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A model of the cerebellum in adaptive control of saccadic gain

I. The model and its biological substrate

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Abstract. We review data showing that the cerebellum is required for adaptation of saccadic gain to repeated presentations of dual-step visual targets and thus, presumably, for providing adaptive corrections for the brainstem saccade generator in response to any error created by the open-loop saccadic system. We model the adaptability of the system in terms of plasticity of synapses from parallel fibers to Purkinje cells in cerebellar cortex, stressing the integration of cerebellar cortex and nuclei in microzones as the units for correction of motor pattern generators. We propose a model of the inferior olive as an error detector, and use a 'window of eligibility' to insure that error signals that elicit a corrective movement are used to adjust the original movement, not the secondary movement. In a companion paper we simulate this large, realistic network of neural-like units to study the complex spatiotemporal behavior of neuronal subpopulations implicated in the control and adaptation of saccades.

1 Introduction

Saccades are high-velocity eye movements of very short duration. As visual feedback delays are longer than the movement itself, saccades cannot be controlled by on-line visual feedback. The rapidity of a saccade further attenuates the registration of visual feedback during the movement. Due to this 'saccadic suppression', the system is open loop. Therefore, accurate saccades require, to use terminology from control theory, an adaptive-parametric controller.

Experiments involving weakening of the eye muscles or target perturbation have shown the adaptability of the saccadic system. When eye muscles are surgically weakened (Optican and Robinson 1980), saccades to a visual target undershoot the target initially, and one or a few corrective saccades are generated in order to acquire the target. Over time, the size of the initial saccade progressively increases until corrective saccades are no longer necessary. In the target perturbation experiment, a naive monkey has to make a saccadic eye movement towards a target. However, during the saccade the target is shifted to a new position and, because of saccadic suppression, this shift is not perceived before the end of the movement (Goldberg et al. 1993). As the first saccade appears incorrect, a corrective saccade is generated (Fig. 1, left-hand panel). Gradually, the amplitude and direction of the initial saccade changes and the amplitude of the corrective saccade decreases until the subject makes an adaptive saccade directly to the displaced target (Fig. 1, right-hand panel). The gain for similar directions and amplitudes is also changed (Goldberg et al. 1993). The left-hand panel of Fig. 2 depicts the exponential time course of the adaptation.

Several researchers (e.g., Ritchie 1976; Optican and Robinson 1980; Fitzgibbon et al. 1986; Noda 1991; Goldberg et al. 1993) have pointed out that cerebellar lesion yields saccadic dysmetria and loss of adaptive capabilities. Figure 2 (right-hand panel) shows the learning curve for the target perturbation experiment described earlier, run with monkeys with lesions of the deep cerebellar nuclei (Goldberg et al. 1993): no adaptation is seen, and due to the loss of the modulation supplied by the cerebellum, the saccades are hypermetric. Thus, the specialized role of the cerebellum for the saccadic system involves two separate time frames (Keller 1989). First, an on-line correction affects individual saccades. The presence of a modulatory cerebellar signal is particularly important for large saccades and to insure the equal accuracy of movements from different initial eye positions. Second, a longer-term adaptive modulation compensates for saccadic dysmetria due to orbital or central lesions or other changes in system characteristics.

The saccade generation model developed by Dominey and Arbib (1992) (henceforth referred to as the D&A model) takes into account many brain regions involved in the generation of saccades in the monkey. The primary

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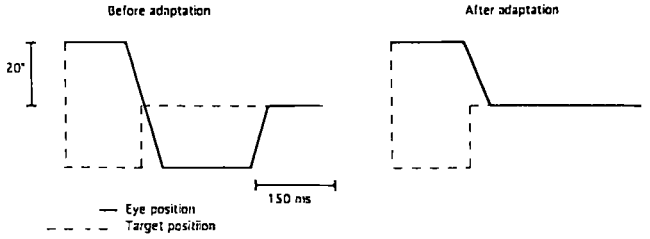

Fig. 1. Technique for inducing saccadic adaptation. In both panels, eye and target position are plotted against time. The *continuous line* represents the horizontal component of eye position, and the *dashed line* represents the horizontal component of target position. In this example, the target steps 40° rightward at the beginning of the epoch, and when the monkey starts to make a saccade, the target steps 20° back. Initially (unadapted, *left*) a corrective saccade is generated. After several hundred trials (adapted, *right*) the monkey makes an accurate saccade to the ultimate target position, not its location at the beginning of the trial (Adapted from Goldberg et al. 1993)

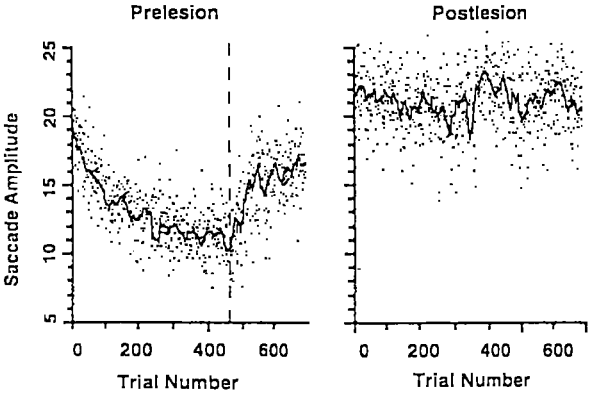

Fig. 2. Effect of cerebellar lesion on saccadic adaptation. Each *dot* is a single trial. The *continuous line* is a ten-trial average of saccade amplitude plotted against the trial number of the middle of the epoch. *Left*: Prelesion. The *dashed line* marks the end of the adaptation run, after which the target is no longer displaced. *Right*: Postlesion. There is no adaptation. (From Goldberg et al. 1993, with kind permission from Elsevier Science – NL, Sara Burgerhartstraat 25, 1055 KV Amsterdam, The Netherlands)

goal of this model was to comply with the well-known anatomy and neurophysiology of the saccade system in simulating a variety of saccade paradigms. In the D&A model, the control of voluntary saccades to visual and remembered targets is modeled in terms of interactions between posterior parietal cortex, frontal eye fields, mediodorsal thalamus, the basal ganglia (all grouped in Fig. 3 under the 'cerebral cortex' label), superior colliculus, and the brainstem saccade generators. The topography of saccade direction and amplitude is preserved through multiple projections between brain regions until they are finally transformed into a temporal pattern of activity that drives the eyes to the target. This sensory-motor transformation occurs at the level of the LLBNs (long lead burst neurons) as shown in Fig. 3. The saccade generator is modified from Scudder (1988). Dominey and Arbib (1992) present a more thorough description of these interactions and mechanisms.

