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FROM VISION TO ACTION: A NEUROMIMETIC MODEL OF THE SACCADIC SYSTEM

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Chapter 1

Introduction

Saccadic eye movements (saccades) are the fast eye movements that we commonly use to redirect our gaze. They include both voluntary and involuntary (i.e., reflexive) changes of fixation, the quick phases of vestibular nystagmus, and the rapid eye movements (REM) that occur during sleep.

The goal of this study is to model the neural processes and circuitry underlying the generation of the first two types of movements, which are usually referred to as goal-directed saccades. The function of these movements is to move the eyes to bring a pre-determined point of interest in the visual scene (the goal) onto the center on the fovea (the region of the retina characterized by the highest density of receptors). As they must be fast and accurate, goal-directed saccades can be considered the most complex and demanding type of eye movements. They also happen to be the most studied motor acts in neuroscience.

There is a very good reason for the large interest in studying this system: The saccadic system represents a unique window through which we can analyze the processes that "convert" a sensory input into a motor output. It could be argued that any other motor system would offer the same opportunity. However, no other system is as simple as the saccadic system: it must control a single joint that can not be loaded. This makes it easier (even though it
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is still far from easy!) to characterize the role of the various neural signals involved in saccade generation, and to establish causality relationships.

Historically, models of the neural control of movement have been designed by applying standard control theory principles to the system under examination. The knowledge about neural patterns of activity or interconnections available at the time, or acquired subsequently, was then either squeezed into the model, or used to refine it. A classic example of this approach is represented by the model of the saccadic system proposed by D.A. Robinson over 25 years ago (Robinson 1975a; Zee, et al. 1976), and by its many data-driven modifications (e.g., Jürgens, et al. 1981; Van Gisbergen et al. 1985; Scudder 1988). Such models have helped us to formalize the problems that the brain faces, provided insights into adaptive processes, and often inspired further experiments. However, control system models have limited predictive power (e.g., they don’t allow predictions of brain activation patterns under novel experimental conditions, or the simulation of lesions of specific brain regions) and can impede the achievement of a thorough understanding of the brain by forcing our interpretations of experimental data to match arbitrary expectations. Nonetheless, the control theory approach was certainly justified in the past, when not much more than an input/output description of the system was available. However, in the last few decades we have come a long way in understanding the brain at the neuronal level, and we feel that it is now essential to work on neuromimetic models, i.e., models that mimic actual brain structure and neuronal activity. This class of models has much more predictive power than the control system models, and can provide insight into the nature of neural signals as well as their encoding, at both the single neuron and population level.

The model that we describe here can undoubtedly be classified as neuromimetic. As such, its foundation and the standard against which it must be evaluated are the experimental data available. Accordingly, we start this work by summarizing the results of several behavioral, physiological, and anatomical studies of the saccadic system of human and non-human primates (Background). In addition, throughout this work we indicate the experimental data
that motivated our choices in assigning roles, connectivity, and patterns of activation to the various brain areas modeled. Of course, the data often leaves the door open to multiple interpretations. When that happens a modeler is forced to make somewhat arbitrary decisions. In all those cases, we clearly indicate to the reader the assumptions we made, and what data support them. When no data were available, common sense was our guide.

After this brief initial review, the rest of this work describes our own contributions to the field. We first (*Input-Output Analysis*) clearly formulate the problem to be addressed, and perform an input-output analysis of the system. This step is often taken for granted, but we consider it crucial as it reveals several constraints that any model of the saccadic system must not violate.

We then move on (*Slide-Step Generation*) to describe what characteristics the innervation signal must have to guarantee a good transition from the high speed saccadic movement to the steady fixation required by the visual system. Because the properties of the components of the innervation signal that we describe in this chapter are strongly affected by the rotational mechanics governing the movements of the eye, a large part of this chapter is devoted to the development of an accurate tri-dimensional dynamic model of the ocular plant. This model allows us to demonstrate how the eye plant can play a considerable, and unexpected, role, simplifying the neural controller.

In the next chapter (*Pulse Generation*) we describe the core of our model, i.e., the circuitry that generates the pulse of innervation that makes saccades so fast. Particular emphasis is given to explaining how the inputs and internal connectivity of the various brain areas modeled produce patterns of activity that closely resemble those experimentally observed.

This descriptive analysis is followed (*Implementation and Simulations*) by a distributed implementation of the model, which is then used to perform a large number of simulations. Through these simulations we show how our model can generate realistic saccades as well as reproduce the effects of paradigm changes, electrical stimulation, natural perturbations, and brain lesions.

In the next chapter (*Analysis and Inferences*) we perform a detailed comparison between our model, previously proposed models of the saccadic system
and of neural motor controllers in general, and classic control schemes used in engineering. From this comparison we conclude that our model is not only different from the other models proposed so far, but that it also does not adhere to classic control theories. In particular, our model does not internalize physical signals (e.g., motor error or desired ocular displacement) but uses instead signals that represent desired sensory states, approximate motor drives, and distributed motor commands. We also argue that a non-classical controller like this may have several advantages for the brain, such as reduced complexity and enhanced tolerance to partial failures. The downside is that the quality of the movements produced is considerably sub-optimal, but good enough to serve vision appropriately.

Finally, we conclude (Future Directions) by outlining some experimental tests for our model, and by illustrating some unresolved issues which we plan to tackle in the future.

Note that, as large parts of this work have already been published in peer-reviewed journals or as book chapters, the focus here is on describing how all the parts fit together. For this reason, on several occasions we only describe the general results, while pointing the reader to the published material for a more detailed analysis.
Chapter 2

Background

The saccadic system has attracted the attention of many investigators over the last forty years. Thanks to the combined efforts of so many researchers, a great deal of data is now available about the pattern of neural activity, the anatomy of functional connections, and the effects of lesions and electrical stimulation in several brain areas involved in controlling saccades.

The number of brain areas that is involved in the generation of saccades is very large. However, by restricting our attention to the execution of goal-directed saccades, we can limit our analysis to only a subset of these areas: the superior colliculus, the brain stem saccadic network, and the cerebellum. Other areas that provide inputs to these structures, such as the frontal eye fields (FEF), the lateral intraparietal cortex (LIP), and the substantia nigra pars reticulata (SNr), will also be considered, but in lesser detail. Needless to say, in addition to these brain areas, the eye plant (i.e., the controlled system) also needs to be carefully studied.

In this chapter we summarize the behavioral characteristics of saccades, the physiology and the anatomy of the brain structures mentioned above, and previous models of their role in determining saccade characteristics. Throughout the rest of this work, we will use this background information both to support the functional role we attribute to these structures, and to justify our
approach. Before starting we will briefly describe some basic mathematical tools necessary to describe rotations.

## 2.1 Quantifying Eye Rotations

The first issue that must be addressed to describe the rotation of a rigid body, or its orientation, is the selection of a set of coordinates, i.e., a set of three Cartesian axes. When studying eye rotations, we have three options: we can consider the three main axes of rotation as fixed in space, fixed in the head, or moving with the eye. Of course, keeping the axes fixed in space would be of little help, as the eyes rotate relative to the head. However, each of the other two solutions has both advantages and disadvantages; the decision of which one to use depends both on the specific oculomotor task under study and on the choice of mathematical tools used to quantify eye rotations.

This latter element is particularly important. In fact, whereas translations, and the resulting positions, can be described by simply specifying the Cartesian coordinates of the center of the eye, rotations, and the resulting orientations, can not be described by any simple (i.e., intuitive) set of coordinates. One of the fundamental reasons for this complexity is that the space of all rotations is curved. This can be easily noted by considering that if one keeps rotating an object around the same axis, eventually (after $360^\circ$) it will get back to the initial orientation. In contrast, the more familiar space of translations (i.e., the Euclidean space) is flat, and moving in one direction will never result in getting back to the initial position.

To address this inherent complexity several mathematical tools have been developed, such as quaternions, sequences of rotations, rotation matrices and rotation vectors, and each one has some advantages and some drawbacks (Tweed 1997a). Of these many equivalent descriptions of rotations, the one we prefer (for reasons that will become clear later on) is the so-called axis-angle form, which follows from Euler’s theorem (Goldstein 1980). This theorem states that
2.1. QUANTIFYING EYE ROTATIONS

Figure 2.1: Description of rotations using the axis-angle form.
Any orientation of a rigid body with one point fixed can be achieved, starting from a reference orientation, by a single rotation around an axis (through the fixed point) along a unit-length vector \( \hat{n} \) by an angle \( \Theta \).

When this method is employed, the natural choice is to consider the main axes of rotation as fixed in the head. The advantage of using this representation over others in studying the oculomotor system is that Euler's vector represents the vector around which the eye must be rotated to take the shortest path from the current orientation to the reference orientation (Nakayama and Balliet 1977; Schnabolk and Raphan 1994a). As we will see later on, this makes it easier to compute the torques acting on the eyeball.

Euler's theorem highlights an aspect common to all the methods that can be used to represent rotary motion: the need to define a reference orientation. Although its choice is totally arbitrary, only two orientations represent a sensible choice for eye movement research. The first is the orientation with the head upright and the eye looking straight ahead. The three main axes of rotation then point straight up, straight ahead and straight to the left, respectively, defining the system of coordinates that is used to describe, for each eye orientation, Euler’s axis of rotation, \( \hat{n} \). With this convention, for example, if the eye is rotated 45° to the left, its orientation is described by \{45, (1, 0, 0)\}, as that orientation is achieved by rotating the eye, starting from the reference orientation, by 45° around the vertical axis (Fig. 2.1A; note that we are looking at the camera from the front, so the main axes point up, out of the page, and to the right, respectively). Similarly, if the eye were rotated 45° up and to the left, its orientation would be \{45, (0.707, 0, -0.707)\} (Fig. 2.1B). The second possible choice for the reference orientation is to have it coincide with the primary position, behaviorally defined by identifying Listing’s Plane (see below). Throughout this work we define the reference orientation as the orientation in which the eye looks straight ahead. However, for simplicity we will also assume that Listing’s Plane coincides with the frontal plane, in which case the reference orientation is also equal to the primary position.
2.2 Behavioral Characteristics

2.2.1 Metrics of Saccades

Velocity

Saccades exhibit a feature unique amongst eye movements: there is a consistent relationship between the size of the movement and its peak speed. The larger the movement, the greater its peak speed (see Fig. 2.2A and B). For small amplitudes this relationship is linear, but then it gradually saturates, with asymptotic values of around $500^\circ/s$ in humans and $1000^\circ/s$ in monkeys (see Fig. 2.2C). This relationship is usually called main sequence (Bahill et al. 1975), and can be used to identify eye movement as saccades or to diagnose pathological conditions. It is important to note that this relationship varies as the experimental paradigm changes. So, for example, saccades in different directions fall on different main sequences, saccades directed to auditory or flashed targets are slower than saccades directed to stable visual targets, centripetal saccades are faster than centrifugal saccades, and so forth. Accordingly, the existence of the main sequence must not be interpreted as evidence that saccade amplitude determines saccade velocity in general (as saccades of the same amplitude can have dramatically different velocities under different experimental conditions), but only that saccade velocity strongly correlates with saccade amplitude, other things being equal. This point is important as the ability to reproduce the main sequence has always been one of the basic requirements of models of the saccadic system.

Duration

Because of the main sequence, amplitude and duration are also expected to be related. It turns out that their relationship is linear over the whole oculomotor range, even though it is also subject to the same dependency on experimental conditions described above.
Figure 2.2: Behavioral characteristics of saccades.  


B: Time course of eye velocity for same saccades as in A. C: Main sequence of saccades. Monkey data provided by Dr. H. Aizawa. 

D: Saccades of different speed to the same target. Human data from (Jürgens et al. 1981). 


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Accuracy

This is the most important measure of saccade performance, as, after all, a correct saccade is a saccade that brings the target on the fovea. In general saccades are pretty accurate, and when a series of saccades to the same target is considered, the end point scatter is usually smaller than the scatter in velocity or duration. This is because velocity and duration are anti-correlated, so that slower saccades last longer. In humans it has been reported (Jürgens et al. 1981) that the compensation is, on average, perfect, i.e., there is no correlation between movement amplitude and velocity (see Fig. 2.2D). However, we have found (Quaia, et al. 2000) that in monkeys this is not the case, and the compensation is only partial (i.e., slower saccades tend to be shorter). Similar compensatory mechanisms seem to be at work to compensate for directional errors, so that if the saccade starts to the left of the target it then bends to the right and vice-versa. Again, the extent of this phenomenon is different in humans and monkeys. Whereas in humans there is over-compensation (Erkelens and Sloot 1995; Erkelens and Vogels 1995), i.e., if the saccade start to the left of the target, it ends to its right and vice-versa, in monkeys the situation is more complex, with partial compensation for small saccades and over-compensation for large saccades (Quaia, et al. 2000).

Of course, what we have just described holds true only on average, but saccades often miss the target. When that occurs usually a corrective saccade follows after a short latency (around 100 ms). Such corrective movements can occur even when the target is no longer present, indicating that non-visual information can be used to trigger the movement. However, this does not mean that vision is not important, as both the probability of occurrence and the accuracy of corrective movements increase, and their latency decreases, if a visual signal is available at the end of the initial saccade (Prablanc et al. 1978; Deubel et al. 1982).
Latency

The interval between the presentation of the target and the initiation of a saccade has been the subject of intensive study, as it reflects various aspects of visual processing, target selection, and motor programming. As such, it depends heavily on the experimental conditions.

By studying saccades under different experimental conditions it has been shown that there is a bimodal distribution of saccade latencies, with early saccades (called express saccades) at latencies shorter than 110 ms (and as low as 80 ms), and regular saccades at latencies of 140 ms or more (see Fig. 2.2E). Saccades at latencies between 110 and 140 ms are virtually absent. The frequency of express saccades varies from subject to subject, is influenced by the amount of training, and can be manipulated by appropriate experimental settings. Furthermore, it is target specific, and thus can be different for saccades directed at different parts of the visual field (Paré and Munoz 1996).

Waveform

Another characteristic of saccades, this one common to many other types of movements (even limb movements), is that the eye velocity tends to follow a bell-shaped profile (see Fig. 2.2B). For small saccades the acceleration and deceleration phases have approximately the same duration, while for large saccades the profile is skewed, with a longer deceleration phase (Van Opstal and Van Gisbergen 1987).

Trajectory

The trajectory of saccades is usually pretty straight, even though there is often some mild curvature (see Fig. 2.2F). This curvature is highly idiosyncratic, as it varies from subject to subject and it is different for different movement directions. It is interesting to note that, because of the main sequence, this behavior is not what would be expected if the horizontal and vertical com-
2.2. Behavioral Characteristics

Figure 2.3: Example of Listing's plane in a human subject. A: Horizontal and vertical components of the vectors of rotation (Euler's axis). B: Corresponding vertical and torsional components. Adapted from (Crawford 1998).

Components of an oblique saccades were controlled independently. If that were the case, because short saccades last less time than long saccades, the smaller component of an oblique saccades would not last as long as the other, and thus the saccade would be curved. However, the duration of the smaller component is stretched to match the duration of the other component, so that saccades are pretty straight (Becker and Jürgens 1990).

2.2.2 Listing's Law

One problem that the brain has to address to control eye orientation is that, even though each eye has three degrees of freedom, the direction of gaze has
only two degrees of freedom, because the eye can be rotated about the line of sight without changing the direction of gaze. This situation is called *kinematic redundancy* (Crawford and Vilis 1995), and implies that each direction of gaze can be achieved through an infinite number of different eye orientations. Despite this potential redundancy, observation of actual eye orientations reveals that the brain does not use all three degrees of freedom, and that each gaze direction corresponds to a unique eye orientation, regardless of previous movements and orientations. This observation, known as Donder’s Law (Leigh and Zee 1999), holds when the head is kept fixed, and it was further extended by Listing to actually specify the space of possible orientation. This is Listing’s Law (Leigh and Zee 1999), which states that if the vectors describing the eye orientations attained by a subject having his head fixed in space are plotted, they form a plane (the so-called Listing’s Plane). Fig. 2.3 shows an example of orientation measurements made from a human subject, where each point indicates the orientation of the eye during a period of fixation. Fig. 2.3A shows, from the subject’s point of view, the vertical and horizontal components of the Euler’s axes for each fixation, whereas Fig. 2.3B shows their vertical and torsional components. It is clear that the points in Fig. 2.3B form a thin plane, i.e., Listing’s Plane. The eye orientation in which the line of sight is orthogonal to Listing’ plane is usually called the *primary position*. Consequently, if this position is taken as the reference orientation to compute Euler’s vectors (see above), and torsion is defined as rotation around a vector collinear with the line of sight in primary position, Listing’s Law simply states that only eye orientations with zero torsion are allowed. This lack of torsion should not be confused with the alignment of the retina with the local gravitational vertical. In fact, when the eye is in a tertiary position (e.g., not on the horizontal or vertical meridian), it appears to be twisted (see Fig. 2.1B), even though the torsional component of orientation is null. To distinguish this twist from real torsion, it is called *false torsion* (Carpenter 1977). It must be stressed that Listing’s law is enforced only when the head is fixed, and it breaks down when the head is freely moving (for example, vestibuloocular slow phases can carry the eye out of Listing’s plane by as much as 30°). Furthermore, when binocular movements are considered, Listing’s plane varies as a function of the depth
of the target, so that Listing’s plane for each eye rotates outward as the eyes rotate inward during vergence (Mok et al. 1992). This implies that Listing’s Law cannot arise from a mechanical, hardwired, property of the ocular plant, but must be enforced by providing the appropriate innervation signals to the oculomotor plant.

2.3  Anatomy and Physiology

In this section we describe the anatomical and physiological characteristics of the main components of the saccadic system, pointing out, when necessary, inconsistencies in the data. Because this analysis is not meant to be a complete review of the literature, we will refer the reader to existing reviews for more detailed explanations.

2.3.1  The Oculomotor Plant

The most essential motor structures of the eye plant are six striated muscles, usually referred to as extraocular muscles (see Fig. 2.4). They have been named according to their location with respect to the eyeball. They are: the medial rectus, the lateral rectus, the superior rectus, the inferior rectus, the superior oblique and the inferior oblique.

The four recti muscles originate in a common ring tendon located at the apex of the orbit and known as the annulus of Zinn. Diverging from this toward the globe, the four recti muscles eventually insert, through their tendons, into the sclera of the anterior half of the globe (see Fig. 2.5). The superior oblique, like the recti muscles, also originates at the apex of the orbit. However, it then runs forward above the medial rectus, becomes tendinous and passes through a cartilaginous pulley (the trochlea). Leaving the trochlea, it turns sharply backward laterally and downward, and inserts in the posterior superior quadrant of the globe. Unlike the other muscles, the inferior oblique does not originate at the apex of the orbit. Its origin is in the front of the orbit, just
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Figure 2.4: Eyeball and extraocular muscles: frontal view

Figure 2.5: Extraocular muscles: lateral view of the left orbit
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below the fossa for the lacrimal sac, and it inserts in the outer lower quadrant of the posterior part of the globe.

The innervation to these muscles is provided by motoneurons located in three nuclei, part of the ipsilateral brain stem. The motoneurons of the lateral rectus are located in the VI (abducens) nucleus, and those innervating the superior oblique are located in the IV (trochlear) nucleus. The other four muscles receive their innervation from neurons located in different subdivisions of the III (oculomotor) nucleus.

These six muscles are usually functionally studied as three agonist-antagonist pairs: the horizontal recti (medial and lateral), the vertical recti (superior and inferior), and the obliques. To characterize their action, we can look at the axes around which they tend to rotate the globe. When the eyes are pointing straight ahead, the horizontal recti rotate the globe around a vertical axis, while the vertical recti induce a large rotation around the horizontal axis, and a smaller, but still very significant, rotation around the line of sight. Finally, the oblique muscles rotate the eyes mainly around the line of sight, but they also induce a significant rotation around the horizontal axis. From these considerations we can conclude that to make a horizontal eye movement it is sufficient to activate the horizontal eye muscles. However, to make a vertical eye movement (rotation around a horizontal axis) it is necessary to coordinate the action of vertical recti and oblique muscles.

It is important to note that the extraocular muscles are different from skeletal muscles in almost every respect: they have different fiber types, innervation patterns, contractile properties, motoneuron firing rates, and proprioceptors. Even the way disease affects them is different (Porter et al. 1995; Porter and Baker 1996). Such specialization must be related to the unique requirements of the tasks that the extraocular muscles need to accomplish, and it shows that Nature can lighten the burden on a neural controller by working on the mechanical properties of the controlled system. In a further chapter we will analyze another example of eye plant mechanics' specialization aimed at simplifying the control problem.

The eyeball is suspended in the orbit by the muscles above described and
to a great extent by a complicated system of ligaments, fascias and other membranes which generally originate or terminate on the orbital walls. There is no anatomical structure that could be designated as the socket within which the eyeball rotates. Even the filler substance of the orbit, the orbital fat, moves with ocular rotations to a degree depending on its proximity to the eyeball. Accordingly, each eye has six degrees of freedom: three for rotation, and three for translation. In reality, the amount of translation possible is very limited (approximately 2 mm along the antero-posterior axis, and 0.5 mm in the frontal plane (Carpenter 1977)), so that the eyeball can be considered, with good approximation, as a spherical joint with its center fixed in the head. With this approximation in place, we only need to consider rotations around three orthogonal axes (which define a system of coordinates) passing through the center of the eye.

2.3.2 The Brain Stem Circuitry

The brain stem saccadic network, which includes the motoneurons that innervate the extraocular muscles, has been the subject of several studies, and our current understanding of it is supported by a great deal of experimental evidence. Here we just briefly describe its fundamental aspects; several reviews describing it in detail have been published (e.g., Fuchs et al. 1985; Büttner-Ennever and Büttner 1988; Hepp et al. 1989; Moschovakis and Highstein 1994).

The basic structure of the horizontal channel of the brain stem circuitry implemented in our model is shown in Fig. 2.6. The muscles innervated to move the eyes in the horizontal plane (i.e., to rotate the eyeball around the vertical axis) are the lateral recti (LR), which rotate the left eye to the left and the right eye to the right (i.e., they rotate the eyes temporally), and the medial recti (MR), which have opposite effects (i.e., they rotate the eyes nasally). When a conjugate movement of the eyes is produced, the LR of one eye and the MR of the other eye act as agonists (i.e., the force they generate is increased), whereas the other two muscles act as antagonists (i.e., their tension is decreased). The
2.3. ANATOMY AND PHYSIOLOGY

Figure 2.6: Brain stem circuitry for generating saccadic eye movements. Dashed lines indicate inhibitory connections. The pathway providing the tonic signals is omitted for clarity.
innervation to the lateral recti is provided by motoneurons (MN) located in the ipsilateral abducens (VI) nucleus; intermixed with these motoneurons are interneurons (IN), which presumably receive the same inputs and project to the motoneurons of the contralateral MR, located in the contralateral oculomotor (III) nucleus.

Each side of the brain stem contains two populations of medium lead burst neurons (MLBNs): one (EBNs) excites the ipsilateral MNs and INs, while another (IBNs) inhibits contralateral MNs and INs. These populations of MLBNs fire phasically during ipsilateral saccades, and are inhibited by OPNs (located across the mid-line), which fire tonically during periods of fixation and pause during saccades, thus acting as a gate. In turn, MLBNs inhibit the OPNs, helping to keep them inactive during saccades. Because no direct projections from the IBNs to the OPNs have been found (Büttner-Ennever and Büttner 1988), we assume that the EBNs inhibit the OPNs through an inter-neuron.

The difference between the signal carried by the ipsilateral EBNs and that carried by the contralateral IBNs determines the speed of the horizontal component of the movement. This velocity signal is then fed to neurons located in the nucleus prepositus hypoglossi and in the vestibular nuclei (for clarity this pathway has been omitted in Fig. 3); the output of these neurons, which constitute the so-called neural integrator, goes to the motoneurons, which use it to hold the eyes in an eccentric position at the end of the saccade.

The scheme for the vertical channel is similarly organized (e.g., Crawford and Vilis 1992), even though two pairs of muscles for each eye (vertical recti and obliques) are activated during vertical movements.

2.3.3 The Superior Colliculus (SC)

Since the early 70s, single-unit recordings (Wurtz and Goldberg 1971; Schiller and Stryker 1972; Wurtz and Goldberg 1972) and electrical stimulation experiments (Robinson 1972; Schiller and Stryker 1972) have indicated that the intermediate layers of the SC must play an important role in producing sac-
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Figure 2.7: Topographical organization of the Superior Colliculus.

cades. Cells in the SC (from now on we always refer implicitly to the intermediate layers of the SC) are characterized by fairly large movement fields (i.e., the range of movements associated with activation of a neuron) (Sparks et al. 1976), which are topographically organized (i.e., cells close together have similar movement fields). Neurons that discharge in correspondence with small saccades are located rostrally, whereas large movements are associated with more caudal sites (Fig. 2.7). Accordingly, electrical stimulation at rostral sites results in small saccades, whereas at more caudal sites larger saccades are evoked. These results indicate that the saccadic (or target) vector is spatially, and not temporally, encoded on the SC; movements toward targets in the left visual hemifield are encoded in the right SC and vice-versa (for a review see, Sparks and Hartwich-Young 1989; Guitton 1991; Wurtz 1996).

Recently, saccade-related neurons in the SC have been divided into three classes, according to their pattern of activity and location: burst neurons, buildup neurons and fixation neurons (Munoz and Wurtz 1992; Munoz and
Figure 2.8: Activity of collicular cells. A: Burst neuron. B: Buildup neuron. C: Fixation neuron. A and B adapted from (Munoz and Wurtz 1995a). C adapted from (Munoz and Wurtz 1993a).

The burst neurons, as classified by Munoz and Wurtz (1995a), are characterized by a brisk discharge synchronized with saccade onset (Fig. 2.8A), have a closed movement field (i.e., they discharge only for saccades around an optimal vector) and are probably the same cells described by Sparks and colleagues as saccade-related burst neurons (SRBNs) (Sparks 1978; Sparks and Mays 1980). Fixation neurons, located in the rostral pole of the SC, behave in an opposite manner (Fig. 2.8C), i.e., they discharge during active fixation and pause during saccades in any direction (except sometimes they do not pause, or even burst, for small, contraversive saccades). These cells pause immediately before the onset of a saccade and resume firing at the time of saccade termination (Munoz and Wurtz 1993a). Electrical stimulation delivered to this rostral area interrupts on-going saccades, while stimulation in the rest of the SC induces...
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contralateral saccades. The third class of cells is represented by the so-called buildup neurons (located amongst and just below the burst neurons), which are characterized by a small build up of activity preceding saccades (hence their name, Fig. 2.8B) and have an open movement field (i.e., they discharge, albeit with different intensities, for all saccades in one direction larger than a certain amplitude). Some, but not all, buildup cells are characterized by a burst occurring at saccade onset, similar to that of the burst cells. In the majority of buildup cells this burst component has a closed movement field, similar to that of the burst neurons (see Munoz and Wurtz 1995a, their Figs. 7B and 8). One striking characteristic of the buildup neurons is that some of the activity (but not the burst component) in the buildup layer seems to spread rostrally across the SC during a saccade (Munoz and Wurtz 1995b). This observation, based upon the analysis of the time course of cells’ discharge during saccades of different amplitude, is reminiscent of the finding that in the cat the locus of collicular activation appears to move rostrally during a saccade (Munoz et al. 1991a), possibly encoding instantaneous gaze error spatially (Munoz et al. 1991b; Guitton et al. 1993).

2.3.4 The Cerebellum

A great deal of evidence points toward lobuli VIc and VII of the cerebellar vermis as being involved in the control of saccadic eye movements. First of all, only very small currents are needed to evoke saccades from this region (Noda and Fujikado 1987), whereas much higher currents are needed to evoke saccades from nearby lobuli (Ron and Robinson 1973; Keller et al. 1983). Second, ablations of this area result in dysmetric movements (Ritchie 1976; Takagi et al. 1998). Finally, neurons in this area present saccade-related activity (Sato and Noda 1992a; Helmchen and Buttner 1995; Ohtsuka and Noda 1995), whereas activity in neurons belonging to other vermal lobuli is not modulated during saccades (Sato and Noda 1992a). Unfortunately, there is not much agreement regarding the pattern of saccade-related activity of these neurons. Whereas Ohtsuka and Noda (1995) reported that neurons in the oculomotor vermis produce an early burst for ipsilateral saccades and a
Contralateral Saccade

Ipsilateral Saccade

Figure 2.9: Activity of FOR cells for movements in the preferred (left column) and non-preferred direction (right column). Note the different timing of the discharge. Adapted from (Ohtsuka and Noda 1991).

late burst for contralateral movements, Helmchen and Butter (1995) reported that the direction associated with the early burst is ipsilateral for half the cells and contralateral for the other half.

In turn the oculomotor vermis projects to an ellipsoidal region in the caudal fastigial nucleus (Yamada and Noda 1987), the so-called fastigial oculomotor region (FOR). These projections are strictly ipsilateral and topographically organized (Courville and Diakiw 1976; Carpenter and Batton 1982; Noda et al. 1990). Because the vermis does not project directly outside the cerebellum, the signals present in the FOR determine the effect of the cerebellar vermis on saccades. Consequently, any model that is concerned with the control of saccades by the cerebellum has to give strong import to the saccade-related
discharge of the FOR neurons. Fortunately, there is general agreement on the pattern of activity recorded in these neurons (Ohtsuka and Noda 1990; Ohtsuka and Noda 1991; Fuchs et al. 1993; Helmchen et al. 1994). They produce an early burst of activity for movements in one direction (preferred direction), and a late burst, time-locked with the end of the movement, for saccades in the opposite direction (Fig. 2.9). The preferred direction always has a contralateral horizontal component.

2.4 Models

In 1975 a milestone in the history of saccadic modeling, the Robinson model, was published (Robinson 1975a; Zee et al. 1976). The central idea of that model, inherited by almost all subsequent models of the saccadic system, was that saccades are controlled by a local feedback loop, which in Robinson’s model was used to compare the desired position of the eyes with an internal estimate of their actual position, thus producing an estimate of the instantaneous (or dynamic) motor error (Fig. 2.10). This model, as well as others
derived from it, was based on control systems principles, and its building blocks were not closely associated with anatomical structures. However, the growth of anatomical and physiological knowledge, due to the large number of experiments carried out after 1975 (largely prompted by the many predictions of Robinson's model), impelled modelers to identify at least some of the different parts of their models with specific regions of the brain.

