate threshold \( \theta \) (Figs. 5B and 6A). It is possible to overcome this problem with the use of the summed INN input (details in APPENDIX, Intrinsic current thresholds in common-drive model), which gives the estimates for \( I_{RS} \) values shown in Fig. 8A.

2) The actual values of the \( I_{RS} \) estimates are determined by the value of weight term, which was chosen arbitrarily as 0.01. It can be seen from Fig. 8A that, in comparison with data from cat abducens MNs (see METHODS), setting \( w = 0.01 \) produces

**FIG. 6.** A: comparison of experimental data and simulation results for MR-MN \#8, with firing rate threshold \( \theta = -37.3^\circ \). B: summed firing rates of simulated INNs (\( n = 25 \), artificial distribution) as a function of eye position.

**FIG. 7.** A: summed firing rates of simulated INNs (\( n = 25 \)) for 3 different distributions as a function of eye position. Actual output of the Fuchs et al. (1988) distribution (FSK88), which was from \( n = 36 \) INNs, has been multiplied by 0.694 (\( = 25/36 \)) for comparability with the other 2 distributions. \( B \): error scores from the equal-weight version of the common-drive mode, as a function of MR-MN firing rate threshold \( \theta \), for 3 different INN distributions. GGM89, Gamlin et al. 1989a distribution.
for each INN distribution, to give an \( I_R \) estimates that are generally higher than the 1–13 nA recorded experimentally. Appropriate choice of weights (details in APPENDIX, Intrinsic current thresholds in common-drive model) removes this mismatch and gives the \( I_R \) estimates shown in Fig. 8B (which uses an ordinate scaled logarithmically to show the values of \( I_R \) for low \( \theta \)s more clearly).

It is apparent from Fig. 8B that, even after the two problems in the model have been removed, the range of \( I_R \) values required by the equal-weight version of the common-drive hypothesis still tends to be higher than that observed experimentally. The precise values depend on both the INN and MN distributions used in the simulation: for example, if the conservative range of \(-40 \) to \(+5^\circ\) is taken for the MR-MN \( \theta \)s (see METHODS), the value of the ratio is 44 for Fuchs et al. (1988), 226 for Gamlin et al. (1989a), and 8.3 for the artificial INN distribution. More importantly, these values are underestimate because the equal-weight version of the common-drive hypothesis needs to be altered to account for the experimental data on the f-I slopes of OMNs.

**MR-MNs: f-I slopes**

Measurements from cat abducens MNs indicate that the slope \( \gamma \) of the f-I relation is inversely related to \( I_R \) (see METHODS). In contrast, Fig. 5C shows that the model’s estimates for \( \gamma \) increase with MR-MN firing rate thresholds, as do the estimates for \( I_R \) (Fig. 5B). The MR-MNs in the model, therefore, have \( \gamma \)s that increase with \( I_R \), as can be seen in Fig. 9, which plots the \( \gamma \) estimates directly against the (uncorrected) \( I_R \) estimates for the three INN distributions. It is possible to avoid this problem by adopting a different version of the common-drive hypothesis in which the weights from INNs to MR-MNs are larger for MR-MNs with higher firing rate thresholds. For the simulations it was decided to choose weight values that kept \( G \) constant, rather than allowing it to vary inversely with \( B \), for two reasons. One was that Eq. 14 is derived from a small number of points, and studies with larger numbers of spinal MNs suggest that \( I_R \) and \( \gamma \) are largely independent (see DISCUSSION). The second reason was the practical difficulty of calculating weight values that gave appropriate covarying values of \( B \) and \( G \). The values for the weights required for \( \gamma \)s that do not vary with MR-MN properties can be estimated (APPENDIX, f-I slopes in common-drive model) given the constraint that the weights to the MR-MN with the median firing rate threshold (\( \theta = -20^\circ \)) are set to give an \( I_R \) of 5 nA (cf. Fig. 8B).

The results of training the model with the artificial INN distribution, and with the weights set to the required values \((w = 0.0018 \text{ for MR-MN with } \theta = -50, \text{ to } w = 0.0062 \text{ for MR-MN with } \theta = +20^\circ\)) are shown in Fig. 10. Figure 10A compares the estimates of \( \gamma \) with the new and old weights and shows that the new weights do abolish the increase of \( \gamma \) with \( \theta \), although the nonlinearity of the INN input prevents perfect compensation at low \( \theta \)s. The model’s estimates of \( I_R \) (calculated as above to avoid the nonlinearity problem) are shown in Fig. 10B. The effect of altering the weights is to increase the estimated ratio of \( I_R \) values (APPENDIX, f-I slopes in common-drive model): for the range of MR-MN firing rate thresholds \( \theta = -40 \) to \(+5^\circ\), the estimates are 100 (Fuchs et al. 1988), 4,750 (Gamlin et al. 1989a), and 19 (artificial INN).

The implication is that the version of the common-drive
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to MR-MNs were fixed and independent of the properties of the parent INN, three problems were revealed.

1) The nonlinearity of the massed INN input to MR-MNs with low firing rate thresholds prevented a close fit between model output and experimental data for these MNs.

2) For the equal-weight condition, the estimated f-I slopes increased with $I_R$, contrary to measurements in cat.

3) Altering the model weights to counteract this problem produced a range of MR-MN $I_R$s greater than that observed experimentally in cat trochlear MNs.

These problems were found with both experimentally obtained distributions of INN thresholds and with an artificial distribution. They are therefore unlikely to be the result of sampling artifacts.