This model, however, does not include the cerebellum. Our goal is to implement a cerebellar-like neural

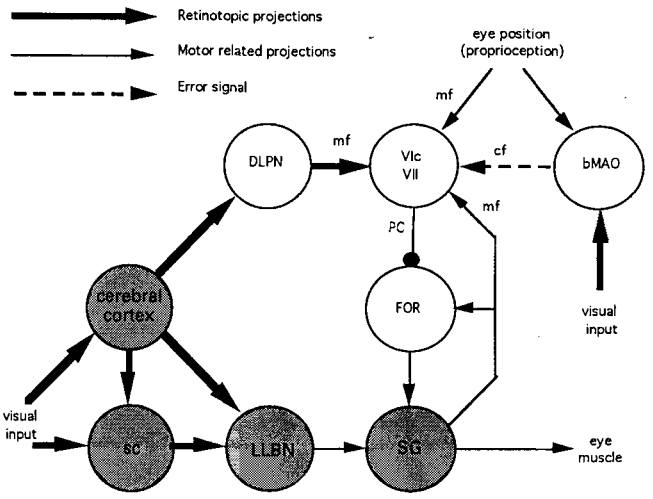

Fig. 3. Functional anatomy of the cerebellar pathways associated with the formation of saccades. The *shaded circles* are part of the D&A model; the *empty circles* represent the new cerebellar model. There are two sites where sensory-motor transformation occurs: the brainstem and the cerebellum. *VIc*, *VII*, vermal lobules VIc an VII; *FOR*, fastigial oculomotor region; *DPLN*, dorsolateral pontine nucleus; *SC*, superior colliculus; *bMAO*, group b of the medial accessory olive; *LLBN*, long lead burst neurons; *SG*, saccade generators (one per eye muscle); *PC*, Purkinje cells; *mf*, mossy fibers; *cf*, climbing fibers. Important projections to the oculomotor vermis from the SC through the nucleus reticularis tegmonti pontis (NRTP) also exist; they are however, not modeled

network to augment the D&A model, in order to account for the adaptive capabilities of the saccadic system. In the present paper, we further develop the D&A model in three phases.

First, we argue that it is the role of the cerebellum to learn to compensate any error generated by the nonlinear frontocollicular pathway. We then modify the D&A model to account for nonlinearities existing in the brainstem saccade generator system and in the eye muscles.

Second, we study the on-line control of the brainstem saccade generator by the oculomotor vermis and build a cerebellar network. Noda et al. (1991) showed that the cerebellum is not the primary controller and that cerebellar impulses are projected downstream to saccade-programming circuits where visual information has already been converted into motor-commanding signals. The cerebellar side path is shown by the unshaded circles in Fig. 3. We briefly review the microcomplex model (Ito 1984) and we carefully review the three types of mossy fiber inputs to the oculomotor cerebellum ('mf' in Fig. 3): visual, proprioceptive and feedback from the brainstem saccade generator. The nature of the cerebellar modulation on the final saccadic circuitry is discussed, based on functional and anatomical considerations.

Third, we address the adaptation issues. We review the functional and anatomical evidence accounting for the role of the inferior olive (more specifically the bMAO as shown on the right-hand side of Fig. 3) as an error detector mechanism. We propose a new neural model of the inferior olive (IO) which gates the adaptation when needed. Then, we study the adaptability of the cerebellar network. Taking into account the significant delay

between the efferent motor command and the afferent error information, we develop a learning rule based on neurochemical study of long-term depression (LTD) and on previous cerebellar learning models.

2 Nonlinearities of the saccadic system

Due to saccadic suppression, the saccadic system cannot tell the difference between a correct motion in a moving world (e.g., the target perturbation experiment) and an incorrect one in a stationary world (e.g., an error due to a wrong system parameter or a weakened muscle). Therefore, the adaptive system is general, i.e., it compensates for all errors produced by the nonadaptive part of the system (the frontocollicular pathway) – but since the adaptation is averaged over many trials, only systematic forms of error are compensated for. These errors are generated by poorly tuned genetically defined connections, cell loss, injuries, and orbital nonlinearities, as well as consistently repeated, artificial target perturbations.

Since the muscle plant is a nonlinear function of the movement signal, different motor commands are necessary to bring the eyes on target for the same target displacement from different initial eye positions. As the muscle plant characteristics are not known *a priori* by the system (and will change over time due to growth, aging, or injury), the retinal and position signals must be part of an adaptive component of the total movement that activates the muscles.

In the D&A model, the eye position is linearly derived from the tonic neurons in each direction. Here, we take the muscle contraction function given in Grossberg and Kuperstein (1989) for a 'slower than linear' muscle nonlinearity, while any inertial or viscous forces are neglected. The eye position depends on the motor neuron firing rate TN in the following way:

$$Pos(TN) = G\frac{(kTN - l)}{a + (kTN - l)} \tag{1}$$

where a is an arbitrary parameter chosen to be large enough to insure that the nonlinearity is significant, and G is a gain factor (k and l are parameters defined in Robinson 1970).

We consider a second source of nonlinearity in our model: within the brainstem spatiotemporal transformation. In the D&A model, it is postulated that spatial gradients that implement the spatiotemporal transformations are generated during an early stage of development: a light on the right hemifield of the retina will move the eye toward the right. This process is achieved by masks with increasing connection strengths from the LLBNs to the medium lead burst neurons, when going from the center of the retinotopic map to more eccentric positions. The connection strengths were derived in a linear fashion in the D&A model: this assumes that the gain between saccadic vector and motor command is constant for all target displacements. As these precisely derived weights are unrealistic, we will assume instead that these connections' strengths are generated by a uniform probabilistic distribution. Optican and Robinson (1980) noted that the saccadic gain of the system with a lesioned cerebellum is approximately between 2 and 3. To reproduce those data and to introduce a high degree of variability (and then further show the adaptive capabilities of the system), we randomly generate the weights in a range 30–100% larger than the ones required for a linear transformation. Then, the gain of the brainstem saccade generator is between 1.3 and 2, and the gain of the whole system (which includes the muscular nonlinearities described above) is approximately between 1.5 and 3 for different saccade amplitudes as shown in figure 7 (dotted curve) of the companion paper (Schweighofer et al. 1996).

