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Hybrid Nonlinear Model of the Angular Vestibulo-Ocular Reflex

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Abstract— **A hybrid nonlinear bilateral model for the horizontal angular vestibulo-ocular reflex (AVOR) is presented in this paper. The model relies on known interconnections between saccadic burst circuits in the brainstem and ocular premotor areas in the vestibular nuclei during slow and fast phase intervals. A viable switching strategy for the timing of nystagmus events is proposed. Simulations show that this hybrid model replicates AVOR nystagmus patterns that are observed in experimentally recorded data.**

I. Introduction

The vestibulo-ocular reflex is an involuntary ocular movement that serves to stabilize gaze in space during head movements to provide clear vision. The *three neuron arc* [1] of the VOR system makes it an appropriate model for studying sensory-motor behavior. The sensors to detect angular and linear head perturbations are semicircular canals and the otholith organs. The sensory information is relayed to the vestibular nuclei (VN) and prepositus hypoglossi (PH) centers in the brainstem which act as the main system controller. By combining the sensory drive with eye position information, the neural pathways in the brainstem provide motor-neurons with proper commands to drive the extraocular muscles. Eye movements are then generated as a result of torques applied to the eyeball by the extraocular muscles.

The VOR consists of compensatory (slow phase) and reorienting (fast phase) segments. While the slow phases serve to stabilize gaze in space by moving the eyes in the opposite direction to the head movement, the fast phases redirect the gaze at high speeds in the direction of the head movement. These slow and fast intervals constitute VOR nystagmus (see Fig.3). We focus on the angular VOR (AVOR), tested with passive whole-body rotation in the dark while recording conjugate or monocular horizontal eye movements. In clinical tests, the VOR is characterized by its gain defined as the ratio of peak eye velocity to peak head velocity during harmonic testing or short pulse perturbations.

The function of the VOR is influenced by contextual factors such as viewing distance [2], [3]. For instance, holding gaze on a near target requires more ocular rotation than for a relatively far target during head movements since the eyes are not centered on the head. In our recent work [4], we presented a nonlinear bilateral model for AVOR slow phases in the dark. By assigning proper nonlinear neural computations at the premotor level, this slow phase model is capable of replicating target-distance dependent VOR responses that are in agreement with geometrical requirements. Due to nonlinearities in the sensors and premotor circuits, this bilateral model predicted a disconjugate VOR in the dark. However, explorations of the model behavior examined only high frequency head pulses or low amplitude sinusoidal rotations to remain in the range of feasible eye rotations. In order to have more relevance to the clinical VOR, we now examine the predicted responses to low frequency sinusoidal rotations. This requires the implementation of the fast phase circuit to replicate nystagmus patterns in the AVOR and compare them to experimental data.

Classically, the two phases of the VOR are believed to be generated by independent and parallel pathways [5]. However, more recent data demonstrate that slow and fast phases of the VOR share efference copies of eye position from PH and premotor cells in VN [6]. Therefore, instead of separate subsystems to generate VOR nystagmus, distinct dynamics for slow and fast phases are generated here through structural modulation [7]. In other words some of the projections during slow phases alter their response characteristics during a fast phase: e.g. position vestibular pause (PVP) and eye head velocity (EHV) cells pause for ipsilaterally directed fast-phases [8] and burster cells that are only active during fast phases or saccades, play an important role in facilitating response changes on premotor cells [9]. It should be noted that structural modulation does not refer to any change in anatomical connectivity, but rather to changes in the available set of active pathways [7].

In this work, a fast phase circuit is presented that shares premotor centers with the bilateral nonlinear slow phase circuit previously presented [4] to form the VOR hybrid model. A viable switching strategy is also implemented to trigger and stop VOR fast/slow phases. Simulation results are presented to evaluate the performance of this hybrid model under different rotation profiles.

II. Methods

A. Reference Coordinate

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.

B. Slow phase model

The original nonlinear model for slow phases of the AVOR is presented in detail in [4]. The model includes semicircular canals modeled as high-pass filters of head velocity,