**Fixed intrinsic properties: synaptic weights variable**

In this condition, the variables $B$ and $G$ were fixed ($\lambda_B = \lambda_G = 0$, Eq. 9 and 10), and the weights were allowed to vary, to see what connections between INNs and MR-MNs would be consistent with experimental measurements of INN and MR-MN firing rates. The results shown in Fig. 11 were

![Fig. 10. Version of the common-drive model with bigger weights on MR-MNs with higher firing rate thresholds $\theta$. A: estimates of the f-I slope $\gamma$ (corresponding to model parameter $G$) plotted against MR-MN firing rate threshold $\theta$ for 3 different INN distributions. Weight values have been adjusted to give, after training, estimates of $\gamma$ that are roughly independent of $\theta$ (details in text). B: estimates of $I_R$ (corresponding to model parameter $-B$) as a function of MR-MN firing rate threshold $\theta$ for the 3 different INN distributions shown in A. Vertical lines: range of MR-MN $\theta$ values reported by Gamlin and Mays (1992), i.e., $-40$ to $+5^\circ$.

model that gives more realistic values for the f-I slope $\gamma$ produces estimates of the MR-MN $I_R$ range that are greater than the 13-fold found experimentally for cat abducens MNs. In fact the estimates obtained were conservative: weight values were chosen to make the values for $\gamma$ independent of $I_R$ (see above) rather than to vary inversely with them, and the range for MR-MN firing rate threshold $\theta$ of $-40$ to $+5^\circ$ is almost certainly too low (see DISCUSSION). Even so, the estimates from the model were too high, and in the case of the experimental INN distributions very markedly so (100- and 4,750-fold vs. 13-fold). The extremely high value of 4,750 for the Gamlin et al. (1989a) distribution follows from the distribution containing only one INN with firing rate threshold $T < -40^\circ$: but even for a reduced MR-MN $\theta$ range of $-30$ to $+5^\circ$, the estimated $I_R$ range is still high at 64-fold.

**Fixed weights: summary**

When the neural network shown in Fig. 2 was trained under the constraint that the weights from simulated INNs

![Fig. 11. A: error scores from the specific-synapse model plotted against firing rate threshold $\theta$ of the simulated MR-MNs, for the artificial INN distribution. Error scores from the common-drive model (Fig. 5A) are shown for comparison. In the specific-synapse model the parameter $B$ (corresponding to $-I_R$) was set to $-0.5$ nA and the parameter $G$ (corresponding to the f-I slope $\gamma$) was set to 10 Hz/nA. B: size of weights on different MR-MNs (specified by firing rate threshold $\theta$) plotted against firing rate threshold of their INN of origin. Weights of size 0 are not plotted.
obtained with the artificial INN distribution, with the bias term $B$ set for all MR-MNs to -0.5 and the gain term $G$ to 10. Figure 11A compares the error scores obtained after training the model in this condition with those obtained after training in the fixed-weights condition (Fig. 5A). Allowing weights to vary greatly reduces the error scores for MR-MNs with low $\theta$s. The distributions of weights that achieved this result are shown for selected MR-MNs in Fig. 11B. The main feature of these distributions is that the effective inputs to a particular MR-MN only arise from INNs with similar firing rate thresholds. This restriction solves the nonlinearity problem associated with massed INN input. Two other features of the weight distributions are that the size of the weights tends to increase with MR-MN firing rate threshold $\theta$ and that the shape of the weight distribution is different for MR-MNs with $\theta$s near the top or bottom of the range than for MR-MNs with midrange $\theta$s.

Values of intrinsic MR-MN properties

The particular values chosen to represent intrinsic MR-MN properties used in the simulation of Fig. 5 (i.e., corresponding to $I_R = 0.5$ nA, $\gamma = 10$ Hz/nA) enabled a good fit to be obtained between model output and experimental data. However, there are restrictions on the values that will do this. These are determined by the range of INN firing rate thresholds (see Appendix, Weight values and intrinsic OMN properties). For the two experimentally obtained INN samples used in the simulations, it is possible to estimate the range of MR-MN intrinsic properties required for a given range of MR-MN $\theta$s. For the Fuchs et al. (1988) distribution, a $-BG$ value of 100 Hz covers the $\theta$ range of $-30$ to $+20^\circ$. A 10-fold range of $-BG$ (from 10 to 100 Hz) covers the $\theta$ range of $-50$ to $+20^\circ$. [For comparison, the mean value of $I_R \times \gamma$ reported for cat abducens MNs by Grantyn and Grantyn (1978) was 4.7 $\times$ 27 = 127 Hz.] For the Gamlin et al. (1989a) distribution, a $-BG$ value of 100 Hz covers the $\theta$ range of $-20$ to $+18^\circ$; a 13-fold range of $-BG$ (from 10 to 130 Hz) covers the $\theta$ range of $-40$ to $+20^\circ$.

These estimates were checked by running simulations. Data for the Fuchs et al. (1988) distribution are shown in Fig. 12. In this simulation, the variable $G$ was kept constant at a value of 10: $B$ was made to vary linearly with $\theta$ such that $B = -1$ when $\theta = -50^\circ$ and $B = -10$ when $\theta = +20^\circ$ (positive $B$ values generated by this procedure were replaced with $B = -0.001$). Figure 12A indicates that allowing the weights to vary with this set of $B$ and $G$ values markedly reduced errors scores in comparison with the fixed-weights condition. Figure 12B shows, for selected MR-MNs, the weight distributions that produced the good fit between model and data. As expected from the analysis in Appendix, Weight values and intrinsic OMN properties, the weights on the high- and low-$\theta$ MR-MNs came from a single INN. In contrast, a substantial number of INNs contributed to the midrange MR-MNs. Qualitatively similar results were obtained for the Gamlin et al. (1989a) distribution (Fig. 13). As with the Fuchs et al. (1988) simulation, the variable $G$ was kept constant at a value of 10. $B$ varied linearly with $\theta$ such that $B = -1$ when $\theta = -37^\circ$ and $B = -13$ when $\theta = +20^\circ$ (positive $B$ values generated by this procedure were replaced with $B = -0.001$). Again, error scores were much reduced in this simulation compared with those produced in the fixed-weights condition (Fig. 14A). (No condition eliminates errors for MR-MN $\theta < -40^\circ$, because $-40^\circ$ is the lowest INN firing rate threshold in the Gamlin et al. 1989a sample.) As with the Fuchs et al. (1988) simulation, the shape of the weight distributions that produced the improved fit varied with MR-MN $\theta$ (see next section).