Initially models included only the brainstem circuitry, but soon the great amount of data available about the superior colliculus made it essential to find a role for this mid-brain structure. Accordingly, models focused on the role played by the SC in controlling saccades and in determining the firing pattern observed in brain stem neurons. However, over the last ten years new experimental evidence has induced modelers to attribute an increasing importance to the SC. This trend has lead to the development of a fairly large family of models that impute to the SC a dominant role in determining saccade metrics, and that could thus be dubbed colliculocentric (Droulez and Berthoz 1988; Waitzman et al. 1991; Lefèvre and Galiana 1992; Van Opstal and Kappen 1993; Arai et al. 1994; Optican 1994). One of the major problems with colliculocentric models is that they have difficulties in explaining why lesions of the SC do not result in large and enduring deficits. In particular, it is well known (Schiller et al. 1980) that collicular ablations impair the ability to make saccades only for a brief time. Furthermore, even in the acute phase of a collicular lesion, the trajectory and speed of saccades can be dramatically affected without a striking loss of accuracy (Aizawa and Wurtz 1998; Quaia et al. 1998a).

On the other hand, it has been shown that cerebellar lesions (e.g., Optican and Robinson 1980) induce permanent deficits, affecting dramatically the accuracy and consistency of saccades. Nonetheless, the large majority of models has downplayed the role of the cerebellum.

We will now briefly review the roles that different models have attributed to the SC and cerebellum, pointing out what we believe are their inconsistencies with the available data. Finally, we will conclude this background chapter by describing a model of the oculomotor plant.
The function classically attributed to the SC is to provide the desired displacement signal to the brain stem circuitry (e.g., Scudder 1988; Grossberg and Kuperstein 1989; Tweed and Vilis 1990). Thus, in these schemes the SC is outside the local feedback loop that has been postulated to control saccades. In many of these models, the collicular output is processed by a spatial-to-temporal transformation (STT, a process or mechanism used to transform information from a spatial encoding to a temporal encoding) which converts the location of the activated locus on the collicular map into a temporal signal encoding the desired displacement of the eyes (Fig. 2.11).

Recently, the finding that there is a fairly good correlation between the level of activity of some collicular neurons and the residual motor error prompted the development of a model (Waitzman, et al. 1991), in which the burst
neurons encode motor error with their temporal discharge (Fig. 2.12). In this case, as well as in similar models (Van Opstal and Kappen 1993; Arai, et al. 1994), the SC becomes part of the local feedback loop. One of the major advantages of these schemes is that they do not require an STT, because the information that is encoded spatially on the SC (i.e., the desired displacement) is never converted into a temporal code and the dynamic motor error is encoded temporally in the brain stem as well as in the SC. The lack of an STT, which is a feature of several other models as well as the model presented here (see below), is very important, because it simplifies considerably the connectivity from the SC to the brain stem (Quaia and Optican 1997).

Unfortunately, there are some major problems with the scheme proposed by Waitzman and colleagues: first of all, because it posits that only the level of collicular activation, but not its spatial distribution, is under feedback control,
it can not account for the purposeful curvature of saccades. In fact, when the eyes are not headed in the correct direction they are brought back toward the target (Becker et al. 1981; Erkelens and Sloot 1995; Erkelens and Vogels 1995; Quaia et al. 2000). This behavior is particularly prominent following collicular reversible inactivation (Aizawa and Wurtz 1998), but it cannot be predicted by Waitzman’s model. Another problem with this scheme is that it does not explain why sustained electrical stimulation of the colliculus produces movements whose amplitude is a function of the rostro-caudal position of the electrode on the SC map (Robinson 1972; Paré et al. 1994; Stanford et al. 1996).

Because of these problems, we think it is unlikely that the collicular burst neurons are part of a feedback loop used to tightly control saccade amplitude. Nonetheless, we think that the correlation between burst neuron discharge and dynamic motor error is not just an epiphenomenon. In fact, when saccades are interrupted in mid-flight by electrical stimulation of the region containing omnipause neurons (OPNs), the burst neurons’ activity goes temporarily to zero (supposedly because of antidromic stimulation of collicular fixation neurons) and then resumes a level of activity that is again compatible with the encoding of dynamic motor error (Keller and Edelman 1994). This last finding makes the hypothesis that the burst neurons’ discharge is simply preprogrammed very unlikely.

The peculiar characteristics of the buildup neurons’ discharge, and particularly the rostral spread of activity during a saccade, makes it tempting to ascribe to this class of neurons a distinct function (e.g., Wurtz and Optican 1994). In particular, it has been proposed (Optican 1994) that the displacement of the center of activity on the buildup layer could represent an internal estimate of the progress of the saccade toward the target (i.e., functionally represent the output of a displacement integrator, Fig. 2.13). This role for the spread of activity is similar to the role attributed to the SC by models based on cat data (Droulez and Berthoz 1988; Lefèvre and Galiana 1992).

Unfortunately, a close inspection of the pattern of activity of monkey buildup neurons reveals that an interpretation of the spread of activity as
Figure 2.13: Optican model of collicular involvement in saccadic control. Unlike the model proposed by Waitzman and colleagues (Fig. 2.12), in this model the displacement integrator is inside the SC. The feedback signal to the SC is thus a velocity, as opposed to position, signal.

functionally important in controlling the movement is problematic. For example, in order to have a significant effect, the change of spatial distribution of activity during a saccade should be quite dramatic. However, the activity that spreads across the buildup layer during a saccade is only a small fraction of the activity that is produced at the site corresponding to the target (often characterized by a burst, see above). Thus, the center of gravity of the activated area in the buildup layer does not change much during the movement (Anderson et al. 1998). One could argue that the spread of activity over the SC map could have an effect by inducing a timely reactivation of the fixation neurons, contributing to stopping the movement. However, under this hypothesis lesions of the rostral pole of the colliculus are expected to induce dysmetria (in particular hypermetria), whereas such lesions do not seem to affect saccade amplitude (Munoz and Wurtz 1993b). Thus, even though it is certainly possible that the reactivation of the fixation zone plays a role in stabilizing the system, we think that it is unwarranted to attribute to it a dominant role in the determination
of saccade amplitude. Finally, it should be noted that this spread of activity begins well before saccade onset (e.g., during a 50° saccade the 3° buildup cell gets activated between 100 and 50 ms before saccade onset and reaches its maximal activation at least 20 ms before saccade onset) (Munoz and Wurtz 1995b, their Fig. 3). This observation makes the hypothesis that the spread is controlled by feedback information tightly related to the movement pretty unlikely, even though it does not rule out less tight feedback schemes.

One final problem common to all colliculocentric models is that they can not easily account for some recent findings suggesting a dissociation between saccade metrics and the collicular locus activated. For example, it has been shown that the collicular movement fields are different when comparing visually-guided movements with saccades to remembered targets (Stanford and Sparks 1994). Analogous results have been obtained using the averaging saccade task (Edelman and Keller 1998), after adaptation induced with the double step paradigm (Goldberg et al. 1993; Frens and Van Opstal 1997) and when saccades to moving targets are considered (Keller et al. 1996). In all these cases the collicular locus activated appears to be tightly related to the retinotopic location of the target and not to the movement evoked.

### 2.4.2 Role of the Cerebellum in Current Models

For decades the role attributed to the cerebellum by the few models of the saccadic system that considered it (e.g., Optican and Miles 1985; Optican 1986; Grossberg and Kuperstein 1989; Dean et al. 1994), has been to compensate for alterations of the oculomotor plant due to age or injury, and to adjust the saccadic command as a function of the orbital position, compensating for plant non-linearities. Such an approach was justified on the basis that cerebellar lesions impair the ability of the system to compensate for changes in the oculomotor plant (Optican and Robinson 1980) and induce saccadic dysmetria (e.g., Ritchie 1976; Optican and Robinson 1980; Sato and Noda 1992b; Robinson et al. 1993; Takagi, et al. 1998), often as a function of orbital position. In all those schemes the assumption was made (implicitly or
explicitly) that the extra-cerebellar pathway generates, using a feedback loop controller, a command that is a fixed function of the desired displacement of the eyes; that command is then supplemented by a fixed (but adaptable over the long term) command produced by the cerebellum (Fig. 2.14). Thus, in those schemes the extra-cerebellar pathway guarantees the consistency of saccades, whereas the cerebellum is responsible for their accuracy. The major failure of this scheme is that it does not account for one of the most striking effects of cerebellar lesions: the increased variability of saccades. In fact, after cerebellar impairment, saccades not only lose their characteristic accuracy, becoming dysmetric (hypermetric or hypometric depending upon the cerebellar area(s) affected by the lesion), but they also become subject to a conspicuous trial-to-trial variability, affecting both amplitude and direction (Robinson, et al. 1993; Robinson 1995; Takagi, et al. 1998).

Recently some models that address the role of the cerebellum in the in-flight control of saccades have appeared; however, in only one of those models (Houk et al. 1992; Houk et al. 1996) is the cerebellum part of the feedback loop. The theory proposed by Houk and colleagues posits that the Purkinje cells in the

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Figure 2.14: Classical model of cerebellar function. The cerebellum (CBLM) is in a side pathway under long adaptation.
cerebellar cortex are trained to recognize particular configurations of the proprioceptive inputs (carried by the mossy fibers), and when these patterns occur they fire to stop an on-going movement. The pattern-recognition mechanism proposed by Houk and colleagues works well to control limb movement, where the delays in the system are shorter than the duration of the movement and proprioceptive feedback can be used to track (and even predict) the on-going movement (Barto et al. 1999). However, we think there are some fundamental problems in extending their model to the control of saccadic eye movements. First of all, in Houk’s model the movement is interrupted when a given final position, and not displacement, is attained. Thus, the cerebellar cortex should work in head coordinates; however, it has been shown recently that saccadic adaptation, which is almost certainly controlled by the cerebellum (Optican and Robinson 1980; Goldberg, et al. 1993), occurs in oculocentric coordinates (Frens and van Opstal 1994). Furthermore, it is known that proprioceptive feedback plays no role in the in-flight control of saccades (Guthrie et al. 1983); one could argue that an internal estimate of the position of the eyes could be used instead, but no signal encoding the position of the eyes during saccades has been found in the mossy fibers. One could overcome these problems by postulating the presence of a displacement integrator in the brain stem, whose output could then be fed to the cerebellum. However, to the best of our knowledge, such a signal has not been observed in the mossy fibers. Finally, in its present form the scheme proposed by Houk and colleagues predicts a pattern of activity for the FOR that mirrors the activity in the SC, i.e., a burst of activity only for saccades in one direction, which is not compatible with the experimental data. For these reasons we think that even though Houk’s scheme is consistent with data on limb control, it is at odds with some crucial data regarding the saccadic system.

Another theory of cerebellar function is the one proposed by Grossberg and colleagues, both for saccadic (Grossberg and Kuperstein 1989) and limb control (Contreras-Vidal et al. 1997). One of the major differences between Houk’s and Grossberg’s models, is that Grossberg proposes an extra-cerebellar loop to compute the residual motor error and to generate a desired velocity signal, which is then fed to the cerebellum. Thus, the cerebellum is part of a side loop,
and it works with velocity (as opposed to position) signals. This theory has two major problems: first, it requires a spatial-to-temporal transformation (part of the extra-cerebellar loop). Second, it also cannot predict the large increase in variability observed after cerebellar lesions.

Recently, Dean (1995) proposed a model of the saccadic system that deals with the role played by the fastigial nuclei in on-line control of saccades, taking particular care in reproducing the pattern of FOR activation. The role attributed by Dean to the FOR is to ensure saccadic accuracy; because of the timing of the FOR bursts, this is achieved by contributing to the acceleration of the eyes at the beginning of saccades and to their deceleration at the end of the movement. According to this theory, which has also been proposed in other studies, the cerebellum only makes a pre-programmed contribution to a saccade whose end is controlled by the local feedback loop in the brain stem. This works because in Dean's model the brain stem circuit (extra-cerebellar pathway) consists of a feedback loop with a gain lower than one. Unfortunately, Dean's model does not predict the increased variability in saccades observed after cerebellar lesions, because it is the brain stem that guarantees the consistency of saccades.

2.4.3 Models of the Oculomotor Plant

As the goal of the saccadic system is to generate appropriate eye movements, it is then necessary, for both the brain and for an external observer trying to understand its operation, to model the oculomotor plant (extraocular muscles, eye globe, orbital tissues and Tenon's capsule). In fact, since the early sixties the oculomotor plant has been the subject of considerable interest, especially by Robinson and Collins (Robinson 1964; Robinson et al. 1969; Collins 1970; Collins 1975; Collins et al. 1975; Robinson 1975b; Robinson 1981; Miller and Robinson 1984), who conducted both experimental and modeling studies of the eye plant.

These initial studies were substantially extended by Inchingolo, who provided a more realistic model of the plant. More importantly, Inchingolo (1995)
radically changed the focus of these studies: while previous studies simply described and modeled the individual plant elements, he focused on the constraints that these elements impose on the neural controller. In Inchingolo's model of the horizontal channel of the eye plant (Fig. 2.15) we can recognize all the anatomical elements previously described: there is an agonist-antagonist pair of muscles (the horizontal recti), the supporting structures (called orbital tissues) and the eyeball.

The eyeball is simply modeled by its inertia, which has been estimated to be equal to $6.12 \cdot 10^{-5} \, \text{g/}(°/s^2)$. Three forces act on the eyeball: the force developed by the lateral rectus, the force developed by the medial rectus, and the force exerted by the orbital tissues. The limp-leash elements indicate that the muscles can only pull, and not push.

The orbital tissues are modeled as two Voigt elements connected in series,
characterized by time constants of 20 ms and 1 s. These elements tend to pull the eye towards its resting position (i.e., the position where it would end up if the muscles were resected).

The extraocular muscles are by far the most complex elements of the model. In series with the whole muscle there is the so-called *series elastic element*, which delivers the force to the tendon while smoothing out changes in overall muscle length. Unfortunately, reliable quantitative data about the value of its stiffness is still lacking. Consequently, in all the implementations of the plant model this element has been neglected. The rest of the muscle is then represented by the parallel of *passive* and *contractile* elements. The passive elements can be modeled as a Voigt element, with a viscosity $R_p$ and a stiffness $K_{cp}$. The contractile elements can also be represented as a Voigt element (viscosity $R_a$ and stiffness $K_c$), but in parallel to this element there is also the *active state tension* ($F_i$), due to the innervation provided to the muscle. When the system has reached an equilibrium (i.e., when the eye is not moving), each muscle delivers to its tendon a force that is the sum of its innervational force $F_i$, the elastic force of the passive element and the elastic force of the contractile element. The difference between the force exerted by the two muscles must then balance the force exerted by the orbital tissues, so that Newton’s law is obeyed.
Chapter 3

Input-Output Analysis

In the previous chapter we have described several experimental findings regarding the patterns of neural activity and the connectivity of several brain areas involved in controlling saccades. In developing our model, we have used these data extensively; however, in several cases the data lends itself to multiple interpretations, and in other cases there is simply not enough data. In all those cases, a modeler is forced to make some assumptions, which need to be justified. Our experience has been that, in almost all cases, a clear understanding of the role of the saccadic system is sufficient to guide these choices. Accordingly, in this chapter we perform an input-output analysis of the saccadic system to describe some general aspects that should be obvious but are often overlooked. Later on it will become clear that this simple analysis can be extremely useful in clarifying our understanding and in guiding us through some complex decisions.

3.1 The Goal of the Saccadic System

Clearly, the first question that we have to address when we model any system is: What is its goal? In the case of the saccadic system, this is pretty clear:
its role is to serve vision by redirecting the eyes to bring a different part of the visual scene onto the fovea (the region of the retina characterized by a high density of light sensors; it is the only part of the eye that can be used to perform fine visual discrimination).

Unlike quick phases of nystagmus and REM movements, goal-directed saccades must be pretty accurate. This requirement stems from a property common to all the animals in which the saccadic system is well developed: the fovea is usually very small (not more than a couple of degrees across in primates). Accordingly, it is important that saccades do not miss the target by more than one degree, so that the point of interest ends up on the fovea.

In addition to being accurate, saccades also need to be fast and to stop abruptly. The reason for this is that, when the eyes are moving at more than a few degrees per second, vision is seriously degraded (Westheimer and McKee 1975; Chung et al. 1996a; Chung et al. 1996b; Haarmeier and Thier 1999). And even a movement as slow as one degree per second (i.e., a point will take almost three minutes to cross the visual field) has an effect comparable to that produced by three diopters of myopia (Robson 1966). This implies that saccades should be as brief as possible, and they must not be followed by slow drifts of the eyes (called post-saccadic drifts or glissades). Thus what matters is the overall time during which the eyes are moving (it would make no sense to produce very fast saccades if these were followed by large drifts). This guarantees that the period of time during which vision is poor is minimized.

The goal of the saccadic system can then be summarized as follows: To serve vision by generating the innervation signals required to redirect the gaze towards an area of interest quickly, accurately, and without any post-saccadic drift.

There is one caveat to all this, though. There is no evidence that small improvements in saccade speed or accuracy constitute an evolutionary edge. Accordingly, there is no real need for the system to strive to reach a state of optimality (i.e., to produce the fastest and most accurate possible movements), especially when this requires a more complex circuitry. Thus, we feel that a model that is compatible with the neurophysiological data, requires simple
circuitry and learning algorithms, and is robust to failure and noise, is much more realistic than models derived from optimality theories based on control principles. In fact, nature’s solutions to problems are often suboptimal (Gould 1992).

3.2 Voluntary Control of Saccades

As hinted at above, the goal-directed saccades that we focus on here can be either voluntary (e.g., when a subject decides to point the eyes somewhere) or reflexive (e.g., when a subject’s gaze is drawn by the sudden appearance of a novel stimulus). Before moving on to study the saccadic system itself, we want to clarify to what extent volition can influence the execution of voluntary saccades. We feel that this is an important point, as these volitional influences must be considered as external inputs to the saccadic system, and thus need to be accounted for by any model of that system.

Certainly, subjects have the ability to decide whether to make a movement, and toward which target. And it is even possible to make a saccade without a target being present at all. However, common sense rules out any other influence of volition over saccades. We have already pointed out that, because of the peri-saccadic degradation of vision, saccades need to be fast and free of post-saccadic drifts. In addition, the suppression of vision makes the trajectory followed by the eyes during the saccade irrelevant. The system is thus an endpoint controller, meaning that all that matters is the foveation of the desired target. Accordingly, it would make absolutely no sense for the system to grant voluntary control over saccadic speed or trajectory. Indeed, all evidence available indicates that this is the strategy adopted by the saccadic system: Once a target has been selected, the saccadic system automatically generates the fastest movement possible.

One might argue that it is also possible to voluntarily control when to make a saccade, and to a certain extent this is indeed true. However, even this variable is subject to a series of automatic processes - which determine the
exact timing (or latency) of a saccade - over which we have no control. In this sense, it is as if all we are able to do is to open a gate, after which everything else happens automatically (Quaia and Optican 1999).

### 3.3 The Input to the Saccadic System

In the vast majority of the literature on the subject, it is commonly postulated that the input to this neural system is either the desired final orientation (often referred to as desired position) or the desired eye rotation (often referred to as desired displacement). In other words, it is almost always assumed that the saccadic system receives a *motor command*.

However, from the considerations that we have made above regarding the goal of the saccadic system and the extent to which it is subject to voluntary control, we conclude that this is unlikely to be the case. We propose instead that the input to the saccadic system is a *desired sensory state*: the movement has to be such that when it ends the selected target is on the fovea. Whatever system sends down the command to the saccadic system does not need to know, nor should it care about, the magnitude of the motor command that will be required to foveate the target. All that matters are the sensory consequences of the movement (i.e., whether or not the target ends up on the fovea). Accordingly, it makes sense for the input to the saccadic system to simply encode the current location of the target of interest. This might seem to be a subtle distinction, but its consequences for the organization of both the sensory and motor systems are not trivial.

There are two reasons why the saccadic system’s input should not be a motor command. First, because the eye is a rotational joint, there is not a one-to-one relationship between retinal locations and the eye rotations needed to foveate such locations (Crawford and Guitton 1997). Accordingly, a target falling on a fixed retinal location will require different rotations to be foveated, depending upon the current orientation of the eyes.

Second, we are often required to make saccades to moving targets, in which
3.4. The Output of the Saccadic System

Obviously the output of the saccadic system is the innervation signal that must be supplied to the extraocular muscles to move the eyes appropriately. As delays in sensory pathways are relatively long (around 50 ms in monkeys, equal to the duration of a fairly large saccade), and vision is poor when the eyes are moving (see above), visual feedback cannot be used to guide the eyes towards the target. In this sense we can say that saccades are ballistic movements: sensory inputs are collected at the beginning, but then the saccadic system must generate the innervation signal without external assistance. To infer what this signal should look like, we will first determine what force needs to be applied to the eyeball to produce the desired movement, and then what innervation force (or active state tension) must be generated by the muscles.
to transfer that force to the tendons.

### 3.4.1 Force at the Tendon

To determine the force that must be applied to the globe to produce a movement, we can turn to the model of the plant previously described (Fig. 2.15), and invert the transfer function of orbital tissues. For reasons that will become clear later on, it is convenient to determine the relationship between the force applied to the eyeball ($F_{OT}$) and the speed of the eye. Using the Laplace transform, it is very easy to get the following relationship:

$$F_{OT}(s) = K_{OT} \frac{(1 + sT_1)(1 + sT_2)}{s(1 + sT_3)} sE(s)$$

(3.1)

where $E(s)$ is the Laplace-transform of eye position and

$$T_1 = \frac{R_1}{K_1} = 0.02 \text{ sec}$$

$$T_2 = \frac{R_2}{K_2} = 1 \text{ sec}$$

$$T_3 = \frac{(R_1 + R_2)}{(K_1 + K_2)} = 0.614 \text{ sec}$$

$$1 / K_{OT} = 1 / K_1 + 1 / K_2 = 1 / 0.48 \text{ deg/g}$$

(Note: all the values refer to the human orbit). Eq. 3.1 can be decomposed as follows:

$$F_{OT}(s) = \left[ A + \frac{B}{1 + sT} + \frac{C}{s} \right] sE(s)$$

(3.2)

For the human orbit, the values of the constants are:

$$A = 0.0156$$

$$B = 0.1793$$

$$C = 0.48$$

$$T = 0.614 \text{ sec}$$
3.4. THE OUTPUT OF THE SACCADIC SYSTEM

Eq. 3.2 tells us that the force delivered by the muscles to the eyeball to produce an eye movement can always be interpreted as the sum of three components (see Fig. 3.1): a pulse, proportional (by a factor $A$) to the velocity of the movement, a slide, proportional (by a factor $B$) to the low pass filter (with time constant $T$) of eye velocity, and a step, proportional (by a factor $C$) to the position of the eye. The step is needed to compensate the elastic force exerted by the orbital tissues, while the pulse and the slide counteract the viscous forces generated by the orbital tissues. Note that the three components have, during a normal saccade, similar strength. Of course this would not be the case for other, slower, movements. The overall force, also shown in Fig. 3.1, can then be described as a pulse-slide-step command.

3.4.2 Force Dissipated by the Muscles

Now that we know what the force delivered at the tendon looks like, we can infer the characteristics of the innervation force by summing to $F_{OT}$ the force needed to change the length of the muscles (for brevity we will refer to this force as the force dissipated or absorbed by the muscles). To compute such force it is useful to first combine the two muscles into an equivalent ideal muscle (i.e., a muscle able to both push and pull). Given that the two muscles operate in push-pull, the equivalent muscle will simply be a muscle with a stiffness equal to the sum of the stiffness of the two muscles, and with a viscosity equal to the sum of the viscosity of the two muscles (see Fig. 3.2).

Making the (acceptable) assumption that the two muscles in a pair have identical characteristics, the equivalent muscle can then be considered as the parallel of a stiffness $K_M = 2(K_c + K_{cp})$, a viscosity $R_M = 2(R_a + R_p)$, and an innervation force $F_I$ (that can be positive or negative). The length of the muscle is measured in degrees, as it is implicitly transformed in the eye position corresponding to that muscle length. Accordingly, the rate of muscle length change is measured in degree/second. The force dissipated by the muscles can
Figure 3.1: Force at the tendon during a saccade: individual components and overall force. The relative weight of the various components is appropriate for a human eye plant.
3.4. THE OUTPUT OF THE SACCADIC SYSTEM

Figure 3.2: Simplified eye plant obtained combining each agonist-antagonist pair into equivalent ideal muscles. The series-elastic element is also ignored.

then be easily expressed as a function of the velocity of the movement:

\[ F_I(s) - F_{OT}(s) = K_M \frac{(1 + sT_M)}{s} sE(s) \]  \hspace{1cm} (3.3)

where \( T_M = R_M / K_M \). Typical values for human muscles are \( K_M = 1.58 \text{ g/deg} \), \( R_M = 0.316 \text{ g sec/deg} \), and \( T_M = 0.2 \text{ sec} \). As done previously, we can now decompose Eq. 3.3:

\[ F_I(s) - F_{OT}(s) = \left[ P + \frac{Q}{s} \right] sE(s) \]  \hspace{1cm} (3.4)

with \( P = 1.58 \) and \( Q = 0.316 \) for human muscles. Thus, the force dissipated by the muscles can be interpreted as the sum of two components (see Fig. 3.3): a pulse, proportional (by a factor \( P \)) to the velocity of the movement, and a step, proportional (by a factor \( Q \)) to the position of the eye. The step is needed to compensate the elastic force absorbed by the muscles, while the pulse counteracts the viscous forces generated by the muscles. The total force
Figure 3.3: Force dissipated by the muscles during a saccade: individual components and overall force. The relative weight of Pulse and Step is appropriate for a human eye plant.
dissipated by the muscle, also shown in Fig. 3.3, can then be described as a pulse-step signal. Note that, for a normal saccade, the pulse is very large compared to the step, and the step is already 3.3 times larger than the step for the orbital tissues (1.58 / 0.48). This means that the dominant time constant in the eye plant is the one determined by the extraocular muscles (i.e., around 200 ms in humans).

### 3.4.3 Innervation Signal

As the innervation force is, by definition, the sum of the force absorbed by the muscles plus the force delivered to the tendon, we can compute it by combining Eqs. 3.3 and 3.1:

$$F_I(s) = \left[ K_M \frac{(1 + s T_M)}{s} + K_{OT} \frac{(1 + s T_1)(1 + s T_2)}{s (1 + s T_3)} \right] s E(s)$$

Some trivial algebra shows that the inverse transfer function of the eye plant is equivalent to:

$$F_I(s) = K_I \frac{(1 + s T_A)(1 + s T_B)}{s (1 + s T_C)} s E(s) \tag{3.5}$$

where (human orbit):

$$T_A = 0.136 \text{ sec}$$
$$T_B = 0.726 \text{ sec}$$
$$T_C = 0.614 \text{ sec}$$
$$K_I = 2.06 \text{ g/deg}$$

This function is similar to the one describing $F_{OT}$ (Eq. 3.1), and thus it can also be described as the sum of three components:

$$F_I(s) = \left[ A + \frac{B}{1 + s T} + \frac{C}{s} \right] s E(s) \tag{3.6}$$
Figure 3.4: Innervation delivered to the muscles (and innervation force generated by the muscles) during a saccade: individual components and overall force. The relative weight of the components is appropriate for a human eye plant.
3.4. THE OUTPUT OF THE SACCADIC SYSTEM

For the human orbit, the values of the constants are:

\[ A = 0.3316 \]
\[ B = 0.1793 \]
\[ C = 2.06 \]
\[ T = 0.614 \text{ sec} \]

In other words, the innervation force is also the sum of a pulse, proportional to the speed of the movement (and often referred to as a *velocity* command), a slide, proportional to the low pass of the speed of the movement, and a step, proportional to the position of the eye. Of course these components are nothing more than the sum of the individual components described earlier for muscles and orbital tissues. As the innervation force is directly proportional to the innervation command supplied to the muscle, the latter can then also be described as a *pulse-slide-step* command. In Fig. 3.4 we show the time course of eye position for a typical saccade, together with the decomposition of the innervation signal (or force) into the three components aforementioned. If we were to measure the work done by the force used to actually move the eyeball (i.e., \( F_{OT} \)) and the work done by the force necessary to shorten/lengthen the muscles (both computed as the integral of the force over the displacement of the eye/muscles), we would find that the work done to move the eye is only 8% of the total work. The remaining 92% is wasted by the muscles. Similarly, during fixation 23% of the innervation force is transferred to the tendons, while the remaining 77% is used to maintain the muscle length. In other words, the muscles are truly pathetic actuators.

Is there any experimental evidence to support these inferences, and thus to validate Inchingolo's plant model and its analysis? As it turns out, there is plenty. For example, Miller and Robins (1992) have measured, in monkeys, the force delivered at the tendon of extraocular muscles. During saccades this force follows a slide-step profile, as predicted (see Fig. 3.5, left column). Similarly, several studies of extraocular motoneurons in monkeys have shown that, during saccades, these neurons discharge following a pulse-slide-step pattern.
(see Fig. 3.5, right column). Obviously the time constant of the slide in our simulations does not perfectly match the data, but it should be noted that 1) the eye movement is also affected by some drift (possibly due to mechanical alterations induced by the presence of the strain gauge used to measure the force), and 2) this data refers to monkeys while the plant model we used is based on data from human subjects.

There is one important caveat to what we have shown so far: we have casually summed together the force components relative to the muscles and to the orbital tissues. However, this is possible, and thus we can simply talk about a pulse, a slide, and a step, only because we assumed a direct proportionality between muscle length and eye position on one side, and eye velocity and rate of change of muscle length on the other. While this is true (at least to a very good extent) when one pair of muscles is considered, this assumption does not hold when the action of all three pairs of muscles is considered. In that case, which we will address in the next chapter, several problems arise, and the various components must be considered separately.

3.5 Intrinsic Signals

The decomposition of the innervation signal that we have described above, first proposed by Inchingolo, follows from the properties of the eye plant, and thus holds for any movement, regardless of its dynamics or of the innervation pattern. However, it cannot be stressed enough that the only signal that must exist in the brain is the overall innervation command, which is carried by the motoneurons. In contrast, the pulse, slide, and step signals are the result of an artificial decomposition that we have applied to the overall command, and do not need to exist as separate signals in the brain. To indicate this fact, from now on we will refer to these signals with the terms Pulse\textsubscript{X}, Slide\textsubscript{X}, and Step\textsubscript{X}, where the subscript X indicates that these signals are extrinsic to the brain. When needed, we will further divide these signals into their basic components, indicating whether they are associated with the muscles or with the orbital tissues (e.g., Step\textsuperscript{M} or Pulse\textsuperscript{QT}).
Figure 3.5: Force delivered at the tendon and innervation pattern during saccades.

