Hypothetical Explanations for Fusion Maldevelopment Nystagmus Syndrome and Infantile Nystagmus Syndrome using a Behavioral Ocular Motor System Model

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ABSTRACT

For best possible vision, the ocular motor system (OMS) continually has to keep the eyes properly aimed and stable, despite challenges to this stability, whether external or internally generated, such as in the case of nystagmus. We have developed a behavioral model of the OMS that can simulate both normal operation as well as two forms of congenitally present nystagmus, without the need for additional mechanisms to compensate for the nystagmus. The model is capable of performing saccadic and smooth pursuit tracking accurately by keeping track of commands issued to move the eyes as well as resulting position and velocity errors and the internal state of key subsystems. This information is used to calculate the necessary commands to correct errors, and perhaps more importantly, to decide when *not* to respond to target motion models of the normal ocular motor system (OMS) that cannot accurately simulate nystagmus—the involuntary oscillation of the eyes towards and away from an intended point of fixation. These models often propose abnormal structures and/or behaviors to allow the OMS to generate the oscillation underlying nystagmus [1-3], and to counter it when attempting to fixate a target.

It is our contention that the OMS is fundamentally the same whether in a "normal" subject or in one with certain congenital forms of nystagmus. Furthermore, we suggest that the mechanisms that allow people with these disorders to perceive a stable world, and that underlie their ability to fix a target with–in some cases–only minimal decrease of visual acuity are not special to these forms of nystagmus, but are simply the fundamental capabilities of the normal OMS performing under extraordinary circumstances, providing stability despite the continuous oscillation of the eye. We hypothesize, in a behavioral model of the OMS, a functional grouping of capabilities, called the "Internal Monitor" (IM), that keeps track of efferent commands issued to move the eye as well as actual eye position. It automatically accounts for discrepancies, allowing for the calculation of perceived target location regardless of the confounding effect of the oscillation, regardless of its internally generated source.

Of the more than forty types of nystagmus recognized [4], two congenital forms are of the greatest interest clinically and scientifically, and have driven the development of our model:

Infantile Nystagmus Syndrome (INS–formerly known as Congenital Nystagmus–CN) is the most common congenital form of nystagmus, affecting between 1 in 3000 and 1 in 6000 people. INS waveforms can be variations of either pendular or jerk waveforms, and the slow phases are increasing velocity (or across the retina, such as during the particular portions of the uncontrolled nystagmus waveform. The resulting output of the model accurately reproduces the responses of the human OMS, and generates complex-appearing pendular nystagmus waveforms bases on the interaction of a simple set of rules.

Keywords: Nystagmus; Ocular Motor System; Eye Movements; Saccades; Smooth Pursuit

1. INTRODUCTION

Visual acuity is greatly dependent upon the ability to hold the fovea on a given point of interest with minimal slip velocity, requiring effective ocular motor control. Superficially this process seems trivial; as a result, this line of thought has led to overly simple
"runaway") exponentials, though approximately linear slow phases can be found in some less-common waveforms [4]. There are additional characteristics of INS that help to distinguish it from the many other types of nystagmus (e.g., the failure of saccades to damp the underlying pendular oscillation, the intervals of extended foveation imposed on the oscillation, the ability to accurately foveate new targets, and the ability to accurately pursue moving targets). A realistic control-system model of INS must be capable of reproducing these basic behaviors to be considered biologically relevant. Many of the ocular motor subsystems have been suggested as the origin of CN, or at least to be severely deficient, including the optokinetic subsystem [5,6], the saccadic subsystem [7,8], and the smooth pursuit (SP) or vestibular subsystems [6,9,10]. However, careful observation and study of most of these candidate systems led us to rule them out as the source of the more common INS waveforms. Instead, we chose to look inside the SP subsystem at a parameter that controls the *onset* of pursuit, rather than the overall gain of the pursuit itself, as first modeled by Robinson [11]. Changes to this internal gain do not affect either the latency or accuracy of pursuit.

