A PHYSIOLOGICAL NEURAL NETWORK FOR SACCADIC EYE MOVEMENT CONTROL

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13. ABSTRACT *(Maximum 200 words)*

Based on electrophysiological evidence, eye-movement measurements and systems control theory, a new physiological neural network model of horizontal saccadic control is described. The neural control mechanism is first-order, time-optimal, and is initiated by the deep layers of the superior colliculus and terminated by the cerebellar fastigial nucleus. The neural circuit consists of neurons in the paramedian pontine reticular formation, the vestibular nucleus, abducens nucleus, oculomotor nucleus, cerebellum, substantia nigra, nucleus reticularis tegmenti pontis, the thalamus, the deep layers of the superior colliculus and the oculomotor plant for each eye. Each of the neural sides in the model produce firing rates matching experimental data, and simulate fast eye movements that match the recorded data extremely well for saccades of all sizes. All features of these simulations, including peak velocity, duration, and amplitude conform to published observations.

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Summary

Response in the natural environment involves the integration of sensory and motor inputs from the simplest reflex arc to the most complex cortical processing. Current understanding of how the central nervous system processes multisensory information is quite complex and not well understood. In this paper, theoretical and experimental results are presented and extrapolated tc described a physiological neural network responsible for oculomotor control in response to visual stimuli.

The overall goal of this investigation is to ultimately produce a model that will predict the head and eye movement responses to any combination of visual, auditory, and vestibular inputs in a changing environment. Theoretical models presented in this report will be used as a component in a neural network responsible for all sensorimotor control. The ultimate goal of this research is to enhance our understanding of how the brain monitors, integrates and adaptively controls neurosensory information.

Previously, the operation of a time-optimal control mechanism was demonstrated during horizontal goal-directed visual eye movements. This study involved an extensive time optimal control investigation using a direct method, and parameter and control estimation using the system identification technique. Since these studies, a new linear homeomorphic model of muscle was developed that has the static and dynamic properties of muscle. An initial study on a time-optimal neural network for the control of horizontal saccades elicited from visual stimulus has also been published. This neural network is the first saccade generator model to include the cerebellum as an important element in the network, and also incorporate the new linear muscle model within the oculomotor plant.

For many years, scientists have obtained data on the firing patterns of neurons at various neural sites during eye and head movements, and developed conceptual models of their behavior. One of the most puzzling aspects of oculomotor research is assessing the role of the cerebellum during saccades. While some neural networks have been proposed which included some sites important for the control of eye movements, the time optimal control and adaptive features of the true biological controller have not been fully explored during saccades. An adaptive control system is developed here that models the cerebellum's function during eye movements in response to sensory information. Presented in this report is a single input time optimal control system depicting the functioning of important nuclei operating during a saccade.

Based on electrophysiological evidence, eye-movement measurements and systems control theory, a new local feedback model of horizontal saccadic neural control is described. The neural control mechanism is first order time optimal with pronounced stochastic rebound neural firing after marked inhibition. The neural circuit consists of neurons in the paramedian pontine reticular formation (burst, tonic and pause cells), the vestibular nucleus, abducens nucleus, oculomotor nucleus, cerebellum, substantia nigra, nucleus reticularis tegmenti pontis, the thalamus, the deep layers of the superior colliculus and the oculomotor plant for each eye.

Agonist burst cell activity is initiated with maximal firing due to an error between the target and eye position, and continues until the internal eye position in the

cerebellar vermis reaches the desired position, then decays to zero. The cerebellar vermis is also responsible for adapting the duration of maximal firing based on the initial position of the eye. Due to prior pause cell inhibition of the burst cells, stochastic rebound burst cell firing occurs, resulting in a temporary rise and fall firing above the maximal steady state burst firing level. Tonic cells "mathematically integrate" burst cell activity to yield an internal estimate of the current eye position. There are two sets of neural integrators in the neural network. One operates within the cerebellar vermis to predict the width of the pulse, and the other within the paramedian pontine reticular formation to maintain the eyes at their destination.

Antagonist neural activity is inhibited during the agonist burst activity. After the agonist burst, antagonist neural activity rises with a stochastic rebound burst and from input from the fastigial nucleus, then falls to a tonic firing level necessary to keep the eye at its destination. The onset of the antagonist tonic firing is stochastic, weakly coordinated with the end of the agonist burst, and under cerebellar control.

A common mechanism of action is described, based on cerebellar gating, through the fastigial nucleus, that explains a number of different saccadic eye movement types, including dynamic overshoot, glissadic overshoot and undershoot, and undershoot.

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Introduction

The visual system is our most important sensory system. The oculomotor system is responsible for movement of the eyes so that images are centered on the central region of the retina, called the fovea. The oculomotor system responds to visual, auditory and vestibular stimuli, which results in one of five types of eye movements: saccadic eye movements, smooth pursuit eye movements, vestibular ocular movements, vergence eye movements and optokinetic eye movements. Each of these movements is controlled by a different neuronal system, and all of these controllers share the same final common pathway to the extraocular muscles. In addition to the five types of eye movements, these stimuli also cause head and body movements. Thus, the visual system is part of a multiple input-multiple output system. Because of the importance of fast or saccadic eye movements in scanning for objects of interest in space, saccadic eye movements are the primary focus of this investigation. A saccade is a quick eye movement that places a visual target on the high resolution region of the retina. Numerous investigations, particularly in recent years have greatly contributed to our knowledge of the elementary control mechanism during saccadic eye movements. Yet, many aspects of the basic control mechanism during saccadic eye movements are still uncertain [1].

In the sections that follow, the long term objective of the overall project is described. After this, a description of the research in this project is described and related to the overall project objectives. Following the description of the project, a detailed top-down description is given for the saccadic control mechanism for a visual stimulus, saccades and the oculomotor plant, and the muscle model. Simulations are then presented which describe a common mechanism for all post saccade phenomenon.

Central Nervous System Sensory Processing

The central nervous system (CNS) processing of multisensory information is quite complex and not well understood. Visual, auditory and vestibular sensory data are all initially encoded in various frames of reference that are different from the coordinate system of the eyeball. It is assumed that this sensory data is translated into a common coordinate system by the CNS, and then sent to the extraocular muscles along a final common pathway. The translation of sensory data must be combined with CNS information about the current position of the eyes and the head to direct the eyes to the target location. While a common coordinate system for translation of sensory data is assumed to exist, its description is unknown at this time [2]. Furthermore, the interaction among multisensory data, and how conflicting information is arbitrated, is not well understood [2].

Numerous investigators have experimentally examined the single stimulus CNS response to visual, auditory or vestibular stimuli. While attempts have been made to examine how the human CNS integrates and processes multisensory information from combined visual, auditory and vestibular stimuli to direct the head and eye responses, much remains unknown [3]. Most researchers have investigated animal model multisensory stimuli sensorimotor integration from an electrophysiological, anatomical and a neural pathway methodology (see Sparks for a review of the literature [2]). However, since little is known about the detailed intrinsic organization of the superior colliculus, cerebellum, thalamus, cortex and other midbrain nuclei, the anatomical and neural pathway methodology is not suffi-

cient alone to be useful in constructing a comprehensive model of the CNS control of multisensory information. A special need for additional approaches is identified by Sparks as necessary to help delineate the CNS control of multisensory information [2].

The effect of combinations of sensory stimuli on the head and saccadic eye movement response has been studied by Meredith and Stein [4]. They examined cell responses in cat and hamster to combinations of visual, somatic and auditory stimuli, and noted dramatic enhancement and inhibitory effects in microelectrode studies. The effectiveness of each stimulus is noted to be a function of the environment, that is, auditory stimuli are more effective in darkness or low level illumination, whereas visual stimuli are more effective in higher levels of illumination. Moreover, the responsiveness of one stimulus can dramatically affect the responsiveness of other stimuli.

The neural response to combinations of sensory stimuli all flow along the same common pathway to the extraocular muscles to control saccadic eye movements. The functional consequences of combined stimulus interactions is not well understood. Certainly, a saturation phenomenon occurs in the neural control mechanism to combinations of sensory stimuli [1]. Thus, the control signal generated by the neural control mechanism does not equal the sum of the controllers for each separate stimulus. Meredith and Stein noted that knowledge of cell responses to individual stimuli could not predict the response to combined stimuli [4]. Furthermore, the CNS processing of sensory stimuli occur in different locations of the brain, and thus (stochastic) timing differences are important.

Investigators have reported a tightly coupled relationship between eye and head movements toward visual targets in monkeys [5] [6]. Moreover, a time optimal control mechanism for human head rotations has been postulated [7]-[12]. Coordinated eye and head movements have not yet been identified as time optimal. Qualitatively, a natural orienting movement to a visual target typically involves the following three steps [13]. First, a saccadic eye movement is executed which moves the eyes towards the target. Approximately 25 to 40 msec after the saccadic eye movement begins, a head movement of the same magnitude as the eye movement is executed. Finally, as the head moves, a vestibular response due to the head motion causes the eyes to be rotated in the opposite direction that the head is moving. Other investigators have indicated the rotation of the eyes during the head movement is not caused by a vestibular mechanism, but by a reset mechanism [14].

Despite many experimental studies that qualitatively describe eye and head coordination, a *quantitative* description of the eye and head neural control mechanism has not been reported, particularly small amplitude target movements under 15°. Two specific *qualitative head* movement patterns have been identified. For small amplitude target stimuli (under 15°), the majority of responses involved movement of the eyes only, the head voluntarily remained fixed [15]. For large amplitude target stimuli (greater than 15°), almost all responses involved coordinated eye and head movement [5] [6],[14]-[17]. Neither the head movement paradigm or the neural control mechanism has been reported in these studies. However, some investigators have noted a neural control strategy that operates to maintain the fovea on the target [15], [17].

Analysis of EOG data indicates that the peak velocity of large amplitude saccades are lower during combined eye and head movement than when the head was restrained [16]. Clearly, small amplitude saccades have the same peak velocity since there is no head movement. From Fig. 1 in Morasso *et al.* [16], it appears that the time to complete the sac-

cadic eye movement is shorter during the combined eye and head movement than in the case where the head was restrained (for larger, not smaller movements). Since visual perception is suppressed during a saccade, minimizing saccade duration is important [18], [19]. Thus, it appears that for a large target amplitude, combined head and eye movements might restore visual perception faster than an eye movement alone.

To direct the eyes towards a target, one possible neurosensory control mechanism for head and eye movements is to minimize the saccade duration. This is a time optimal controller. Such a controller would explain why most naturally occurring saccades are less than 15° in amplitude, with no head movement [20]. A small amplitude eye movement is executed without a coordinated head movement since the head movement does not decrease the time it takes to move the eyes onto the target because of inherent time delays. Moreover, a combined head and eye movement is executed when target amplitudes are larger than 15° since it takes less time to move the eyes to the target than with an eye movement only.

Figure 1 describes a block diagram of the eye and head movement system. The relationship between the input and the output is given by

$$\theta_1 = H_1 x_1$$
$$\theta_2 = H_2 x_2$$

where H_1 is the input independent transfer function for the eye movement system, H_2 is the transfer function for the head movement system, x_1 is the neural control mechanism for the saccadic eye movement system, and x_2 is the neural control mechanism response for the head movement system. Note that a possible vestibular feedback due to the head movement is included to the oculomotor neural control mechanism. The control signal, x_1, sent to the oculomotor system depends on the nonlinear interactions that take place in the CNS. A saturation phenomenon most likely occurs in the neural control mechanism. Thus, the control signal generated by the neural control mechanism does not equal the sum of the controllers.

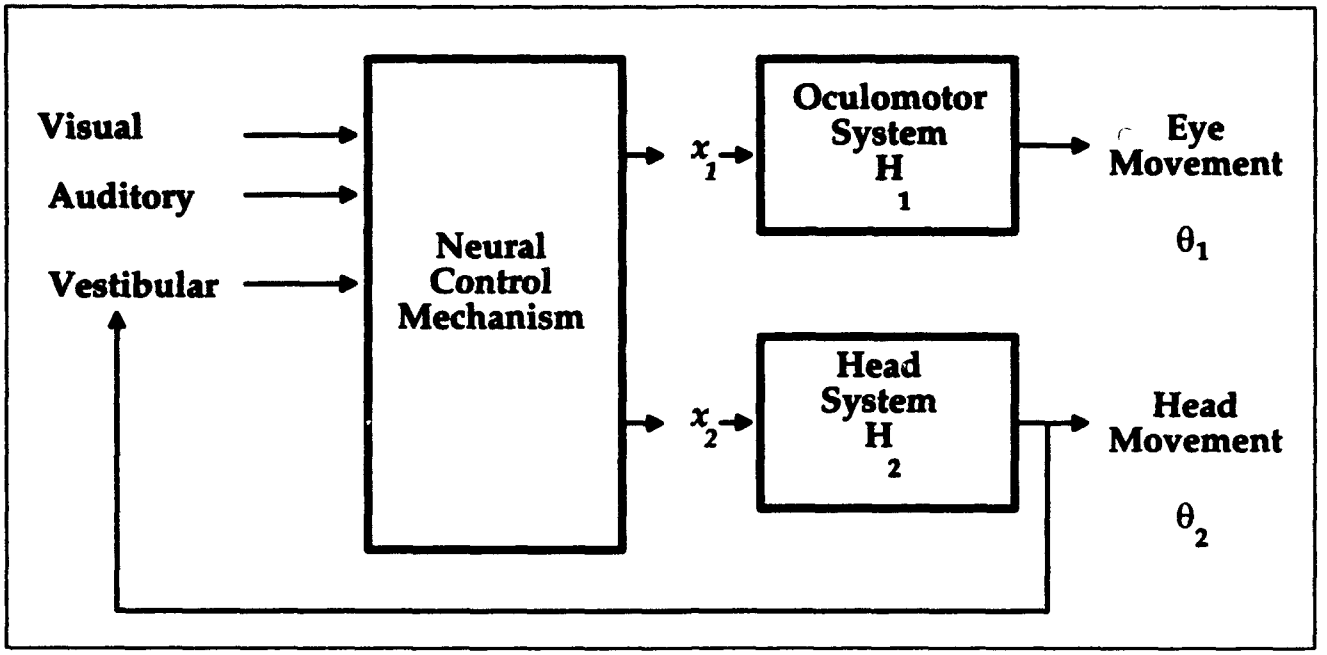

Figure 1. A block diagram of eye and head movement system.

In order to better understand the eye and head movement system, it is necessary to partition the study into smaller studies that will increase our understanding of how the brain integrates and controls information. To use systems analysis for theoretical model development of a complete multiple-input, multiple-output eye and head movement model for single and multiple sensory sources, it is important to partition the study into a series of interdependent models involving neural networks and Newtonian mechanics. Each model is designed to increase our understanding of how the brain integrates and controls information. Only by systematic and thorough investigation of these models of increasing complexity, is it possible to gain an understanding of all the experimental data, data that are often times in confliction. Therefore, this investigation is limited to the development of a neural network for horizontal goal directed visual saccades, and will be presented in two stages. The first stage will deal with the development of a physiological neural network for horizontal saccades, and the second stage will deal with the development of an oculomotor plant model for horizontal saccades. Models for a two-dimensional neural network, auditory and vestibular stimuli, and head movements will be carried out in future studies.

Current Project for a Goal Directed Visual Saccade Circuit

The primary focus for the research in this project is to extend our knowledge of how the CNS interprets visual information, and adaptively monitors and controls the saccadic eye movement system without head movements. Physiological evidence indicates that saccades are controlled through a parallel distributed network involving the cortex, cerebellum, and brain stem. A number of important and critical questions still remain regarding the operation of the saccade generator such as:

- Does the cerebellum have a role in the control of saccades? It should be noted that none of the current functional models for a saccade generator include the cerebellum (with the exception of a preliminary study by Enderle and coworkers [21]).
- What is the mechanism for translation of sensory signals into motor commands to initiate and adaptively control saccades?
- What causes stochastic post saccade phenomenon such as dynamic overshoot and glissades?

The work carried out in this project will begin to provide quantitative and qualitative answers to the previous questions. Toward this goal, a theoretical neural circuit for an adaptive controller for goal directed visual saccades is presented involving the cerebellum, superior colliculus, thalamus, cortex and other nuclei in the brain stem. Of central importance to this effort is the monitoring and adaptive control activity of the cerebellum.

Shown in Figure 2 is a diagram illustrating important sites for the generation of a conjugate horizontal saccade in both eyes. It consists of the familiar premotor excitatory burst neurons (EBN), inhibitory burst neurons (IBN), long lead burst neurons (LLBN), omnipause neurons (OPN), tonic neurons (TN), and the vestibular nucleus, abducens nucleus, oculomotor nucleus, cerebellum, substantia nigra, nucleus reticularis tegmenti pontis (NRTP), the thalamus, the deep layers of the superior colliculus (SC), and the oculomotor plant for each eye. Excitatory inputs are shown with an arrow, inhibitory inputs are shown with a $\perp$. Consistent with current knowledge, the left and right structure of the neural circuit model are maintained. This circuit diagram was constructed after a careful review of the current literature. Each of the sites and connections are supported by firm physiological evidence. Since we are interested in goal directed visual saccades (as opposed to voluntary saccades), the cortex has not been partitioned into the frontal eye field and posterior eye field (striate, prestriate, and inferior parietal cortices). Both the neural circuit and the oculomotor plant will be described in detail throughout the remainder of the report.

