The vestibulo-ocular reflex: computation in the cerebellar flocculus

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Abstract

The function of the vestibulo-ocular reflex, commonly known as the VOR, is to stabilise an image on the surface of the retina during head movement. One of the parts of the brain involved in this reflex is the flocculus in the cerebellum, which integrates information from multiple sources, including the vestibular apparatus in the labyrinth of the middle ear, motion detectors in visual cortex, and afferents from the muscles of the neck and eye. Research has shown (van der Steen et al[44] and others) that the flocculus is organised in a topographically ordered way, such that oculomotor responses elicited by stimulation of neighbouring areas of flocculus are close together in rotational-geometric space. This paper describes the vestibulo-ocular reflex in some detail, both from the mathematical and neurophysiological perspectives, and presents a computational model of how this topographic organisation can come to be learned from the information presented to the structure.

Contents

1 Introduction

1.0.1 Stimulus

The stimulus for the VOR is head acceleration, detected by the vestibular apparatus of the middle ear, which is comprised firstly of the labyrinth, three semicircular canals at approximately 90° to each other, which can gauge acceleration around the three (roughly) orthogonal axes, and secondly of the otoliths, the utricle and the saccule, which are primarily concerned with acceleration with respect to gravity. The labyrinthine canals are filled with endolymph fluid, which moves relative to the walls of the canal during head acceleration as a result of inertia; this movement disrupts hair cells or follicles which protrude into the canals, bending them in one direction or another, and thus causing them to depolarise or hyperpolarise according to their orientation.

1.0.2 Response

The VOR achieves stabilisation of the object in the visual field by controlling the eye muscles in such a way as to compensate for this head acceleration. If this control were calculated cortically (smooth pursuit), the object would smear over the retina as the cortical pathways are too long and involved, and hence slow. This would be a very bad thing for predatory agents, since they would have to stop every time they wanted to get an adequate fix on their prey, and possibly equally disabling for the prey itself. Thus, the VOR must be a fast, accurate reflex. Compensatory eye movements begin approximately 14ms after initiation of head acceleration, depending on the head velocity (we will return to this later).

1.0.3 Normal performance

The *gain* of the VOR is defined as eye speed over head speed, a simplistic and inaccurate measure of the performance of a complex three-dimensional rotation, yet often used to describe this performance. In these terms, the gain of the VOR in normal mammals is very close to 1 even in darkness at head speeds of up to 300°/s due to its dependence on vestibular rather than visual stimuli. To demonstrate the VOR in action, try this small experiment:

1. Keep your head facing in one direction, and move your hand fairly quickly backwards and forwards in front of you, trying to track only with your eyes. The image of your hand is blurry.

2. Now keep your hand still and move your head from side to side. Even when the speeds are about the same, the image of your hand is much crisper in this condition.

In the second condition, information from the vestibular apparatus is integrated with visual information to provide much faster responses for the eye muscles. The image of your hand will not appear smeared unless the slip over your retina is greater than about four degrees per second.

1.0.4 Conventions

Many neurophysiologists describe head and eye movements with respect to planes: the frontal, sagittal, and transverse (horizontal) planes. In this paper I shall consistently use descriptions of eye and head movements as rotations around axes with such terms as pitch, yaw, and roll. These terms are defined as follows: pitch is rotation about the horizontal (interaural) axis, yaw is rotation about the vertical (ground-orthogonal) axis, and roll, or torsion, is rotation around the

line of sight (naso-occipital) axis. These terms are normally intended to refer to eye orientations in a head-centred coordinate system.

I shall use the terms "saccade" and "saccadic eye movement" to describe both a vector representing VOR gain and the fast component of nystagmus (a vestibular-oculomotor disorder, sometimes very brief, characterised by the eyes "following" an imaginary target from one side to the other and then quickly jumping back to the first side to begin the scan again). In these cases, all that is being referred to is "some fast eye rotation", in contrast to smooth-pursuit eye movements such as the slow component of nystagmus.

Some neurophysiologists have been concerned over the use of the nomenclature describing cerebellar components of the VOR. In this paper, as in the vast majority of the research done on the VOR, I use the term "cerebellar flocculus" to cover a structure that, it has been pointed out, consists of the ventral paraflocculus rostrally and the flocculus caudally (Lisberger et al[29]). This may be of concern, since the ventral paraflocculus and flocculus differ in the origin of their visual mossy fibres despite being anatomically similar in other respects (their inputs and outputs). However, since it has not yet been shown that one or other of these structures is not definitively involved in the VOR, and they do both appear to be involved in such motor learning, I consider the distinction unnecessary.

2 Kinematics of the vestibulo-ocular reflex

2.1 Coordinate systems: defining rotations

2.1.1 Rotation matrices

In order to define eye movements in three dimensions we must first establish two coordinate systems, one head-fixed ($\{h_1, h_2, h_3\}$) and one eye-fixed ($\{e_1, e_2, e_3\}$), where 1, 2, and 3 in each case refer to torsional, horizontal, and vertical components of the coordinate system. We can then describe any eye rotation by means of a matrix multiplication operating over the head coordinates; for instance, a purely torsional eye movement with an angle of θ could be described by the matrix

$\parallel v^L - w_{c^L}^L \parallel \leq \parallel v^L - w_i^L \parallel \forall i,$

a movement around the horizontal axis with the same angle could be described as

$\Delta w_i^L = \eta^L h_{i,c^L}^L (v^L - w_i^L) \forall i,$

and a movement around the vertical axis would be

$v^S = v^L + \frac{\sum_i h_{i,c^L}^S w_i^S}{\sum_i h_{i,c^L}^S}.$

However, despite the simplicity with which such matrices are applicable in one dimension at a time, pure three-dimensional rotations cannot be determined straightforwardly from these equations.

One of the most salient questions in defining a coordinate system for describing three-dimensional rotational eye movements is the *order* the rotations are carried out. Normally two such orders are considered: the Helmholtz-gimbal and the Fick-gimbal. The Fick-gimbal, initially considered a sensible reference system for eye movements, relies on the idea of first specifying horizontal movement, then vertical, and finally torsion. The Helmholtz-gimbal, in contrast, is characterised by a rotation about the horizontal axis, then a rotation about the vertical axis, and finally a rotation around the line of sight. This was considered to be advantageous by von Helmholtz[**?**] since variations of head pitch make the concept of a horizontal eye movement (i.e. rotation about earth-vertical) difficult; however, it is in fact quite arbitrary.

Different gimbal systems will specify different values for the components in the rotation matrices required to perform the same rotation. Experimentation Tweed et al[41] and others with scleral search coils (a means of converting 3D orientation into voltages using oscillating

magnetic fields) has led to a much-discussed problem, that of *false torsion*: torsion values in one gimbal system will differ from those in another, and therefore the values must be specified relative to one gimbal system or another.

