A MODEL FOR THE TRANSLATIONAL VESTIBULO-OCULAR REFLEX

by

Wissam Musallam

A thesis submitted in conformity of the requirements for the degree of Master of Science
Department of Physiology
University of Toronto

© Copyright by Wissam Musallam 1997
The author has granted a non-exclusive licence allowing the National Library of Canada to reproduce, loan, distribute or sell copies of this thesis in microform, paper or electronic formats.

The author retains ownership of the copyright in this thesis. Neither the thesis nor substantial extracts from it may be printed or otherwise reproduced without the author’s permission.

L’auteur a accordé une licence non exclusive permettant à la Bibliothèque nationale du Canada de reproduire, prêter, distribuer ou vendre des copies de cette thèse sous la forme de microfiche/film, de reproduction sur papier ou sur format électronique.

L’auteur conserve la propriété du droit d’auteur qui protège cette thèse. Ni la thèse ni des extraits substantiels de celle-ci ne doivent être imprimés ou autrement reproduits sans son autorisation.
ABSTRACT
A MODEL FOR THE TRANSLATIONAL
VESTIBULO-OCULAR REFLEX

Wissam Musallam
Master of Science
1997

Department of Physiology
University of Toronto

The vestibular system is the system of balance. The vestibulo-ocular reflex (VOR) moves the eyes in response to head movements by using information from the angular motion detectors, the semi-circular canals (AVOR), and linear motion detectors, the otolith organs (TVOR). In order to move the eyes, the oculomotor neurons are known to require signals in phase with velocity and position. However, the primary afferent signal carrying information from the otolith organs is in phase with acceleration. To complicate matters, the TVOR is a function of target distance and target position and the otoliths are also sensitive to gravity. The model in this thesis differentiates the primary afferent signal making it in phase with velocity. The signal's gain is then adjusted and is merged with the canal signal and it is the combination of the two signals that will reach the motor neurons.

Tilts on the other hand cause the gravity vector to shift with the respect to the otolith organs. How do central mechanisms differentiate between an imposed tilt and an imposed linear acceleration? We have proposed that if both the otolith organs, the utricle and the saccule, are taken into account, then the ambiguity in the signal is removed. A simple function is presented that considers different cases of tilt and translations and eliminates any ambiguity.
ACKNOWLEDGMENTS

I would like to thank Dr. David Tomlinson for his endless advice, support, and understanding. Dr. Tomlinson showed me the patience of a kindhearted person and I am very grateful to him. I have benefited greatly from being in his lab, both as a student and as a person. I am thankful for the freedom he gave me to learn on my own and the support he provided along the way.

I would also like to thank Mary and my parents, Suleiman and Siham, for their endless support, Peter for his inspiring belief in me, and Irene for making it all mean something.
TABLE OF CONTENTS

Acknowledgments.................................................................................................................. iii
List of Tables.......................................................................................................................... vi
List of Figures ........................................................................................................................ vii
List of Appendices ................................................................................................................... ix
List of Abbreviations .............................................................................................................. x

1.0 Introduction ....................................................................................................................... 1
  1.1 Peripheral Vestibular Organs ......................................................................................... 2
    1.1.1 Blood Supply ...................................................................................................... 2
    1.1.2 Hair Cells .......................................................................................................... 2
    1.1.3 The Semicircular Canals .................................................................................... 3
      1.1.3.1 Structure ..................................................................................................... 5
      1.1.3.2 Mechanics .................................................................................................... 5
    1.1.4 The Otolith Organs .............................................................................................. 8
      1.1.4.1 Sensitivity Vectors ..................................................................................... 8
      1.1.4.2 Mechanics .................................................................................................. 10
  1.2 Innervation of the Peripheral Vestibular System ............................................................... 11
    1.2.1 Efferent Fibers .................................................................................................. 11
    1.2.2 Primary afferents ............................................................................................... 12
      1.2.2.1 Canal Primary afferents ........................................................................... 15
      1.2.2.2 Otolith Primary Afferents ......................................................................... 15
    1.2.3 Primary Afferent Input To The Vestibular Nuclei .................................................. 20
  1.3 Extraocular Muscles ........................................................................................................ 21
  1.4 The Vestibulo-Ocular Reflex .......................................................................................... 24
    1.4.1 Oculomotor Neurons .......................................................................................... 25
    1.4.2 Pathways Linking the Horizontal Canals to the Oculomotor Neurons ................ 26
    1.4.3 AVOR .............................................................................................................. 26
    1.4.4 TVOR ............................................................................................................... 28
      1.4.4.1. Dependence of the TVOR on Target Position and Distance ..................... 29
      1.4.4.2 AVOR-TVOR Interaction ......................................................................... 31
  1.5 Cells in the Vestibular Nuclei Mediating the VOR .......................................................... 34
    1.5.1 PVP Cells ......................................................................................................... 34
    1.5.2 EHV Cells ........................................................................................................ 35
    1.5.3 Otolith Only, Canal Only, and Canal Otolith Cells. ............................................. 36
  1.6 Models of the VOR ........................................................................................................ 36
    1.6.1 Robinson's Model of the AVOR ................................................................. 36
    1.6.2 Models of the TVOR ...................................................................................... 36
  1.7 Cancellation, suppression and adaptation ........................................................................ 38
  2.0 Methods ............................................................................................................................ 40
    2.1 Oculomotor Neurons ................................................................................................. 40
      2.1.1 Transfer function of an oculomotor neuron .................................................... 41
    2.2 The Model ............................................................................................................... 43
3.1 Differences Between Tilts and Translations ........................................ 51
3.2 H3[s]............................................................................................. 53
3.3 H1[s]............................................................................................. 54
3.4 H2[s,w]........................................................................................ 58
3.5 Output of H1 and H2 ................................................................. 62
3.6 AVOR-TVOR Interaction ......................................................... 67
4.0 Discussion .................................................................................... 70
  4.1 Predictions and experiments ................................................... 74
Appendix A ..................................................................................... 84
Appendix B ..................................................................................... 85
REFERENCES .................................................................................. 87
LIST OF TABLES

Table 1.1  Approximate on direction of Canals  14
Table 1.2  Primary afferent projection onto the Vestibular Nuclei  31
Table 1.3  Effects of right eye muscle activation  33
Table 1.4  Primary effect of canal stimulation  34
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1.1</td>
<td>Orientation of the semicircular canals</td>
<td>4</td>
</tr>
<tr>
<td>Figure 1.2</td>
<td>Cupula deflection of the hair cells</td>
<td>6</td>
</tr>
<tr>
<td>Figure 1.3</td>
<td>Gain and phase of canal primary afferents</td>
<td>9</td>
</tr>
<tr>
<td>Figure 1.4</td>
<td>Orientation of the utricle and saccule</td>
<td>10</td>
</tr>
<tr>
<td>Figure 1.5</td>
<td>Histogram of the coefficient of Variations</td>
<td>14</td>
</tr>
<tr>
<td>Figure 1.6</td>
<td>Adaptation of an Irregular afferent</td>
<td>16</td>
</tr>
<tr>
<td>Figure 1.7</td>
<td>Bode plots for Regular otolith primary afferents</td>
<td>17</td>
</tr>
<tr>
<td>Figure 1.8</td>
<td>Bode plots for Irregular otolith primary afferents</td>
<td>19</td>
</tr>
<tr>
<td>Figure 1.9</td>
<td>The vestibular nuclei and its innervations</td>
<td>22</td>
</tr>
<tr>
<td>Figure 1.10</td>
<td>Muscular innervation of the right eye</td>
<td>22</td>
</tr>
<tr>
<td>Figure 1.11</td>
<td>Horizontal canal excitatory projections</td>
<td>27</td>
</tr>
<tr>
<td>Figure 1.12</td>
<td>The dependence of the TVOR on target distance</td>
<td>27</td>
</tr>
<tr>
<td>Figure 1.13</td>
<td>Signal ambiguity in the otolith organs</td>
<td>30</td>
</tr>
<tr>
<td>Figure 1.14</td>
<td>Disjunctive eye movements</td>
<td>30</td>
</tr>
<tr>
<td>Figure 1.15</td>
<td>Eccentric rotation</td>
<td>32</td>
</tr>
<tr>
<td>Figure 1.16</td>
<td>Eye position for eccentric rotation for different vergence angles</td>
<td>33</td>
</tr>
<tr>
<td>Figure 1.17</td>
<td>Robinson's model for visual-vestibular interaction</td>
<td>37</td>
</tr>
<tr>
<td>Figure 2.1</td>
<td>Bode plot for an oculomotor neuron</td>
<td>42</td>
</tr>
<tr>
<td>Figure 2.2</td>
<td>A model for the TVOR</td>
<td>47</td>
</tr>
<tr>
<td>Figure 2.3</td>
<td>Program that simulates the model in figure 2.2</td>
<td>48</td>
</tr>
<tr>
<td>Figure 3.1</td>
<td>Torsional eye produced by the model compared with experimental values</td>
<td>55</td>
</tr>
<tr>
<td>Figure 3.2</td>
<td>Bode plot of $H_1(s)$</td>
<td>56</td>
</tr>
<tr>
<td>Figure 3.3</td>
<td>Bode plot of $H_1(s)$ cascaded with otolith primary afferents</td>
<td>57</td>
</tr>
<tr>
<td>Figure 3.4</td>
<td>Bode plot of $H_1(s)$</td>
<td>60</td>
</tr>
<tr>
<td>Figure 3.5</td>
<td>Bode plot of $H_1(s)$ cascaded with otolith primary afferents</td>
<td>61</td>
</tr>
<tr>
<td>Figure 3.6</td>
<td>Output of the model for various vergence angles</td>
<td>63</td>
</tr>
</tbody>
</table>
Figure 3.7  Model's eye velocity divided by theoretical eye velocity 65
Figure 3.8  Sensitivities vs. Frequency of the TVOR 66
Figure 3.9  Sensitivities vs. Vergence of the TVOR 66
Figure 3.10  Firing rates of central canal and otolith neurons 68

Figure 4.1  Slow phase eye velocity produced by the model 72
Figure 4.2  Torsional amplitudes for various frequencies 75
# LIST OF APPENDICES

<table>
<thead>
<tr>
<th>Appendix 1</th>
<th>Proof that $F(\theta,a) &gt; 0$</th>
<th>83</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendix 2</td>
<td>List of parameters</td>
<td>84</td>
</tr>
</tbody>
</table>
# LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATD</td>
<td>Ascending Tract of Deiters</td>
</tr>
<tr>
<td>AVOR</td>
<td>Angular Vestibulo-Ocular Reflex</td>
</tr>
<tr>
<td>CA</td>
<td>Canal Only</td>
</tr>
<tr>
<td>CAOT</td>
<td>Canal-Otolith</td>
</tr>
<tr>
<td>EHV</td>
<td>Eye Head Velocity</td>
</tr>
<tr>
<td>EPSP</td>
<td>Excitatory Post-Synaptic Potential</td>
</tr>
<tr>
<td>FTN</td>
<td>Floccular Target Neurons</td>
</tr>
<tr>
<td>g</td>
<td>$9.8m/s^2$</td>
</tr>
<tr>
<td>IO</td>
<td>Inferior Oblique</td>
</tr>
<tr>
<td>IR</td>
<td>Inferior Rectus</td>
</tr>
<tr>
<td>LR</td>
<td>Lateral Rectus</td>
</tr>
<tr>
<td>LVOR</td>
<td>Linear Vestibulo-Ocular Reflex</td>
</tr>
<tr>
<td>MA</td>
<td>Meter Angles</td>
</tr>
<tr>
<td>MLF</td>
<td>Medial Longitudinal Fasciculus</td>
</tr>
<tr>
<td>MR</td>
<td>Medial Rectus</td>
</tr>
<tr>
<td>OT</td>
<td>Otolith Only</td>
</tr>
<tr>
<td>OVAR</td>
<td>Off Vertical Axis Rotation</td>
</tr>
<tr>
<td>PVP</td>
<td>Position-Vestibular-Pause</td>
</tr>
<tr>
<td>SO</td>
<td>Superior Oblique</td>
</tr>
<tr>
<td>SR</td>
<td>Superior Rectus</td>
</tr>
<tr>
<td>TVOR</td>
<td>Translational Vestibulo-Ocular Reflex</td>
</tr>
<tr>
<td>VN</td>
<td>Vestibular Nuclei</td>
</tr>
<tr>
<td>VOR</td>
<td>Vestibulo-Ocular Reflex</td>
</tr>
<tr>
<td>COV</td>
<td>Coefficient of Variation</td>
</tr>
</tbody>
</table>
Chapter 1

1.0 INTRODUCTION

The vestibular system is the system of balance and is necessary for clear vision. It is responsible for moving the eyes so as to compensate for motion of the head and body. This is accomplished by using head movement information supplied by the vestibular labyrinth. When the head is rotated in one direction, the vestibulo-ocular reflex (VOR) generates a compensatory eye movement that is in the opposite direction leaving the direction of the visual axis unchanged. Failure of the VOR results in a movement of retinal images during head movement and in a marked decrease in visual acuity.

The vestibular system is divided into two distinct sensory organs; the semicircular canals, which sense head rotation, and the otolith organs, which sense linear head movement. Because of this distinction between stimuli, the VOR can also be subdivided into two classes: the Translational VOR (TVOR, also known as the Linear VOR (LVOR)) which is mediated by the otolith organs, and the Angular VOR (AVOR) which is mediated by the semicircular canals. Other vestibular reflexes include the vestibulo-colic reflex, which activates neck muscles, and the postural reflexes which active the lower limbs. The vestibular response to head rotation, or the AVOR, is probably the most thoroughly studied of all eye movement systems and thus clinical testing that can assess canal function is routine. However, due to a lack of basic research into the mechanism of otolith function, a clear diagnosis of otolith pathology cannot currently be made.

The work in this thesis grew out of the interesting question of how the vestibular nuclei process signals that originate in the otolith organs. A model has been written that takes as input linear acceleration, processes it, and produces an output in phase with eye velocity.
1.1 PERIPHERAL VESTIBULAR ORGANS

The vestibule is located in the inner ear at the base of the skull just posterior to the cochlea which is connected to the vestibule by the ductus reuniens. The vestibular system functions as a sensor of head motion, responding to head acceleration. Each ear has three semicircular canals: a horizontal, anterior and posterior canal, and two otolith organs, the utricle and the saccule. Both of these organs are capable of generating a VOR (Lysakowski et al., 1993).

Information about head movement is carried by the eighth nerve, which enters the vestibule via Scarpa's ganglion from the internal auditory meatus. The vestibular (Scarpa's) ganglion is divided into a superior and an inferior section. The superior vestibular nerve associated with the superior portion of Scarpa's ganglion supplies the anterior and horizontal canal and the utricle, while the inferior vestibular nerve supplies the posterior nerve and the saccule (Lysakowski et al., 1993).

1.1.1 Blood Supply

Blood supply to the vestibular end organs is through the internal auditory artery, which becomes the anterior vestibular artery and the common cochlear artery. The anterior vestibular artery provides the blood supply to most of the utricle and to the superior and horizontal canals and to a small portion of the saccule. The common cochlear artery divides into the proper cochlear artery and the vestibulocochlear artery, which gives rise to the posterior vestibular artery. The latter supplies primarily the posterior canal and the saccule (Lysakowski et al., 1993).

1.1.2 Hair Cells

Information from the vestibular system is initiated by movement of cilia on hair cells (See section 1.1.3.1). The hair cells are mechanoreceptors with a resting membrane potential of about -60 mV. The mechanoreceptive organelles of the hair cells is a stereocilia bundle numbering 40 to 200 and arranged in a staircase pattern bounded at the tallest end by a single kinocilium. Deflection of the stereocilia towards the kinocilium depolarizes the hair cell decreasing the potential to about -40mV; deflection away from the kinocilium hyperpolarizes it to -64 mV, and a stimulus directed perpendicular to the kinocilium should elicit no response.
This rectification greatly emphasizes the excitatory response making the cell morphologically polarized. Depolarizing the hair cell leads to primary afferent activation. Thus a functional polarization vector exists as well (Schwarz and Tomlinson, 1993).

The hair cells are divided into Type I and Type II cells. Type I hair cells are flask shaped, and are concentrated in the center of the neuroepithelium in the monkey. They are innervated by a calyx shaped dendritic afferent and generally gives rise to an irregular firing rate (see section 1.2.1) and can be innervated by efferent synapses (Fernandez et al., 1990). Type II hair cells are phylogenetically older and are located mostly in the periphery of the neuroepithelium. They are cylindrical in shape, are innervated by bouton endings, and generally give rise to regular firing rates (see section 1.2.1).