The differences between the common-drive and specific-synapse models regarding required $I_R$s are summarized in Fig. 14. This figure shows the required $I_R$ range for different INN distributions and for a restricted (Fig. 14A) and wider (Fig. 14B) distribution of MR-MN firing thresholds $\theta$. The restricted MR-MN $\theta$ range is $-40$ to $+5^\circ$ for the artificial and Fuchs et al. (1988) distributions and $-30$ to $+5^\circ$ for the Gamlin et al. (1989a) distribution. The reduced $\theta$ range for the Gamlin et al. (1989a) distribution was chosen because of the small number of INNs in that distribution that have firing rate thresholds less than $-30^\circ$. The $I_R$ ranges are based on the assumption that the value of the $f$-$f$ slope $\gamma$ is (roughly) constant and independent of the value of $I_R$ (cf. Fig. 10). It can be seen that for each of the five parameter combinations illustrated, the common-drive model required an $I_R$ range greater than the 13-fold found for cat abducens MNs, whereas the specific-synapse model required an $I_R$ range less than or approximately equal to it.
As training proceeds, the distribution both narrows (so that the peak weights become larger) and becomes asymmetric, with weights from INNs with thresholds greater than $-20^\circ$ dropping out. Training was stopped after 7,000,000 trials (error score 0.014). An important point is that the performance of the simulated MR-MN after 2,000 trials was very close to that observed experimentally (Fig. 15B). As in the common-drive model, inputs from INNs with firing rate thresholds greater than that of the MR-MN do introduce nonlinearity to the response, but the effect is very small (cf. DISCUSSION).

For these two reasons there is a variety of receptive-field "shapes" possible for MR-MNs with firing rate thresholds toward the middle of the distribution.

**DISCUSSION**

The purpose of this study was to investigate the origin of conjugate eye-position-related discharges in ocular MNs by modeling the well-characterized projection from INNs to MR-MNs. Two main versions of the model were compared. In one, the common-drive model, each MR-MN received identical synaptic input from every INN. In the second, the specific-synapse model, the weights between individual

**Fig. 13.** As in Fig. 11, for the INN distribution of Gamlin et al. (1989a).

**Distributions of synaptic weights**

Figures 11B, 12B, and 13B show that, in the specific-synapse model, MR-MNs with either high or low firing rate thresholds $\theta$ receive inputs from a small number of INNs with similar firing rate thresholds. By analogy with the receptive fields of sensory neurons, these simulated MNs could be said to have very restricted receptive fields from the INN pool. The input stream from INNs to MR-MNs is channeled rather than lumped at the extremes of the distribution of firing rate thresholds.

Figures 11B, 12B, and 13B also show that, for MR-MNs with firing rate thresholds closer to the middle of the distribution, the pattern of INN weights is more variable. The main reason for this is indicated in the APPENDIX, Weight values and intrinsic OMN properties. There are two equations that need to be satisfied for realistic MR-MN firing rates to be produced, and for MR-MNs with firing rate thresholds away from the edges of the distribution these equations have more than two unknowns (i.e., weights). The equations do not therefore specify a unique combination of weight values.

There is also a second reason for weight variability, which is illustrated in Fig. 15. Figure 15A shows the distribution of weights onto a midrange simulated MR-MN (firing rate threshold $\theta = -20^\circ$) for different amounts of training. After 2,000 trials (error score 559), the distribution is broad and roughly symmetrical about INN firing rate threshold of $-20^\circ$.

As training proceeds, the distribution both narrows (so that the peak weights become larger) and becomes asymmetric, with weights from INNs with thresholds greater than $-20^\circ$ dropping out. Training was stopped after 7,000,000 trials (error score 0.014). An important point is that the performance of the simulated MR-MN after 2,000 trials was very close to that observed experimentally (Fig. 15B). As in the common-drive model, inputs from INNs with firing rate thresholds greater than that of the MR-MN do introduce nonlinearity to the response, but the effect is very small (cf. DISCUSSION).

For these two reasons there is a variety of receptive-field "shapes" possible for MR-MNs with firing rate thresholds toward the middle of the distribution.

**Fig. 14.** Estimates from the common-drive and specific-synapse models of range of MR-MN $I_R$ (corresponding to model parameter $-B$) required to produce the observed range of MR-MN firing rate thresholds $\theta$. A: for a restricted range of $\theta$ ($-40 \rightarrow +5^\circ$ for the artificial and Fuchs et al. 1988 distributions; $-30 \rightarrow +5^\circ$ for the Gamlin et al. 1989a distribution). Dotted line: $I_R$ range of 13, as found for cat trochlear MNs by Nelson et al. (1986). B: for a wider range of $\theta$. Dotted line as in A.
described in the INTRODUCTION, the simulations did not support the first (the common-drive mechanism), but were consistent with the second (synaptic specificity only) and third (synaptic specificity combined with intrinsic OMN properties).

Three features of the modeling results are discussed: their dependence on the assumptions used to construct the models, their congruence with experimental findings, and their implications.

Assumptions used in the model

Two major assumptions used in building the model were that the INN input to MR-MNs is the only important input for generating eye-position-related discharges and that the simplifications successfully used for modeling spinal MNs are also applicable to ocular MNs.

INPUTS TO MR-MNs. The main justification for concentrating on the INN input to MR-MNs was the clinical and experimental evidence that, after interruption of this input by damage to the medial longitudinal fasciculus, adduction beyond the midline is lost during conjugate movements (e.g., Cogan 1970; Evinger et al. 1977; Gamlin et al. 1989b). This evidence suggests that the excitatory eye position signals conveyed to MR-MNs via the ascending tract of Deiters from neurons in the ipsilateral ventral lateral vestibular nucleus (Baker and Highstein 1978; Highstein and Baker 1978; Highstein and Reisine 1981; McCrea et al. 1987; Reisine et al. 1981), which is spared by medial longitudinal fasciculus interruption, “are insufficient by themselves to strongly activate the medial rectus extraocular muscle” (Reisine et al. 1981, p. 156). Moreover, the eye position signals carried in the ascending tract of Dieters appear to be broadly similar.