2.1.2 Quaternions and rotation vectors

Although rotation matrices are an intuitively simple tool for describing rotations, they are not the most efficient or useful. *Euler's theorem* dictates that any three-dimensional position can be reached from a base position by means of a rotation around some fixed axis. Thus, a more efficient means of describing rotations is to use a vector such that the direction of that vector is the axis of rotation and the extent of the vector is the angle of rotation: this obviates the need for procedural calculation. *Quaternions*, four-component vectors with some specific properties invented by Hamilton in 1899 to convert one vector into another by multiplication with yet another, are an elegant way to view such a process. A quaternion q which describes a rotation around an axis a by an angle of θ is given by

$q = q_0 + (iq_1 + jq_2 + kq_3).$

This is also often written as

$q = q_0 + q \cdot I.$

with q and I defined as

$\| v^S \| < r_{fovea}$ and $\| v^S - w_{cS}^L \| \leq \| v^S - w_i^L \| \ \forall i$

as q_0 is seen to represent the scalar component of the quaternion, and q the vector component. Quaternions have stringent constraints on both the real and imaginary components, such that the real elements $\{q_0, q_1, q_2, q_3\}$ have the properties

- $v^{S'} = v^S + \dfrac{\sum_i h_{i,cS}^S w_i^S}{\sum_i h_{i,cS}^S}$

- $\| v^{S'} \| < \| v^S \|$

- q is parallel to a

and the imaginary elements $\{i, j, k\}$ are governed by

$i \cdot i = -1, j \cdot j = -1, k \cdot k = -1, i \cdot j = k, j \cdot k = i, k \cdot i = j, j \cdot i = -k, k \cdot j = -i, i \cdot k = -j.$

From the above equations we can see that quaternions that describe rotations must have length 1: these are called *unit quaternions*. If a quaternion is not 1, then it will combine a rotation with a change in the scalar component q_0, i.e. it will stretch the vector as well. In eye kinematics, we use only unit quaternions. To combine two quaternions we use the formula

$\Delta w_i^S = \eta^S h_{i,cL}^S ((w_{cL}^S + w_{cS}^S) - w_i^S) \forall i$

from which we can see that the sequence of quaternions is important (as with the ordering of rotation matrix calculations): $h_{i,u}^L$, but leads to a different eye orientation. A combination of quaternions in this way can be interpreted to mean "p after q" in a head-fixed rotation (Haslwanter[14]).

As we have seen, the scalar component of a quaternion does not provide any further information than the vector component with regard to head rotations (i.e. when we are concerned only with unit quaternions). Therefore, it can be eliminated, leaving a *rotation vector*. For instance, a rotation vector r corresponding to our quaternion q above can be written as

$h_{i,u}^S.$

What can we use rotation vectors for? Primarily, since we can measure the orientation of the eye in absolute space (*gaze*), and also the orientation of the head, using dual scleral search coils, we will want to know the position of the eye relative to the head. Given r_{head} the rotation vector describing the orientation of the head (in a head-fixed reference system), and r_{eye} the orientation of the eye with respect to the head, we can specify r_{gaze} the absolute rotation of the eye in terms of the other two givens as

$\| i - u \|$

which can be rearranged to give r_{eye} our target

$\| i - u \| = \sqrt{[(r_i \sin(\frac{2\pi c_i}{C})) - (r_u \sin(\frac{2\pi c_u}{C}))]^2 + [(r_i \cos(\frac{2\pi c_i}{C})) - (r_u \cos(\frac{2\pi c_u}{C}))]^2}.$

The inverse quaternion q^{-1} for unit quaternions is given by

$E = \frac{\sum_i \|w_i^L - w_i^S\|}{N},$

therefore the inverse rotation vector r^{-1} is, straightforwardly, $-r$.

2.2 Effects of eye position

Experiments carried out by Misslisch et al[33] on the slow phase velocity vectors of subjects tested during roll, pitch and yaw rotations show that the axis of eye rotation tilts systematically depending on eye position. For instance, responses to pitch rotation while looking to the left are biased slightly to the left, and, vice versa, responses to pitch while looking to the right are tilted to the right, whereas responses to roll near the abscissa (the naso-occipital axis) show the opposite effect.

There have been three main hypotheses posed to explain these effects of eye position and the weakness of torsional VOR. Firstly, the degrees of eye rotation that actually occur do not correspond in a linear fashion to the degrees of activation of the innervation of the extraocular muscles. This argument is known as the *orbital mechanics hypothesis*. Alternatively, the neural control mechanisms may cause different rotations in different eye positions for some functional reason. If we abandon the assumption that the VOR is attempting to stabilise the entire retinal image, and imagine that fovealisation of the stimulus is more important, then we have a greater degree of freedom in that for any given head acceleration, an infinite number of eye movements could be triggered with velocity vectors identical except for the torsional component, all of which would correctly fovealise the stimulus. There are two hypotheses that have been developed in line with this suggestion: firstly, that the smallest velocity vector of these possible eye movements is chosen (the *minimum-velocity strategy*), and secondly, that the eye velocity consistent with *Listing's law* is chosen, given that this principle holds for fixation, pursuit and saccadic movements.

2.2.1 Listing's Law

The definition of Listing's law is as follows: for any position q taken up by the eye, there exists a head-fixed plane VP_q associated with that position such that all possible eye positions can be reached by a single rotation around a fixed axis in VP_q (von Helmholtz[45]). This plane VP_q is also known variously as *Listing's plane*, the *velocity plane*, and the *displacement plane*. Thus, there is a simple experiment that can be performed: if an oculomotor system obeys Listing's law, the quaternion vectors that describe eye position will be confined to the velocity plane of reference position. However, this assessment has not been found to be useful with respect to the VOR, and therefore a modified version developed by Helmholtz[45] is generally applied: if the eye is in position q, the velocity vector must lie in the associated velocity plane VP_q, given that the velocity planes of different eye positions are different. It can be shown that an oculomotor system that follows Listing's law in this way cannot perfectly stabilise a retinal stimulus.

One of the difficulties facing 3D modellers in this respect is the non-commutativity of 3D rotations. If the eyeball is rotated in any direction, the axes about which it must rotate from the centre postion will always lie in some displacement plane. Moving back to the primary position taking the reverse path from that taken to arrive at the eccentric position always leads to zero torsion. However, let us imagine a situation where three movements are taken in sequence: one 30° around the horizontal axis, then one 30° around the vertical axis, and then one back to primary position. If Listing's law were obeyed in this position, the torsion would be the same as a the start. In fact, however, this leads to negative torsion (see Figure 2.2.1) because the
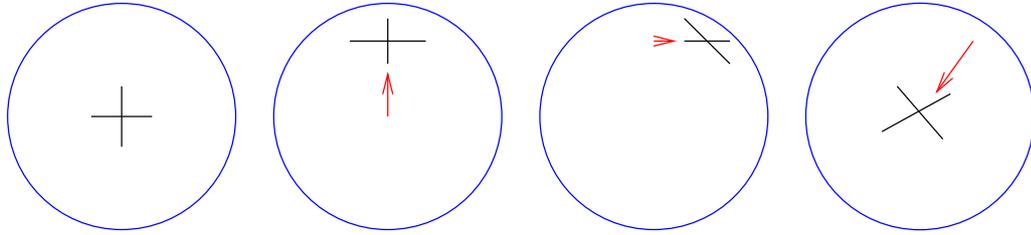
Figure 1: The non-commutativity of 3D rotations

second rotation is not in a radial direction. If torsion remains unchanged, the rotation vector between two orientations in Listing's plane cannot itself be in Listing's plane except in radial movements.

What does this mean for the VOR? It seems that two radical possibilities could be in effect: either the velocity vectors point directly in the direction of the VOR gain independent of eye position, in which case the rotation vectors during the slow phase of nystagmus would always have a torsional component, or the eye rotation vectors describing the eye position point directly in the direction of the VOR gain, in which case the velocity vectors would have a torsional component dictated by the orientation of the eye around the axis orthogonal to the direction of the gain.

Experimentation has shown (Misslisch et al[33]) that the orbital mechanics hypothesis predicts smaller responses in the yaw and pitch planes than were observed (in humans) and that roll responses would be around axes of gaze direction, which was not the case. The qualitative aspects of the results obtained from this experimentation were consistent with both the minimum-velocity strategy and the Listing's law hypothesis, but these hypotheses erroneously predicted greater yaw and pitch tilts than were observed: the minimum-velocity strategy predicts angles four times greater, and the Listing's law hypothesis predicts angles twice as large.

These results seem to suggest that in the VOR a compromise position is taken up somewhere between compliance with Listing's law and perfect retinal stimulus stabilisation.