1.1.3 The Semicircular Canals

The semicircular canals are arranged as a set of three mutually orthogonal sensors with each canal being maximally sensitive to rotations that lie in the plane of that canal. The response of each canal is proportional to the cosine of the angle between the plane of head rotation and the plane of the canal (Leigh and Zee, 1991). There are two vertical canals on each side, the anterior and posterior, that lie perpendicular to each other and are oriented roughly 45 degrees to the sagittal plane, and one horizontal canal tilted upward about 30 degrees (Figure 1.1) (Lysakowski et al., 1993). The canals are organized as functional pairs. The anterior canal on one side is paired with the posterior on the opposite side while the horizontal canals form a synergistic pair (Table 1.1) (Leigh and Zee, 1991).
Figure 1.1 Orientation of the semicircular canals. The three canals on each side of the head are mutually orthogonal to each other. The Left AC and the Right PC form a synergistic pair. Likewise for the Right AC and the Left PC. The Lateral Canals also form a synergistic pair and are tilted 30 degrees from the horizontal in the upright position.

<table>
<thead>
<tr>
<th></th>
<th>YAW right</th>
<th>YAW left</th>
<th>PITCH forward</th>
<th>PITCH backward</th>
<th>ROLL right</th>
<th>ROLL left</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hor Right</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>Hor Left</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Sup Right</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>Post Left</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Sup Left</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>Post Right</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 1.1 Approximate 'ON' direction of canals. +:stimulation. -:inhibition. For a particular movement (yaw, pitch or roll), conjugate pairs are activated for all directions of that movements, so that sensation occurs in any direction. Conjugate pairs are indicated by the same row number.
1.1.3.1 Structure

The semicircular canals can be thought of as a thin circular tube filled with endolymph that is secreted by specialized cells in each sensory organ similar to the stria vascularis of the cochlea. At one end of each canal is an enlargement known as the ampulla, which contains the cupula and the sensory epithelium (figure 1.2a). The lumen of the canals is occluded by the cupula, a gelatinous membrane which protrudes into the ampulla spanning the entire cross section of the canal so that it stops the endolymph from flowing past it (Hillman, 1979). The cupula is bent by the relative flow of the endolymph during head rotation. The three semicircular canals converge upon the utricle which provides a fluid continuity among the three canals. Since the saccule is in fluid continuity with the utricle, then by association, it also is in continuity with the canals (Wilson & Jones, 1979).

At the bottom of the ampulla lies the crista ampullaris, the neuroepithelium that gives rise to the hair cells embedded in the cupula. The processes of each hair cells that lie in the crista consists of many stereocilia and one kinocilium aligned so that they respond to cupula bending in a specific orientation. It is the bending of the cupula that stimulates the hair cells that lie in its base leading to the firing of the vestibular primary afferent neurons (Lysakowski et al., 1993). Deflection of the stereocilia towards the kinocilium causes depolarization of the hair cell; deflection in the opposite direction causes hyperpolarization (figure 1.2b).

1.1.3.2 Mechanics

The crista and the surrounding endolymph have been likened to an overdamped torsion pendulum (Wilson and Melville Jones, 1979). The diameter of the semi-circular canals is small compared to their curvature (Leigh and Zee, 1991) so that when the canal is rotated, the fluid lags behind because of its inertia. This causes the flow of the endolymph to be proportional to head velocity making the canals integrating accelerometers. The idea that the canals mechanically integrate head acceleration has been confirmed electrophysiologically (Goldberg and Fernandez, 1971).
FIGURE 1.2a Hair cells protrude from the crista into the cupula. When the head rotates, the endolymph pushes on the cupula which in turn deflects the hair cells embedded in it.

FIGURE 1.2b Deflection of the stereocilia (short lines) towards the kinocilium (dark lines) causes depolarization (right hair cell). Deflection away from the kinocilium (left hair cell) causes hyperpolarization.
The mechanics of cupular and endolymph displacement have been described by a torsion-pendulum model (Steinhause, 1933):

\[
I \frac{d^2q}{dt^2} = I \frac{d^2E}{dt^2} + B \frac{dE}{dt} + kE
\]  

(1.1)

where \( I = 2.54 \times 10^4 \text{g/cm} \) is the moment of inertia, \( q \) is the angular displacement of the head (or canal) in radians, \( B = .08 \) poise is the viscous damping couple, \( k = .008-.016 \text{ g/cm}^2\text{s}^2 \) is the elastic restoring force of the cupula and \( E \) is the angular displacement of the cupula relative to the canal in radians (Schwarz and Tomlinson, 1993). Equation 1.1 relates the angular deflection of the cupula to the angular acceleration of the head. The response of the cupula is characterized by two time constants; \( \tau_1 = L/B \) and \( \tau_2 = B/k \). \( \tau_1 \) defines the minimum duration of the stimulus which can accurately be transduced by the canals and has been calculated to be 3 ms. \( \tau_2 \) is the time constant of the cupula's return to its resting point. Since \( k \) cannot be measured directly, the value of \( \tau_2 \) has been inferred from primary afferent activity and its current accepted value is about 6 seconds (Schwarz and Tomlinson, 1993).

The variables in the torsion-pendulum model are related to canal dimensions which vary across species. Large animals tend to be sluggish and require a more sensitive peripheral apparatus with longer time constants. This is accomplished by having a large radius of curvature along with a large lumen radius.

There is one drawback to equation 1.1. The angular acceleration stimulus is integrated reasonably well for physiological frequencies and one would expect the primary afferent gain and phase to follow the movement of the cupula fairly well. However, at higher frequencies, primary afferent behaviour show a gain increase and a consistent phase lead throughout the frequency range (figure 1.3) (Femandez & Goldberg, 1971). Rabbit and Damiano (1991) modeled the cupula as an elastic plate and the endolymph as an incompressible Newtonian fluid governed by the Navier-Stokes and continuity equations. They took into account the frequency dependence of the endolymph velocity distribution and the fluid structure interaction at the cupula. Although they ran simulations using data from human infants, their results follow the experimental findings of Fernandez & Goldberg (1971). However, sensory receptors are
generally sensitive to both the stimulus and its rate of change mediated by synaptic dynamics. In the vestibular system this would appear as a high frequency gain increase and phase lead. Therefore, since equation 1.1 does not take into account synaptic mechanisms, we cannot assume that it does not correctly model the endolymph-cupula interaction.

1.1.4 The Otolith Organs

The otolith organs sense linear acceleration in contrast to the semicircular canals, which sense angular acceleration. They are endolymph filled sacs with a sensory epithelium known as the macula. The utricular macula lies approximately in the horizontal plane and its anterior portion is tilted up about 25 to 30 degrees such that normal head position would orient it somewhat horizontally. It can best detect either fore and aft or lateral translations of the head and tilts of the head. The saccular macula lies parallel to the sagittal plane perpendicular to the utricle with its lowest end deflected laterally by 18 degrees. It can best detect up and down translations and tilts of the head. The hair cells in the macula protrude into a gelatinous matrix in which calcium carbonate crystals (otoconia) are embedded. Due to the otoconia, the specific gravity of the otolithic membrane is about 2.7 times greater than the surrounding endolymph (Money et al., 1971). This results in a greater inertia, and causes a displacement of the membrane, and thus a deflection of the hair cells, in the direction opposite to an imposed linear acceleration.

1.1.4.1 Sensitivity Vectors

The macula is divided down the midline by a thin stripe known as the striola. The directional sensitivities of the hair cells point towards the striola in the utricle and away from the striola in the saccule (figure 1.4). Directional sensitivities are in line with the morphological sensitivities that will be described in section 1.2.3. Deflection of the cilia along its directional axis leads to maximal excitation. At other angles of deflection, the response amplitude is proportional to the response along the directional axis multiplied by the cosine of the angle. Unlike the canals, hair cells in the macula of the utricle and saccule do not face a single direction. Linear accelerations in all directions could activate some hair cells and inhibit others (Schwarz and Tomlinson, 1993).
This dual signal might aid the brain in discerning the direction of movement.

Although it has been suggested that the otolith organs might respond to angular accelerations since such a stimulus would cause a torsional motion of the membrane, Goldberg & Fernandez, (1975) found that otolith neurons are unaffected by angular accelerations. This can be explained if the membrane has a high torsional rigidity, or because torsional movements induced by angular accelerations would deflect most sensory hair cells in a direction perpendicular to their polarization axes which is presumably ineffective.

Figure 1.3 Gain and phase in the frequency domain of canal primary afferents. The solid lines are theoretical values while the dotted lines are the results of experimental data and deviate from the values predicted by equation 1.1. Experimental values from Fernandez & Goldberg, (1971) (Adapted from Milsum, 1966).
Figure 1.4. Orientation of the utricle and the saccule in the right side from the subject's point of view. Hair cells in the saccule point away from the striola (midline), while those in the utricle point towards the striola. In the upright position, the hair cells ventral to the striola in the saccule are continuously excited due to the presence or the gravity vector. The otolith organs on the contralateral side are the mirror image of the picture presented here. So a translation towards the right will excite the hair cells that are lateral to the striola of the utricle in the right side and excite the hair cells that are medial to the striola in the left side.

1.1.4.2 Mechanics

The mechanics of the otolith membrane can been described by (Goldberg & Fernandez, 1975):

$$\frac{d^2 x}{dt^2} + \frac{b}{m_e} \frac{dx}{dt} + \frac{k}{m_e} x = \alpha(t) \rho$$  \hspace{1cm} (1.2)

relating otolith displacement $x(t)$ to input acceleration $\alpha(t)$. $m_e$ is the effective mass of the otolith membrane ($1.9 \times 10^4$ g), $\rho = \frac{\rho_0 - \rho_e}{\rho_0 + \rho_e} = 320$ is the density of the otolith membrane relative
to the density of the endolymph, $b$ is a viscous damping constant (1 g/s), and $k$ is the spring constant (1200 dynes/cm). The smallest detectable displacement of the otolith membrane $x(t)$ that can be detected by humans is $10^{-6}$ cm. This corresponds to a human threshold for perception of linear acceleration of $2 \times 10^{-2}$ g (Grabiel et al., 1955).

**1.2 INNERVATION OF THE PERIPHERAL VESTIBULAR SYSTEM**

The Vestibular system is innervated by both afferent and efferent fibers in the eight cranial nerve. The bipolar cells that make up the afferent fibers have their cell bodies in Scarpa's ganglion (see section 1.2). These cells will be discussed in detail in the following section.

**1.2.1 Efferent Fibers**

In the monkey, the few efferent fibers that supply the vestibular end organs arise lateral to the abducens nucleus and from a region dorsolateral from the genu of the facial nerve (Goldberg and Fernandez, 1980). In the frog, efferent fiber discharges have a time course similar to that of the canal primary afferents in response to constant angular acceleration and velocity steps. After the cessation of an acceleration step, the time course for the falling phase of the response was irregular and prolonged indicating possible multisensory convergence on efferent neurons. These neurons discharged by passive and active limb movement and gentle pressure applied to the skin or eyes (Precht et al., 1971) and also increase their firing rate in response to visual and auditory stimuli.

The experimental results of Precht, (1974) indicate that the efferent system is inhibitory in nature. Some possibilities for the function of the efferent system were postulated by Brichta and Goldberg (1996). They found that the efferent system in the turtle posterior crista inhibited some units and excited others. They suggested that if the efferent system is activated in anticipation of movement, then it could be used to switch the vestibular system from a "postural" mode to a "volitional" mode by inhibiting units that could be saturated by large head movements and activating units that have large dynamic ranges. Other possible functions were postulated by Schmidt et al., (1972) when they found that the efferent neurons in fish changed their firing rate prior to the onset of eye movements. Although the efferent affect on the
afferent signal has been characterized as weak (Precht et al., 1971) all this evidence suggests that it might play a role in suppressing the undesired afferent signal from the labyrinth when making an active head movement accompanied by an eye movement in the same direction (Precht, 1978). However, Khalsa et al., (1981) presented evidence that this is not so. They propose that the role of the efferent system is a global baseline regulation during a wide range of stimuli. This is supported by findings of extensive branching of efferent fibers onto afferents (Khalsa et al., 1981). Evidence in primates favouring this hypothesis is provided by (Louie and Kimm, 1978).

1.2.2 Primary afferents

The primary afferent neurons encode the degree of stimulation of the peripheral organs and relay this information primarily to the vestibular nuclei. At the peripheral end of the neuron, the afferent can have a bouton, calyx or a dimorphic ending. Anatomically, the calyx endings are found in the central regions of the neuroepithelium and receive synapses from Type I hair cells and sometimes from Type II hair cells (Goldberg et al., 1990). These neurons have low sensitivities and lead to irregular firing patterns. Bouton endings are found in the peripheral regions of the neuroepithelium and have regular firing rates. Dimorphic endings can be either regular or irregular in their firing pattern and innervate both Type I and Type II hair cells. The dimorphic synapses that lead to regular firing patterns are found in the peripheral zones while those that result in irregular firing patterns are found in the center of the neuroepithelium. Generally, regardless of the innervation, irregular firing neurons are concentrated centrally on a neuroepithelium while regular firing neurons are concentrated in the periphery. The different localization of the fibers exhibiting different activity may lead to different central terminations but their significance is not yet known (Schwarz & Tomlinson, 1993).

The primary afferents are not quiet in the absence of stimulus but maintain a constant discharge in response to the constant neurotransmitter release from the hair cells. Goldberg & Fernandez, (1971a) reported and average resting discharge rate of 90 spikes/sec. This allows for bi-directional change depending on the direction the hair cells bend. The regularity of discharge is defined by the coefficient of variation (COV) which is computed as the standard deviation divided by the mean interspike interval and is therefore somewhat arbitrary because of the different interspike intervals that may be used. At an interspike interval of 17.5 ms, the mean
COV of all primary afferents was reported as \( \mu = 0.3072 \pm 0.024 \) (mean \( \pm \) standard error mean) (Goldberg & Fernandez, 1971c). The regular firing fibers, which have slower conduction velocities and a smaller diameter than irregular firing fibers have a COV less than 0.1, while irregular firing patterns have a COV greater than 0.4. A frequency histogram of COV is shown for a squirrel monkey using an interspike interval of 12.5 ms resulting in a mean COV of \( \mu = 0.1854 \pm 0.0139 \) (figure 1.5). Two peaks can be seen, one centered around COV of 0.6 and a second around 0.4 corresponding to regular and irregular fibers. The function of regular and irregular neurons will be discussed in section 1.2.2.

The afferents innervating the canals are activated by head accelerations in the ipsilateral direction and inhibited by rotations in the contralateral directions (Fernandez & Goldberg, 1971b) with the degree of activation being proportional to the cosine of the angle between the canal plane and the stimulus plane. Similarly, in the monkey, even though the hair cells in the utricular macula are distributed around the striola, the utricular afferents have a preponderance of afferents responding to forces directed towards the ipsilateral ear. However, unlike the canal afferents, the otolith primary afferents may respond to stimuli in one or more directions (Fernandez & Goldberg, 1976b). They also may be excited by forces directed perpendicular to their polarization vector. Fernandez & Goldberg, (1976b) suggested that the otolith mechanics may involve complex non-linear mechanical interactions. Dickman et al., (1991) also reported otolith afferents in the gerbil that responded to stimuli directed orthogonal to their sensitivity vectors. Angelaki (1992a) explained these "broadly tuned" neurons with a model utilizing the spatio-temporal convergence between hair cells with different temporal and spatial properties. Two hair cells with different phase characteristics and different directional sensitivities could produce the "broadly tuned" behaviour observed in these neurons. The different phase characteristics could be produced by the different membrane properties of Type I and Type II hair cells (Correia and Lang, 1990). This would make the dimorphic neurons suited to carry "broadly tuned" signals.
Figure 1.5 Histogram showing the Coefficient Of Variation for the primary afferents of the squirrel monkey. Interspike interval = 12.5ms. Regular units are defined as having a COV<1. Irregular units have a COV>4. Units in between are defined as dimorphic. Note that the amount of regular units found is greater than both the dimorphic and the irregular. Data from Fernandez & Goldberg, 1971c.
1.2.2.1 Canal Primary afferents

Canal primary afferent neurons carry a signal that is approximately in phase with angular velocity of the head (Fernandez & Goldberg, 1971). The transfer function that describes the behaviour of the canal primary afferent is:

\[ H(s) = \frac{1}{(1+sT_1)(1+sT_2)}(\frac{sT_A}{1+sT_A})(1+sT_L) \]  

(1.3)

where \( s \) is the Laplace transform. The first part of equation 1.3 is the laplace transform of equation 1.1 and corresponds to the cupular dynamics. As before, \( T_1 = 6 \) seconds, \( T_2 = .003 \) seconds. The second bracket corresponds to an adaptation operator. In the time domain, this high pass filter is proportional to \( e^{-TA} \) so that as \( T_A \) decreases, the neurons adapt faster. Even though the value of \( T_A \) varied for irregular units, their mean is \( T_A = 34 \) seconds indicating a relatively rapid adaptation. In contrast, the regular units' adaptation operator is omitted (or equivalently set to infinity). Figure 1.6 shows the time course of a representative irregular afferent with \( T_A = 34 \) seconds and \( T_L = .08 \) seconds. Finally, the last bracket indicates a high frequency gain enhancement and phase lead, with \( T_L = .08 \) for irregular units and .017 in regular units (Fernandez & Goldberg, 1971a).

