

The Horizontal Angular Vestibulo-Ocular reflex: A Non-Linear Mechanism for Context-Dependent Responses

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Abstract—A bilateral model for the horizontal angular vestibulo-ocular reflex (AVOR) is presented in this paper. It is shown that by assigning proper non-linear neural computations at the premotor level, the model is capable of replicating target-distance dependent VOR responses. Moreover, the model behavior in case of sensory plugging is also consistent with reported experimental observations.

I. INTRODUCTION

The vestibulo-ocular reflex (VOR) is a type of involuntary eye movement that stabilizes retinal images during head perturbations to maintain clear vision. The vestibular apparatus consists of the semicircular canals and the otolith organs to detect head movements during angular and translational motion, respectively. Circuits in brainstem, including vestibular nuclei (VN) and prepositus hypoglossi (PH), act as the main system controller to integrate sensory drive and eye position information and provide motor neurons with proper commands. Motor neurons in turn activate the extraocular muscles that apply torques on the eyeball and produce rotational eye movements. These three rather simple sensory-motor components constitute the main VOR path, the so-called *three neuron arc* [1].

Although the head movements sensed by the vestibular apparatus initiate this reflex, the response is also influenced by contextual factors such as viewing distance [2], [3]. It can be demonstrated geometrically that the magnitude of the ocular deviations required for compensating a translation of the eyes depends on the location of the fixation target relative to the observer. Such ocular deviations increase as a function of decreasing fixation distance [2]. In other words, holding gaze on a near target requires more ocular deviations than for a relatively far target during head movements since the eyes are not centered on the head. The site and underlying mechanism of such adjustments are still unknown. The majority of models proposed to generate target-distance dependent VOR responses relate this property to *i*) an internal signal proportional to the inverse of target distance that scales VOR gain [2], [4], *ii*) cortical computations [5] or *iii*) forcing parametric changes [6]. Zhou et. al. [7] suggested instead a multiplication of vestibular and eye position signals within the direct VOR pathway as the neural substrate that mediates VOR gain modulations. Theoretical work by Khojasteh and Galiana [8] also suggests that integrating proper sigmoidal functions in the response of bilateral VOR interneurons enables the model to generate context dependent responses.

This work is supported by CIHR and NSERC.

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Their proposed mechanism uses monocular efferent copies of eye position that are known to converge on premotor cells in the medial VN as the signal to modulate VOR gain. However, a major shortcoming of their model was that the use of a signal in a loop also causes the dynamics of the system to vary as the VOR gain modulates. Moreover, it could not achieve VOR gains in complete agreement with the geometrical requirements for eccentric targets.

The present study expands the concept of non-linear neural computation in a simple bilateral model for slow phase horizontal AVOR in the dark, based on premotor anatomy and physiology. This model can replicate binocular responses for targets at different depths and eccentricities during short duration head velocity bumps. In this model it is postulated that non-linear computations, appearing at the level of premotor cells in the VN, are a function of both monocular eye position and vergence angle estimates to generate target-distance dependent VOR gains for each eye. The model includes non-linear vestibular sensors [9] for a more realistic sensory system in the VOR. Simulation results are presented to evaluate the performance of the model under different viewing distance conditions. Moreover, the model is able to generate responses in cases of unilateral canal plugging that are consistent with published results [10], [11].

II. METHODS

Reference coordinates in this model are selected such that for each eye, zero position is defined as looking straight ahead at optical infinity; temporal deviations are considered positive and nasal deviations, negative. Conjugate and vergence eye positions are thus defined as $E_{conj} = \frac{1}{2}(E_R - E_L)$ and $E_{verg} = -(E_R + E_L)$, where E_R and E_L refer to the right and left eye position, respectively.

According to geometrical requirements (Fig.1-(a)), the ideal monocular VOR gains at high frequencies, angular eye velocity/ angular head velocity, for any target distance D and eccentricity θ can be approximated with [2],

$$\frac{\partial E_{R,L}}{\partial H} \approx -1 - \frac{R}{I} (E_R + E_L) \cos(E_{R,L}) = -1 + \frac{R}{I} E_{verg} \cos(E_{R,L}) \quad (1)$$

where H refers to head position, R is the radius of rotation and I is the inter-ocular distance. In Equ. 1, target distance and eccentricity from the midline are approximated by $D = \frac{I}{E_{verg}}$ and $\theta = \tan^{-1}(E_{conj})$. Equ. (1) implies that approximating the target location with respect to the eyes (for different depths and eccentricities) in the horizontal plane, requires an estimate of binocular angles, or a combination of them, e.g. monocular eye position and vergence state. In