INNs and MR-MNs varied. The results of the simulations indicated that the common-drive model faced three difficulties.

1) The simulated discharges of MR-MNs with low firing rate thresholds did not vary linearly with eye position.

2) In the simplest version of the common-drive model, which had identical synaptic weights on each MR-MN, the intrinsic f-I slopes of the simulated MR-MNs increased with current threshold.

3) To avoid this increase, the weights on high-current threshold MR-MNs had to be made larger than those on MR-MNs with low-current thresholds. In the adjusted common-drive model, the required range of intrinsic MR-MN current thresholds was much greater than that found experimentally for cat abducens MNs.

In the specific-synapse model, values of synaptic weights were obtained that overcame each of these difficulties. For some parameter values in the model, synaptic specificity alone was sufficient to produce realistic MR-MN firing rates: for others a contribution from intrinsic MR-MN properties was also required. Thus, of the three possible arrangements

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**FIG. 15.** A: size of weights on a simulated MR-MN with firing rate threshold \( \theta = -20^\circ \), plotted against firing rate threshold of their INN of origin, after different numbers of training trials. Weights of size 0 are not plotted. Error scores: 2,000 trials, 559; 20,000 trials, 77.1, 200,000 trials, 12.3, 7,000,000 trials, 0.014. B: comparison of experimental data and simulation results for MR-MN firing rates. Model performance is shown after 2,000 and 7,000,000 trials of training.
even greater than estimated here (cf. Fig. 3 in Baker et al. 1981). If, on the other hand, the prepositus input were distributed differentially to target MR-MNs, it could take over some of the synaptic specificity assigned by the present model to the INN projection alone. This would leave the broad conclusion concerning the need for synaptic specificity unaltered, but would raise important questions about its precise origins.

A third source of eye position signals to MR-MNs is related to the degree of convergence of the two eyes (Gamlin and Mays 1992; Mays and Porter 1984) and originates from “near response” cells located just dorsal and lateral to the oculomotor nucleus (Judge and Cumming 1986; Mays 1984; Zhang et al. 1991, 1992). These signals were ignored in the present simulations, dealing as they did only with conjugate eye positions and implicitly assuming zero vergence. Nonetheless, at zero vergence the near-response cells provide a tonic excitatory drive to MR-MNs (Zhang et al. 1992). This could prove to be important for estimates of intrinsic threshold values, because it has been shown for spinal MNs that appropriately distributed tonic excitatory drive can powerfully reinforce a recruitment order based on intrinsic MN properties (Heckman and Binder 1993b). However, electrophysiological evidence indicates that the vergence drive to an MR-MN is only weakly related to its conjugate drive. The firing rates of MR-MN cells vary linearly with degree of vergence above their thresholds, and the slope $K_v$ of this line for an individual MR-MN can be compared with its slope $K_c$ for conjugate eye position (called simply $K$ in the present study). The correlation between the two is 0.31 (Mays and Porter 1984). In addition, existing data (Zhang et al. 1992) can be used to estimate the synaptic drive to MR-MNs at zero vergence, giving an approximate value of 0.5 nA (calculation based on equations in APPENDIX, Errors in common-drive model). Given the probable existence of an inhibitory input to MR-MNs from the nucleus prepositus hypoglossi, the neglect of this weak tonic excitatory input appears reasonable at this early stage of modeling.

**INTRINSIC PROPERTIES OF MR-MNS.** The second major assumption underlying the model was that OMNs could be treated in the simplified manner that has proved successful for spinal MNs (Heckman 1994; Heckman and Binder 1990, 1991, 1993a, b). “The simplest model of how synaptic inputs control MN discharge posits that they simply deliver current to the MN’s spike generating conductances and thereby alter the discharge rate in accord with the cell’s intrinsic frequency-current ($f-I$) relation” (Binder et al. 1993, p. 1028). Treating spinal MNs as if they were platonic neurons (Llinás 1988), that is, neglecting any nonlinearities produced by dendritic geometry or spike-generating conductances, appears empirically justified under some steady-state conditions. In particular, the effective synaptic current $I_s$ (defined as the total current that reaches the soma) modulates firing rates in a manner reasonably predictable from the effects of injected currents (Powers and Binder 1995a; Powers et al. 1992).

The adapted response of OMNs to injected currents is an increase in firing rate linearly related to current amplitude over a wide range of firing rates up to 10 times higher than those observed in spinal MNs (Baker and Precht 1972; Grantyn and Grantyn 1978; Remmel and Marrocco 1975). This and other considerations such as the lack of development of the dendritic tree suggested to Grantyn and Grantyn (1978) that abducens MNs represented a separate, specialized cell type compared with lumbar alpha-MNs, with the primary function of adding together commands already computed at the premotor level. Consistent with this proposed function, “(t)he mechanisms of frequency regulation in LR-MNs are comparable to those described for a particular type of dorsal spino-cerebellar tract neuron.... Such a similarity to relay cells may reflect a specialization of oculomotor MNs for faithful and efficient transmission of signals generated by premotor interneurons” (Grantyn and Grantyn 1978, p. 270). But, in opposition to these conclusions, other workers have emphasized the complexities of OMN dendritic morphology and electrical properties (Bras et al. 1987; Deschênes et al. 1979; Durand et al. 1994). For example, N-methyl-D-aspartate (NMDA) receptors appear to mediate highly nonlinear changes in the firing patterns of rat abducens MNs (Durand 1991, 1993). As far as the present model is concerned, an important point is that iontophoretic application of the NMDA blocker aminophosphonovalerate to abducens MNs in alert cats does not alter the firing rate parameters $\theta$ and $K$ (Cheron et al. 1994). It is possible that NMDA receptors on OMNs are involved not in steady-state behavior but in processing transient signals or in the adjustments required during development (see below) or recalibration.

To summarize, the present model is intended only for highly restricted conditions (steady-state operation) and has been used to draw a very general conclusion (synaptic specificity is necessary). Because of these limitations, the assumptions used in building the model appear to be justified. However, an improved version of the model would need to take into account possible contributions to synaptic specificity from projections to MR-MNs besides the one from INNs. In particular, the role of the putative inhibitory projection from the nucleus prepositus hypoglossi needs to be addressed.