1.2.2.2 Otolith Primary Afferents

The otolith primary afferents are of great interest in this study since they supply the input to the circuitry that is being modeled. The transfer function that describes the behaviour of the otolith primary afferents is given by (Fernandez & Goldberg, 1976c):

\[ H(s) = \frac{1+k_A T_A s}{1+T_A s} \left( \frac{1+k_s (T_v s)^{k_v}}{1+T_M s} \right) \]  

(1.4)

The term \( H_v = 1+k_s (T_v s)^{k_v} \) is a velocity sensitive operator with fractional component \( (k_v < 1) \) which provides most of the gain enhancement and phase leads seen in irregular units. The value of \( k_v \) reflects the amount of differentiation that takes place (the effectiveness of the velocity
operator. The factor \( H_A = \frac{1 + k_A T_A s}{1 + T_A s} \) is an adaptation operator. It contributes to the phase leads seen at low frequencies and to the large increase in gain observed in going from DC to .006 Hz (figure 1.8). (Note that in figures 1.7 and 1.8, the values from DC to .006 where interpolated using equation 1.4.)

![Graph showing adaptation of a canal irregular primary afferent using \( T_A = 34 \) seconds. Gain is maintained at about .2 spikes/sec/deg/sec for about 1 second.](image)

Figure 1.6 Adaptation of a canal irregular primary afferent using \( T_A = 34 \) seconds. Gain is maintained at about .2 spikes/sec/deg/sec for about 1 second.
The last term $H_m = 1/(1 + T_m s)$ is a first order lag operator and may reflect the mechanics of otolith motion. It accounts for the high frequency phase lags seen in regular units (figure 1.7) and accounts for the small phase lead seen in irregular units which are usually smaller than would be predicted solely from the fractional velocity operator. Figure 1.8b depicts the phase of an irregular afferent with $k_r = 0.44$. Based on this information, the phase lead should be close to 40 degrees especially at high frequencies. However, as can be seen from figure 1.8b, due to $H_m$ the phase begins to decline as the frequency increases. Fernandez & Goldberg, (1976c) estimated four of the parameters ($k_r, k_A, T_A, T_m$) using a least square fit to the experimental frequency plots but held $T_v$ constant at 40 seconds. The median values reported are used throughout the simulations in this theses. For irregular afferents, the medians were: $k_r = 0.44$, $k_A = 1.9$, $T_A = 101$ seconds and $T_m = 0.009$ seconds. Regular units had $k_r = 0.188$, $k_A = 1.12$, $T_A = 69$ seconds and $T_m = 0.016$ seconds.

Figure 1.7 and 1.8 depict the dynamics of a regular and irregular otolith neuron in the frequency domain. The irregular unit increases its gain by 40 times and has an average phase lead of 30 degrees with respect to head acceleration as the frequency increases from .006 Hz to 2 Hz. Surprisingly, the regular unit shows very little variation with frequency. Its phase hovers around 0 degrees at low frequencies and dips to around a 20 degrees lag at higher frequencies. The average gain for an irregular otolith afferent is about 200 spikes/sec/g at 1 Hz while that for a regular afferent is around 40 spikes/sec/g at 1 Hz. On average, the resting rate of otolith afferents was found to average 60 spikes/sec, considerably less than the average found for the canal afferents (Fernandez & Goldberg, 1971a).
Figure 1.7 Bode plots for regular otolith primary afferents. $k_v = .188$, $k_A = 1.12$, $T_A = 69s$, $T_M = 16ms$, $T_v = 40s$. a: Gain in spikes/sec/g where $g = 9.8m/s^2$. As the frequency increases from 0.01 to 2 Hz, the gain exhibits a very flat frequency response. Compare with figure 1.8a. b: Phase re acceleration in degrees. At low frequencies, the phase leads acceleration by a few degrees. After 1Hz, the phase begins to lag and reaches -5 degrees at 2Hz.
Figure 1.8 Bode plots for irregular otolith primary afferents. $k_v = 0.440, k_A = 1.90, T_A = 10\text{s}, T_M = 9\text{ms}, T_v = 40\text{s}$. a: Gain in spikes/sec/g where $g = 9.8\text{m/s}^2$. In contrast to the regular afferent's gain (figure 1.7a), the gain of the irregular neuron is dynamic and responds with a large gain for an increase in frequency. Note the difference in scale. b: Phase re acceleration in degrees. At low frequencies, the phase leads acceleration as described by the velocity operator. At 1 Hz, the phase begins to lag due the input of the lag operator.
1.2.3 Primary Afferent Input To The Vestibular Nuclei

There is a fundamental difference between the signals originating from the otolith organs and for those originating from the canals. The signals are in phase with head acceleration (Fernandez & Goldberg, 1976c), and head velocity respectively. The oculomotor neurons are known to require input signals proportional to eye velocity and eye position (see section 1.4). Therefore for the AVOR, the velocity signal is readily obtained from the semi-circular canals making its raw signal adequate to drive the velocity component of the oculomotor neurons. The situation for the TVOR is more complex. Since the signal from the otoliths is in phase with acceleration, further processing is needed in order to obtain the necessary commands to drive the ocular motoneurons. The circuitry that accomplishes this feat is not yet known but because of the high latencies of the TVOR, the circuitry probably extends beyond the vestibular nuclei into the cerebellum.

The vestibular nuclei occupy a large portion of the medulla and extend rostrally into the pons. Primary afferent fibers from semicircular canals and the otolith organs run into the vestibular division of the vestibulocochlear nerve (VIII) to terminate in the vestibular nuclei. In addition, high frequency stimulation of the utricular nerve evoked EPSPs in the abducens motoneurons with latencies between 0.9 ms and 1.2 ms. This suggests that the abducens motoneurons make monosynaptic connections with the vestibular nerve (Uchino et al., 1994). This is a surprising result since the latency of the TVOR is around 30 ms (see section 1.4.4).

The vestibular nuclei consists of four main nuclei termed superior, descending (inferior), lateral and medial nuclei (figure 1.9) and several minor groups termed Y, L, F, X and Z groups (Schwarz & Tomlinson, 1993). Each main nuclei and the Y group has distinct connections with the periphery as shown in table 1.2. All the primary afferents connections are excitatory. The inhibitions shown in table 1.2 are mediated by inhibitory interneurons.

The medial and superior vestibular nuclei receive input from the semicircular canals. These nuclei participate in the vestibulo-ocular reflex and make monosynaptic connections with motoneurons innervating the neck muscles and are the primary source of the reflex control of
neck movements (Leigh & Zee, 1991). The medial nucleus also receive utricular input resulting in a small amplitude response to forward and backward tilts (Gacek, 1969).

The descending vestibular nucleus receives some input from the semicircular canals and a significant input from the utricle and correspondingly has a large response to tilt (Wilson & Melville Jones, 1979). The rostral part of the nucleus is believed to receive saccular input (Gacek, 1969). The descending nucleus sends the majority of its efferents to the vestibulospinal pathways and projects to the spinal cord.

The lateral vestibular nucleus has main inputs from the macula of the utricle, semicircular canals (Gacek, 1969) and from the cerebellum and the spinal cord (Wilson & Melville Jones, 1979). Neurons in the lateral vestibular nucleus also respond to tilt in one direction and decrease their response to tilt in the opposite direction. The magnitude of the response increases with increasing tilt (Schor, 1974).

<table>
<thead>
<tr>
<th>Canal</th>
<th>Vestibular Nucleus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horizontal</td>
<td>Excitation</td>
</tr>
<tr>
<td></td>
<td>Medial &amp; Lateral</td>
</tr>
<tr>
<td></td>
<td>Inhibition</td>
</tr>
<tr>
<td></td>
<td>Medial</td>
</tr>
<tr>
<td>Anterior</td>
<td>Excitation</td>
</tr>
<tr>
<td></td>
<td>Medial &amp; Lateral</td>
</tr>
<tr>
<td></td>
<td>Inhibition</td>
</tr>
<tr>
<td></td>
<td>Superior</td>
</tr>
<tr>
<td>Posterior</td>
<td>Excitation</td>
</tr>
<tr>
<td></td>
<td>Medial &amp; Lateral</td>
</tr>
<tr>
<td></td>
<td>Inhibition</td>
</tr>
<tr>
<td></td>
<td>Superior</td>
</tr>
<tr>
<td>Utricle</td>
<td>Excitation</td>
</tr>
<tr>
<td></td>
<td>Lateral &amp; inferior</td>
</tr>
<tr>
<td>Saccule</td>
<td>Excitation</td>
</tr>
<tr>
<td></td>
<td>y-group &amp; Inferior</td>
</tr>
</tbody>
</table>

Table 1.2 Projections of semicircular canals and otolith primary afferents onto the vestibular nuclei. Inhibitory responses are due to inhibitory interneurons. Adapted from Leigh & Zee, 1991.

1.3 EXTRAOCULAR MUSCLES

The eyes are innervated by six extraocular muscles. These are the medial and lateral recti, the superior and inferior recti, and the superior and inferior obliques (figure 1.10). The effect of
Figure 1.9 Sections of the four major vestibular nuclei and its innervations. The primary afferents from the canal terminate in all four vestibular nuclei while the utricle terminates onto the inferior and lateral portions and the Saccule on the lateral portions. Solid light line: Horizontal and anterior canal. Solid dark line: Saccule. Dashed light line: Posterior canal. Dashed dark line: Utricle.

the lateral and medial recti are almost purely a horizontal rotation since these muscles are attached in the plane of the center of rotation of the eye. But things are not that well structured for the other muscles. The superior and inferior recti are displaced in a medial direction and have a line of action that is displaced 23 degrees to the visual axis in the primary position. Their main action in this position respectively is elevation and depression together with a slight intorsion from the superior rectus and an extorsion from the inferior rectus. The superior oblique uses a pulley, the trochlea, to change its direction and inserts itself laterally along the top of the eye. Its line of action then is displaced 53 degrees from the visual axis in the primary position. The inferior oblique inserts itself in the inferior lateral portion of the globe with the posterior section close to the optic nerve, making its line of action not coincident with that of the superior oblique. Their main action in the primary position respectively is intorsion with a secondary action of depression and extorsion with a secondary action of elevation (Wilson & Melville Jones, 1979). Table 1.3 summarizes the actions of the right eye muscles for certain movements from the primary position.

<table>
<thead>
<tr>
<th>Right Eye</th>
<th>Adduction</th>
<th>Abduction</th>
<th>elevation</th>
<th>depression</th>
<th>intorsion</th>
<th>extorsion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral Rectus</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Medial Rectus</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Superior Rectus</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Inferior Rectus</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Superior Oblique</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Inferior Oblique</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Yaw Right</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Yaw Left</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Pitch backward</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Pitch forward</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Roll In (CCW)</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Roll out (CW)</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 1.3 Effects of the activation of the right eye muscles and the movement that stimulates them. +: stimulation. -: inhibition. +: main action. +: minor action. For a particular movement (yaw, pitch or roll), conjugate pairs are activated for all directions of that movements.
Comparing table 1.3 with table 1.1, it becomes evident that each pair of canal influences a pair of extraocular muscles that moves the pair in the plane of that canal. The utricle and the saccule on the other hand can move the eyes in any direction (Fluur & Mellstrom, 1970). Primary effects of canal stimulation are shown in table 1.4.

<table>
<thead>
<tr>
<th>Canal stimulated</th>
<th>Excites</th>
<th>Inhibits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horizontal</td>
<td>iMR cLR</td>
<td>iLR cMR</td>
</tr>
<tr>
<td>Anterior</td>
<td>iSR cIO</td>
<td>iIR cSO</td>
</tr>
<tr>
<td>Posterior</td>
<td>iSO cIR</td>
<td>iIO cSR</td>
</tr>
</tbody>
</table>

Table 1.4 Primary effects of canal stimulation on the extraocular muscles. i: ipsilateral, c: contralateral, MR: medial rectus, LR: lateral rectus, SR: superior rectus, IR: inferior rectus, SO: superior oblique, IO: inferior oblique.

Innervation of the six extraocular muscles originate in three nuclei located in the brainstem; the oculomotor nucleus (III), the trochlear nucleus (IV) and the abducens nucleus (VI). In the monkey, the abducens and the trochlear nucleus each supply only one muscle, the ipsilateral lateral rectus and contralateral superior oblique respectively. The oculomotor nucleus supplies the other four muscles; the ipsilateral inferior rectus, ipsilateral medial rectus, ipsilateral inferior oblique and contralateral superior rectus (Warwick, 1953).

1.4 THE VESTIBULO-OCULAR REFLEX

The vestibulo-ocular reflex (VOR) generates eye movements that compensate for head movements sensed by the vestibular system. There are two classes of VOR, the Angular VOR (AVOR) governed by the semicircular canals, and the Translational VOR (TVOR) driven by the otolith organs. Failure of the VOR results in movement of retinal images and a marked decrease in visual acuity. Little is known about the TVOR since research has concentrated on the AVOR. This thesis will be mainly concerned with the TVOR.
1.4.1 Oculomotor Neurons

The TVOR has a latency of 30-40 ms (McConville et al., 1996). This is because the primary afferent signals require processing before they can be fed to the oculomotor neurons. The AVOR on the other hand has a latency of 10-14 ms (Lisberger, 1984) and is based on a 3 neuron arc consisting of:

1. the primary afferent neuron,
2. the secondary neurons in the vestibular nucleus,
3. the oculomotor neurons.

The primary afferents have already been described in section 1.2 while the neurons in the vestibular nucleus will be described in the next section. The oculomotor neurons are used by both the TVOR and the AVOR pathways and will be briefly described here.

The ocular motoneurons are known to require input signals proportional to eye velocity and eye position as motoneuron firing rate can be described by the equation:

\[ R = R_c + kE - r \frac{dE}{dt} \]  

(1.5)

where \( R \) is the firing rate in spikes/sec, \( R_c \) is the firing rate when the eye is in primary position, \( E \) and \( \frac{dE}{dt} \) are the eye position and eye velocity respectively, \( k = 4 \) spikes/sec/deg, and \( r = 0.95 \) spike/sec/deg/sec (Robinson, 1981). As can be seen, equation 1.5 carries signals proportional to eye velocity and eye position. In the case of the AVOR, the eye velocity command is obtained from the canal signal and the position signal is obtained by integration. A central neural integrator has been proposed to perform this task (Robinson, 1968). However, unlike the AVOR, the unprocessed otolith afferent signal is inappropriate to supply the velocity command for driving the motoneurons since it is in phase with head acceleration.
1.4.2 Pathways Linking the Horizontal Canals to the Oculomotor Neurons

The model of the TVOR presented in this thesis describes the behaviour of eye movements to interaural translations. In the model (see section 2.1), the horizontal TVOR reflex eventually adds to information from the labyrinth and uses the labyrinthine pathways to the extraocular muscles. Therefore, only a description of the pathway from the horizontal canals to the extraocular muscles will be given.