3 Neurophysiology of the vestibulo-ocular reflex

3.1 Anatomy and function

Essentially, the VOR circuit consists of detection by follicle transducers, projection from there to the vestibular nuclei in the brain stem, projection from the vestibular nuclei to the extraocular muscle nuclei of the third, fourth, and sixth cranial nerves, sometimes referred to as the preextraocular nuclei, and projection via the aforementioned nerves to the extraocular muscles, comprising a three-layer computation, or vector transformation. This circuit represents the feedforward component of the VOR, which is actually used to generate the saccadic eye movements given some head acceleration stimulus originating in the vestibule, and is known as the *reflex arc*. However, there are a number of other components which must be taken into consideration in order to complete the picture of the VOR. Firstly, and perhaps predominantly, we must take into account the role of the cerebellar flocculus. This receives innervation from both the labyrinth and the retina, in a chain involving the pretectal nucleus and inferior olive, and is also massively recurrently connected. Cells in the extraocular muscle nuclei and motion detectors in visual cortex also project via climbing fibres to Purkinje cells in the cerebellum, with different path lengths in such a way as to provide information about the eye movements both before and after execution: the signal from labyrinthine detectors will standardly arrive around 15-30ms after the onset of the stimulus, whereas feedback from the visual cortex regarding retinal slip would arrive at around the 80-90ms mark. This arrangement, along with
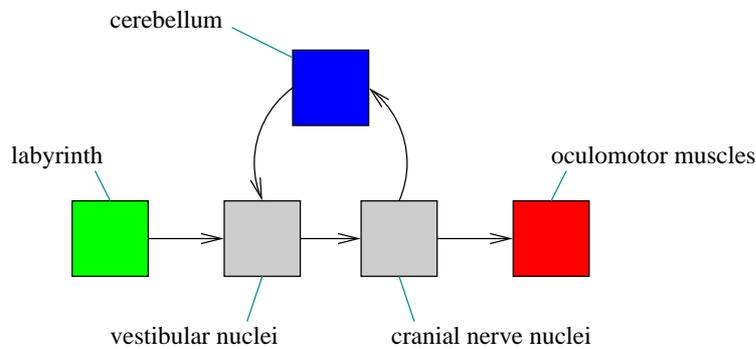
Figure 2: Greatly simplified schematic of the architecture of the vestibulo-ocular reflex.
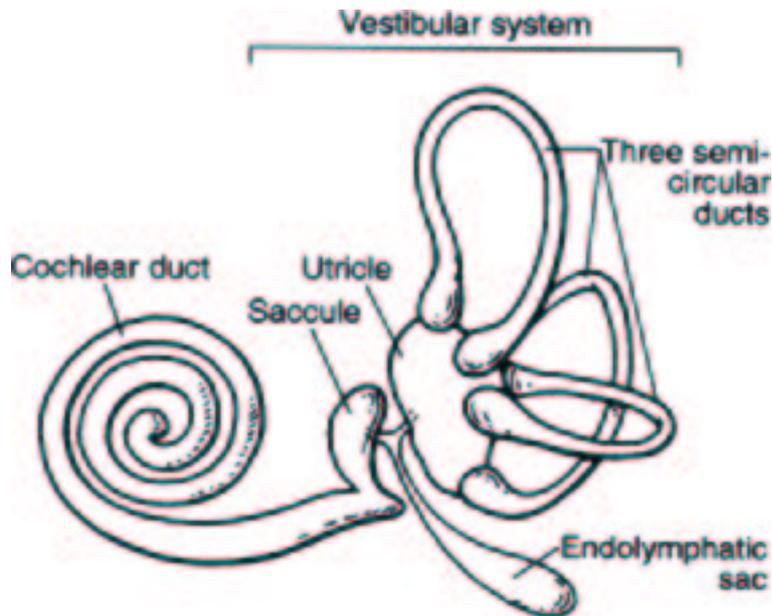

Figure 3: The labyrinth.

the recurrent connections within the floccular layer, allows the flocculus to integrate the reflex information over time and hence provide some measure of error to train the synaptic connections in the reflex arc. Additionally, it is likely that information from the neck muscles is also partially involved in the VOR since feedback from the skeletal muscles also arrives in lateral and medial areas of the vestibular nuclei involved in the reflex arc.

Let us examine the architecture of the vestibular system in a little more detail.

3.1.1 Receptors and afferent vestibular fibres

The labyrinth is composed of two parts: the vestibular apparatus and the cochlea. The cochlea is not involved in the vestibulo-ocular reflex, so we will ignore it. The vestibular apparatus is further composed of the three *semicircular canals* and two smallish vesicles known as the *utricle* and the *saccule*. The semicircular canals are oriented roughly orthogonally, and terminate at the utricular end in a swelling known as the ampulla. The orientation of the three canals is as follows: the *posterior vertical* is oriented around the horizontal axis, the *lateral* (also confusingly known as the horizontal) canal is oriented around the vertical axis, and the *anterior vertical* is oriented approximately around the torsional axis (see Figure 3.1.1).

As in the cochlea, *epithelium* with hair cells is found in several locations in the vestibular system: the *ampullar crista*, a mound found in each of the ampullae where hair cells project into a material known as the *cupula*; and the utricular and saccular *maculae*, where the cupula-like material contains small crystalline deposits known as *otoliths* (Brodal[4]). The utricular

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macula is oriented in the horizontal plane, and the saccular macula is oriented more or less in the vertical plane at about 45° off sagittal. The cilia of the ampullae bend when the surrounding endolymph fluid moves relative to them during head movement (due to inertia), depolarising or hyperpolarising the cell. The stimulus for the cilia in the maculae is bending due to distortion of the jelly-like material they are embedded in, which is further due to the mass of the otolith membrane (Lindeman[24]). Thus, the construction of the vestibular apparatus is such that the semicircular canals can detect head rotation around each of the three axes, whereas the utricle and saccule can detect linear acceleration in the vertical and horizontal planes (the saccules on the different sides of the head are aligned at approximately 90° to one another and hence three-dimensional linear acceleration can be detected). The semicircular canal receptors are only slightly affected by linear acceleration, and have a dynamic response – they are only affected by changes in velocity. Cilia in the utricular and saccular maculae, in contrast, can provide information about all the possible head orientations due to their static response and relative orientations (in gravity: these mechanisms are effectively neutralised in weightless conditions), and also provide dynamic information, since the firing frequencies are greater with increasing acceleration.

Primary afferent fibres from the vestibule terminate in various locations in the vestibular nuclei, sometimes collectively called the *vestibular complex*, consisting of four large nuclei: superior, lateral, medial, and inferior (or descending); and a number of smaller nuclei on the dorsolateral side of the brain stem. Fibres from the semicircular ducts primarily terminate in the superior and medial nuclei, whereas fibres from the maculae terminate for the most part in the lateral. The vestibular nuclei also receive innervation from a number of other CNS structures, including the cerebellum, the reticular formation, the spinal cord, and other oculomotor nuclei in the mesencephalon as well as commissural connections linking the two sides of the brain (Brodal[4]).

3.1.2   Efferent vestibular fibres and the extraocular system

The vestibular nuclei primarily innervate three systems: the cranial nerve nuclei responsible for stimulation of the extraocular muscles, spinal cord motoneurons responsible for maintenance of equilibrium, and the cerebellum. We will ignore those fibres descending to spinal motoneurons, since they are not involved in the VOR. Those fibres terminating in the abducens, trochlear, and oculomotor nuclei have their perikarya primarily located in the superior and medial vestibular nuclei (which, as we have seen, are innervated primarily by semicircular canal receptors), and leave the vestibular nuclei in a large cluster known as the *medial longitudinal fasciculus*, some crossing the midline commissurally. Fibres terminating in the cerebellum have their perikarya in medial and inferior areas of the vestibular nuclei that do not receive primary afferents from the vestibule.