Fusion Maldevelopment Nystagmus Syndrome (FMNS–formerly known as Latent/Manifest Latent Nystagmus–LMLN) occurs subsequent to strabismus in some people [12,13]. It may be confused with INS in patients who also have strabismus [14,15]. Accurate eye-movement recordings can reliably differentiate the type of nystagmus by identifying the respective waveforms and their variation with gaze and convergence angle. Unlike INS, whose amplitude grows as gaze is directed to either side of the null position, the amplitude of FMNS usually follows Alexander's law: it increases as the fixating eye moves into abduction and decreases in adduction. The slow phases of FMNS may be either linear or of decreasing velocity in the same

patient. Depending on their slow-phase velocity, FMNS fast phases can be programmed to cause the target image to fall either within (foveating) or outside (defoveating) the foveal area [16]. Higher slow-phase velocities have been found to precipitate defoveating fast phases [17]. Several mechanisms have been proposed as the cause of FMNS. Confusion of egocentric direction secondary to strabismus may result in a constant-velocity drift of the eyes in the direction opposite to the fixating eye [13,18]. Alternatively, it has been suggested that a naso-temporal asymmetry in the optokinetic system may cause the tonic drift of the eyes [6]. Finally, a proprioceptive imbalance has also been suggested as being responsible for the slow-phase genesis of FMNS [19]. For the sake of our modeling it is not important to decide between these putative mechanisms, as each results in a linear slow phase in the direction opposite to the fixating eye.

Despite the oscillation, individuals with INS and FMNS exhibit normal visual function (albeit often with reduced acuity) unless additional afferent deficits are present. Because of that, behavioral models of the ocular motor system of individuals with CN can provide valuable insight into the mechanisms by which the ocular motor system ensures good visual function.

2. METHODS

The ocular motor recordings and observations used to specify the model's performance came from approximately 1000 subjects with nystagmus, recorded in our laboratory and others over the past 35 years. We measured eye movements using a variety of techniques: infrared reflection, magnetic scleral search coil; or high-speed video. Data from all systems were digitized at 500 Hz with 16-bit resolution. Data filtering and analysis were performed using the OMtools software available from http://www.omlab.org ("Software and OMS Models" page).

We developed the model in Simulink, using a modular approach allowing each subsystem to be implemented and tested separately from the others before incorporation into the greater model.

The IM is the "brains" of this model, keeping track of several crucial signals including: efference copy of eye position and velocity; output from the NI; saccadic commands; and position and velocity errors. It uses this information to: detect target changes; reconstruct the target's position and velocity, and their errors; determine when a saccade must be made and then program an appropriate magnitude; control whether or not the NI should integrate its input; and provide reconstructed target velocity information to the fixation system to help it act to prolong target foveation in the presence of disruptive signals such as nystagmus oscillations. Because of the complexity of this major subsystem, each added function required strenuous testing to insure that it did not compromise already-demonstrated capabilities. In addition to the IM, the OMS model is composed of these additional major subsystems (Figure 1):

THE PLANT—A two-pole transfer function is used to model the eye's (globe and muscle) response to movement commands. It provides an adequate saccadic trajectory, far better than a single-pole plant and almost as accurate as a one-zero, two-pole plant.

THE OCULAR MOTOR NEURONS—The summation of tonic and phasic signals at the ocular motor neurons was simulated by a summation with logic to ensure that the output was that of the pulse when a pulse was present.