A linear homeomorphic oculomotor plant is used with the agonist and antagonist neural activity separately maintained. Shown Figure 3 is a model of the oculomotor plant for each eye. Stochastic muscle saturation and pronounced stochastic post inhibitory rebound burst firing in the premotor neurons are implicitly included in the model as supported by physiological evidence [1]. Muscle saturation is illustrated in the block diagram in Figure 4. Parameter estimates for the oculomotor plant shown in Figure 3 were obtained using the system identification techniques [22]. The saccade generator model, as will be described, is rigorously tested against experimental data, including electrophysiological data, and eye movements with dynamic overshoot, glissadic overshoot and undershoot, and undershoot. Examples of eye movement recordings with these characteristics are shown in Figure 5. A common mechanism of action, dependent on the gating effects of the cerebellum, is described in this report which accounts for all types of saccades.

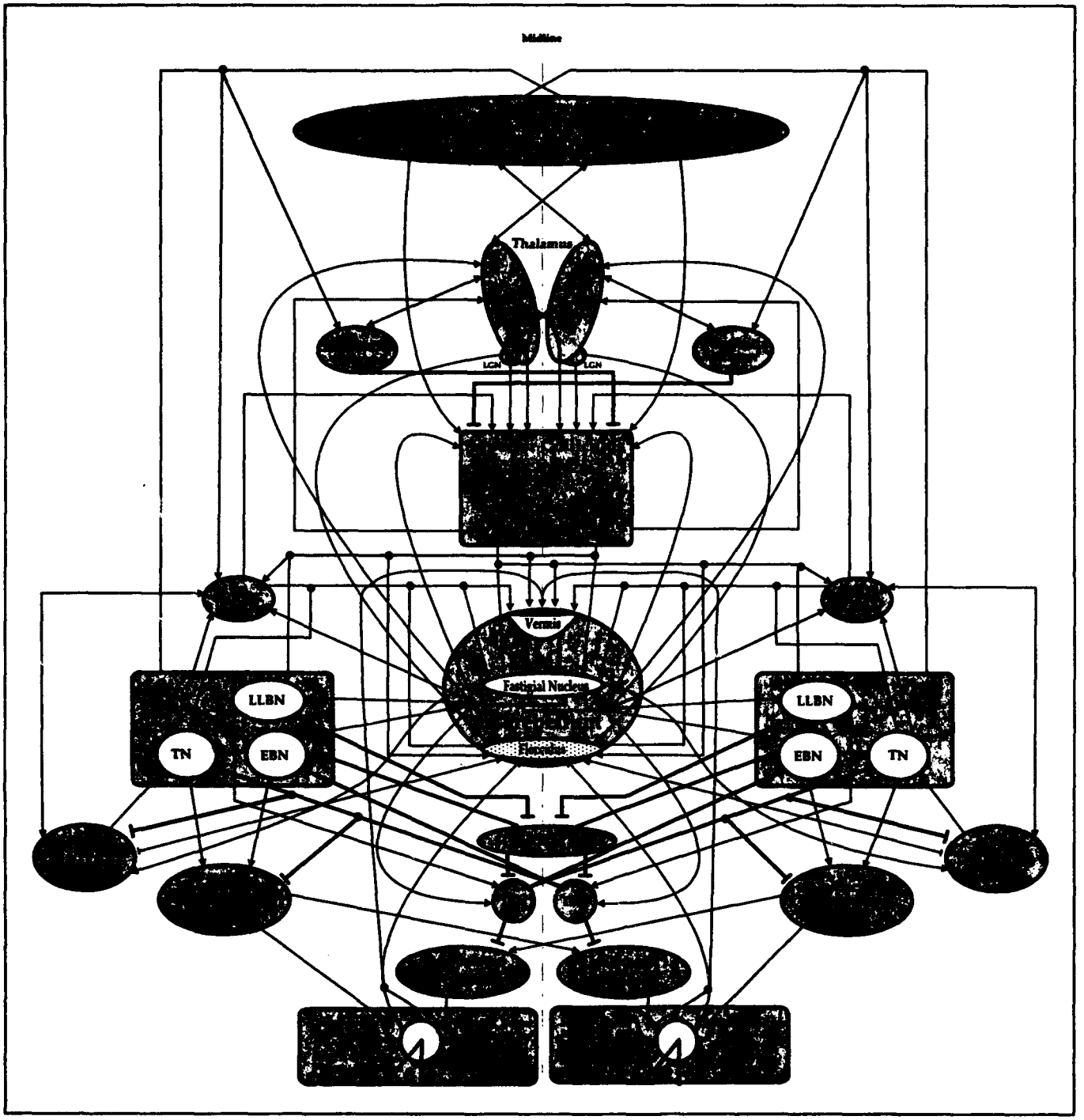

Figure 2. A physiological neural network for human eye movement control.

Saccade Pathways

The axons of retinal ganglion cells exit and join other neurons to form the optic nerve. The optic nerves from each eye then join at the optic chiasm, where fibers from the nasal half of each retina cross to the opposite side. Axons in the optic tract synapse in the LGN (a thalamic relay), and continue to the visual cortex. This portion of the saccade neural

network is concerned with the recognition of visual stimuli. Axons in the optic tract also synapse in the superior colliculus. This second portion of the saccade neural network is concerned with the location of visual targets and is primarily responsible for goal directed saccades. The frontal eye fields are concerned with generating saccades to complex visual

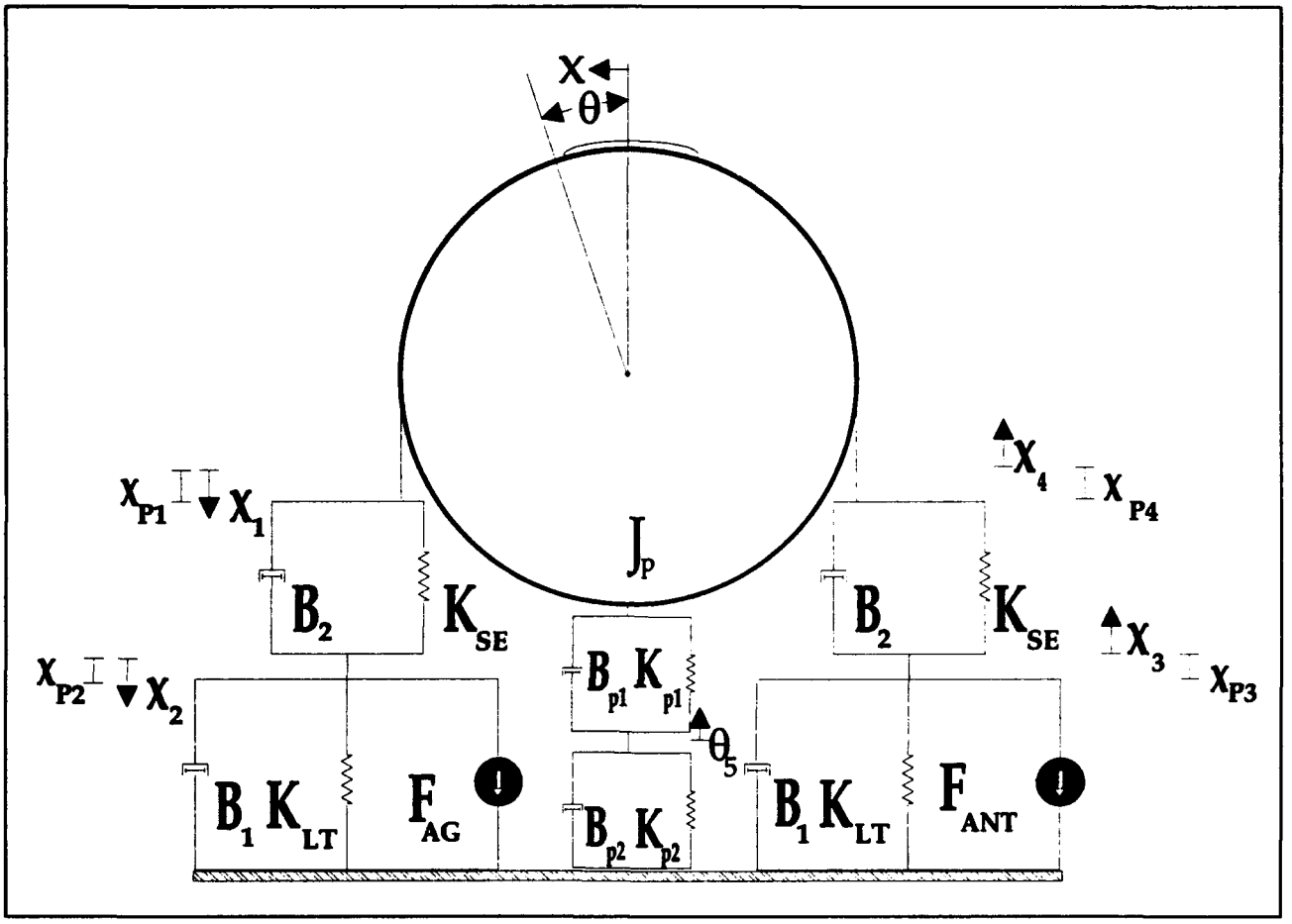

Figure 3. Oculomotor plant for each eye.

stimuli after receiving input from the visual cortex. Note that these pathways are not explicitly depicted in the physiological neural network in Figure 2, but are implicitly assumed to be part of the network.

Clinical evidence, lesion and stimulation studies all point toward the participation of vitally important neural sites in the control of saccades, including the cerebellum, superior colliculus, thalamus, cortex and other nuclei in the brain stem (for example, see [23]-[24]). Through many clinical, experimental, lesion and stimulation studies, it is clear that a number of neural sites are active during saccades, and that saccades are driven by parallel neural networks. The saccadic neural activity of the superior colliculus and cerebellum, in particular, have been identified as the saccade initiator and terminator, respectively, although neither is required for a saccade. The impact of the frontal eye field and the thalamus, while very important, have less important roles in the generation of goal-directed saccades to visual stimuli. The frontal eye field are primarily concerned with voluntary saccades, and the thalamus appears to be involved with corrective saccades. Therefore, this report primarily

describes the oculomotor neural activity within the superior colliculus and cerebellum responsible for goal-directed saccades.

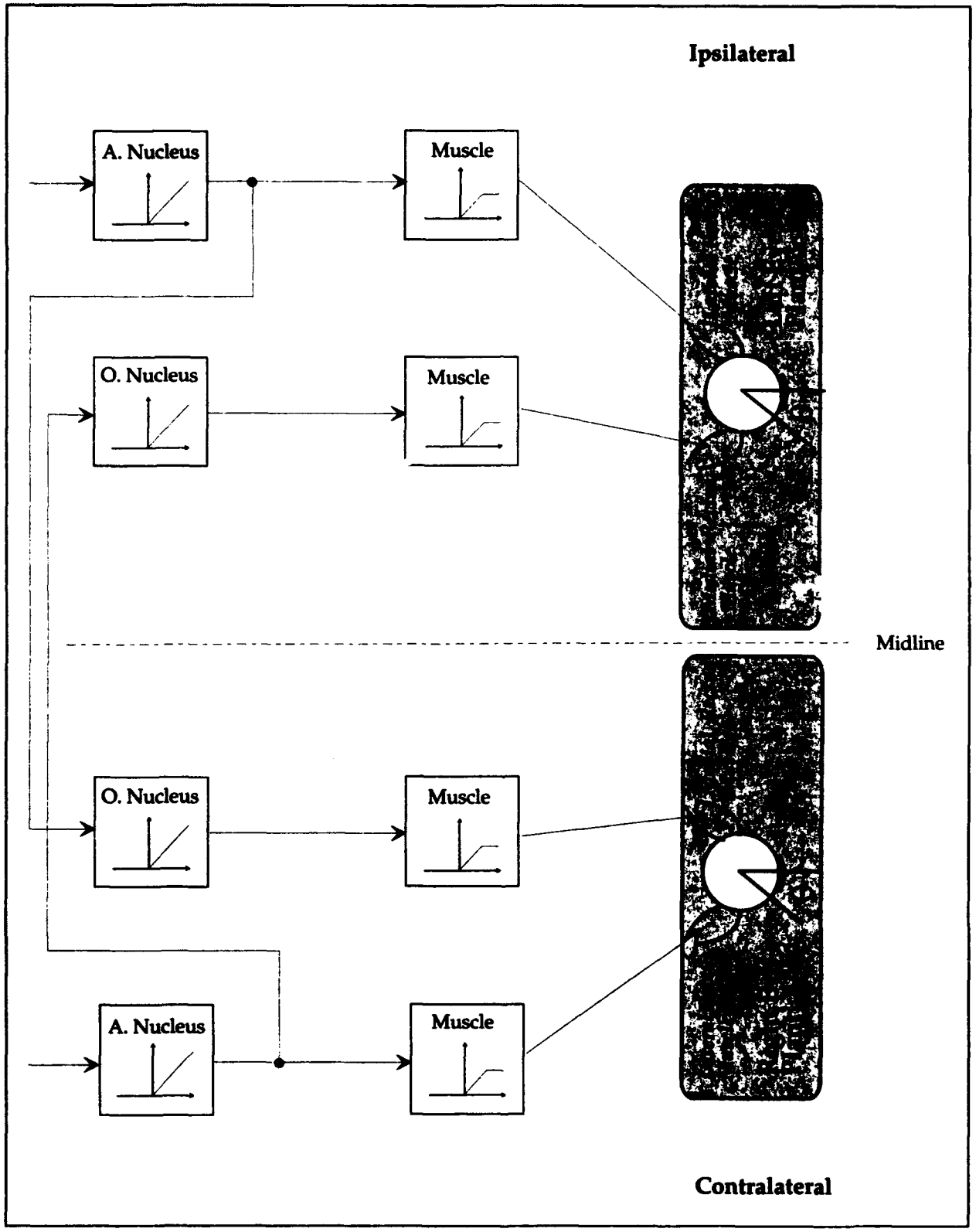

Figure 4. Block diagram of muscle saturation.

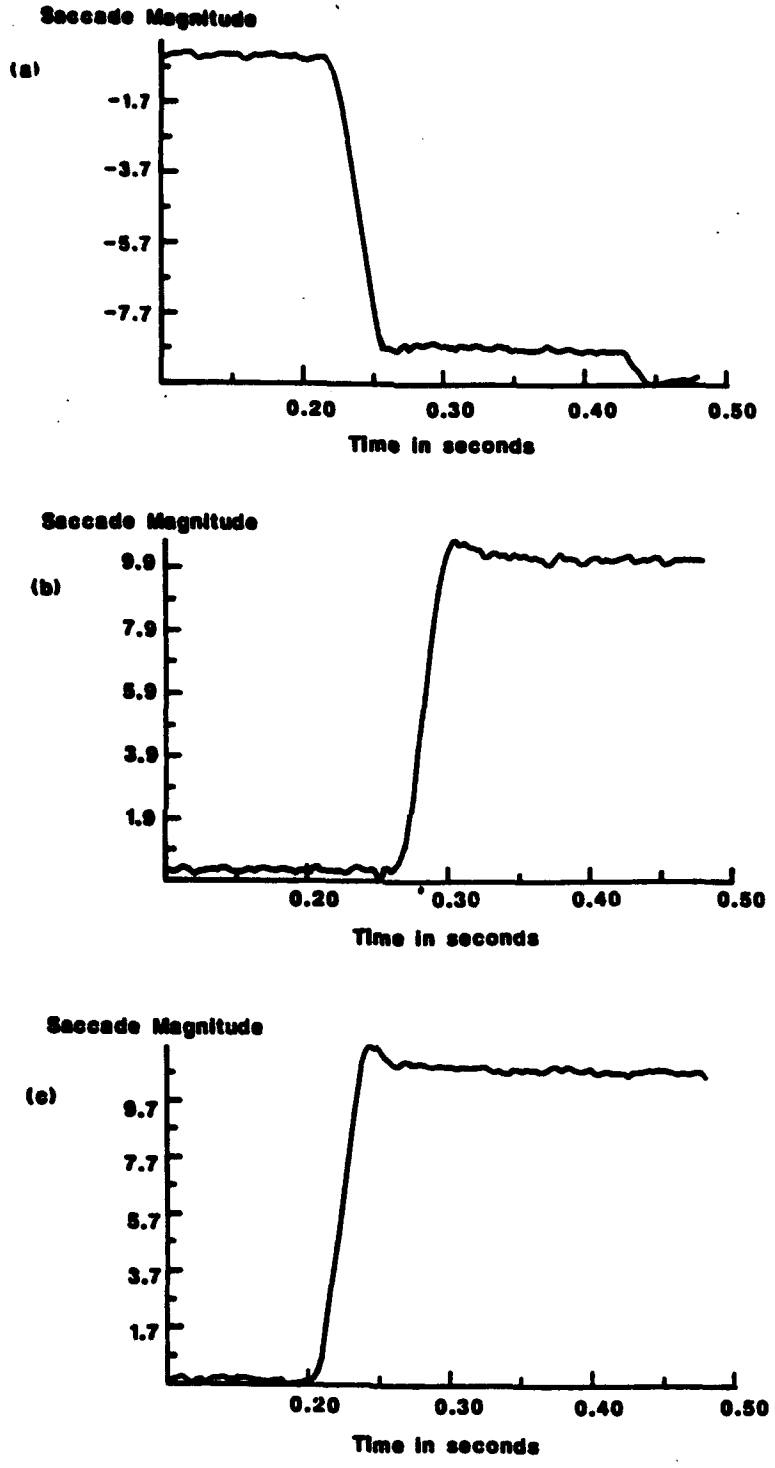

Figure 5. Various eye movement recordings: (a) a normal saccade, (b) a glisssadic eye movement, and (c) a saccade with dynamic overshoot.