Miller and Robins, 1992
Goldstein, 1983
Having said this, the next question that we need to answer is: what kinds of signals would it make sense to find in the brain? In principle, to generate an eye movement the brain could simply change the innervation signal in a step-wise manner, from its current value to the value needed to keep the eyes in the desired final position. However, we have just shown that the damping induced by the viscous elements of the plant is quite strong. Thus, such a pattern of innervation would induce a slow movement, having an exponential time course. For any movement, at least 600 ms (three times the dominant time constant) would be required to foveate the target. To speed up the movement, the brain must add to this tonic component an initial phasic component, so that at the beginning of the movement the eyes accelerate faster. The problem with this solution is that, if the phasic and the tonic components are not appropriately matched, the eyes will initially move fast (under the influence of the phasic component), but then they will slowly drift toward the equilibrium position that is associated with the tonic component. Again, the time during which the eyes are not stable, and vision is poor, would be fairly large. There is one, and only one, way to avoid such drifts: the phasic and the tonic components must be appropriately matched.

As both the phasic and the tonic components need to be under independent adaptive control (the plant changes through time), the only viable way to guarantee an appropriate matching is to compute these signals separately, and then to sum them together, with adaptable weights, at the level of the motoneurons. Such signals have in fact been found in the brain stem: they are carried by the MLBNs (phasic) and by the neural integrator (tonic) (see Fig. 2.6). However, because they exist as separate signals, it does not mean that they have to be computed independently. In fact, compelling physiological evidence suggests that quite the opposite is true. For example, when saccades are interrupted in mid-flight by stimulation of the omnipause neurons (see Fig. 2.6), the eyes do not drift toward the goal or the initial orientation, as they should if the tonic component were computed based on the initial and/or final eye position, but stay still (Keller 1974). Furthermore, when the phasic component is produced by electrically stimulation of the MLBNs, no target is specified. In this case, the eye displacement is a function of the duration
and intensity of the stimulation; however, when the stimulation is over the eye does not drift but maintains its current orientation (Cohen and Komatsuzaki 1972; Keller 1974; Crawford et al. 1991; Crawford and Vilis 1992). In other words, the tonic component is always appropriate to keep the eyes where they are, even when the phasic component is artificially generated or modified; we infer from this that the tonic component must be calculated dynamically from the phasic component, so that they are always matched [Note that this is certainly not true in pathological conditions (e.g., see Fioravanti et al. 1995)]. But saying that the tonic component of innervation (a signal intrinsic to the brain, which contributes to determining the characteristics of eye movements) is always appropriate to keep the eyes where they are, implies that this signal is always equal to $\text{Step}_X$ (the fraction of the innervation signal needed to compensate the elastic forces in the plant, see above).

Now, if the tonic component is equal to $\text{Step}_X$, it means that the phasic component of innervation must be equal to the sum of $\text{Pulse}_X$ and $\text{Slide}_X$. But as $\text{Pulse}_X$ and $\text{Slide}_X$ have potentially very different adaptation requirements, it would then make perfect sense for the brain to generate internal signals that mirror the decomposition of the overall innervation signal into $\text{Pulse}_X$, $\text{Slide}_X$ and $\text{Step}_X$. Such neural signals could then be simply termed Pulse, Slide, and Step, to indicate that, when they are appropriately matched, they correspond to $\text{Pulse}_X$, $\text{Slide}_X$, and $\text{Step}_X$, respectively. We have already pointed out that the Step is carried by the neural integrator, and we have indicated that the MLBNs carry the phasic component of innervation. In reality, though, the MLBNs carry only the Pulse, as they fire only during the saccade (while the Slide outlasts the movement). Accordingly, some other neurons, currently not identified, must be responsible for generating the Slide component of innervation.

Through this reasoning, we have now defined six signals. Three (Pulse, Slide and Step) are actual neural signals, carried by different populations of neurons, and summed together at the level of the motoneurons to generate the innervation signal. The other three ($\text{Pulse}_X$, $\text{Slide}_X$, and $\text{Step}_X$) are extrinsic signals, which we derive by decomposing the innervation signal into
three components. This decomposition is based on the characteristics of the plant. To efficiently produce accurate movements the brain needs to generate neural signals that match the corresponding extrinsic signal. Accordingly, the brain then needs to solve two problems: generate the appropriate Pulse, and compute the corresponding Slide and Step from it. If either of these steps fails, the internal signals will not match the extrinsic signals, and the resulting movement will be inappropriate (i.e., with the wrong metrics and/or followed by post-saccadic drift).

3.6 What’s Ahead

With these considerations in mind, we can now decompose the saccadic system into two subsystems: the first one is mainly feed-forward, receives as an input the Pulse of innervation, and generates the Slide and Step appropriate to match the ever changing characteristics of the eye plant. As this system needs to be adjusted only as a function of the characteristics of the eye plant, it is not specific to the saccadic system and it can be shared amongst all oculomotor systems. In this sense one could argue that it is not even part of the saccadic system. However, its correct functioning is so crucial to the generation of saccades that it would be difficult not to consider it in a model of the saccadic system. Accordingly, we will outline and address some of the most important problems that make this subsystem more complex than was originally thought.

The second subsystem is the one responsible for generating the Pulse of innervation. This is an even more complex system as, to operate correctly, it needs to integrate information about the location of the target, the current orientation of the eyes, contextual cues, and mechanical properties of the plant. The reason for this complexity is that this system needs to convert its input, which, as noted above, is a desired sensory state, into a motor command, providing, implicitly or explicitly, all the necessary transformations.
Chapter 4

Slide-Step Generation

As noted in the previous chapter, there is sufficient experimental data, and compelling reasons, to support the hypothesis that the brain partitions the task of generating the innervation signal necessary to generate a saccade into the computation of three signals: the Pulse, the Slide and the Step. In this chapter we will model the neural circuitry that is required to generate the Slide and the Step. As we have presented evidence that these two signals are generated from the Pulse of innervation, we will assume that this signal is available. Its generation will be the subject of the following chapter.

In the previous chapter we have already discussed at length how, to produce an appropriate movement, the Slide and the Step must be appropriately matched to the Pulse. We have also noted that, for this to occur, Pulse, Slide, and Step must correspond to the extrinsic signals \( \text{Pulse}_x \), \( \text{Slide}_x \), and \( \text{Step}_x \). Thus, for example, the relationship between Pulse and Step must be the same as the one between the \( \text{Pulse}_x \) and the \( \text{Step}_x \), and to unveil the computations that the brain must carry on to get the Step from the Pulse we only need to find out the relationship between the \( \text{Step}_x \) and the \( \text{Pulse}_x \).

In this chapter we describe these computations, and we show that they are not as simple as it was initially thought. We will also show how, thanks to a clever mechanical solution, Nature has simplified this task, making it more
approachable for the brain. But before getting into all this, we will start by considering the simplified case in which there is only a pair of muscles and the eyes are then able to move only around one axis. This situation was the first considered by modelers, and it represent a good basis to fully understand the general problem described later.

4.1 The Problem in One-Dimension

As noted above, in these conditions the speed of lengthening/shortening of the muscles is directly proportional to the speed of the eye, and the length of the muscles is directly proportional to the position of the eye. In particular, as we always measure the length of the muscles in degrees of eye rotation, the proportionality factor is equal to one in both cases. Thus, the innervation force can be considered as the sum of a $Pulse_X$, proportional to eye speed, a $Slide_X$, proportional to a low pass filtered version of eye speed, and a $Step_X$, proportional to eye position:

$$
\begin{align*}
    Pulse_X(t) &= k_1 \omega(t) \\
    Slide_X(t) &= k_2 \text{LP}[\omega(t)] \\
    Step_X(t) &= k_3 E(t) = k_3 \int \omega(t) dt
\end{align*}
$$

where $\text{LP}[]$ is a shorthand for a low pass filter operator. From this simple considerations it follows that, if a Pulse signal is available, a Slide and a Step appropriately matched to the Pulse can be obtained by carrying out the following computations:

$$
\begin{align*}
    Slide(t) &= K_2 \text{LP}[Pulse(t)] \\
    Step(t) &= K_3 \int Pulse(t) dt
\end{align*}
$$

An appropriate choice of $K_2$ and $K_3$ (based on the characteristics of the plant) then guarantees a perfect match between the three components, and the absence of any post-saccadic drift. When this happens, Pulse, Slide, and Step
4.1. THE PROBLEM IN ONE-DIMENSION

Figure 4.1: Slide-Step generation in one dimension.

correspond to $Pulse_X$, $Slide_X$, and $Step_X$; accordingly, the Pulse correlates well with eye velocity, while the Step correlates well with eye position. It is important to note, though, that this is not true in general: whenever the three components are not matched, the Pulse does not correlate with velocity, and the Step does not correlate with position. For this reason, it is incorrect to say that the Pulse encodes velocity, or that the Step encodes position. It is true though that, regardless of the matching between components, the Step always determines the steady-state position of the eye.

This brief analysis allows us to conclude that, in this simplified case, the Step of innervation can be obtained simply by integrating the Pulse. Similarly, the Slide can be obtained by simply low pass filtering the Pulse. It turns out that it is relatively easy to perform these operations with neural circuits. After all, a neuron is a low pass filter with a fairly low time constant (around 1 ms). Thus, some positive feedback is sufficient to turn it into a low pass filter with a higher time constant. To realize an integrator this concept must be pushed to the extreme (see Fig. 4.1), as an integrator can be seen as a low pass filter with a very high time constant (conversely, a low pass filter can be seen as an
integrator with a large leak). The problem in this case is that, to obtain a
circuit with a high enough time constant (around 20s), the gain of the positive
loop must be very close to 1 (0.99995), thus taking the system very close to
instability. The calibration of this parameter must then be very accurate,
otherwise oscillations would ensue.

This solution has been known for a long time, and has been used in essen-
tially all the models of the saccadic system. The problems start when we try
to extend these concepts to rotations around arbitrary axes (three-dimensional
rotations).

4.2 Does This Work in the General Case?

To extend models of Slide-Step generation from one to three dimensions, sev-
eral problems must be addressed. First, when rotations around arbitrary axes
(all passing through one point fixed in space) are considered, the concept of
position must be replaced by the concept of orientation, which is less intuitive
and more difficult to define mathematically. Second, the concept of velocity
must be replaced by the concept of angular velocity. Third, and most im-
portant, it must be kept in mind that for rotations around arbitrary axes the
derivative of orientation is not angular velocity (Goldstein 1980).

This last property, which applies to any rigid body rotating around a point
fixed in space, is due to the non-commutativity of rotations, which can be
described geometrically as follows: starting from the same initial orientation,
a rotation of a $\alpha$ degrees around an axis $\hat{x}$ followed by a rotation of $\beta$ degrees
around $\hat{y}$ (with $\alpha$, $\beta$, $\hat{x}$, and $\hat{y}$ arbitrary, as long as $\hat{x}$ is not parallel to $\hat{y}$)
does not produce the same final orientation obtained when the order of the
rotations is reversed. For example, in the two panels of Fig. 4.2 a camera,
starting from the same initial orientation (leftmost column), is rotated around
the same pair of axes (arrows in the figure) but in different order; clearly, the
final orientations (rightmost column) are different for the two sequences of
rotations.
Figure 4.2: Non commutativity of rotations. Arrows indicate that the image on the right of each arrow is obtained by rotating by $90^\circ$ the image on the left around an axis collinear with the arrow. The direction of rotation corresponds to the direction in which a right-hand screw advances. **A**: The camera is rotated first around a vertical axis, and then around an horizontal axis. **B**: The order of rotations is reversed. The final orientation is clearly different.
Because rotations around a single axis (i.e., when $\hat{x}$ and $\hat{y}$ are parallel) are commutative, in one dimension eye position is equal to the time integral of eye velocity, and thus it is possible to use a simple integrator to compute the Step from the Pulse (see above). However, because of the non-commutativity of arbitrary rotations, it is logical to conclude that a model that relies on the angular velocity being the derivative of orientation can not be used to control a rotational plant in three dimensions.

Accordingly, Tweed and Vilis (1987) developed a model that uses non-commutative, rotational operators to generate the components of the innervation signals. Subsequently Schnabolk and Raphan (1994a; 1994b) proposed that, in fact, a non-commutative neural system is not needed to control eye movements. Schnabolk and Raphan argued that the non-commutativity of rotations is not relevant because the innervation signals determine muscle torques (which are vectors, and thus commute), not eye orientation.

There is a fundamental difference in the behavior of the two models. The model developed by Tweed and Vilis is the correct extension to three-dimensions of the model proposed by Robinson in one dimension (Robinson 1975a; Zee et al. 1976), because eye orientation and angular velocity are neurally represented by the Step and the Pulse, respectively. This is because this model assumes that the goal of the saccadic system is not only to move the eye from its current to a new orientation, but also to accomplish this as quickly as possible. In particular, any post-saccadic drift is avoided by guaranteeing a Pulse-Step matching. Thus, the Tweed-Vilis model (as well as the Robinson model) focused not only on the steady-state conditions (i.e., after stabilization of eye orientation) but also on the dynamics of the movement used to foveate the target. In contrast, Schnabolk and Raphan concentrated exclusively on the issue of eventually acquiring the target, without making any attempt to make a model that, by achieving a Pulse-Step match, avoids (or minimizes) post-saccadic drifts. In fact, they explicitly stated: "there is of necessity a mismatch between the plant dynamics and the pulse-step driving it" (Schnabolk and Raphan 1994a, Pg. 634). However, as we noted above, there is compelling physiological evidence suggesting that a model that does not ac-
count appropriately for the dynamics of the movement (i.e., that produces movements with large post-saccadic drifts) is not a good approximation of the system implemented by the brain to control saccades. In fact, movements produced by normal subjects (either primates or humans) have very little post-saccadic drift, and when the drift is induced artificially the innervation signals are adaptively modified to reduce the retinal slip (Optican and Miles 1985).

Thus, the fact that a commutative controller is sufficient to guarantee a good steady-state behavior of the system does not imply that the brain can use such a strategy to drive the eye plant, as erroneously concluded by Schnabolk and Raphan. In other words, the Pulse-Slide-Step matching issue can not be ignored. Nevertheless, the need to account for the dynamics of the plant does not necessarily imply that the neural controller must be non-commutative. In fact, a non-commutative controller is necessary only if the computation of Slide and Step from the Pulse, or the computation of the Pulse itself, requires non-commutative operators. To verify whether that is the case, we need to analyze the relationship between Step$_X$, Slide$_X$, and Pulse$_X$.

4.3 Pulse, Slide and Step in 3D

In the one-dimensional case we saw that the Step$_X$ was proportional to the mathematical integral of the Pulse$_X$ of innervation. This was true because, in that limited case, the Pulse$_X$ is proportional to the speed of the eye while the Step$_X$ is proportional to the position of the eye. Similarly, the Slide$_X$ was proportional to the low pass filter of the Pulse$_X$. In 3D things are not so simple, and intuition must yield to a rigorous approach. Moreover, the components associated with orbital tissues and muscles must be kept separate. We then need to compute five signals: two relative to the muscles (Pulse$_X^M$ and Step$_X^M$), and three relative to the orbital tissues (Pulse$_X^{OT}$, Slide$_X^{OT}$, and Step$_X^{OT}$).

If we collapse each pair of muscles into an equivalent ideal muscle (see Fig. 3.2), we can describe the innervation provided to the eye muscles as a 3D
CHAPTER 4. SLIDE-STEP GENERATION

vector (in muscle space):

\[ \vec{I} = [I_1, I_2, I_3]^T \]

The innervation \( \vec{I} \) will produce an innervation force, \( \vec{F}_I \), which is directly proportional (through the innervation/tension ratio \( S \)) to the innervation (except for a slight low pass filter effect that can be safely ignored). Part of this force (the \( \text{Pulse}^M_X \) and the \( \text{Step}^M_X \)) will be dissipated by the muscle, while the rest (\( \text{Pulse}^{OT}_X, \text{Step}^{OT}_X \) and \( \text{Slide}^{OT}_X \)) will be delivered to the tendon. Of course, these forces can also be represented vectorially (again, in muscle space):

\[
\begin{align*}
\vec{\text{Pulse}}^M_X &= [\text{Pulse}^M_{X_1}, \text{Pulse}^M_{X_2}, \text{Pulse}^M_{X_3}]^T \\
\vec{\text{Step}}^M_X &= [\text{Step}^M_{X_1}, \text{Step}^M_{X_2}, \text{Step}^M_{X_3}]^T \\
\vec{\text{Pulse}}^{OT}_X &= [\text{Pulse}^{OT}_{X_1}, \text{Pulse}^{OT}_{X_2}, \text{Pulse}^{OT}_{X_3}]^T \\
\vec{\text{Slide}}^{OT}_X &= [\text{Slide}^{OT}_{X_1}, \text{Slide}^{OT}_{X_2}, \text{Slide}^{OT}_{X_3}]^T \\
\vec{\text{Step}}^{OT}_X &= [\text{Step}^{OT}_{X_1}, \text{Step}^{OT}_{X_2}, \text{Step}^{OT}_{X_3}]^T
\end{align*}
\]

If we now indicate with \( F_{OT_i} \) the force delivered to the tendon by the \( i \)-th pair of muscles, the torque applied by that pair of muscles to the eye globe can be computed by multiplying this force by the axis of action of that pair of muscles (\( \hat{m}_i \), the unit-length vector around which the globe rotates under the action of that pair of muscles, in Cartesian space):

\[
\vec{T}_{OT_i}(t) = F_{OT_i}(t) \cdot \hat{m}_i \tag{4.1}
\]

(the radius of the eye, being a constant, can be assimilated in other constants and ignored). The total torque applied to the globe (in Cartesian space) is then the sum of the three vectors obtained by applying Eq. 4.1 to each pair of
4.3. PULSE, SLIDE AND STEP IN 3D

muscles:

\[ \vec{T}_{OT}(t) = [F_{OT_1}(t) \cdot \hat{m}_1 + F_{OT_2}(t) \cdot \hat{m}_2 + F_{OT_3}(t) \cdot \hat{m}_3] \]

\[ = [\hat{m}_1 \ \hat{m}_2 \ \hat{m}_3] \cdot [F_{OT_1}(t) \ F_{OT_2}(t) \ F_{OT_3}(t)] \]

\[ = \overline{M} \cdot \vec{F}_{OT}(t) \] (4.2)

where \( \overline{M} \) is the so-called muscle matrix, which allows us to move from the muscle space into Cartesian space. As we know that the force delivered to the tendon is equal to the sum of Pulse\(^{QT}\), Slide\(^{QT}\) and Step\(^{QT}\), from Eqs. 4.2 and 3.2 it follows that:

\[ \vec{T}_{OT}(t) = \overline{M} \cdot \left[ \text{Pulse}\(^{QT}\) + \text{Slide}\(^{QT}\) + \text{Step}\(^{QT}\) \right] \]

\[ = \overline{K}_{pl} \cdot \vec{\omega}(t) + \overline{K}_{sl} \cdot LP[\vec{\omega}(t)] + \Phi(t) \overline{K}_{sl} \cdot \hat{n}(t) \] (4.3)

where \( \vec{\omega} \) is the angular velocity of the eye, \( \Phi \) and \( \hat{n} \) describe its orientation using Euler’s angle-axis form, and the various \( \overline{K} \) are constant diagonal matrices defined in Cartesian space. If we assume, as it is reasonable to do, that the orbital tissues are isotropic, the diagonal matrices can be replaced by scalar constants:

\[ \vec{T}_{OT}(t) = K_{pl} \vec{\omega}(t) + K_{sl} \cdot LP[\vec{\omega}(t)] + K_{sl} \Phi(t) \hat{n}(t) \] (4.4)

The advantage of using Euler’s theorem, hinted at above, is now clear, as the passive torque exerted by the orbital tissues can be easily expressed in terms of Euler’s axis-angle. In addition (see Eq. 3.4), the force dissipated by each pair of muscles can be described as

\[ \text{Pulse}^{M}_{X_i}(t) + \text{Step}^{M}_{X_i}(t) = K_{pl} \cdot v_i(t) + K_{sl} \cdot l_i(t) \] (4.5)
where \( v_i \) is the speed of lengthening/shortening of the muscle pair, and \( l_i \) is its differential length (null when the two muscles are in equilibrium). In vectorial form we have that

\[
\overrightarrow{\text{Pulse}}^M_X(t) + \overrightarrow{\text{Step}}^M_X(t) = K_{plM} \cdot \vec{v}(t) + K_{stM} \cdot \vec{l}(t)
\]

where the various \( K \) are constant diagonal matrices defined in muscle space.

If we now assume that all the muscles have the same characteristics, we can replace the diagonal matrices with constants:

\[
\overrightarrow{\text{Pulse}}^M_X(t) + \overrightarrow{\text{Step}}^M_X(t) = K_{plM} \vec{v}(t) + K_{stM} \vec{l}(t)
\]

(4.6)

Finally, as the angular velocity of the eye is determined by the speed imposed on the eyeball by all three pairs of muscles, it is always true that

\[
\vec{\omega}(t) = v_1(t) \cdot \vec{m}_1 + v_2(t) \cdot \vec{m}_2 + v_3(t) \cdot \vec{m}_3
\]

\[
= \overrightarrow{M} \cdot \vec{v}(t)
\]

(4.7)

Now that we have mathematically formalized the problem, we can identify the operations that the brain needs to perform to compute the innervation signal for the three pairs of muscles.

### 4.3.1 Pulse\(_X\) in 3D

We saw previously that in one dimension the Pulse\(_X\) is proportional to the speed of the eye. In 3D we have that (Eq. 4.4):

\[
\overrightarrow{\text{Pulse}}^{\text{OT}}_X(t) = K_{\text{plot}} \overrightarrow{M}^{-1} \cdot \vec{\omega}(t)
\]

\[
= K_{\text{plot}} \vec{v}(t)
\]

(4.8)

Also from Eqs. 4.6 and 4.7 it follows that

\[
\overrightarrow{\text{Pulse}}^M_X(t) = K_{plM} \vec{v}(t)
\]

\[
= K_{plM} \overrightarrow{M}^{-1} \cdot \vec{\omega}(t)
\]

(4.9)
4.3.2 \textit{Step}_X \textbf{in 3D}

From Eq. 4.4 it follows:

\[ \overrightarrow{\text{Step}}_X^{OT}(t) = K_{stot} \overrightarrow{M}^{-1} \cdot \Phi(t) \cdot \hat{n}(t) \]  

(4.10)

Similarly, Eqs. 4.6 and 4.7 imply that

\[ \overrightarrow{\text{Step}}_X^M(t) = K_{stM} \vec{l}(t) \]

\[ = K_{stM} \int_0^t \vec{v}(t) \, dt \]

\[ = K_{stM} \int_0^t \overrightarrow{M}^{-1} \cdot \vec{w}(t) \, dt \]  

(4.11)

4.3.3 \textit{Slide}_X \textbf{in 3D}

From Eqs. 4.4 and 4.7 we conclude that

\[ \overrightarrow{\text{Slide}}_X^{OT}(t) = K_{slot} \overrightarrow{M}^{-1} \cdot LP[\vec{w}(t)] \]

\[ = K_{slot} \overrightarrow{M}^{-1} \cdot LP[\overrightarrow{M} \cdot \vec{v}(t)] \]

(4.12)

4.3.4 The Relationship Between Extrinsic Signals

As done for the one dimensional case, we now need to explore the relationship between the extrinsic signals \textit{Pulse}_X, \textit{Slide}_X, and \textit{Step}_X. Knowing this relationship will enable us to infer what operations the brain needs to carry out to compute Slide and Step from the Pulse of innervation (again, we assume that the appropriate Pulse has already been computed).

From Eqs. 4.8 and 4.9 it follows that

\[ \overrightarrow{\text{Pulse}}_X(t) = (K_{pltot} + K_{pltM}) \overrightarrow{M}^{-1} \cdot \vec{v}(t) \]

\[ = (K_{pltot} + K_{pltM}) \vec{v}(t) \]  

(4.13)
From Eqs. 4.13 and 4.11 it follows that

$$\overrightarrow{\text{Step}}_X^M(t) = \frac{K_{stM}}{K_{ploT} + K_{pIM}} \int_0^t \overrightarrow{Pulse}_X(t) \, dt$$ \hspace{1cm} (4.14)

Thus, the \( \overrightarrow{\text{Step}}_X^M \) is always proportional to the integral of the \( \overrightarrow{Pulse}_X \). Similarly, from Eqs. 4.13 and 4.12 it follows that

$$\overrightarrow{\text{Slide}}_X^{OT}(t) = \frac{K_{stM}}{K_{ploT} + K_{pIM}} \overrightarrow{M}^{-1} \cdot \text{LP}[\overrightarrow{M} \cdot \overrightarrow{Pulse}_X(t)]$$ \hspace{1cm} (4.15)

If we now assume that the axis of action of the muscles do not change as the eye rotates in the orbit, \( \overrightarrow{M} \) can be considered constant, and Eq. 4.15 can be reduced to

$$\overrightarrow{\text{Slide}}_X^{OT}(t) = \frac{K_{stM}}{K_{ploT} + K_{pIM}} \text{LP}[\overrightarrow{Pulse}_X(t)]$$ \hspace{1cm} (4.16)

Thus, in this special case, the \( \overrightarrow{\text{Slide}}_X \) is proportional to the low pass filter of the \( \overrightarrow{Pulse}_X \).

So far then the three dimensional case is the natural extension of the one dimensional case (at least if the muscles are stable in the orbit). Unfortunately this is not true for the \( \overrightarrow{\text{Step}}_X^{OT} \), as it is not proportional to the integral of the \( \overrightarrow{Pulse}_X \). The reason for this discrepancy is that, because of the non-commutativity of rotations (see above), the orientation of the eye is not equal (or even proportional) to the integral of its angular velocity. To quantify the dissimilarity between these two quantities, we can now introduce a new measure \( \Delta \):

$$\Delta = \frac{\| \vec{\omega}(t) - \ddot{\vec{\omega}}(t) \|}{\| \vec{\omega}(t) \|} = \frac{\| \Delta \vec{\omega}(t) \|}{\| \vec{\omega}(t) \|}$$ \hspace{1cm} (4.17)

where

$$\ddot{\vec{\omega}}(t) = \frac{d}{dt}[\Phi(t) \cdot \hat{n}(t)] \hspace{1cm} (4.18)$$
and the operator $\| \cdot \|$ indicates the Euclidean norm of a vector. From Eqs. 4.17 and 4.18 it follows that

$$\Delta \tilde{\omega} = \tilde{\omega} - \frac{d}{dt} (\Phi \cdot \hat{n}) = \tilde{\omega} - \frac{d}{dt} (\Phi) \cdot \hat{n} - \Phi \cdot \frac{d}{dt} [\hat{n}]$$

(time dependency implicit). As Schnabolk and Raphan (1994a) showed, the derivative of $\Phi$ and $\hat{n}$ can be expressed as:

$$\frac{d}{dt} [\Phi] = \tilde{\omega} \cdot \hat{n} = \| \omega \| \cos(\alpha)$$

(4.20)

$$\frac{d}{dt} [\hat{n}] = \frac{\tilde{\omega} \times \hat{n}}{2} + \frac{\hat{n} \times (\tilde{\omega} \times \hat{n})}{2} \cot \left( \frac{\Phi}{2} \right)$$

$$= \frac{\| \tilde{\omega} \| \sin(\alpha)}{2} \hat{x} + \frac{\| \tilde{\omega} \|}{2} \cot \left( \frac{\Phi}{2} \right) (\hat{n} \times \hat{x}) \sin(\alpha)$$

(4.21)

where $\hat{x}$ is a unitary vector parallel to $\tilde{\omega} \times \hat{n}$, and $\alpha$ is the angle between $\tilde{\omega}$ and $\hat{n}$. As it is easy to demonstrate that

$$(\hat{n} \times \hat{x}) \sin(\alpha) = \tilde{\omega} - \cos(\alpha) \hat{n}$$

(4.22)

we can now substitute Eq. 4.22 into Eq. 4.21 and Eqs. 4.20 and 4.21 into Eq. 4.19 to conclude that

$$\Delta \tilde{\omega} = \| \tilde{\omega} \| \left[ (1 - H) \tilde{\omega} - (1 - H) \cos(\alpha) \hat{n} - \frac{\Phi}{2} \sin(\alpha) \hat{x} \right]$$

(4.23)

where

$$H = \frac{\Phi}{2} \cot \left( \frac{\Phi}{2} \right)$$

(4.24)

Now, because the norm of a vector is equal to the square root of the dot product of the vector by itself, and given that

$$\tilde{\omega} \cdot \hat{n} = \cos(\alpha)$$

$$\hat{n} \cdot \hat{x} = 0$$

$$\tilde{\omega} \cdot \hat{x} = 0$$

(4.25)
Figure 4.3: $\Delta$ plotted as a function of eye eccentricity. The case when the angular velocity is orthogonal to the orientation (worst case scenario) is plotted.

It follows that

$$\Delta = \frac{\|\Delta \omega(t)\|}{\|\omega(t)\|} = |\sin(\alpha)| \sqrt{(1 - H)^2 + \left(\frac{\Phi}{2}\right)^2}$$

which can be approximated to

$$\Delta \approx |\sin(\alpha)| \frac{\Phi}{2}$$ (4.27)

Thus, the relative difference between the angular velocity and the derivative of orientation increases almost linearly with the eccentricity $\Phi$, and it is a function of the angle between orientation and angular velocity. This equation reveals that, as $\Delta$ is not a constant, an integrator with a fixed gain can not be used to compute orientation from angular velocity. This is possible only when rotations around one axis are considered, as in that case $\alpha$ is equal to zero and $\Delta$ is always null. Eq. 4.27 conveys an important message: because the $\text{Step}_{X}^{QT}$
is not proportional to the integral of the $\overrightarrow{\text{Pulse}}_x$, if the brain were to compute the fraction of the Step associated with the orbital tissues by integrating the Pulse, a post-saccadic drift would occur. Note however that the fraction of the Step that is used to maintain the desired muscle length, could be obtained simply by integrating the Pulse.