**Evidence relevant to simulation results**

**PROBLEMS WITH COMMON DRIVE.** The first problem to appear with the common-drive model was that the firing rates of simulated MR-MNs with low $\theta$s did not vary linearly with eye position (Fig. 6A). The reason is that in this model each MR-MN receives input from all the INNs and summed INN output necessarily varies nonlinearly with eye position as a result of recruitment (Fig. 7A). However, it is unlikely that the mild degree of nonlinearity observed in the simulations would be in conflict with experimental evidence. For example, the line of best fit for the model unit illustrated in Fig. 6A gives a correlation coefficient of 0.98. This is very close to the average correlation coefficient of 0.99 for abducens MNs and INNs (Fuchs et al. 1988). In addition, real OMNs start firing at a steady minimum firing rate of 10–20 Hz (Fuchs et al. 1988). Elimination from Fig. 6A of the points corresponding to firing rates $<$20 Hz increases the correlation coefficient to 0.991.

The second problem that emerged with the common-drive model was that the estimated $f-I$ slope $\gamma$ of its simulated
MR-MNs increased with current threshold $I_R$ (Fig. 9). This relationship arises because the firing rate slope $K$ of MR-MNs increases with their firing rate threshold $\theta$. If all synaptic weights are equal, the only way $K$ can increase with $\theta$ is if $\gamma$ increases with $I_R$ (APPENDIX, f-1 slopes in common-drive model). Although there have been hints that such a relationship might obtain for spinal MNs (Kernell 1966), it appears to hold at best over a limited range of $R_{\text{syn}}$ (Schwindt 1973), and computer simulations of spinal MN pools typically use fixed values for $\gamma$ (e.g., Binder et al. 1993; Heckman 1994). Moreover, the low values of $\gamma$ for spinal MNs compared with most other mammalian neurons suggest that they are specially adapted to produce sustained low rates of firing and are therefore atypical (Schwindt and Crill 1989, al. 1988; Gamlin et al. 1989a) that describe significantly different populations (Fig. 3). Studies of burst-tonic units in the medial longitudinal fasciculus report yet a third distribution [$n = 20; T_{\text{min}} = -65^\circ, T_{\text{max}} = -15^\circ$ (King et al. 1976) and $n \approx 10; \theta_{\text{min}} = -64^\circ, \theta_{\text{max}} = -10.7^\circ$ (Pola and Robinson 1978)].

Disagreement over firing rate threshold ranges also surfaces in two accounts of identified primate INNs (Fuchs et al. 1988; Gamlin et al. 1989a) that describe significantly different populations (Fig. 3). Studies of burst-tonic units in the medial longitudinal fasciculus report yet a third distribution [$n = 20; T_{\text{min}} = -65^\circ, T_{\text{max}} = -15^\circ$ (King et al. 1976) and $n \approx 10; \theta_{\text{min}} = -64^\circ, \theta_{\text{max}} = -10.7^\circ$ (Pola and Robinson 1978)].

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common-drive model is ≈5 times greater than the 13-fold estimate for cat OMNs.

3) A crucial requirement of the common-drive model is that the $I_{K}$ of an OMN pool must vary directly with the firing rate thresholds $\theta$. This requirement holds independently of the strengths of the motor units involved (Dean 1996). Again, in the absence of any direct measurements of $I_{K}$ it is necessary to rely on indirect measures. As far as soma size in primate abducens nucleus is concerned, McCrea et al. (1986) could find no clear relation between firing rate threshold and soma size, or proximal dendritic volume ($n = 6$). They concluded that “the size of the soma and the size of the proximal dendrites of motoneurons and internuclear neurons are poorly correlated with either their threshold for recruitment or tonic eye position sensitivity.... The structural characteristics responsible for the recruitment threshold and tonic eye position sensitivity are probably better related to factors that are not immediately apparent at the light microscopic level such as the relative weight and distribution of different inputs, or idiosyncratic membrane characteristics” (p. 307). Another indicator used for $I_{K}$ has been conduction velocity, itself an indirect measure of soma size (Eq. 3). Conduction velocity is inversely related to $R_{s}$ in cat OMNs ($r = -0.73$ in Grantyn and Grantyn 1978; $r = -0.74$ in Nelson et al. 1986). It is not, however, closely related to firing rate threshold in monkeys (Fuchs et al. 1988) ($n = 7$, $r = 0.24$ for firing rate threshold versus latency of antidromic stimulation, p. 1888). Although in both these studies the sample size is small, it seems likely that the very strong relationship between firing rate and intrinsic thresholds required by the common-drive model would have been apparent with such numbers.

To summarize this section on observed and simulated $I_{K}$ ranges in primate MR-MNs, the general conclusion is that the $I_{K}$ ranges required by the common-drive model are probably larger than those observed experimentally, even allowing for the current uncertainties in INN and MR-MN sampling and in $I_{K}$ estimation itself. This conclusion is also consistent with the evidence suggesting at best a weak relation between $I_{K}$ and $\theta$ in primate OMNs.

SYNAPTIC SPECIFICITY. The final conclusion drawn from the simulation results was that the threshold problem can be resolved by allowing the synaptic weights between INNs and MR-MNs to vary such that an individual INN projects to some MR-MNs but not others. In this version of the model, each MR-MN has in effect a receptive field of inputs from selected INNs. The simulation results indicate that, given the assumptions discussed above, these restricted receptive fields are necessary to account for the transformation of INN firing rate patterns into MR-MN firing rate patterns. This conclusion is independent of the origin of the experimentally observed INN firing rates (although INNs themselves may also have receptive fields; see next section).