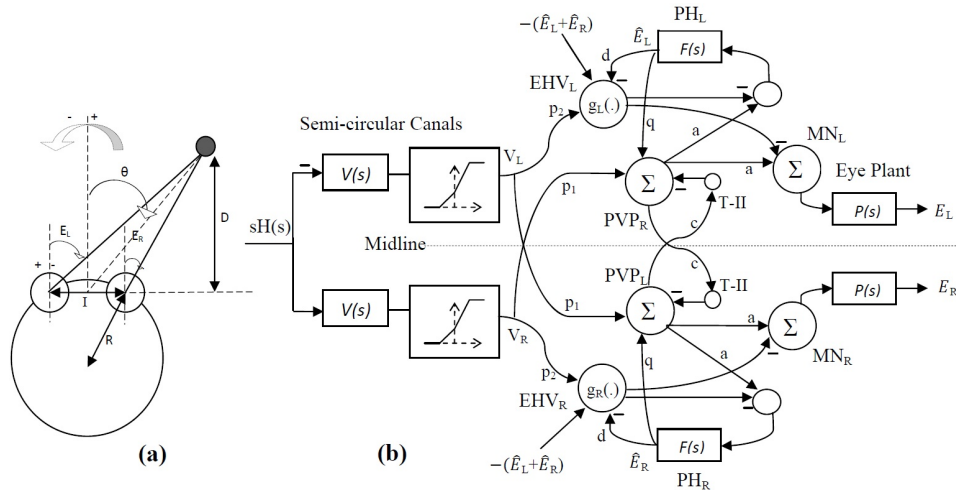


Fig. 1. (a) Right and left eye positions for an eccentric target.(b) Bilateral model of horizontal AVOR in dark.

TABLE I
NUMERICAL VALUES OF THE MODEL PARAMETERS

p_1	p_2	c	q	a	d	k_f	k_p	T	T_c
0.75	0.75	0.013	1.43	0.8	1	0.85	0.55	0.3	6

other words, there is no one-to-one mapping between the ideal monocular VOR gain and monocular eye position - the latter is not sufficient to define target location in space.

Fig.1-(b) presents our bilateral model for the AVOR in the dark. In this model, population responses of cells are considered. The input is head velocity, $sH(s)$, sensed by semicircular canals. The canals are modeled as high pass filters: $V(s) = \frac{sT_c}{sT_c+1}$ followed by a static non-linearity [9]. The non-linear block has asymmetric gains around zero ($k_{negative} = 0.4$ and $k_{positive} = 0.6$) and limits the primary afferent output $V_{R,L}$ by saturation and cut off levels. Position-Vestibular-Pause (PVP), type I Eye-Head-Velocity neurons (EHV) and type II (T-II) neurons in the premotor circuit receive vestibular and eye position information from canals and PH, respectively. MN represents the sum of the excitatory abducens and inhibitory oculomotor motoneurons for horizontal eye rotation. The eye plant is modeled with first order low pass dynamics, $P(s) = \frac{k_p}{sT+1}$. The neural filters in PH generate internal estimates of eye position \hat{E} with similar dynamics to the eye plant, $F(s) = \frac{k_f}{sT+1}$. The output signal is eye position E . Subscripts R and L refer to the right and left side of the brainstem.

The model structure and connections are similar to the one developed in [8] with linear summing junctions except for non-linear sensors and non-linear EHV cells. In the former model [8], context dependency relied on a single non-linearity applied after the sum of EHV afferent signals. Therefore, as different gains were generated with viewing context, the dynamics of the system also changed. Moreover, relying only on internal estimates of ipsilateral monocular eye position did not allow reaching ideal gain modulation. In order to preserve the dynamics with ideal gain modulations,

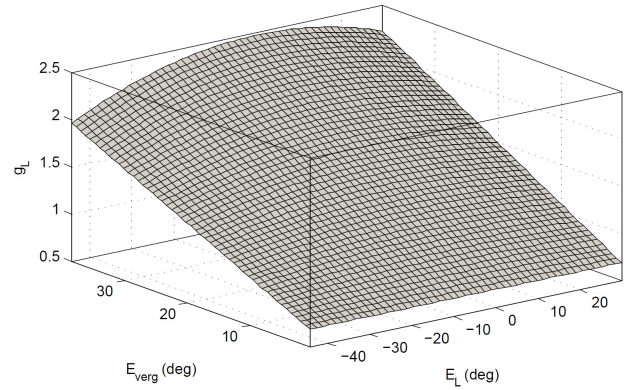


Fig. 2. Non-linear surface computed as the sensitivity of the left EHV to vestibular afferent projections as a function of \hat{E}_L and \hat{E}_{verg}