Of course, saying that post-saccadic drifts would arise is not enough without a quantitative analysis of the magnitude of such drift. After all, if the drift were very small the system could simply tolerate it, and use an integrator to compute both parts of the Step from the Pulse. Unfortunately, such quantification is far from trivial. This is because, as noted above, as soon as a mismatch ensues none of the intrinsic signals (Pulse, Slide and Step) matches the corresponding extrinsic signals. Consequently, $\Delta$ can not be used to quantify the effect of a mismatch (as soon as there is a mismatch, the Pulse is not equal to the $\overrightarrow{\text{Pulse}}_x$, and thus it is not proportional to angular velocity). The only viable solution is then to use simulations. In doing this knowing $\Delta$ is very helpful, as it allows us to identify, and test, the worst case scenario: $\alpha = 90^\circ$ and large eccentricity $\Phi$ (see Fig. 4.3).

4.4 Modeling the Eye Plant in 3-D

Ultimately, the goal of a model of the eye plant is to compute the instantaneous orientation and angular velocity of the eyeball as a function of the innervation provided to the six extraocular muscles. In the previous section we have demonstrated that the forces involved in the control of the eye are a function of the muscle matrix, the length and speed of lengthening/shortening of the muscles, the orientation and angular velocity of the eye, as well as of intrinsic properties of the muscles and orbital tissues. Because of the complex relationship between these parameters, it would be very hard to extract the closed-form differential equations that describe the instantaneous eye velocity as a function of the innervation signal. Instead, it is much easier to find the instantaneous eye velocity iteratively by changing it until the overall sum of active and passive forces is zero (which is required by D’Alambert’s theorem).
Accordingly, we have decided to go down this path, and we have used the following algorithm to simulate the movements of the eye:

1. Define the desired rotation
2. Define the initial orientation \((\Phi, \hat{n})(0)\)
3. Define the innervation vector \(\vec{I}(t)\)
4. Compute the vector of muscle length \(\vec{l}(t)\) associated with the current orientation
5. Compute the muscle matrix \(\overline{M}\)
6. Compute the innervation force \(F_I(t)\)
7. Guess the angular velocity \(\vec{\omega}(t)\) (Initial guess: \(\vec{\omega}(t) = \vec{\omega}(t - \Delta t)\))
8. Compute the corresponding rate of muscle length change \(\vec{v}(t)\)
9. Compute the passive torque exerted by the orbital tissues \(\vec{T}_{OT}(t)\)
10. Compute the force dissipated by the muscles
11. Compute the torque delivered to the tendon by the muscles
12. Compare this torque to \(\vec{T}_{OT}(t)\). If they are not equal, go back to step 7
13. As \(\vec{\omega}(t)\) has been correctly guessed, the orientation \((\Phi, \hat{n})(t + \Delta t)\) can now be computed (assuming \(\vec{\omega}\) constant between \(t\) and \(t + \Delta t\))
14. Go back to step 4

In the previous sections we have already seen how steps 6, 8, 9, 10, and 11 can be carried out. Now we will present a solution for steps 4, 5, and 13.
4.4.1 Muscle Matrix

To realistically simulate the operation of the eye plant, it is crucial to determine, for each orientation of the eyes, the axes of action $\hat{m}_i$ of the six extraocular muscles. These are the unitary vectors around which each muscle tends to rotate the eye, and thus determine how the force exerted by each muscle is converted into a torque applied to the globe. If we assume that the center of the eyeball is stable in the orbit (which is a reasonable approximation), the computation of these vectors is fairly simple. In fact, each vector $\hat{m}_i$ must be orthogonal to the plane that contains the vector $\vec{g}_i$ that goes from the center of the globe to the muscle insertion on the globe, and the vector $\vec{\sigma}_i$ that goes from the center of the globe to the muscle’s origin. Computing $\hat{m}_i$ is then a simple matter:

$$\hat{m}_i = \frac{\vec{\sigma}_i \times \vec{g}_i}{||\vec{\sigma}_i \times \vec{g}_i||}$$  \hspace{1cm} (4.28)

where $\times$ indicates the cross product operator.

Because the muscles operate as agonist-antagonist pairs, and we are interested in modeling the differential innervation, things can be slightly simplified by considering the axis of action of each pair of muscles. This can be defined as the average of the axes of action of the muscles in the pair. We then find that, in primary position, the axes of action for the right human eye (see Table 4.1) are:

$$\begin{align*}
m_h &= - 0.9998 \ x - 0.0157 \ y + 0.0091 \ z \\
m_v &= - 0.0826 \ x - 0.4401 \ y - 0.8942 \ z \\
m_o &= - 0.1409 \ x - 0.7859 \ y + 0.6020 \ z
\end{align*}$$ \hspace{1cm} (4.29)

with the $x$ axis pointing up, the $y$ axis pointing ahead, and the $z$ axis pointing to the left.
### Table 4.1: Orbital geometry (all measures in millimeters) of a right human eye. From Miller and Robinson (1984).

Of course, as the eye moves in the orbit these axes can change, because the insertion point moves with the eye, and thus its location relative to the center of the globe changes as a function of eye orientation. This implies that, to make an accurate simulation of an eye movement we need to recalculate these axes at each orbital position. If we describe the orientation of the eye using the axis-angle form that follows from Euler’s Theorem (see Section 2.1), the location of the muscle insertion points can be obtained simply by multiplying the matrix of rotation $\overline{R}(\Phi, \hat{n})$ by the coordinates of the insertion point with the eye in primary position (it is implicit that we are using the primary position as the reference orientation for the Euler’s axes):

$$\begin{bmatrix} g'_x \\ g'_y \\ g'_z \end{bmatrix} = \overline{R}(\Phi, \hat{n}) \cdot \begin{bmatrix} g_x \\ g_y \\ g_z \end{bmatrix}$$ (4.30)

where

$$\overline{R}(\Phi, \hat{n}) = 
\begin{bmatrix}
  n_z (1 - \cos \Phi) + \cos \Phi & n_x n_y (1 - \cos \Phi) - n_z \sin \Phi & n_x n_z (1 - \cos \Phi) + n_y \sin \Phi \\
  n_x n_y (1 - \cos \Phi) + n_z \sin \Phi & n_z (1 - \cos \Phi) + \cos \Phi & n_y n_z (1 - \cos \Phi) - n_x \sin \Phi \\
  n_x n_z (1 - \cos \Phi) - n_y \sin \Phi & n_y n_z (1 - \cos \Phi) + n_x \sin \Phi & n_z^2 (1 - \cos \Phi) + \cos \Phi
\end{bmatrix}$$ (4.31)
4.4.2 Orbital Dynamics

The next step required to perform a simulation of the eye plant, is to determine the relationship between the instantaneous angular velocity of the eye and the change in orientation it produces. As noted above, the latter is not simply the integral of the former, as would be the case for translational systems. For a rotational system, the equations that describe the change (i.e., the derivative) of orientation as a function of angular velocity are the following:

\[
\frac{d \Phi}{dt} = \vec{\omega} \cdot \hat{n}
\]

and

\[
\frac{d \hat{n}}{dt} = \frac{\vec{\omega} \times \hat{n}}{2} + \frac{\hat{n} \times (\vec{\omega} \times \hat{n})}{2} \cdot \cot \left( \frac{\Phi}{2} \right)
\]

As we are interested in performing a discrete-time simulation, these equations could be discretized to compute, given \( \vec{\omega} \) and the current orientation, the orientation at the next simulation step. However, it turns out that it is simpler and more robust (i.e., larger simulation steps can be used) to update instead the rotation matrix \( R(\Phi, \hat{n}) \) using the finite rotation formula (Goldstein 1980). In fact, if we define an incremental rotation vector

\[
\hat{n}_{inc} = \frac{\vec{\omega}}{\|\vec{\omega}\|}
\]

and an incremental eccentricity

\[
\Phi_{inc} = \|\vec{\omega}\| \Delta t
\]

we can then compute an incremental rotation matrix \( R_{inc}(\Phi_{inc}, \hat{n}_{inc}) \), using the same rotation matrix formula previously described (Eq. 4.31). The updated rotation matrix is then

\[
R(t + \Delta t) = R_{inc}(t) \cdot R(t)
\]
Euler’s axis and angle can then be extracted from the rotation matrix using the Euler-Rodriguez relationships:

\[
\begin{bmatrix}
    n_1 \\
    n_2 \\
    n_3
\end{bmatrix} = \begin{bmatrix}
    \frac{R_{32} - R_{23}}{\sin \Phi} \\
    \frac{R_{13} - R_{31}}{\sin \Phi} \\
    \frac{R_{21} - R_{12}}{\sin \Phi}
\end{bmatrix}
\]

\[
\Phi = \arccos \left[ \frac{\text{Trace}(R) - 1}{2} \right]
\]

### 4.4.3 Muscles’ length

The final parameter that we need to compute to accurately simulate eye rotations is the length of each of the extraocular muscles. This is a more complex problem, as the muscles do not go from the origin point to the insertion on the globe in a straight line. Instead, they roll around the globe from the insertion point to a point of tangency; from there they go straight to the origin (as we will see later on, this is not entirely true). To compute the length of the muscles, we then need to first find the point of tangency. This can be defined as the point of tangency between the eye globe and the straight line \( r \) that is tangent to the eyeball, passes through the origin \( P_o \) and lies on the plane \( \pi \) that contains the origin point, the insertion point, and the center of the globe (the so-called muscle plane). \( r \) can be defined as the intersection of the plane \( \pi \) with the star of planes \( \pi_s \) going through \( P_o \). If we now approximate the globe as a perfect sphere \( \Sigma \), the problem can be expressed in terms of the following equations:

\[
\Sigma: \quad x^2 + y^2 + z^2 = r_E^2
\]
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\[ \pi : \ ax + by + cz = 0 \]

\[ P_o = \begin{bmatrix} x_o \\ y_o \\ z_o \end{bmatrix} \]

\[ \pi_s : \ a_1 (x - x_o) + b_1 (y - y_o) + c_1 (z - z_o) = 0 \]

where \( r_E \) represents the eye radius (12.43 mm in humans) and the expression for \( \pi \) takes into account the fact that the plane goes through the center of the coordinate system (i.e., the center of the globe). If we now define

\[ d_1 = -(a_1 x_o + b_1 y_o + c_1 z_o) \]

\( \pi_s \) can be described as

\[ \pi_s : \ a_1 x + b_1 y + c_1 z + d_1 = 0 \]

The intersection between \( \pi \) and \( \pi_s \) can be solved pairing their equations:

\[
\begin{align*}
ax + by + cz &= 0 \\
ax_1 + by_1 + cz_1 + d_1 &= 0
\end{align*}
\]

Using Cramer's rule to solve these equations as a function of \( x \), we obtain:

\[
\begin{align*}
y &= \frac{-a c_1 x + c a_1 x + c d_1}{b c_1 - c b_1} \\
z &= \frac{-b a_1 x + a b_1 x - b d_1}{b c_1 - c b_1}
\end{align*}
\]
If we now convert this system of equations into parametric form, we can express the intersection between the planes as:

\[
\rho : \quad t \begin{bmatrix} 1 \\ \frac{c a_1 - a c_1}{b c_1 - c b_1} \\ \frac{a b_1 - b a_1}{b c_1 - c b_1} \end{bmatrix} + \begin{bmatrix} x_o \\ y_o \\ z_o \end{bmatrix} = t \mathbf{v} + P_o
\]

As we are interested in the line tangent to the sphere, we can add the constraint that the distance between \( \rho \) and the center of the sphere must be equal to the radius of the sphere. In formulas:

\[
d(0, \rho) = \frac{|(0 - P_o) \times \mathbf{v}|}{|\mathbf{v}|}
\]

\[
= \frac{\left| \begin{array}{c} a_1 (y_o b + z_o c) - b_1 y_o a - c_1 z_o a \\ b c_1 - c b_1 \\ a_1 x_o b - b_1 x_o a \\ b c_1 - c b_1 \\ c_1 x_o a - a_1 x_o c \\ b c_1 - c b_1 \end{array} \right|}{\sqrt{1 + \left( \frac{c a_1 - a c_1}{b c_1 - c b_1} \right)^2 + \left( \frac{a b_1 - b a_1}{b c_1 - c b_1} \right)^2}} = \tau_E
\]

As the plane \( \pi \) goes through the center of the sphere \( \Sigma \), it is an equatorial plane, and thus the plane \( \pi_s \) must be orthogonal to it. This implies that

\[
a a_1 + b b_1 + c c_1 = 0
\]
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Assuming that \( c \) is not equal to zero (this can always be guaranteed by temporarily swapping the axes), we can then express \( c_1 \) as:

\[
c_1 = -\frac{a a_1 + b b_1}{c}
\]  

(4.33)

Finally, if we impose \( a_1 = 1 \) (which can always be done), we obtain the following second-order equation for \( b_1 \):

\[
K_1 b_1^2 - 2 K_2 b_1 + K_3 = 0
\]

(4.34)

where

\[
K_1 = x_o^2 \left( a^2 + \frac{a_2 b_2}{c^2} \right) + y_o^2 \left( a^2 + c^2 + \frac{b_4}{c^2} + 2 b_2 \right) + z_o^2 \left( c^2 + \frac{a_2 b_2}{c^2} + \frac{b_4}{c^2} + 2 b_2 \right) - r_E^2 \left( a^2 + c^2 + \frac{a_2 b_2}{c^2} + \frac{b_4}{c^2} + 2 b_2 \right) - y_o z_o \left( \frac{2 b a^2}{c} \right) + x_o y_o \left( \frac{2 a b^3}{c^2} + 2 a b \right) + x_o z_o \left( 2 a c + \frac{2 a b^2}{c} \right)
\]

\[
K_2 = -x_o^2 \frac{a^3 b}{c^2} - y_o^2 \frac{a b^3}{c^2} - z_o^2 \left( \frac{a^3 b}{c^2} + \frac{a b^3}{c^2} + 2 a b \right) + r_E^2 \left( a b + \frac{a_3 b}{c^2} + \frac{a b^3}{c^2} \right) + y_o z_o \left( a c - \frac{a b^2}{c} + \frac{a^3}{c} \right) - x_o y_o \left( a^2 + b^2 + c^2 + 2 \right) + 2 \frac{a^2 b^2}{c^2} + x_o z_o \left( b c + \frac{b^3}{c} - \frac{a^2 b}{c} \right)
\]

\[
K_3 = x_o^2 \left( 2 a^2 + b^2 + c^2 + \frac{a^4}{c^2} \right) + y_o^2 \left( b^2 + \frac{a^2 b^2}{c^2} \right) + z_o^2 \left( 2 a^2 + c^2 + \frac{a^4}{c^2} + \frac{a^2 b^2}{c^2} \right) - r_E^2 \left( 2 a^2 + b^2 + c^2 + \frac{a^4}{c^2} + \frac{a^2 b^2}{c^2} \right) + y_o z_o \left( 2 b c + \frac{2 a^2 b}{c} \right) + x_o y_o \left( \frac{2 a^3 b}{c^2} + 2 a b \right) - x_o z_o \left( \frac{2 a b^2}{c} \right)
\]

Equation 4.34 obviously has two solutions, as there are two lines that lie on \( \pi \), go through \( P_o \), and are tangent to \( \Sigma \). It is our responsibility to pick the correct
one. To compute the tangent point we can then consider the intersection between this line and the plane \( \pi_2 \) orthogonal to it and containing the center of the sphere. This plane can be described as:

\[
\pi_2 : \quad x + \left( \frac{ca_1 - ac_1}{bc_1 - cb_1} \right) y + \left( \frac{ab_1 - ba_1}{bc_1 - cb_1} \right) z = 0
\]

Thus, the point of tangency is:

\[
P_t = t \left[ \begin{array}{c}
1 \\
\frac{ca_1 - ac_1}{bc_1 - cb_1} \\
\frac{ab_1 - ba_1}{bc_1 - cb_1}
\end{array} \right] + \begin{bmatrix}
x_o \\
y_o \\
z_o
\end{bmatrix} = tv + P_o
\]

(4.35)

where \( t \) is

\[
t = -\frac{x_o + \left( \frac{ca_1 - ac_1}{bc_1 - cb_1} \right) y_o + \left( \frac{ab_1 - ba_1}{bc_1 - cb_1} \right) z_o}{1 + \left( \frac{ca_1 - ac_1}{bc_1 - cb_1} \right)^2 + \left( \frac{ab_1 - ba_1}{bc_1 - cb_1} \right)^2}
\]

4.4.4 Simplifications

Now that we have found a way to compute all these parameters, we could simulate the eye movements produced by any pattern of innervation. However, as we are interested mainly in understanding how the non-commutativity of rotations affects the Slide-Step generation process, we think that some small alterations to the plant model would considerably aid our efforts. More precisely, if we make the plant symmetric by having the three muscle pairs act in orthogonal planes (at least when the eye is in primary position), it would become much easier to compare the movements produced with our expectations. For example, we could slightly displace the origin and insertion of the extraocular muscles so that, in primary position, the horizontal recti rotate the eyes
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<table>
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<tr>
<th>Parameter</th>
<th>LR</th>
<th>MR</th>
<th>SR</th>
<th>IR</th>
<th>SO</th>
<th>IO</th>
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</thead>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>$o_x$</td>
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<tr>
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</tr>
<tr>
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<td></td>
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<td>-10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$g_y$</td>
<td>7.5</td>
<td>7.5</td>
<td>7.38</td>
<td>7.38</td>
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</tr>
<tr>
<td>$g_z$</td>
<td>-9.91</td>
<td>9.91</td>
<td>0</td>
<td>0</td>
<td>-12.43</td>
<td>-12.43</td>
</tr>
</tbody>
</table>

Table 4.2: Orbital geometry (all measures in millimeters) of our symmetric plant model.

around a purely vertical axis, the vertical recti rotate the eyes around a purely horizontal axis, and the obliques rotate the eyes around the torsional axis. Under these conditions, if rotations were commutative we would expect that simply providing innervation to only the horizontal and vertical recti would be sufficient to ensure that the eye orientation stays in Listing’s Plane. Thus, we have designed a symmetric eye plant (see Table 4.2), which we will use for all our simulations.

4.4.5 Simulations

The goal of these simulations is to find out how large the post-saccadic drifts would be if we were to use a commutative controller to generate the innervation signals provided to the extraocular muscles. As noted above, the portion of the step of innervation that is needed to compensate the passive torque exerted by the orbital tissues, $Step_{X}^{OT}$, is not equal to the mathematical integral of the pulse of innervation. And the measure $\Delta$ tells us that the difference between these two signals gets larger as the eccentricity increases and as the angle between orientation and angular velocity increases. To evaluate the effects of
this difference in a realistic setting, we could then think of moving the eyes first 30° up and 30° to the right, and then from there 60° to the left. We chose this sequence of movements for several reasons: first of all, the Δ measure indicates that they should theoretically induce the largest drifts; second, they are realistic, as they are within the human oculomotor range; and third, there is experimental data available that shows how human subjects perform this task (Tweed et al. 1994). More precisely, it is known that when humans make the second movement, the eyes essentially stay in Listing’s Plane, with only a small transient deviation out of it (see Fig. 4.4), and there is not much drift around the other two axes. So the question that we now need to answer is whether a commutative controller would be able to generate the innervation signal needed to produce such movements like human subjects do.

Before showing that simulation we need to validate our model and approach by showing that, when Δ is null, no mismatch occurs, and thus the movement is not followed by post-saccadic drifts. In Fig. 4.5 we simulate a 30° rightward movement starting from the primary position. In this case α (the angle between
Figure 4.5: Simulation of 30° rightward movement induced by driving our symmetric eye plant model with a commutative innervation signal.
eye velocity and eye orientation) is zero throughout the movement, and so is $\Delta$; thus no mismatch should occur. And this is exactly what happens. Thus, in these conditions it is true that a commutative controller is sufficient to generate appropriate patterns of innervation.

However, when we simulate the off-axis sequence of movements previously described (Fig. 4.6), the result we obtain is considerably different from the movements produced by human subjects. The first thing that we note is that there is a very large torsional movement (dashed line). Second, even the horizontal and vertical components (gray and black lines, respectively) are characterized by drifts and bumps. Third, and most surprising, both after the first and after the second movement, the eyes tend to stabilize to an orientation in which the torsion is not null. In other words, the eyes land outside of Listing's Plane and do not simply go out of it transiently like humans do.

To understand why and how these movements are affected by such undesired properties, we must first note that, in our symmetric plant, the center of the globe and the origin of the horizontal/vertical recti lie on the torsional axis. Consequently, the axes of action of these muscles cannot have a torsional component, and thus they must lie in Listing's Plane. With this consideration in mind, it is now fairly simple to understand the cause of the large torsional movement occurring during the second saccade, which we fully expected. In fact, because during this saccade the angular velocity is confined to Listing's Plane (as only the horizontal and vertical recti receive a pulse of innervation), the orientation of the eyes must exit this plane. In contrast, if we wanted to confine the orientation into Listing's Plane, we would need to induce an angular velocity vector that stays outside of Listing's Plane. More precisely, this vector should be tipped backwards by an angle equal to half of the eccentricity. This follows from the well known half-angle rule, which has been shown to be respected during eye movements (Tweed and Vilis 1988). Thus, if we wanted to avoid these drifts we would have to rotate the eye around an axis that is not in Listing's Plane. But it is not possible to actively induce such a rotation without innervating the oblique muscles.

On the basis of these consideration one would expect the eyes to go outside
Figure 4.6: Simulation of a movement induced by driving our symmetric eye plant model with a commutative innervation signal. Note that the oblique muscles receive no innervation.
Listing's Plane transiently, and then to drift back into it. After all, if the horizontal and vertical recti generate a torque in Listing's Plane, and the oblique muscles are not innervated, why should the equilibrium orientation of the eye lie outside Listing's Plane? This is a question that puzzled us considerably at first, as we did not expect this behavior. Actually, we do not know of any study that ever suggested or predicted this kind of behavior. However, a close inspection of the system revealed that the cause of this behavior is not that mysterious after all. We have shown before that the equilibrium is reached when the active torque delivered by the tendons of the eye muscles counteracts the passive forces exerted by the orbital tissues. And it is true that for any orientation in Listing's Plane the torque exerted by the orbital tissues has no torsional component. However, this does not mean that for any orientation in Listing's Plane the oblique muscles exert no torque on the globe, even when they are not innervated. This is clear if we recall (see Eq. 4.11) that, in steady state, the force delivered by a muscle to its tendon (which, when its innervation is null, is the opposite of the force absorbed by the muscle) is a function of the length of the muscle. So, the only situation in which a pair of non-innervated muscles does not exert any torque is if the length of the two muscles in the pair is the same (so that their passive tension cancels out). As the reader might now guess, this condition does not hold true for all orientations in Listing's Plane, because the length of the oblique muscles varies as a function of the horizontal and vertical orientation of the eye. This point can be made more clearly by plotting the length difference between the superior and inferior oblique for all the possible eye orientations in Listing's Plane (see Fig. 4.7). Clearly, the difference in length can be quite large, up to 15° at the limit of the oculomotor range. And when this length difference is not null, the eye will rotate, in the torsional plane, until the torque exerted by the orbital tissues compensates the muscular torque due to the muscle length difference. When this equilibrium is reached, the length difference will be somewhat smaller, but the eye orientation will be outside Listing's Plane. And this is why in our simulations the eye drifts towards orientations that do not belong to Listing's Plane.

From these considerations it appears clear that it is simply impossible to keep the eyes in Listing's Plane while providing no innervation to the oblique
4.4. MODELING THE EYE PLANT IN 3-D

Figure 4.7: Difference between the length of the inferior oblique and superior oblique muscles for orientations in Listing's Plane. The length difference is expressed in degrees of eye rotation.
Figure 4.8: Simulation of a movement induced by adding some torsional components to the innervation signal used in the previous simulation.
muscles. This holds true not only during the saccades, when, because of the non-commutativity of rotations, we expected it, but also during periods of fixation, when the brain must generate a tonic innervation signal that compensates the oblique muscles' length difference corresponding to the desired orientation. This last task could be simply accomplished by also generating for each saccade an appropriate torsional movement. In Fig. 4.8 we show one such example. Here we have simply generated 3-D innervation signals appropriate to produce the desired 2-D movement and to ensure that, at least in steady state, the eye orientation is in Listing's Plane. Unfortunately, this adjustment does not solve all the problems. First of all, as the torsional component of the movement is also a saccade, during the first movement the pulse of innervation delivered to the oblique muscles causes the eyes to transiently go out of Listing's Plane. By doing so we have actively induced a post-saccadic drift in the torsional plane. Furthermore, the large torsional blip during the second movement is still there, even though its magnitude is now reduced.

We could try to fix the first problem by assuming that the torsional system under-estimates the torsional viscosity of the eye plant. For example, in Fig. 4.9 we show what happens when the size of the torsional pulse is reduced by a factor of four. Clearly the torsional transient occurring during the first movement is reduced, but the one occurring during the second movement is enhanced. In other words, with this kind of solution we would improve matters in some situations, and make them worse in others. Furthermore, the disturbances on the horizontal and vertical position traces are always present, and do not seem to be affected by these adjustments.

From these simulations of the plant model we can draw the following conclusion: it is simply not possible to use a commutative neural controller to generate the innervation signal necessary to appropriately drive the plant model here presented. Does this hold true for the saccadic system? As we will demonstrate in the next section, it does not.
CHAPTER 4. SLIDE-STEP GENERATION

Figure 4.9: Same simulation as above, but with smaller torsional pulses.
4.5 EXTRAOCULAR PULLEYS

4.5 Extraocular Pulleys

The plant model that we have presented in the previous chapter has one major flaw: it assumes that the extraocular muscles can move freely within the orbit. However, Miller, Demer, and colleagues (Miller et al. 1993; Miller and Demer 1994; Demer et al. 1995; Demer et al. 1996; Clark et al. 1997; Demer et al. 1997; Miller and Demer 1997; Clark et al. 1998; Clark et al. 1999; Clark et al. 2000; Demer 2000; Demer et al. 2000) have demonstrated beyond doubt that the path of the muscles does not change from the origin point to some point behind the insertion point; from there the muscles go straight to the insertion point. This intermediate point corresponds to the location of orbital tissues that act on the muscles as pulleys, constraining their movements. As Miller and coworkers (Miller, et al. 1993) pointed out "orbital mechanics is fundamentally different under a pulley model. Here, the axis of rotation is determined by the center of rotation, the effective location of the pulley, and the anatomic insertion. Unlike the conventional model, the pulley model predicts that gaze movements out of the muscle plane will cause the axis of rotation to tilt with the globe".

Accordingly, we have added to our model of the eye plant four extraocular pulleys, one for each rectus muscle. The location of the pulleys has been inferred from experimental measurements (Clark, et al. 2000), again with small adjustments to enforce symmetry (see Table 4.3). In addition, we have also allowed the pulleys to move backward and forward with their corresponding muscle, in accordance with Demer's active pulley hypothesis (Demer 2000). As no definitive data is available at this moment, we have used an estimate of the magnitude of this pulley movement (6 mm over 28° of eye rotation) kindly provided to us by J.L. Demer (personal communication). The rest of the model is then identical, as the only change required is to consider the pulleys as the point of origin of the muscles.
### Table 4.3: Location of the extraocular pulleys (all measures in millimeters) with the eye in primary position for an human eye plant and for our symmetric plant model.

<table>
<thead>
<tr>
<th>Plant</th>
<th>LR</th>
<th>MR</th>
<th>SR</th>
<th>IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Plant</td>
<td>-0.3</td>
<td>-0.3</td>
<td>11.8</td>
<td>-12.9</td>
</tr>
<tr>
<td></td>
<td>-9</td>
<td>-3</td>
<td>-7</td>
<td>-6</td>
</tr>
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<td></td>
<td>-10.1</td>
<td>-14.2</td>
<td>1.7</td>
<td>4.3</td>
</tr>
<tr>
<td>Symmetric Plant Model</td>
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<td>0</td>
<td>13</td>
<td>-13</td>
</tr>
<tr>
<td></td>
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<td>-6</td>
<td>-6</td>
</tr>
<tr>
<td></td>
<td>-14</td>
<td>14</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

4.5.1 Simulations

We will now illustrate the results of simulations of the same movements that we tried to generate with the model without pulleys. In Fig. 4.10 we simulate a 30° rightward movement starting from the primary position. As before, the movement is perfect, and it does not show any post-saccadic drift or anomalies. Also, deviations around the other axes are absent. The only point worth noting is that, because the movement of the pulleys induces a slight change in muscle length, to avoid a slight post-saccadic drift we had to reduce the neural estimate of the plant stiffness from \(2.06 \text{ g/deg} \) to \(2.01 \text{ g/deg}\).

When we simulate the sequence of large movements the we used earlier, relatively large rotations around the torsional axis are still present (see Fig. 4.11), and the steady-state orientations are still outside of Listing's Plane. However, this is to be expected, as the presence of the pulleys does not change the fact that the length of the two oblique muscles is not the same for different orientations in Listing's Plane. In fact, if we plot the length difference of the obliques muscles, we find a pattern of deviation virtually identical to the one observed without pulleys. Nonetheless, there are two considerable improvements in this simulation: first of all, the torsional deviations are smaller. Second, and more important, there are virtually no bumps, anomalies or sizeable drifts around
Figure 4.10: Simulation of 30° rightward movement induced by driving our eye plant with active pulleys model with a commutative innervation signal.
Figure 4.11: Simulation of a movement induced by driving our eye plant with pulleys model with a commutative innervation signal. The obliques receive no innervation.
4.5. EXTRAOCULAR PULLEYS

the horizontal and vertical axes.

Similarly to what we have done before, we can now try to fix the steady-state orientation by adding some innervation to the oblique muscles. When we do so (see Fig. 4.12) we note immediately that the pulse of innervation to the oblique muscles is too strong. If we reduce it by a factor of four (see Fig. 4.13) the torsional blips become much smaller (around $4^\circ$ for the second movement). Note also that the already small drifts around the horizontal and vertical axes are now completely gone. If we now look back at the performance of human subjects (see Fig. 4.4), we find that during that saccade there is a small blip in the torsional trace. It is definitely smaller (around $2^\circ$) than the one produced in our simulations (around $4^\circ$), but the speed of the movement is also considerably lower. It is also worth noting that this blip does not arise because of the non-commutativity of rotations, but it is determined by the passive characteristics of the muscles; if the muscles were ideal, so that they would not exert any tension in absence of innervation, this blip would not occur at all.