Superior Colliculus

The superior colliculus contains two major functional divisions· a superficial division and an intermediate or deep division, and has been identified as an important neural site during saccades, [2] [25]-[31]. Inputs to the superficial division are almost exclusively visual and originate from the retina and the visual cortex [2]. Most efferent projections of the superficial layers ascend in fiber tracts that terminate in the thalamus [2] [24]. The deep layers provide a convergence site of convergence for sensory signals from several modalities and a source of efferent commands for initiating orienting movements. The deep layers of the superior colliculus sends input to the contralateral LLBN, NRTP, cerebellar vermis and flocculus, and ipsilateral thalamus, cerebellar fastigial nucleus. The deep layers of the superior colliculus receives input from the ipsilateral thalamus and cortex, and contralateral input from the substantia nigra (inhibitionary) and the cerebellar fastigial nucleus. The substantia nigra fires tonically at 40-100 Hz and pauses during saccades (approximately 40 ms before and up to 150 ms after) [2], [28], [32]. After a retinal error has been detected, the error is represented within the movement field of the deep layer of the SC (indicating the motor error). The SC is the initiator of the saccade and thought to translate visual information into motor commands.

The deep layers of the superior colliculus initiate a saccade based on the distance between the current position of the eye and the desired target [2]. The neural activity in the superior colliculus is organized into movement fields that are associated with the direction and saccade amplitude, and does not involve the initial position of the eyeball whatsoever. The movement field is shown in Figure 6 for a twenty degree saccade. Neurons active during a particular saccade are shown as the dark circle, representing a desired 20° eye movement. Active neurons in the deep layers of the superior colliculus generate a high frequency burst of activity beginning 18-20ms before a saccade and end sometime toward the end of the saccade; the exact timing for the end of the burst firing is quite random and can occur slightly before or slightly after the saccade ends. Each active bursting neuron discharges maximally, regardless of the initial position of the eye. Neurons discharging for small saccades have smaller movement fields, and those for larger saccades have larger movement fields. All of the movement fields are connected to the same set of LLBN [2].

As reported, information concerning the saccade direction and amplitude is not contained within the discharge of a single cell. The location of active neurons specifies saccade direction and amplitude. There has been no experimental support for a direct coupling between the superficial to deep superior colliculus. Apparently, the role of the deep layers is to specify, by activating a particular subset of collicular neurons, the change in eye position required to look at a target. One of the major questions regarding the superior colliculus is the mechanism by which the signals that precisely control the direction and amplitude of the saccade are extracted from the activity of a population of neurons [27]. Interestingly, the neural activity within the superior colliculus often does not end with the end of the saccade. The results of lesions restricted to the superior colliculus indicate that it is not an essential structure for saccades–an increase in saccade latency and a small reduction in accuracy are the only observed effects.

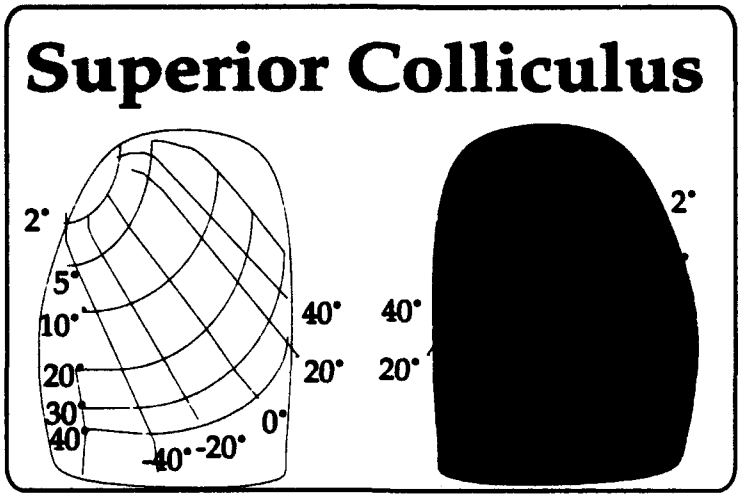

Figure 6. Movement field of Superior Colliculus.

Cerebellum

The cerebellum is responsible for the coordination of movement. The cerebellum is composed of a cortex of gray matter, internal white matter and three pairs of deep nuclei: fastigial nucleus, the interposed and globose nucleus, and dentate nucleus. The deep cerebellar nuclei and the vestibular nuclei transmit the entire output of the cerebellum. Output of the cerebellar cortex is carried through Purkinje cells. Purkinje cells send their axons to the deep cerebellar nuclei and have an inhibitory effect on these nuclei. The cerebellum is involved with both eye and head movements, and both tonic and phasic activity are reported in the cerebellum.

Ito reports that the cerebellum is not directly responsible for the initiation or execution of a saccade, but contributes to saccade precision [24]. Sites within the cerebellum important for the control of eye movements include the oculomotor vermis, fastigial nucleus and the flocculus (for example, see [23]-[49]). Consistent with the operation of the cerebellum for other movement activities, the cerebellum is postulated here to act as the coordinator for a saccade. The cerebellum receives input from three sources: the periphery (including oculomotor muscle spindles or proprioceptors), the brain stem, and the cerebral cortex. Cerebellar input connects to the cerebellar cortex and the deep nuclei [24]. Most of the outflow from the cerebellar cortex projects back to the deep nuclei (rather than out of the cerebellum). As a result, neurons in the deep nuclei compare afferent input reaching them directly with the same information after it has been processed by cerebellar cortex. Ito has described this type of connection as providing a precise gating mechanism [24].

In addition to the outflow to the deep nuclei, some portions of the cerebellar cortex project directly to the vestibular nuclei (VN). Together, the deep cerebellar nuclei and the VN transmit the entire output of the cerebellum. The upper surface of the cerebellum is divided into an anterior and posterior lobe. The posterolateral fissure on the underside of the cerebellum separates the large posterior lobe from the small flocculonodular lobe. The surface of the cerebellum has two longitudinal furrows that separate three sagittal areas from one another: a thin longitudinal strip in the midline (known as the vermis), and a left and right cerebellar hemisphere. The vermis and the hemispheres are connected to differ-

ent deep cerebellar nuclei. The vermis projects to the fastigial nucleus, and the hemispheres to the interposed nucleus and the dentate nucleus. The cerebellar cortex is a simple and uniform structure consisting of three layers with five types of neurons: stellate, basket, Purkinje, Golgi, and granule cells. The Purkinje neurons send their axons down through the third layer of the cortex into the underlying white matter, and provide the sole output of the cerebellar cortex.

Cerebellum and Saccades

The cerebellum is included in the saccade generator as a time-optimal gating element, using three active sites during a saccade: the vermis, fastigial nucleus and flocculus. The vermis is concerned with the absolute starting position of a saccade in the movement field, and corrects control signals for initial eye position [50]. Using proprioceptors in the oculomotor muscles and an internal eye position reference, the vermis is aware of the current position of the eye. The vermis is also aware of the signals (dynamic motor error) used to generate the saccade via the connection with the NRTP and the superior colliculus.

With regard to the oculomotor system, the cerebellum has inputs from superior colliculus, lateral geniculate nucleus (LGN), oculomotor muscle proprioceptors, and striate cortex via NRTP. The cerebellum sends inputs to the NRTP, LLBN, EBN, VN, thalamus, and superior colliculus. The oculomotor vermis and fastigial nuclei are important in the control of saccade amplitude, and the flocculus, perihypoglossal nuclei of the rostral medulla, and possibly the pontine and mesencephalic reticular formation are thought to form the integrator within the cerebellum [28], [51]-[52]. One important function of the flocculus may be to increase the time constant of the neural integrator for saccades starting at locations different from primary position.

Oculomotor Vermis

The oculomotor vermis is concerned with the absolute starting position of a saccade [53]. The vermis is topographically organized as determined through stimulation studies [35] [50]. It is known that nonprimary position saccades have different characteristics than saccades initiated from primary position. For instance, a saccade starting from 30° and moving to primary position has higher peak velocity, and shorter duration than a saccade moving from primary position to 30° (this is due to the oculomotor plant elastic elements, etc.). The cerebellum, as envisioned in our model, adaptively controls the duration of the agonist pulse, depending on initial and final position of the saccade. This is similar to its role in other systems whereby it plays a crucial role by adjusting (reducing the duration) the output of motor systems of the brain. Thus, when the cerebellum is removed (in lesion studies), a saccade is still executed, but it is larger than it should be (it is inaccurate), and has marked post saccadic drift [51]. The following table illustrates some complex results when the left cerebellum is lesioned and saccades are elicited, as reported in a 1983 paper by Vilis, Snow and Hore [53].

Left Eye		*Right Eye*	
Movement Left	*Movement Right*	*Movement Left*	*Movement Right*
Normal	Larger aptitude & lower velocity than right eye. No glissades or dynamic overshoot observed.	Smaller saccade amplitude than target movement. Glissadic undershoot observed to destination.	Larger saccade amplitude than target movement. Higher velocities than left eye. Dynamic overshoot observed.
Normal	*Abnormal*	*Abnormal*	*Abnormal*

With the cerebellum included in the saccade generator model presented here, predictions of the model have all of the characteristics of experimental data, including normal, lesion and stimulation data. As reported elsewhere, the cerebellum is also involved in long term adaptive control in addition to its role as a coordinator for saccadic eye movements, [51]-[52].

Fastigial Nucleus

The fastigial nucleus receives input from the superior colliculus, as well as other sites. The output of the fastigial nucleus is excitatory and projects ipsilaterally and contralaterally as shown in Figure 2 [23] [50]. During fixation, the fastigial nucleus fires tonically at low rates [36], [50]. Twenty ms prior to a saccade, the contralateral fastigial nucleus bursts, and the ipsilateral fastigial nucleus pauses and then discharged with a burst (see Figure 13 in this report) [35]. The pause in ipsilateral firing is due to Purkinje cell input to the fastigial nucleus. According to Ritchie, the sequential organization of Purkinje cells along beams of parallel fibers suggests that the cerebellar cortex might function as a delay, producing a set of timed pulses which could be used to program the duration of the saccade [54]. This type of model is referred to as a side path model [24]. If one considers nonprimary position saccades, different temporal and spatial schemes, via cerebellar control, are necessary to produce the same size saccade. It is postulated here that the cerebellum acts as a gating device which precisely terminates a saccade based on the initial position of the eye in the orbit.

The vermis and fastigial nucleus also act as a short term adaptive controller. There have been many lesion and stimulation studies carried out with regard to the cerebellum, including those by Optican and coworkers, Vilis and coworkers, Noda and coworkers, and McElligott and coworkers [35] [51] [53] [52] [55]. The saccade generator model developed here reproduces the effects noted in these reports, that is, vermis stimulation produces ipsilateral saccades and fastigial nucleus stimulation produces contralateral saccades.

Flocculus

The flocculus receives visual input from LGN and other sites as described in Figure 2, and are primarily driven by the VN. The flocculus monitors retinal slip and responds to oculomotor errors between brainstem predictions of the saccade and the actual eye movement. Based on performance, the flocculus adjusts the connectivity of the TN integrator

network to fine tune its ability to hold fixation eye position. The flocculus also participates in the vestibulo-ocular reflex. The overall activity of the flocculus is one of long term adaptability.

Paramedian Pontine Reticular Formation

The Paramedian Pontine Reticular Formation (PPRF) has neurons that burst at frequencies up to 1000 Hz during saccades and are silent during periods of fixation, and neurons that fire tonically during periods of fixation. Neurons that fire at steady rates during fixation are called tonic neurons (TN) and are responsible for holding the eye steady. The TN firing rate depends on the position of the eye (presumably through a local integrator type network). The TN are thought to provide the step component to the motoneuron. There are two types of burst neurons in the PPRF called the long-lead burst neuron (LLBN) and a medium-lead burst neuron (MLBN); during periods of fixation, these neurons are silent. The LLBN burst at least 12 ms before a saccade and the MLBN burst less than 12 ms (typically 6-8 ms) before the saccade. The MLBN are connected monosynaptically with the Abducens Nucleus.

There are two types of neurons within the MLBN, the excitatory burst neurons (EBN) and the inhibitory burst neurons (IBN). The EBN and IBN label describes the synaptic activity upon the motoneurons; the EBN excite and are responsible for the burst firing, and the IBN inhibit and are responsible for the pause. A mirror image of these neurons exists on both sides of the midline. The IBN inhibits the EBN on the contralateral side.

Also within the brain stem is another type of saccade neuron called the omnipause neuron (OPN). The OPN fires tonically at approximately 200 Hz during periods of fixation, and is silent during saccades. The OPN stops firing approximately 10-12 ms before a saccade and resumes tonic firing approximately 10 ms before the end of the saccade. The OPN are known to inhibit the MLBN, and are inhibited by the LLBN. The OPN activity is responsible for the precise timing between groups of neurons that causes a saccade. The existence of each of these PPRF neuron groups is uniformly accepted [1] [2]. The manner in which these neurons are connected, however, is not uniformly accepted.

Other Neural Sites

Activity within other neural sites associated with saccades are briefly described here. In general, neural connections and firing patterns are described.

As previously described, the FEF are primarily concerned with generating saccades to complex visual stimuli after receiving input from the visual cortex. The FEF project to a number of neural sites, including the superior colliculus, certain regions of the PPRF, thalamus and basil ganglia. The mapping of neural activity with the FEF is similar to the superior colliculus. Consistent with the superior colliculus, electrical stimulation of the FEF on one side produces conjugate saccades toward the opposite side. A unilateral lesion of the FEF causes an inability to voluntarily make a saccade to the side opposite of the lesion. A bilateral destruction of the FEF causes a complete loss of voluntary saccades.

The thalamus provides sensory input to the primary sensory areas of the cerebral cortex, and input about ongoing movements to the motor areas of the cortex. The thalamus acts as a relay, receiving sensory information and projecting that information to various cortical regions. Fibers also project from the cortex to the thalamus. The thalamus also receives input from the cerebellum (fastigial nucleus) and superior colliculus, which then

projects to the motor cortex [2] [24]. Patterns of thalamic activity during saccades are characterized by: bursts accompanying saccades, pause-rebounds, and sustained firing at a frequency determined by the eye position in the orbit [56]. A typical thalamic saccade unit discharges vigorously before a purely horizontal contralateral saccade, and pauses before an ipsilateral saccade. The thalamus is identified as important for timing control, and not signal generation, during saccades. Lesions of the internal medullary lamina of the posterior-medial thalamus cause severe deficits in the accuracy of saccades. Monkeys with thalamic saccade lesions are unable to make hypometric saccades to targets without corrective saccades [25].

The substantia nigra, a part of the basal ganglia, has mutual connections to the thalamus, receives input from the FEF, and has an inhibitory connection to the superior colliculus. During periods of fixations, neurons within the substantia nigra fires at high tonic rates, and during saccades, neurons within the substantia nigra decrease their firing rate associated with visual stimuli in the receptive field, and before saccades to visual targets [2]. Neurons in the substantia nigra inhibit cells in the deep layer of the superior colliculus. The decrease in substantia nigra firing release collicular neurons from inhibition, thus facilitating in the initiation of a saccade. The decrease in substantia nigra neural firing occurs at approximately 40 ms before the saccade, and resumed firing approximately 40-150 ms after the onset of the saccade.

Neurons in the NRTP fire at high rates during saccades and display few initial condition tendencies [57]. The primary input to the NRTP is from the contralateral superior colliculus, fastigial nucleus, and the cortex. The NRTP has a firing rate and movement fields similar to the superior colliculus. Almost the entire output of the NRTP goes to the cerebellum: projecting to the vermis for pulse control, and to the flocculus for step control. The role of the vermis and NRTP, as presented in this report, are as a pre-event integrator, which is used to predetermine the duration of the pulse, based on the orbital position of the eye before the saccade [58]. The NRTP is also thought to mediate visual signal to the flocculus via mossy fibers and relays to the VN [24].

Saccades

To execute a saccade, a sequence of complex activities takes place within the brain, beginning from the detection of an error on the retina, to the actual movement of the eyes. The work in this report concentrates on the neural activity occurring approximately 25 ms before the eyes begin to move, and excludes the previous 175 ms of CNS processing activity. The saccade generator model shown in Figure 2 is consistent with the connections of neurons as reported in the literature, and also accounts for the lesion and stimulation studies. This model is first-order time optimal [59], with activity initiated by the superior colliculus, and ended by the cerebellum.

A saccade is directly caused by a burst discharge from motoneurons in the agonist muscle and a pause in firing from motoneurons in the antagonist firing (pulse). During periods of fixation, the motoneurons fire at a rate necessary to keep the eye stable (step). The pulse-step discharge in the motoneurons is caused by discharges in the PPRF.

Final Common Pathway

Regardless of the sensory input causing the fast eye movement, neural commands generating the saccade flow along a pathway called the final common pathway. The neurons within the final common pathway include the MLBN, Abducens Nucleus and the Oculomotor Nucleus. While saccades can be stimulated from a variety of different sites, if the final common pathway is removed, no saccade will occur. From the final common pathway, a variety of pathways are capable of causing a saccade–for goal directed saccades, it is commonly acceptable that the PPFR is intimately involved.

Qualitatively, a saccade occurs according to the following sequence of events within the PPRF. First, the ipsilateral LLBN are stimulated by the CNS neurons which initiate the saccade. The LLBN then inhibits the tonic firing of the OPN. When the OPN cease firing, the MLBN is released from inhibition and begins firing (these neurons fire spontaneously and also stimulated by the fastigial nucleus). The ipsilateral IBN are stimulated by the ipsilateral LLBN and the contralateral fastigial nucleus of the cerebellum. The ipsilateral EBN are stimulated by the contralateral fastigial nucleus of the cerebellum, and when released from inhibition fire spontaneously. Except for the fastigial nucleus, there are no other accepted excitatory inputs to the EBN. The burst firing in the ipsilateral IBN inhibit the contralateral EBN and abducens nucleus, and the ipsilateral oculomotor nucleus. The burst firing in the ipsilateral EBN cause the burst in the ipsilateral abducens nucleus, which stimulates the ipsilateral lateral rectus muscle and the contralateral oculomotor nucleus. With the stimulation of the ipsilateral lateral rectus muscle by the ipsilateral abducens nucleus and the inhibition of the ipsilateral medial rectus muscle via the oculomotor nucleus, a saccade occurs in the right eye.