the EHV cells in the new model only modulates the gain related to the sensory inputs, $V_{R,L}$, but uses the eye context information. We assume that there are two signals in the premotor circuit related to binocular eye position that trigger the context-dependent gain modulation. Although there is evidence that the majority of premotor cells (saccadic Burst neurons, PVPs) encode monocular eye movements [12], [13], there are other neurons that encode binocular eye movements with ipsilateral preference or mixed sensitivities [13]. Thus the ipsilateral eye position efference copy is available from PH, while binocular information or at least contralateral eye position is also available to the EHV cells through commissural pathways and interneuron connections. EHV cells are known to behave non-linearly and also exhibit vergence dependent behavior [14], [15], [16]. The source of such an input could be through projections from the so-called *vergence neurons* in the midbrain reticular formation that discharge proportional to the vergence angle [17]. Access to cells with such characteristics is essential to tune the non-linear gain of EHV cells for different target distances and eccentricities. Therefore, we assume that ipsilateral monocular and vergence eye position inputs to the EHV

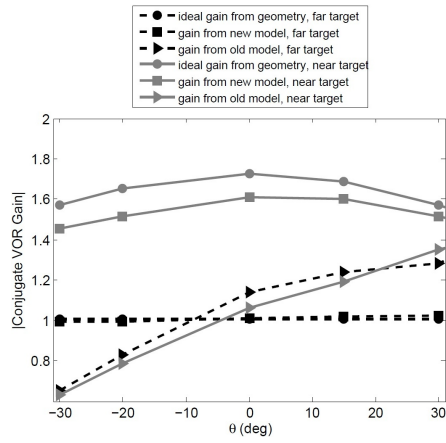


Fig. 3. Absolute conjugate gains vs. target eccentricity for a far target, $D=10$ m, and a near target, $D=11$ cm.

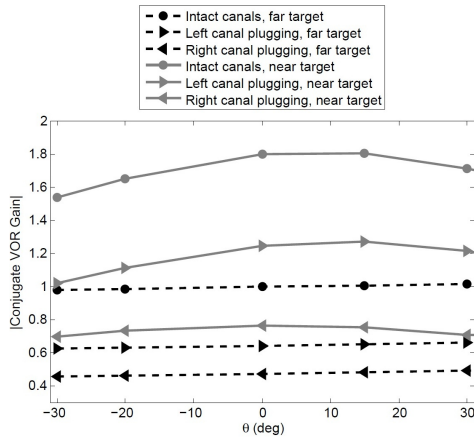


Fig. 4. Absolute conjugate gains vs. target eccentricity for a far target, $D=10$ m, and a near target, $D=11$ cm, in response to rightward head impulse.

cells define their sensitivities (gain) to vestibular signal in a non-linear fashion; i.e. $E_{HV_{R,L}} = g_{R,L}(\hat{E}_{R,L}, \hat{E}_{verg}) \times V_{R,L}$, where $g_{R,L}(\cdot)$ is the non-linear sensitivity of EHV cells to vestibular afferents. Given these assumptions, the equations for conjugate and vergence angles in the model are

$$E_{conj} = \frac{k_p (V_L g_L p_2 - V_R g_R p_2) + a k_p p_1 (V_L - V_R)(c+1)}{2(Ts - adk_f(c+1) + 1)} \quad (2a)$$

$$E_{verg} = \frac{k_p (V_L g_L p_2 + V_R g_R p_2) + a k_p p_1 (V_L + V_R)(c-1)}{2(Ts + adk_f(c-1) + 1)} \quad (2b)$$

Modulation of g_R and g_L clearly only changes the overall gain but not the system dynamics (poles). The parameter set used provides system stability and approximates recorded time constants for version and vergence [6], (see Table I).

We computed the optimum values for $g_{R,L}$ so that the high frequency monocular gains in the model match the ideals from Equ. (1) for different target depths and eccentricities with $R = R_{head} = 8.8$ cm and $I = 6$ cm. A surface fit optimization is performed to describe the desired $g_{R,L}$ as a 4th order polynomial function of $\hat{E}_{R,L}$ and 1st order polynomial of \hat{E}_{verg} . Fig. 2 depicts this surface for g_L . The non-linear functions are then assigned to the left and right EHV cell processes.

All simulations were performed using MATLAB Simulink (The MathWorks Inc., MA, USA). The solver used was first order Euler approximation with a step size of 1 ms. The behavior and performance of the model under different conditions are provided next.

III. RESULTS

The model is designed to simulate human AVOR responses during yaw rotations in darkness around a vertical axis passing through the center of the head. The performance of the non-linear model was examined during brief high-velocity head perturbations in different binocular context. We also replicated behavior after unilateral vestibular sensory loss by canal plugging. The simulation results are compared with published experimental data.