We have verified that this behavior holds for various movement directions and eye orientations, and it is thus not just specific to the movements we have simulated here. Therefore, we can safely conclude that the presence of the pulleys reduces considerably the drifts and the blips due to the non-commutativity of rotations, making a commutative saccadic generator sufficient to produce eye movements that can serve vision appropriately.

4.5.2 Pulleys’ Action

Although we have shown with simulations that the presence of the pulleys somehow solves the non-commutativity related problems, a mathematical demonstration of this process would almost certainly yield deeper insights. Unfortunately, we already pointed out how it would be extremely difficult to address this problem mathematically, and that is why we used simulations in the first place. However, this does not mean that we can not try to address a simplified version of the problem. In particular, if we consider the pulleys’ role, we see that their major effect is to change the axes of action of the muscles
Figure 4.12: Simulation of a movement induced by adding some torsional components to the innervation signal used in the previous simulation.
Figure 4.13: Same simulation as above, but with smaller torsional pulses.
as a function of the orientation of the eyes. In a first order approximation, we could then simply hypothesize that the pulleys make the axes of action of the muscles rotate around the axis of rotation \( \hat{n} \) by a fraction \( K_\Phi \) of the angle of rotation \( \Phi \).

Under this hypothesis, the muscle matrix \( \overrightarrow{M} \) is then equal to the product of the rotation matrix \( \overrightarrow{R}(K_\Phi \Phi, \hat{n}) \) by the muscle matrix in primary position \( \overrightarrow{M}_0 \). If we now look back at Eqs. 4.8, 4.9 and 4.10 we see that while the Pulse is proportional to the product of the inverse of the muscle matrix by the eye velocity, the fraction of the Step relative to the orbital tissues is proportional to the product of the inverse muscle matrix by Euler’s vector of orientation:

\[
\overrightarrow{\text{Pulse}}_X(t) = K_p \overrightarrow{M}(t)^{-1} \cdot \overrightarrow{\omega}(t)
\] (4.36)

\[
\overrightarrow{\text{Step}}^{\text{OT}}_X(t) = K_s \overrightarrow{M}(t)^{-1} \cdot \Phi(t) \cdot \hat{n}(t)
\] (4.37)

If we now define \( \delta = K_\Phi \Phi \), recall the following properties of rotation matrices (\( \alpha \) and \( \hat{n} \) generic)

\[
\begin{cases}
\overrightarrow{R}(\alpha, \hat{n}) \cdot \hat{n} = \hat{n} \\
\overrightarrow{R}(\alpha, \hat{n})^{-1} = \overrightarrow{R}(\alpha, \hat{n})^T = \overrightarrow{R}(-\alpha, \hat{n})
\end{cases}
\] (4.38)

and assume that in primary position the muscle matrix is equal to the identity matrix (as is the case in our symmetric model, and thus in all the simulations presented above), Eqs. 4.36 and 4.37 are equivalent to:

\[
\overrightarrow{\text{Pulse}}_X(t) = K_p \overrightarrow{R}(\delta(t), \hat{n}(t))^T \cdot \overrightarrow{\omega}(t)
\] (4.39)

\[
\overrightarrow{\text{Step}}^{\text{OT}}_X(t) = K_s \cdot \Phi(t) \cdot \hat{n}(t)
\] (4.40)

To try to quantify the amount of mismatch that would arise if the Step were computed by integrating the Pulse, we can now compute again the measure
4.5. EXTRAOCULAR PULLEYS

\[ \Delta, \text{this time defined as the difference between the Pulse and the derivative of the Step:} \]

\[ \Delta = \frac{\| \overline{R}(\delta(t), \hat{n}(t))^T \cdot \vec{w}(t) - \frac{d}{dt} [\Phi(t) \cdot \hat{n}(t)] \|}{\| \overline{R}(\delta(t), \hat{n}(t))^T \cdot \vec{w}(t) \|} \] (4.41)

As \( \Delta \) is defined as the ratio of the magnitude of two vectors, any transformation that does not change the ratio can be applied to the two vectors without affecting the result. In particular, pre-multiplying a vector by a rotation matrix does not change its magnitude. Thus, we can redefine \( \Delta \) as follows (time dependencies implicit):

\[ \Delta = \frac{\| \vec{w} - \overline{R}(\delta, \hat{n}) \frac{d}{dt} [\Phi \cdot \hat{n}] \|}{\| \vec{w} \|} = \frac{\| \Delta \vec{w} \|}{\| \vec{w} \|} \] (4.42)

where

\[ \Delta \vec{w} = \vec{w} - \overline{R}(\delta, \hat{n}) \cdot \frac{d}{dt} [\Phi] \cdot \hat{n} - \overline{R}(\delta, \hat{n}) \cdot \Phi \cdot \frac{d}{dt} [\hat{n}] \] (4.43)

From the properties above described (Eq. 4.38) it now follows that

\[ \Delta \vec{w} = \vec{w} - \frac{d}{dt} [\Phi] \cdot \hat{n} - \overline{R}(\delta, \hat{n}) \cdot \Phi \cdot \frac{d}{dt} [\hat{n}] \] (4.44)

From Eq. 4.31 it also follows that

\[ \overline{R}(\delta, \hat{n}) = \]

\[ \begin{bmatrix}
    n_z^2(1-\cos \delta)+\cos \delta & n_x n_y (1-\cos \delta)-n_z \sin \delta & n_x n_z (1-\cos \delta)+n_y \sin \delta \\
    n_x n_y (1-\cos \delta)+n_z \sin \delta & n_z^2(1-\cos \delta)+\cos \delta & n_y n_z (1-\cos \delta)-n_z \sin \delta \\
    n_x n_z (1-\cos \delta)-n_y \sin \delta & n_y n_z (1-\cos \delta)+n_x \sin \delta & n_z^2(1-\cos \delta)+\cos \delta
\end{bmatrix} \] (4.45)
which can be decomposed as

\[
\overline{R}(\delta, \hat{n}) = \cos(\delta) \cdot I_d + [1 - \cos(\delta)] \cdot \begin{bmatrix}
  n_x^2 & n_x n_y & n_x n_z \\
  n_x n_y & n_y^2 & n_y n_z \\
  n_x n_z & n_y n_z & n_z^2
\end{bmatrix} + \\
+ \sin \delta \cdot \begin{bmatrix}
  0 & -n_z & n_y \\
  n_z & 0 & -n_x \\
  -n_y & n_x & 0
\end{bmatrix}
\]

(4.46)

where \( I_d \) is the 3 x 3 identity matrix.

This decomposed form becomes very useful when the product of the matrix \( \overline{R} \) by a vector is considered. In fact, from Eq. 4.46, it follows that

\[
\overline{R}(\delta, \hat{n}) \cdot \vec{v} = \cos(\delta) \vec{v} + [1 - \cos(\delta)] (\vec{v} \cdot \hat{n}) \cdot \hat{n} + \sin \delta \hat{n} \times \vec{v}
\]

(4.47)

where \( \vec{v} \) is a generic vector. By using Eqs. 4.20, 4.21, 4.22, 4.44, and 4.47, it is easy to show that

\[
\Delta \vec{\omega} = ||\vec{\omega}|| \left\{ \left[ 1 - H \cos(\delta) - \frac{\Phi}{2} \sin(\delta) \right] \vec{\omega} - \\
- \left[ \frac{\Phi}{2} \cos(\delta) - H \sin(\delta) \right] \sin(\alpha) \hat{x} - \\
- \left[ 1 - H + [1 - \cos(\delta)] H - \frac{\Phi}{2} \sin(\delta) \right] \cos(\alpha) \hat{n} \right\}
\]

(4.48)

with \( H \) defined in Eq. 4.24. From the relationships described in Eq. 4.25 and Eq. 4.48 it finally follows that

\[
\Delta = |\sin(\alpha)| \sqrt{(1 - H)^2 + \left( \frac{\Phi}{2} \right)^2 + 2 H [1 - \cos(\delta)] - \Phi \sin(\delta)}
\]

(4.49)
4.5. EXTRAOCULAR PULLEYS

Figure 4.14: \( \Delta \) plotted as a function of eye eccentricity considering the effect of the pulleys. Five values of \( K_\Phi \) are used, each corresponding to different locations of the pulleys. The case when the angular velocity is orthogonal to the orientation (worst case scenario) is plotted.

In Fig. 4.14 we plot the value of \( \Delta \) when \( \alpha \) is equal to 90°, as we did in Fig. 4.3. We plot several curves, showing the value of \( \Delta \) for different values of \( K_\Phi \) (0, 0.25, 0.5, 0.75, and 1). It appears clear from Fig. 4.14 (and it can be easily verified by setting the derivative of \( \Delta \) to 0) that the optimal value of \( K_\Phi \) is 0.5. If the pulleys are located so as to produce a 50% muscular slip (\( K_\Phi = 0.5 \)), the value of \( \Delta \) always stays below 0.025. This means (see above) that the overall mismatch will always be smaller than 2.5%, regardless of the movement. This is in fact what one would have expected from the half-angle rule (see above).

This simplified mathematical approach allows us to conclude that a proper placement of the pulleys turns the integral of the Pulse into a very good approximation of orientation. This statement is apparently at odds with the fact that rotations do not commute, and thus the integral of angular velocity is not orientation. In fact, both statements are true, and this is possible simply
because in the pulley model the Pulse does not correlate with angular velocity. Instead, the Pulse vector is proportional to the angular velocity vector $\vec{\omega}$ rotated by $-\delta$ degrees around the orientation axis $\hat{n}$ (see Eq. 4.39); and we have shown that the integral of this Pulse signal (but not of the angular velocity) is a very good approximation of the eye orientation.

This concept is elucidated graphically in Fig. 4.15, where the direction of the Pulse (green dotted line) and the direction of the angular velocity (red dashed line) are indicated. Suppose that the Pulse vector is colinear with the vertical axis (i.e., in our symmetric model the Pulse is applied to the horizontal recti only). Now, because of the presence of the pulleys, the pulling direction of the horizontal recti changes as a function of the elevation of the eye. When the eye is in primary position (panel A), the axis of rotation of the horizontal recti is vertical, and thus the Pulse and angular velocity coincide. In contrast, when the eye is elevated (panel B) the axis of rotation of the muscles is tilted back, and the angular rotation vector (which is always colinear with the axis of rotation) does not coincide with the Pulse. Thus, the Pulse does not always correlate with angular velocity, and its integral can encode orientation. The fact that $\Delta$ is small indicates that the Pulse of innervation is actually close to the derivative of orientation. Consequently, the pulley model can be considered, to a very good approximation, as a mechanical implementation of the linear plant model proposed by Tweed and coworkers (1994; 1997b); the principal difference is that we have made explicit here the mechanism that underlies the effect of the plant on the neural signals. Furthermore, this finding supports and gives larger significance to other studies that modeled the Pulse as the derivative of eye orientation (Crawford 1994; Crawford 1997; Crawford and Guitton 1997).

To conclude that this is indeed the effect of the pulleys, we now need to show that the actual location of the pulleys is well approximated by our mathematical model when $K_\Phi$ is close to 0.5. It comes as no surprise that the asymmetry of the arrangement of the three pairs of muscle (even in our modified plant) makes it impossible to find a value of $K_\Phi$ that perfectly fits the actual mechanical model for all possible orientations of the eye. Nonetheless, if
Figure 4.15: Schematic representation of the effect of the pulleys. A Pulse of innervation is provided to the horizontal recti alone. When the eye is in primary position (panel A), the angular velocity is colinear with the Pulse. However, when the eye is elevated (panel B), the same Pulse will make the eye rotate around a different axis.
we consider only orientations in Listing's Plane, and we limit our observations to the effects of the pulleys on the axes of action of the horizontal and vertical recti, we find that a value of $K_\Phi$ of 0.61 represents a reasonable approximation of the pulleys' action. This value being different from 0.5 justifies the small drifts observed in our simulations; yet the value is low enough to guarantee that the magnitude of the drifts due to the non-commutativity of rotations is behaviorally acceptable.

The role that we propose here for the pulleys can be further tested by verifying the strongest prediction of the pulley model, i.e., that the Pulse of innervation is closer to the derivative of orientation than to the eye angular velocity. To verify this prediction, recordings in the medium lead burst neurons (i.e., the neurons that carry the Pulse) during movements from secondary to tertiary positions are necessary. Because of the relatively large span of burst-neurons' on-direction, to have a good estimate of the signal they carry it is important to average over a fairly large population of neurons (Quaia and Optican 1997). Although the results of such an experiment have not been published yet, it has been reported (van Opstal et al. 1996, Pg. 7294) that: "recordings from both the riMLF and the oculomotor nucleus so far indicate that saccade-related burst activity is better correlated with the rate-of-change of 3-D eye position than with eye angular velocity (our unpublished observation)". As similar activity was recorded in both burst and motor neurons, the only place left to perform the needed conversion of the Pulse into angular velocity is the plant. Accordingly, these preliminary observations strongly support the model proposed here, as well as all the studies in which it has been proposed that the Pulse encodes the derivative of eye orientation (again, this is not true in the mathematical sense, but their difference, $\Delta$, is very small).

It is important to note that, for the pulleys to exert the required action, not only they must be properly placed (between the equator and the posterior pole of the globe), but, as the eye turns, they must also move. More precisely, as a muscle contracts the corresponding pulley must be pulled backwards, so that the distance between the location of the pulley and the insertion point of the muscle on the globe is approximately constant. This is the kind of behavior
that was found by Demer and colleagues with high-resolution MRI studies of the human orbit (Demer, et al. 2000), and that we included in our model of the plant (see above). The mechanism proposed to achieve such a dynamic relocation of the pulleys turns out to be quite simple, albeit surprising. It has been known for a long time that the fibers that make up each extraocular muscle can be histologically differentiated into two groups: the global fibers and the orbital fibers (Leigh and Zee 1999). It turns out that while the global fibers of the rectus muscles go through the pulley and insert anterior to the globe equator, the orbital fibers insert directly on the pulley (Demer, et al. 2000), and never reach the tendon. Thus, if the whole muscle is contracted, part of the tension will be delivered to the globe, and part will be delivered to the pulley itself, moving it as required.

4.5.3 Implications for the saccadic system

The results we have presented in this chapter have two main implications for the saccadic system. First of all, there is no need to employ non-commutative operators to generate the Step and the Slide from the Pulse of innervation. An integrator and a low pass filter do just fine. Second, to keep the eyes in Listing’s Plane at all times we need to provide to the oblique muscles an appropriate innervation, which is a function of the desired orientation of the eyes. If the innervation signal is so generated, the extraocular pulleys take care of the conversion of the Pulse into the appropriate angular velocity signal. Thus, while the presence of the pulleys makes it easier for the saccadic system, and for the oculomotor system in general, to produce eye movements with the correct dynamics, it is not sufficient to guarantee either the absence of drifts or the obedience to Listing’s Law, and it certainly does not represent a mechanical implementation of Listing’s Law.

Nonetheless, the presence of the pulleys considerably simplifies the neural implementation of the saccadic generator. In fact, without pulleys the brain would need to use non-commutative operators to generate the Step and the Slide from the Pulse (requiring the accurate multiplication of two fast-changing
neural signals, certainly not an easy task). In contrast, thanks to the pulleys, all that is needed is the conversion of the retinal error (a 2-D signal) into the appropriate 3-D innervation. But this can be implemented very easily with an associative memory that has access to both the retinal error and the current orientation of the eyes. As we will show in the next chapter, the cerebellum appears to be perfectly suited to carry out this task. It must also be kept in mind, that this operation is required regardless of the presence of the pulleys, and it can be easily combined with the sensorimotor transformation between the retinal location of a target and the eye rotation required to foveate it, which is also a function of the orientation of the eyes (Crawford 1997; Crawford and Guitton 1997; Klier and Crawford 1998).

The presence of the pulleys also has implications for other oculomotor systems, and for the treatment of strabismus, but we have addressed those issues elsewhere (Quaia and Optican 1998).
Chapter 5

Pulse Generation

In this chapter we describe in detail our model of the pulse generator. To provide a general idea of the role that the various areas play in the overall picture, we first outline the structure of the model. To avoid any misunderstanding, we stress that all the connections and patterns of activity described hereafter refer to our model, and we will indicate, by means of citations to the relevant literature, when they are supported by experimental findings. Similarly, when we make assertions relative to the role played by brain areas in controlling saccades we refer to our model of the saccadic system, not to the saccadic system itself, even when this is not explicitly stated.

5.1 Overall Structure

As noted above, in designing this model we gave primary significance to the patterns of saccade-related activity recorded from single cells in the SC, in the cerebellum (especially the fastigial nuclei, which contain the cerebellar neurons that project to the brain stem saccadic circuitry) and in the brain stem. Using many of the known anatomical connections between these different areas, we have created a model in which the metric and dynamic characteris-
Figure 5.1: Overview of model structure. There are two major pathways, one through the superior colliculus (SC) and the other through the cerebellum. Solid lines for excitatory signals; dashed lines for inhibitory signals.
tics of saccades are determined by the cooperation of two parallel pathways (Fig. 5.1). The first pathway (collicular pathway) involves the cerebral cortex (which provides the target location in retinotopic coordinates), the SC, the premotor medium-lead burst neurons (MLBNs) [which are divided into excitatory (EBN) and inhibitory (IBN) burst neurons] and the motoneurons (MNs) that innervate the extraocular muscles. The core structure of this pathway is the SC, which plays two roles: first, it determines the onset of the saccade, by releasing the excitation provided to the omnipause neurons (OPNs) which tonically inhibit (gate) the MLBNs in between saccades. Second, it drives the eyes toward the target. Thus, this pathway provides a veto signal and what we call a directional drive.

The second pathway (cerebellar pathway) involves the cerebral cortex, the SC (which just relays the target information), the cerebellum (vermis lobules VIc and VII and FOR), MLBNs and MNs. The cerebellum, which is the central structure of this second pathway, plays three roles: (1) it provides an additional directional drive, (2) it monitors the progress of the saccade toward the target (acting as a displacement integrator, DI), adjusting its output to compensate for directional errors, and, when the eyes approach the target, (3) it chokes off the drive provided by these two pathways to the motoneurons, ending the saccade. Thus, this pathway also provides two signals to the brain stem circuitry: a directional drive and a choke signal.

As will become clear further on, there is a fundamental difference in our model between the collicular and the cerebellar drives: whereas the first cannot change direction during a saccade (i.e., the ratio between the horizontal and vertical components of the collicular drive is fixed throughout the movement), the second is adjustable in direction.

5.2 Brain Stem circuitry

As the brain stem network that we use in our model is supported by a great deal of experimental evidence, and is essentially identical to that used in several
other models, we have described it in section 2.3.2 of the Background chapter (see also Fig. 2.6).

5.3 Superior Colliculus

5.3.1 Inputs to Burst Neurons

We have modeled four inputs to the collicular burst neurons: the first input comes from the frontal eye fields (FEF), and it encodes the location of the target for the impending saccade in retinotopic coordinates (saccadic command) by providing a topographically organized excitatory input to the SC. Each input fiber discharges maximally for one target vector; its discharge decreases following a Gaussian function as the direction of the target vector deviates from the preferred vector, and following a log-Gaussian function as its amplitude deviates from the preferred vector. This is in agreement with recordings from movement cells in FEF (Bruce and Goldberg 1985). The width of the FEF movement fields is larger than that of collicular burst neurons, and we assume that they are narrowed by intra-collicular on-center-off-surround connections (Grossberg 1973; Grossberg 1988), which determine the size of the burst neurons movement fields. Similarly, we modeled the temporal characteristics of this signal as being less brisk than those of the collicular burst neurons; in particular, the FEF activity rises earlier compared to saccade onset, the activation outlasts the saccadic movement, and the activity does not decay much during the saccade (Fig. 5.2A). Such characteristics are compatible with recordings from cortico-tectal neurons in FEF (Segraves and Park 1993), which probably are the movement cells studied by Bruce and Goldberg (1985).

The second input to the burst neurons (fixation command) is provided by the collicular fixation neurons, which provide inhibition until just before saccade onset, when they turn off allowing the burst neurons to start discharging (Fig. 5.2B). These neurons are then reactivated around the end of the saccade. This is compatible with recordings in the rostral pole of the SC (Munoz and Wurtz 1993a; Everling et al. 1998). The relative weight of these first two
5.3. SUPERIOR COLLICULUS

Figure 5.2: Schematic of the temporal characteristics of the inputs to model collicular burst neurons. **A:** Cortical saccadic command. **B:** Collicular fixation command. **C:** Feedback inhibition input. **D:** Output of collicular burst neurons.
inputs determines, in our model, the onset of the burst neurons discharge, and thus the latency of the movement.

The third input to the burst neurons encodes, in a relatively sloppy way, the magnitude of the displacement since the beginning of the saccade. This signal, which we call feedback inhibition, inhibits the burst neurons, thus determining the observed decay of activity as a function of dynamic motor error (Fig. 5.2C); as we will explain below, it does not need to be particularly accurate. Such an extra-collicular signal is necessary in our model to reproduce the results of Keller and Edelman (1994) and Waitzman et al. (1991), but there is no direct experimental evidence for (or against) the existence of such a feedback inhibition signal.

The fourth and final input to the collicular burst neurons also comes from the cortex, but, because it is weak and has minimal effect on the burst neurons' discharge, we will describe it later. For now it suffices to say that this fourth input is the source of the early activity observed in buildup cells. It will be made clear below why we propose that the burst neurons receive this input as well.

### 5.3.2 Activity of SC Burst Neurons

We modeled the output of the burst neurons as a burst of activity that starts just before the beginning of the saccade and is almost over by the end of the saccade (Fig. 5.2D). Thus, in our model the burst neurons are only partially clipped, i.e., the neurons are still active at the end of the movement, even though at a fairly low level (approximately 20% of maximum activation). The choice of keeping this residual activity at the end of the movement is due to the experimental finding that, even though some burst cells are clipped (i.e., their activity is over by saccade end), most burst cells (probably as many as 70%) are only partially clipped (Waitzman, et al. 1991; Munoz and Wurtz 1995a). The presence of unclipped activity is not a problem because, as stated above, in our model the collicular output does not encode dynamic motor error, which has to be zero at the end of the saccade. In fact, later on it will become
clear that the presence of unclipped activity is an indispensable feature of the
model.

It is important to point out that the spatial characteristics of the first three
inputs described above (which essentially determine the activity of burst neu-
rons, because the fourth input is very weak) are not under feedback control
and, except for noise-related variations, do not change during a saccade. Con-
sequently, in our scheme the activity in the burst layer maintains its spatial
distribution throughout the saccade, and it is modulated only in intensity by
feedback signals. Accordingly, only the magnitude of the output of the burst
cells changes during the saccade, and thus in our model the purposeful curva-
ture of saccades (which reflects a feedback-driven directional control) can not
be due to this collicular output.

5.3.3 Outputs of Burst Neurons

In our model the burst cells excite the contralateral MLBNs (both EBNs and
IBNs) (see Chimoto et al. 1996), with weights that are a function of the
position of the cell on the collicular map (caudal sites have stronger projec-
tions than rostral sites), as originally proposed by Edwards and Henkel (1978).
Cells in the lateral and medial part of the SC project preferentially to verti-
cal MLBNs, whereas cells along the central meridian project preferentially to
horizontal MLBNs (see Grantyn et al. 1997). However, the input provided by
the SC to the MLBNs is a directional drive signal and no spatial-to-temporal
transformation (see section 2.4.1) is performed. Thus, the input provided to
the MLBNs by the SC can be the same even if two different collicular loci are
activated at different levels (e.g., a 20° locus weakly activated compared with
a 10° locus strongly activated). In contrast, by definition the output of an
STT must always be different when different loci are activated, regardless of
the level of activity (see Fig. 2.11).

Thus, in our scheme the SC burst cells provide a signal that only drives
the eyes approximately in the right direction. The direction of the movement
is determined by the latero-medial location of the collicular site activated,
whereas its speed depends upon (but is not strictly encoded by) the level of activation of the burst neurons and the rostro-caudal location of the active site. This last aspect is in agreement with results from single unit recordings (Berthoz et al. 1986), collicular lesions (Hikosaka and Wurtz 1985; Hikosaka and Wurtz 1986; Lee et al. 1988; Aizawa and Wurtz 1998; Quaia, et al. 1998a), and electrical stimulation of the SC (Paré, et al. 1994; Stanford, et al. 1996).

In our model the burst neurons also provide a topographically organized input to the NRTP and to the pontine nuclei (see Thielert and Thier 1993), which in turn project heavily to the cerebellum. As we will describe below, we propose that the function of these projections is to relay to the cerebellum information regarding the target location, retaining the spatial code and thus avoiding the need for an STT. Finally, the burst neurons inhibit the fixation neurons, thus helping to keep them off during the saccade.

### 5.3.4 Inputs to Buildup Neurons

In our model the second cortical input to the SC, which we call the saccadic plan input and briefly introduced in the previous section, is the source of the early activation and of the rostral spread of activity in buildup neurons. We call this signal the saccadic plan because it indicates the presence and location of an area of interest in the visual scene. Any such location is a potential target for a saccade, but a saccade to it is not necessarily generated. In our model this signal starts exciting buildup neurons soon after the target has been designated, and is characterized by a perisaccadic spread (i.e., a particular input fiber is activated later for larger saccades in one direction). Recordings from lateral intraparietal cortex (LIP) neurons projecting to the SC (Paré and Wurtz 1997) revealed the presence of a signal that could be compatible with these requirements. Actually, because of the breadth of the cortical movement fields, there is no need for the input to spread: all that is needed is a step-like remapping of the target from its initial eccentric position to a foveal position (Fig. 5.3, left column). In Fig. 5.3 (right column) we show the effect of such a remapping of the saccadic plan input on collicular buildup neurons (this
Figure 5.3: Schematic outlining the effect of a cortical predictive remapping of the saccadic plan input on the activity of collicular neurons. Note that this figure does not account for the other inputs to collicular neurons, which were shown in Fig. 5.2.
Figure 5.4: Pattern of activation of collicular neurons. Spatial distribution of activity is shown at different times before and during an horizontal saccade (saccade onset = 0 ms, duration = 60 ms). Only the activity in the area of the SC corresponding to horizontal targets/saccades is shown. The activity of fixation neurons is shown around the vertical line indicating the rostral pole of the SC.
must not be confused with the actual pattern of activation of buildup neurons, shown in Fig. 5.4, which is also determined by other inputs). If the cortical activity is remapped from the locus corresponding to the position of the target to the foveal zone, starting approximately 80 ms before saccade onset, the effect on collicular buildup neurons is a pattern of activation that resembles a spread of activity toward the rostral pole of the SC. One characteristic of this spread/remapping is that, in order to start before saccade onset (see section 2.4.1), it must be predictive, and can not depend on feedback information regarding an on-going movement. The presence of such a signal is supported by the findings of predictive target remapping in LIP by Goldberg and colleagues (Goldberg and Bruce 1990; Goldberg et al. 1990; Duhamel et al. 1992; Quaia et al. 1998b). The onset of such remapping (80 ms before saccade onset) is consistent with the timing of the spread observed in the SC. It should also be noted that such remapping has been reported in Frontal Eye Fields only in visual neurons (Umeno and Goldberg 1997), and not in movement neurons, which in our model carry the saccadic command input to the SC (and thus can not show remapping).

Besides the saccadic plan input, in our model the buildup neurons receive three other inputs, described in a previous section: the saccadic command, the fixation command and the feedback inhibition (Fig. 5.2).

5.3.5 Activity of the Buildup Neurons

In Fig. 5.4 we show how, in our scheme, the spatial distribution of neuronal activity across the SC changes before and during the movement. Here the case of a horizontal saccade having a duration of approximately 60 ms is illustrated. As already pointed out, only the burst neurons around the optimal vector are activated during a saccade (Fig. 5.4, left column). The activation starts just before, and it peaks around, saccade onset (see also Fig. 5.2D); no change in the spatial distribution of the activity occurs. The fixation neurons (Fig. 5.4, right column, rostral neurons) are inactive during the saccade and are otherwise firing tonically (see also Fig. 5.2B). Buildup neurons are instead characterized
by the superposition of the burst and of the input described in Fig. 5.3, which produces a pattern of activation that resembles a rostrally directed spread of activity.

It is important to note that because, in our model, feedback information controls the strength of the burst input but not the spread (or remapping) of activity toward the rostral pole, the buildup neurons can not contribute to the goal-directed curvature of saccades (i.e., even if there is a change in spatial distribution, it does not depend on the trajectory of the eyes and thus is not part of a trajectory control mechanism).

5.3.6 Outputs of the Buildup Neurons

In our scheme the buildup neurons project to the same recipients as the burst neurons. Thus they provide an excitatory input to MLBNs (directional drive), an inhibitory input to the collicular fixation neurons, and topographically organized inputs to NRTP and pontine nuclei. Thus, we propose that, as far as movement execution is concerned, buildup neurons are not functionally different from burst neurons.

5.3.7 Fixation Neurons

In our model the fixation neurons receive five inputs: an excitatory visual input from targets on the fovea, an excitatory input that is related to the desire to keep the eyes steady (active fixation), an excitatory input from the caudal fastigial nucleus, an inhibitory input from the ipsilateral caudal SC (burst and buildup neurons), and an excitatory input from the contralateral rostral pole of the SC. Several investigators have provided experimental evidence that supports this scheme (e.g., May et al. 1990; Munoz and Wurtz 1993a; Munoz and Istvan 1998).

The role of the fixation neurons is to provide a veto signal for the saccade. They carry out this role by turning off just before the beginning of each saccade, thus reducing the excitatory input of the OPNs, and allowing the MLBNs to
turn on and start the saccade. The role of this gate circuitry is twofold: first, it stabilizes the circuit during periods of fixation, avoiding the onset of oscillations. Second, the presence of a gating mechanism allows the collicular signal to rise to its maximum just before saccade onset, thus providing the MLBNs with the strongest possible drive, which in turn results in the maximum acceleration of the eyes.

Furthermore, in our scheme the fixation neurons are reactivated after the end of the saccade to help maintain fixation. As we will show later on, by means of simulations, the diminished activation of the burst neurons and the increased overall activation of the FOR at the end of the saccade is sufficient to induce a timely reactivation of the fixation neurons.