There are six extraocular muscles in the eye, which attach the wall of the orbit to the sclera of the eye. These muscles are: the *superior* and *inferior oblique*, the *superior* and *inferior rectus*, and the *medial* and *lateral rectus*. The oblique muscles are torsional, rotating the eye clockwise (left superior / right inferior) or anticlockwise (right superior / left inferior) from the point of view of the observer, as well as directing gaze approximately 60° upwards or downwards. The superior and inferior rectus muscles are also involved in torsional movements as well as equal and opposite movements in planes described by the oblique muscles, and the medial and lateral rectus cause rotation around the vertical axis, as shown in Figure 3.1.2 (Carpenter[5]). The abducens nucleus is located in the pons, and the abducens nerve runs forward close to the midline, supplying only the lateral rectus muscle and causing the cornea to move laterally (also known as *abduction*). The trochlear nucleus is located ventrally to the aqueduct in the mesencephalon, and the trochlear nerve leaves the brain stem dorsally by the inferior colliculus to innervate the superior oblique muscle. The oculomotor nucleus is
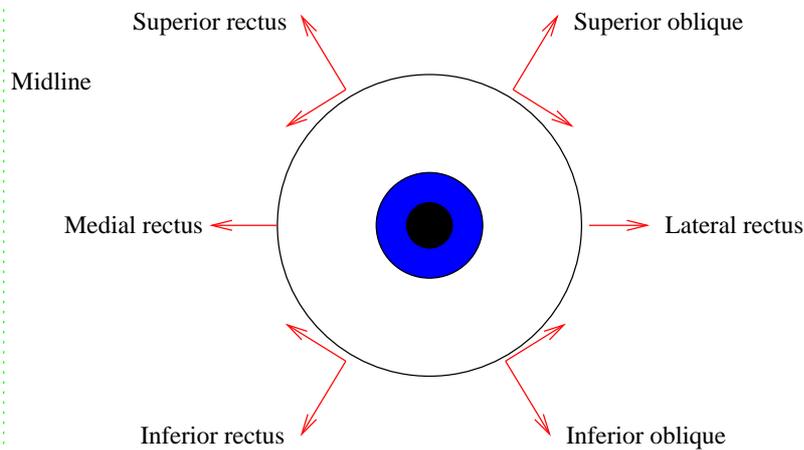
Figure 4: Forces exerted by the extraocular muscles.

situated near the medial longitudinal fasciculus and the other nuclei, and the oculomotor nerve emerges ventrally from the mesencephalon. This nerve contains not only somatic fibres but also visceral (parasympathetic) efferents from the Edinger-Westphal nucleus - however, only the somatic efferents are relevant here: they innervate the remaining four extraocular muscles and the *levator palpebrae superioris* (upper eyelid lifting muscle) (Brodal[4]).

3.1.3   The vestibulocerebellum

Like the cerebrum, the cerebellum is enclosed by grey matter (cortex) with underlying white matter, and extensively folded. At the midline is a narrow area known as the *vermis*, which sprouts two small bulbs on thin stalks on either side; the anterior of these is the cerebellar peduncle, and the posterior and more lateral is called the *flocculus*. The flocculus and that part of the vermis connected to it (the *flocculonodular lobe*) is phylogenetically one of the earlier structures in the brain, and varies little between mammalian species. The flocculonodular lobe receives input for the most part from the vestibular nuclei and primary vestibular afferents (cells with their perikarya in the vestibule) and is also known as the *vestibulocerebellum*; efferents from this area terminate in the vestibular nuclei (Brodal[3]).

3.2   Pathology

In general, since the (involuntary) eye movements on each side of the head are conjugated, they require a cooperation of various muscles. The simplest case is that of the lateral and medial rectus: if one lateral rectus is stimulated, the contralateral medial rectus will also be activated and the ipsilateral medial rectus and contralateral lateral rectus will be inhibited. (The case with other groups of muscles is similar but more complex, due to the different forces they exert on the eye.) This is to ensure that the eyes both point in approximately the same direction, and that therefore the image falling on corresponding points of the two retinae are relatively similar. If the control of some subset of these muscles fails (which usually happens by lesion of one of the extraocular cranial nerves), diplopia always results, often accompanied by vertigo and postural anomalies (Carpenter[5]).

Lesion of the abducens nerve leads to compensation for the deficit in lateral motion by turning the head ipsilaterally. Damage to the oculomotor nerve produces laterally directed strabismus, since the abduction of the eye remains unopposed. Diplopia (double vision) results in all three cases of extraocular cranial nerve injury.

Lesion of the vestibular nuclei or interruption of the vestibular nerve leads to ipsilateral stumbling and falling, as the normal side continues to function by pushing towards the lesioned

side. Such lesions also result in nystagmus to the contralateral side - the slow component occurs for the same reason, and corrective saccades - the fast component - occur in order to attempt to correct the deficit internally. Lesion in the paramedian pontine reticular formation (PPRF), en route from the contralateral vestibular nuclei to the abducens nucleus, results in an inability to turn both eyes ipsilaterally past the midline in attempted horizontal gaze towards the ipsilateral side, as would be expected (atrophy of the ipsilateral lateral rectus occurs). Interruptions of the abducens nerve cause deviation of the ipsilateral eye position medially and diplopia, often compensated for by head rotation to the lesioned side. Lesions of the medial longitudinal fasciculus, especially in the pathway from the vestibular nuclei to the oculomotor nucleus, result in the inability to move the ipsilateral eye medially in attempted horizontal gaze to the contralateral side (atrophy does not occur).

3.2.1 Clinical conditions

The two main vestibular disorders that can be evaluated with an understanding of the vestibulo-ocular system are *benign paroxysmal positional vertigo* (BPPV) and *ocular tilt rection* (OTR).

   BPPV is the most common form of vertigo, affecting up to 15% of people acutely at some point during their lives. It is characterised by transient attacks of intense rotatory vertigo precipitated by rapid head extension with lateral head tilt ipsilaterally. This paroxysmal vertigo is inevitably associated with a characteristic positioning nystagmus with the following properties, compatible with excitation of the posterior vertical canal induced by ampullofugal cupular deflection:

1. nystagmus and vertigo begin with a one or more second(s) *latency* from completion of head tilting;

2. nystagmus and vertigo *paroxystically* increase and then decrease over a *transient* period of 10-40s even with maintenance of the precipitating head position;

3. nystagmic saccades are directed *geotropically* (towards the lowest ear);

4. repositioning (returning to the original position) may cause *reversal* of the vertigo and nystagmus;

5. repetition of the positioning manoeuvre gradually reduces the effects of vertigo and nystagmus (this is known clinically as *fatigability*).

   These effects were originally explained by the theory of *cupulolithiasis*, given the incidence of basophilic deposits on the cupula of the posterior vertical canal in patients with this condition. This material, probably originating from the otolith layer in the utricle, adheres to the surface of the cupula opposite the utricle and renders the cupula gravity-sensitive due to its mass. If these fragments are dislodged from the cupula and expelled into the utricle, the symptoms will be relieved. However, the cupulolithiasis hypothesis does not explain several important features of BPPV:

1. nystagmus and vertigo are associated with acceleration rather than orientation (*positioning* rather than positional): effects disappear rapidly after tilting if the head is kept steady;

2. nystagmus and vertigo do not occur if the positioning is performed slowly;

3. nystagmus and vertigo reappear a few hours after disappearing due to fatigability;

4. a clinical procedure known as the Semont manoeuvre shows that the direction of the nystagmus in the last phase is opposed to that predicted by the cupulolithiasis hypothesis, i.e. apogeotropic.