If the head is rotated to the right, then in order to compensate for this movement, the eyes must move to the left. For the right eye, this results in excitation of the medial rectus and inhibition of the lateral rectus. In general, excitation of a horizontal canal on one side causes excitation of the contralateral and inhibition of ipsilateral abducens (table 1.4) (Precht et al., 1969). The second order neurons that relay this information to the abducens lie in the rostral medial nucleus (Gacek, 1971). In the cat, Baker et al., (1969) showed that stimulation of the vestibular nerve evokes EPSPs in the contralateral abducens with a latency of 1.2-2.0 ms making these connections disynaptic confirming the AVOR 3 neuron arc. Internuclear neurons in the abducens project to the third nucleus via the medial longitudinal fasciculus (MLF) to contact medial rectus neurons. Excitatory neurons in the medial vestibular nucleus cross the midline at the level of the abducens and synapse on the contralateral abducens nucleus. From there, excitatory projection is sent to the lateral rectus while other neurons cross the midline via the abducens interneurons, back to the half of the excited canal, and synapse onto the third nucleus exciting the ipsilateral medial rectus. The ipsilateral medial rectus is also excited via the Ascending Tract of Dieters (ATD) which does not project to the other side. This gives the ATD the ability to send signals to the motoneurons that do not match those going to the contralateral lateral rectus. This is exactly what is needed for disjunctive eye movements and will be discussed further in section 1.4.4 A summary of excitatory connections for the horizontal canal is shown in figure 1.11.

1.4.3 AVOR

The AVOR is the most thoroughly studied vestibular reflex (see Schwarz & Tomlinson, 1993 for a review). The gain of the AVOR is defined as the eye velocity divided by angular head
Figure 1.11 Horizontal canal excitatory projections. Ipsilateral vestibular nuclei neurons project contralaterally to the abducens. In turn, the Abducens projects to the ipsilateral lateral rectus and contralaterally to the III nucleus. The ATD does not project contralaterally. MLF: Medial Longitudinal Fasciculus, III: Oculomotor nucleus. VI: Abducens nucleus. LR: Lateral rectus. MR: Medial Rectus. VN: Vestibular nucleus. ATD: Ascending Tract of Deiters. HC: Horizontal Canal.

Figure 1.12 Translation is highly dependent on target distance. Translating a distance $L$ to the right requires the eye to move an angle $\arctan(L/D)$ to the left where $D$ is the target distance. As $D$ approaches infinity, $E \rightarrow 0$. 
velocity and the temporal difference between the output and the input is described as phase. For natural head frequencies (5-5 Hz), the gain is almost ideal and is close to 1 while the phase has a value of 0 degrees. Since the eye moves in the opposite direction to the head, perfect compensation requires a phase shift of 180 degrees (which by convention is taken to be 0 degrees). At frequencies of rotation less than .01 Hz, the gain decreases and a phase lead develops. But in this range, the visual system helps to compensate for the rotation.

For sustained rotations at constant velocity, vestibular eye movement velocity declines with a time constant around 15 seconds. The decline is due to the elastic properties of the cupula but 15 seconds is much greater than the cupula’s time constant (5-6 seconds). The prolongation of the signal is achieved by the velocity storage integrator which combines vestibular and optokinetic input in a positive feedback loop (Raphan et al., 1978, Cohen et al., 1981). The output (eye velocity) of the velocity storage is the sum of the direct vestibular pathway, direct visual pathway (retinal slip) and the output of the positive feedback loop. The canal time constant \( T_2 \) would result in a new system time constant \( T_s = \frac{T_v}{1 - \gamma} \) where \( \gamma \) is the gain of the loop. In the monkey, \( \gamma = .7 \) which causes \( T_s = 3 \times T_2 \), which is what is observed (Waespe & Henn, 1977).

1.4.4 TVOR

There are several different manifestations of the otolith-ocular reflexes that are aimed at accomplishing visual stability. These include counter-rolling of the eyes during head tilts, context specific ocular reflexes during translation (Paige & Tomko, 1991a) and a sustained nystagmus during Off Vertical Axis Rotation (OVAR), a paradigm that tilts the axis of the rotation from the vertical. Even though the otolith primary afferents have been well quantified (Fernandez & Goldberg, 1976, Goldberg et al., 1990), little is known about the TVOR reflex and its central connections. This is partly due to the difficulty in obtaining equipment that can produce controlled linear stimuli and partly due to early TVOR results. Niven et al., (1965) performed experiments in darkness and found the TVOR response in humans to be very small. From the geometric understanding of the reflex (figure 1.12), this is what is expected, since in darkness the eyes are diverged as if there existed a target at visual infinity. Recently, the TVOR
response has been shown to be a function of target distance (Buizza et al., 1981) and further experiments have shown it to be substantial when the target distance is small (Paige, 1989, Paige & Tomko, 1991, Schwarz et al., 1989). When the head is translated through a distance $L$ from $P_1$ to $P_2$, the required compensatory eye movement is given by $\arctan(L/D)$ where $D$ is the target distance (figure 1.12).

The otolith organs respond to linear acceleration including gravity. Since gravity is normally present, it has always been assumed that the otolith signal generated by a head tilt to one side will be the same as that generated by translational acceleration to the other side. The ocular response to a translation is a horizontal eye movement while that to a head tilt is a torsional eye movement while high frequency stimuli result in horizontal ones, with considerable overlap. The ambiguity mentioned is true for the utricle, but is not true if both the utricle and the saccule are taken into consideration. The utricular signal that develops when a subject is tilted by an angle $\theta$ is the same as during a translation in the opposite direction of the tilt with an acceleration $-g\sin(\theta)$ where $g = 1g_0 = 9.8m/s^2$ (figure 1.13). However, during translation, the saccule does not modulate its discharge rate as it would during a tilt. Therefore, we conclude that if information from both endorgans is taken into consideration by the brain, then this would eliminate the ambiguity discussed above.

Signal ambiguity can also arise with the saccule. Dorsoventral translation at some acceleration $a_\phi$, would cause the saccule to sense an acceleration $g - a_\phi$ in one direction. This same acceleration can be repeated with a tilt by an angle $\phi$ such that the $g\cos(\phi) = g - a_\phi$, leading to the proposed ambiguity. For falling, which is a dorsoventral translation, the compensatory eye movement is vertical but for tilting it is torsional. Again, this ambiguity can be eliminated by considering both otolith organs. During dorsoventral translation, the utricle does not modulate but during tilts, it does.

1.4.4.1. Dependence of the TVOR on Target Position and Distance

In the dark, the gain of the TVOR defined here as eye velocity divided by head acceleration is 13 deg/sec/g at a frequency of 1.5 Hz. However, in the light, the sensitivity of the TVOR (defined
Figure 1.13. To the utricle, tilting the head is equivalent to accelerating interauraly with \( a = g \cdot \sin(\theta) \) leading to an ambiguity in the signal. To the saccule, no interaural translation can replicate the acceleration it senses during tilt hence eliminating the ambiguity once the discharge of both organs is taken into account.

Figure 1.14. When a subject is accelerated in the naso-occipital axis, the right left eye move independently of each other. In this case, the target is located in front of the right eye. As the subject approaches the target, the left begins moving the amount shown while the right eye does not move. Such eye movements may be mediated by the ATD.
here as eye position over head position in degrees/meter) is a function of target distance. In addition, during interaural translations and after travelling a distance \( x \) in one direction, the target distance increases to \( (L^2 + (x^2 + D^2))^{1/2} \) so that the gain of the TVOR needs to be dynamic to compensate for the changing target distance. The dependence of the TVOR on target distance is manifested by the degree of convergence of the eyes. The stimulus to change vergence is retinal disparity and the degree of vergence is measure as Meter Angles (MA) which is equivalent to the inverse of target distance.

The gain of TVOR also is a function of target and eye position. Consider the effect of the target position on the gain of each eye during naso-occipital translation. If the target is located directly in front of the right eye, then the right eye does not have to move to maintain fixation during the movement but the left eye needs to rotate to the right (Figure 1.14). Such changes in the TVOR have been shown to occur by Paige & Tomko, (1991b) and may be mediated by the fibers in the ATD. Indeed naso-occipital translations can lead to a variety of eye movements. If a target is located to one side of a subject as they are translated in the naso-occipital axis, then horizontal eye movement will result. Similarly, if the target is located above or below the subject, then vertical eye movements will result. Vergence eye movements (both eyes moving in opposite direction towards the nose) are expected to occur during forward translation when the target is located between the eyes. This is exactly what is observed experimentally (Tomko & Paige, 1992).

Vergence eye movements are much faster if they occur at the same time with a head or eye movement towards a target rather than by themselves (Paige & Tomko, 1991b). It was believed that vergence information is simply superimposed onto oculomotor neurons (Mays et al., 1986) but this is inconsistent with the observed TVOR results. Instead, vergence information must be supplied to central neurons that mediate the TVOR to produce the observed system behaviour.

### 1.4.4.2 AVOR-TVOR Interaction

Rotation about an axis removed from the center of the head (eccentric rotation) will excite both the canals and the otolith organs (figure 1.15). Equations 1.6 and 1.7 describe the theoretical left and right eye movements for a given head movement (Viirre et al., 1986).
\[ \theta_1 = \text{ArcTan}\left(\frac{(D + R)\sin(-\phi) + I}{2(D + R)\cos(-\phi) + R}\right) \]

\[ \theta_r = \text{ArcTan}\left(\frac{(D + R)\sin(-\phi) - I}{2(D + R)\cos(-\phi) - R}\right) \]

where \( D \) is the target distance, \( R \) is the radius of rotation, \( I \) is the interaural distance, \( \phi \) is head position and \( \theta_l \) and \( \theta_r \) are the left and right eye positions respectively. Figure 1.16 depicts movements for the right eye based on equation 1.7 with \( R = .2 \) meters, \( D = .3, .2 \) and \( .10 \) metres.

When the subject is facing the center of rotation as in figure 1.15, a leftward eccentric rotation will cause the head to rotate to the right but translate to the left. Both the AVOR and the TVOR are active but each system wants to drive the eye towards the opposite direction. As the target distance goes from being farther to being closer than the axis of rotation, the eye movement decreases and eventually reverses. For \( D > R \), the eyes must rotate towards the right and the AVOR dominates (figure 1.16) while for \( D < R \), the eyes must rotate to the left and the TVOR dominates. When \( D = R \), the eye position in the head is geometrically not expected to change. From figure 1.16, it can be seen that the absolute change in the amplitude of eye position around \( D = 0.2 \) meters is exactly the same for \( D = 0.3 \) metres and \( D = 0.15 \) meters even though the former is 10 cm farther than the axis of rotation and the latter is 5 cm closer to the subject than the center of rotation. However, the eye movement is a function of vergence angle which is the inverse of target distance. The change in vergence angle induced by going from \( D = 0.3 \) meters to \( D = 0.2 \) meters is \((1/0.3) - (1/0.2) = 1.667 \) MA. This is exactly the same as going from \( D = 0.2 \) meters to \( D = 0.15 \) meters since \((1/0.2) - (1/0.15) = 1.667 \) MA.
Figure 1.15. Eccentric rotation excites both the canals and the otolith organs. Rotating to the left around an axis in front of the subject causes the AVOR and the LVOR to oppose each other.

Figure 1.16. Eye position during eccentric rotation with the radius of rotation 20 cm in front of the head and a frequency of 2 Hz. If the gaze is directed at the center of rotation, then no eye movement is expected to occur. As the target distance increases, the AVOR dominates while if it decreases, the TVOR dominates.
1.5 CELLS IN THE VESTIBULAR NUCLEI MEDIATING THE VOR

Single cell recordings from the vestibular nuclei have elucidated many of the mysteries underlying the sensory to motor transformations that occur in the brain stem (McConville et al., 1996, McConville et al., 1994, Tomlinson et al., 1996, Tomlinson & Robinson, 1984, Scudder & Fuchs, 1992, Lisberger & Miles, 1980, Fuchs & Kimm, 1975). Early classification labeled cells in the vestibule nuclei as Type I, Type II or Type III. Type I cells were defined as those excited by head rotations to the ipsilateral side, Type II were defined as head rotations to the contralateral side, and Type III are excited by rotations in both directions (Fuchs & Kimm, 1975). A different cell type classification identified cells according to their relevance to the horizontal VOR (Fuchs & Kimm, 1975). In the rostral medial vestibular nucleus, some of these cells are: Position Vestibular Pause (PVP), Eye Head Velocity (EHV), Burst-Tonic neurons (BT) and Floccular Target Neurons (FTN). FTN probably correspond to EHV cells since they have the same behaviour and are found in the same region of the vestibular nuclei (McConville et al., 1996). The behaviour of these cells will be discussed in the next section.

Some of the other neurons found in the rostral medial and medial lateral vestibular nuclei include Canal only cells (CA), otolith only cells (OT), and cells that receive combined canal and otolith input (CAOT) (Tomlinson et al., 1996).

Of all these neurons, only the PVP cells and the EHV (or FTN) cells contribute to the vestibular information supplied to the motoneurons (Scudder and Fuchs, 1992). There are distinct differences between the behaviour and inputs of EHV and PVP neurons as discussed in the next section.

1.5.1 PVP Cells

PVP cells provide the main contribution to the horizontal VOR. Their firing rate is proportional to eye position when the head is stationary and to angular head velocity. Almost all PVP cells are Type I, being excited for ipsilateral rotations. They pause during saccades (Scudder & Fuchs, 1992). Robinson (1981) gave the following equation for PVP cells for the vertical VOR.
where \( R \) is the discharge rate in spikes/sec, \( \frac{dE_p}{dt} \) is the eye velocity in degrees/sec during pursuit of a moving target with the head stationary, \( \frac{dE_s}{dt} \) is the eye velocity during saccades and indicates that the cell stops firing during all rapid eye movements. \( \frac{dH}{dt} \) indicates the vestibular component of the signal. The presence of an eye position signal in these neurons suggests that they receive input from the neural integrator. The PVP cell has many eye signals converging onto it and can be assigned a function of converting the sensory signals from the vestibular system into a motor one.

In the situation depicted in figure 1.15, eye movements induced by the AVOR are directed to the left while those from the TVOR are directed to the right. Using targets with different distances while eccentrically rotating rhesus monkeys, McConville et al., (1996) found that the otolith signals are supplied to PVP cells but they first must undergo processing. As mentioned earlier, the gain of the TVOR is strongly dependent on target distance. McConville et al., (1996) observed that PVP cells did not modulate their firing rate significantly when the target distance was altered during eccentric rotation. The EHV cells on the other hand showed a large increase in gain and are candidates for this effect.

1.5.2 EHV Cells

Along with PVP cells, EHV cells are also known to contact motoneurons (Scudder & Fuchs, 1992). EHV cells exhibit large changes in gain when the target distance is changed and probably represent a dominant pathway for the TVOR. The large target distance sensitivity might be accomplished by using floccular input from the cerebellum (McConville et al., 1996) and hence may correspond to the Floccular Target Neurons (FTN). Snyder & King (1995) demonstrated that the flocculus is supplied with the necessary otolith signal although it is not known whether the EHV's receive a direct input from otolith afferents in addition to Cerebellar input. The large modulation of EHV's to a change in target distance during otolith stimulation is easily illustrated by considering their sensitivities. If the axis of rotation intersects the interaural line, then the

\[
FR = 130 + 2.5E^+.47\frac{dE_p}{dt} - .98\frac{dH}{dt} - \frac{dE_s}{dt}
\]
sensitivities of EHV neurons are .41 spikes/sec/deg/sec and .56 spikes/sec/deg/sec for far and near targets respectively. But when the axis of rotation is moved 14 cm in front of the eyes, the sensitivities become 1.36 spikes/sec/deg/sec for far targets and 2.2 spikes/sec/deg/sec for near targets, a 62% increase.

1.5.3 Otolith Only, Canal Only, and Canal Otolith Cells.

Others cells in the medial and lateral vestibular nucleus include cells that have response characteristics consistent with combined canal and otolith signals (CAOT), cells that only have canal inputs (CA) and cells that only have otolith inputs (OT) (Tomlinson et al., 1996). These cells had response dynamics that are intermediate between those observed in primary afferents and those required to drive the motoneurons and therefore may represent an intermediate stage in the signal processing (Tomlinson et al., 1996).

1.6 MODELS OF THE VOR

Several models have been designed to explain how the TVOR might operate during OVAR (Hain, 1986; Raphan & Schnablock, 1988) and during translation (Angelaki, 1992). But first a simple model for the AVOR will be described (Robinson, 1981). The model we have written utilizes Robinson's model as the final common pathway.

1.6.1 Robinson's Model of the AVOR

Eye movements are driven by visual inputs and vestibular inputs and these two inputs generally act in synergy. Visually driven eye movements include the pursuit system, where a target in motion is kept on the fovea, and the optokinetic system, where the eyes move in response to the movement of the entire visually field. Studies of the optokinetic system have shown that it uses the same circuitry as the vestibular system (Robinson, 1981). Figure 1.17 shows the model proposed by Robinson, (1981) in which the vestibular and the optokinetic system are combined.