In our model the fixation neurons project to both the OPNs and to the collicular burst/buildup neurons; both these connections are supported by experimental evidence (Büttner-Ennever and Horn 1994; Paré and Guitton 1994; Gandhi and Keller 1997; Munoz and Istvan 1998). It must be noted that, because the activity of the fixation neurons is influenced by the activity of burst and buildup neurons, the onset time of the saccade is not under direct voluntary control (even though it is possible to voluntarily prevent the execution of a saccade).

5.3.8 Difference Between Burst and Buildup Neurons

Physiological recordings indicate that the early activity observed in collicular neurons can vary, in the same cell, from a significant level to essentially zero activity, depending upon the experimental conditions, such as likelihood of appearance of a target in the response field or initial eye position (Paré and Munoz 1996; Basso and Wurtz 1997; Dorris et al. 1997). Thus, if, as we propose here, this same low level component confers to the buildup neurons their open-movement field characteristics, the same neuron could be classified as burst or buildup depending upon the conditions under which it is observed.

To account for these observations, in our model burst and buildup neurons share the same inputs and constitute a single class of neurons. Neurons that
Figure 5.5: Classification of collicular neurons.
5.3. **SUPERIOR COLLICULUS**

receive a strong cortical saccadic command show a strong burst of activity, whereas neurons for which that input is weaker produce a smaller burst, or no burst at all. Similarly, the stronger the cortical saccadic plan input, the larger the buildup (Fig. 5.5). The characteristics of individual neurons, which form a continuum, are then just the result of the different relative contribution of the four inputs shown in Fig. 5.5. What we call burst and buildup neurons are then just the extremes of this continuum. However, this does not mean that they cannot play different roles for other aspects of eye movements, like target selection (Optican 1994), learning of consistent maps for different modalities (Grossberg, et al. 1997) and determination of reaction time (Dorris, et al. 1997).

**5.3.9 Collicular Inhibitory Connections**

It must be noted (see Fig. 5.5) that in our scheme the inhibition from the fixation neurons acts on the saccadic command input at the dendritic level, shunting that signal, and not (or only weakly) on the soma of the burst/buildup neurons. This arrangement allows our buildup neurons to be active long before the saccade (when the fixation neurons are active) and to have a burst closely synchronized with the saccade. Such connections have not been shown experimentally, but under these conditions it should be possible to find a frequency of stimulation in the fixation zone that would prevent the occurrence of the burst but not the early activity in the buildup cells. Lower frequencies would not be sufficient to prevent the occurrence of the burst, and higher frequencies might also inhibit the early activity if a fraction of the inhibition acts at the level of the soma. In fact, such a finding has been recently reported (Munoz and Istvan 1998).

The same consideration holds for the intra-collicular excitation-inhibition that narrows the movement field of the collicular burst; in our scheme these connections directly shunt the burst input, otherwise it would not be possible to have a narrow movement field for the burst and a large movement field for the buildup. Finally, for the same reasons, in our scheme the feedback
inhibition also acts at the dendritic level (Fig. 5.5).

An alternative scheme (Optican 1994; Grossberg et al. 1997) posits that only the buildup neurons receive the saccadic plan input, and that the burst neurons generate the burst from the buildup activity using a winner-take-all network. The burst is then imposed on the buildup neurons by the burst neurons and there is resonant feedback between the two layers. In these schemes inhibition from the fixation neurons is provided only to the burst neurons, and can be applied directly to the soma. Currently, no experimental evidence conclusively differentiates between these two schemes. Nonetheless, both schemes are compatible with the rest of our model, and in particular with the function exerted by the cerebellum in controlling saccades.

5.4 Cerebellum

5.4.1 Inputs

To keep track of how far the eyes have turned since the beginning of the saccade, the cerebellum needs accurate information about eye movements. In our model the cerebellum obtains this information by monitoring the output of the MLBNs (i.e., velocity efference copy). In support of this hypothesis bilateral projections from regions containing MLBNs to the cerebellum have been reported (Yamada and Noda 1987; Noda, et al. 1990; Thielert and Thier 1993), and MLBN-like activity has been recorded in mossy fibers (Kase et al. 1980; Ohtsuka and Noda 1992). However, in one study no direct projections from the MLBNs to the cerebellum have been reported (Strassman et al. 1986a; Strassman et al. 1986b), thus an alternative would be to extract the velocity signal from the burst-tonic signal provided (presumably by the nucleus prepositus hypoglossi) to the cerebellum, which has also been documented (Kase, et al. 1980).

The signals just described enable the cerebellum to act as a displacement integrator (DI, Fig. 5.1); however, to generate the choke signal at the appro-
appropriate time, the cerebellum also needs to know the desired amplitude of the movement. In our scheme this information is not directly available to the cerebellum, but it is computed by the vermis using several inputs. The first piece of information needed is the target location, which is spatially encoded in the NRTP (Crandall and Keller 1985). We propose that this area sends topographically organized projections to the cerebellum. In support of this hypothesis, recordings in mossy fibers (Strassman et al. 1986a; Strassman et al. 1986b) revealed the presence of signals similar to those reported by Crandall and Keller in NRTP. Alternatively such signals could be provided by the pontine nuclei, and more precisely by the dorsomedial pontine nuclei (DMPN), which receive strong projections from the FEF and project heavily to the cerebellum (Noda, et al. 1990). In addition, the cerebellum needs information about the speed of the target, the current eye position, and various contextual information to determine the displacement of the eyes needed to foveate the target. We propose that all this information is available to the vermis, and that it uses an associative network to extract the desired displacement.

As we will describe in detail below, we propose that the cerebellum uses these two signals (eye velocity and desired displacement) to keep track of the residual motor error, enabling it to issue the choke signal at the appropriate time.

5.4.2 Activity

The discharge characteristics of fastigial neurons have played a significant role in guiding our modeling effort. In our model each fastigial neuron produces an early burst for saccades in one direction (having a contralateral horizontal component), and a late burst for saccades in the opposite direction. The early burst occurring in the contralateral FOR provides, through crossing connections from the FOR to the MLBNs, an additional directional drive. Thus, the sum of the FOR and the collicular inputs to MLBNs determines the initial direction and speed of the saccade (Fig. 5.6). However, because of the relatively mild effects on initial acceleration of muscimol injections in the FOR
Figure 5.6: Contributions to the overall saccadic drive (Pulse).
(Robinson, et al. 1993), we posit that, at the very beginning of the saccade, the cerebellar contribution to the overall directional drive is not very intense (approximately 20-30% of the total drive). Accordingly, in our model the collicular pathway is stronger than the cerebellar pathway.

In contrast to the early burst observed for saccades in the preferred direction, a late burst is produced in correspondence with saccades in the opposite direction. This burst occurs later and later for larger and larger saccades (see Ohtsuka and Noda 1990; Ohtsuka and Noda 1991; Fuchs, et al. 1993; Helmchen, et al. 1994); it had been proposed that such a signal contributes to the deceleration of the eyes at the end of the movement (Noda 1991; Fuchs, et al. 1993; Robinson 1995). In our model this signal exerts a more fundamental role: we propose that this late burst is generated by the cerebellum to actually end the saccade when the eyes are approaching the target, similar to the proposal by Sparks and Barton (1993); this function is performed in our model by activating the IBNs contralateral to the movement (Fig. 5.6).

An important novel aspect of our scheme is that the early and late bursts are not two distinct bursts, but a single burst that spreads from the contralateral to the ipsilateral FOR during horizontal saccades, and within each FOR during vertical movements. The major consequence of this spreading mechanism is that, if the speed of the spread (which in our model is controlled by the vermis), is an appropriate function of the velocity of the movement, the FOR acts as a spatial displacement integrator that keeps track of the residual motor error. The integration of the velocity signal is carried out by the cerebellum in the spatial, as opposed to the temporal, domain. To perform a spatial integration of the velocity signal some sort of topographic organization has to exist (Optican 1995); accordingly, in our model the FOR is topographically organized. Under this assumption there are regions of the FOR that project preferentially to vertical bursters and others that project more heavily to horizontal bursters; furthermore, the preferred directions of neurons spans the whole contralateral hemifield. In fact, recordings in the FOR appear to be compatible with this scheme (Ohtsuka and Noda 1991; Fuchs, et al. 1993).

Furthermore, thanks to this topographical organization of the FOR, a di-
Figure 5.7: Directional control by the FOR. The two fastigial nuclei are represented as a single map. Neurons in the left half of the map drive the eyes toward the right (R), neurons in the top half of the map drive the eyes downward (D), etc. E = initial eye position; T = target position.
5.4.  **CEREBELLUM**

Directional control over the saccade automatically arises. When a horizontal saccade starts, the activated area is in the contralateral FOR at a location proportional to the amplitude of the movement (Fig. 5.7, top panels), and thus its contribution is collinear with the collicular drive. As the saccade progresses, the activity spreads across the map; if the eyes are moving straight toward the target (Fig. 5.7, central column, blue arrow), the FOR activity spreads into an area having the same amount of projections to the upward and downward MLBNs (Fig. 5.7, left column). However, if the saccade is bending away from a straight trajectory, going for example upward (Fig. 5.7, central column, red arrow), the activity spreads toward an area that projects more heavily to the downward MLBNs (Fig. 5.7, right column), compensating for the directional error. Thus, in our model the FOR exerts a directional control over the saccade, redirecting the eyes toward the target, and, even though the output of the collicular pathway is unidimensional, saccades can be purposefully curved. As the eyes approach the target, the activity reaches the other side of the FOR, and the choke signal is applied to the brain stem circuitry (Fig. 5.6). Because the collicular drive to the EBNs is choked off by the cerebellar input acting on the contralateral IBNs, and not on OPNs, the two components of a saccade can terminate at different times, as occasionally observed (Bahill and Stark 1977; King et al. 1986; Becker and Jürgens 1990). Note that the spread of activity in the FOR is very different from the spread of activity in the buildup layer of the SC, which in our model begins before the saccade and is not under feedback control.

### 5.4.3 Outputs

As indicated in the previous section, in our model the FOR projects to the contralateral MLBNs, stronger to the IBNs than to the EBNs. Experimental evidence supports this hypothesis (Gonzalo-Ruiz et al. 1988; Noda, et al. 1990).

At the beginning of horizontal saccades, the FOR contralateral to the direction of the saccade produces a burst, exciting the MLBNs ipsilateral to the
saccade and thus supplying an additional drive. In contrast, toward the end of
the movement the FOR ipsilateral to the direction of the saccade bursts, thus
exciting the MLBNs contralateral to the saccade. The activity induced in the
contralateral EBNs is canceled out, at the level of the MNs, by the activity
still present in the ipsilateral IBNs because of the collicular drive. At the same
time the ipsilateral FOR also excites the contralateral IBNs, with stronger
weights (as supported by anatomical studies, see above); this late activity in
the contralateral IBNs cancels out, at the level of the MNs, the activity present
in the ipsilateral EBNs because of the collicular pathway and of the contralat-
eral FOR, thus stopping the saccade. In other words, the late excitation of
the contralateral IBNs is used to choke off the activity still present in the
ipsilateral EBNs. We call this a choke and not a brake because the saccade
is terminated by removing the pulse component of the drive to the agonist
muscle, and not by activating the antagonist. Thus, no co-contraction of the
agonist-antagonist pair of muscles is produced. The same line of reasoning
can be applied to vertical and oblique saccades; however, in those cases the
concepts of ipsilateral and contralateral are lost, and it is useful to visualize
the two FORs as a single map.

It now becomes clear why we said earlier that the presence of unclipped
activity in the SC is an indispensable feature in our model: if the collicular
drive were over at, or before, the end of the saccade there would be nothing
left for the cerebellar pathway to choke off. Furthermore, the lack of activity in
the caudal SC would cause the reactivation of the collicular fixation neurons,
which in turn would reactivate the OPNs, opening the gate and making the
positive drive produced by the contralateral FOR useless. When this happens,
the accuracy of the saccade can not be controlled by the cerebellum. Thus, the
collicular pathway must always supply a drive that would produce hypermetric
saccades, so that the cerebellum can turn them into normometric movements
by choking off the collicular drive at the appropriate time. After the saccade
has been stopped in this way, the OPNs reactivate, stabilizing the saccadic
circuit. Nevertheless, in our model neither the removal of excitatory input to
the ipsilateral EBNs nor the reactivation of the OPNs is necessary to stop the
movement.
5.4.4 **Action of the Vermis**

As we already pointed out, in our scheme the desired displacement signal is delivered to the cerebellum by connections from the NRTP, which is characterized by a retinotopic organization (i.e., cells have retinotopic response fields) (Crandall and Keller 1985). So, the earliest burst on the FOR is imposed by topographic inputs from NRTP (or from DMPN). However, in our scheme the connections from NRTP (or from DMPN) to the FOR need to be bilateral; this aspect, which is supported by experimental evidence (Noda, et al. 1990), is extremely important. In fact, during small saccades there is no time for the ipsilateral burst to be generated by making the contralateral burst spread across the FOR under the effect of velocity feedback. Thus, in these conditions the ipsilateral FOR, which in our model provides the choke, should start discharging before the onset of the saccade (this is in agreement with experimental findings) (see Fuchs, et al. 1993, their Fig. 1). Another reason for
having bilateral projections from the NRTP to the FOR is related to the fact that the vermis, which in our model controls the spread, can only disinhibit the FOR neurons.

A mechanism that the vermis could use to control the spread of activity in the FOR is illustrated in Fig. 5.8. Suppose that throughout the movement, the NRTP provides a bilateral, widespread excitatory input to the FOR. At the beginning of the movement the vermis releases inhibition at a site located in the contralateral FOR (at least for not too small saccades). The location of this site will determine the final metrics of the movement, and thus is a function of the desired displacement of the eyes. As noted above, the vermis can compute such signal by using the target location information (provided by the NRTP), possibly the speed of the target (from the pontine nuclei), the current eye position (from the nucleus prepositus hypoglossi), and other contextual information. Once the eyes start moving, the vermis will use the velocity feedback (from the MLBNs) to sequentially disinhibit the FOR. If the speed of this wave of inhibition release is directly proportional to the speed of the eyes, a sort of spatial integrator emerges. An appropriate choice of the weights will ensure that by the time the eyes approach the target the ipsilateral FOR has been disinhibited (dashed annulus), so that the FOR can choke off the saccadic drive and guarantee the accuracy of the movement.

Two relationships then need to be learned to produce accurate saccades: the correspondance between the desired displacement and the site of initial activation, and the relationship between the velocity of the movement [which is a function of the output of the MLBNs and the orbital position of the eyes (Collins 1975)] and the speed and direction of the spread. It should also be noted that, because in our model the SC encodes (spatially) the location of the target and not the desired displacement, eye position information could also be used by the cerebellum to implement the visuo-motor transformation needed to convert a target location from retinotopic coordinates into the displacement of the eyes required to foveate it (Klier and Crawford 1998).
Chapter 6

Implementation and Simulations

We have implemented a slightly simplified version of the pulse generator model described in the previous chapter using a network composed of a large number of simple elements (low pass filters and summing junctions). The advantage of using a distributed implementation of the model, as opposed to some lumped circuit producing an equivalent behavior, is that it allows a direct comparison of simulations of the activity of cells with recordings from individual neurons. Furthermore, effects of partial lesions and other unusual conditions can be more thoroughly tested. In this chapter we present this distributed implementation, together with several simulations that demonstrate its ability to reproduce a wide body of experimental data.

6.1 Implementation

6.1.1 Cortical Structures

We have modeled the motor layers of the frontal eye fields (FEF) as a lattice of 33 by 33 neurons, covering target locations ranging from $-40^\circ$ to $+40^\circ$ horizontally and vertically and uniformly distributed. All the other areas implemented
in our model are organized in the same way. This is of course a simplification of the actual organization of neural maps and it does not account for their well known logarithmic warping (Robinson 1972; Schwartz 1980). However, this assumption simplifies the implementation of the model, without affecting its functionality.

The FEF motor map, which encodes the target location $T$, projects, in a topographically organized fashion, to both the SC and the NRTP, and contributes to the perisaccadic burst of activity observed in both these areas. We modeled the activity $x_{FEF}(i, j, t)$ on this map as a gaussian profile centered around the cell $(i_T, j_T)$ that is associated with the target location $T$:

$$x_{FEF}(i, j, t) = I(t) \exp \left( -\frac{(i - i_T)^2 + (j - j_T)^2}{\sigma^2} \right)$$

(6.1)

To fit the experimental data we chose $\sigma^2 = 5$; $I(t)$ becomes active some time during the simulation, and is maintained constant (150 spikes/s) until after the end of the saccade [it must be removed, or at least weakened, around 50 ms after the end of the saccade, otherwise it could induce a second saccade; however, such a time course is compatible with experimental evidence (Segraves and Park 1993)].

In addition to the FEF we have modeled another cortical area, the lateral intraparietal cortex (LIP). In our model this area projects to the collicular buildup neurons (BUNs) and is responsible for their early activation and for the spread of activity across the collicular BUN layer. As noted in the previous chapter, this spread of activity (which starts well before saccade onset, i.e., it is predictive) plays no functional role in our model, which only focuses on saccade execution, but may play a role in the preparation of the saccade and can affect the balance between collicular burst neurons (BNs) and collicular fixation neurons (FNs).

To simulate the long prelude of activity in the BUNs, while keeping the simulation time as short as possible, in our model the LIP output that is associated with the target location $T$ becomes active at the very beginning of the simulation. When the FEF output starts, the LIP activity spreads to cells
that encode smaller movements in the same direction. This spread starts and continues throughout the saccade with a time constant $\tau_{LIP}$ of 50 ms. More precisely, the output of this layer is described by

$$x'_{LIP}(t) = -\frac{x_{LIP}(t)}{\tau_{LIP}} + \frac{I_{LIP}}{\tau_{LIP}}$$  \hspace{1cm} (6.2)$$

$I_{LIP}$ represents the input from neighboring LIP cells, and it is used to make the activity spread. This input is obtained by convolving the parietal activity $x_{LIP}$ with a matrix $\overline{K}$ that is a function of the location of the target $T$:

$$\overline{K} = \frac{T_H \overline{M}_H + T_V \overline{M}_V}{\sqrt{2} \begin{bmatrix} 1 & 1 & 1 \\ \sqrt{2} & 1 & \sqrt{2} \end{bmatrix}}$$  \hspace{1cm} (6.3)$$

where the division indicates element-by-element division, $T_H$ and $T_V$ are the horizontal and vertical components of the target location, and $\overline{M}_H$ and $\overline{M}_V$ are defined below (see section 6.1.3). The LIP output is normalized to have a peak of 75 spikes/s for the whole duration of the simulation; furthermore, it cannot cross the midline.

### 6.1.2 Superior Colliculus

As we have already pointed out, we have modeled three classes of collicular cells: BNs, BUNs and FNs. We now define the equations that determine the firing patterns of these classes of cells. The burst neurons receive an excitatory input from the FEF just before and during the saccade, an inhibitory input from the cerebellum (CBLM) which grows during the saccade and is an approximate function of the residual error, and an inhibitory input from the FNs. To avoid the need for different connectivity for BNs and BUNs, we hypothesize the inhibitory signals act by shunting the dendritic FEF input,
and not directly on the soma of the cell. Then, we can represent the BNs by the equation:

\[
x'_BN(t) = -\frac{x_{BN}(t)}{\tau_{BN}} + \frac{I_{BN}}{\tau_{BN}}
\]  

(6.4)

where

\[
I_{BN} = [k_{FEF} x_{FEF} (1 - k_{FB} x_{FB}) - k_{FN} x_{FN}]^+
\]  

(6.5)

with

\[
[x]^+ = \begin{cases} 
  x & \text{if } x \geq 0 \\
  0 & \text{otherwise}
\end{cases}
\]

In Eq. 6.5 \( x_{FEF} \) represents the activity of the FEF neurons (defined by Eq. 6.1), \( x_{FB} \) the feedback cerebellar input (defined as the ratio between the norm of displacement since the beginning of the saccade and the norm of the desired displacement), and \( x_{FN} \) the activity of the fixation neurons; the values for the constants are \( k_{FEF} = 4, k_{FB} = 0.85, \) and \( k_{FN} = 3. \)

In addition to the three inputs we have just described, the BUNs also receive an input from LIP. However, this input is applied directly to the soma and is not affected by the two inhibitory signals described above. The need for having an early activation of the BUNs, even when the FNs are still strongly activated, is what has induced us to use the inhibition to shunt the dendritic FEF input to the SC as opposed to directly inhibiting the SC cells. Then, the activity of the BUNs can be described by:

\[
x'_BUN(t) = -\frac{x_{BUN}(t)}{\tau_{BUN}} + \frac{I_{BUN}}{\tau_{BUN}}
\]  

(6.6)

where

\[
I_{BUN} = [k_{FEF} x_{FEF} (1 - k_{FB} x_{FB}) - k_{FN} x_{FN}]^+ + x_{LIP}
\]  

(6.7)
Thus, except for the input from LIP, the BNs and the BUNs are governed by the same equation.

The FNs receive different inputs: first, they are inhibited by the BNs; second, they receive a cortical fixation input $FIX$; and third, they receive an excitatory input from the oculomotor region of the fastigial nucleus (FOR) (May, et al. 1990). They are described by:

$$x'_F(t) = \frac{-x_F(t)}{\tau_F} + \frac{I_F}{\tau_F} \quad (6.8)$$

where

$$I_F = FIX + k_{FOR}x_{FOR} - k_{BN}max(x_{BN}) \quad (6.9)$$

and where $k_{BN} = 0.001 \|T\|^2 + 0.6$ is used to simulate a stronger inhibition from BNs and BUNs encoding larger displacements; $k_{FOR}$ is equal to 0.0073. $FIX$ is set to 150 spikes/s during periods of fixation, it is set to zero just before the onset of the movement and it is reactivated at the end of the movement. However, this input plays no role in determining the end of the movement; it is used only to stabilize the system after the saccade. This input is present all the time during simulations of electrical stimulation. The time constant of BNs ($\tau_{BN}$) and BUNs ($\tau_{BUN}$) is set to 7.5 ms, whereas for FNs ($\tau_F$) it is set to 20 ms.

### 6.1.3 Cerebellum

Our major goal in modeling the cerebellum was to reproduce the pattern of activation that is observed in FOR neurons during saccades. Thus, we have built a circuit that generates a burst of activity synchronized with saccade onset in the FOR contralateral to the direction of the saccade (for horizontal saccades) and a burst synchronized with the end of the saccade in the FOR ipsilateral to the saccade. Furthermore, the duration of the contralateral (early) burst should be correlated with the duration of the movement. In our model such signals are generated by imposing a burst of activity in the contralateral FOR
and causing the activity to spread, with a speed proportional to the velocity of the eyes, from the contralateral to the ipsilateral FOR.

To generate the initial burst we connected the NRTP (which in turn receives topographically organized projections from the SC and the cortex) to the FOR in a topographically organized manner. By doing so, we have established a one-to-one relationship between target location $T$ and desired displacement. This is only an approximation of the model’s design, but, as it simplifies the implementation, we felt that it was appropriate for the tests we wished to conduct at this stage. The FOR cells, which are modeled as a low pass filter with saturation of their inputs, are then connected to each other, and the strength of these projections is linearly modulated by the efference copy of the phasic input provided to the motoneurons (i.e., the Pulse). More precisely, the output of the FOR neurons is generated using the following equation:

$$x'_{FOR}(t) = -\frac{x_{FOR}(t)}{\tau_{FOR}} + \frac{k_{NRTP} I_{NRTP} + k_{CBLM} I_{CBLM}}{\tau_{FOR}}$$

(6.10)

where $I_{NRTP}$ represents the input from the NRTP, and it is defined by:

$$I_{NRTP} = k_{FEF} x_{FEF} + k_{BUN} x_{BUN} + k_{BN} x_{BN}$$

(6.11)

with $k_{FEF} = 0.8$, $k_{BUN} = 0.4$, and $k_{BN} = 0.4$. $\tau_{FOR}$ is the time constant of the cells (20 ms during saccades, 40 ms during fixation), and $I_{CBLM}$ is the input from neighboring cells, which is obtained by convolving the FOR activity with a matrix $\overline{M}$ that is a function of the efference copy of the horizontal and vertical components of the Pulse ($P_H$ and $P_V$, respectively):

$$\overline{M} = \frac{|P_H| \overline{M}_H + |P_V| \overline{M}_V}{\sqrt{2} \ 1 \ \sqrt{2} \ \sqrt{2} \ 1 \ \sqrt{2} \ 1 \ \sqrt{2}}$$

(6.12)
where the division indicates element-by-element division and

\[
\overline{M}_H = \begin{cases} 
0.707 & 0 & 0 \\
1 & 0 & 0 \\
0.707 & 0 & 0
\end{cases} & \text{if } P_H \geq 0 \\
0 & 0 & 0.707 \\
0 & 0 & 1 \\
0 & 0 & 0.707 & \text{if } P_H < 0
\end{cases}
\]

\[
\overline{M}_V = \begin{cases} 
0.707 & 1 & 0.707 \\
0 & 0 & 0 \\
0 & 0 & 0
\end{cases} & \text{if } P_V \geq 0 \\
0 & 0 & 0 \\
0 & 0 & 0 & \text{if } P_V < 0
\end{cases}
\]

With the strength of the connections chosen in such a way that the FOR cells never reach saturation \((k_{NRTP} = 0.7 \text{ and } k_{CBLM} = 0.0032)\), simulations (see next section) show that such a simple scheme is sufficient to implement a very accurate spatial integrator. Because the integration is performed spatially, the initial location of the activated FOR area plays a major role in determining the amplitude of the movement. However, note that the central region is reached when the eyes are still a few degrees away from the fovea. Consequently, if we produce a movement of amplitude \(x\) by imposing the activity \(y\) cells away from the central cell, to obtain a movement of amplitude \(2x\) we can not simply
impose the activity $2y$ cells away from the central cell. To avoid a complex remapping from the NRTP to the cerebellum, and given that the exact location of the activated zone in the SC does not have a strong effect on the amplitude of the movement (which is determined by the cerebellum), we decided to simply impose the target on the cortical map (and thus on all the maps) at a location appropriate for the cerebellum. So, given the target location (eccentricity and direction), we find a corrected eccentricity, and we center the cortical activity around the cell that encodes that eccentricity. The equation that describes this corrected eccentricity is

$$\left\{ 1 + 0.3 \left[ 1 - \frac{4}{\pi} \left| \theta \% \frac{\pi}{4} - \frac{\pi}{4} \right| \right] \right\} (1.7 \|T\| - 12.7) \quad (6.13)$$

where $\%$ indicates the modulus operation.

We emphasize that such a mechanism is not necessarily implemented physiologically; all we are interested in is reproducing a pattern of activation that closely resembles neural recordings, so that we can study the effects of such activities and make predictions regarding the function of the cerebellum.

### 6.1.4 Brain Stem Network

The two parallel pathways from SC and cerebellum converge at the level of brain stem MLBNs and provide inputs to excitatory and inhibitory burst neurons (EBNs and IBNs). We simulated the activity of eight neurons, one excitatory (EBN) and one inhibitory (IBN) for each of the four cardinal directions: right, left, up and down. For simplicity we describe here what determines the activity of the rightward EBN and IBN. The activity of the six other neurons are computed similarly.

All MLBN cells have a time constant of 1 ms; their discharge can not be negative and saturates at 1000 spikes/s. Right EBNs and IBNs receive four inputs: from the BNs, BUNs, FOR and OPNs. The input from the SC is such that neurons that are active before a rightward saccade excite rightward MLBNs; similarly neurons that are active before an upward saccade excite
upward MLBNs. The weight of the projections from the SC to the MLBNs is a function of the location of the cell on the SC, with cells encoding larger movements having stronger weights.

The projections from the OPNs is inhibitory, and is equally applied to all MLBNs. Like the one from the SC, also the input from the FOR is characterized by different weights depending on the position of each cell on the FOR map. For example, the leftward FOR excites rightward MLBNs, and the weights of this projection are larger for cells that are far away from the midline. However, in this case the weights to the IBNs are 5 times stronger than those to the EBNs.

We did not introduce any dynamical element to model OPNs; their output is the sum of their inputs, it cannot be negative and saturates at 300 spikes/s. They receive two excitatory inputs: a constant bias input (100 spikes/s) and an input from FNs (gain = 15). They also receive three inhibitory inputs: the sum of the activity of all BNs and BUNs weighted by 0.05 (which mimics the inhibitory input that they receive from long lead burst neurons) and the sum of the activity of all EBNs.

The eye plant was modeled as a second order system, with time constants of 150 ms and 5 ms. Of course this is only an approximation of a real plant model (which we have described and analyzed at length in a previous chapter), but we had to use it to keep simulation times reasonable. As shown earlier, the phasic input to the plant, which is represented by the output of the MLBNs and is defined as the difference between ipsilateral EBNs and contralateral IBNs, is a good approximation of the rate of change of eye orientation, and is also used in the feedback pathway to the cerebellum. Whereas in the actual plant this relationship is enforced by the pulleys, in our simplified model we have enforced it by considering the system commutative (i.e., as if it were a translational system). Furthermore, we only consider movements in Listing's Plane.
6.2 Simulations

In this section we report a series of simulations of the model implementation above described. Through these simulations we demonstrate that this model:

- Produces normal saccades that lie on the so-called main sequence.
- Guarantees the accuracy of saccades regardless of their speed.
- Replicates the patterns of activation observed in collicular burst, buildup and fixation neurons, as well as in FOR neurons.
- Exerts a partial trajectory control.
- Replicates the effects of sustained electrical stimulation of the SC (i.e., it generates staircases of saccades).
- Reproduces the main effects of collicular lesions
- Reproduces the effects of cerebellar lesions

To produce these results we have manipulated two of the model’s parameters: the weight that determines the speed of the cerebellar spread as a function of the speed of the movement and the mapping of connections from the NRTP to the cerebellum (see above). However, once we found the desired set of parameters they stayed fixed. Thus, all the results shown here were obtained using the same set of parameters. Furthermore, even though in most of the cases we test the model for horizontal (usually rightward) saccades, the behavior reported above holds for vertical and oblique saccades as well (one example of an oblique movement will be shown later), as long as the saccades are not so large that edge effects (caused by the limited size of our maps) become a problem.