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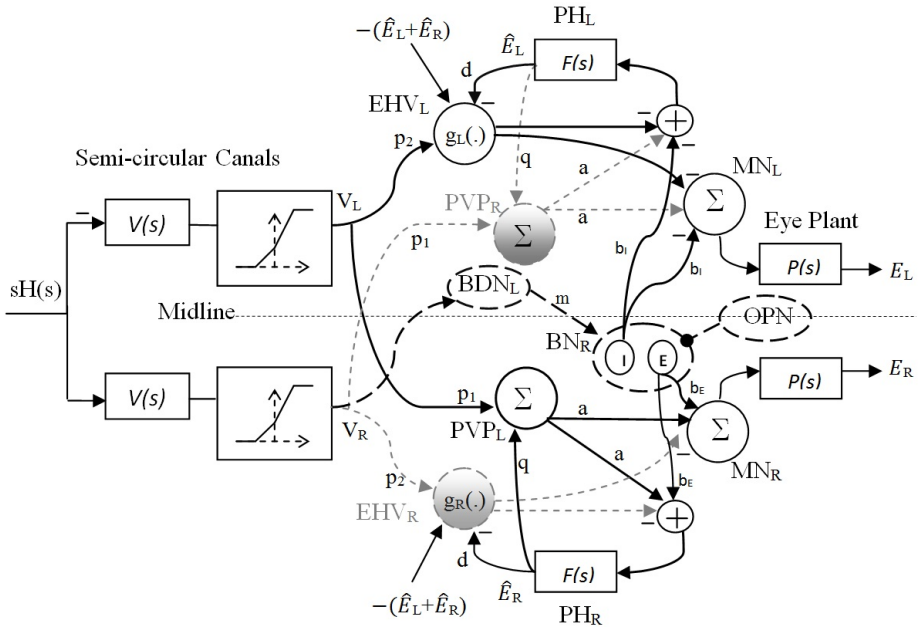

Fig. 1. Model structure for a rightward fast phase. Inactive projections and paused cells are indicated by dashed gray lines. Long dashed black lines are the centers that are only active during fast phase and solid black lines are shared projections during both slow phase and rightward fast phase of the VOR.

$V(s) = \frac{sT_c}{sT_c+1}$, followed by a static nonlinearity on sensory modulation. Type I PVP, EHV and type II cell populations in the VN are distinct in the model and receive sensory projections from the canals as well as efferent copies of eye position from PH. They support commissural pathways across the midline. Premotor PVP and EHV cells project to motor neurons (MN) to drive the eye plants. The eye plants as well as neural filters in PH are modeled with first order low pass dynamics as $P(s) = \frac{k_p}{sT+1}$ and $F(s) = \frac{k_f}{sT+1}$. Nonlinear computations in form of nonlinear surfaces, $g(.)$, are assigned to the response of EHV cells to account for the target distance related gain modulations of the VOR. These nonlinear computations modulate the sensitivity to sensory projections according to the concurrent monocular eye position and vergence angle [4].

C. Fast phase model

Fig.1 represents the model structure for a rightward fast phase circuit. A mirror image of this circuit would hold for leftward fast phases. Similar to the slow phase model, cell populations are represented. Summing junctions are linear except nonlinear EHV cells [4]. Unlike the bilateral structure of the slow phase system with reciprocal signals across the midline, during fast phases VN cells such as ipsilateral PVPs and EHVs are suddenly silenced, as well as their cross-midline projections (gray dashed lines and circles in Fig.1, cross midline projections are not shown for simplicity). Omnipause neurons (OPN) and burster-driving neurons (BDN) as well as excitatory and inhibitory burst neurons (EBN and IBN) are included in the fast phase circuit (long dashed black lines and circles in Fig.1). OPNs located near the midline of the pons act as triggers for the initiation of fast eye movements in all directions. During fixation and slow eye movements, the OPNs discharge at high firing rate and exert a tonic inhibition on premotor BNs. OPNs cease firing prior to a saccade, remain silent for the duration of the saccade and resume firing at the saccade end [10]. In addition to other sources such as afferents from superior colliculus, OPNs receive signals from the cells in the medial vestibular nuclei [11]. BDNs are located below the PH and are found to be excited by contralateral horizontal head rotation and project to contralateral BNs [9]. In our model, we assume that this contralateral excitatory vestibular drive to BDNs comes from contralateral vestibular-only (VO) cells. BDNs also modulate with a PH response to close the loops and shape bursts during fast phases [9]. Therefore, the output signal from left BDNs during rightward fast phase is: $BDN_L = V_R - \alpha \times E_R^*$ (connections are simplified in Fig.1). EBNs and IBNs are located in the reticular formation, receive projections from BDN, and have monosynaptic connections to abducens motoneurons. EBNs excite ipsilateral MNs while IBNs with similar firing patterns inhibit contralateral MNs. The same projections to MNs are sent to PH neurons [6]. In order to achieve faster dynamics in the fast phase circuit, it is assumed that the feedback loops including PVP and EHV cells around the VN and PH filters change their sign as originally suggested in [7], for example using competition between parallel inhibitory and excitatory projections whose strength is modified by EBN/IBN effects. As in the slow phase model [4], the nonlinear function $g(.)$ does not appear in the system poles thereby preserving the system dynamics during modulations of gain with target distance; that is, fast time constant$= \frac{T}{1+k_f(a*d+\alpha)}$. The model parameters (Table.I) are selected to preserve stability of the fast phase system with a small time constant (≈ 0.5 sec) - only values different from the slow phase model in [4] are provided.