3 On-line cerebellar control of the saccadic system

3.1 The microcomplex model

The cerebellar architecture is very uniform and regularly divided into small structural and functional units inserted into various extracerebellar systems. These units are called cerebellar corticonuclear microcomplexes (Ito 1984). A microcomplex is composed of a cerebellar microzone and a small number of nuclear cells. Oscarsson (1980) defined the microzone as a narrow longitudinal zone in the cerebellar cortex receiving climbing fibers from a small group of IO neurons and having a particular bodily function. Indeed, the IO is divided into small clusters of electrotonically coupled cells (Llinás et al. 1974). The set of mossy fiber inputs to the microcomplex, relayed by the granule cells and their long parallel fibers (Mugnaini 1983), is characterized by its considerable divergence across many other microzones. According to the hypothesis of Marr (1969) and Albus (1971), this set constitutes a 'context' (tunable by experience) for present sensorimotor actions.

The basic, simplified mode of function of a microcomplex is (Ito 1990): (1) As Purkinje cells (PCs) have an inhibitory action upon nuclear cells (while collaterals of mossy fibers excite the nuclear cells), the signal flow from the nuclear cells is modulated by the microzone action. (2) Climbing fibers convey signals encoding error in the performance of the system in which the microcomplex is installed. (3) Climbing fiber signals induce LTD in those parallel fiber–PC synapses which were activated with the climbing fibers (but within a certain time window, as we shall emphasize below). Due to the uniformity of the cerebellar cortex, the cerebellar functions are primarily defined by the nature of the inputs to particular cerebellar regions and by the locus of the projections from the deep cerebellar nuclei.

3.2 Mossy fiber inputs provide adaptation parameters

3.2.1 Visual inputs. The target perturbation experiments and the related cerebellar saccadic adaptation, suggest that the oculomotor vermis has access to visual information. Goldberg et al. (1993) found that stimulation of the superior colliculus produces saccades which are not adapted to target perturbations. This result suggests that

the side path concerned with cerebellar adaptation in this paradigm starts 'higher up' than the superior colliculus.[1] Yamada and Noda (1987) have shown anatomical evidence for a path involving the pontine nuclei,[2] lobule VII of the oculomotor vermis and the fastigial oculomotor region (FOR). We further assume that the pontine cells are mere relays, in which the precise target map is somewhat lost by divergence-convergence. The spread of activity is modeled by a gaussian distribution of synaptic efficacies (or 'weights') to form a 'blurry' topographic connection from the motor layer of the FEF to the cerebellum (the equations are given below).

Since the model is computationally expensive, we model cerebellar control and adaptation of horizontal saccades only. The membrane potentials of the retinotopic mossy fiber coding for the horizontal retinal position are formally described by *mfret*, a 19-element vector (since the D&A model generates saccades in the range $[-45°;45°]$, the discretization sample is 4.75°) given by:

$$\tau_{mf} \frac{d\mathit{mfret}}{dt} = -\mathit{mfret} + w_g * \mathit{FEFsac} \tag{2}$$

where w_g is a vector of weights whose values form the discrete gaussian distribution, *FEFsac* is the output layer of the FEF in the D&A model, and $*$ is the convolution operator.[3] The generic equation ruling each neuron's membrane potential is given in the Appendix.

3.2.2 Proprioceptive inputs. As discussed earlier, cerebellar lesions yield dysmetria of varying amplitudes depending on the initial eye position. Thus, the cerebellum has to have access to such information. Fuchs and Kornhuber (1969) showed the existence of mossy fibers carrying extraocular muscle proprioceptive signals in the cat, which coincide with projections from the FEF. Kase et al. (1980) recorded tonic mossy fibers carrying a high-fidelity eye position signal. The firing level of these cells was proportional to eye positions within *a limited range only*, and did not respond for other eye positions. To approximate this phenomenon, we use a coarse coding similar to the one described earlier for visual inputs. This coding has the important implication of speeding the adaptation (see Sect. 4.2).

In the model, a set of 11 tonic mossy fibers carry horizontal eye position, in the range $[-45°, 45°]$. We have, for each cell i, a corresponding coordinate (in degrees) $H(i)$, in which a position maximally stimulates the cell, with the response dropping off in a gaussian fashion as the horizontal coordinate H of the current position departs from this optimum:

$$\mathit{mfpos}(i) = \exp[-(H(i) - H)^2/s^2] \tag{3}$$

3.2.3 Brainstem saccade generator feedback. Ohtsuka and Noda (1992) have shown that a significant proportion of mossy fibers carry a signal very similar to the excitatory burst neuron (EBN) activity in the saccade generator. Moreover, Yamada and Noda (1987) revealed a significant number of connections from the horizontal saccade burst neurons to the oculomotor cerebellum. There are two functional interpretations of this type of mossy fiber: (1) Since they fire distinctively for left and right saccades, the whole granule cell population is activated quite differently for left and right saccades. This allows a sharp differentiation in the adaptation of left and right saccades, as shown by experiments (Houk et al. 1992). (2) Their excitatory collaterals to the FOR allow proper cerebellar control of the saccadic gain, since the bursts match the PC inhibition.

On the basis of satisfactory preliminary simulations, we chose to model ten of these fibers (this allows us better separation of learning between the left and right saccades).

$$\tau_{mf} \frac{d\mathit{mfburst}}{dt} = -\mathit{mfburst} + w_{mf}\mathit{EBNr} \tag{4}$$

where *EBNr* is the firing rate of either the left or the right excitatory burst neuron projecting to the resettable integrator (five cells encode the 'left' EBNr, five others the 'right' EBNr). See Sect. 3.4 for the meaning of 'r'.

3.3 Cerebellar cortex and fastigial nuclei compute the adaptive correction

We model two microcomplexes, each modulating the activity of the one saccade generator with which it is associated. In the present model, we define three types of cerebellar neurons: granule cells, PCs and nuclear cells (Fig. 4, top). However, we do not take any cerebellar interneurons into consideration. For clarity, we describe only one microcomplex.

Each of the granule cell's four dendrites (Ito 1994) receives a distinct mossy fiber input, and the cell cannot fire if it receives only one mossy fiber input. To allow a rich combination of inputs, and to reproduce the very large divergence between the mossy fibers and the granule cells, we model 1000 granule cells, which gives us a divergence ratio of 40:1000 between the mossy fibers and the granule cells. The granule cells generate a

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[1] As a consequence of this stimulation experiment, we do not consider the projections from the superior colliculus to the oculomotor cerebellum. [A functional study of these (reciprocal) projections can be found in Houk et al. (1992).]