The simulations were carried out using MATLAB/SIMULINK (The Mathworks Inc., Mass.) running on a Challenge-L computer (Silicon Graphics Inc., California).
6.2. SIMULATIONS

6.2.1 Characteristics of Saccades

We have simulated saccadic eye movements by driving a second-order model of the oculomotor plant with a distributed network that encompasses the SC, the cerebellum and several brain stem structures. As we have previously pointed out, this model departs considerably from earlier approaches; in particular, here the phasic input to the motoneurons is not determined by a local feedback loop that continuously reduces an estimate of the motor error to zero. Consequently, it is not even obvious, a priori, that our model can produce accurate saccadic eye movements for saccades of different amplitudes or for saccades having the same amplitude but different speeds. Clearly, a model unable to reproduce these basic characteristics of saccades (using a fixed set of connections between its elements) would be worthless.

Consequently, we started by simulating saccades of different amplitudes, setting the weights of the connections so that the movements produced fall on the so called main sequence (Bahill et al. 1975) for monkeys (whose saccades...
are faster than humans' saccades). In Fig. 6.1 we show velocity (A) and position (B) profiles of three horizontal saccadic eye movements (10°, 20°, and 30°). The saccades produced are accurate and have a peak speed which is compatible with the speed of monkey saccades. The velocity profiles are slightly skewed, especially for large saccades, but this can be accounted for by our use of a first order controller to drive a second order plant.

Next, we simulated a family of saccades to the same target (20° to the right) but with different speeds (peak speed varying from 800 to 160 deg/s). To produce movements of different speeds we used different levels of cortical activation (100, 80, 60, 40 and 20% of maximum). A lower level of cortical activation resulted in a lower collicular activation and thus in a reduced drive to the motoneurons. In Fig. 6.2 we show the results of these simulations. Panel A shows the velocity profiles of the saccades obtained; it is clear that slower saccades are stretched, i.e., their duration is increased. This is due to the different feedback signals that affected both the decay of the collicular drive and the
6.2. SIMULATIONS

timing of the cerebellar choke signal. Because of this stretching, the amplitude of the saccades does not vary much (panel B) despite the large variation in the dynamics of the movements. However, in agreement with recent data we have collected in monkeys (Quaia, et al. 2000), there is a slight tendency for slower movements to be smaller. Actually, in monkeys the magnitude of this effect is even stronger; to reproduce this degraded behavior with our model we could either impose a slightly incorrect mapping between the speed of the eye and the speed of the activity spread in the FOR, or use an imperfect estimate of eye speed. Finally it should be noted that in our simulations the slowest saccade simulated is appreciably dysmetric (hypometric); interestingly, such hypometria is not due to an untimely application of the choke but to the early reactivation of the OPNs. In this case the signals that are supposed to keep the OPNs off (i.e., the caudal SC and the EBNs) are not strongly activated and can not keep the OPNs off long enough for the eye to get on target. Interestingly, this is the same mechanism that we have recently proposed (Quaia, et al. 1998a) to account for the widespread hypometria observed following collicular inactivation (Aizawa and Wurtz 1998). To summarize, these simulations demonstrate that the scheme we have proposed can suppress noise and achieve accuracy in spite of its lack of a classic motor error feedback loop. It also can reproduce some second order phenomena that would not be predicted by classic feedback models.

6.2.2 Collicular activity

As repeatedly noted, our first goal in designing this model was to reproduce the neural patterns of activation observed in the various brain areas modeled. After all, this is what the term neuromimetic is all about. To verify whether we succeeded, in Fig. 6.3 we plot the activity across the collicular map during a 20° rightward saccade. In this figure the SC (in this case the left SC, which controls rightward saccades) is represented as a two-dimensional map; as noted above, for the sake of simplicity we have used a linear map, as opposed to a more realistic logarithmically warped map (Robinson 1972; Ottes et al. 1986; Optican 1995). Each panel in Fig. 6.3 represents the spatial distribution of the
Figure 6.3: Spatial distribution of BUN activity during a 20° rightward saccade. FNs are represented on the right side of each panel (dark spot on the first panel). Time zero refers to saccade onset.
BUNs activity at different times: 100 ms before saccade onset, 30 ms before saccade onset, at saccade onset (0 ms) and 50 ms after saccade onset. The fixation neurons (FNs) are located at the rostral pole of the left SC, on the right of each panel. The level of activation is represented using a color scale image.

The first two panels reveal the prelude of activity observed in BUNs. During that time, the FNs are still active (on the extreme right of the panels), and thus they prevent a saccade from occurring by inhibiting the BNs and exciting the OPNs. Initially (time = -100 ms) the prelude is localized around the site that corresponds to the saccadic target (i.e., the site where the burst will occur), but before the onset of the saccade (time = -30 ms) it starts spreading towards the rostral pole of the SC. At saccade onset (time = 0 ms), this ongoing spread of activity is supplemented by a strong burst of activity, which occurs at the site corresponding to the target and does not spread. Around saccade end (time = +50 ms), the residual unclipped activity of the burst is combined with the late spread near the rostral pole, and the FNs are slowly reactivated by the large amount of activity present in the fastigial nucleus (see below).

The pattern of activity in the burst neuron layer is very similar to the one reported in Fig. 6.3, except that BNs do not exhibit a prelude of activity. Thus, the activity in the BN layer is simply a spatially localized burst of activity that starts just before saccade onset and decays during the saccade, without any rostral spread.

To better illustrate the evolution of the collicular activity in the different classes of collicular cells modeled, we have plotted the time course of activation of some collicular cells (all located along the horizontal meridian) during the same saccade (Fig. 6.4). In panel A we show the time course of the firing rate of four different BNs: the one that discharges maximally for a 20° rightward saccade (cyan), and three other cells located more rostrally. The burst of activity starts around 50 ms before saccade onset, peaks around saccade onset and is almost over by saccade end (the net drive to the motoneurons is over around time 40 ms, even though the saccade ends approximately 10 ms later). Neurons that discharge optimally for different saccades start discharging later
and stop discharging earlier. These characteristics are in agreement with neurophysiological recordings in the SC of monkeys (Sparks, et al., 1976). The decay of activity during the movement is due to an inhibitory feedback from the cerebellum, and is also in agreement with neurophysiological recordings in the SC of monkeys (Waitzman, et al. 1991).

In panel B we report the activity of three buildup neurons and one fixation neuron (red line). We show one buildup neuron (cyan) that discharges maximally for the saccade simulated. The activity of this neuron is characterized by a prelude of activity that starts more than 100 ms before saccade onset, and by a burst of activity essentially identical to the one carried by the burst neurons. The prelude of activity is initially localized at the site where the burst will later emerge, but around 80 ms before the onset of the saccade it starts spreading toward the rostral pole (green), and some time during the saccade it reaches the most rostral cells (black). In our model this spread is not due to intracollicular mechanisms, but to an external cortical input, which has predictive properties (see above).
The fixation neurons (red) are tonically active in between saccades, and stop discharging just before saccade onset. The time course of the decay in FN activity before saccades is determined by two factors: first, the removal of a cortical tonic input, which simulates the removal of a cognitive fixation command; second, the rise of the burst of activity in the caudal SC (which inhibits FNs). Around the end of the saccade the FNs start discharging again. This reactivation is due to several factors: first, the increased excitation from the fastigial neurons; second the decreased inhibition from the collicular BNs; and third, the reactivation of the cortical fixation command. When FNs are tonically active again, the system reenters fixation mode.

Note that in our model we simulate only the saccade-related activity of distributed SC and cerebellum networks. Accordingly, all the activity that is not directly related to saccades (e.g., visual signals in the SC) are ignored.

### 6.2.3 Fastigial Activities

The FOR plays a central role in our model. In Fig. 6.5 we plot the pattern of activation of FOR neurons at four different time instants during a 20° rightward saccade (the same movement used to illustrate the collicular activity). The contralateral FOR starts firing first, with a weak prelude of activity (time = -100 ms). At saccade onset (time = 0 ms), a strong burst of activity is present in the contralateral FOR, complementing the collicular drive for the saccade.

Initially the FOR burst is centered in the contralateral FOR at a location that is a function of the amplitude and direction of the desired movement. Once the saccade starts, the burst of activity spreads across the FOR with a speed and direction that is proportional to the velocity of the movement, estimated using an efference copy of the phasic signal sent by the EBNs and IBNs to the motoneurons. When the activity reaches the other side, which occurs around 30 ms before saccade end (i.e., around 10 ms into the saccade for the movement simulated here), the FOR starts driving the IBNs/EBNs contralateral to the direction of the movement, with stronger weights to the IBNs than to the EBNs. Because the contralateral EBNs are inhibited by the
Figure 6.5: Spatial distribution of bilateral FOR activity during the simulation of the same saccade illustrated in Fig. 6.3. Time zero is saccade onset. Same color scale as in Fig. 6.3.
ipsilateral IBNs, the only important effect of the ipsilateral FOR firing is that the contralateral IBNs turn on. These contralateral IBNs choke off the residual drive input provided to the ipsilateral IBNs by the contralateral SC and FOR. By the time the saccade is over (time = +50 ms) a large part of the ipsilateral FOR is activated, guaranteeing that the eyes will always stop.

As we did previously for the SC, we now plot the time course of the activity of four FOR cells, all located along the horizontal meridian, during the same saccade (Fig. 6.6). The black line corresponds to the activity of the optimal cell for this movement (i.e., the cell that gets activated first). This cell starts discharging weakly well before saccade onset, and essentially reflects the activity of the SC cell that is maximally activated. The cyan line corresponds to the activity of a cell that is located in between the optimal cell and the midline. This cell is characterized by a burst that starts around saccade onset

Figure 6.6: Time profile of the activity of FOR neurons during the simulation of the same saccade illustrated in Fig. 6.3. Time zero is saccade onset.
Figure 6.7: Comparison of two saccades directed to the same target. Solid line: straight saccade. Dashed line: curved saccade (curvature induced by transient perturbation). The inset focuses on the residual error after correction: $\Delta r$ is the residual error, while $\Delta c$ is the amount of correction produced by the model.

and peaks some time later. The third cell illustrated (red) is located near the midline, whereas the last one (green) is located in the ipsilateral FOR. It is clear that these cells start discharging later and later, so that the front of the spreading activity on the FOR map is correlated with the residual motor error.

### 6.2.4 Control of Saccade Trajectory

We will now show that the model presented here is also able to compensate, at least partially, for trajectory perturbations. In particular, errors in initial
saccade direction are common in normal saccades (Becker et al. 1981; Erkelens and Sloot 1995; Erkelens and Vogels 1995; Quaia et al. 2000), and their subsequent compensation produces a curved trajectory. In Fig. 6.7 we show two simulated saccades directed toward the same target (approximately 14° up and 14° to the right).

In the normal case (solid line) the eyes go essentially straight to the target. In the other case (dashed line) we caused a deviation in the initial trajectory by transiently decreasing the gain of the horizontal EBNs (gain = 0.8; duration = 10 ms). As a result of the perturbation, the eyes initially moved more quickly up than to the right, so that the initial direction (thin line a) deviated from the normal trajectory (solid line). If there were no compensating mechanism built into the model, once the perturbation was over the eyes would proceed parallel to the normal direction (thin line c). However, soon after the perturbation was over, the eyes steered back toward the target, even though the final overall direction (thin line b) did not coincide with the desired overall direction (i.e., the compensation wasn’t perfect). This compensation, which is due to the cerebellar contribution to the generation of the saccade, is highlighted in the inset figure, which enlarges the final part of the two saccades. The residual error in eye orientation (i.e., the difference between the actual and the desired eye orientation) is represented by the segment \( \Delta r \), whereas \( \Delta c \) corresponds to the correction in trajectory due the cerebellar contribution (i.e., the difference between the final position and the position that would have been achieved without a compensation mechanism). A perfect compensation (which would be produced by any model based on a closed-loop feedback mechanism) can not be achieved because our model is not an end-point controller in the strict sense. Furthermore, in our implementation only a small fraction of the drive is controllable in direction. Thus, partial compensation is a prediction of our model. This suggests a limit to the maximum compensation for errors in initial saccade direction. Furthermore, perturbations near the end of the movement, or for small saccades, should be compensated less, because there will not be enough time to redistribute activity on the FOR map.

To further investigate this correction mechanism, in Fig. 6.8 we illustrate
Figure 6.8: Spatial distribution of FOR activities during the curved saccade represented in Fig. 6.7 (dashed line). The white spot represents the center of activity on the of FOR map. The dashed oblique line is where this spot lies during a normal straight saccade. Time zero is saccade onset.
the activity in the FOR map during the perturbed saccade. The center of gravity of FOR activities is represented by the white spot; it is clear on the third panel (FOR activities at time = 15 ms) that, by pushing the eyes upward, the perturbation induces a shift of activity in the FOR. This is because the trajectory of the center of activity on the FOR map follows the trajectory of the eye. Thus, the cerebellum is aware of the current heading of the eyes and can automatically produce a drive that compensates, at least partially, any misdirection. Under the influence of the cerebellum (exerted through the connections between the FOR and the MLBNs), the trajectory of the eyes can then be corrected in mid-flight, as illustrated in Fig. 6.7.

6.2.5 Electrical Stimulation of the SC

The first experimental evidence for the role of the SC in the control of saccades comes from early stimulation studies of this structure (Adamük 1872; Apter 1946). For example, by briefly passing electrical current through an electrode inserted in the SC, Robinson (1972) was the first to describe in quantitative detail the retinotopic organization of the SC motor map. The similarity between saccades electrically evoked (EE) and natural movements of the eyes has led many investigators to conclude that electrical stimulation of the SC mimics natural SC activation and provides downstream structures with an identical motor command. This view has been reinforced by the tight correspondence between the movement field of SC cells as recorded during natural saccades and the characteristics of saccades evoked by electrical stimulation of the same collicular site (Van Opstal et al. 1990; Paré, et al. 1994; Paré and Guitton 1994).

Also of interest is the fact that, if the electrical stimulation is sustained for a prolonged period, a first saccade (which has approximately the same size as that evoked by a brief stimulation from that site) is followed by a series of saccades of similar (but slightly smaller) amplitude. Because of the time profile of eye position during the stimulation period, this series of movements is then called a staircase. Other characteristics of staircases of saccades are that the
amplitude of the first saccade increases with the intensity of the stimulation. In contrast, both the interval between two saccades (inter-saccadic interval) and the amplitude of the saccades after the first, decrease when the intensity of the stimulation is increased (Stryker and Schiller 1975).

To simulate sustained electrical stimulation of the SC, we imposed on the SC a gaussian activity profile, having a constant amplitude throughout the stimulation period. Thus, we made the assumption that the cerebellar inhibitory feedback had no effect on SC drive as long as the SC was stimulated (i.e., the SC burst does not decay during the saccade). The rationale behind this assumption is that electrical stimulation probably directly excites the soma and the axon of collicular neurons, and it is thus not affected by dendritic inhibition. Accordingly, during our simulations the only significant effect of cerebellar feedback was on the FNs that receive a direct input from the FOR. Furthermore, during the stimulation we did not provide any spreading cortical input to the SC. The reason for this is that no signal in the brain could predict the onset of electrical stimulation, and thus it would make no sense to have a predictive signal in the model. Similarly, the cortical fixation input to the FNs was not withdrawn at the beginning of the first saccade; instead, it was kept constant during the whole duration of the stimulation. It must be noted that the model neither contains a mechanical limit to the displacement of the eye in the orbit, nor takes into account the well known effects of orbital eye position on the dynamics of eye saccades. These two characteristics, though important, are beyond the scope of this paper.

The simulations that we present here show that our model can produce staircases of saccades that closely match those generated by sustained electrical stimulation of the SC (Fig. 6.9). In all cases the same collicular site was activated; panel A corresponds to the case where no delays are included in the circuit, whereas panel B shows the results obtained by introducing a 6 ms delay in the feedback pathway that provides the eye velocity signal to the cerebellum. Different position traces correspond to different intensities of the collicular activity (see legend). Note how as the intensity of the stimulation is increased the amplitude of the first saccade increases, while both the
Figure 6.9: Simulations of electrical stimulation of the SC. SC peak discharge $= k \cdot 600$ spikes/s. Time zero is stimulation onset. Different position traces correspond to different intensities of SC stimulation. A: No delays are considered. Red line, $k = 1$; cyan, $k = 0.675$; black, $k = 0.6$; green, $k = 0.5$; magenta, $k = 0.475$. B: A 6 ms delay is introduced in the feedback pathway. Red line, $k = 0.9$; cyan, $k = 0.7$; black, $k = 0.6$; green, $k = 0.5$; magenta, $k = 0.475$. 
CHAPTER 6. IMPLEMENTATION AND SIMULATIONS

inter-saccadic interval and the amplitude of the other saccades is decreased. Furthermore, the strength of the stimulation also strongly affects the latency of the first movement; this aspect is also supported by experimental data (Stryker and Schiller 1975).

It is also interesting to note that, while strong stimulations yielded saccades that had an amplitude corresponding roughly to the site activated, weak stimulations were cut short because of an early reactivation of the OPNs (due to the persistent cortical fixation input provided to the FNs). Finally, in the case of very strong stimulations, the first saccade is followed by a smooth eye movement (red line in panel A), or by a series of very small saccades in the case where the 6 ms delay is introduced (red line in panel B).

6.2.6 Effects of cerebellar lesions

Lesions of the oculomotor cerebellum have a large impact on the characteristics of saccades. Because in our implementation we have focused on the role of the FOR, and we have not directly addressed the issue of how the cerebellar cortex carries out its function, we will describe here simulations of lesions of the FOR. All the simulations we show refer to the effects of FOR lesions on a saccade to a target located 20° to the right of the center. In all figures the pre-lesion (control) saccades are indicated with a dashed line, whereas the post-lesion saccades are indicated with a solid line.

It has been shown (Robinson, et al. 1993) that when the fastigial nuclei are lesioned bilaterally saccades become hypermetric, regardless of their direction. Furthermore, their speed is lower than expected for saccades of their size, and even lower than the speed of normal (i.e., pre-lesion) saccades to the same target. To simulate these conditions with our model we assumed that the effect of a lesion of the FOR is to attenuate its output (because some of the FOR is possibly spared). For example, when we imposed an attenuation of 60%, we obtained saccades that are hypermetric (Fig. 6.10A) and slower (Fig. 6.10B) than normal, just as reported in the literature. Effects on latency by actual lesions seem to be very inconsistent; in our simulations we observed a very
6.2. SIMULATIONS

Figure 6.10: Simulation of the effects of FOR lesions on a 20° rightward saccade. **A-B**: Eye position and velocity before (dashed) and after (solid) a bilateral FOR lesion. **C-D**: Effects of a lesion of the right (ipsilateral to the movement) FOR. **E-F**: Effects of a lesion of the left (contralateral) FOR. All results obtained by reducing the output of the FOR by 60% (see text).

small latency decrease due to a decrease in the excitatory drive provided by the FOR to the collicular fixation neurons.

With unilateral lesions of the FOR it is possible to evoke a much larger range of effects (Robinson, et al. 1993; Ohtsuka et al. 1994). First of all, ipsilateral saccades become hypermetric, while their velocity (at least for 20° saccades) slightly increases. Our simulations (performed by attenuating by 60% the output of the right FOR for a 20° rightward movement) are in agreement with such findings (Fig. 6.10C-D). Conversely, after contralateral lesions saccades become hypometric and slower. However, when we simulated this
condition with our model (using the same attenuation as before) we could reproduce the slowing down, but not the hypometria (Fig. 6.10E-F). This is due to the fact that we assumed that altering the activity in the contralateral FOR (the one that is active at the beginning of the movement) does not affect in any way the functioning of the spatial integrator. Thus, even though the saccade started slower, the choke signal supplied by the ipsilateral FOR was delivered later, and the eyes landed on target. However, it should be noted that the FOR projects to the NRTP (Noda, et al. 1990), which in turn projects to the vermis; thus a lesion of the FOR could very well disrupt the mechanism underlying the spatial integration of the velocity signal, inducing an early activation of the choke (in our simulations we only attenuated the output of the cells). To clarify this issue a better understanding of the NRTP-vermis interaction is needed.
6.2. SIMULATIONS

Unilateral lesions of the FOR also affect vertical saccades, which become slightly hypermetric and bend toward the side of the injection (Robinson, et al. 1993). Because of a large edge effect (due to the need to activate both collicular maps), the current implementation of our model is not very well suited to simulate vertical saccades. However, because of our models structure, the effects of a lesion of the left FOR on an upward saccade are equivalent to the effects of a lesion of the upper half of the FOR (see Fig. 5.7) on a rightward saccade. This allows a vertical saccade to be simulated by interchanging of horizontal and vertical in our model. The results of such a simulation (Fig.6.11) are very similar to what has been reported in the literature (see Robinson, et al. 1993, their Fig. 2). In particular, note that the saccade started in the correct direction and then bent away from the target. Furthermore, the saccade was also slower (not shown), as reported by Robinson and colleagues (1993).

Another study of unilateral injections of muscimol in the fastigial nuclei of the head- free cat (Goffart and Pelisson 1994) showed that ipsilateral saccadic deficits were compatible with a remapping of the target, rather than with a generalized hypermetria. In contrast, contralateral saccades were hypometric, as expected. Our model, in its present form, does not predict such results, which could be due to the disruption of some additional mechanism (perhaps related to the removal of the tonic level of activity that is normally present in fastigial neurons, which we have not modeled here). Nonetheless, it should be noted that the effect of unilateral FOR lesions on vertical saccades, which is reproduced very well by our model, would be very difficult to explain with a theory that posits a role for the FOR in specifying the target.

Finally, we previously pointed out that when the FOR is lesioned, the variability of saccades is considerably increased, both in amplitude and in direction. As pointed out above, this increased variability is incompatible with classic models of cerebellar contribution that use only long-term adapted control signals. On the other hand, the increased variability is compatible with our model, where the cerebellum is the structure that accounts for both the accuracy and consistency of saccades. Because noise sources have not been
included in this implementation of our model, we did not use simulations to demonstrate this property. However, because without a cerebellum our model of the saccadic system would simply be a feed-forward controller, the results are obvious.

6.2.7 Effects of Collicular Lesions

Even though the SC is not necessary to produce saccadic eye movements (Schiller, et al. 1980), it is well known that its partial chemical inactivation causes, at least in the acute phase of the lesion, changes in all saccadic parameters. Typical effects of reversible partial deactivation of the SC are increased latency, decreased peak velocity, and dysmetria of the movements (Hikosaka and Wurtz 1985; Hikosaka and Wurtz 1986; Lee et al. 1988; Aizawa and Wurtz 1998; Quaia, et al. 1998a). Furthermore, it has been recently reported that the trajectory (Aizawa and Wurtz 1998) and the initial velocity and direction (Quaia, et al. 1998a) can also be systematically affected.

We have simulated a collicular lesion by attenuating the output of a region of the SC. We have reduced the activity of one cell by 70%, of its 8 neighbors by 60% and of the successive 12 neighbors by 50% (both buildup and burst neurons were affected in the same way), with the central cell corresponding to a $15^\circ$ saccade at $45^\circ$ of elevation. Then we have looked at the effect of this lesion on a $10^\circ$ and a $20^\circ$ saccade, both at $45^\circ$ of elevation. In another paper (Quaia, et al. 1998a), we suggested that the effects of SC lesions on the initial direction of saccades can be accounted for if it is assumed that the lesion always causes a change in the horizontal drive larger than what would be expected given the location of the lesion. To include this assumption in our simulations, we have also reduced the drive of the SC to the horizontal MLBNs by 30%.

When, under the above mentioned conditions, a saccade to a $20^\circ$ target is simulated (Fig. 6.12A-B), the eyes deviate upward and then curve back toward the target. However, the compensation is only partial, so that the saccade falls short of the target. The speed (both initial and peak) of the movement
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Figure 6.12: Simulation of the effects of a collicular lesion, centered at 15° of amplitude and 45° of elevation, on trajectory and eye velocity. A-B: Effect on a 20° oblique saccade. C-D: Effect on a 10° oblique saccade. (See text for details about the parameters used to simulate the lesion.)
is considerably lower than in the control situation, even though the amplitude of the movement is not much different. When a $10^\circ$ saccade is simulated (Fig. 6.12C-D), a similar pattern of curvature is observed, and again both peak and initial speed are considerably affected. However, in this case the eyes fall considerably short of the target.

All these characteristics are in agreement (at least qualitatively) with the results presented by Aizawa and Wurtz (1998); however, our simulations clearly fail to show the large change in latency which is a trademark of collicular lesions. This failure is due principally to the fact that the cortical fixation input provided to the collicular fixation neurons (see above) is, in our current implementation, removed abruptly, and not gradually. A more gradual removal of this input would make the timing of the saccade onset more sensitive to the balance between the activity of the burst/buildup neurons and that of the fixation neurons, thus allowing a much larger spread of latencies.

6.2.8 Sensitivity to Parameter Changes

As expected, our model is very sensitive to the relationship between the MLBNs activity, which determines the speed of the eyes, and the speed of the spread of activity in the FOR. If this relationship is not precise, saccades will not be accurate. A second important factor is the mapping from NRTP/DMPN to the cerebellum. This mapping determines the area of the FOR that bursts at the beginning of the movement; the location of this area is also very important to ensure the accuracy of the movement. On the other hand, saccade accuracy turned out to be fairly insensitive to changes in the speed of the movement, and thus to the weight of the connections between the SC and the MLBNs; furthermore, altering the feedback inhibition signal to the SC has little affect on the metric of saccades. Similarly, the weight of the connections between the FOR and the MLBNs is not very important, as long as the input to the IBNs (the choke) is strong enough to overcome the collicular input to the EBNs (otherwise the movement would not stop).

Finally, the OPNs deserve a special note: we have noticed that, even though
under normal circumstances they play essentially no role in determining the characteristics of saccades, they can become very important when abnormal conditions are considered. For example, they can have important effects after lesions or during electrical stimulation. Thus, we suggest that it would be interesting to study their behavior under these conditions, or, for example, to study how a lesion of the OPNs affects electrically evoked saccades.
Chapter 7

Analysis and Inferences

In the previous chapters, we have presented a model in which saccades are generated by the cooperation of two pathways, both influenced by feedback information. In this sense, our model departs from the Robinsonian scheme that has dominated saccadic modeling for the last 25 years, where the saccadic drive was generated by a single feedback loop. The main concepts that characterize our scheme are: (1) the saccade ends not because the motoneurons run out of drive from the EBNs, but because that drive is actively choked off; (2) only one part of the drive can be controlled in direction; (3) the cerebellar contribution depends upon feedback information, and it is carefully tailored for each movement; (4) no classical spatial-to-temporal transformation (which would produce a temporally coded dynamic motor error) is performed; (5) the displacement integrator (or, more precisely, a functionally equivalent circuitry) is implemented in the spatial domain in the cerebellum.

We have also shown that the presence of extraocular pulleys simplifies the task of generating the Slide and Step components of the innervation signals, considerably reducing the control problems related to the non-commutativity of rotations. We believe that this finding is very important, as it indicates that Nature goes to great lengths to simplify the neural controller. This contrasts sharply with the widely held belief that, because neural networks can solve
problems of great complexity, Nature should simplify the structure of the plant.

When coupled with a plant model with pulleys, our model of the controller, which faithfully reproduces the patterns of activity observed in several brain areas, is able to generate realistic saccades as well as to simulate the effects of paradigm changes, electrical stimulation, natural perturbations, and lesions. The model's ability to reproduce all these data prompted us to investigate whether some general principles about the neural control of movement can be inferred from it.

We will carry out this analysis by comparing our model to classic control schemes, highlighting their differences in structure and performance, as well as their phylogenetic impact. But before doing so, we will first make a thorough functional analysis of our model.

### 7.1 Model Analysis

#### 7.1.1 Overview

The schematic diagram of our model of the saccadic system is shown in Fig. 7.1. Briefly, it consists of cortical regions (such as the frontal eye fields and the lateral intraparietal cortex) that provide information about the location of the target to be foveated to both the superior colliculus (SC) and the cerebellum. The SC produces three signals. The first is a veto signal, tonically active in between saccades and silent during saccades. This signal directly excites the omnipause neurons (OPNs), which strongly inhibit the saccadic pre-motor neurons (MLBNs) carrying the pulse of innervation required to make a saccade. The SC also directly provides to the MLBNs part of the pulse of innervation used to move the eyes. We call this a directional drive, as it simply moves the eyes in a given direction. The direction of the drive is determined by the latero-medial location of the activated site, whereas its intensity is a function of both the rostro-caudal location of the active site, and of the level of activation. As this signal is simply a weighted sum of all the activity on the SC map,
in this pathway there is strong convergence. Finally, the SC provides information about target location to the cerebellum [through the nucleus reticularis tegmenti pontis (NRTP)]. This information is distributed, so that different SC cells project to different cerebellar neurons. In other words there is no convergence, and there may even be divergence.

The cerebellum also generates multiple signals. During the first part of the saccade, the cerebellum provides an excitatory drive to the excitatory MLBNs ipsilateral to the movement, increasing the initial acceleration of the eyes. Thus, this signal can also be considered a directional drive; the main difference between the collicular and the cerebellar drives is that the direc-
tion of the latter can be modified during a saccade. Toward the end of the saccade, the cerebellum starts exciting the inhibitory MLBNs contralateral to the movement, choking off the drive to the motoneurons and thus providing a functionally different signal. The speed with which the transition from driving to choking occurs is directly proportional to the speed of the movement (i.e., to the intensity of the pulse). Thus, the faster the movement, the faster the transition. In our model the cerebellum also provides a third signal to the SC which encodes, in a very approximate way, the progress of the saccade toward the target. This signal is used in the SC to reduce the activity in the caudal SC, so that at the end of the saccade the rostral, or fixation, neurons in the SC can resume firing and excite the OPNs, preventing further saccadic movements.

One of the most important innovations of the model that we presented here is that in this scheme the cerebellum carries out the function that in previous models was ascribed to the displacement integrator and feedback summing junction, i.e., monitoring the dynamic motor error. Here, the cerebellum plays a pivotal role in guaranteeing both the accuracy and the consistency of saccades. This role is accomplished by choking off the collicular drive at the appropriate time and by compensating for directional errors by providing an appropriate directional drive to the brain stem circuitry. Thus, the signal provided by the cerebellum is subject not only to long term adaptation, as often suggested, but is adjusted during each saccade to compensate for the instantaneous behavior of the rest of the system.

### 7.1.2 The Pulse of Innervation

In Fig. 7.2 we show a functional representation of the model that focuses on the signals contributing to the pulse of innervation. The collicular contribution is always positive, peaks at saccade onset, decays throughout the saccade, but is not over by saccade end. This signal is a function of the initial location of the target and it simply drives the eyes approximately in the right direction. The overall cerebellar contribution (i.e., the difference between the drive and
Figure 7.2: Time course of the collicular and cerebellar contributions to the pulse of innervation.
Figure 7.3: Cerebellar mechanism for generating accurate movements.