A more recent theory known as *canalolithiasis* explains these effects as follows: the degenerative débris does not adhere to the cupula but instead remains in the endolymph of the semicircular canal. Since these particles are heavier than the endolymph they always gravitate towards the lowest part of the canal producing positive or negative pressure forces on the cupula. Acceleration into the precipitating position deflects the cupula in an ampullofugal excitatory direction, and, after a 180° contralateral tilting (the second phase of the Semont manoeuvre), a further progression of the material along the arm of the canal still results in this deflection, providing compatibility with all the aforementioned features. Relief will be obtained by moving the head through an appropriate sequence of positions relative to gravity, resulting in the débris clearing the crus and returning to the utricle (Mira[32]).

OTR is a coordinated ipsilateral torsional deflection of both head and eyes, also involving hypotropia. Head tilt direction is towards the side of the lowest ear, eye torsion towards the side of rotation of the 12 o'clock meridian, and the ocular skew direction is determined by the side of the lower (hypotropic) eye. Symptoms of tonic OTR are minimal, being vertical or torsional diplopia or tilting of subjective vertical. It is caused by lesion of the graviceptive pathway leading from the utricle and posterior vertical canal to the contralateral interstitial nucleus of Cajal, and leads to a compensatory head tilting postural reflex elicited by changes in orientation and magnitude of the linear acceleration vector about the naso-occipital axis. The proportions of the effect with regard to head tilt, eye torsion and vertical eye skew is dependent on species differences, particularly with respect to the orientation of the optic axes: the owl, for instance, having little or no eye movement, displays the greatest head tilt component, whereas the skew eye movement is most prominent in fish, which have mobile, laterally placed eyes but no torsional head movement. OTR in humans is probably a vestigial remnant of an otolithic righting reflex seen only in the pathologic case. Partial or complete ipsiversive tonic OTR occurs in patients with acute lesion of a labyrinth or vestibular nerve. Peripheral OTR gradually dissipates according to the degree of vestibular compensation (Mira[32]).

From these cases we can see how an understanding of vestibulo-ocular pathways can provide a more complete and valuable insight into the processes underlying clinical symptoms.

3.3   Learning

3.3.1   Sites of learning

Where are the neurons located that actually train the VOR? A great deal of information regarding the synaptic connections and spike properties of the kinds of neurons that change their behaviour subsequent to VOR learning and relearning is available. Essentially, three kinds of cell have been identified:

1. *Position-Vestibular-Pause* (PVP) cells are so named because they spike according to eye position and vestibular rotation and are silent during saccadic movements. These cells, some of the main interneurons in the VOR pathways, are located in the vestibular nuclei, receiving monosynaptic input from the vestibular nerve and provide monosynaptic output to extraocular motoneurons (Scudder & Fuchs[37]).

2. *Floccular Target Neurons* (FTNs) receive monosynaptic inhibition from the flocculus and ventral paraflocculus (Lisberger & Pavelko[27]) and there is evidence that at least some FTNs project directly to extraocular motoneurons (Scudder & Fuchs[37]). FTNs are also located in the vestibular nuclei and, like PVP cells, also receive monosynaptic input from the vestibular nerve.

3. *Horizontal-Gaze Velocity Purkinje* (HGVP) cells owe their name to the fact that they spike according to horizontal-gaze velocity in periods of interaction of visual and vestibu-
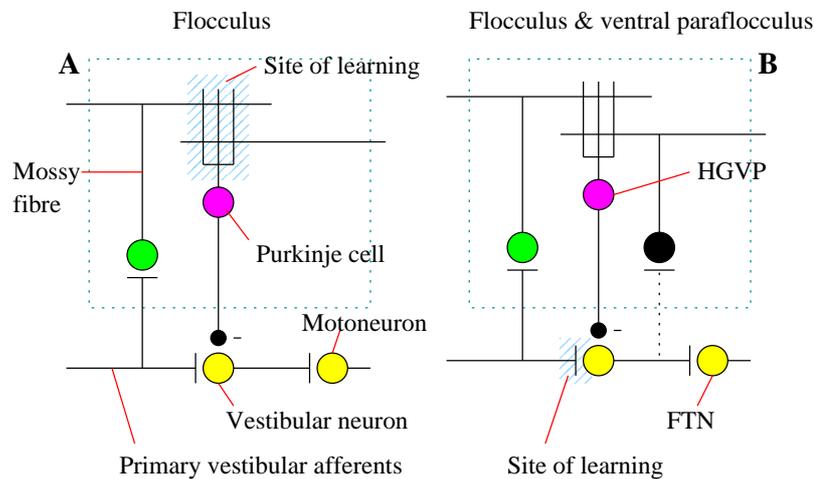
Flocculus Flocculus & ventral paraflocculus

A Site of learning **B**

Mossy fibre HGVP

Purkinje cell

Motoneuron

Vestibular neuron FTN

Primary vestibular afferents Site of learning

Figure 5: Two theories of the site of adaptation of the VOR. A: Ito's[16] hypothesis. B: Miles & Lisberger's[**?**] hypothesis. FTN: floccular target neuron. Adapted from Lisberger et al[28].

lar stimuli. HGVP cells are located in the flocculus and ventral paraflocculus, and project directly to FTNs and other interneurons in the vestibular nuclei (Langer et al[22]).

Regarding the actual site of learning (assuming that there is only one), there have been at least two schools of thought: Ito[16][17] has suggested that learning occurs in the flocculus, guided by the conjunction of vestibular mossy fibre inputs and visual climbing fibre inputs, whereas Miles & Lisberger[**?**] argue that the primary site of learning is in the brain stem, accounting for cerebellar lesion symptoms by suggesting that training is supervised by an error signal coded in the spike frequency of HGVP cells (see Figure 3.3.1). These cells are located primarily in the ventral paraflocculus, and have also been shown to be present in the flocculus as well (Lisberger et al[28]).

Miles et al[31] attempted to determine the role of cerebellar structures in VOR relearning by recording from Purkinje cells before and after VOR adaptation in monkeys, using magnifying spectacles or symmetrically reversing prisms. They found both increases and decreases in VOR gain to be associated with changes in the magnitude of the head velocity stimulus to HGVP-cells, in the *wrong* direction to cause changes in the VOR. They therefore concluded that the mossy fibre vestibular afferents to the Purkinje cells were not the site of learning for the VOR, disproving Ito's hypothesis at least in the case of the HGVP-cells. For a more specific model that accounts for some data that shows that the pathways involved in smooth-pursuit reflexes are distinct from those involved in retraining the VOR, see Lisberger[25].

3.3.2 Properties of VOR pathways

FTNs and PVPs are located in the direct VOR pathways, and therefore the pattern of activation over these cells is representative of the motor responses that are triggered by the corresponding head acceleration. Increases in the amplitude of FTN or PVP cell spiking control corresponding increases in the gain of the VOR, and hence decreases in their spiking amplitude reduce the gain of the VOR. The HGVP story is a little more complex, but essentially an increase in the amplitude of an HGVP cell's response contributes to an overall decrease in the gain of the VOR as the greater the spike from the HGVP cell, the greater the inhibition to the corresponding FTNs in the brainstem (du Lac et al[10]).

As has been noted earlier, VOR latency is approximately 14ms for ramps of head velocity. This figure corresponds to the initial, unmodified eye velocity component of the VOR. Typically, PVP cells respond with a latency of 7ms after onset of the stimulus. Extraocular motoneurons have been shown to respond, on average, 7ms before onset of the evoked eye

movements (Lisberger et al[29]), and the time between the response of the PVP cell and that of the motoneuron is taken to be 1ms or less since at least some PVP cells have been shown to project monosynaptically to motoneurons (above). Thus, the total latency of the VOR via the PVP pathway is approximately 15ms, which tallies well with the 14ms unmodified component. The latency of FTN responses, however, is approximately 11ms, which would be too long for the initial unmodified component but corresponds closely to the initial modified component with an overall latency of 19ms.