1.6.2 Models of the TVOR

Hain, (1986) proposed a three-dimensional model that extends the idea of velocity storage (section 1.4.3). The otolith information about the orientation of the head to gravity changes the
time constant of vestibular responses by modulating the gain of the velocity storage feedback loop. Hain, (1986) also proposes that otolith signals in response to translations are fed into the vestibular system through the velocity storage integrator. The velocity storage integrator makes up part of the low pass filter feedback loop in the velocity storage that extends the time constant of the AVOR. This paper suggests that the bias eye velocity observed during OVAR could be estimated by cross-correlation of linear acceleration signals and their derivatives. Hain could generate the bias eye velocity during OVAR but does not take into account the target distance dependence of the TVOR and therefore the model is inadequate for interaural translations.

Figure 1.17 Robinson's (1981) model for visual-vestibular interaction. The signal existing form OKS is inserted in the vestibular nuclei (vn). This in turn is added with the semicircular canal signal. OKS: Optokinetic system. de: retinal slip velocity. dW: visual surround velocity. dE: eye velocity, dH: head velocity S=switch (closed for daylight, open for night).

Raphan & Schnabolk, (1988) proposed that during OVAR, a dynamic pattern of neural activation produced by the sequential activation of regular otolith neurons with different polarization vectors by the rotating gravity vector resembles a traveling wave that can be detected centrally. The velocity of the travelling wave is then used to drive the velocity storage
integrator. Again this model simulates OVAR and not interaural translations and assumes that there exists a delayed signal that drives the system. However, temporal properties of central vestibular neurons show no such time delays (Schor et al., 1985).

Angelaki, (1992) suggested that otolith afferents with different dynamics and polarization vectors might be summed in such a way as to produce a signal proportional to translational velocity. Before the Angelaki model, vestibular nuclei neurons were described to behave as one-dimensional linear accelerometers characterized by a response along the neuron's polarization vector. Angelaki, (1992) transforms the response vector into a response plane having complicated spatial characteristics. Otolith afferents with different polarization vectors and dynamics would converge onto central neurons producing a neuron that exhibits a responses that map out this plane, defined as a response ellipse. These neurons respond to the component of a stimulus vector on a plane rather than on a single axis characterizing neural response in two rather than one dimension. Stimulation in the direction of the minor axis of the ellipse produces a response that is in phase with jerk while stimulation along the major axis would produce a response in phase with acceleration. The velocity vector is then encoded as the vector that is normal to the response plane.

During eccentric rotations, otolith organs are excited by the tangential acceleration and the canals are excited by the rotation. However, there also exists centripetal acceleration, which occurs at twice the frequency of tangential acceleration. Since the neurons in Angelaki's (1992) model have a broad range of input, then they should show responses related to centripetal acceleration. McConville et al., (1996) failed to find evidence of neurons modulating at twice the frequency. But these results are inconclusive since the stimulus intensity was very low leading to the explanation that the stimulus was too weak to elicit any such response. More experiments are needed to determine whether the Angelaki model is correct.

1.7 CANCELLATION, SUPPRESSION AND ADAPTATION

If a target is pursued with the head and not with the eyes, then the VOR needs to be eliminated. There are two ways that this can be done. Cancellation refers to a central process where the target velocity as interpreted by smooth pursuit is subtracted from the head velocity as
interpreted by the vestibular system. Tomlinson & Robinson (1984) showed that secondary vertical VOR neurons do not show a linear addition of the vestibular and pursuit signals during cancellation of the VOR. Instead, the cancellation may be provided by cells that receive cerebellar input (Chubb & Fuchs, 1982). A second way to eliminate the vestibular contribution is by way of suppression. This method turns down the gain of the VOR. It is likely that the system uses a combination of these methods to eliminate the VOR (Leigh & Zee, 1991).

If retinal slip increases, then the VOR will adjust its gain as to minimize the slip. Adaptation refers to the ability of the vestibular system to adjust its gain in response to long term changes in stimulus. Miles et al., (1980) proved that VOR adaptation was motor learning by recording the gain of the VOR after a x2 lenses where placed on monkeys. Appropriately, the VOR gain increased reaching an asymptote after 4 days of wearing the lenses. Ito, (1972) suggested that the site of these adaptive changes reside in the cerebellum. Specifically, Ito proposed that the coincident excitation of parallel fibers and Purkinje cells in the Nodulo-Floccular lobe of the cerebellum could strengthen the synapse responsible for VOR motor learning. The Purkinje cells would then keep the modulation of the Medial Vestibular neurons down. Therefore, to increase the gain of the VOR, decrease the Purkinje cell's firing rate. This was investigated by Lisberger & Fuchs, (1978) by recording from Purkinje cells in the cerebellum during the VOR, pursuit and cancellation. These authors found that the firing rate of the Purkinje cells was proportional to gaze velocity (head velocity + eye velocity). Therefore for a low gain cancellation, this gaze velocity Purkinje cell should show a slight modulation in the direction of head movement. Miles et al., (1980) found that the Purkinje cells modulated but in the wrong direction with a long latency disproving Ito's hypothesis. Lisberger, (1984) searched for the site of adaptive changes to the vestibular nucleus and showed that PVP cells have very little change in their gain response when the gain of the VOR changed. However, Lisberger found that Floccular Target Neurons (FTN, which might include EHV's (McConville et al., 1996)) changed their discharge rate early enough to be responsible for motor learning making the brainstem a likely place for motor learning.
Chapter 2

2.0 METHODS

The TVOR system can be viewed as a control system for eye movements. Single cell recordings from alert animals (Tomlinson et al., 1996, McConville et al., 1996, Fuchs et al., 1975 to name a few,) coupled with experimental data on eye movements and some simplifying features of the eye (Robinson, 1981), have made this system ideal for a quantitative analytical methods that describe oculomotor control. There are five major systems for oculomotor control. These are the vestibulo-ocular system, vergence, pursuit, saccadic, optokinetic and the pursuit system. The function of each of these systems is known and therefore one can concentrate on how the systems achieves its results (Robinson, 1981). Because of its simplicity, we will first use control systems analysis to derive a transfer function for the firing rate of an oculomotor neuron before proceeding to a description of the model presented here.

2.1 OCULOMOTOR NEURONS

The discharge rate of oculomotor neuron depends on eye position and eye velocity (Henn & Cohen, 1973). For an abducens motoneuron, the discharge rate increases as a subject looks ipsilaterally and decreases for contralateral eye positions. The equation for the firing rate of a typical motorneuron in the monkey was presented on page 25 as equation 1.5 as is repeated below as equation 2.1.

\[ R = R_0 + kE + r \frac{dE}{dt} \] (2.1)

Where \( R \) is the firing rate, \( R_0 \) is the resting discharge. \( E \) and \( \frac{dE}{dt} \) are the eye position and eye velocity respectively, \( k=4 \) spikes/sec/deg and \( r=1 \) spike/sec/deg/sec. Each extra-ocular muscle is defined as having an on direction and an off direction. When the monkey is fixating at a target located straight ahead, so that eye position is zero and eye velocity is zero, then the firing
rate of the motorneuron is just $R_0 \sim 100$ spikes/sec (Robinson, 1981). If the monkey fixates a target located in a particular muscle's on direction or off direction then $R$ will increase by $kE$ or decreases by $kE$ respectively. For example, if a monkey fixates at a target located 20 degrees in the on-direction, then $R=180$ spikes/sec but if the monkey fixates 25 degrees in the off-direction, then $R=0$. If the eye is in motion, $R$ will further change by $r \frac{dE}{dt}$. Therefore if the eye is passing the position where $E=0$ with a velocity of 150 deg/sec, then $R= 250$ spikes/sec.

2.1.1 Transfer function of an oculomotor neuron.

In applying control systems analysis to ocular motoneurons, we must regard the eyeball and its muscles simply as a device to be controlled so that we may observe its behaviour to any signal that reaches the motoneurons. By using equation 2.1, we can say that given any signal that reaches the motoneuron, we know what eye movement $E$ it will produce.

Another way to describe how a system will respond to a variety of signals is by use of frequency analysis. The ratio between the input and the output is represented by the transfer function $H(s)$ where $s$ is the complex frequency (having a real and an imaginary part). If one delivers a sinusoidal signal with complex frequency $s$ to a linear system (such as equation 2.1), then the output will also be a sinusoid of frequency $s$. The amplitude of the output divided by the amplitude of the input is termed the gain of the system while the ArcTangent of the imaginary part of $H$ divided by the real part of $H$ defines the phase shift. All signals can be thought of as sums of sinusoids. Therefore, the gain of $H$ will define how the system will respond to different signals at all frequencies.

The transfer function of a differential equation is readily obtained by the use of Laplace Transforms. The transfer function of equation 2.1 defines the change in eye position in response to a change in firing rate and is defined as

$$H(s) = \frac{1}{sT + 1} \quad (2.2)$$
Figure 2.1 Gain and phase in the frequency domain of equation 2.2. The gain (a) and phase (b) are representative of a low pass filter. As the frequency increases, the gain decreases and the phase leads by 90 degrees.
where $T$ is the time constant defined as $r/k=.25$ seconds. The time constant describes how rapidly the eye will respond to changes in the firing rate and represents the time needed for the eye to reach 63% of its final destination. This response is exponential. If for example, the firing rate in equation 2.1 changes suddenly, the eye will respond with an exponential movement with a time constant of .25 seconds. Figure 2.1 shows the gain and phase of equation 2.2. As the frequency increases, the gain reduces to $(sT)^{-1}$ with the output lagging the input by 90 degrees. While at very low frequency, the gain is just one and no phase shift is seen.

### 2.2 THE MODEL

The program to simulate the model presented in figure 2.2 was written in Mathematica Student Version 2.2 on a Pentium-166 with 32 MB of RAM. Mathematica was chosen over other simulation software because of its portability and its ability to carry out neural network simulations, which we plan to do in the future. Simulation time ranged between a few seconds to about 5 minutes. The program that implemented the TVOR for interaural translations and eccentric rotations is shown in figure 2.2.

Several models were investigated before the final design of figure 2.2 was decided upon. All models had the following inputs:

1) They received both regular and irregular otolith inputs as described by Fernandez & Goldberg, 1976c.

2) They received information regarding vergence angle.

The output of the model had to meet certain criteria so that it might be consistent with experimental data. These criteria were:

1) The output had to be a linear function of the vergence angle.

2) The output (slow phase eye velocity) had to lead head velocity by approximately 50 degrees below 1 Hz and approach head velocity as the frequency increased.
Both of these output criterions were satisfied by using the model in figure 2.2. In order to obtain a signal in phase with velocity from an acceleration signal, we partially differentiated the outputs of the primary afferents and adjusted the sensitivities of the resultant jerk vector. At high frequencies, where the Otolith-Ocular Reflex (OOR) is most robust, the irregular otolith afferent signal was already partially differentiated making it more suited for further differentiation rather than integration as is mathematically required. Integration of the signal would lead to a low pass filtering effect, an attribute not observed for the TVOR.

Although the otolith-ocular reflex is a bilateral system, the model presented here assumes it is driving a cyclopean eye. Our most important goal was to design a model to see if utilizing the jerk vector could in fact reproduce experimental data. Many transfer functions were designed that took advantage of the phase lead exhibited by the primary afferents and differentiated this signal as a function of frequency. The ones chosen for this thesis do not provide the best fit for the data but are a compromise between complicated functions and accurate results. Indeed some transfer functions that reproduced the means of the experimental data accurately were functions of real and complex frequency and even had the laplace transform $S$ raised to the 4th power which increased simulation time considerably. One must remember that the experimental data is subject to variation and although the model presented here does not accurately reproduce the experimental means (see figure 3.8), its output is contained between the maximum and the minimum sensitivities obtained in experiments by Telford et al., (submitted).

The easiest of the transfer functions to design was that for the torsional eye movements (equation 3.2). We simply started with a low pass filter and wrote a simple program in C that would iteratively raise the laplace transform in the denominator to various powers less than one. The program would then check the gain of the transfer function using a least square method approximation to a logarithmic fit of the experimental data (Telford et al., submitted). Figure 3.1 shows the output of this transfer function cascaded with regular afferent input as a function of frequency along with the fitted experimental values for the gain of the torsional eye movements. (Here gain is defined such that a gain of one is a 90-degree torsional eye movement).
The irregular afferents were not included in the design of the torsional system for several reasons. Upon tilting, the vertical canals cause the eye to undergo torsion while the otolith system actually maintains the torted position. The dynamics of the irregular afferents is not suited for maintaining a position because it is too phasic. Recall that the irregular afferents are very highly sensitive to changes in frequency and they adapt very fast (see figure 1.7). The regulars, with their small gains and poor frequency dependence proved more than adequate to serve as the peripheral signal that can sustain torsion.

$H_i[s]$ and $H_f[s,w]$ were obtained in a similar way to $H_o[s]$ but their derivation was not as simple. Many variables had to be considered in designing these two functions. The output of the model is a cascade of four transfer functions so that as the design process continued, the interaction between the four functions needed to be monitored. Therefore, both $H_i[s]$ and $H_f[s,w]$ were designed simultaneously. The reason behind $H_f[s,w]$’s dependence on both complex and real frequency is discussed later in the Results and Discussion.

Not only are we interested in the question of how the Otolith-Ocular reflex obtains a velocity signal, but also in the interaction between the TVOR and the AVOR. As shown in figure 4.1, the TVOR is non-ideal. Even at 4 Hz where it is most robust, it only reaches 60% of the theoretical value. This may be a consequence of the system’s inability to properly adjust the sensitivity after differentiating to a jerk vector. We believe that the TVOR is more robust if the canals are stimulated (such as during eccentric rotations). This gives the system the ability to measure the relative quality of the otolith signal in comparison to the canal signal. Central canal neurons already have at their disposal information about frequency giving them a good measure of how much enhancement the otolith signal will need. $F[c,o]$ is actually another network (or several cascading transfer functions) that will accomplish this task. A simplified version of this network was used for the purposes of this thesis but a time sampling mistake alerted us to the multidimensionality and complexity of $F[c,o]$. This simplified equation correctly simulated AVOR+TVOR for a particular frequency and vergence but any adjustments made to the variables caused a marked instability which proved this equation to be useless and warrants no more explanations. One consequence of this attempt is that the AVOR+TVOR reflex is not a linear function of vergence. This idea will be presented in more detail in the Discussion.
Experiments have been planned where single cell recordings from the vestibular nucleus of awake rhesus monkeys will help us elucidate the interaction between the two reflexes. We will then use this data to complete the model for how the AVOR and the TVOR interact.
Figure 2.2 Model used in this thesis to simulate the TVOR. 