[2] Large groups of mossy fibers were found in the paramedian pontine nuclei and the dorsolateral pontine nucleus (DLPN), which are the primary targets of the frontal eye fields (FEF), organized in terms of saccade displacement. To comply with the anatomical constraints in the D&A model, and to fit best the anatomical and neurophysiological data, we consider a side path starting from the FEF, going through the DLPN, then through lobules VIc and/or VII of the vermis. Several sources of visual information reach the oculomotor vermis (for a review see Blanks 1988). However, given the lack of functional data and the sufficiency of one visual projection for our purpose, we do not take them into account.

[3] Note that only here do we use the convolution operator since w_g is a 'gaussian mask'. In the membrane potential equations below, the weights are either constant scalar values, in which case a simple scalar multiplication is performed, or they are represented as a vector of modifiable weights, in which case a point-to-point multiplication is performed.

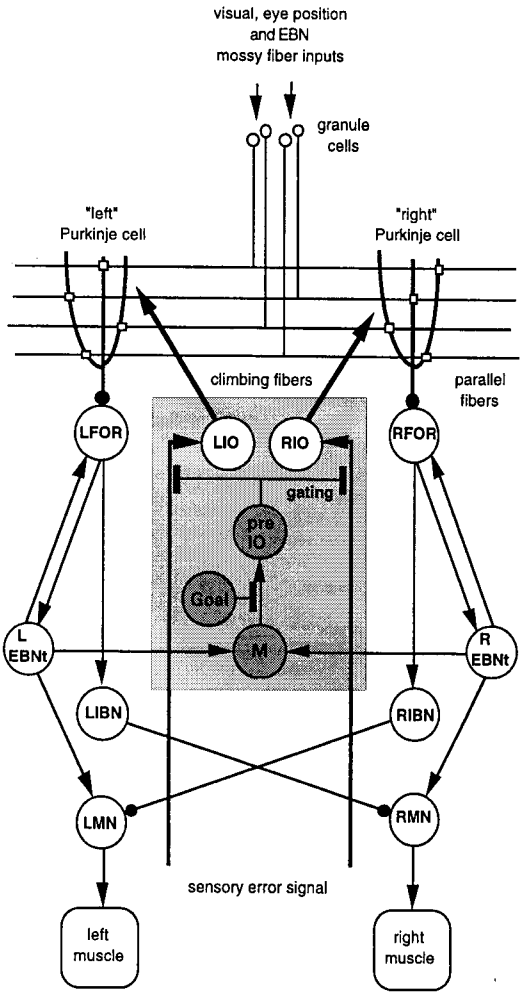

Fig. 4. The cerebellar model for control and adaptation of horizontal saccades. Most of the neurons are labeled left (*L*) or right (*R*) in order to refer to the underlying left or right eye muscle. The cerebellar neural network comprises granule cells, Purkinje cells (PCs) and fastigial oculomotor region (*FOR*) cells. The dendritic trees of the PCs are shown crossing the parallel fibers. The modifiable parallel fiber–PC synapses are represented by *small empty squares*. The FOR cells receive convergent inputs from the burst neurons EBNr (for clarity, cross-projections from the EBNr cells to the FOR cells are not drawn) and project to the excitatory burst neurons *EBNt* and to the inhibitory burst neurons (*IBN*), which then project to the motor neurons (*MN*) and the tonic neurons (*TN*). Notice the competition achieved between the IBNs and EBNts. The inputs to the brainstem saccade generator stemming from the D&A model are not drawn for clarity. The error detector network (*light shaded area*) contains a gating network and the inferior olive (*IO*). The IO transmits direction and amplitude information for adaptation. The three *dark shaded neurons* constitute the gating network: pre-IO neuron, goal neuron and M neuron ('memory' neuron). The sensory error signal can derive from either proprioceptive or retinal inputs, but in the present model we assume that the error has a proprioceptive nature. Notice that the midline is not the midline of the real brain, as only one eye is modeled. For more details on the functioning of this circuit see the text

(uniform) statistical distribution of combinations of mossy fibers carrying retinotopic signals, position signals and motor signals. Therefore some granule cells will tend to carry unimodal signals, but, due to their high firing threshold, most will carry bi- or trimodal signals. The equation ruling the membrane potential gc_n of the nth granule cell is given by:

$$\tau_{gc}\frac{dgc_n}{dt} = -gc_n + w_{mf-gc}(MFx1 + MFx2 + MFx3 + MFx4) \quad (5)$$

where $MFxi$ represents the firing rate of a mossy fiber, which can be of any modality (due to the statistical distribution described above). The sum of four distinct mossy fiber firing rates represents the effect of the four dendrites of a granule cell.

As the granule cells give rise to long parallel fibers, we posit that the set of parallel fibers make synaptic connections with all the PCs. This divergence is supported by the findings of Kase et al. (1980) who reported that the PCs, unlike the mossy fibers, respond to all eye positions. To make the model computationally tractable and to avoid unnecessary speculations on the relative spatial distributions of the different layers (mossy fiber–granule cell–PC–FOR), we model only one PC per microcomplex. Therefore, the PCs receive a very rich combination of inputs, as the convergence ratio is 1000:1. The two PCs receive the same set of granule cell inputs; only the climbing fiber input differs (see below). The PC membrane potential equation is given by:

$$\tau_{pc}\frac{dpc}{dt} = -pc + w_{ltd}GC + B_{pc} \quad (6)$$

where w_{ltd} is a vector of adjustable synaptic weights [see (12)] initially randomly generated, GC is the vector of firing rates of the granule cells, and B_{pc} gives the cell's background activity.[4]

Ohtsuka and Hiroharu (1991) showed that the control of saccades by the cerebellum depends upon the output signal conveyed by the FOR neurons. These neurons coincide anatomically with the area receiving PC projections from the oculomotor vermis. The duration of the pre-saccadic burst seen in the nuclear neurons being correlated with saccadic duration (Noda 1991), we assume that only mossy fibers arising from the EBN give collaterals to the FOR. This assumption is similar to the distinction between fast and slow responding mossy fibers made by Eccles (1973). In our case the fast mossy fibers are the visual mossy fibers, which start firing much earlier than the (slow) mossy fibers arising from the brainstem saccade generator. Eccles proposed that the fast mossy fibers pass by the deep nuclei, giving only very few collaterals to the nuclear cells, whereas slow mossy fibers give off many collaterals. This becomes very

[4] We note here that, by not taking into account the climbing fiber afferents either in the PC or in the FOR cell equation [(7)], we implicitly make the following assumption: The climbing fibers send collaterals to the deep nuclei, on their way to the cerebellar cortex; the excitation of the fastigial neurons by these collaterals would nullify the strong inhibition caused by the complex spikes, which are the response of the PCs to the climbing fiber firing.

important in the broader context of how the cerebellum modifies motor commands. If the nuclear cell excitation were derived mainly from visual signals, the temporal order of excitation would be: (1) visual (long lead) mossy fibers, (2) FOR and granule cells carrying mostly visual information, (3) PCs and, finally, (4) short lead mossy fiber burst neurons. These many temporal mismatches would allow only poor control of saccade generation by the cerebellum.