Anatomic evidence points to some kind of selective projections onto MR-MNs. In primates these particular OMNs have a distinctive organization, being arranged in three subgroups within the oculomotor nucleus (see also Augustine et al. 1981; Büttner-Ennever 1981; Porter et al. 1983). In the terminology of Büttner-Ennever and Akert (1981), subgroup A is located ventrally and ventrolaterally and contains medium sized MR-MNs (mean diameter 26 µm). Subgroup B lies dorsally in the caudal third of the oculomotor nucleus and contains slightly larger MR-MNs (mean diameter 30 µm). Subgroup C lies in the dorsomedial corner of the oculomotor nucleus, outside the “classical” boundary of large MNs. It contains the smallest MR-MNs (mean diameter 18 µm), which alone are labeled after injections of retrograde tracer into the orbital layer of the medial rectus muscle. The grouping, which is more pronounced than that observed in cat (e.g., Miyazaki 1985), suggests some form of functional specialization among MR-MNs (Büttner-Ennever and Akert 1981), which in turn suggests that different subgroups might receive different afferent inputs.

As far as the INN projection is concerned, large injections of orthograde tracer into the abducens nucleus produce multiple foci of label in the oculomotor complex neatly matched to the three MR-MN subgroups (Büttner-Ennever 1981; Büttner-Ennever and Akert 1981; Carpenter and Batton 1980), although label in subgroup C may be lighter than in the other two groups (McCrean et al. 1986). Filling individual INNs with tracer (McCrean et al. 1986) showed the patterns of their terminal arborizations in the oculomotor nucleus: of four cells, all had terminals in subgroup A, one had collaterals in subgroup B, and none showed terminals in subgroup C. “Thus, it is likely that some internuclear neurons project to only one subgroup of medial rectus subdivision of the oculomotor nucleus, and that internuclear neurons may be specialised in respect to the motoneurons that they innervate” (McCrean et al. 1986, p. 306). For other MR-MN inputs, axons in the ascending tract of Dieters also have restricted terminal arbors in cat (Furuya and Markham 1981), and in primate the nucleus of the optic tract and the olivary pretectal nucleus project only to subgroup C (Büttner-Ennever et al. 1996).

The scattered spatial distribution of MR-MNs might underlie the possible problem of sampling MR-MNs discussed above. It might also underlie the INN sampling problem, provided that, with the specific-synapse model, INNs projecting to different subgroups have different firing rate thresholds (see next section). At present, the main physiological evidence about selective MR-MN afferents concerns the vergence-related input described in Assumptions used in the model. The fact that the correlation between the firing rate slopes for vergence and conjugate eye position is 0.31 (Mays and Porter 1984) implies that at most one of these slopes can be determined by the intrinsic characteristics of the MR-MN. Thus either the vergence signal or the conjugate signal or both is delivered via afferents specific to individual MR-MNs (cf. King et al. 1994).

In summary, the anatomic evidence indicates that the INN input is not uniformly distributed within the MR-MN pool, consistent in broad terms with the specific-synapse model and not the common-drive model. However, the physiologic properties of these specific projections are not known.

Implications of simulation results

PREDICTIONS FOR EXPERIMENTAL STUDIES. The main predictions of the present simulation results would be tested if both firing rate threshold and $I_{K}$, together with eye-position-related synaptic drive (cf. Powers and Binder 1995a), could
all be measured in the same set of MR-MNs. Unfortunately, this requires overcoming the technical problems of intracellular recording in alert animals.

It might, however, prove possible to exploit the idiosyncratic anatomic distribution of MR-MNs described above. For example, if it were established that MR-MNs in subgroup C had firing rate thresholds that differed from those of MR-MNs in subgroups A or B, then it would be predicted that those INNs antidromically activated by selective stimulation within subnucleus C would have related firing rate thresholds (cf. Figs. 11B, 12B, and 13B). In general, if the firing rate thresholds in any subgroup were particularly low (or high), then those INNs innervating that subgroup would be predicted to have firing rate thresholds that were correspondingly low (or high). This prediction may be related to the INN sampling problem mentioned above: Gamlin et al. (1989a) identified INNs by antidromic activation from stimulation delivered to the contralateral medial longitudinal fasciculus (p. 73), whereas Fuchs et al. (1988) used a stimulating electrode implanted in the oculomotor nucleus itself, “usually located toward the caudal end of the oculomotor complex” (p. 1876). Most MR-MNs in the caudal region of the oculomotor complex belong to subgroup B (Büttner-Ennever and Akert 1981). It is possible that the difference between the distributions of INN firing rate thresholds in the two studies arises in part because INNs projecting to subnucleus B were sampled more frequently by Fuchs et al. (1988).

The question arises of whether a similar strategy could be applied to the OMNs for eye muscles besides the medial rectus. For example, there is evidence consistent with synaptic specificity in the premotor inputs to abducens MNs (Broussard et al. 1995; Gamlin et al. 1989a; Ishizuka et al. 1980; Mays and Porter 1984; McCrea et al. 1986; Ohgaki et al. 1988; Spencer and Sterling 1977). Moreover, the position-related firing patterns of the cells that project to primate abducens MNs are broadly similar to that seen in INNs, i.e., linearly related to eye position above a threshold (McFarland and Fuchs 1992; Scudder and Fuchs 1992). Thus the problems faced by a common-drive model in extracting the correct abducens MN firing rate properties from this input pattern are likely to be similar to those found in the present simulations. If so, abducens MNs (and indeed INNs themselves) would also have a form of motor receptive field. Testing for the precise form of synaptic specificity predicted by the simulations might be possible if MNs in the abducens nucleus were segregated into subgroups like those seen for MR-MNs (Buettner-Ennever et al. 1983).

MOTOR UNIT ORGANIZATION AND DEVELOPMENT. A previous study of motor control during conjugate fixation (Dean 1996) suggested the existence of three main types of oculomotor units. These types may be related to the three broad categories of OMNs that emerged from the present simulations as follows.

1) Simulated OMNs with low firing rate thresholds receive input only from premotor cells that also have low firing rate thresholds, and may themselves have low I_h. In the previous study, OMNs with low firing rate thresholds were found to control relatively strong muscle units, possibly containing multiply innervated fibers specialized for providing steady force output at low input frequencies (cf. Robinson 1978).