- Multiplication of signals. Inputs to the model are regular and irregular otolith afferents. These signals initially pass through the Tilt/Translation box where it is decided whether a tilt or a translation is taking place. If a translation has been detected, vergence and irregular afferents multiply and adjust the gain of the horizontal eye movement to be performed while simultaneously inhibiting the torsional pathway. After a phase adjustment has occurred at $H_1$, the signal that slightly leads velocity emerges and, if the canals are active, is modified, and summed with the canal signal. The pathway that leads to tilts is always on and is inhibited by the horizontal pathway. Numbers in brackets represent equations in text.
FIGURE 2.3 Program that carried out the simulations of Figure 2.2

(*A Program to simulate the TVOR with stimulus interaural translations or eccentric rotation*)

<<Statistics`LinearRegression``

(*Irregular afferent constants.  See equation 1.4.  Constants are taken to be the medians presented in Fernandez & Goldberg, (1976c)*)

\[
\begin{align*}
&kvi = .44; \\
&kai = 1.9; \\
&tai = 101; \\
&tmi = .009; \\
&tv = 40; \\

&(*Regular*) \\
&kv = .188; \\
&kar = 1.12; \\
&tar = 69; \\
&tm = .016; \\
&t = 40; \\

&(*canal*) \\
&T1 = .003; \\
&T2 = 6; \\

&(*Save* "const", kvi, kai, tai, tmi, tv, k, kar, tar, tm, t, T1, T2)*
\]

(*........otolith afferents From Fernandez & Goldberg, (1976a)*)

(*........GLOBAL FUNCTIONS*******)

\[
\begin{align*}
&Irreg[w_] := 23.5*(1-kai*tai*I*w)/(1+kvi*(tv*I*w)^kvi)/(tai*I*w+1)*(tmi*I*w+1)); \\
&Regul[w_] := 25.8*(1-kar*tar*I*w)/(1-kvi*(tv*I*w)^kvi)/(tar*I*w+1)*(tm*I*w+1)); \\
&Canal[w_] := (1/.003)*(I*w*T1+T2)/(I*w*T2+1);
\]

(* H[s] in figure 2.2*)

\[
\text{NEURON1} [w_, verg ] := \text{Module} [ 0 ]; \\
\text{tcon} = .27; (*seconds*) \\
\text{amplitude} = 2.5; (**) \\
\text{numeratorexp} = 2.5; \\
\text{denominatorexp} = \text{numeratorexp}; \\
\text{H1} := \text{amplitude} \cdot \text{Irreg}[w] \cdot \text{verg} \cdot \text{numeratorexp} / (\text{tcon} \cdot \text{w} \cdot \text{denominatorexp});
\]

Return[H1]];

(*H2[s,w] in figure 2.2*)

\[
\text{NEURON2} [w_] := \text{Module} [ 0 ]; \\
\text{amplitude} = .06; (**) \\
\text{tcon} = .45; (*seconds*) \\
\text{numeratorexp} = 1.95; \\
\text{denominatorexp} = \text{numeratorexp};
\]
\[ H = \text{amplitude} \times \text{Regul} \{ w \} \times \left( \frac{\{ I \times w \}^{\text{numeratexp}}}{(1+\{ I \times w \}^{\text{denominatexp}})} \right) \]

Return \[ H \];

adjust = .001;

\[ \text{NEURON3} \{ w,\text{verg} \} = \text{adjust} \times (\text{NEURON1} \{ w,\text{verg} \} \times \text{NEURON2} \{ w \}) ; \]

\[ N[\text{Arg}[\text{NEURON3} \{ \pi,1 \}]] \]

\[ \text{For}[i=1,i<5,i++1, \]

\[ N[\text{Arg}[\text{NEURON3} \{ 2\pi \times i,1 \}]] \]

(* from Paige 1997*)

\[ \text{sens} = \{.1, .23, .26, .3 \} ; \text{(means 1, 2, 3, 4 hz)} \]

\[ \text{senupper} = \{.15, .4, .4, .4 \} ; \text{(upper and lower for 1, 2, 4 hz)} \]

\[ \text{senslower} = \{.5, .12, .17, .2 \} ; \]

\[ \text{phasemodel} = \{2.19, 1.868, 1.683, 1.528 \} ; \text{(cut down on simulation time)} \]

(* the phase of the model was not calculated independently of the simulations and inserted into simulations as a constant. This will cut on simulations time*)

\[ t = . \]

\[ \text{For}[j=1,j<8,j=j+2, \]

\[ \text{For}[i=1,i<5,i=i+1, \]

(* go through 4 frequencies...namely f=1Hz, 2Hz, 3Hz, 4Hz *)

\[ w = 2\pi \times i; \]

(* used small amplitudes for all simulations*)

\[ \text{amp} = .01 ; \text{(meters)} \]

\[ \text{amp1} = 1 ; \text{(cm)} \]

(* stimulus*)

\[ x[t_] = \text{amp} \times \text{Sin}[w \times t]; \]

\[ y[t_] = \text{D}[x[t],t]; \]

\[ z[t_] = \text{D}[y[t],t]/10; \]

(*r is the target distance. 4 target distances used here are r=1m, 1/3m, 1/5m, 1/7m*)

\[ r = 1/j; \]

(*verge is the reciprocal of the target distance used above*)

\[ \text{verg} = 1/r; \]

(* The verge changes as the subject is translated. But since the amplitude used was 1 cm, then this change is negligible. v[t] was used to show that this is true*)

\[ v[t_] := (\text{verg}^2 + x[t]\^2)^.5; \]

(*Print[] ;
Print["amp" = , \text{amp}, "m w =", w, 
phasemol = , a[w], "vergence =", \text{verg}];
Print[] ; *)

(* Since experimental values were given in sensitivity defined as deg/cm/MA, then the firing rate corresponding to the eye velocity at a certain sensitivity can be obtained by using the following formula:

sensitivity*vergence*headVelocity*1spike/sec/deg/sec*)

(*Plot[{senupper[[i]]*verg*amp1*\{w*Cos[w*t+phase][[i]]\}+
4*Sin[w*t+phase][[i]]\} ,Abs[NEURON3\{w,v[t]\}]*(w^2*amp*Sin[w*t+
phasemodel[[i]]]}/10- 

49
4*w*amp*Cos[w*t+phasemodel[[i]]]/10,
(* upper and lower sensitivities correspond to upper and lower
eperimental values *)
senslower[[i]]*verg*ampl*(w*Cos[w*t+phase[[i]]]+4*Sin[w*t+phase[[i]]]),{t,0,2*Pi/w},
AxesLabel->{"time (s)","sp/s"}];

(*)
t=0;
Print[N[senupper[[i]]*verg*ampl*(w*Cos[w*t+phase[[i]]]+4*Sin[w*t+phase[[i]]]),"
"N[Abs[NEURON3[w,verg]]*(w^2*amp*Sin[w*t+phasemodel[[i]]])/10-
4*w*amp*Cos[w*t+phasemodel[[i]]]/10]],"
"N[senslower[[i]]*verg*ampl*(w*Cos[w*t+phase[[i]]]+4*Sin[w*t+phase[[i]]])," a="N[amp*w^2/10],"g",
" theory="N[(w+4)*amp*180/Pi/r]," td="r,"m"," "];
t=.;

(*t=0;
Print[N[sens[[i]]*verg*ampl*(w*Cos[w*t+phase[[i]]]+4*Sin[w*t+phase[[i]]]),"
"N[Abs[NEURON3[w,v[t]]]*(w^2*amp*Sin[w*t+phasemodel[[i]]])/10-
4*w*amp*Cos[w*t+phasemodel[[i]]]/10]],"
"a="N[amp*w^2/10],"g",
" theory="N[w*amp*180/Pi/r]," td="r,"m"];
t=.;*)
Chapter 3

3.0 RESULTS

TVOR responses where simulated based on experimental data obtained from Telford et al., (submitted). The gains and phases of the transfer functions that make up the model will now be presented along with the sensitivities and responses they invoke.

The Tilt/Translation box in figure 2.2 decides whether a horizontal movement is being made or the excitation of the afferents is due to a tilt. This box is not based on the accepted method that utilizes a frequency filter to eliminate the assumed ambiguity in the signal (see page 28). Instead, we have employed a method that takes into consideration the modulation of both the utricle and the saccule under the assumption that there does not exist an ambiguity (actually, the model proposed eliminates any ambiguity). This signal is then used to either turn on (allow a signal to pass) or keep off (inhibit) a pathway for horizontal movements (pathway H in figure 2.2). Note that a pathway leading to torsional eye movements is always on (pathway through the low pass filter H₄[s], see below) so that horizontal eye movements of low frequency will also cause some torsion (Paige & Tomko, 1991a).

3.1 DIFFERENCES BETWEEN TILTS AND TRANSLATIONS

The function that arrives at the decision about the type of movement taking place is \( F(\theta,a) \) and is defined as:

\[
F(\theta,a) = pq + a
\]

The output of \( F(\theta,a) \) will determine whether pathway H in figure 2.2 will be turned on or off. We shall adopt the convention that a negative output from \( F \) will be a result of a pure tilt and will inhibit the horizontal eye movement pathway. Conversely, a positive output will be a result of a horizontal movement (either alone or during a tilt) and will excite the horizontal eye
movement pathway. Work has begun on functions that will replace equation 3.1 and will supply the junction at the irregular utricular afferent (figure 2.2) with a scaling factor determined by the degree of tilt and the magnitude of the horizontal acceleration. Here we will only be concerned with whether the pathway is turned on and off.

Equation 3.1 must satisfy certain conditions: 1) It must maintain both pathways off in the absence of a stimulus, 2) it must inhibit the horizontal eye movement pathway during a pure tilt so that no horizontal eye movements (in head coordinates) can be initiated and 3) it must turn on the horizontal eye movement pathway during a horizontal translation regardless of whether a tilt exist. Parker et al., (1985) observed that after landing, astronauts exhibited horizontal eye movements in response to a head tilt but in the absence of translation. This gives us the fourth criterion that equation 3.1 must satisfy, namely that 4) after the conditions described above have been met, equation 3.1 must turn on the horizontal eye movement pathway in response to a tilt but in the absence of horizontal translations in effect contradicting criterion 2. Actually, it will be shown that after being in space, central mechanisms change and the behaviour of eye movements switch from criterion 2 to criterion 4.

Let \( p = (S_a - g_i) \), where \( g_i \) is an internal memory of 1g of acceleration where 1g is the acceleration due to gravity measured in units of \( 9.8 \text{ m/s}^2 \), \( (g_i = g = 1 \text{ on earth under normal conditions}) \), let \( a \) be the acceleration in the horizontal plane and let \( 0<\theta<90 \) degrees be the deviation from the vertical. Then \( S_a = g \cos(\theta) + a \sin(\theta) \) is the acceleration felt by the saccule for an interaural translation \( a \) after tilting an angle \( \theta \) from the vertical \((S_a = g \text{ in the upright position}). \) \( p \) will then be defined as the acceleration felt by the saccule relative to gravity. Also let \( q = U_a \) where \( U_a = g \sin(\theta) + a \cos(\theta) \) is the acceleration felt by the utricle for an interaural translation \( a \) after tilting an angle \( \theta \) from the vertical \((U_a = a \text{ in the upright position})\), then \( F(\theta, a) \) is a simple function that determines the magnitude of the degree of tilt relative to any interaural acceleration.

In the absence of any tilts or horizontal translations, \( a = 0, g = 1 \) and \( \theta = 0 \). It follows that \( S_a = g \) and \( q = U_a = a = 0 \). However, \( p = (S_a - g_i) = 0 \) giving us the result that \( F(0,0) = 0 \) satisfying the first condition.
The second condition that needs to be satisfied has \( a = 0 \) but \( \theta > 0 \). This gives \( S_x = g \cos(\theta) \) and \( U_x = g \sin(\theta) \) so that \( p = g \cos(\theta) - g_i = g (\cos(\theta) - 1) \) which is less than zero since \( \cos(\theta) < 1 \). Then, since \( a = 0 \), \( F(\theta, 0) < 0 \) and the horizontal pathway is inhibited.

The third condition occurs during a translation without a tilt. In the absence of a tilt, \( a > 0 \) and \( \theta = 0 \). Therefore, \( S_x = g \) making \( p = 0 \). Therefore, \( F(0, a) = 0 \) and \( a > 0 \) and the pathway for horizontal eye movements is turned on.

Now suppose \( \theta > 0 \) and \( a > 0 \), so that an earth horizontal translation is taking place during a tilt, then \( S_x = g \cos(\theta) + a \sin(\theta) \) and \( U_x = g \sin(\theta) + a \cos(\theta) \). Proof that \( F(\theta, a) > 0 \) for all \( \theta \) and \( a \) satisfying the third condition is provided in appendix A.

Before we show that the 4th condition is also satisfied, note first that memory of 1g acceleration is assumed to exist and is subtracted from the saccule in order to obtain \( p \) (figure 2.2). We hypothesize that this memory is forgotten after being in gravity free space so that for this situation and for several hours after landing, \( p = S_x - g_i \) where \( g_i < g \). We will assume that the magnitude of \( g_i \) continues to decrease as long as a subject is in space. Therefore after all the memory is forgotten, \( g_i = 0 \). A head tilt in the absence of translation (\( a = 0 \)) would then result in \( p = g \cos(\theta) \) and \( q = g \sin(\theta) \) so that \( F(\theta, a) = g' \cos(\theta) \sin(\theta) > 0 \) turning on the horizontal eye movement pathway in response to a pure tilt.

### 3.2 H3[S]

Whether a horizontal translation or a tilt is taking place, regular afferents continuously drive \( H_3[s] \) and produce torsional eye movements. In other words, the pathway to \( H_3[s] \) is always turned on. It is up to the horizontal pathway to inhibit the torsional pathway once the horizontal pathway becomes active. \( H_3[s] \) is just a low pass filter defined by:

\[
H_3[s] = 0.05 \left( \frac{1}{(sT_{\text{tilt}})^{0.5} + 1} \right)
\]

3.2
where $T_{r_t} = .5$ seconds. The gain and phase of equation 3.2 after receiving regular otolith input are shown below in figures 3.1a and 3.1b. Actually, this low pass filter is a function of the synapse of a collateral that extends from the horizontal pathway to the torsional pathway inhibiting it (see figure 2.2). So that as the horizontal pathway $H$ is activated, the torsional pathway is inhibited according to $H_3[s]$.

3.3 $H_1[s]$  

Pathway $H$ in figure 2.2 represents the Horizontal TVOR pathway. Once it has been interpreted that a horizontal movement is taking place, information about the amplitude of the movement as interpreted by the irregular otolith afferents and the vergence angle of the eyes is passed on to $H_2[s]$. $H_2[s]$ is a high pass filter described by the transfer function:

$$H_1[s] = \frac{-(sT_1)^{2.5}}{1 - (sT_1)^{2.5}}$$

where $T_1 = 270$ ms. $H_2[s]$ has the responsibility of controlling the gain subject to input from the irregular afferents and the vergence angle. Bode plots for the gain and phase of $H_2[s]$ is shown in figure 3.2. As can be seen, it is merely a high pass filter that changes its phase by 45 degrees throughout the frequency range simulated. The primary afferents have their own transfer function so that irregular primary afferent input into $H_2[s]$ will change its characteristics. Bode plots for the $H_2[s]$ after receiving otolith input is shown in figure 3.3.
Figure 3.1 Gain (where a gain of 1 is a 90-degree torsional eye movement) and phase re acceleration of the torsional VOR as predicted by $H_i(s)$ after receiving regular otolith input. A: Gain of the Torsional VOR. As the frequency increases, the amplitude of the torsional eye movement decreases by continues with very small tilt angles even at high frequencies. Throughout the frequency range simulated, the output of the model closely follows that of the experimental values. B: The phase re acceleration of the torsional VOR. As the frequency increases, the phase approaches head velocity (the phase of the horizontal TVOR. Experimental values from Telford et al., (submitted)
Figure 3.2 Gain and phase of $H_{ij}[s]$. A: $H_{ij}[s]$ has the simple characteristics of a high pass filter. B: The phase starts out at 45 degrees and approaches zero as the frequency increases. This will become important during the discussion about $H_{j[s,w]}$. 
Figure 3.3. Gain and phase of $H_s(s)$ after it receives input from the irregular primary afferents. The differences between the gain and phase presented here and that of figure 3.2 are due to the effect the irregular afferents transfer function has on $H_s(s)$. A: The filter is designed in such a way that otolith input will increase its high pass filter characteristics. M: Meter Angles. B: Phase lead increases after otolith input and continues to lead throughout the frequency range simulated.
$H_i[s]$ is designed in such a way such that its product with irregular otolith input increases the resultant corner frequency. The phase of $H_i[s]$ leads linear acceleration by 45 degrees at 0.1 Hz and is in phase with acceleration at frequencies greater than 1 Hz. (figure 3.2) Due to the phase characteristics of the irregular otolith afferents, upon irregular otolith input the phase lead is increased to 70 degrees at 0.1 Hz and to around 40 degrees at 1 Hz. The phase continues to approach acceleration as the frequency increases but maintains a lead even at high frequencies (figure 3.3b). This phase adjustment will become important later where simulations will show that low frequency translations exhibit a phase lead to head velocity and that the phase of the eye velocity approaches head velocity as the frequency increases (see Paige et al., 1991a, 1991b. Paige et al., 1991 for experimental results). The output of $H_i[s]$ will dictate the amplitude of the eye movement and will be one of the inputs into $H_i[s,w]$.

3.4 $H_2[S,W]$ 

$H_i[s,w]$ is another high pass filter but with different characteristics than $H_i[s]$. Its main goal is to partially differentiate incoming signals as functions of frequency so that they are in phase with the jerk vector (and hence velocity, see page 26). $H_i[s,w]$ was designed as a function of 2 variables; real and complex frequency (equation 3.4). One of the major consequences of this design is that the time constant of decay of a signal going through $H_i[s,w]$ is a function of frequency. The probability for the existence of a neuron that perseverates its signal for a longer period of time after high frequency stimulation in the direct TVOR pathway is presumed low but is unknown. Nevertheless, this transfer function proved highly efficient in reducing simulation time and achieving its desired results. Some of its consequences will be described in the discussion.

$$H_2[S, W] = \frac{s^{1.95}}{(1 + (wT_{reg})^{0.5} (sT_{reg}))}$$  \hspace{1cm} (3.4)

$T_{reg}$ = 1second  
$T_{reg}$ = 0.195 seconds
$H_{fs,w}$ receives input from the regular otolith afferents and its output is multiplied by the output of $H[z]$. The regular otolith input turns on this function but provides minimal high frequency enhancement. Most of the enhancement and amplitude adjustments have been taken care of by $H[z]$ and therefore what is left is the appropriate phase adjustment. Bode plots of the gain and phase of $H_{fs,w}$ before and after receiving regular utricle afferent but without the input from $H[z]$ are shown in figures 3.4 and 3.5 respectively.