HGVP cells show a marked change in their responses after learning has taken place, either inducing an increase or a decrease in the gain of the VOR. However, when the gain is normal, these cells show little or no response during the course of the reflex (Lisberger & Fuchs[26]). HGVPs respond with a latency of approximately 23ms, which, when combined with a motoneuron-to-eye-movement delay of 7ms and and additional 2ms latency for the HGVP spike to affect the firing of motoneurons, provides a total latency of 32ms through the HGVP pathway. Thus, HGVPs respond too late to affect the earlier components of the reflex but do contribute to later components of the modified VOR.

3.3.3   Neural learning mechanisms

At least two mechanisms of cellular plasticity suggest themselves for the function of converting the behavioural and informational requirements of the VOR into real cellular behaviour changes: the presynaptic and the postsynaptic. These mechanisms would allow the integration of transient stimuli represented by the patterns of spiking in the vestibular and floccular/parafloccular inputs to flocculus target neurons to train the inputs to these neurons. Firstly, the Purkinje cell axon terminals could release modulatory transmitter substances that would selectively or dynamically interact with axon terminals of vestibular afferents. Alternatively, inhibition from the Purkinje cells (specifically the HGVPs) could provide a basis for learning via effects on the state of activation of the postsynaptic FTNs. There have been a number of relevant models of regulation of potentiation and depression by implementation of thresholds in neurons that are contemporally active (for a review, see Artola & Singer[1]).

4   A computational model of floccular development

4.0.4   Motivation

Van der Steen et al's[44] experiments on rabbit cerebellar flocculus strongly indicate a topologically ordered arrangement of cells in this area, similar to the topographic effects of orientation selectivity observed in primary visual cortex by Hubel & Wiesel[15]:

> "A zonal representation also is indicated from the CF studies showing that the different CF classes that signal retinal slip in reference to specific axes of visual world rotation arise from different parts of the dorsal cap and ventrolateral outgrowth of the inferior olive. When this relation is combined with the general anatomic and physiological finding ... that the inferior olive can be subdivided such that each subdivision's terminal field in the cerebellar cortex has the form of a parasagittal zone, then the importance of a zonal configuration in the floccular representation of eye movements is further apparent."

These results are quite specific, localising the correspondence of electrical stimulation in zone 2 with rotation around the vertical axis as well as stimulation in zones 1 and 3 with rotation around the 135° horizontal axis identified as equivalent to the human interaural horizontal axis in rabbits (given the different orientation of their eyes). The zones so described were delineated on an anatomical basis by histological analysis of the tissues in the flocculus: five such

compartments, separated by dark raphes, were discovered in transverse sections of an AChE stain, running obliquely in a caudomedial to rostrolateral direction.

However, a number of such studies have taken place (Dufossé et al[8], Ito et al[19], and Balaban & Watanabe[2] to name but a few), and many of the specific localisation results do not correspond between experiments, a few being even mutually inconsistent:

> "The anatomic organization of the floccular white matter into compartments separated by raphes, as revealed by AChE histochemistry, is directly related to the physiologically distinguishable classes of eye movements and probably to specific VOR pathways. The existence of a zonation of the rabbit flocculus has been proposed by Ito and colleagues ... on the basis of the distribution of sites where microstimulation evoked either different patterns of eye movements or influenced specific VOR pathways. Throughout the years, however, the localization and the extent of these different areas has shown a considerable variability. In addition, the proposed organization of the zonation is contrary to the basic principle of cerebellar zonation because the rotary zone ran sharply across the horizontal and vertical zones."

Some of the reasons that such inconsistencies could come about include the lack of accuracy of measurements and a lack of a sensible measure of anatomic delineation of the tissues of the flocculus that could be identified on a species-independent basis, especially in the earlier studies. Despite these caveats, it seems likely that the specific eye rotations that come to be represented in the flocculus are much more dynamic than the neurophysiologists appear to give them credit for, i.e. that they are learned: the adaptive mechanism regulating the performance of the vestibulo-ocular reflex is itself adaptive. Intuitively, this seems obvious, since the specific properties of both the vestibule and the vestibular nuclei may be different between individuals even within the same species, and therefore a genetically predetermined response will always result in some degree of error. The VOR itself must be learned as some process governed by the cerebellar flocculus, after all. Additionally, experimentation has shown that the VOR can be relearned in time after damage to the vestibular system. In order for this to occur, the representation of vestibular space in the VOR must be adaptable.

This paper details a system by which the cerebellar flocculus can come to represent vestibular inputs in the form of head position and acceleration as a topologically ordered motor map, and use this topographic representation to compute saccadic outputs. It is a highly simplified version of that part of the vestibulo-ocular reflex reponsible for the analysis of head movements and prediction of the corresponding eye rotations that must be executed in order to train the reflex, and without which the VOR will not be learned or recalibrated after damage to the oculomotor system. Such a *vestibulotopic map* must be formed in order to adequately represent the space of possible head movements before a degree of error between the eye movement actually executed and the correct eye movement can be calculated.

The method by which this map is formed is in accordance with the principles of competitive unsupervised learning. Given that the flocculus has access to feedback information from the visual system regarding whether or not a particular saccade actually succeeded, a linear, Hebbian learning rule can then train a second set of output connections to predict the correct motor vectors required for a stimulus at these vestibular coordinates. These vectors can then be fed back into the vestibular nuclei as error, allowing the vestibular system to compare its actions with the correct motor output in a Hebbian manner.

4.0.5   Method

The architecture of the model is as follows: there are three nodes representing the stimulus in the form of a three-dimensional rotation from a static head position. This is a simplification of a more detailed model in which this rotational vector (information from the semicircular canals)

would be specified in addition to a linear (Cartesian) acceleration vector as an offset from a static head position vector supplied by the utricle and saccule. These units feed into a three-dimensional lattice of Gaussian feature detectors. This means that there is a number of units for which the situational geometry is defined in three dimensions (they exist at relative distances from one another as distinct points in cortical space), and that for each unit, the receptive field is of the centre-surround kind common in cortical representations of perceptual stimuli. The lattice architecture is in the form of a cube with 10 nodes on each side, leading to 1000 units in all in this layer; the dimensionality of the lattice is suggested by the dimensionality of the input space. These lattice units further feed into three nodes representing the necessary rotations around orthogonal axes that specify the ultimate eye movements required given the stimuli. Therefore there are two sets of synaptic connection weights: those connecting the stimulus with the lattice units, which will be referred to as the *lattice weights* (w^L), and those connecting the lattice units with the outputs, which will be called the *saccade weights* (w^S).

This model is not intended to represent successive stimuli occurring in time, and therefore no attempt to limit the values of the three dimensions of input space has been implemented; these are chosen with equal probability. All stimuli are intended to represent the extent of head rotations around three orthogonal axes.