We model two FOR cells associated with the right and left microzones. There is a one-to-one correspondence between the PC and the FOR cells, and convergence from both left and right EBNs to each FOR cell. Each nuclear cell's membrane potential equation is:

$$\tau_{nu}\frac{dnu}{dt} = -nu - w_{pn}PC + w_{mn}step(LEBNr + REBNr) + B_{nu} \qquad (7)$$

with w_{pn} being the projection strength from the PCs to the nuclear cells, w_{mn} the strength of the EBNr inputs, *LEBNr* and *REBNr* the left and right burst neurons and B_{nu} the background activity (again see Sect. 3.4 for the meaning of 'r'). The step function, *step* ( ), insures that the nuclear cell fires with a burst of similar 'height' for different saccades, and with a duration proportional to the duration of the saccade, as in the experimental findings. Note that each nuclear cell will be activated during every saccade.

3.4 Cerebellar outputs

The FOR neurons project primarily to the saccade-related structure of the brainstem (Noda et al. 1990). The projections are (1) to the inhibitory burst neurons (IBN), which deliver an inhibitory burst to motor neurons during saccades, (2) to the omnipause neurons, which by ceasing firing during all saccades allow each saccade to occur, and (3) to the EBNs, which encode the saccade velocity. As omnipause neurons behave in a similar manner for all saccades, they probably receive inputs from all the FOR areas. Fuchs et al. (1993) suggested, on the basis of anatomical and neurophysiological evidence, that the IBNs are the main fastigial link to the saccade brainstem generators. This is consistent with the fact that saccades performed with a lesioned vermis are mostly hypermetric. Optican and Robinson (1980) proposed that the brainstem saccadic system of the monkey has a gain of 2–3 (depending on the saccade vector, initial eye position) and that the gain is brought back to 1 by cerebellar action. Thus, the IBNs would regulate the gain by subtracting the FOR output from the fixed-gain, frontocollicular pathway.

However, a sole projection to the IBNs would not be sufficient for the following reason. As Grossberg and Kuperstein (1989) noted, in order to correct for errors, the adaptive system has to be unconstrained by retinotopy. For instance, suppose that in the target perturbation experiment the first target falls on the right sector of the retinotopic map and the second target on the left half. In this case, the first saccade amplitude should be decreased as it is hypermetric. To compensate for this error, a decrease of the agonist innervation pulse and an increase of the antagonist pulse is needed. In other words, for each direction for the first saccade, adaptation can occur in the same direction or in the opposite direction. However, because of the unidirectional functional change in weights due to LTD (which results in an increase in nuclear output due to the inhibitory nature of the PCs), the system requires competition between agonist and antagonist microcomplex outputs. Thus, we predict that projections to IBNs *and* EBNs are necessary (Fig. 4, bottom). Before learning, the net influence of the cerebellum on the saccadic circuitry will be close to zero, and will soon become either positive or negative, depending on the direction of the error: a saccadic overshoot will increase the antagonist microcomplex output and an undershoot will increase the agonist microcomplex output. This suggests that the adaptive saccadic system requires not just simple gain control, but *adaptation of coordination* between the different saccade generators.

In the D&A model, the velocity of the saccade is determined by a loop comprising the EBN, a resettable integrator and the omnipause neurons. The difficulty is that if the EBN activity is modified inside the loop, it does not change the amplitude, but just the velocity of the saccade. [We refer the reader to figure 3 in Dominey and Arbib (1992) for more details.] To solve this problem, we model two subpopulations of EBN cells: one projecting to the cerebellum, the other receiving cerebellar inputs. The first subpopulation, EBNr, would project to the resettable integrator (RI) cells and to FOR, while the second, EBNt, would project to the tonic neurons and to the motor neurons (MN) to yield the pulse-step firing pattern. Both subpopulations receive the same input from the LLBNs and the omnipause neurons, but only the subpopulation EBNt receives the FOR inputs (Fig. 4). Consequently, for saccades that have gain increase adaptation, there is increased velocity and amplitude but unchanged duration. The existence of these two EBN subpopulations would have to be verified experimentally, since no cells with a resettable firing pattern have been found.

4 Adaptation: problems and solutions

4.1 Modeling of the inferior olive as an error detector

A position 'error' between the fovea and the target cannot be used for adaptation without a mechanism which knows that this error was not expected. Indeed, after an incorrect saccade is generated, the retina is in the same state as before the generation of the first saccade: a target is present on the retina but not on the fovea.

The error is presumably carried by the climbing fibers stemming from a subdivision of the IO, the group b of the medial accessory olive (bMAO) (Ikeda et al. 1989;

Gonzalo-Ruiz and Leitchnetz 1990).[5] As adaptation should occur only if the main saccade is not accurate, the IO should be activated only in this case. Weiss et al. (1990) showed that the afferent sensory responsiveness of the IO is blocked during movement by motor signals. Therefore, along with Houk et al. (1992), we assume that only when a corrective saccade is generated will be appropriate IO cell fire and send an error signal to the appropriate microcomplex.

We propose that a 'pre-IO' neuron will gate the IO (Fig. 4, light shaded area) and here we discuss how this neuron is activated. To make sure that the nonfoveation is the result of an incorrect saccade, we assume that an error will be detected if (a) a target is on the retina but not on fovea, *and* (b) a saccade has just been completed. To fulfill (a), we model a 'goal' neuron which carries a signal that lasts until target acquisition is complete: it encodes the goal of the saccadic system. Such a cell type has been found in the FEF, where some neurons have an on or off response to visual stimulation of the fovea (Segraves and Goldberg 1987). In the D&A model, these cells are called Fon cells; for convenience we model the 'goal' neuron with the opposite response. It fires when no targets stimulate the fovea, i.e., soon after a target displacement, and keeps on firing until the end of the saccade (if the latter is accurate enough to bring the fovea on target; if not it fires until the end of the corrective saccade). Condition (b) is made possible in the model by a movement 'memory cell', which receives convergent signals from both left and right EBNts and has a long time constant (alternatively, a reverberating circuit could sustain the activity). The 'goal' and the 'memory' cell project to the 'pre-IO' neuron, which fires only when the two inputs are active simultaneously, i.e., only if the main saccade *did not* bring the eye on target. The equation ruling the membrane potential of the pre-IO neuron is:

$$\tau_p \frac{dp}{dt} = -p + M\ Goal \tag{8}$$

The product between the 'memory' cell firing rate M and the 'goal' cell firing rate *Goal* reflects the necessary co-activation of these two neurons to activate the pre-IO neuron.