The major contribution of $H_{fs,w}$ to the model in figure 2.2 is the phase advancement it provides the regular signal along with the signal coming out of $H[z]$. At low frequencies (below 0.6 Hz), the phase lead is huge reaching up to 180 degrees for frequencies less than 0.1 Hz. This 180-degree phase lead is equal to a 90-degree phase lead with respect to the jerk vector. However, as stated earlier, the jerk vector is in phase with velocity and hence a 90-degree lead with respect to the jerk is in fact a signal that is in phase with acceleration. In other words, if the movement is a low frequency movement, then this transfer functions merely maintains the signals' phase. As the frequency increases, the phase approaches that of the jerk vector. This will ensure that the slow phase eye velocity at low frequencies will lead head velocity.
Figure 3.4 Gain and phase of the high pass filter $H_{a}[s, w]$. Although this filter does affect the amplitude of the incoming signal (especially at low frequencies), its main function is adjusting the phase. A: Like $H_{a}[s]$, $H_{a}[s, w]$ is a simple high pass filter. B: Phase of $H_{a}[s, w]$. As the frequency increases, the phase hovers around 90 degrees leading acceleration.
Figure 3.5 Gain and phase of $H(z,w)$ after receiving regular afferent input. A: Unlike the cascaded gain of $H(z)$ with the irregular input, the gain curve is only slightly affected. B: The phase of $H(z,w)$ begins to lag jerk at high frequencies after receiving regular otolith input.
3.5 OUTPUT OF H1 AND H2

In the absence of canal input, the eye velocity response to a translation is determined by the output of the junction labeled 'jerk' in figure 2.2. At this point, the otolith signal has been made to be in phase with velocity and its sensitivity adjusted accordingly. The velocity commands will then get integrated for the position commands in the box labeled "Canal Processing". Note that the TVOR is a non-ideal system (ideal meaning behaving as is geometrically required) and the sensitivity adjustment that has taken place up to this point reflects this weakness.

The firing rate of a neuron representing a velocity signal that is to be sent to the oculomotor nuclei is shown in figure 3.6a. Recall that the ocular motoneurons require a velocity signal and its integral (position) as described by equation 1.5. However, integration tends to enhance low frequency signals and reduce the amplitude of high frequency ones. Since the TVOR operates best at high frequency, then figure 3.6a is also an approximate description of the firing rate of the oculomotor nuclei as a function of acceleration and vergence since the contribution of the position signal will be small. Figure 3.6b shows that as the frequency increases, the phase of the slow phase eye velocity approaches head velocity. These results compare well with experimental results (see Paige et al., 1991, 1991a, 1991b, Telford et al., 1996, Telford et al., (submitted)).

The gain of the TVOR defined as the peak slow phase eye velocity predicted by the model divided by the peak theoretical slow phase eye velocity is shown in figure 3.7. From the phase difference shown in figure 3.6b (the theoretical phase resides on the 90-degree line), it is apparent that the theoretical and experimental peaks occur at different times for a translation of the form $x(t) = A\sin(\omega t)$. 

Figure 3.6 Velocity command that will feed the oculomotor neurons and its phase. A: Simulations for 4 values of the vergence angle as a function of frequency. The system begins responding after 0.3 Hz because of the filtering achieved by $H_1$ and $H_2$. B: The phase reposition (90 degree line is velocity) is independent of the vergence angle of the eyes and approaches the jerk vector as the frequency increases.
Figure 3.7 shows that the output of the model is always less than what is expected theoretically but approaches the theoretical values as the frequency increases. At 4 Hz, it seems that the model's output reaches 70% of the theoretically ideal value but due to the phase differences, this value is actually smaller (~64%). Nevertheless, the overall shape of the curve still maintained and is consistent with the fact that the TVOR is not a robust system. The theoretical values where obtained from the fact that if we let x(t) be the position at any time t of a subject undergoing interaural translation, let A be the amplitude of the interaural translation and let d be the target distance, then after a time t, one of the eyes has moved θ degrees where θ = ArcTan(\( \frac{x(t)}{D} \)) (figure 1.11). The theoretical slow phase eye velocity will then be defined by equation 3.4 as:

\[
\frac{dθ}{dt} = \frac{x'(t)}{D(1 + \frac{x^2(t)}{D})}
\]

Note that the target distance d is also a variable of time since as a subject is translated, the distance increases. But the simulations carried out in this thesis used A<.05 meters making the change in d negligible.

Another measure of the performance of the TVOR is its sensitivity measured as eye velocity divided head velocity and is expressed as deg/cm/MA for particular accelerations. Figure 3.8 compares the sensitivities obtained from the model (0.25-g peak acceleration) to that obtained experimentally for 0.2-0.3 g peak accelerations. Experimental values were obtained from Telford et al., (submitted) and represent the mean of 3 squirrel monkeys. The sensitivity predicted by the model actually lies within the experimental maximum and minimum range. The slope of the sensitivity curve increases significantly with increasing frequency as expected. The ideal TVOR has a sensitivity slope of 0.57 degrees/cm/MA (Paige et al., 1994), and the experimental values obtained by Telford et al., (submitted) at 4 Hz averaged 0.31 degrees/cm/MA, 54% of the ideal value) and that of the model 0.33 degree/cm/MA.
Figure 3.7 Peak eye velocity produced by the model divided by theoretical peak eye velocity. The sharp rise in the curve indicates the robust high frequency response of the model, reaching 70% of the theoretical value at 4 Hz (see text for further clarification of this value). Note that the peaks occur at different times since the phase produced by the model leads the theoretical phase throughout the frequency simulated. Vergence = 3MA. See figure 3.6b for phase description.

Figure 3.9 show sensitivities as a function of vergence. The influence of vergence on the TVOR response is clearly linear. The slopes of the regression lines agree well with experimental values for high frequencies (4Hz, model: 0.340 deg/cm, experiment: 0.32 deg/cm. 2Hz, model: 0.196 deg/cm, experiment: 0.19 deg/cm), but not for low frequencies (1Hz, model: 0.041 deg/cm, experiment: 0.08 deg/cm, 0.5Hz, model: 0.007 deg/cm, experiment: 0.02 deg/cm) (experimental values from Telford, et al., submitted).
Figure 3.8 Sensitivities obtained from the model compared with the experimental values (Telford, et al., submitted). Experimental values are the means of three monkeys.

Figure 3.9 Sensitivities produced by the model as a function of vergence during interaural translations for several frequencies. Acceleration = 0.2g.
3.6 AVOR-TVOR INTERACTION

One way to excite both the canals and the otolith organs is by eccentrically rotating a subject. Eccentric rotation refers to rotation around an axis that is removed from the center of the head and is useful in studying the interaction between the AVOR and the TVOR. If a subject is eccentrically rotated to the left (figure 1.14), then this is equivalent to a leftward translation and a rightward rotation about a head-centered axis. If the gaze is directed towards the axis of rotation, then the AVOR and the LVOR should cancel resulting in no eye movements (Vürre et al., 1986). If the gaze is directed to a target located farther away than the center, then the AVOR should dominate and if the gaze is directed to a target located closer to the subject than the center of rotation then the TVOR should dominate.

During eccentric rotation, the otolith organs are stimulated by the resultant tangential acceleration, where \( a_{\text{tangential}} = Arw^2\sin[wt] \) where \( A \) is the amplitude of the movement and \( r \) is the radius of rotation. The signal generated by the model in spikes/sec is not sufficient to cancel the AVOR signal which is proportional to the frequency of rotation with 1 Spike/sec/deg/sec (Robinson, 1981). Evidence that the TVOR is more robust when the canals are simultaneously activated was presented by Anastasopoulos et al., (1996). A network of neurons is being developed for the model in figure 2.2 that enhance the TVOR when the canals are activated.

The interaction between the signals coming from the canals and the otolith is predicted to be non-linear. The discharge rate of secondary neurons receiving canal stimulation is proportional to head velocity (Robinson, 1982) which is a linear function of frequency. However, according to the model in figure 2.2, the frequency characteristic of a secondary vestibular neuron receiving otolith input has the shape of a high pass filter (figure 3.6). Suppose that a subject is being eccentrically rotated at a frequency \( \omega_1 \) with the axis of rotation located \( r \) cm infront of the subject with the gaze directed towards the center of rotation. Then the AVOR and the TVOR should add and cancel. Now if the frequency is doubled to \( \omega_2 = 2 \omega_1 \) and the gaze is maintained towards the axis of rotation, then the AVOR and the TVOR should again cancel. \( F[\omega_0] \), the function which we will design to handle this interaction will be both a function of frequency and vergence of the eyes. A simplified version of \( F \) is shown as equation 3.6.
\[ F = \frac{(C + O)^2}{O} \]  

where \( C \) is the signal that originated from the canals and \( O \) is the signals that originated from the otoliths. Simulations showed that canals signals at the junction \( F[c,o] \) always dominated the otolith signal up to a frequency of 4 Hz so that for low at frequencies less than 4 Hz, the output of \( F \) is greater than the Otolith input. Note that in the absence of canal stimulation, such as during a pure linear translation, or when there is a large otolith signal, such as during eccentric rotation with a close target, \( F \) simply reduces to \( O \). Figure 3.10 depicts frequency characteristics of central Canal (Robinson, 1981) and Otolith neurons as predicted by the model.

![Frequency (Hz)](image)

**Figure 3.10.** Firing rates of the central canal neurons (Robinson, 1980) compared to the predicted firing rate of central otolith neuron for different vergence angles. The nonlinearity of the central firing rate of otolith neurons force the interaction between the AVOR and the TVOR to be nonlinear.

According the anatomy in figure 2.2, even in the absence of an otolith signal, an increase in vergence can in effect increase the discharge rate of the horizontal pathway as long as the background discharge of the Otolith primary afferent is maintained. It is possible then that the AVOR receives its information about vergence from this pathway. A lesion that might abolish
the background discharge rate of otolith primary afferents could then reduce the AVOR's dependance on vergence.
Chapter 4

4.0 Discussion

This thesis presents a systems model that simulates the eye movements produced during sinusoidal linear interaural translations. This kind of modeling leads to certain disadvantages since often, the signals that are created in a systems model are not found in the brain making the model unrealistic. Another disadvantage is that such a model does not include thresholds or saturation of single neurons but attempts to simulate the population behavior of the system. Nevertheless, the advantage of such modeling is the ability to understand the system in terms of mathematical principles and derive experiments based on the predictions of the model.

Two types of TVOR are described. The first maintains ocular fixation during interaural translation and the second causes torsion of the eyes in response to a head tilt. For horizontal translations, the model utilizes signals recorded from otolith afferents by Fernandez & Goldberg (1976) and attempts to manipulate these real signals into a form (Robinson, 1980) that would produce compensatory eye movements. Several important variables that influence the TVOR, including the vergence angles of the eyes (target distance), amplitude of the translation and the frequency of translation where manipulated in order to quantify the TVOR.

One of the flaws of the model is that it is a unilateral model that drives a cyclopean eye. Contralateral otolith input might play a role in the control of eye movements even though if they do it is probably minimal. It may be that commisural pathways are not a property of the otolith-ocular system (Wilson & Melville Jones, 1979). If they are, we expect to be able to adjust the gains of the transfer functions presented here in order to accommodate the contralateral otolith input. Our major goal was to reproduce experimental data (Paige et al., 1991, Paige et al., 1991a, Telford et al., submitted) using primary afferent input as described by Fernandez and Goldberg (1976c) and we believe we have succeed at that task as shown in figure 4.1. On the other hand, the experimental results on which we based our model are actually the product of a bilateral system. Although the architecture is different between the model and the real system, our main concern is with procedure. Can the jerk vector be used in obtaining an accurate central representation of head velocity? We believe that it can. With this established, some of
our future goals are to extend the model to accommodate contralateral vestibular input. Another flaw is that we have assumed that the population of the regular and irregular otolith afferent is the same. Figure 1.5 shows a histogram of the number of units with a particular coefficient of variation (COV). The COV of regular and irregular afferents are less than 0.1 and greater than 0.4 respectively. It is obvious from figure 1.5 that the regular primary afferents outnumber the irregular ones, something we have not taken into consideration when designing the model. The reason for this is we believe that the regular and irregular afferents have different functions in driving the TVOR. The irregulars dictate the size of the movement to be performed while the regulars inform the system of the type of movement that needs to be performed. Recall that regular otolith afferents have a flat frequency response and we believe that the regulars are inadequate to set the required output amplitude for different frequencies of stimulation. Also, because of their low gain, modestly increasing their number in the model would have little effect on the frequency dependence of the system as designed. Modeling the neurons they feed ($H_1$ and $H_2$) as we did, led us to believe that regular afferents serve another purpose. As shown in figure 1.6, irregular afferents also adapt quite significantly in a very short period of time. Recall that the time constant of $H_2[s,w]$ is a function of frequency such that as the frequency increasing, so does the time constant. The slight increase in gain of a regular afferent due to an increase in frequency is sufficient to alter the time constant of $H_2$. Therefore, this neuron will be used in subsequent modeling to perseverate the signal driven by the irregular afferent so that as the irregular signal adapts, the reflex will maintain its functionality. Regular otolith afferents have been designed to drive $H_2[s,w]$ and therefore we hypothesize that their greater population serves to compensate for the irregular otolith afferents adaptation. No work has been undertaken to develop this idea but it is also part of our future goals.

One of the advantages of the model is that the primary afferent signals used are provided by the transfer function derived by Fernandez & Goldberg, (1976c). Using the real otolith signal made the model more realistic and restricted us with the kind of processing we could do on them since the afferents dynamics had to be taken into consideration. The transfer functions shown in chapter 3 proved to be the most efficient and several predictions could be made based on their functionality. These predictions are listed in the next section.
Figure 4.1 Slow phase eye movements for translations with different frequencies. Amplitude = 0.2 g for all plots. A: For high frequency, the model and experimental values approach that of the theoretical but still lead in phase by less than 10 degrees. B, C: As the frequency decreases, the experimental and model output become even more non-ideal and increase their phase lead. The model and the experimental values are in good agreement for all 3 frequencies simulated.
4.1 PREDICTIONS AND EXPERIMENTS

The first predictions we will mention have to do with torsional eye movements. In place of the frequency filter hypothesis that presumably allows the otolith ocular system to distinguish between an interaural translation and a tilt of the head (Paige et al., 1991a), we have taken into consideration the modulation of both the saccule and the utricle and have come up with a function (equation 3.1) that can distinguish between the two stimuli. The model in figure 2.2 has two independent pathways, one for the horizontal eye movements (horizontal pathway) and one for the torsional eye movements (torsional pathway). The torsional eye movement pathway has been modeled to continuously receive regular otolith afferent input and is therefore always on ("on" meaning carrying a signal). The signal coming from the regular afferents is then passed through a low pass filter restricting the torsional eye movements to low frequency translations mirroring experimental results (Paige et al., 1991a). Actually, the low pass filter $H_t[s]$ has taken the place of a synapse that extends from the horizontal pathway to the torsional pathway (figure 2.2). In this design, the torsional pathway is always kept on during any movement in any direction by the modulating regular afferents, but as soon as the horizontal pathway is turned on, a collateral extending from this pathway to the torsional one will inhibit the torsional eye movements with low pass filtering characteristics. Therefore, the first prediction that is produced from this design is that

P1) The torsional eye movements can be inhibited only if the horizontal eye movement pathway is turned on.