The algorithm for the development of this model of the flocculus follows this schedule:

1. Set w^L and w^S to small random values

2. Present a vestibular stimulus vector v^L over the input units

3. Find the unit in the lattice representing the centre of excitation c according to
$$\parallel v^L - w_c^L \parallel \leq \parallel v^L - w_i^L \parallel \forall i$$

4. Update the lattice weights to form the vestibulotopic map over the lattice units according to
$$\Delta w_i^L = \eta^L h_{i,c}^L (v^L - w_i^L) \forall i$$

5. Execute a normalised saccadic eye movement centred on c such that the response vector v^S occurs according to
$$v^S = v^L - \frac{\sum_i h_{i,c}^S w_i^S}{\sum_j h_{j,c}^S}$$

6. If the horizontal and vertical components of the saccade v^S are equal and opposite to the horizontal and vertical components of the stimulus v^L, perform the learning step for the saccade weights according to
$$\Delta w_i^S = \eta^S h_{i,c}^S (v^S - w_i^S) \forall i$$

7. Go to step (1)

The terms $h_{i,j}^L$ and $h_{i,j}^S$ are Gaussian functions of the magnitude of the distance $\parallel i - j \parallel$, contingent on σ^L and σ^S, respectively, which in turn decrease over time, like the learning rates η^L and η^S, according to a standard exponential decay. These parameters were chosen as

- $\eta^L(t) = 0.3 \exp(-0.0002t)$

- $\sigma^L(t) = 5.5 \exp(-0.0003t)$

- $\eta^S(t) = 0.2 \exp(-0.0001t)$

- $\sigma^S(t) = 4.0 \exp(-0.0003t)$

where t indexes the presentation of the stimulus (trial). The choice of parameters in the model is relatively arbitrary: what is required is that the learning rate for the saccade weights starts lower than that for the lattice weights but is still relatively strong in the later trials, since the receptive fields of the lattice units must be learned before any significantly useful information can be gleaned from the saccade weights.

4.0.6 Results

The above algorithm was implemented over 20,000 trials. Due to the multidimensional nature of the stimulus and saccade vectors, I have not attempted to provide a graphical representation of the results. However, I determined two measures which appear to be adequate yardsticks of the network's performance during the trials. The first is a global error measure E^G, which is defined as

$$E^G = \frac{\sum_i \|w_i^L + w_i^S\|}{N}$$

with N representing the number of lattice units. E^G thus measures the distance by which the saccade weight vector differs from the idealised saccade, which is equal and opposite to the stimulus, represented as the lattice weight vector. Note that the network is not guaranteed to learn the torsional components of w^L and w^S according to the algorithm, and therefore E^G is not expected to reach 0 in the limit, only approach it closely. The second measure E^R is of how well the lattice comes to represent the input space. Note that all that is required is for units in the lattice to represent stimuli closer in lattice weight space to their situational neighbours than to those units in the lattice further away. Therefore, for each lattice unit i we can define a measure E_i^R which is dictated by

$$E_i^R = \sum_j \frac{f_{i,j}(\|g(w_j^L) - g(w_i^L)\|)}{f'_{i,j}(\|g(w_j^L) - g(w_i^L)\|)}$$

such that the function $f_{i,j}$ is a function involving the normalised Manhattan-distance between i and j of the magnitude of the distance between the weight vectors of i and j, and the function $f'_{i,j}$ is the inverse of that function. The function g is simply a modification to take into account the fact that high values of the components of W^L are closer to the low values than the intermediary values (due to the rotational geometry). Thus, the measure E_i^R is smaller when the units closer to i have weight vectors more similar to i than the units further away, and vice versa. This allows us to define the whole-lattice measure E^R as the sum of the E_i^R for all i

$$E^R = \frac{\sum_i E_i^R}{N}.$$

In ten sets of trials of 20,000 trials each, with both sets of weights being set to small random values at the start of each set of trials, E^R initially reduced to <0.001 after 12,000 trials, and E^G reduced to <0.001 after 16,000 trials. After approximately 4,000-5,000 trials each of the error values was decreasing monotonically (see Figure 4.0.6).

4.0.7 Learning

When we address the question of where learning takes place in this model, the answer is that it is not as straightforwardly localisable as, for instance, Lisberger[25] would have us believe. In connectionist networks, learning resides in all the modifiable weights between units, hence, in this model, all the connections are responsible for producing the ultimate correct result. However, it is interesting to note that in all cases of the development of the model over time, a characteristic pattern of learning, as is clearly revealed in Figure 4.0.6, can be determined. In the time period between 2,000-3,000 trials, the error measure associated with the receptive field formation, E^R, drops sharply; approximately 700 trials later, the error measure E^G also falls by a similar amount. This is attributable to the fact that the overall development of the model's responses depends to a great extent on the stability of the lattice, since the weights w^S are being trained on the basis of the determined centre of excitation c in the lattice, which will
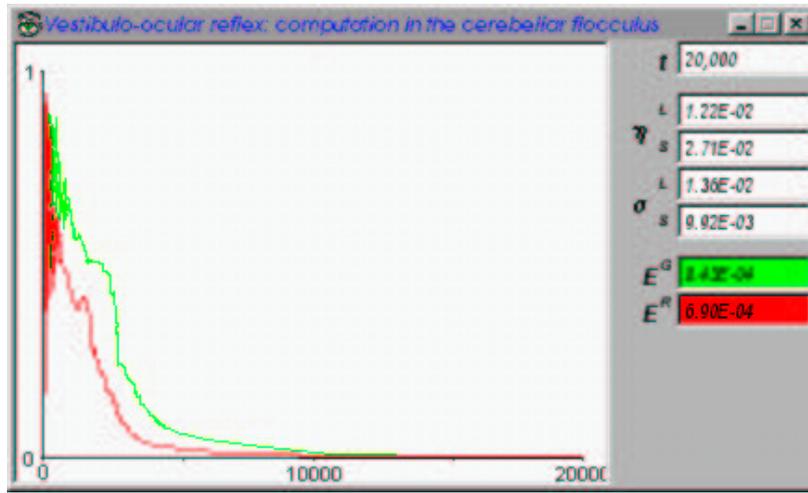
Figure 6: Evolution of the error terms in the model over time.

be more or less accurate depending on how well the vestibulotopic map covers the space of inputs.

5   Conclusion

In recurrent neural circuits such as exist in the majority of circuits in the brain, an explanation of behaviour and learning in the circuit must involve both cellular mechanisms and the architecture and dynamics of the neural network in which the circuit is embedded. Positive feedback can act computationally as an integrator to mediate sustained change in the system given transient stimuli or as an amplifier to convert small cellular changes into global behaviours. The potential effects of using a recurrent model may well invalidate chains of reasoning that seem straightforward if applied to feedforward networks. Thus, it is not always a simple matter to determine the cause of some observed behaviour, to attribute it to some localisable site, since the behaviour may receive contributions from many dynamically interacting sources, both cellular and informational. In this paper I have attempted to present a holistic view of the neurophysiological and mathematical constraints on the vestibulo-ocular reflex, along with a computational model of a fundamental part of that reflex. Hopefully, as a result of this window on the VOR process, a greater understanding of both cellular responses and their computational semantics in the reflex can be achieved.

References

[1] Artola, A & Singer, W [1993] 'Long-term depression of excitatory synaptic transmission and its relationship to long-term potentiation' *Trends in Neuroscience* 16:480-87

[2] Balaban, C D & Watanabe, E [1984] 'Functional representation of eye movements in the flocculus of monkeys (*Macaca fuscata*)' *Neuroscience Letters* 27: 101-105

[3] Brodal, P [1967] *The cranial nerves: Anatomy and anatomico-clinical correlations* (2nd edition) (Elsevier)

[4] Brodal, P [1992] *The Central Nervous System* (Oxford University Press)

[5] Carpenter, R H S [1977] *Movements of the Eyes* (London, Pion)

[6] Churchland, P S [1989] *Neurophilosophy - Toward a Unified Science of the Mind/Brain* (MIT Press)

[7] Churchland, P S & Sejnowski, T [1990] *The Computational Brain* (MIT Press)

[8] Dufossé, M, Ito, M & Miiyashita, Y [1977] 'Functional localization in the rabbit's cerebellar flocculus determined in relationship with eye movements' *Neuroscience Letters* 5: 273-277

[9] Demer, J L [1992] 'Mechanisms of Human Vertical Visual-Vestibular Interaction' *Journal of Neurophysiology* 68, 6: 2128-2146