Simultaneously, with the contralateral medial rectus muscle is stimulated by the contralateral oculomotor nucleus and with the inhibition of the contralateral lateral rectus muscle via the abducens nucleus, a saccade occurs in the left eye. Thus the eyes move conjugately under the control of a single drive center. The saccade is terminated with the resumption of tonic firing in the OPN via the fastigial nucleus. While there are a number of uncertainties, a significant uncertainty involves site for the termination of the saccade and the mechanism of action.

Visual Saccade Control Mechanism

Although the purpose for a saccadic eye movement is clear, that is, to quickly redirect the eyeball to the destination, the neural control mechanism is not. Direct evidence through electrophysiological techniques have demonstrated that activity patterns of motoneurons during visually elicited saccades are manifested by a pulse-step discharge rate [60] [61].

Until quite recently, generator models of the saccadic eye-movement system involved a ballistic or preprogrammed control to the desired eye position based on retinal error alone [58] [62]-[66]. Today, an increasing number of investigators are putting forth the idea that visual goal-directed saccades are controlled by a local feedback loop that continuously drives the eye to the desired eye position. This hypothesis, first presented by Vossius in 1960, did not start to gain acceptance until 1975 when Robinson re-examined it [67] [68]. Robinson suggested that saccades originate from neural commands to the pulse generator that specifies the desired position of the eye rather than the preprogrammed distance the

eye must be moved. The value of the actual eye position is subtracted from the desired position to create an error signal that completes the local feedback loop that drives a high gain burst element to generate the neural pulse. This neural pulse continuously drives the eye until the error signal is zero. According to the local feedback theory, saccade velocity and duration are a function of the error signal, and subject to variation dependent on a number of performance factors.

Subsequently, a number of other investigators have modified the local feedback mechanism proposed by Robinson [68] to better describe the neural connections and firing patterns of brainstem neurons in the control of horizontal saccadic eye movements [1] [21] [69] -[73]. Two models of the saccade generator have evolved: the Robinson model (as modified by van Gisbergen *et al.* [72]) and the Scudder model [70]. Enderle and coworkers have also developed a preliminary saccade generator model [21]. All of the models involve three types of premotor neurons: burst, tonic and pause cells, as previously described, and involve a pulse-step change in firing rate at the motoneuron during a saccadic eye movement [60] [61].

Qualitative Discharge Pattern

While the general pattern of motoneuron activity is qualitatively accepted during a saccadic eye movement, there is little agreement on a quantitative discharge description. In 1970, Fuchs and Luschei presented microelectrode results that indicate discharge frequency during the pulse phase of saccadic eye movements is *independent* of saccade amplitude, and that the duration of the pulse alone determines the size of the saccade for saccades greater than 10° [61]. Similar discharge frequency results are also seen in Robinson (Fig. 4 in [1]) and in van Gisbergen *et al.* (Figures 2 and 4 in [72]) for saccades as low as 7°. Investigators have also reported that the discharge frequency during the pulse phase of saccadic eye movements is *dependent* on saccade amplitude (for example, see [63], [69] [73] [74]). One reason for the conflicting interpretation of the microelectrode studies is the stochastic variability within the saccadic eye-movement controller.

The saccade generator models by Robinson and Scudder are structured to provide a control signal that is proportionally weighted (or *dependent*) to the desired saccade size, as opposed to the saccade generator model proposed here, structured to provide a control signal that is *independent* of saccade amplitude and stochastically maximal. The Robinson saccade generator provides a controller that changes the premotor firing frequencies ($B_L(t)$ and $B_R(t)$ in Fig. 10 of [72]) according to the desired saccade size, while the Scudder saccade generator provides a controller via the superior colliculus that is topographically weighted to create an "excitatory burst proportional to the desired saccade size" [70].

Post Inhibitory Rebound Burst Firing

Ipsilateral IBN's inhibition of the contralateral EBN's, TN's and abducens nucleus, the ipsilateral oculomotor nucleus, and OPN's may result in post inhibitory rebound burst firing activity within these cells, shortly after the dynamic motor error (DME) returns to zero as observed in the cerebellar vermis. Additionally, OPN's inhibition of the ipsilateral EBN's before a saccade may result in post inhibitory rebound burst firing activity within the ipsilateral EBN's at the start of a saccade. Electrophysiological evidence for the post inhibitory rebound burst firing during saccadic eye movements is prevalent in the literature. Further support for this post inhibitory rebound burst firing activity is derived from the reports by

Jahnsen and Llinas [75]-[76]. These investigators describe rebound burst responses from thalamic neurons after very marked hyperpolarizations. Because the EBN have no known inputs besides the fastigial nucleus, the EBN are modeled as firing spontaneously when released from inhibition since EBN fire even after the fastigial nucleus is lesioned. The occurrence of post inhibitory rebound bursts are a random and unplanned portion of the firing frequency. However, the average effects of the rebound burst are adaptively compensated through cerebellar interaction. Fastigial nucleus firing rates also contribute to EBN firing.

Post Saccade Phenomenon

A number of theories have been reported on post saccade phenomenon describing dynamic overshoot, glissadic overshoot and undershoot, and undershoot [77]-[82], all naturally and frequently occurring saccadic eye movements. Undershoot is the phenomenon whereby the final eye position falls short of the target position [58]. Dynamic overshoot is an eye position overshoot, followed by a quick saccade-like return to a lower steady state eye position. Glissadic overshoot is similar to dynamic overshoot, but with a return to steady state that is more gradual. Glissadic undershoot is an initial eye position undershoot, followed by a gradual rise to a higher steady eye position.

Neither the Robinson or Scudder saccade generator models provide a mechanism of action for dynamic overshoot, glissadic overshoot and undershoot, and undershoot. The Robinson model presented simulations (see Fig. 11 in [72]), and a mechanism of action for dynamic overshoot in monkey saccadic eye movement data with amplitudes 3° and smaller [72]. Human saccadic eye movements with dynamic overshoot have characteristics that significantly differ with monkey data; nearly all human saccades with dynamic overshoot occur in the abducting direction; as saccade amplitude increases, the incidence of dynamic overshoot decreases [82]. Robinson model's dynamic overshoot mechanism of action [72] fails to explain these human characteristics. Moreover, the Robinson saccade generator model does not describe the mechanism of action for the other post saccade phenomenon.

Muscle Model

A new linear homeomorphic third-order model for rectus eye muscle was recently reported that has the static and dynamic properties of muscle, and is based on physiological evidence [83]. The muscle is modeled as a viscoelastic parallel combination connected to a parallel combination of active state tension generator, viscosity element and length tension element, and shown in Figure 3 within the oculomotor plant. The new muscle model has been thoroughly tested and validated against published rectus eye muscle; the length tension characteristics are in good agreement with the data within the operating region of the muscle, and the force-velocity curves match the data, even under different stimulus rates without parametric changes. Shown in the following two figures are the length-tension curves (static characteristics) and the force velocity characteristics (dynamic characteristics illustrated via predicted vs. data).

The length-tension characteristics of the model match human data extremely well as shown in Figure 7. The force-velocity characteristics of the linear muscle model (shown in the solid line with triangles) have a nonlinear shape that match the data (shown in the solid line) very well as shown in Figure 8. It should be noted that no investigator has ever presented a linear muscle model with a nonlinear shaped force-velocity curve in the literature;

all other published articles present linear force-velocity characteristics for a linear muscle model.

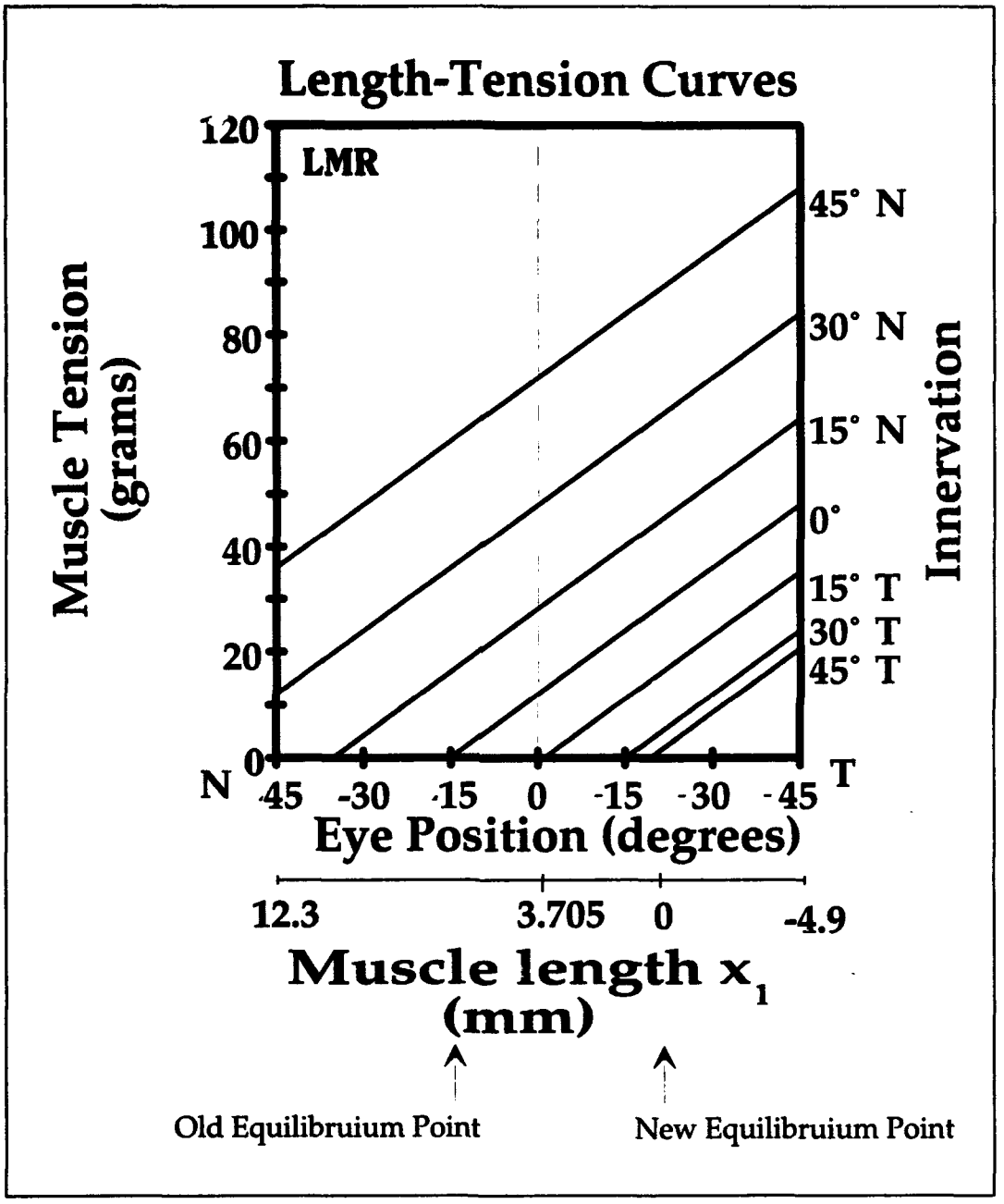

Figure 7. Length-tension curve from [83].

Previously, investigators were faced with using a nonlinear muscle model or a linearized nonlinear muscle model. Nonlinear muscle models used in oculomotor studies have not been fruitful. Extremely complex nonlinear muscle models have been proposed, *without verification*, for the oculomotor system [1]; however, these models are unusable in complex system studies involving neural networks (e.g., see [69]). When investigators model the

muscles of the oculomotor plant in neural network studies, these models are simple linear models.

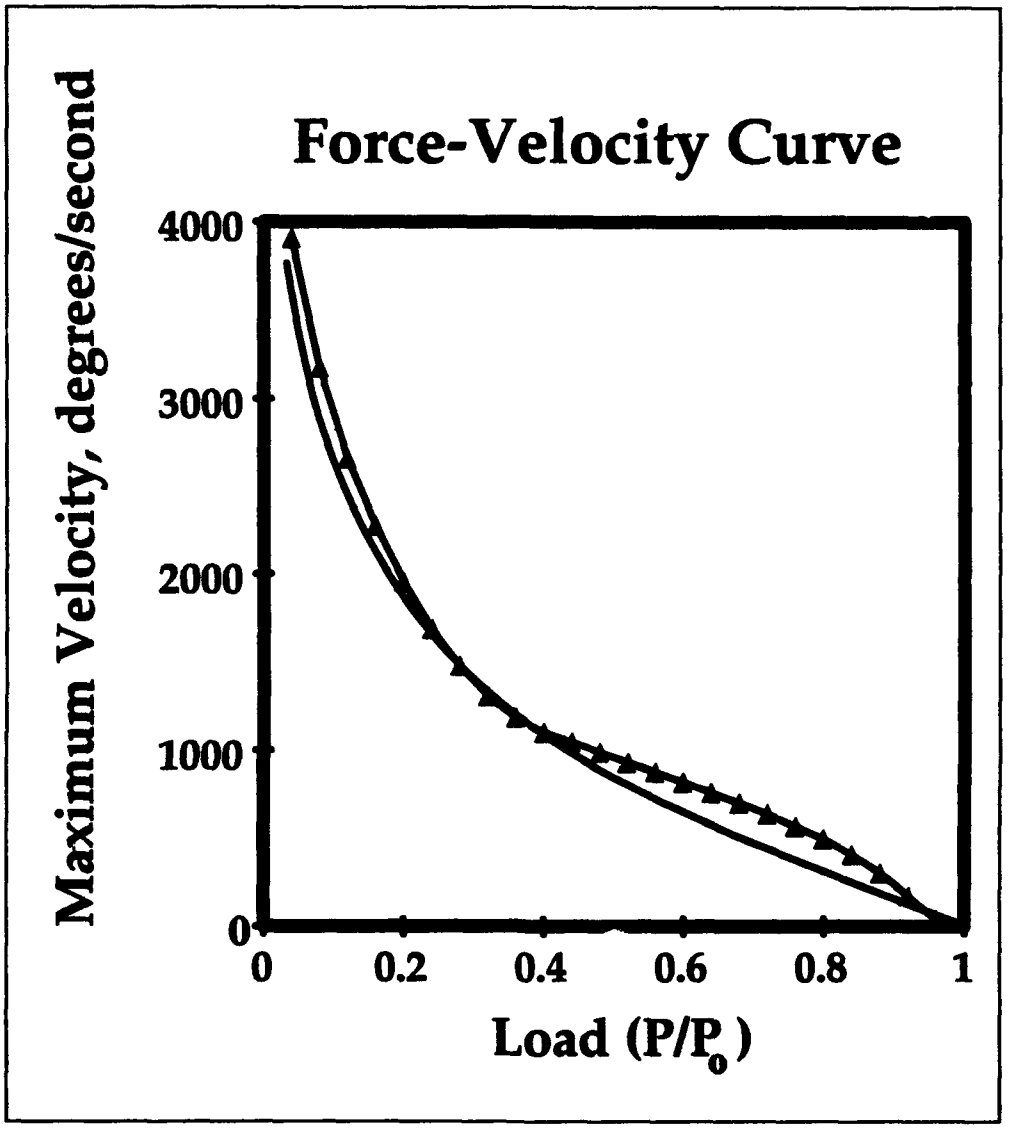

Figure 8. Force-velocity curve from [83].

Linear muscle models prove to be the most popular in systems applications because of the relative mathematical ease in analysis, as well as their simplicity. However, linear muscle models, and linear oculomotor muscle models in particular, have been criticized because they have not successfully accounted for the nonlinear interpretations of experimental evidence. The linear oculomotor muscle model in [83] has been validated against the static and dynamic properties of experimental medial and lateral rectus eye muscle data. The simplicity of the model makes it an ideal component for the muscles in the oculomotor plant. This muscle model, suitably parameterized, may also be applicable for modeling other muscles in the sensorimotor system, such as the neck and other eye muscles.

Saccades and the Oculomotor Plant

Saccadic eye movements, among the fastest voluntary muscle movements the human is capable of producing, are characterized by a rapid shift of gaze from one point of fixation to another. Stimulated by target displacement, information from the retina periphery is used to direct the eyeball to place the high resolution fovea on the target. Neglecting vestibulo-ocular input, saccadic eye movements are conjugate and ballistic with a typical latency of 150-300 ms. The latent period is thought to be the time interval during which the CNS calculates the distance the eyeball is to be moved, transforming retinal error into transient muscle activity.

A large variability in saccade dynamics exists, either executed by a single subject or a group of subjects, for saccades of the same size [84] [85]. Saccade peak velocity, time to peak velocity, duration and latency are observed to exhibit random behavior under conditions without the influence of fatigue or drugs [22] [84]-[86]. These variations have been attributed to stochastic motoneuronal activity that is first-order time-optimal [59] [22] [84]-[86].

Models of oculomotor function are important in the development of clinically useful diagnostic tools and in understanding the neurophysiology of eye movements [69], [77]-[78], [87]-[92]. The complexity of these models and their correlation with physiological evidence has increased since Westheimer first presented a model of saccadic eye movements in 1954 [62]. Recently, a sixth-order linear homeomorphic horizontal saccadic eye movement model was developed that provides an excellent match between the model predictions and the data [63]. Enderle *et al.* modified the linear homeomorphic horizontal saccadic eye movement model to a form that makes it ideal for use in the development of more sensitive tests of oculomotor pathology and in the description of normal oculomotor function [91].