Since the IO cells fire at a very slow rate, they are modeled in the following way. We let *io* be the membrane potential of an inferior olive cell. IO = 1 represents an IO spike, while *hyper* is the hyperpolarization immediately following a spike. This hyperpolarization brings the potential below threshold again.

$$\text{If } io(t) \geqslant \theta, \quad \text{then } io(t + \partial) = \theta - hyper,$$
$$and\ IO(t + \partial) = 1, \quad \text{for } 0 < \partial \leqslant d \tag{9}$$

where θ is the threshold for an IO spike and d the duration of a spike. Otherwise, we have:

$$\tau_{io} \frac{dio}{dt} = -io + PE + noise \tag{10}$$

where P is the pre-IO neuron firing rate and E is a phasic proprioceptive input that drives the appropriate cluster to firing level. The firing rate E, along with the added noise term, insures that the larger the amplitude of the error, the higher the probability that the IO cell will fire. The product of P and E reflects the gating by the pre-IO neuron, and signals the need for adaptation. When the pre-IO neuron is activated, the IO cells are allowed to fire in response to its sensory input. Thus, a motor command gates a sensory input in the IO.

4.2 Learning

The commonly agreed requirements for LTD in the parallel fiber–PC synapse is a rise of postsynaptic Ca^{2+} induced by climbing fiber action, with concurrent activation of metabotropic glutamate receptors by the parallel fiber input (Crepel and Krupa 1988). Recently, Linden et al. (1993) showed that Na^+ influx through AMPA receptors at the parallel fiber–PC synapse is also necessary for LTD induction.

Since the climbing fiber carrying the error information is delayed relative to the efferent signal, a short-term memory system capable of retaining the appropriate parameters of the first saccade is needed. To account for this fact and to solve the credit assignment problems, we assume synapse eligibility (Klopf 1982; Sutton and Barto 1981) due to the existence of a second messenger system. This concept has been successfully applied to cerebellar learning by Houk et al. (1990). These authors proposed a model suggesting how a second messenger would effectively tag a synapse as eligible for modification. The synapses participating in a computation are said to be eligible when a second messenger, in this case diacylglycerol, is released in the PC dendritic spine following parallel fiber activation. The location of the 'tagged' synapses solves the spatial credit assignment problem

[5] Two types of post-saccadic information have been proposed to correct an erroneous motor command (Albano and King 1989), and anatomical paths carrying both types have been found: (1) A post-saccadic visual error carried by the climbing fibers would drive the adaptation, as in the vestibulo-ocular reflex (Ito 1984). Visual signals are known to reach the bMAO through the superior colliculus (Frankfurter et al. 1976). (2) An error in motor coordinate, i.e., the motor activity from a visually guided corrective saccade, or its sensory consequences from the oculomotor muscle stretch receptors. Proprioceptive climbing fiber inputs to the posterior vermis have been demonstrated (Baker et al. 1972). At present, there are no convincing data to favor one strategy (visual error) or the other (motor error). However, both show a consequent delay between the efferent motor command corresponding to the erroneous saccade and the corresponding error. The delay for a visual error would correspond to visual preprocessing after the first saccade is terminated, which typically takes 40–80 ms. The delay associated with the proprioceptive strategy corresponds approximately to the time between the first saccade and the corrective saccade, so typical values would be around 100–150 ms. Models using proprioceptive IO cells have been proposed for limb control (Berthier et al. 1993) and saccade control (Houk et al. 1992). Similarly, here we consider an error in motor coordinate, as this strategy does not require a visuo-motor transformation. Instead, this assumes a one-to-one anatomical correspondence between the muscles, the IO clusters (modeled as single cells) and the microcomplexes. We model direct projections from the stretch receptors to the IO cells and assume that these proprioceptive projections are direction specific, and carry phasic signals.

and reproduces the specificity of LTD: If a parallel fiber–PC synapse participates in synaptic transmission, it becomes eligible to be weakened by LTD if a climbing fiber signal is received somewhat later. Moreover, this temporary activation of the second messenger acts as a short-term memory. Due to the important delay in the error system, the climbing fiber error signal corresponding to the erroneous first saccade reaches the cerebellar cortex at approximately the same time as the signal carried by the parallel fibers corresponding to the second saccade. A monotonically decaying eligibility signal would not be sufficient to solve this temporal problem, as learning might then be erroneously associated with the corrective saccade. When the error signal arrives, we need the concentration of the messenger to be largest for synapses involved in the initial saccade. We introduce the concept of a 'time window of eligibility'. We posit that the concentration of the second messenger diacylglycerol ([2nd]) has the response of a second-order system (although, alternatively, we can imagine a second messenger following a first-order equation but starting with a significant delay). In the synapse of index i for either PC, we have:

$$\frac{d^2[2nd]_i}{dt^2} + l_1 \frac{d[2nd]_i}{dt} + l_2 [2nd]_i = K w_{ltdi} GC_i \qquad (11)$$

where l_1 and l_2 are properly chosen so that the response is damped and K is a gain factor. The presence of w_{ltdi}, the adjustable synaptic weight of the parallel fiber–PC synapse, in the right-hand side of the equation reflects the amount of Na^+ within the spine. Ideally, the concentration matches in time the occurrence of the error signal and the concentration decays relatively fast to insure a minimum of interference with the next saccade.