If P1 is true, then it is possible to activate the torsional VOR pathway with a high frequency signal and still get torsional eye movements if the horizontal eye movement pathway is not turned on. This could be accomplished by using galvanic currents while recording torsional eye movements for a variety of frequencies. Irregular afferents can be selectively and reversibly silenced by applying a DC anodal current of 100 µA unilaterally or bilaterally to both ears (Goldberg et al., 1992, Angelaki et al., 1992b). If in fact the horizontal pathway inhibits the torsional pathway, then by applying galvanic currents we expect the amplitude of the torsional TVOR to maintain a somewhat constant amplitude across frequencies.
According to the anatomy shown in figure 2.2, the torsional VOR is at most a di-synaptic reflex. Evidence has already been obtained by Uchino et al., (1994) that there do exist connections from otolith primary afferents onto the abducens nucleus in cats. Torsional eye movements do not result from abducens activation but from activation of the oculomotor and trochlear nuclei. We are predicting that these connections also exist. Our second prediction then states:

P2) The latency of the torsional eye movements should be equal to the time it takes for a signal to cross a synapse and for the eye muscles to be activated. In total, the latency is predicted to be less than 10 ms. This can only be accomplished if there exist direct regular otolith afferent connections onto the trochlear and oculomotor nuclei.

Torsion of the eyes is of very low amplitude during horizontal translation so why even have a torsional eye movement? During translations and upon an abrupt change in the direction of motion, processing delays might cause objects to be perceived as twisting causing the eye to undergo torsional movements. However, the error associated in aligning a bar vertically on earth is about 2-3 degrees making any twisting effects that might be perceived negligible. It also may be a by-product of the design of the TVOR. We can test this idea by noting that the combination of P1 and P2 suggests that every horizontal eye movement is preceded by a torsional one. This idea is not only a result of the differences in latencies, but of our anatomical design. The torsional pathway can only be inhibited after the horizontal pathway has been turned on.

The torsional pathway is activated by regular otolith input. Recall that firing rate of regular afferents is almost constant across frequencies so that a large increase in frequency would not cause a large change in the attributes of the torsional VOR if it were not for the presence of the horizontal pathway. Regular afferents are the only input to the torsional mechanism and this design gives us our third prediction:

P3) Removing the regular otolith afferent would eliminate the torsional eye movements during tilts and horizontal translations. Also applying galvanic currents to the ear (galvanic currents have been shown to silence the irregular afferents, see below) should have no effect on the torsional eye movements.
One of the consequences of this prediction is that the torsional TVOR is not driven by irregular otolith afferents. Currently there is no method by which regular otolith afferents can be silenced making this prediction difficult to test directly. The experiment used to prove prediction 1 could be utilized even though this only gives us some proof that the irregulars do not drive torsional eye movements rather than that the regular input drives them. The simulated torsional eye movements' responses are shown in figure 4.2 for interaural translations for frequencies of 1 Hz and 3 Hz at an acceleration of 0.2g.

![Graphs showing torsional amplitudes for various head translations.](image)

Figure 4.2 Torsional amplitudes for various head translations. Acceleration = 0.2g. A: Very low frequency movements yield the highest amplitude (2.5 degrees) and a phase very close to linear head acceleration. B, C: As the frequency increases, the phase approaches head velocity but the amplitude decreases considerably. D: A typical head velocity profile at 1Hz.

Note that there is no vergence information supplied to these pathways (figure 2.2) maintaining experimental consistency that the torsional part of the TVOR is not a function of vergence (Telford et al., submitted)). But as mentioned earlier, the degree of activation of the horizontal
pathway will dictate the degree of inhibition of the torsional VOR pathway. The TVOR is a linear function of vergence (Paige & Tomko, 1991b). Therefore, an increase in the vergence angle should increase the activity of the horizontal pathway, which in turn decreases the activity of the torsional pathway. This attribute would make the torsional VOR a function of vergence angle even though the effect is indirect. This leads us to our fourth prediction:

P4) The torsional VOR is a function of vergence angle only during horizontal translation.

This is fairly easy to test. Torsional eye movements could be measured during translation with the gaze of the subject directed at targets with different distances. As the target distance increases, so should the amplitude of the torsional eye movement.

According to the model, horizontal eye movements are mediated by regular and irregular afferents and are a function of vergence. Both the TVOR and the AVOR use a final common pathway instead of parallel pathways and it will be argued later that when both are active, the AVOR enhances the TVOR. Our fifth prediction states that

P5) The AVOR and the TVOR use the same pathway and share the neural integrator. So that destroying the integrator will affect the ability to hold gaze for both translations and rotations for a particular direction of movement.

Simulations showed that otolith velocity signals are always dominated by canal velocity signals and that canal activation can enhance otolith velocity signals. After receiving this enhancement, the otolith signal is modeled to add to the canal signal. Although not shown here, this can provide a central measure of the robustness of the signal coming in and merging with the canal cells. This might even be a site for adaptation since the strength of enhancement can be adjusted. This idea has not be pursued in detail but led to the idea that the merged signals continue on to a common integrator.

The model has the vergence angle of the eyes (or target distance) affecting the reflex at the level where the irregular otolith afferents act in the brainstem, we predict that:
P6) Silencing the irregular otolith afferents will also reduce the systems dependence on the vergence angle.

According the anatomy presented in the model, this would be difficult to verify. Angelaki et al., (1992b) found that applying galvanic stimulation during Off Vertical Axis Rotation (OVAR) reduced the amplitude of the slow phase eye velocity by 70%. Goldberg et al., (1992) on the other hand showed that the effect of such a current applied to the inner ear while the monkey was undergoing motion in a centrifuge was minimal. Simulations of the model presented here tend to agree with the Angelaki result. Removing the irregular afferent input reduced the slow phase eye velocity by up to 80%. Therefore applying galvanic currents to the ears in order to verify prediction 6 will not work. As mentioned earlier, the slow phase eye velocity is expected to be reduced but what we would like to ascertain is how much of this reduction is due to the silencing of the irregular otolith afferents and how much of it is due to the reduced sensitivity to the vergence angle. If information about vergence affected the system at a different site, then the reduction in eye velocity when applying galvanic currents can be attributed to its effect of silencing the irregular afferents. But if information about vergence affected the system as indicated in figure 2.2, then the reduction in eye velocity will also be due to the lack of information about vergence. The methods in which we have tied both of these variables together make it difficult to disable one and observe the effect on the other.

Our seventh prediction deals with the contribution of the regular otolith afferents to the slow phase eye velocity. Specifically, we predict that

P7) Silencing the regular otolith afferent is predicted to reduce the slow phase eye velocity by up to 85%.

Regular afferents can not be silenced as of yet. But like the irregulars, simulations showed that slow phase eye velocity was reduced by up to 85% if the regular input was removed from the model. This result is indirectly supported by Goldberg et al., (1992) who supports the idea that regular afferents drive the VOR while irregulars drive the vestibulo-spinal tract. Their argument is based on the relative gains of the primary afferents. They argue that the irregular afferents have a large enough gain as to be able to move a heavy body. On the other hand, the eyes carry
no load (Robinson, 1980) and are easy to move so that the regular afferent signal is sufficient for their reflex. The design we have used here use both the regular and irregular signals for the TVOR and eliminating either one proved to reduce the slow phase eye velocity.

As mentioned earlier, the model utilizes memory of a 1g acceleration in deciding whether a movement made is a tilt or a translation. We further hypothesized that this memory is forgotten after space flight and returns with a certain time constant when the astronauts return to earth. Immediately after landing, the memory of a 1g force is at its minimum causing a tilt of the head to be interpreted as a linear translation (Parker et al., 1985) (how the model accomplished this was shown in the results). Other predictions that can be made from such a design are listed below but involve experiments that need to be conducted in space. If the canals of an animal are plugged as to eliminate their contribution, then on earth the amplitude of the eye velocity during horizontal translations with an animal in the upright position should be greater than the amplitude during a horizontal translation with the animal tilted some angle $\theta$ from the vertical (where the vertical is defined as the axis perpendicular to the axis of translation.) If the interaction between the saccule and the utricle is as defined by the anatomy of the model, then we predict that

P8) The opposite is true in space. That is, after tilting an animal, the amplitude of the slow phase eye velocity is expected to increase.

This prediction relies on the absence of the 1g memory in space. Recall that the function of equation 3.1 is to decide whether a tilt or a translation is taking place. Although in the Results section we treated equation 3.1 as having a digital output, its future function is to provide a degree of activation that is dependent on the degree of tilt. We shall utilize this fact here in providing basis for prediction 8. The 1g memory does not exist in space resulting in no input from the saccule in the upright position reducing equation 3.1 to $a$ (see the Results section for a definition of these variables). The acceleration detected by the saccule in space during a horizontal translation while tilted an angle $\theta$ from the vertical is $S = a\sin(\theta)$ reducing equation 3.1 to $a^2\sin(\theta)\cos(\theta) + a$ which is clearly greater than the acceleration felt in the upright position. This is predicted to increase the activation of the horizontal pathway leading to larger
amplitude eye movements during horizontal translations than during a tilt. Note that the product \( \sin(\theta)\cos(\theta) \) is generally a small number, and since the horizontal acceleration \( a \) is measured in g's, the increase in the perceived acceleration will be small.

Further predictions can be made concerning signals that could be found in the vestibular nucleus. The model in figure 2.2 achieves a signal that is in phase with velocity by differentiating the acceleration signal and not integrating it as is mathematically required. Integration is not suited for the TVOR because integration enhances low frequency signals and reduces the gain of large frequency signals. The TVOR is known to be a high frequency system and if subjected to a double integration would develop characteristics that are inconsistent with experimental values. Specifically, it would exhibit sensitivities (defines as eye velocity/head velocity) that are low pass filtered and not high pass filtered. Therefore, signals that lead linear acceleration are predicted to exist in the central vestibular neurons. Recall that irregular otolith afferents show partial differentiation in their signal since they lead linear acceleration by up to 30 degrees at 2 Hz (figure 1.8d). Our ninth prediction involves these phase values and states that:

P9) There exist signals in the vestibular nucleus that lead linear acceleration as a function of frequency. As the frequency increases, so should the phase lead.

Single cell recording in the brain stem of alert animals is the only way to search for these signals. We expect to start single cell recordings by September, 1997.

Simulations of eccentric rotations where carried out to study the AVOR-TVOR interactions. In all cases except for frequencies greater than 4 Hz, the processed otolith signal proved inadequate to add to the dominating canal signal to exhibit the observed behaviours. Although linear translations simulated eye movements that are consistent with experimental values, eccentric rotations did not. After enhancing the otolith signal with the canal signal, we were able to improve the simulations. Although preliminary results have shown that the TVOR is more robust when the canals are activated (Anastasopoulos et al., 1996), we found that this design is necessary for explaining the AVOR-TVOR interaction, and specifically the cancellation of eye movements observed when the subject is facing the center of rotation. Contralateral otolith input is expected to provide some of the enhancement but as mentioned earlier, high frequency
rotations caused the otolith signal at the summing junction with the canals to be very large. Contralateral input would then compound this problem. It is expected that both canal enhancements of otolith signals and contralateral otolith signal take part in adjusting the signal. We believe that the canal signal is important here since it gives the otolith signal a relative rather than absolute measure of how well it is doing. Based on our simulation, we can predict that

P10) The central otolith signal is more robust when the canals are activated.

We have just started modeling this interaction. It is expected to take the shape of a network of neurons that analyze the canal and otolith activation rates and provide enhancement to the otolith signal accordingly. As mentioned earlier, if the target is located farther than the axis of rotation, then the AVOR should dominate, and if the target is located closer than the axis of rotation, then the TVOR should dominate. One of the characteristics of this network of neurons is to provide this phase change based on information about vergence. It will also be a function of frequency since the otolith require more enhancement at low frequencies (note that when talking about low frequencies, we are actually referring to magnitudes of about 1 Hz since anything lower than that causes the pursuit system to be active).

We have mentioned earlier that the AVOR and the TVOR use a final common pathway on their way to the neural integrator and to the plant. Actually, it is the pathway of the AVOR that the otolith signals use and therefore our next prediction is that

P11) The gain of the TVOR is predicted to decrease with canal lesions but the gain of the AVOR is predicted to be unaffected by otolith organ lesions.

Plugging the canals maintains the baseline-firing rate causing no change in the way the TVOR operates in the absence of canal input. But if this baseline-firing rate can be abolished, then the gain of the TVOR is expected to decrease. During linear translation, the junction where the canal signal sum with the otolith signal would be affected since there is no longer a steady state baseline firing rate coming into the junction. Eccentric rotations would affect the TVOR to a greater degree since the canal enhancement of an otolith signal would also be eliminated. The
only way to test this result is by measuring slow phase eye movements with an animal that has a lesioned canal.

An increase in frequency (acceleration), or an increase in vergence will cause the central otolith neurons to increase their discharge rates (Fernandez & Goldberg, 1976c, Paige et al., 1991). Simulations showed that increasing the radius of rotations during eccentric rotation has the same but opposite effect as increasing the vergence angle by the same amount provided that the gaze is directed at the center of rotation. After further thought, it becomes clear that this is what is geometrically expected. Consider an eccentric rotation with a radius \( r \), and vergence \( V = 1/r \), then theoretically there should be no eye movements.(Vührre et al., 1986) If the radius is now increased, the frequency kept constant and the vergence decreased according to the equation above then the eye movement should still be zero. Therefore increasing the radius of rotation (increasing the acceleration) and decreasing the target distance by the same amount have the same but opposite effect on the TVOR if the gaze is directed at the center of rotation. If gaze is directed away from the center of rotation, then we do not expect this result to be true. Therefore, interaction between the canal signal and the otolith signal is expected to make the TVOR a nonlinear function of vergence for gazes that are directed away from the center of rotation. This cannot be listed as a prediction since the network of neurons that accomplished this task has not yet been developed.

After many simulations, the following observation was made regarding the behaviour of eye velocity as a function of frequency.

P12) During horizontal translations, the slow phase eye velocity increases as a function of the square root of the frequency.

In contrast to this observation, the AVOR is a linear function of frequency. Why the TVOR in the model behaves this way is not yet known but we believe this will further enhance our understanding of the non-linear interaction between the AVOR and the LVOR.

The model in figure 2.2 was successful in reproducing most of the experimental results. Its major flaw is that it is not a bilateral system and the effect of contralateral input has not yet been
assessed. We also want to develop a model for $H_{[5]}$ that will shed some light on the interaction between the otolith organs and the canals. Nevertheless, we believe that the model shows us a way in which eye velocity can be extracted from the raw otolith signals without using a double integration.
Appendix A

PROOF THAT $F(\theta, a)>0$

Proof that $F(\theta, a)>0$ when $F(\theta, a) = (g\cos(\theta)+a\sin(\theta)-g)(g\sin(\theta)+a\cos(\theta))+a$.

Multiplying through, we have:

$F(\theta, a) = g\cos(\theta)\sin(\theta)+ga\cos^2(\theta)+ga\sin^2(\theta)+a^2\sin(\theta)\cos(\theta)-g^2\sin(\theta)g\cos(\theta)+a$

Rearranging:

$F(\theta, a) = \sin(\theta)\cos(\theta)(g^2+a^2) + ag-a\cos(\theta)+1-g^2\sin(\theta)$

Clearly, $ag > a\cos(\theta)$ and since $g=1$, then $1 > g^2\sin(\theta)$ making $F(\theta, a)>0$ for all $\theta$ and $a$. 

83
Appendix B

LIST OF PARAMETERS

The following parameters were used for all simulations presented in this thesis.

Otolith Primary Afferents

\[ H(s) = \frac{1 + k_A T_A s}{1 + T_A s} \left( \frac{1 + k_v (T_v s)^k_v}{1 + T_M s} \right) \]

Irregular Afferents:
- \( k_v = 0.44 \)
- \( k_A = 1.9 \)
- \( T_A = 101 \) seconds
- \( T_M = 0.009 \) seconds
- \( T_v = 40 \) seconds

Regular Afferents:
- \( k_v = 0.188 \)
- \( k_A = 1.12 \)
- \( T_A = 69 \) seconds
- \( T_M = 0.016 \) second
- \( T_v = 40 \) seconds

\( H_1[s] \):

\[ H_1[s] = \frac{-(sT_1)^{2.5}}{1 - (sT_1)^{2.5}} \]

\( T_1 = 0.27 \) seconds
Gain = 1

\( H_2[s, w] \):

\[ H_2[s, w] = \frac{s^{1.95}}{(1 + (wT_{regr})^{0.95}(sT_{regc}))} \]

\( T_{regr} = 1 \) second
\( T_{regc} = 0.195 \) seconds
Gain = 1

$H_3(s)$:

$H_3(s) = 0.05 \left( \frac{1}{(sT_{ult})^{95} + 1} \right)$

$T_{ult} = 0.5$ seconds
Gain = 0.5
REFERENCES


89


Telford, L., S. H. Seidman, et al. (submitted, 1997). "Dynamics of Squirrel Monkey Linear Vestibuloocular Reflex and Interactions with Fixation Distance"