Using the updated linear muscle model [83], Enderle and coworkers have further updated and validated the oculomotor plant using the new model of eye rectus [21] [83] [93]. The lateral and medial rectus muscle of each eye is modeled as a parallel combination of an active state tension generator with a viscosity and elastic element, connected in parallel to a series elastic and viscosity element as previously described. The eyeball is modeled as a sphere connected to a parallel combination of elastic and viscosity elements connected in series with another parallel combination of elastic and viscosity elements.

The simplicity of the previous linear models in [63] and [91], and ease in use in systems studies, is preserved with our current oculomotor plant model as shown in Figure 3. Moreover, the criticisms previously expressed by many other investigators concerning linear models that do not successfully account for the nonlinear interpretations of experimental evidence, are now removed with our current model. The characteristics of the new oculomotor plant model has been extensively tested against experimental data. Moreover, simulation results for eye position and higher derivatives are in good agreement with the eye position data and the data derived estimates of the higher derivatives.

Experimental Data and Results

To gain an understanding of the eye movement control system, extracelluar single-unit recordings from within the PPRF (for EBN, LLBN and Burst-Tonic neurons) and eye position were obtained from rhesus monkeys during horizontal and oblique saccadic eye

movements (data provided by Dr. David Sparks from his laboratory while at the University of Alabama). Samples of the data are given in Figures 9-11. Details of the experiment and training are reported elsewhere, and briefly described here [94]. Horizontal and vertical eye position data were recorded using magnetic coils, and neural activity were recorded using tungsten microelectrodes. The data was stored onto hard disk of a computer. Recording sites were verified from histological sections. Data were collected from monkeys seated before a target display with a sampling rate of 1000 Hz. The monkeys were trained to follow target movements with saccades. No filtering of the data was carried out, but the firing frequency was placed in the usual format of frequency of firing over 1ms intervals, rather than the electrical activity itself.

This data, and other data reported in the literature, are used to describe the sequence of neural events (firing patterns) of each of the neural sites detailed in Figure 2, and are also used to simulate all types of saccades, including those with dynamic overshoot and glissades, using a common mechanism of action. Ito points out that there is a significant gap in our knowledge concerning this sequence of events [24], and Noda points out that there are no saccade generator models which include the cerebellum as an integral element [35].

In addition, data were collected from five normal human subjects seated before a target display of nine small red light emitting diodes (LED's), each separated by five degrees. The subject was instructed to follow the "jumping" target, which moved from the center LED to one of the other LED's, and then returned to the center LED. The subject first observed twenty-eight 5° target movements, then twenty-eight 10°, twenty-eight 15°, and twenty-eight 20° target movements that were randomized between right-left ordering and the time interval between target movements. The subject was allowed to rest after each 28 target movement session to prevent fatigue. Each of the five subjects repeated the combined experiment on three separate days. A total of 1680 eye movements were collected and analyzed.

Data were recorded from the initial displacement from the center LED for the right eye. The horizontal eye movements were recorded using an infrared signal reflected from the anterior surface of the cornea-scleral interface. Signals for bilateral tracking were digitized at a rate of 1000 samples per second for one-half second and stored in hard disk memory of an IBM XT computer. A twenty-point digital filter was used to obtain the velocity estimates.

Figure 5 illustrates a normal saccade, a saccade with glissadic overshoot, and a saccade with dynamic overshoot for one of these five subject's. As shown in Fig. 5(a), a corrective saccade was made by the subject to remove the undershoot error. Figure 12 summarizes the frequency distribution for the five types of different saccadic eye-movement responses from all five subjects (1680 eye movements), partitioned in 5, 10, 15, and 20 degree movements. Nearly all of the dynamic overshoot (85%) occurred in the abducting direction. The dynamic overshoot peak velocities in the abducting direction averaged approximately 70° s, compared with an average of approximately 45°/s in the adducting direction. Subject to subject dynamic overshoot variation ranged from 5% to 40%. Additionally, as the saccade size increased, the incidence of dynamic overshoot decreased. Glissades occurred in approximately 35% of the total saccades recorded with the individual ranges from 22% to 52%. The percentage of glissades increased with increasing saccade size: 5° saccades had 27% glissadic activity, 10° had 31%, 15° had 33%, and 20° had 47%. The peak-velocity dis-

tribution for saccades with glissadic activity did not differ significantly from the peak-velocity distribution from normal saccadic eye movements.

Some movements displayed characteristics of dynamic overshoot followed by a glissade. These movements had peak return velocities and velocity profiles similar to dynamic overshoot and then returned to the tonic state with velocities of a glissade. Another post-saccadic movement that occasionally occurred was a dynamic overshoot followed by a glissadic undershoot. This movement exhibited a dynamic overshoot with normal peak return velocities and velocity profile, directly followed by a slow drift back near the position reached at the extent of the overshoot. Corrective saccades occurred in approximately 26% of the saccades, with individual ranges from 9% to 40%.

Simulation Results

This project involved developing a horizontal saccade generator model based on physiological evidence, eye movement recordings and systems control theory. This model accurately depicts the connections of these saccade neural sites as recorded in the literature, and simulates realistic eye movements of all types.

To test the veracity of the horizontal saccade generator model presented in this paper, saccadic eye movements were simulated using TUTSIM, a continuous time simulation program, and compared with experimental data. Parameter values used for the oculomotor plant are given in [21] [59]. Neural sites (nucleus) are described via a *functional* block diagram description of the horizontal saccade generator model as shown in Figures 13 and 14. Table 1 summarizes additional firing characteristics for the neural sites. The output of each block represents the firing pattern at each neural site observed during the saccade; time zero indicates the start of the saccade and T represent the end of the saccade. Naturally, the firing pattern observed for each block represents the firing pattern for a single neuron, as recorded in the literature, but the block represents the cumulative effect of all of the neurons within that site. Consistent with a time optimal control theory, neural activity is represented within each of the blocks as pulses and/or steps to reflect their operation as timing gates (see discussion). Obviously, individual neurons fire as reported in Figures 9-11. For illustrative purposes, saccadic eye movements for the right eyeball are presented. These results may be easily extrapolated for the left eyeball.

The superior colliculus, as described in Figures 2 and 12, fires maximally as long as the dynamic motor error is greater than zero, in agreement with the first-order time optimal controller and evidence presented by Sparks [2]. Notice that the LLBN's are driven by the superior colliculus as long as there is a feedback error maintained by the cerebellar vermis. In all likelihood, the maximal firing rate by the superior colliculus is stochastic, depending on a variety of physiological factors such as the interest in tracking the target, anxiety, frustration, stress, and other factors.

The actual firing patterns in the superior colliculus, the burst neurons in the PPRF (LLBN, EBN and IBN) and abducens nucleus are simulated with filtered pulse signals, consistent with the physical limitations of neurons [1]. For the superior colliculus and the LLBN, this involves a single pulse, for the EBN and IBN, this involves two pulses with different filters (the first pulse describes the brief rise and subsequent fall within the first 10 ms during a saccade, and the second pulse describes the steady state pulse during the saccade) to match the electrophysiological data.

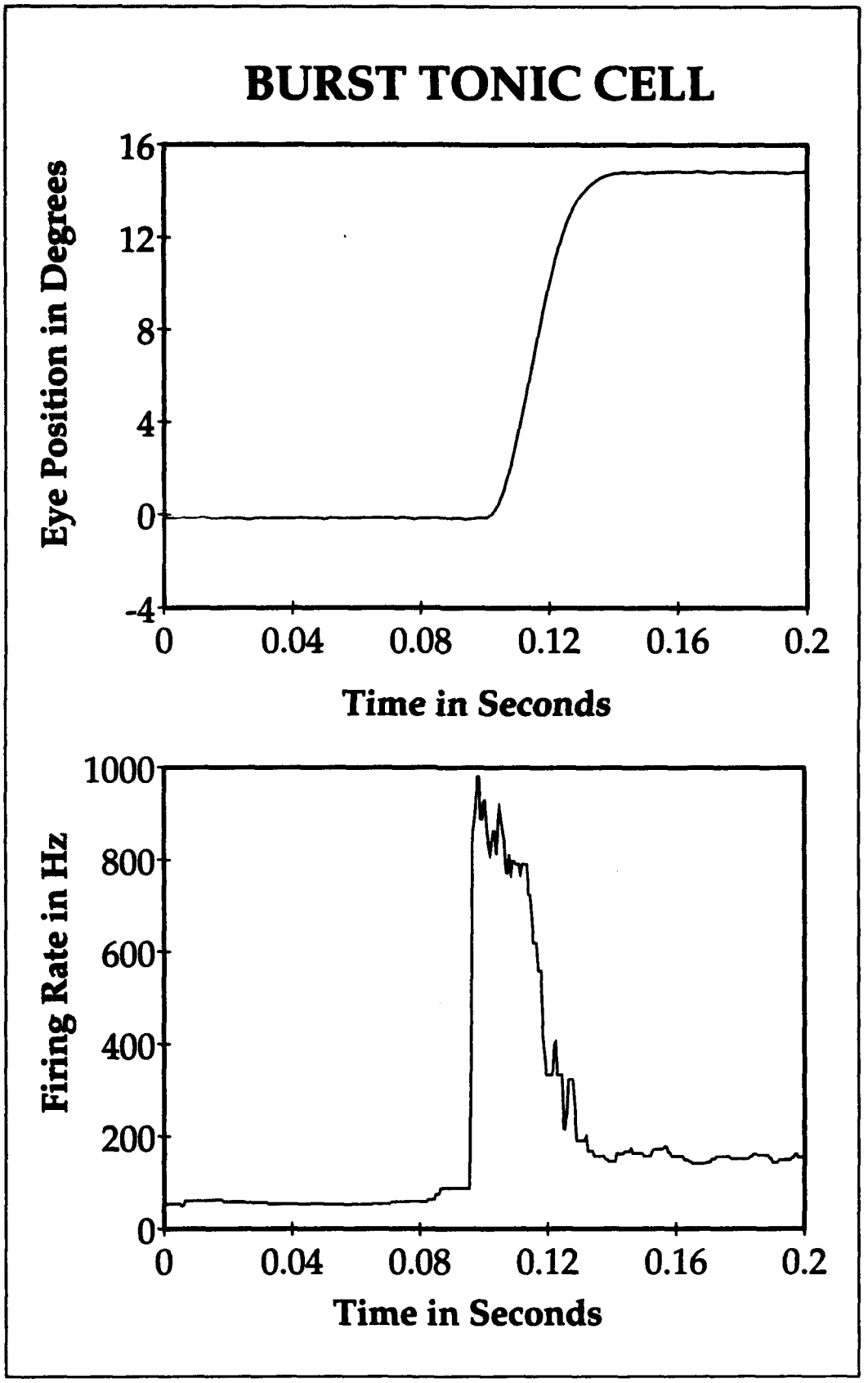

Figure 9. Burst Tonic Cell.

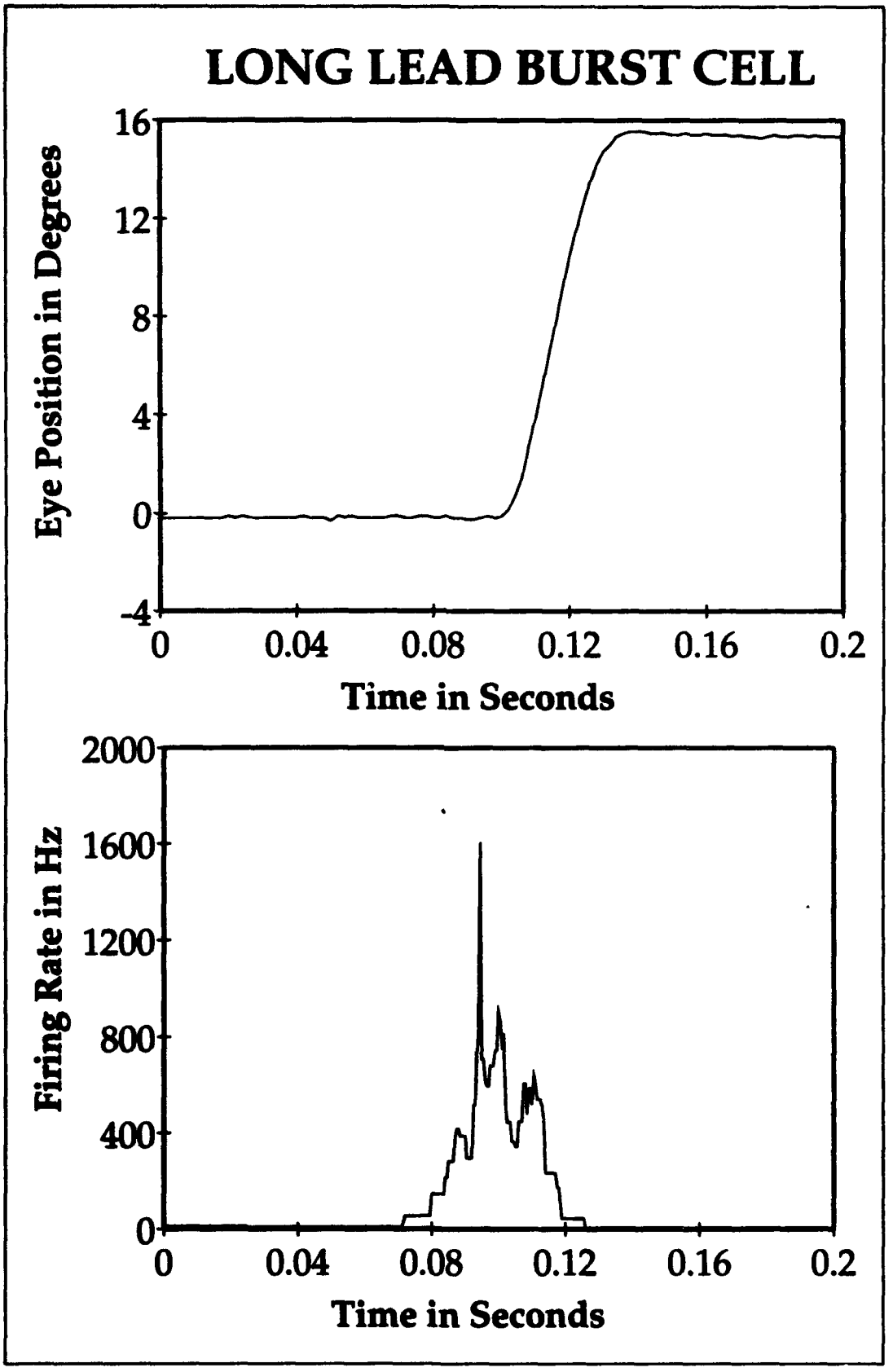

Figure 10. Long Lead Burst Cell.

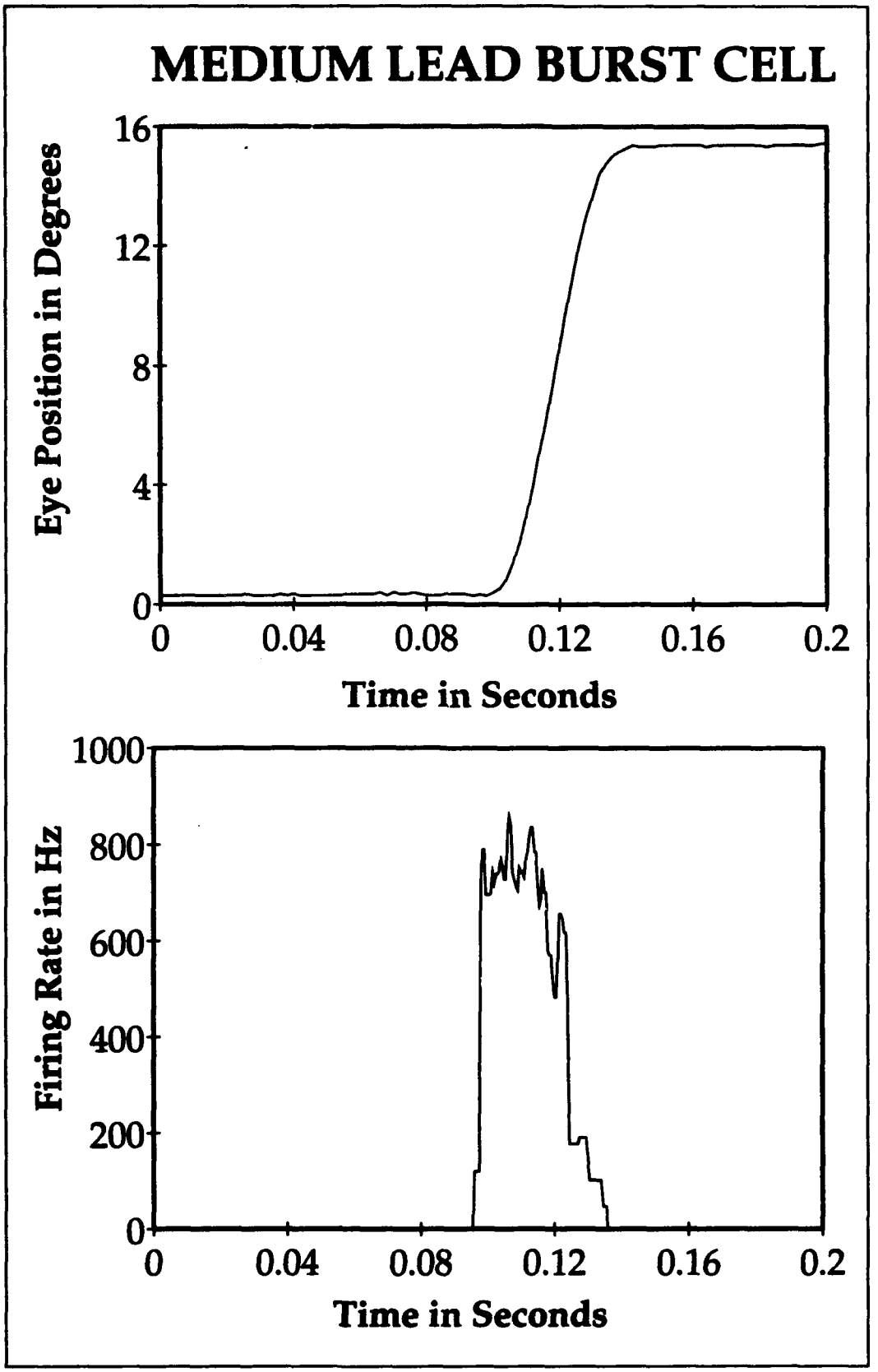

Figure 11. Medium Lead Burst Cell.