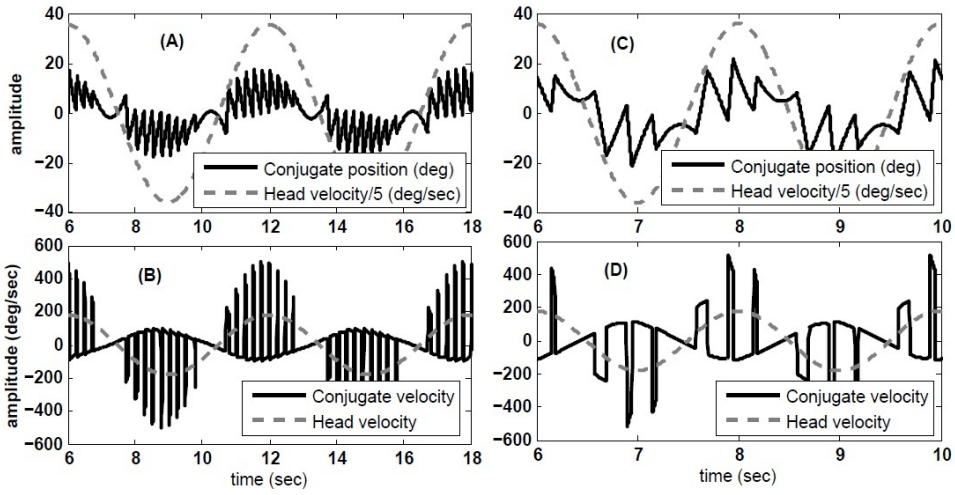

Fig. 2. Simulated conjugate eye position (top) and conjugate eye velocity (bottom) in response sinusoidal head velocity rotation (amplitude=180 deg/s). (A,B) input frequency is 1/6 Hz; (C,D) input frequency is 1/2 Hz.

D. Strategy for nystagmus

Nystagmus serves to improve the linear range of the VOR, since eye excursions are kept inside a reasonable limit; hence, a proposed switching strategy is based on limiting eye deviations by avoiding cut-off and saturation limits in the responses of premotor neurons [7]. It is known that a logical circuit controls the activity of OPNs to trigger and end a fast phase. It's assumed that the OPN circuit constantly monitors the output of PVP neurons. If the activity of PVPs on one side reaches a threshold (ON-Th) a fast phase is triggered ipsilateral to the PVPs' side. During the fast phase the ipsilateral PVPs are silenced and the contralateral PVPs change direction and decay. The fast phase ends as the decay on the contralateral PVPs reaches a second threshold (OFF-Th). This mechanism generates fast phases in the same direction as head movement and limits eye position signals below their physical limit. Given fixed system parameters and dynamics, ON-Th and OFF-Th control the frequency of fast phases and their duration; i.e. increasing ON-Th results in later triggering of fast phases and lowering the OFF-Th leads to longer fast phases. It should be noted that a refractory period (20 ms) is imposed after switching to a fast phase to enforce a minimum time interval before allowing triggering a new fast phase.

The performance of the model under different rotation profiles are provided next. All simulations were performed using MATLAB Simulink (The MathWorks Inc., USA), with a first order Euler solver and 1 KHz sampling rate.

III. Results

The model is designed to simulate the human AVOR responses during yaw rotations in darkness around a vertical axis passing though the center of the head. The ON-Th and OFF-Th are set as 50 and -10 spikes/s. This model only considers cell population firing modulations around their resting rates; resting rates (biases) are not included.

Fig. 2 depicts the response of the hybrid model (conjugate eye position and eye velocity) to two different rotation frequencies: 1/6 Hz (A,B) and 1/2 Hz (C,D) with velocity peaks of 180 deg/s. As in experimental observations, the number of fast phases per cycle decreases for higher frequencies, that is, fast phases are triggered more often in low frequency head rotations. This is due to the band pass characteristics of the central neurons in the VOR pathway. At lower frequencies the gain of central neurons is higher which increases the possibility of exceeding their firing thresholds and triggering a fast phase. Further, at a given input frequency, fast phases appear more often as the amplitude of head velocity increases. This is also consistent with experimental observations.

We have also compared our model performance in response to a specific rotation profile (180 deg/s at 1/6 Hz) where binocular records are available [12]. Fig. 3 shows the recorded conjugate eye position (A) and eye velocity (B) signals (black) as well as our model responses to the same rotation stimulus (blue). Clearly, general nystagmus characteristics from the simulation and data are similar; i.e. the amplitude of conjugate eye position, the number of fast phases and their timing are also similar, suggesting that the switching mechanism in our model is plausible. In addition, the simulation also provides modulation in vergence (shifted down by 20 deg in Fig.3.C) during this AVOR, as observed in the data.