As discussed earlier, the visual and proprioceptive mossy fiber inputs are coded in 'coarse coding' manner. This creates generalization, thus speeding up adaptation (Albus 1975): a group of cells which are 'close' to the selected cell will be updated – the assumption is that similar states will require similar control effort. This is of importance for the learning process, as adaptation is extended to saccades of similar amplitude and direction, as seen in Goldberg et al.'s experiments. This coding is a 'natural' coding for the visual mossy fibers, since they are organized retinotopically and it is expected that exact retinotopy is somewhat lost through multiple projections. For position information the type of coding we use is, *a priori*, at odds with a linear relationship between position and mossy fiber. However, given that the proprioceptive cells recorded by Kase et al. (1980) respond in a ramp-like manner, with an important range of eye position which elicits no activity, coarse coding should be regarded as a useful simplification: it allows a more efficient adaptation than linear coding. If the cells were carrying a signal linearly dependent upon the eye position, learning discrimination would be poor, as a large signal would activate the same subset of parallel fiber–PC synapses as a smaller signal.

In the model there are two weight vectors, one for each PC denoted by w_{ltd}. As each parallel fiber makes a synaptic contact with each PC, these vectors have 1000 elements. Since the rate of change of the calcium concentration is rapid compared with the second messenger dynamics, the weight update rule is at each time step:

$$\Delta w_{ltdi} = -\alpha IO\ [2nd]_i \qquad (12)$$

where i is the ith synapse of a given PC, α is the learning coefficient, IO the binary climbing fiber error signal, and $w_{max} > w_{ltdi} \geqslant 0$. A term showing some kind of long-term potentiation (LTP) in the learning rule is necessary: if only LTD were occurring, all the weights would tend to zero. Thus, we implemented a weight normalization (which can be thought of as providing nonspecific LTP) which keeps the sum of all the synaptic weights constant for each PC.[6] Each weight receives the increment: $\sum \Delta w_{ltdi}/n$, where the sum is over all the weights of one PC, and $n = 1000$ is the total number of synapses per PC. This potentiation has no direct functional role as far as the behavior is concerned, except that it somewhat degrades the performance of the whole system. This effect is reduced by the large number of synapses.

5 Discussion

In the present study we argued that it is the role of the cerebellum to learn to compensate for any error generated by the nonlinear frontocollicular pathway. By carefully reviewing and integrating known biological data, we showed how a semirealistic cerebellar network with adaptive capabilities could potentially learn how to control the highly nonlinear saccadic system. In the companion paper (Schweighofer et al. 1996) we simulate this model, and based on the above analysis and the simulation results, we make several predictions and propose several new experiments.

This work was inspired by pre-existing models of the cerebellum, and notably by the CMAC model (Albus 1975), the cerebellar learning model of Houk et al. (1990), and the theoretical model of saccadic learning and control developed by Grossberg and Kuperstein (1989). It is of interest to relate our model to the feedback error learning scheme (Kawato and Gomi 1991). In the feedback error learning scheme, the feedback controller output provides the training signal. Thus, the IO activity reflects the output of the feedback controller and therefore carries the amplitude and direction of the movement. Over trials the movement execution is taken over entirely by the cerebellum and the feedback controller activity disappears: the inverse model of the plant (the motor neurons, the muscles and the eye ball) resides entirely in the cerebellum, and other brain structures are involved only to assist the cerebellum in case of unexpected deviations. However, we believe that the cerebellum is only part of the inverse model of the plant: the non-adaptive

[6] We modeled a subtractive normalization. In simulations we also tried a multiplicative normalization; however, it gave a learning curve somewhat different from the data.

pathway is an approximate inverse model (which can be thought of as genetically programmed) which is being adaptively compensated by the cerebellum.

Recently, another model of the cerebellar control of saccades (Dean et al. 1994) was proposed. This model was developed with the same goals as ours, i.e., learning the nonlinearities of the plant and learning target perturbations. Moreover, it nicely reproduces experiments in which the eye muscles are weakened. Our model differs from theirs on the following issues: (1) Dean et al.'s model is more of a control system type model, which does not reproduce firing patterns of specific neuronal populations. This approach has the advantage of being computationally easy, and permits a departure from known biological facts to make further predictions (for instance, these authors looked at the performance of the system with different kinds of olivary error signals). In the companion paper (Schweighofer et al. 1996) we carefully ground the model in specific and real neuron subpopulations and as such we are able to study the temporal responses, i.e., the firing patterns of the relevant subpopulations of neurons. (2) The results from Goldberg et al. (1993) show that the visual information for adaptation to target perturbations at least are not carried by the NRTP mossy fibers. (3) The IO error signal must be delayed – hence our model of the window of eligibility which allows to 'reach through time'.

Appendix. Neuronal modeling

The cells in our model interact only via their 'firing rates,' while the firing rate of a cell depends only on its own membrane potential. Computer simulation cycles through two steps:

Step 1. Updating the membrane potentials. The membrane potential of each cell is described by a differential equation of the form:

$$\tau_m \frac{dm(t)}{dt} = -m(t) + S_m(t)$$

The time step Δt is set equal to 5 ms and $dm(t)/dt$ is approximated by the ratio $(m(t+\Delta t) - m(t))/\Delta t$. The subscript 'm' indicates the specific cell type, while $m(t)$ denotes the membrane potential to that cell at time t. τ_m is the time constant for the rate of change of this potential. $S_m(t)$ represents the total input that the cell of type m receives from other cells.

Step 2. Updating the firing rates. Rather than model spike generation (with the exception of the IO cells), we use a coarse approximation. The 'firing rate' of a cell is obtained by passing the membrane potential through a nonlinear function. The result of this transformation is that the firing rate of the neuron increases as the sum of the inputs increases up to a specified maximum at which the firing rate saturates. Except for the IO cells, the function used is a saturation function with a linear range, i.e., the firing rate F is a function of the membrane potential m such as:

if $m < x_1$, then $F(m) = 0$,

else if $x_1 \leqslant m \leqslant x_2$,

then $F(m) = \dfrac{y_1}{(x_2 - x_1)}(m - x_1)$,

else $F(m) = y_1$

with $x_1 < x_2$ and $0 < y_1$.