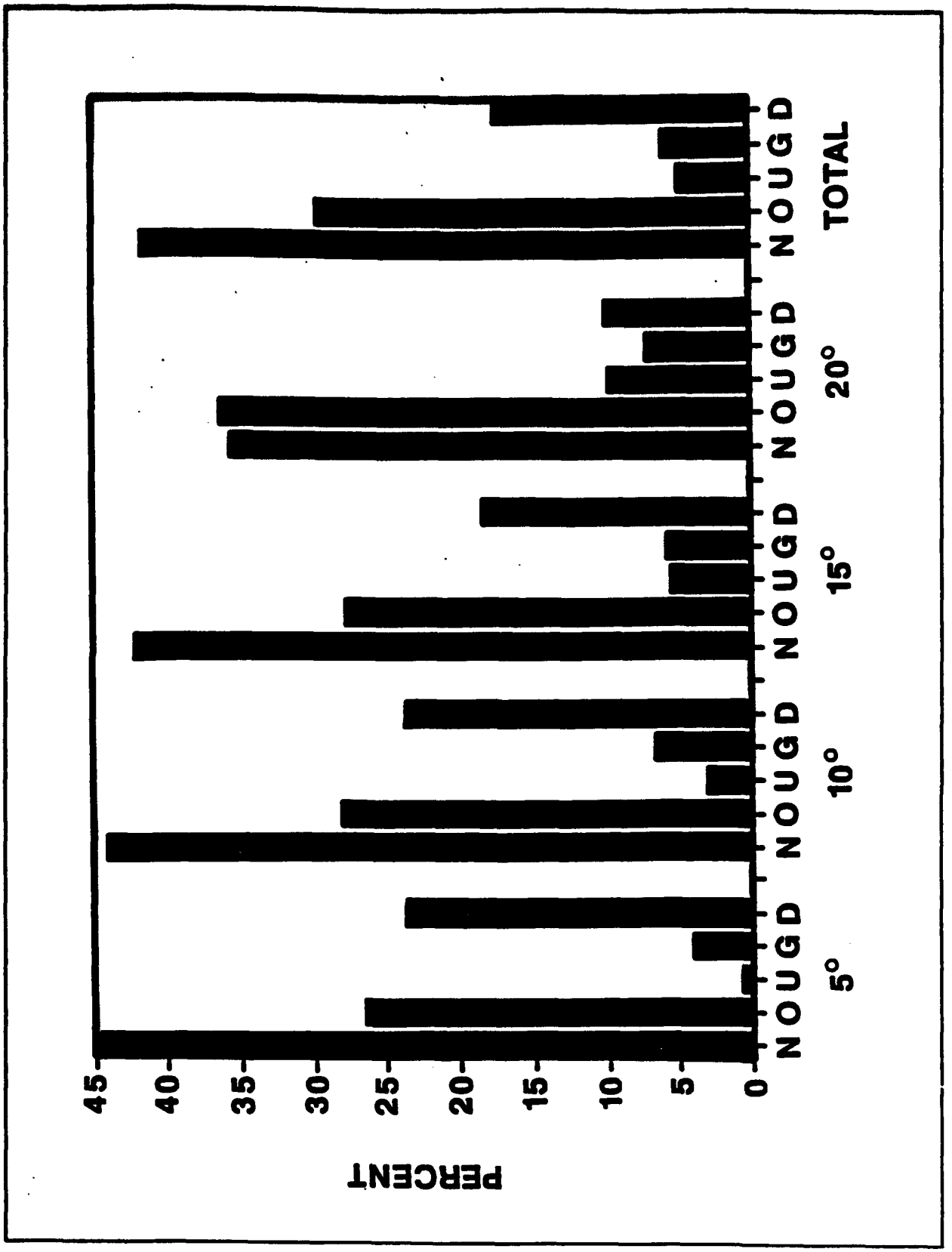

Figure 12. Histogram for all five subjects. all eye movements, describing the frequency of normal saccades (N), glissades with overshoot (O), glissades with undershoot (U), saccades with dynamic overshoot followed by a glissades (G), and dynamic overshoot (D), for 5°, 10°, 15° and 20°, and all saccades.

The movement fields within the superior colliculus also reflects the number of neurons firing for saccades less than 7° are fewer than those firing for saccades greater than 7° [2]. Saccades for a given target position error occur with equal duration in the superior colliculus regardless of initial eye position. Corrections for saccade duration due to the initial conditions are carried out by the cerebellar vermis; this aspect of the saccade generator model is the subject of a future effort. Each of the neural sites firing pattern match the data very well for saccades of all sizes. In fact, the TUTSIM EBN blocks were replaced with EBN data for a 20° saccade, with little difference between the simulation results and the eye movement data, as shown in Figure 15 [21].

Illustrated in Figure 16 are simulation results for abducting 5°, 10°, 15° and 20° saccadic eye movements, simulated by changing retinal error only. Shown are the saccade trajectories, the saccade velocities, and the abducens and oculomotor firing rates. All features of these simulations, including peak velocity, duration and amplitude conform to published observations. Notice that due to the time optimal control structure, the abducens firing rates for the 5°, 10°, 15° are all subsets of the 20° abducens firing rate.

Figures 17 and 18 illustrate TUTSIM simulated saccades generated with the oculomotor model with varying onsets and amplitudes for the contralateral post inhibitory rebound burst firing. Both the amplitude and timing of the rebound bursting are important in the saccade dynamics. In Figure 17, the onset of the rebound burst is varied while the amplitude is held constant. Here, as the onset of the rebound burst is increasingly delayed from the initiation of the DME return to zero at 18ms, simulations change from saccades with glissadic undershoot, to normal saccades, to saccades with glissadic overshoot, to saccades with dynamic overshoot.

In Figure 18, the amplitude of the rebound burst is varied while the onset of the rebound burst is held constant at 15ms after the initiation of the DME return to zero. Increasing the rebound burst amplitude changes the saccade dynamics from a normal saccade, to a saccade with glissadic undershoot, to a saccade with glissadic overshoot, to a saccade with dynamic overshoot.

Illustrated in Figure 19 is a TUTSIM simulation in which muscle saturation is varied from 550 to 750 Hz. The most prominent effects of the change in muscle saturation is the variation in peak velocity and the size of the undershoot error.

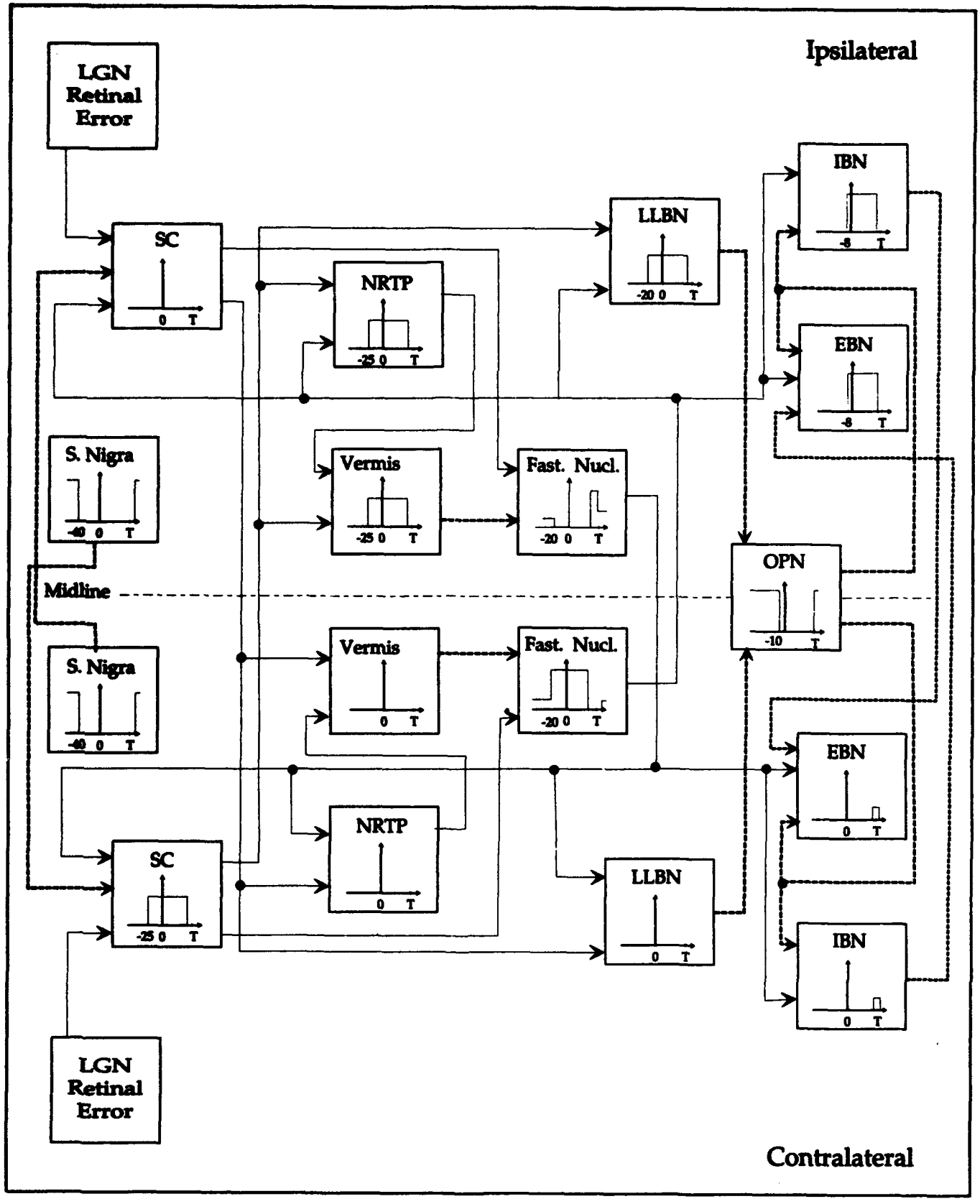

Figure 13. Part A: A functional block diagram of the saccade generator model. Solid lines are excitatory and dashed lines are inhibitory.

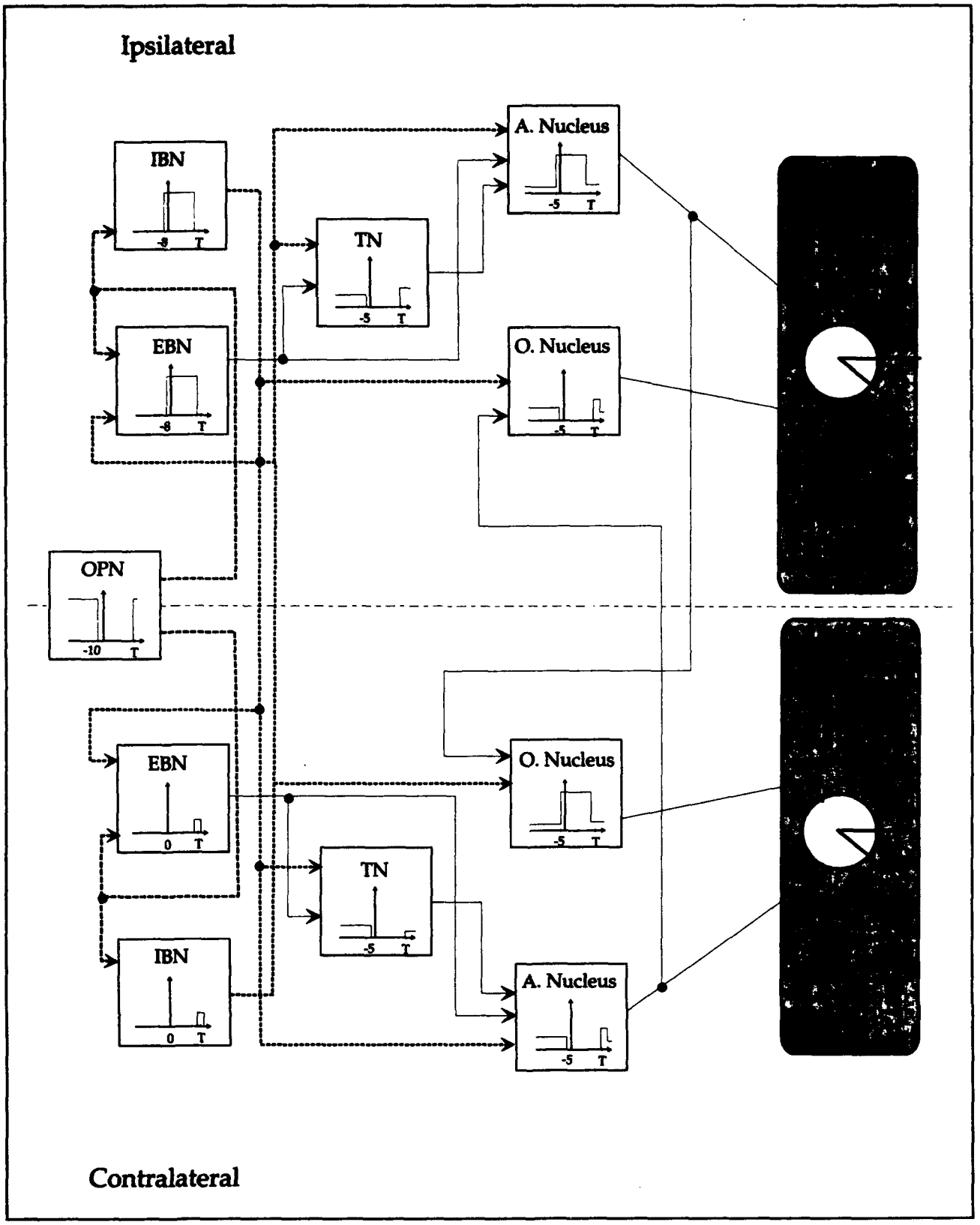

Figure 14. Part B: A functional block diagram of the saccade generator model. Solid lines are excitatory and dashed lines are inhibitory.

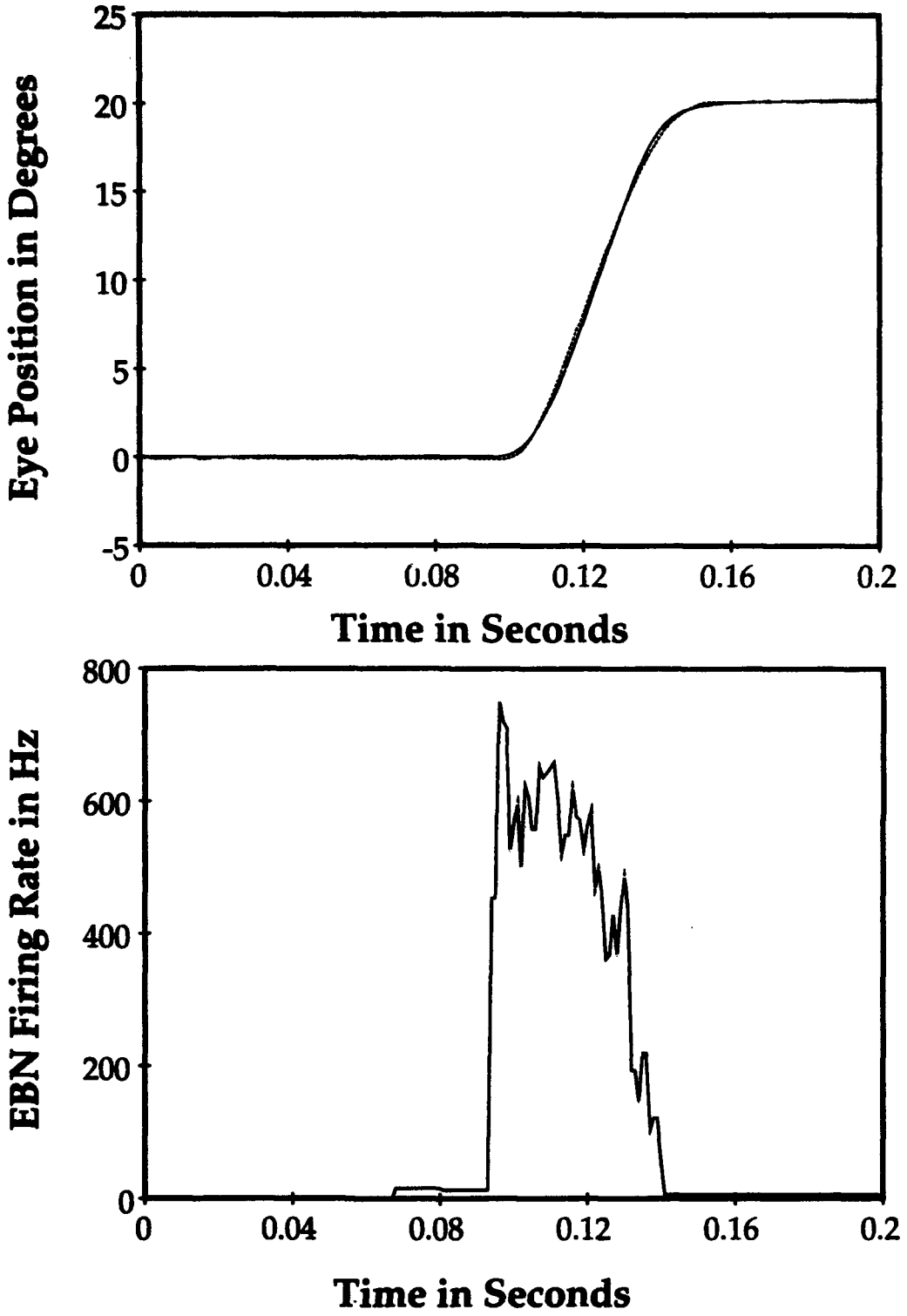

Figure 15. Simulated eye position results, shown in solid line, generated by substituting the EBN TUTSIM blocks with EBN data (shown below), and eye movement data, shown in dashed line.