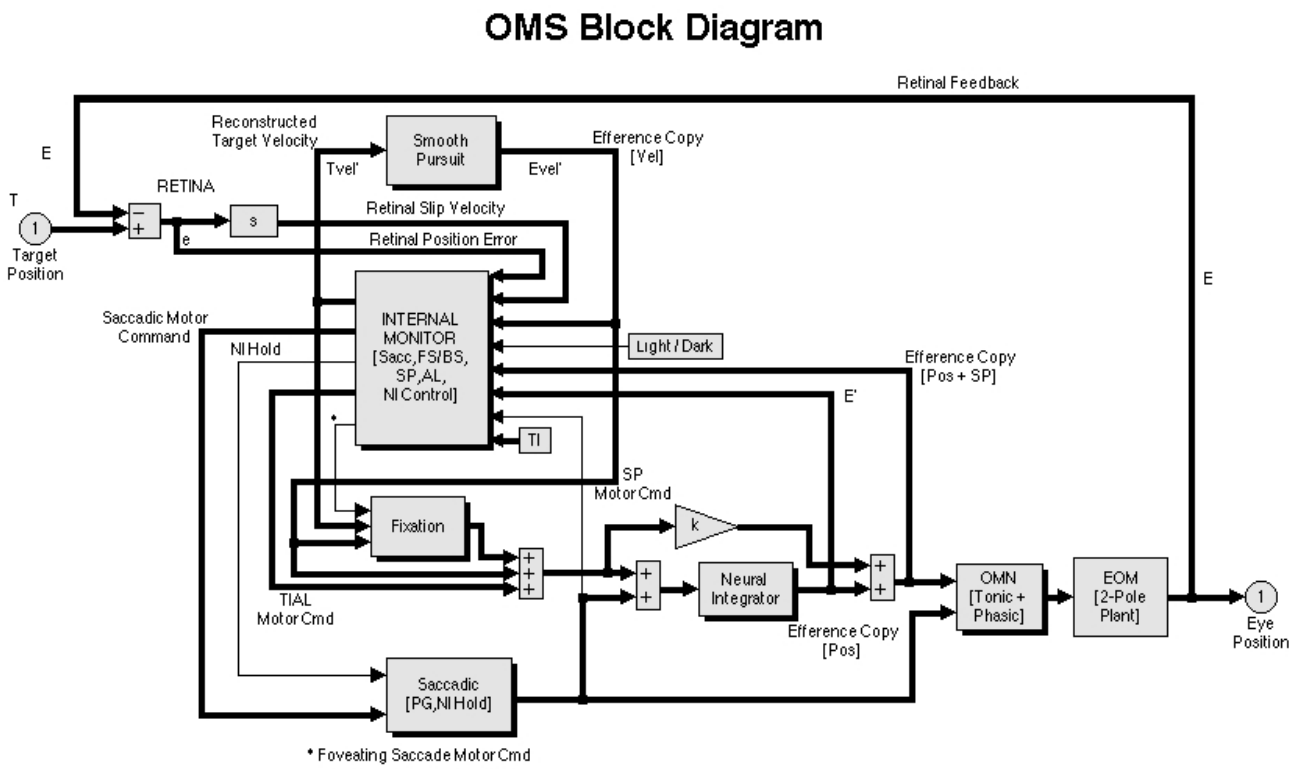

Figure 1. Functional block diagram of the OMS model, showing the major subsystems and their interconnections. Drop shadows indicate that the block contains additional functional blocks. The heavy lines represent main signal pathways, and the light lines control signals.

THE COMMON NEURAL INTEGRATOR—The common neural integrator consists of a leaky integrator (time constant equal to the normal dark-drift time constant of 25 sec) around which is a positive feedback gain to offset that leak and produce a non-leaky integrator.

THE PULSE GENERATOR—The pulse generator produces a pulse whose height is determined by a saturation non-linearity and whose duration is determined by a resettable neural integrator and another non-linearity [20]. A saccadic motor command is passed by a sample-and-hold to both non-linearities. The pulse-height signal is maintained until the pulse-width signal terminates it. The trailing edge of the pulse generator signal is used to initiate a user-definable refractory period only after which time can another saccade be generated.

THE SMOOTH PURSUIT SUBSYSTEM—The smooth pursuit system is a modified version of that proposed by Robinson et al. [11]. The open-loop gain was set to 0.95 to simulate normal smooth pursuit. It responds to the perceived motion of the target, generating an equivalent velocity signal. The forward path contains a low-pass filter, gain, velocity saturation, and a modified premotor circuit (PMC+) containing an acceleration saturation and an integrator in a negative feedback loop; it controls the normally damped oscillatory behavior of the pursuit subsystem.

BRAKING/FOVEATING SACCADE LOGIC—Braking saccades [21-23] are automatically generated to brake runaway eye velocities. If the eye is *running away from* the target at the time of saccade programming, the velocity exceeds 4°/s, and has passed its point of maximum velocity, a braking saccade will be generated. When the eye is *approaching* the target at that time, and meets the other two criteria, then the saccade will be foveating, with the magnitude calculated by the predicting where the eye will be 60 ms later (based on internal delays), when the saccade begins execution.

FIXATION SUBSYSTEM—The fixation subsystem is a velocity-limiting system aimed at reducing retinal slip velocity[24]. Position and velocity errors are passed through a velocity-sensitivity function approximating the general sensitivity of the visual system: high sensitivity (scale factor=1) for lower velocities, with exponentially decreasing sensitivity at higher velocities.