2) Simulated OMNs with high firing rate thresholds receive input only from premotor cells that also have high firing rate thresholds, and may themselves have high I_h. In the previous study, OMNs with high firing rate thresholds were found to control strong muscle units, perhaps specialized to deliver the high levels of force required to achieve eccentric eye positions (cf. Robinson 1978).

3) The third category of simulated OMNs comprises cells with firing rate thresholds toward the middle of the range. According to the simulations, no particular intrinsic properties are required of these cells, and many different combinations of synaptic weights on them will deliver their firing rate properties for conjugate eye position. In the previous study, OMNs with intermediate firing rate thresholds were found to control muscle units that were weak, possibly corresponding to the orbital singly-innervated fibers that are particularly abundant in primates (e.g., Porter and Baker 1992). The properties of this large middle category of OMN appear well suited to the precise control of force for a variety of different oculomotor commands by summing the effects of independently varying sets of synaptic weights. In this context it is interesting to note that, as mentioned previously, the firing rate sensitivities of OMNs to conjugate and disconjugate eye position are at best weakly related (Gamlin et al. 1989a; Mays and Porter 1984).

An important issue is the developmental plausibility of this relationship between OMN inputs and muscle unit properties. It was suggested earlier (see RESULTS) that OMNs could be regarded as having a “receptive field” of premotor neurons, which determines for that OMN the nature of the fixation command \( \psi \) (Fig. 2). If so, ideas concerning the development of receptive fields in other parts of the brain could then be applied to OMNs. For example, if synchronicity of afferent input in the development of tactile receptive fields in cerebral cortex (Wang et al. 1995) were also important for the development of connections between INNs and MR-MNs, the kind of “channeling” shown in Fig. 11B might be accounted for. It is also possible that intrinsic MN characteristics play a developmental role for neurons at either end of the firing rate threshold distribution. Although evidence for OMN recruitment based on intrinsic characteristics is weak for the distribution as a whole, it seems stronger for OMNs with very low and very high firing rate thresholds (i.e., categories 1 and 2 in the preceding text). The intrinsic characteristics of these MNs could then preferentially favor presynaptic terminals with the appropriate activity patterns (Heckman and Binder 1990; Poo 1996) as well as influence the development of the muscle fibers to which they projected.

NEURAL INTEGRATOR. It was argued in the INTRODUCTION that one reason for trying to decide between the common-drive and specific-synapse models is that this would help to characterize the outputs required of prior processing stages in the manufacture of a fixation command. Fixation commands are thought to be generated from eye velocity commands by a process equivalent to mathematical integration (Robinson 1968, 1989). Two kinds of evidence suggest that this process is distributed over a large number of neurons.
Electrophysiological recordings in primates have revealed eye-position-related signals on many neurons in the vestibular nuclei and nucleus prepositus hypoglossi that project to the abducens nucleus (McFarland and Fuchs 1992; Scudder and Fuchs 1992). Partial disabling of the neural integrators for vertical and torsional eye position by injection of muscimol into the interstitial nucleus of Cajal produced a pattern of changes in eye position consistent with “each of several parallel integrators producing a fraction of the eye position command” (Crawford and Vilis 1993, p. 443). In addition, modeling studies of integrator function have shown that large numbers of neuronlike components are necessary to avoid biologically unrealistic constraints on parameter values (Cannon et al. 1983; Seung 1996) and to approximate the fractional-order dynamics of the vestibuloculocreflex (Anastasio 1994). The present study suggests that these and other population models (Arnold and Robinson 1991), which employ many units internally but then sum all the outputs onto two OMNs each representing an entire OMN pool, might be usefully constrained by the requirement of driving realistic populations of OMNs via specific output connections. The channeling of integrator output is more consistent with the idea of a distributed, dynamic representation for eye position commands (cf. Seung 1996) than with treatments of them as a single, lumped variable that is linearly related to eye position.

APPENDIX

Errors in common-drive model

The origin of the effects illustrated in Figs. 6 and 7 can be seen by setting the model output for the jth MR-MN (Eq. 5 and 6) equal to the actual output (Eq. 7). The result (Eq. A1) can then be simplified

$$K_i(\phi - \theta_i) = G_i \left( \sum_j F_{ij} w_j + B_j \right)$$  \hspace{1cm} (A1)

because in the common-drive condition under consideration, all \(w_j\)'s have the same value. The term \(\sum_j F_{ij} w_j\) can be replaced by \(INN_{TOT}(\phi) \cdot w\) where \(w\) is the common weight value and \(INN_{TOT}(\phi)\) is the sum of the INN firing rates for a given eye position \(\phi\) (Eq. A2). Differentiating the result

$$K_i(\phi - \theta_i) = G_i \left( INN_{TOT}(\phi) \cdot w + B_j \right)$$  \hspace{1cm} (A2)

with respect to eye position \(\phi\) gets rid of the threshold terms on both sides of Eq. A2, yielding the slope (Eq. A3)

$$\frac{dINN_{TOT}(\phi)}{d\phi}$$  \hspace{1cm} (A3)

Because the firing rate slope for OMNs is a constant, the model will only produce a good fit to the extent that \(\frac{dINN_{TOT}(\phi)}{d\phi}\) remains constant. Although individual INNs have constant slopes \(T_s\), the sum of their output has increasing slope as more INNs are recruited. The fit will improve for MR-MNs with higher thresholds \(\theta_s\), because, as Fig. 6B shows, the variation in slope reduces as eye position increases. The problem for low-\(\theta_s\) MR-MNs is that, according to the common-drive hypothesis, they receive input from high-threshold as well as low-threshold INNs.

Ir$s in common-drive model

The nonlinearity in the summed INN input caused the model to produce unrealistic values of bias, i.e., \(B = 0\) for MR-MNs with low firing rate threshold \(\theta\). More realistic estimates for the current threshold \(I_r\) were derived from Eq. A2, which gives the conditions for model and data to be equivalent by putting the eye position \(\phi\) equal to \(\theta_i\), the firing rate threshold for the jth MR-MN. This gives the threshold (Eq. A4)

$$INN_{TOT}(\theta_i) \cdot w + B_j = 0$$  \hspace{1cm} (A4)

which was used to provide the estimates for MR-MN current threshold that are plotted in Fig. 8A. The overall shape of the curves relating \(B\) to \(\theta\) is the same as that of those shown in Fig. 7B, because in both cases the shape is determined by the term \(INN_{TOT}\).