A. VOR gain modifies with target depth and eccentricity

Fig.3 shows absolute conjugate VOR gain plotted against target eccentricity for a far target ($D = 10$ m) and a near target ($D = 11$ cm) when head velocity is applied as a short duration (20 ms) impulse of amplitude $100^\circ/s$. Initial eye positions are set for each test to align with targets of variable distance and eccentricity. The gain here refers to the ratio of the peak conjugate eye velocity to the input head velocity peak. We also compared this to the performance of the prior non-linear model [8] under the same conditions. The new model is able to generate conjugate gains very close to the ideal ones required by geometry (SSE=0.0755), much improved over [8], (SSE=4.1768). As expected, relying on binocular eye position information has improved the performance in adjusting target location with respect to head.

B. Target-distance dependent VOR gain with unilateral canal plugging

We studied the model behavior assuming unilateral loss of sensory modulation (i.e. canal plugging). Experimental results report that the gain of the horizontal AVOR evoked by high frequency, high acceleration head impulses in subjects with unilateral lesions show an asymmetry in the contralesional vs. ipsilesional rotations [10], [18]. The AVOR in squirrel monkeys after acute unilateral canal plugging during high frequency and high velocity steps of acceleration shows a gain of 0.61 ± 0.14 for contralesional rotations and 0.33 ± 0.03 for ipsilesional rotations [10]. Interestingly, Migliaccio et. al. [11] also reported that despite lower gains, the target-location dependent modulation of the human AVOR survives after canal plugging. According to the results of experiments on monkeys and toadfish, afferents innervating a plugged canal increase their sensitivities with frequency [19], [20], but show a much reduced gain; this can be modeled as an increase in stiffness and a reduction in the dominant time constant and gain in their transfer function.

In order to evaluate the model behavior in the case of canal plugging, we change the canal dynamics according to [20], that is $T_c = 0.03$ sec and a 30% gain reduction in $V(s)$ for a plugged canal, rather than $T_c = 6$ sec for an intact one. The model is then again stimulated with a *rightward* short

duration (100 ms) head velocity pulse of amplitude $100^\circ/s$. All other model parameters including the non-linear EHV were left unchanged. Again initial eye conditions were varied so that different initial target distance and eccentricities could be tested (Fig.4). The model results confirm an asymmetry consistent with experiments. If the left sensor is plugged, the average generated gain to a rightward contralateral head pulse is 0.67 ± 0.02 . In the case of a right canal plugging, the generated conjugate gain is 0.45 ± 0.02 for the same head pulse, now ipsilateral to the side of lesion. This is consistent with the observations of [10] - a larger gain for contralesional than ipsilesional head rotations. Despite the lesion, there is still an increase in the VOR conjugate gain when the target is closer, in accordance with the observations of [11] - gain modulation of the VOR survives canal plugging, though it may not be as optimal as before lesions. Note that the results from plugging were an emerging property. Model parameters were pre-set to satisfy healthy response dynamics only.

IV. DISCUSSION

This work introduces a physiologically relevant model for the rotational VOR with non-linear computation in dominant classes of vestibular neurons and non-linear sensors. The response of the model in different contextual conditions is consistent with geometrical requirements. Moreover, the model behavior after unilateral canal plugging is in agreement with reported experimental observations during binocular recordings.

Non-linear computation in neural responses, so-called *gain modulation*, exists in many cortical and subcortical areas - it is viewed as a major computation principle in non-linear neural processing [21]. Here, it is postulated that the sensitivity of EHV cells to vestibular signals modulates non-linearly with eye position and vergence state, enabling auto-adjustment of the VOR to the set point of both eyes.

The goal of modeling a sensory-motor system is unmasking potential control strategies used by the brain to gain insight in clinical applications. One prediction of our model is that vergence angle information plays a role in generating disconjugate VOR responses that account for the different target proximities with respect to the eyes during horizontal head rotations. Moreover, another prediction is an increased *vergence* response with unilateral vestibular lesions, also associated with decreased conjugate gains. Due to central non-linearities and non-linear sensors, there is an increase in the VOR common mode response, E_{verg} , related to the sum of bilateral sensory signals (normally modulated in opposite directions). In a bilateral non-linear circuit, we have shown that unbalanced sensory inputs result in an increase in the vergence response compared to the normal case during contralesional rotations and a decrease in vergence during ipsilesional rotations compared to the normal case. These predictions will be explored with binocular VOR recordings; if confirmed new test protocols will follow for the evaluation of VOR performance and degree of compensation in vestibular patients.

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