With nonlinear sensors and computations assigned at the premotor cells, a vergence eye movement is now present in the response of our hybrid model to head perturbations. This vergence component shows a carrier frequency that is twice that of the stimulus. Moreover, compared to the pure slow phase model, the peak-to-peak amplitude of the vergence component is smaller in the hybrid model since nystagmus serves to limit non-linear functions to smaller excursions on non-linear surfaces at the premotor level. Contrary to common belief, the AVOR is not purely con-

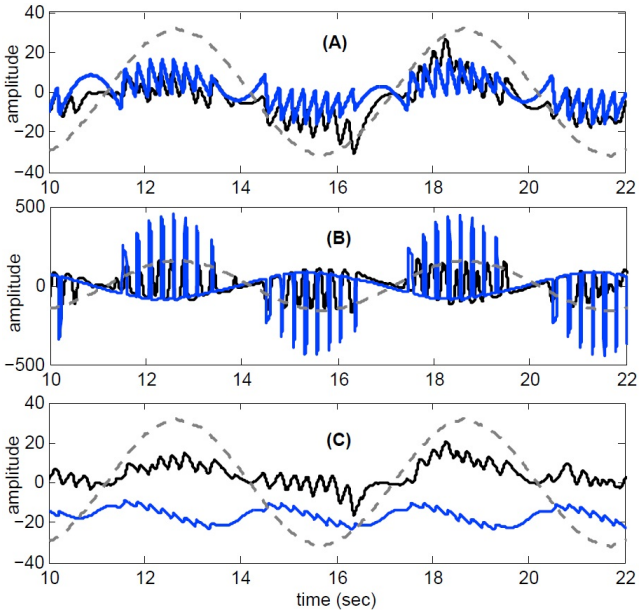

Fig. 3. Simulation results compared to recorded VOR nystagmus. (A) Conjugate eye position (deg) and scaled (1/5) head velocity (deg/s); (B) Conjugate eye velocity (deg/s) and head velocity (deg/s) (C) Vergence eye position (deg) and scaled (1/5) head velocity (deg/s)- blue shifted down. Legend: blue → Simulated, black→ Recorded, dashed gray→ Head velocity.

jugate in the dark; binocular recordings during sinusoidal rotations in darkness clearly show a vergence component in the AVOR [12]. Fig.3.C presents both the recorded and simulated vergence component. The peak-to-peak amplitude of the vergence component in both cases is comparable to that of conjugate VOR, suggesting that it cannot be a result of inappropriate calibration of EOG measurements in these binocular recording. Instead, as predicted from the nonlinear model, this vergence component can be a direct result of nonlinearities at the premotor and sensory levels.

It should be noted that this study did not attempt direct system identification from eye recordings to produce the vergence modulations. A simple comparison of general characteristics without parameter tuning highlights the impact of non-linear gains in this binocular reflex: modulations with target distance will necessarily cause unwanted modulations in vergence, in the dark.

IV. Conclusion

This work introduces a hybrid nonlinear model to replicate AVOR nystagmus in the dark. The bilateral model includes nonlinear sensors as well as nonlinear surfaces assigned to EHV cells to account for target distance dependent behavior of the VOR. A physiologically relevant fast phase circuit and a nystagmus strategy are imbedded to cause the generation of nystagmus and extend the functional range of the AVOR.

The performance of the hybrid model is evaluated through simulations in response to sinusoidal inputs. Similar to experimental observations, there are fewer fast phases per stimulus cycle at higher rotation frequencies. Moreover, the switching frequency also increases with head velocity amplitude.

TABLE I

Numerical values of the model parameters

p_1	p_2	m	b_I	b_E	k_f	k_p	α
1	0.5	5	2	2	0.3	0.15	2

We also compared the simulated eye position and eye velocity signals with experimental data in response to the same rotation profile. It is observed that the general nystagmus characteristics are similar in terms of switching patterns. A considerable *vergence* component exists in experimental data during rotations in the dark as predicted from the bilateral nonlinear model behavior.

Another prediction of our model is an increased vergence response with unilateral vestibular lesions, also associated with decreased conjugate gains. Unbalanced sensory projections due to vestibular lesions result in an increase in the vergence response compared to the normal case. This prediction will be explored by analyzing experimental data from unilateral patients.

This hybrid model of the AVOR can also be used to generate virtual data for validation of algorithms that classify nystagmus segments and identify reflex dynamics.

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