The actual values of the \(I_r\) estimates are determined by the value of \(f\)-weight term, which was chosen arbitrarily as 0.01. Equation A4 was therefore used to derive, for each of the three INN distributions, a value for \(w\) that set the estimated \(I_r\) for the median MR-MN (\(\theta = -20\)) to 5 nA. The resultant range of \(I_r\) estimates is plotted against MR-MN \(\theta\) in Fig. 8B. An MR-MN with a low firing rate threshold \(\theta_{low}\) receives, at its threshold eye position \(\phi = \theta_{low}\), a small massed INN input. Consequently the required MR-MN intrinsic threshold \(I_r\) also has to be small. As Eq. A4 shows, the exact value is determined by the form of the function that relates \(INN_{TOT}(\phi)\) to \(\phi\) (Fig. 7A). For example, the Gamlin et al. (1989a) distribution has few INNs with firing rate thresholds \(T\) below \(-35^\circ\). Thus the values of MR-MN \(I_r\) required by the model drop off very sharply for MR-MNs with \(\theta_s\) of less than \(-35^\circ\). At the other end of the distribution, an MR-MN with a high firing rate threshold \(\theta_{high}\) receives a large massed INN input at eye position \(\phi = \theta_{high}\), and therefore requires a high intrinsic threshold \(I_r\). The range of MR-MN \(I_r\) is required to cover the observed range of firing rate thresholds \(\theta\) is therefore large. Its value can be derived from Eq. A4 by considering the MR-MNs in the model with the highest and lowest \(\theta\). The ratio of their bias values \(B\) (which correspond in the model to \(I_r\)) is given by Eq. A5 for the equal-weight case

$$\frac{B_{high}}{B_{low}} = \frac{INN_{TOT}(\theta_{high})}{INN_{TOT}(\theta_{low})}$$  \hspace{1cm} (A5)

In the equal-weight version of the common-drive model, this ratio is determined only by the function relating \(INN_{TOT}(\phi)\) to \(\phi\), and the values of \(\theta_{high}\) and \(\theta_{low}\).
network, the single MR-MN has firing rate threshold $\theta$ and receives input from just two INNs, both with firing rate thresholds $T_1$ and $T_2$. The basic identity equation (Eq. A1) becomes Eq. A7 in this simple case

$$K(\phi - \theta) = G \cdot [sw_1(\phi - T_1) + sw_2(\phi - T_2) + B]$$  \hspace{1cm} (A7)

Equation A8 is the simplified version of the slope equation (Eq. A2), and Eq. A9 is the simplified version of the threshold equation (Eq. A3)

$$K = Gs(w_1 + w_2)$$  \hspace{1cm} (A8)

$$-B = sw_1(\theta - T_1) + sw_2(\theta - T_2)$$  \hspace{1cm} (A9)

These can be rearranged to give two linear equations for the two unknown weights (Eq. A10 and A11)

$$w_1 + w_2 = \frac{K}{Gs}$$  \hspace{1cm} (A10)

$$(\theta - T_1)w_1 + (\theta - T_2)w_2 = \frac{-B}{s}$$  \hspace{1cm} (A11)

What are constraints on the values of the intrinsic MN properties represented by $B$ and $G$?

For the low end of the distribution, Eq. A12 gives the threshold relation for the first MR-MN, i.e., the one with the lowest firing rate threshold $\theta_1$

$$-B_1 = s[(\theta_1 - T_1)w_1 + (\theta_1 - T_2)w_2]$$  \hspace{1cm} (A12)

The issue is whether there is a maximum value for $-B_1$ (which corresponds to the current threshold of the MR-MN with lowest firing rate threshold). Examination of Eq. A12 indicates that the distribution of weights that maximizes its right side is the one that gives all the weight to the most effective INN, namely the INN with the largest value of $(\theta_1 - T_1)$. This is the INN with the lowest firing rate threshold $T_1$, so $w_2$ must become 0. Therefore

$$-B_1 \approx sw_1(\theta_1 - T_1)$$

and from Eq. 4 with $w_2 = 0$

$$-B_1 \cdot G_1 \approx K_1(\theta_1 - T_1)$$  \hspace{1cm} (A13)

At the high end of the distribution, the important value is now the smallest value for the right side of Eq. A12, consonant with Eq. A10 being satisfied. Because by definition $T_2 > T_1$ (and assuming $\theta > T_1$), this will occur when $w_1 = 0$. Thus

$$-B_{TOP} \cdot G_{TOP} \approx K_{TOP}(\theta_{TOP} - T_{TOP})$$  \hspace{1cm} (A14)

where the suffix TOP refers to the MR-MN and INN with highest firing rate thresholds.

At the low-$\theta$ end, applying Eq. A13 to the three distributions for INN thresholds allows the maximum values for the product of

$$F_1 = s(\phi - T_1)$$

and $F_2 = s(\phi - T_2)$

Fig. 16. Diagram of simplified network, consisting of a single MR-MN and 2 INNs. The 2 INNs have firing rate thresholds $T_1$ and $T_2$ and firing rate slopes $s$. Their firing rates $F_1$, $F_2$ at eye position $\phi$ are therefore as indicated. MR-MN has intrinsic parameters $B$ and $G$ and firing rate threshold $\theta$ and slope $K$. FR as a function of $\phi$ is indicated.

Fig. 17. Limits on the values of model parameters $B$ (corresponding to $-I_b$) and $G$ (corresponding to the $f-I$ slope $\gamma$) in the specific-synapse model for the 3 different INN distributions. A: for MR-MNs with low firing rate thresholds $\theta$, $-B \cdot G$ has a maximum value that varies with $\theta$, $B$; for MR-MNs with high firing rate thresholds $\theta$, $-B \cdot G$ has a minimum value that varies with $\theta$.

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