[10] du Lac, S, Raymond, J L, Sejnowski, T J & Lisberger, S G [1995] 'Learning and Memory in the Vestibulo-Ocular Reflex' *Annual Review of Neuroscience* 18: 409-441

[11] Escudero, M, Dewaele, C, Vibert, N, Berthoz, A & Vidal, P P [1993] 'Saccadic Eye-Movements and the Horizontal Vestibuloocular and Vestibulo-collic Reflexes in the Intact Guinea-Pig' *Experimental Brain Research* 97, 2: 254-262

[12] Gilbert, C D [1983] 'Microcircuitry of the visual cortex' *Annual Review of Neuroscience* 6: 217-47

[13] Guitton, D, Munoz, D P & Galiana, H L [1990] 'Gaze Control in the Cat: Studies and Modeling of the Coupling between Orienting Eye and Head Movements in Different Behavioral Tasks' *Journal of Neurophysiology* 64(2): 509-531

[14] Haslwanter, T [1995] 'Mathematics of Three-dimensional Eye Rotations' *Vision Research* 35, 12: 1727-1739

[15] Hubel, D H & Wiesel, T N [1974] 'Sequence Regularity and Geometry of Orientation Columns in the Monkey Striate Cortex' *Journal of Comparative Neurology* 158: 267-294

[16] Ito, M [1972] 'Neural design of the cerebellar motor control system' *Brain Research* 40: 80-84

[17] Ito, M [1982] 'Cerebellar control of the vestibulo-ocular reflex - around the flocculus hypothesis' *Annual Review of Neuroscience* 5:275-298

[18] Ito, M [1984] *The cerebellum and neural control* (Raven Press)

[19] Ito, M, Orlov, I & Yamamoto, M [1982] 'Topographical representation of vestibulo-ocular reflexes in rabbit cerebellar flocculus' *Neuroscience* 7: 1657-1664

[20] Kaas, J H, Merzenich, M M & Killackey, H P [1983] 'The Reorganization of Somatosensory Cortex Following Peripheral Nerve Damage in Adult and Developing Mammals' *Annual Review of Neuroscience* 6: 325-356

[21] Knox, P C & Donaldson, I M L [1995] 'The effect of afferent signals from extraocular muscles on visual responses of cells in the optic tectum of the pigeon' *Proceedings of the Royal Society, London* B 259: 285-291

[22] Langer, T, Fuchs, A F, Chubb, M C, Scudder, C A & Lisberger, S G [1985] 'Floccular efferents in the rhesus macaque as revealed by autoradiography and horseradish peroxidase' *Journal of Comparative Neurology* 235: 26-37

[23] Leigh, R J & Zee, D S [1991] *The Neurology of Eye Movements* (Philadelphia) (2nd edition)

[24] Lindeman, H H [1992] 'Anatomy of the Otolith organs' *Advances in Oto-Laryngology* 20: 405-433

[25] Lisberger, S G [1994] 'Neural Basis for Motor Learning in the Vestibuloocular Reflex of Primates 3. Computational and Behavioral-Analysis of the Sites of Learning' *Journal of Neurophysiology* 72, 2: 974-998

[26] Lisberger, S G & Fuchs, A F [1974] 'Response of flocculus Purkinje cells to adequate vestibular stimulation in the alert monkey: fixation vs. compensatory eye movements' *Brain Research* 69: 347-353

[27] Lisberger, S G & Pavelko, T A [1988] 'Brainstem neurons in modified pathways for motor learning in the primate vestibulo-ocular reflex' *Science* 242: 771-773

[28] Lisberger, S G, Pavelko, T A, Brontestewart, H M & Stone, L S [1994a] 'Neural Basis for Motor Learning in the Vestibuloocular Reflex of Primates 2. Changes in the Responses of Horizontal Gaze Velocity Purkinje-Cells in the Cerebellar Flocculus and Ventral Paraflocculus' *Journal of Neurophysiology* 72, 2: 954-973

[29] Lisberger, S G, Pavelko, T A & Broussard, D M [1994b] 'Neural Basis for Motor Learning in the Vestibuloocular Reflex of Primates 1. Changes in the Responses of Brain-Stem Neurons' *Journal of Neurophysiology* 72, 2: 928-953

[30] Maxwell, J S & Schor, C M [1996] 'Adaptation of Vertical Eye Alignment in Relation to Head Tilt' *Vision Research* 36, 8: 1195-1205

[31] Miles, F A, Braitman, D J & Dow, B M [1980] 'Long-term adaptive changes in primate vestibuloocular reflex IV. Electrophysiological observations in flocculus of adapted monkeys' *Journal of Neurophysiology* 43: 1477-1493

[32] Mira, E [1995] 'General View of Vestibular Disorders' *Acta Oto-Larygologica* S519: 13-16

[33] Misslisch, H, Tweed, D, Fetter, M, Sievering, D & Koenig, E [1994] 'Rotational Kinematics of the Human Vestibuloocular Reflex III. Listing's Law' *Journal of Neurophysiology* 72, 5: 2490-2502

[34] Rang, H P, Dale, M M, & Ritter, J M [1995] *Pharmacology* (Churchill Livingstone) (3rd edition)

[35] Robinson, D A [1964] 'The mechanics of human saccadic eye movement' *Journal of Physiology, London* 174:245-264

[36] Robinson, D A [1989] 'Integrating with Neurons' *Annual Review of Neuroscience* 12: 33-45

[37] Scudder, C A & Fuchs, A F [1992] 'Physiological and behavioral identification of vestibular nucleus neurons mediating the horizontal vestibuloocular reflex in trained rhesus monkeys' *Journal of Neurophysiology* 68: 244-64

[38] Seidman, S H, Leigh, R J, Tomsak, R L, Grant, M P & del'Osso, L F [1995] 'Dynamic Properties of the Human Vestibulo-ocular Reflex During Head Rotations in Roll' *Vision Research* 35, 5: 679-689

[39] Shelhamer, M, Tiliket, C, Roberts, D, Kramer, P D & Zee, D S [1994] 'Short-Term Vestibuloocular Reflex Adaptation in Humans II. Error Signals' *Experimental Brain Research* 100, 2: 328-336

[40] Tiliket, C, Shelhamer, M, Roberts, D & Zee, D S [1994] 'Short-Term Vestibule-Ocular Reflex Adaptation in Humans I. Effect on the Ocular Motor Velocity-to-Position Neural Integrator' *Experimental Brain Research* 100, 2: 316-327

[41] Tweed, D, Cadera, W & Vilis, T [1990] 'Geometric relation of eye position and velocity vectors during saccades' *Vision Research* 30: 111-127

[42] Tweed, D, Fetter, M, Sievering, D, Misslisch, H & Koenig, E [1994a] 'Rotational Kinematics of the Human Vestibuloocular Reflex II. Velocity Steps' *Journal of Neurophysiology* 72, 5: 2480-2489

[43] Tweed, D, Sievering, D, Misslisch, H, Fetter, M, Zee, D & Koenig, E [1994b] 'Rotational Kinematics of the Human Vestibuloocular Reflex I. Gain Matrices' *Journal of Neurophysiology* 72, 5: 2467-2479

[44] van der Steen, J, Simpson, J I & Tan, J [1994] 'Functional and Anatomic Organization of Three-Dimensional Eye Movements in Rabbit Cerebellar Flocculus' *Journal of Neurophysiology* 72, 1: 31-46

[45] von Helmholtz, H [1867] *Handbuch der Physiologischen Optik* (Hamburg: Voss)

[46] Wiesel, T N & Hubel, D H [1974] 'Ordered Arrangement of Orientation Columns in Monkeys Lacking Visual Experience' *Journal of Comparative Neurology* 158: 307-318