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References

Albano JE, King WM (1989) Rapid adaptation of saccadic amplitude in humans and monkeys. Visual Sci 30:1883–1893

Albus JS (1971) The theory of cerebellar function. Math Biosci 10: 25–61

Albus JS (1975) A new approach to manipulator control: the cerebellar model atriculation controller (CMAC). J Dynam Syst Meas Contr 97:220–227

Baker R, Precht W, Llinás R (1972) Mossy and climbing fiber projections of extraocular muscle afferents to the cerebellum. Brain Res 38:440–445

Berthier NE, Singh SP, Barto AG, Houk JC (1993) Distributed representation of limb motor programs in arrays of adjustable pattern generators. J Cogn Neurosci 5:56–78

Blanks R (1988) Cerebellum. In: Buttner-Ennever JA (ed) Neuroanatomy of the oculomotor system. Elsevier, Amsterdam

Crepel FC, Krupa M (1988) Activation of protein kinase C induces a long-term depression of glumatate sensitivity of cerebellar Purkinje cells: an in vitro study. Brain Res 458:397–401

Dean P, Mayhew JEW, Langdon P (1994) Learning and maintaining saccadic accuracy: a model of brainstem cerebellar interactions. J Cogn Neurosci 6:117–138

Dominey P, Arbib M (1992) A cortico-subcortical model for generation of spatially accurate sequential saccades. Cerebral Cortex: 2: 153–175

Eccles JC (1973) The cerebellum as a computer: patterns in space and time. J Physiol (Lond) 229:1–32

Fitzgibbon EJ, Goldberg ME, Segraves MA (1986) Adaptive processes in the visual and oculomotor systems. Pergamon Press, Oxford

Frankfurter A, Weber JT, Royce GJ, Strominger NL, Harting JK (1976) An autoradiographic analysis of the tecto-olivary projection in primates. Brain Res 118:245–257

Fuchs AF, Kornhuber HH (1969) Extraocular muscle afferents to the cerebellum of the cat. J Physiol (Lond) 200:713–722

Fuchs AF, Robinson FR, Straube A (1993) Role of the fastigial nucleus in saccade generation: neuronal discharge patterns. J Neurophysiol 70:1723–1740

Gilbert P, Thach WT (1977) Purkinje cell activity during motor learning. Brain Res 128: 309–328

Goldberg ME, Musil S, Fitzgibbon E, Smith M, Olson C (1993) The role of the cerebellum in the control of saccadic eye movements. In: Mano N, Hamada I, Delong MR (eds) The role of the cerebellum and basal ganglia in voluntary movement. Excerpta Medica, Amsterdam, pp. 203–211

Gonzalo-Ruiz A, Leitchnetz G (1990) Afferents of the caudal fastigial nucleus in the New World monkey. Exp Brain Res 80:600–608

Grossberg S, Kuperstein M (1989) Neural dynamics of adaptive sensory motor control. Pergamon Press, Oxford

Houk JC, Singh SP, Fisher C, Barto AC (1990) An adaptive sensorimotor network inspired by the anatomy and physiology of the cerebellum. In: Miller WT et al. (eds) Neural networks for control. MIT Press, Cambridge, Mass

Houk JC, Galiana HL, Guitton D (1992) Cooperative control of gaze by the superior colliculus, brainstem and cerebellum. In: Stelmach GE, Requin J (eds) Tutorials in motor behavior II. Elsevier, Amsterdam

Ikeda Y, Noda H, Sugita S (1989) Olivocerebellar and cerebellolivary connections of the oculomotor region of the fastigial nucleus in the monkey. J Comp Neurol 284:463–488

Ito M (1984) The cerebellum and neuronal control. Raven Press, New York

Ito M (1990) A new physiological concept on cerebellum. Rev Neurol (Paris) 146:564–569

Kase M, Miller DC, Noda H (1980) Discharges of Purkinje cells and mossy fibers in the cerebellar vermis of the monkey during saccadic eye movements and fixation. J Physiol (Lond) 300:539–555

Kawato M, Gomi H (1991) A computational model of four regions of the cerebellum based on feedback-error-learning. Biol Cybern 68:95–103

Keller E (1989) The cerebellum. In: Wurtz RH, Goldberg ME (eds) The neurobiology of saccadic eye movements. Elsevier, Amsterdam, pp 391–411

Klopf H (1982) The hedonistic neuron: a theory of memory, learning and intelligence. Hemisphere, Washington, DC

Linden DJ, Smeyne M, Connor JA (1993) Induction of cerebellar long-term depression in culture requires postsynaptic action of sodium ions. Neuron 11:1093–1100

Llinás R, Baker R, Sotelo C (1974) Electrotonic coupling between neurons in cat inferior olive. J Neurophysiol 37:560–571

Marr D (1969) A theory of cerebellar cortex. J Physiol (Lond) 202:437–470

Mugnaini E (1983) The length of cerebellar parallel fibers in chicken and rhesus monkey. J Comp Neurol 220:7–15

Noda H (1991) Cerebellar control of saccadic eye movements: its neural mechanisms and pathways. J Physiol (Tokyo) 41:351–368

Noda H, Sugita S, Ikeda Y (1990) Afferent and efferent connections of the oculomotor region of the fastigial nucleus in the macaque monkey. J Comp Neurol 302:330–348

Noda H, Murakami S, Warabi T (1991) Effects of fastigial stimulation upon visually-directed saccades in macaque monkeys. Neurosci Res 10:188–199

Ohtsuka K, Hiroharu N (1991) Saccadic burst neurons in the oculomotor region of the fastigial nucleus of the macaque monkey. J Neurophysiol 65:1422–1434

Ohtsuka K, Noda H (1992) Burst discharges of mossy fibers in the oculomotor vermis of macaque monkeys during saccadic eye movement. Neurosci Res 15:102–114

Optican L, Robinson D (1980) Cerebellar-dependent adaptive control of primate saccadic system. J Neurophysiol 44:1058–1076

Oscarsson O (1980) Functional organization of olivary projection to the cerebellar anterior lobe. In: Courville J, Lamarre Y (eds) The inferior olivary nucleus: anatomy and physiology. Raven Press, New York

Ritchie L (1976) Effects of cerebellar lesions on saccadic eye movements. J Neurophysiol 39:1246–1256

Robinson DA (1970) Oculomotor unit behavior in the monkey. J Neurophysiol 33:393–404

Schweighofer N, Arbib MA, Dominey PF (1996) A model of the cerebellum in adaptive control of saccadic gain. II. Simulation results. Biol Cybern 75:29–36

Scudder CA (1988) A new local feedback model of the saccadic burst generator. J Neurophysiol 59:1455–1475

Segraves M, Goldberg ME (1987) Functional properties of corticotectal neurons in the monkey's frontal eye field. J Neurophysiol 58: 1378–1419

Sutton RS, Barto AG (1981) Toward a modern theory of adaptive networks: expectation and prediction. Psychol Rev 88:135–170

Weiss C, Houk JC, Gibson AR (1990) Inhibition of sensory responses of cat inferior olive neurons produced by stimulation of red nucleus. J Neurophysiol 64:1170–1185

Yamada J, Noda H (1987) Afferent and efferent connections of the oculomotor cerebellar vermis in the macaque monkey. J Comp Neurol 265:224–241