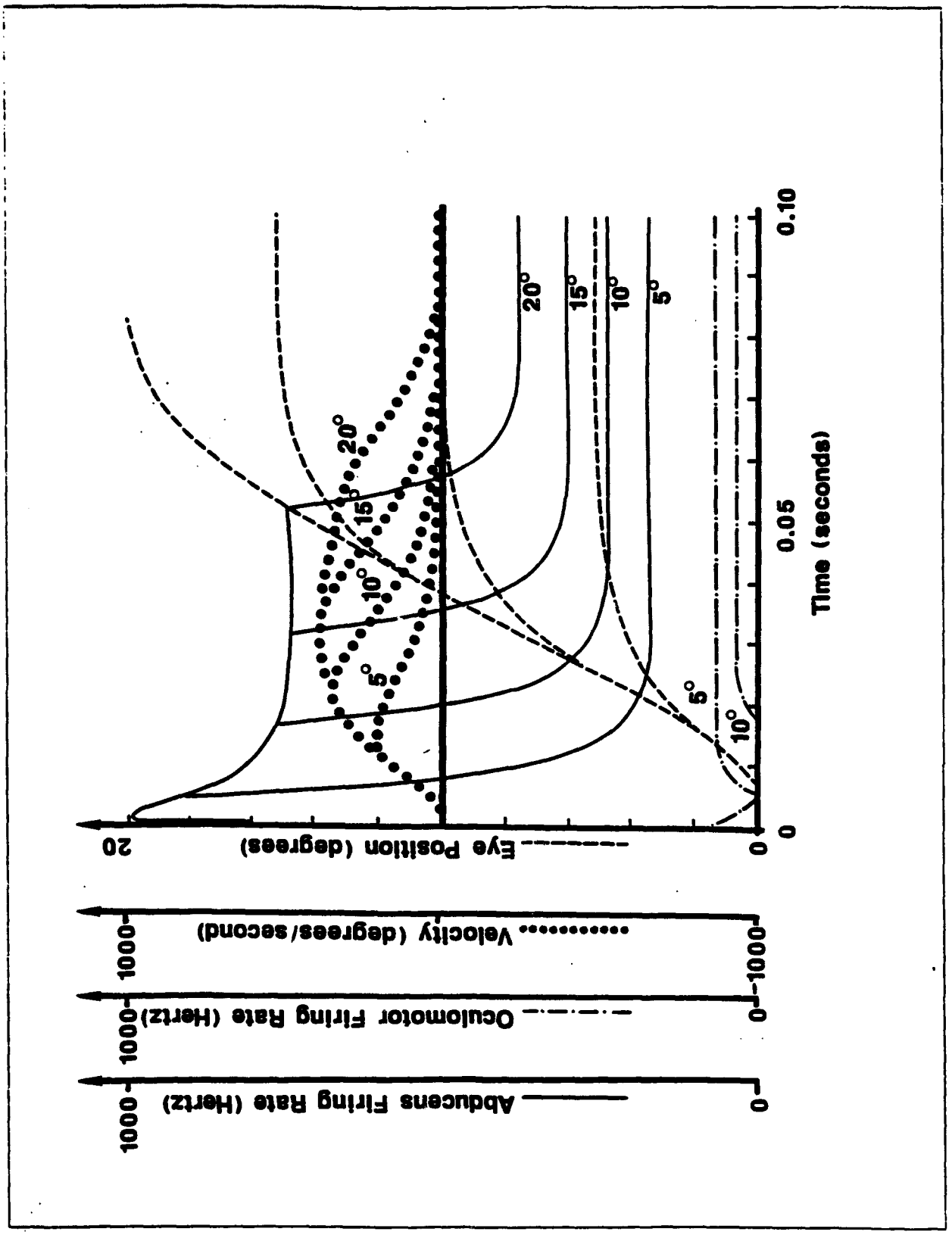

Figure 16. TUTSIM simulations for 5, 10, 15 and 20 degree saccades generated with the saccade generator. Shown are the saccade trajectories, the saccade velocities, and the abducens and oculomotor firing rates. Muscle saturation is set at 714 Hz for each simulation. All features of these simulations, including peak velocity, duration and amplitude conform to published observations.

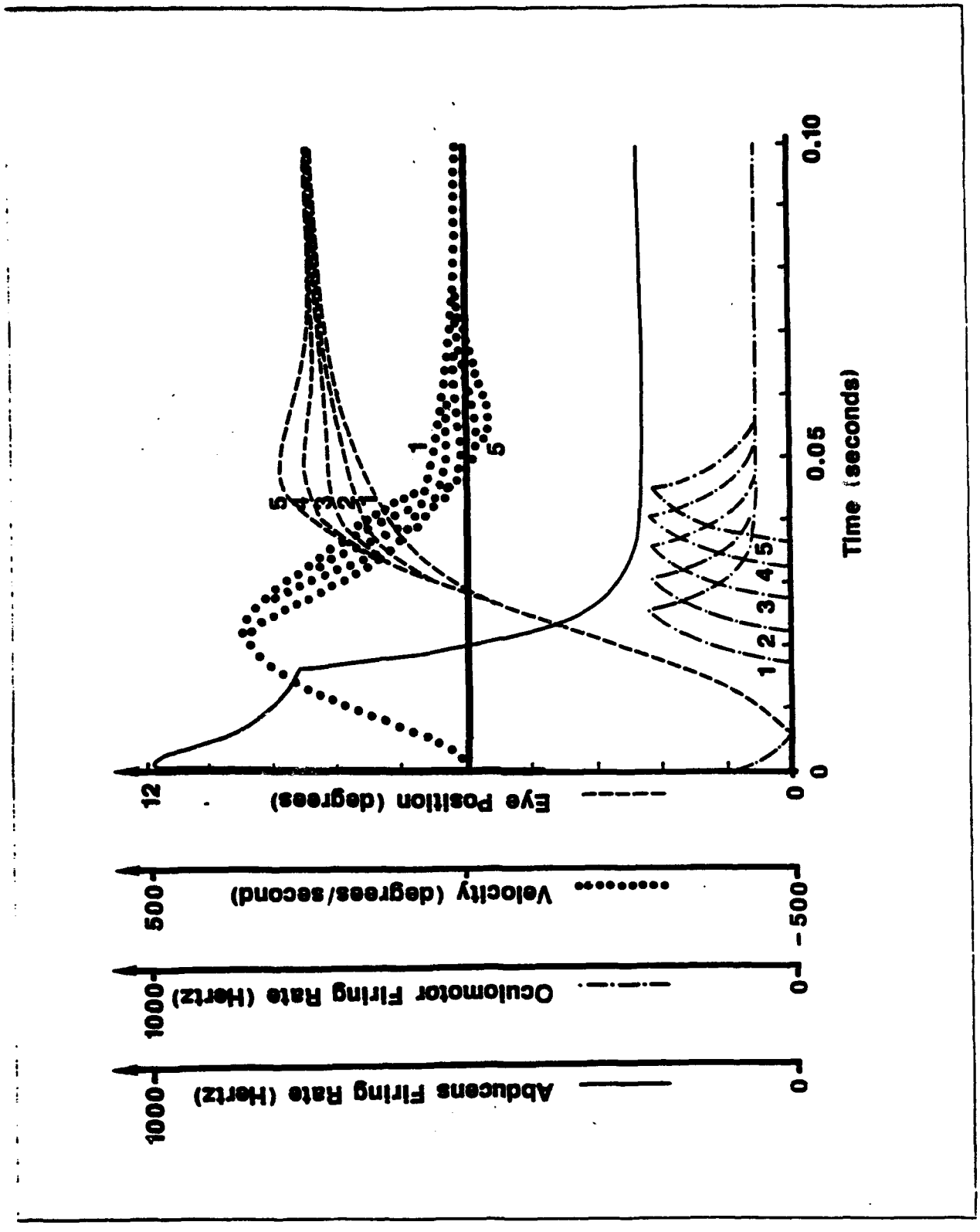

Figure 17. TUTSIM simulated saccades generated with the saccade generator in which the onset of the contralateral EBN's post inhibitory rebound burst firing is varied, while the amplitude is held constant. Shown are the saccade trajectories, the saccade velocities, and the abducens and oculomotor firing rates. Muscle saturation is set at 714 Hz for each simulation. Normal saccades, glissades, and saccades with dynamic overshoot are present in the simulations.

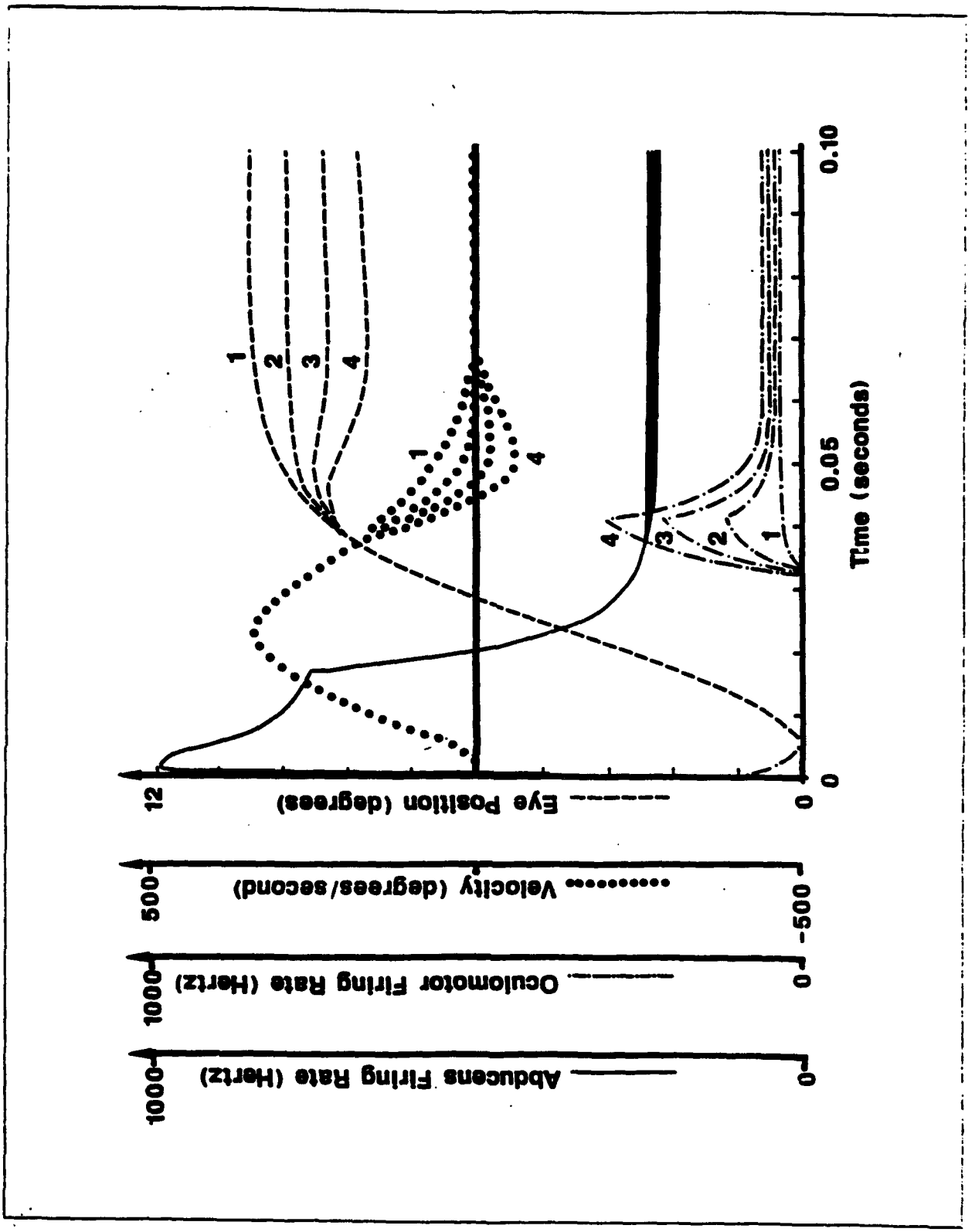

Figure 18. TUTSIM simulated saccades generated with the saccade generator in which the amplitude of the contralateral EBN's post inhibitory rebound burst firing is varied, while the onset is held constant at 15 ms after the DME return to zero. Shown are the saccade trajectories, the saccade velocities, and the abducens and oculomotor firing rates. Muscle saturation is set at 714 Hz for each simulation. Normal saccades, glissades, and saccades with dynamic overshoot are present in the simulations.

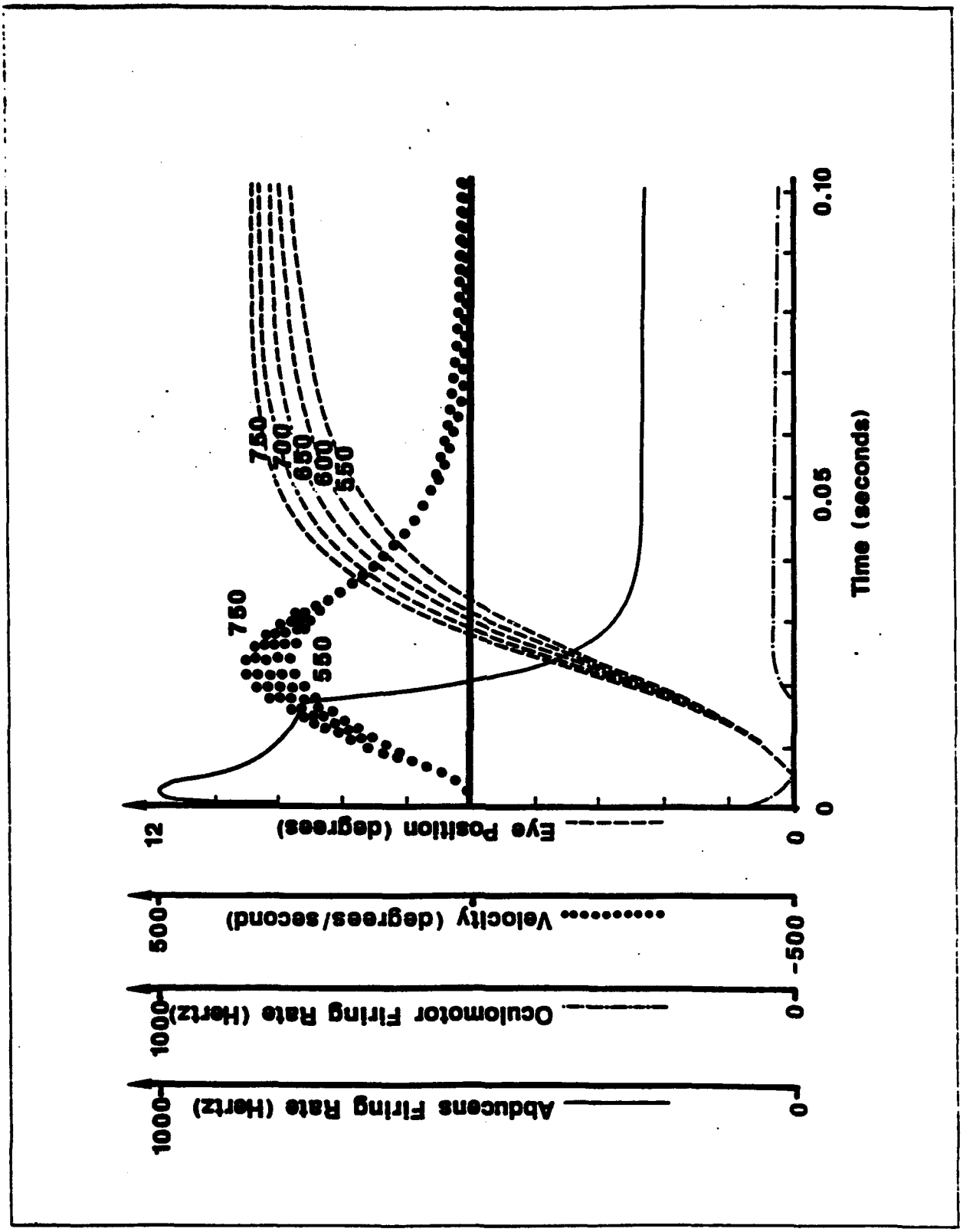

Figure 18. TUTSIM simulated saccades generated with the saccade generator in which the muscle saturation is varied from 550 to 750 Hz, while all other parameters are held constant. Shown are the saccade trajectories, the saccade velocities, and the abducens and oculomotor firing rates. Peak velocity variations of 100 degrees/second are observed, consistent with the variations reported in the literature..

Table 1. Activity of Neural Sites during a saccade.