The choke) is positive at the beginning of the movement, but becomes negative afterwards. The movement is over when this negative contribution offsets the positive drive coming from the SC. The time at which this point is reached is a function of the speed of the movement and of some other information (see below). Thus, in this scheme the cerebellum is the structure that decides when it is time to terminate the movement, determining its exact metrics. Accordingly, to understand how our model generates saccades having the desired amplitude, we have to look at the events that we propose take place in the cerebellum.

As noted above, in our model the NRTP provides a signal encoding the location of the target to both the vermis and the FOR. We posit that the FOR is topographically organized, and that different NRTP neurons project, in a topographically organized manner, to different cerebellar neurons. Actually we
propose that in the FOR there is divergence, so that for each target location a large fraction of the FOR neurons receives excitatory inputs. Just before the beginning of the movement (e.g., a rightward saccade), the vermis releases inhibition at a site in the contralateral FOR whose location is a function of the desired displacement of the eyes (Fig. 7.3, gray circle in left FOR). The larger the movement, the farther away from the midline will be this site of initial activity. In the first phase of the movement this activity will excite the MLBNs, thus driving the eyes in the appropriate direction. As the movement progresses, feedback from the brain stem about saccade velocity (Fig. 7.3, Pulse) causes a wave of inhibition to sweep across the vermis (Fig. 7.3, top gray arrow). This wave in the vermis sequentially disinhibits neighboring parts of the FOR, so that the FOR activity appears to spread towards the opposite side (Fig. 7.3, bottom gray arrow). Eventually the other side of the FOR is activated (Fig. 7.3, dotted gray disk in right FOR). However, the projections from this side go to the inhibitory MLBNs, and thus this activity reduces the pulse. As the inhibition grows the pulse shrinks, until it gets to zero and the saccade ends. At this point the activity in the FOR does not spread any more and it slowly decays toward zero. The speed of this spread is directly proportional to the pulse and thus to the speed of the movement. If the movement is fast, the activity will reach the other side quickly, whereas if it is slow it will get there later. Thus, the duration of the movement becomes inversely proportional to its speed, keeping the amplitude constant.

For this scheme to work, the cerebellum must know, or must be able to infer, the desired displacement of the eyes. However, we already pointed out that in our model this signal is not readily available, as the SC and the other cortical structures encode the location of the selected target, not the amplitude of the movement. Under the simplest behavioral paradigm (i.e., saccades directed to a stable target) these two signals coincide, but simple (and realistic) paradigm changes can break that equality. Consider, for example, saccades to moving targets, or saccades to a target that is moved, in a predictable (but not necessarily perceivable) fashion, during a saccade. It is well known that, in both cases, subjects can make a saccade straight to the predicted location of the target. It has also been shown that, as we posit in our model, under
those conditions the collicular site activated encodes the location of the target and not the desired movement (Goldberg, et al. 1993; Keller, et al. 1996; Frens and Van Opstal 1997). This situation raises two questions: how does our model compute the desired displacement? And why is the system organized this way?

7.1.3 The Desired Displacement Signal

As noted above, in our model the cerebellum receives (from NRTP) an input that only encodes the location of the target. To guarantee that the appropriate movement is produced, additional information, such as the speed of the target, the initial position of the eyes, and perhaps some information about the required behavior (the overall context of the movement) is also provided. In our model, the way in which the cerebellum uses this information is fairly simple, and it can be more easily explained through an example.

Suppose that a target appears in the periphery and moves toward the fovea with a predictable velocity. In this case, the desired target is represented in the SC (and in the NRTP) by the activation of a locus corresponding to the initial target location in retinotopic coordinates (Fig. 7.4, gray disks in SC and FOR). We propose that the additional information about the target speed, conveyed to the cerebellum by the pontine nuclei (Keller, et al. 1996), is used by the vermis to cause the initial locus of activity in the contralateral FOR to shift toward the midline (in Fig. 7.4, from the gray disk, appropriate if the target were stable, to the black disk). The faster the target, the larger the shift. As the eyes start moving, the velocity feedback causes the activity to spread; however, because the site initially activated is more medial, the activity reaches the ipsilateral FOR earlier, ending the saccade sooner and making it smaller than expected from the active site in the SC. The movement will thus have a shorter amplitude than required to acquire a stationary target, because the additional information about target motion was used to move the cerebellar site initially activated closer to the midline.

One might then be tempted to conclude that, in our model, the initially
Figure 7.4: Saccade directed to a target moving towards the fovea. To generate a movement of the right size, the site initially activated in the cerebellum (black disk) need to be closer to the midline than if the target were stable (gray disk).
Figure 7.5: The cerebellar locus initially activated does NOT encode the desired displacement of the eyes. 

**A:** $15^\circ$ saccade to a stable target.  

**B:** $15^\circ$ saccade to a target moving towards the fovea.

active cerebellar site encodes the desired displacement of the eyes. However, a closer inspection reveals that such a conclusion is not warranted. Consider, for example, a $15^\circ$ saccade to a stable target. The SC site activated and the cerebellar site initially active would be the ones indicated in Fig. 7.5A. Now, consider a saccade directed to a target that is moving towards the fovea, and assume that the target location before the saccade starts is $20^\circ$. Assume also that the saccade needs only to be $15^\circ$ long, because the target will move $5^\circ$ closer to the fovea before the eyes get there. In this case, the cerebellar site initially activated (Fig. 7.5B) needs to be closer to the midline than it was
7.2. **COMPARISON WITH CLASSIC CONTROL SCHEMES**

![Diagram of Classic Motor Control Scheme]

Figure 7.6: Classic motor control scheme.

in Fig. 7.5A, even though the movement to be generated is the same. This is because by the time the eyes have traveled $15^\circ$ the collicular drive will be stronger in this case than in the previous (because the SC site activated is different in the two cases). Accordingly, if the site indicated in Fig. 7.5A were initially activated, a saccade larger than $15^\circ$ (but smaller than $20^\circ$) would be produced.

Thus, in our model there is no *explicit* computation of the desired displacement signal. This signal is only *implicit*, and it is *distributed* across both the SC and the cerebellum.

### 7.2 Comparison with Classic Control Schemes

The most fundamental difference between our model and models inspired by classic control theories is that, in all of those models the very first step involves the explicit computation of the desired movement vector or trajectory (Fig. 7.6, $E_d$). This is usually a temporally encoded signal, which is then fed to an inverse model of the eye plant (simply a block that receives as an input the desired movement, and produces as an output the innervation required to produce that movement). The inverse model of the plant is usually not implemented as
Figure 7.7: Inverse model of the plant implemented using a feedback loop.

a feed-forward system. Instead, it is often implemented as a feedback loop in which $E_d$ is compared with another temporal signal representing an estimate of the current ocular displacement (Fig. 7.7, $\hat{E}$). This signal is obtained by feeding the innervation signal to a forward model of the plant. The output of the comparator gives the difference between these two signals, which represents the dynamic motor error (Fig. 7.7, $\hat{m}_e$). The motor error is then used to generate the innervation signal (in our case, the Pulse). The foremost example of the employment of such a scheme in a model of a neural controller is represented by Robinson’s model of the saccadic system (Robinson 1975a; Zee et al. 1976), which we have previously described (Fig. 2.10). In that model, the forward model of the plant was represented by a simple integrator, as the Pulse of innervation encoded eye velocity and only rotations around the vertical axis were considered (which, as noted earlier, are commutative).

An alternative scheme uses a combination of a feed-forward inverse model of the plant and a forward model of the plant working in feedback (Fig. 7.8). In this case the signal generated by the feed-forward pathway is only under
7.2. **COMPARISON WITH CLASSIC CONTROL SCHEMES**

Additional Information

Target Location

Sensory-Motor Transform.

Desired Trajectory

Inverse Plant Model

Feedback Controller

Forward Plant Model

Pulse

Figure 7.8: Inverse model of the plant built as the combination of a feed-forward inverse plant model (under long term adaptation) and a forward plant model working in feedback.
long term adaptation, and, in absence of perturbations or plant alterations, it provides a signal appropriate to generate a movement that matches the desired trajectory. The forward plant model, which can be modified much more quickly to reflect plant changes, generates an estimate of the movement currently generated. This estimate is compared with the desired trajectory, and any discrepancy is passed on to a feedback controller which generates an appropriate compensatory signal (Friedland 1996). Several models of neural controllers based on such a scheme exist (Kawato and Gomi 1992a; Kawato and Gomi 1992b; Wolpert et al. 1998; Bhushan and Shadmehr 1999).

At first sight this latter scheme looks similar to our model, with the feed-forward part corresponding to the collicular pathway and the feedback part corresponding to the cerebellar pathway. However, the similarity is deceiving, as that scheme requires a desired displacement signal (actually a desired trajectory signal), which is not available in our model. Thanks to this difference, our model does not require a spatial-to-temporal transformation between the SC and the brain stem, allowing a much simplified connectivity. Furthermore, in Fig. 7.8 the feed-forward pathway is used to assure that the behavior is accurate on average, while the feedback pathway takes care of the noise, perturbations, and, in the short term, changes in the plant. In our model, instead, the cerebellum takes care of both the accuracy and the consistency of the movements [which is consistent with the findings that, after cerebellar lesions, both the accuracy and the consistency of movements are lost (Optican and Robinson 1980; Robinson, et al. 1993)]. Accordingly, if the cerebellar pathway were suddenly removed, the movements generated would be inaccurate, even on average.

7.3 Experimental Evidence

Now that we have outlined what differentiates our model from others, the next question we need to address is whether there is any experimental evidence that can help us decide which scheme is more realistic. It turns out that there is some evidence, although it is somewhat indirect. First of all, it is well known
from both physiological recordings (Berthoz, et al. 1986), electrical stimulation experiments (Van Opstal, et al. 1990; Paré, et al. 1994; Stanford, et al. 1996), and lesion studies (Hikosaka and Wurtz 1985; Hikosaka and Wurtz 1986; Lee, et al. 1988; Aizawa and Wurtz 1998; Quaia, et al. 1998a), that the level of activation of the SC strongly influences the speed of the movement. Similarly, when saccades to moving targets are compared to identical saccades to stable targets, their dynamics are very different (Keller, et al. 1996). Now, if the SC were to encode only the location of the target and not the desired amplitude of the movement (as suggested by the experimental evidence reviewed above), and the desired displacement were explicitly computed downstream from the SC, there would be no rationale for such a relationship. In fact, as there is no reason to control the speed of the movement at all, if the saccadic system had available a desired displacement signal it would make sense to always produce a movement that is as fast as possible. Thus, both these facts argue against the use of a desired displacement signal as the input to the pulse generator, but are consistent with our hypothesis that the SC provides desired target (spatially coded) and directional drive (temporally coded) signals.

7.4 Advantages of a Non-Classical Controller

Although the simple observations summarized in the previous section support our theory, they certainly do not add up to conclusive evidence in favor of a non-conventional scheme like ours. However, we believe that our case can be considerably strengthen by looking at the phylogenetic advantages that our scheme has over others.

7.4.1 Computational Complexity

The first advantage of using a scheme like ours is that it considerably reduces the complexity of the system. As noted above, our model manages to generate accurate saccades without needing to compute a desired displacement signal.
The cerebellum does so by simply associating a certain pattern of inputs with a specific site of initial activation. The cerebellum only needs to learn this association, and to change it if errors arise. A previously experienced change in context can then lead to sudden changes in behavior, as it only requires the recall of a stored association. The task of computing the desired displacement is then reduced to a pattern recognition task, which the brain is very well suited to carry out.

Consider now a classic scheme that relies on the computation of the desired displacement signal, and then on comparing this signal with an estimate of the current displacement. Such a scheme could be implemented in two ways: the first would be to generate a temporal signal encoding the desired displacement, and then to compare this signal with a temporally coded estimate of the current displacement (readily available from sensory feedback or efference copy). This solution would work very well from the point of view of the performance of the system, but it would be extremely unreliable, as it would require the transformation of a spatial signal (encoding the location of the target) into a temporal signal (encoding the desired displacement). Such transformation would require a mathematical division between two dynamic signals. This operation is certainly easy to perform with an electronic circuit, but it would be very difficult to carry out (with the desired accuracy) using simple neurons. The alternative would be to use a scheme similar to our model of the cerebellum (i.e., an associative memory) to compute the desired displacement on a spatial map and to realize a spatial integrator (like we do in the FOR). This solution would certainly work, and the complexity would not be superior to that of our scheme, but its robustness to failure would be very low, as any lesion to the spatial integrator would be catastrophic (see below).

Another computational advantage of our scheme is that it does not rely on comparators, one of the cornerstones of classic feedback schemes. Comparators present two main problems for the brain: first, because the brain uses a mixture of temporally and spatially coded signals, the comparators would need to compare two signals differently encoded. This would require it to convert one of the two signals, which, as noted above, is no easy task. Second, any noise in
the reference signal would be transferred, as is, to the output, which does not work out very well in a system as noisy as the brain. Of course, in man-made systems there is no such mixed coding, and the noise is usually much lower. Thus it makes perfect sense that control theories rely heavily on comparators.

7.4.2 Sensitivity to Noise

Thanks to the extensive use of spatial codes, our scheme is also very robust to noise in individual elements. Fluctuations in single cell discharges have very little effect, because the output of both the SC and the cerebellum is the sum of the activity of a huge number of neurons. The only element sensitive to noise is thus the pulse generator (Fig. 7.1, MLBNs), where the discharge level is very high and the noise across neurons is likely to be correlated. However, the output of the pulse generator is under feedback control, and so such fluctuations are automatically compensated. In contrast, classic schemes often involve temporally coded signals outside the feedback loop. For example, the computation of the desired displacement is particularly critical, as noise at that stage propagates directly to the output.

7.4.3 Resistance to Failure

That the ability to make saccades is crucial to everyday life is witnessed by the peculiar characteristics of eye muscles, which are resistant to diseases such as dystrophies that devastate skeletal muscles (Porter, et al. 1995; Porter and Baker 1996). Accordingly, it is extremely important not to lose that ability because of damage to the controller. However, a characteristic common to all classic models is that they have almost no resistance to failure. If any one element goes, the ability to make saccades is lost. More importantly, each block is so complex and so critical, that, if it were to fail, it would be almost impossible for another structure to take over its functions. Even models with adaptive controllers can only compensate for simple changes in the gain of the circuit; they cannot overcome structural changes. In our scheme the situation
is very different. Virtually any block (besides the pulse generator) could be destroyed without causing massive deficits. For example, if either the FEF or LIP is damaged, the other can still provide the target location information to the SC. And even if they were both lesioned, a connection from visual cortex (or directly from the retina) could be sufficient to at least generate saccades to highly salient targets. Similarly, if the SC were to be lost, the FEF could still provide the target location to the cerebellum, and all that would be needed to evoke saccades would be a new mechanism to shut off the OPNs. Reinforcing the existing connections between FEF and the OPNs might be sufficient. This is possible because, at least for simple tasks, the role of the SC and the FEF is similar enough that, if one were to fail, only minor reorganizations would be needed for the other to take over. If the cerebellum were to be lesioned, things would be slightly worse, as the complexity of its function would make it impossible for another structure to replace it. However, the effects would not be devastating. Of course, the system would become purely feed-forward, so the accuracy, and consistency, of saccades would be lost. But at least saccades could still be made, and if the lesion were limited to only the vermis, some recovery, at least in the average behavior, would still be possible. The ability to compensate for the motion of a target would also be lost, but that is not a big loss, as saccades wouldn’t be accurate anyway. Only combined damages to at least two structures would completely obliterate saccades; but, as FEF, LIP, SC and cerebellum are far away from each other, it is highly unlikely that a lesion could do so without being fatal to the individual. Of course, destroying the pulse generator or the motoneurons in our model obliterates saccades, but this is consistent with experimental results (Cohen et al. 1968; Henn et al. 1984).

Thus, our model’s resistance to failure can be ascribed to three factors: first, no one block is vital to the functioning of the circuit. Second, the functionality is distributed across areas that are far apart in the brain. And third, the structure is such that one pathway (the collicular one) provides an approximate motor drive that is good enough for survival, while the other pathway (cerebellar) improves the movements’ accuracy and consistency.
7.5 Schemes Based on Learning Theories

In addition to the models based on control system theories, several models of neural control have been inspired by theories of learning in neural networks. These models, which put great emphasis on the role of the cerebellum, stem from the early work by Marr (1969), Grossberg (1969) and Albus (1971); two of the most influential theories in this group are those of Houk, Barto and colleagues (Houk 1989; Houk, et al. 1992; Berthier et al. 1993; Houk, et al. 1996; Houk 1997; Barto, et al. 1999) and of Grossberg and colleagues (Grossberg and Kuperstein 1989; Contreras-Vidal, et al. 1997), which we have described in some detail in the Background chapter.

In many respects these models are similar to ours: they are certainly neuromimetic (at least to the extent to which they reproduce the experimental data), and they share with our model many of the advantages outlined in the previous section. However, we have previously discussed (Section 2.4.2) how all those models fail to reproduce some critical experimental finding. Nevertheless, they have one important advantage as, especially in their most recent versions (Contreras-Vidal, et al. 1997; Barto, et al. 1999), they make testable predictions about the pattern of activities in Purkinje cells and interneurons (especially basket cells) in the cerebellar cortex. This is certainly a most desirable feature, that unfortunately at this stage our model lacks, but that we are planning to incorporate in the future.

7.6 Conclusions

The focus of this chapter was to show that our model of the saccadic system, while reproducing both realistic behavior and neurophysiological data, does not conform to classic control schemes.

We have also shown that a model like ours would have several advantages for the brain, such as its reduced complexity and its enhanced tolerance to partial failures. The downside is that the model does not produce ideal (i.e.,
optimal) movements, and it does not perfectly compensate for perturbations, but neither does the brain (Quaia, et al. 2000). However, both produce movements that are good enough to serve their purpose. Here lies the key to understanding the lack of conformance of our model, and perhaps the brain, to classic schemes: because there is a trade off between complexity and performance, it might be convenient to lose something in performance to reduce, perhaps greatly, the complexity of the system.

If this is the case, it does not mean that control system schemes are not helpful in our struggle to understand the brain. At the very least they are useful to clearly formulate the problems that the brain must solve, and they are the only option when very little physiological data are available. However, once a considerable body of data is available, we might be better served by changing our approach; instead of trying to fit the data into a classic scheme, it might be better to base a new scheme on the data and then figure out what missing pieces must be added to make the system work. In this stage the guiding principles would then mainly be circuit oriented (e.g., reduced complexity and increased robustness), as opposed to purely behavior oriented (e.g., optimal performance, by some measure).
Chapter 8

Future Directions

In this work we have presented a comprehensive model of the saccadic system. However, lots of work remains to be done, both to validate the model and to extend it. In this chapter we summarize both experimental tests aimed at validating our model, and what we regard as the most important unresolved issues.

8.1 Experimental Tests

8.1.1 Ocular Plant Model

We have already pointed out that preliminary results indicate that the activity of burst and motoneurons correlates better with the derivative of eye orientation than with the angular velocity of the eyes, as predicted by our model of the eye plant. However, several other experimental tests can be devised to further support our results regarding the role of the pulleys in simplifying the task of the neural controller.

For example, we could stimulate the sites that contain burst- and motoneurons while the animal fixates different targets. This should elucidate how
the axes of action of the extraocular muscles depend upon orbital eye position. Studies involving stimulation in these areas have been carried out repeatedly but, to the best of our knowledge, no systematic study of the dependence of the effect of stimulation on eye orientation has been published. Because of the fairly complicated organization of burst neurons controlling vertical movements (e.g., see Crawford and Vilis 1992), we think that it would be simpler to electrically stimulate either directly the motoneurons of individual muscles or the burst neurons that control the horizontal recti muscles.

Another test for the pulley hypothesis is represented by the surgical resection of the orbital pulleys. The effect of such a procedure on the steady-state and the dynamics of eye movements would certainly have a great value in evaluating the functional role of the pulleys. Demer and colleagues (1996) have shown that, even though displacement of the pulley of the medial rectus alone is probably not sufficient to cause strabismus (Clark, et al. 1998), surgical destruction of the pulleys can cause strabismus; however, the effects of such a procedure on the dynamics of the movement have yet to be investigated. This test would also have clinical relevance, as it would reveal the consequences of such a procedure if carried out on strabismic subjects.

8.1.2 Neural Controller

Thanks to its neuromimetic nature, our model of the neural controller makes several predictions that can be experimentally tested. Here we will just present those that are easier to carry out.

Activity of FOR Neurons

We have conjectured that the FOR is topographically organized, and that a spatial integration is performed in the vermis and represented on the fastigial map. While we have shown that all the input/output connections needed are in place, several testable predictions can be made about the pattern of activity in FOR neurons:
8.1. EXPERIMENTAL TESTS

1. The ipsilateral burst should occur later and later for larger and larger saccades.

2. For contralateral saccades, the timing of the burst should depend on both the saccadic vector and the location of the cell on the fastigial map.

3. It should be possible to find cells that burst only for contralateral saccades larger than a given amplitude.

4. Adaptive alteration of saccadic size should alter the time of occurrence of the ipsilateral burst, which should remain time-locked to the end of the movement, not its intensity.

5. In analogy with what has been done in the SC (Keller and Edelman 1994), it would be very interesting to observe how the activity of fastigial neurons changes during interrupted saccades. Our model predicts that, under those conditions, the contralateral burst would be prolonged and the ipsilateral burst would be delayed to preserve its timing relative to the end of the movement.

6. For saccades to moving targets, the fastigial site initially activated should correlate more with the metrics of the actual movement than with the location of the target (the opposite of what has been found in the SC).

Because of the short duration of saccades, to test these predictions the activity of FOR cells should be observed during saccades of very different amplitude. Unfortunately, the majority of the studies on FOR activity dealt principally with saccades smaller that 20°; nonetheless, some evidence in support of the first (e.g., Ohtsuka and Noda 1991), third (Fuchs, et al. 1993) and fourth (Scudder 1998) predictions is already available.

Activity of Medium Lead Burst Neurons

The discharge and connectivity of FOR neurons to MLBNs raise some expectations regarding the activity present in MLBNs during saccades. More
specifically, the late burst present in the ipsilateral FOR should induce, toward the end of a saccade, a discharge in the contralateral EBNs and IBNs. In fact, evidence for a late burst in at least some EBNs for contralateral movements has been reported (Keller 1974; Van Gisbergen et al. 1981; Strassman, et al. 1986a). This burst is pretty weak, but that is in line with our prediction: we do not expect these neurons to discharge more than 200 spikes/s, and for no more than 20 ms or so [because of the reactivation of the OPNs (Fuchs et al. 1991; Everling, et al. 1998; Paré and Guitton 1998)]. Thus, only 3 or 4 spikes are expected. This late discharge is exhibited also by a sizable subset of the IBNs (Strassman, et al. 1986b; Scudder et al. 1988), and appears to be stronger, as predicted by our model.

Unfortunately, even though it is clear that IBNs are activated later for contralateral than for ipsilateral saccades, it has not been ascertained whether the burst for contralateral movements is time-locked with the end of the saccade (i.e., it lags saccade onset more and more for larger and larger saccades). Thus, although experimental recordings in these regions support (or at least are compatible with) our interpretation, further exploration is needed for a definitive answer.

Effects of Lesions

We have shown by means of simulations how our model can replicate the effects of lesions in several brain lesions. In addition, we can also make some predictions about the effects of other lesions. For example, it would be interesting to verify the effects of collicular electrical stimulation combined with complete FOR lesions. Our model would predict that the removal of the choke signal normally provided by the FOR paired with the lack of a sizable decay of the collicular output (because of the sustained stimulation) should suppress the generation of staircases, and the eyes should keep turning as long as the electrical stimulation is applied (up to the oculomotor limit).

Another prediction of our model is that lesions of the cerebellum should cause the disruption of the directional control of saccades. Note that this does
not mean that after cerebellar lesions saccades should be straight, but only that the curvature should not indicate the systematic redirection of the eyes toward the target observed in normal subjects (Quaia, et al. 2000). Unfortunately, no systematic study on the curvature of saccades after cerebellar lesions has been carried out, but the data appears to be consistent with the lack of a directional control [for example, see (Robinson, et al. 1993), their Fig. 10 and (Vilis and Hore 1981), their Fig. 7].

It would be more difficult to predict the effects of vermal lesions, as we don’t yet have a real implementation of the vermis. However, we would certainly expect that the feedback compensation would be disrupted, causing a marked increase in the variability of saccades. Also, as a lesion of the vermis would cause an overall disinhibition of the FOR, on average saccades should become hypometric. Such hypometria could be corrected in the long term by reducing the inhibitory action of the FOR on the collicular activity, but we would not expect the variability to disappear, even in the long term. The ability to make accurate movements to moving targets should also be lost. Results in agreement with these prediction have in fact recently appeared (Takagi, et al. 1998; Barash et al. 1999).

Finally, lesions to the NRTP are also expected to have important effects, as this area relays the target location signal to the cerebellum and in turn receives projections from the cerebellum.

8.2 Unresolved Issues

Besides the experiments described above, which are aimed at testing our model, lots of work remains to be done to extend the model and more generally to further our understanding of the saccadic system.
8.2.1 Experimental Projects

Clearly at this point the vermis represents one of the least understood areas of the saccadic system. While almost everything is known about the anatomy of the cerebellar cortex (e.g., see Eccles et al. 1967), we know very little about its functioning. Even worse, in the case of the part of the vermis involved in the control of saccades the data available is not only scarce but it is also contradictory. Accordingly, a thorough study of the activity of vermal neurons during saccades is in order.

Other interesting experiments involve the oculomotor plant. For example, it is still unclear to what extent the extraocular pulleys move as a function of eye position, and whether there is also a pulley for the inferior oblique muscle. In addition, an accurate estimate of the mechanical properties of the orbital tissues is still lacking, as the early experiments carried out in human subjects have a few flaws (e.g., only the horizontal recti muscles had been detached from the globe, which means that some of the stiffness observed could have been due to the vertical/oblique muscles).

8.2.2 Modeling Projects

While the model we have presented in this work covers a lot of ground, there are still quite a few aspects of the saccadic system that we have not investigated thoroughly enough.

For example, we would be very interested in simulating the behavior of the model when electrical stimulation of any area is delivered during an on-going saccade. Experiments of this kind (so-called colliding saccades) have already been carried out, and we believe that our model should be able to reproduce their outcome. Unfortunately, our current implementation of the model is not well suited for carrying out such simulations, and it will need to be modified accordingly.

Another project in its own right is represented by the pairing of our model of the controller with an implementation of a model of the plant that closely
matches the actual orbital geometry (remember that here we have used a more symmetric model of the plant). The major problem that would have to be addressed would then be that of determining the proper innervation for vertical and oblique muscles, which act in non-orthogonal planes. As this could turn out to be more complex than expected, it might be worthwhile to implement a model of the controller that is actually able to automatically learn the appropriate projection strength.

Finally, it would be extremely important to investigate the ability of the model to modify itself in response to changes in the periphery or to behavioral conditions. This would require the introduction in the model of some unsupervised learning scheme, which should make use only of information readily available to the actual saccadic system (e.g., proprioceptive signals from the extraocular muscles, retinal error, retinal slip). While this last project is certainly the most complex, it is also the one that could yield the most profound insights.
Bioengineering is important because organisms are existence proofs for solutions to vexing problems (e.g., movement control and coordination, vision, learning) that engineers would like to solve. In the past, though, the approach to studying organisms, and more specifically their brains, has been to perform an input-output analysis and then to make a synthesis of the system using classic engineering models. Accordingly, throughout history the brain has been associated with the most complex man-made machines of the time. Thus, the brain has been looked upon as a steam engine, a telephone switch-board, a computer, a Kalman filter, etc. However, over the last two decades the biological understanding of the brain has progressed beyond simple input-output descriptions, to looking inside the black box. Needless to say, insights from these studies are very valuable because they reveal the mechanisms behind such well-developed behaviors as vision and movement control.

In this study we took this new approach to the extreme, designing a model of the saccadic system that not only matches the performance of the saccadic system of primates, but that also mimics actual neural activity and organization. While doing so we came to realize that a key step toward achieving our goal was to perform a detailed analysis of the oculomotor plant, which led to some important and novel results. Particularly interesting was the unveiling
Figure 9.1: Block diagram of our neuromimetic model of the saccadic system.

of the role of the pulleys, which showed us that Nature goes to considerable length to simplify the task of the neural controller. This finding reinforced our belief that a key design constraint for the controller had to be the reduced complexity of the neural operations and circuitry.

Following these design principles, which are usually not very prominent in the mind of the control engineer, we designed a neuromimetic model of the saccadic system that, while reproducing human-like behavior down to its suboptimal characteristics, is also able to replicate a wide body of anatomical and physiological data. The close parallel between our model and the actual saccadic system prompted us to carry out a detailed post-hoc analysis of our model, which revealed that it does not conform to any classic control scheme. More precisely, from a block diagram of the model (see Fig. 9.1) it appears clear that the model lacks a signal describing the desired movement, as well as any comparator, both cornerstones of classic control schemes. Such a non-classical model suggests that the encoding of movement signals in the
brain may occur in a completely unorthodox way, one that does not internalize the physical signals (e.g., desired displacement, motor error) associated with the movement. Instead, intrinsic brain signals may represent desired sensory states, approximate motor drives, and distributed motor commands. Furthermore, this analysis led us to infer from our model some general principles about the neural control of movement, and to conclude that a non-classical controller has more advantages than disadvantages for the brain, given its requirements and implementation restrictions.

Another positive aspect of our model, and of neuromimetic models in general, is that it can be a valuable tool for the experimenter. In fact, when the internal signals in the model can be precisely related to brain structures, it becomes much easier to test the model; this is particularly important if we consider that the same neurons can carry more than one signal, as the collicular neurons do in our model. Also, the model can better highlight gaps in the available data, such as the organization and structure of the vermis and caudal fastigial nucleus.

Of course, this particular model may not represent how the brain actually controls saccadic eye movements. However, it demonstrates that it is possible for the brain to control movements using mechanisms that do not conform to any classic control scheme, and it shows that neuromimetic models can be powerful tools in the quest for understanding the brain. Also it suggests that the development of engineering devices that do not directly internalize physical signals may be fruitful, as it may lead to a new emphasis on problem solving through structural design, rather than algorithmic design.
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