Neural Site	Onset before Saccade	Peak Firing Rate	End Time
Abducens Nucleus	5 ms	400-800 Hz	Ends approx. 5 ms before saccade ends
Contralateral Fastigial Nucleus	20 ms	200 Hz	Pulse ends with pause approx. 10 ms before saccade ends, resumes tonic firing approx. 10 ms after saccade ends
Contralateral Superior Colliculus	20-25ms	800-1000 Hz	Ends approx. when saccade ends
Ipsilateral Cerebellar Vermis	20-25 ms	600-800 Hz	Ends approx. 25 ms before saccade ends
Ipsilateral EBN	6-8ms	600-800 Hz	Ends approx. 10 ms before saccade ends
Ipsilateral Fastigial Nucleus	20 ms	Pause during saccade, and a burst of 200 Hz toward the end of the saccade	Pause ends with burst approx. 10 ms before saccade ends, resumes tonic firing approx. 10 ms after saccade ends
Ipsilateral FEF	> 30 ms	600-800 Hz	Ends approx. when saccade ends
Ipsilateral IBN	6-8ms	600-800 Hz	Ends approx. 10 ms before saccade ends
Ipsilateral LLBN	20 ms	800-1000 Hz	Ends approx. when saccade ends
Ipsilateral NRTP	20-25ms	800-1000 Hz	Ends approx. when saccade ends
Ipsilateral Substantia Nigra	40 ms	40-100 Hz	Resumes firing approx. 40-150 ms after saccade ends
OPN	6-8 ms	150-200 Hz (before & after)	Ends approx. when saccade ends

Neural Integrators

It is known that the saccadic system utilizes at least two sets of integrator networks during the execution of a saccade. One is used to adjust the saccade amplitude for initial orbital position, and the other is used to adjust the level of firing for the TN during fixation. The existence of these two integrators have been confirmed via lesion studies. To model the integrator activity, several schemes have been suggested [95]-[98]. A simple weighted mathematical integral of the input firing rate is used in simulating these neural sites.

Post Saccade Phenomenon

One consequence of the termination of the saccade by the cerebellar circuit is that it offers a common mechanism for saccades of all types, including those with dynamic overshoot, glissadic behavior and undershoot. Depending on the timing of the termination sig-

nal by the cerebellum and any rebound burst observed in the antagonist muscle, one of three types of behavior can occur as shown in Figure 20 from the simulations of Figures 16-19.

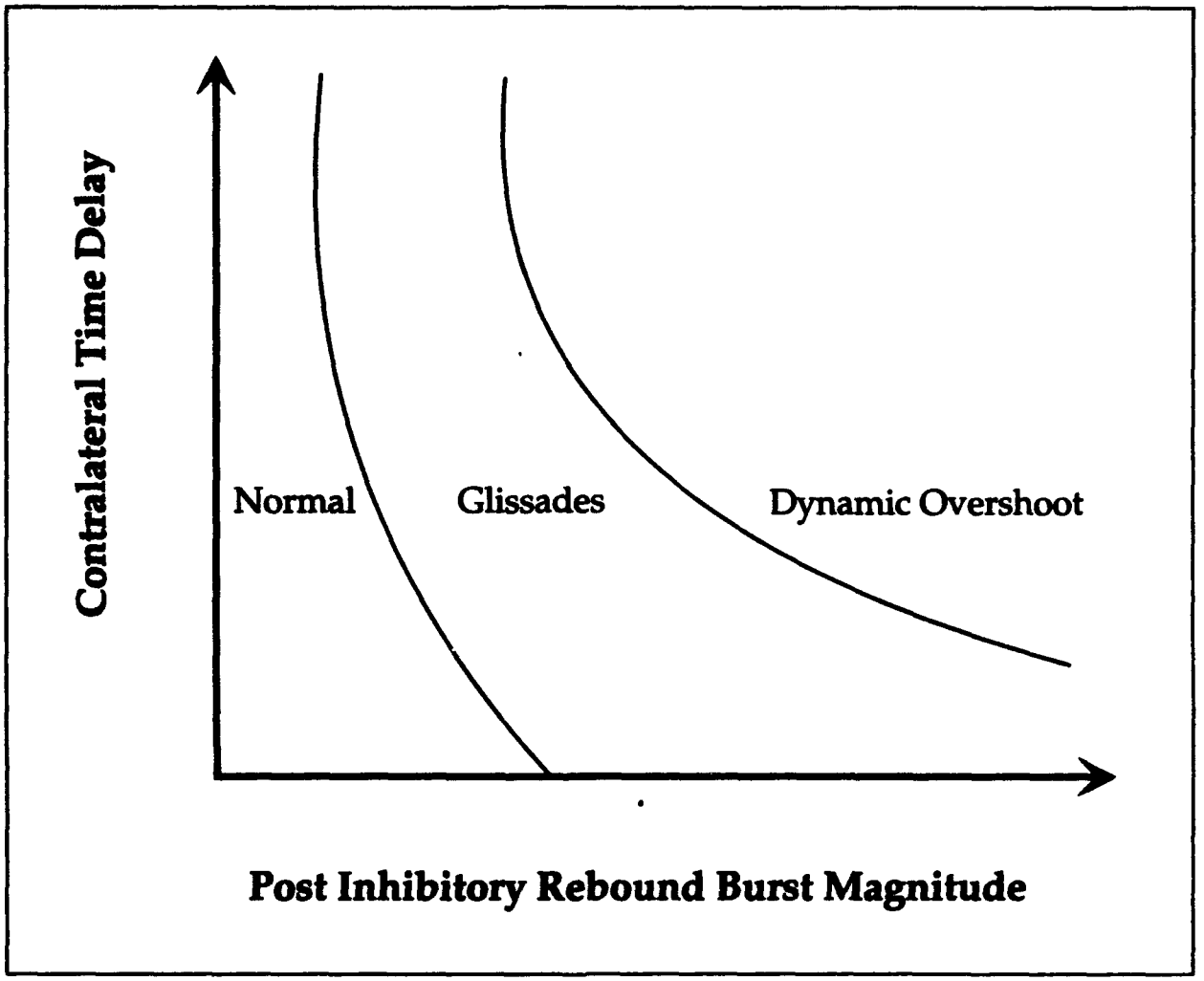

Figure 20. Diagram illustrating a common mechanism of action for post saccade phenomenon.

Discussion

The objective of this paper was to present a new physiolgical neural network more accurately representative of the neural connections and firing patterns of brainstem neurons in the control of horizontal saccadic eye movements. Physiological evidence indicates that saccades are controlled through a parallel distributed network involving the cortex, cerebellum, and brain stem. Important differentiating features of this model from previous models are: 1) the saccade generator is first-order time optimal, 2) the saccade is initiated by the superior colliculus, 3) the saccade is terminated by the cerebellum, 4) neural firing after marked hyperpolarization occurs with pronounced stochastic rebound burst firing, 5) two integrators exist in the network, one in the PPRF and the other in the cerebellar vermis and NRTP, 6) muscle saturation is explicitly included, and 7) a sixth-order linear homeomorphic oculomotor plant is used. Moreover, a common mechanism of action is described which

explains a number of different saccadic eye movement types, including dynamic overshoot, glissadic overshoot and undershoot, and undershoot.

Dynamic Overshoot and Glissades

Reports in the literature on the occurrence of dynamic overshoot during saccadic eye movements have varied from 70% to 5%. Our experimental results indicate that dynamic overshoot occurs predominantly in abducting saccades with an average frequency of 17.5%. Furthermore, the incidence of dynamic overshoot decreases as saccade size increases. Researchers have reported a dynamic overshoot mechanism which relies on a second-order neural control signal; unfortunately, there has been no electrophysiological evidence to support the second-order control mechanism. Here, we suggest that dynamic overshoot is primarily caused by unplanned post inhibitory rebound burst firing as the DME returns to zero and activity caused by the fastigial nucleus. Illustrated in Figures 17 and 18 are examples of dynamic overshoot simulated with varying onsets and amplitudes for the post inhibitory rebound burst firing. In particular, the simulation in Figure 18 (#4) compares favorably with the saccade recorded with dynamic overshoot displayed in Figure 5 (c); the peak velocities during the dynamic overshoot are approximately equal, the size of the overshoots are approximately equal, and the durations of the dynamic overshoot are approximately equal. The timing of the post inhibitory rebound burst is critical for dynamic overshoot; the rebound burst must be delayed approximately 15 ms (or more) after the initiation of the DME return to zero. Moreover, the amplitude of the rebound burst must be of sufficiently high amplitude for dynamic overshoot to occur. This dynamic overshoot mechanism is fully supported by electrophysiological evidence.

One reported mechanism of action for glissadic overshoot describes a central nervous system (CNS) dependent error in computing the duration of the agonist EBN's burst and not the level of EBN's firing. Support for this hypothesis is derived from reported lower peak velocities of glissades, as compared to other types of saccades. Our experimental results, however, indicate that glissades have the same distribution of peak velocities as other types of saccades. Another mechanism of action for glissadic overshoot uses an adaptive mechanism for suppression of post saccadic drift. This mechanism supports a CNS error in the gain of the step and the time constant of the slide for glissade generation. Glissades are quite common, with a frequency of occurrence in our data equal to approximately 35%; a rather high CNS error rate for the pulse width glissadic error mechanism and the adaptive mechanism.

Here we suggest that glissadic overshoot and undershoot are primarily caused by post inhibitory rebound burst firing. Illustrated in Figures 17 and 18 are examples of glissades simulated with varying onsets and amplitudes for post inhibitory rebound burst firing. As with dynamic overshoot, both the amplitude and timing of the rebound burst is important in generating a glissade. Note that this glissadic mechanism presented here predicts that glissades have the same distribution of peak velocities as other types of saccades.

An inherent coordination error exists between the return to tonic firing levels in the abducens and oculomotor nucleus during the completion of a saccade. Ipsilateral abducens nucleus fire uninhibited (although dynamically changing as previously described) during an abducting saccade. Oculomotor nucleus firing activity is inhibited during the pulse phase during an abducting saccade. Because of the ipsilateral IBN's inhibition of the contra-

lateral EBN's and TN's, and ipsilateral oculomotor nucleus, resumption of tonic firing and rebound burst activity in the oculomotor nucleus does not begin until shortly before the ipsilateral IBN's cease firing (from Fig. 17, a delay of approximately 10 ms after the DME initiates the return to zero). This same delay exists in the abducens MN's for adducting saccades.

There are significantly more internuclear neurons between the contralateral EBN's and TN's, and the ipsilateral oculomotor nucleus (antagonist neurons during an abducting saccade), than the ipsilateral EBN's and TN's, and ipsilateral abducens nucleus (antagonist neurons during an adducting saccade). Due to this greater number of internuclear neurons operating during an abducting saccade, a longer time delay exists before the resumption of activity in the oculomotor MN's after the pulse phase for abducting than adducting saccades. This abducting time delay is in addition to the time delay present because of IBN's activity during the pulse phase, as previously discussed. Since the time delay before the resumption of activity in the oculomotor nucleus after the pulse phase of a saccade is greater for abducting saccades than with adducting saccades, the incidence of saccades with dynamic overshoot should be greater for abducting saccades than adducting saccades. This is precisely what is observed in saccadic eye movement recordings. Nearly all saccades with dynamic overshoot occur in the abducting direction. Additionally, because the contralateral TN's firing rate decreases as ipsilateral saccade amplitude increases, the rate of dynamic overshoot decreases since fewer saccades have sufficiently high post inhibitory rebound burst amplitudes. This is also what is observed in saccadic eye movement recordings.

Essentially nothing is known about the distribution of the onset and amplitude of the post inhibitory rebound burst firing. Based on the variability observed in saccadic eye movement response, these variables are stochastic. Based on the central limit theorem, a Gaussian distribution is appropriate to describe the onset and amplitude of the post inhibitory rebound burst firing. Based on the simulation results and experimental data presented in this paper, the mean onset time of the rebound burst (after the DME return to zero is initiated) is approximately 12 ms for abducting saccades and 10 ms for adducting saccades, both with a standard deviation of 2 ms. Moreover, the mean peak amplitude of the rebound burst is approximately 100 Hz, with a standard deviation of 33 Hz for both abducting and adducting saccades. Certainly, appropriate microelectrode studies are needed to more completely describe these distributions.

Saccade Accuracy and Variability

While it is known that saccades nearly always undershoot the target location, a precise mechanism for this phenomenon is not at all understood. The size of the undershoot error between the target and the eye position after the first saccade follows an almost linear relationship to the size of the saccade amplitude. As previously described, the TN's provide an internal representation of the current eye position by mathematically integrating EBN's and IBN's activity.

Since muscle saturation limits the maximum firing rate at which the muscles respond, an error exists between the true and internal eye position. This error is approximately constant during the average bursting phase of the pulse. Therefore, since saccade duration increases as a function of saccade amplitude, the CNS will produce an approximately linear saccade amplitude dependent undershoot error due to this integral error dif-

ference. Note that the CNS is integrating a constant error, which results in a linear function, dependent on saccade duration and saccade amplitude. Notice that when the ipsilateral EBN's and contralateral EBN's rebound bursts cease, the internal representation of the eye is at its final destination. However, the actual eye position is short of its final destination at this time. Because of resultant active state tensions and the dynamics of the oculomotor plant after the EBN's bursts cease, the eye continues to be driven closer to its true destination, but an undershoot error still remains. The predictions of this control mechanism are consistent with the undershoot error observed in eye-movement data. Note also that contralateral post inhibitory rebound burst firing causes undershoot error as illustrated in Figure 18.

Hysteresis has been reported in the electrophysiological results of some investigators and not in others. Hysteresis involves the steady state tonic firing rate differences dependent on the direction of the saccade. The neural model presented here does predict hysteresis based on the TN's integrated stochastic neural activity during the post inhibitory EBN's rebound bursts. Interestingly, while the tonic firing rates are quite variable for a given eye position, the effects of hysteresis are negligible. Moreover, the system is self rectifying, in that any long term drift in the tonic firing rate is effectively removed because of the equal ribution of left and right saccadic eye movements.

With the same target presentation, an individual's saccadic eye movements are quite variable and highly coordinated. Peak velocity variations for the same size saccade have been reported to be approximately 100°/s for saccades of all sizes. Using system identification techniques and optimal control theory, Enderle and Wolfe identified that random variation in the agonist pulse magnitude causes the variation in the peak velocity for saccades of the same size. Moreover, the agonist pulse magnitude is a random variable, and independent of the size of the saccade. The muscle saturation level is the most dominant factor affecting agonist pulse magnitude. Thus, the muscle saturation level must also be a random variable.

Conclusion

One of the strengths of this modeling effort is that the saccade generator model developed here is fully supported by experimental evidence, with neural connections and firing patterns consistent with those reported in the literature. The saccade generator model uses neurons that fire maximally for saccades of all sizes, consistent with the firing patterns observed in the data. Moreover, a realistic oculomotor plant is used within the oculomotor system model, which produces accurate simulations that match the experimental data for all types of saccades using a common mechanism of action.

Future work involves increasing the complexity of the saccade generator model to include oblique saccades. A theoretical model of the oculomotor plant, with six muscle pairs, and a neural circuit will be developed. The six muscle oculomotor plant will be based on the new model of muscle, and constructed using Newtonian mechanics. The saccade generator model will be updated to include the sites for vertical fast eye movement center in the rostral interstitial nucleus of the medial longitudinal fasciculus (iMLF) [99]. Note that there are two separate channels for oblique saccades, one for the horizontal component and one for the vertical component.

It is hoped that the knowledge and insight learned from this study will prepare us for future and more complex studies involving the multiple input-output saccadic eye movement system. The ultimate goal of the research findings will be the development of an adaptive control system based on the known functioning of the cerebellum. The controller is believed to be time optimal and based on a series of switches that control the timing of the pulse-step input to the oculomotor plant. Certainly, the research carried out in this project will be important in assigning qualitative and quantitative role to the cerebellum which should indicate whether it is possible for the cerebellum to control the saccade amplitude for any given initial orbital position of the eye. This research should also provide a mechanism for control of saccade amplitude which is consistent with known sites and firing patterns involved with saccades, and the spatial to temporal transformation.

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ABSTRACT

Based on electrophysiological evidence, eye-movement measurements and systems control theory, a new phsysiological neural network model of horizontal saccadic control is described. The neural control mechanism is first order time optimal, initiated by the deep layers of the superior colliculus and terminated by the cerebellar fastigial nucleus. The neural circuit consists of neurons in the paramedian pontine reticular formation (burst, tonic and pause cells), the vestibular nucleus, abducens nucleus, oculomotor nucleus, cerebellum, substantia nigra, nucleus reticularis tegmenti pontis, the thalamus, the deep layers of the superior colliculus and the oculomotor plant for each eye. Agonist burst cell activity is initiated with maximal firing due to an error between the target and eye position, and continues until the internal eye position in the cerebellar vermis reaches the desired position, then decays to zero. The cerebellar vermis is also responsible for adapting the duration of maximal firing based on the initial position of the eye. Due to prior pause cell inhibition of the burst cells, stochastic rebound burst cell firing occurs, resulting in a temporary rise and fall firing above the maximal steady state burst firing level. Tonic cells "mathematically integrate" burst cell activity to yield an internal estimate of the current eye position. There are two sets of neural integrators in the neural network. One operates within the cerebellar vermis to predict the width of the pulse, and the other within the paramedian pontine reticular formation to maintain the eyes at their destination. Antagonist neural activity is inhibited during the agonist burst activity. After the agonist burst, antagonist neural activity rises with a stochastic rebound burst and from input from the fastigial nucleus, then falls to a tonic firing level necessary to keep the eye at its destination. The onset of the antagonist tonic firing is stochastic, weakly coordinated with the end of the agonist burst, and under cerebellar control. A common mechanism of action is described, based on cerebellar gating, through the fastigial nucleus, that explains a number of different saccadic eye movement types, including dynamic overshoot, glissadic overshoot and undershoot, and undershoot. A linear homeomorphic oculomotor muscle model is used in the simulations of the operation of the neural network. Each of the neural sites in the model fire similar to experimental data, and simulate fast eye movements that match the data extremely well for saccades of all sizes. All features of these simulations, including peak velocity, duration and amplitude conform to published observations.

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