We use a counter-signal equal and opposite to the nystagmus velocity (the difference between reconstructed target and eye velocities calculated within the IM) to cancel out the portion of oscillation immediately following a foveating saccade, corresponding to the time when the target image would be in the foveal area. The product of the foveation-quality signal, the nystagmus velocity, and an additional factor of 4 (compensating for the 0.25 gain of the velocity signal that is passed to the ocular motor neurons) is subtracted from the velocity signal just before the input to the NI.

3. RESULTS

Normal Behavior

We first tested the model for normal behavior in the absence of nystagmus, examining the operation of the saccadic and pursuit systems, acting separately and in concert. Figure 2 shows the model's response to a series of jumps in target position, ranging from 1° to 40°. The left panel shows the smaller-magnitude saccades, up to 10°. Note that the response to the smaller steps can result in a slightly hypermetric saccade, followed by a passive drift ("glissade") back to the desired position, which is a behavior often seen in normal human subjects. Compare this to

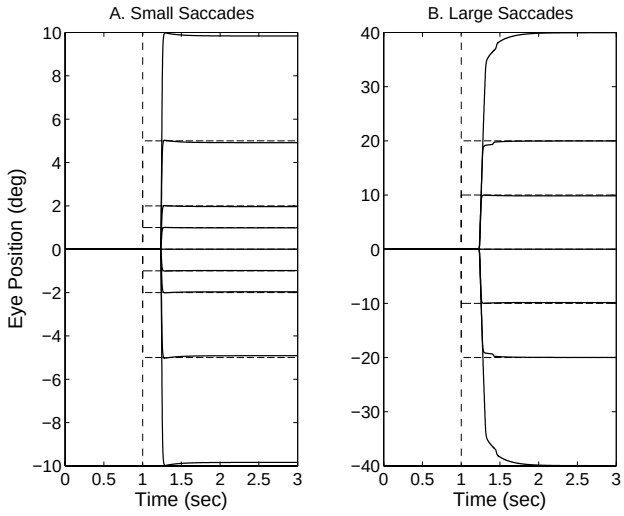

Figure 2. Saccades made in response to target jumps A) <10°, and B) up to 40°. In this and following Figures, dashed lines represent target position; solid lines, eye position.

the saccades on the right side of the Figure, where for target steps of around 20°, the initial response is hypometric, and is quickly followed by a secondary, corrective saccade, programmed using efference copy information executed with much shorter latency (~125 ms) than saccades driven by visual information which typically occur ~250 ms following the stimulus. Again, this is a behavior commonly seen in normal subject data.

The model's ability to accurately track a target moving to either direction, with or without an initial target step, is demonstrated in Figure 3A, for pursuit velocities up to 30°/second. There is a ~125ms latency between the start of target motion and the onset of pursuit, reflecting typical human performance. For the higher velocity ramps, i.e., 20°/sec and greater, the eye cannot keep up and must make a catch-up saccade to recapture the target once the position error exceeds a predefined threshold. This behavior requires precise interaction between the saccadic and SP

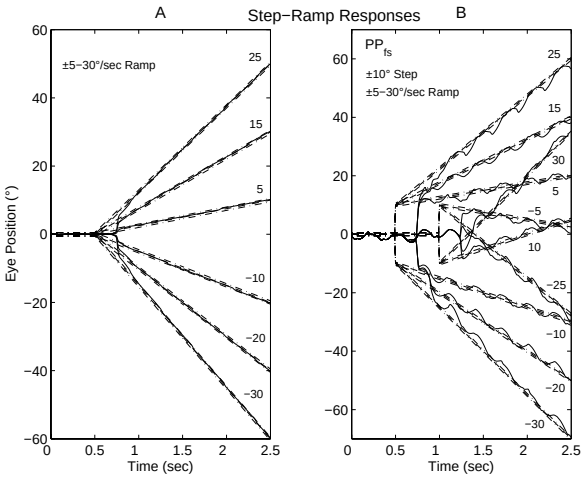

Figure 3. Pursuit A) without nystagmus, and B) in the presence of INS PP_{fs} waveform. Note that the foveation periods in B) always lie along the line of pursuit, and that voluntary saccades, catch-up saccades and nystagmus quick phases do not interfere with each other.

subsystems for it is necessary to accurately predict where the target will be at the time the saccade is executed, which is also required for the a step-ramp (Rashbass) stimulus. In this case it is necessary to make these calculations for steps that either are in the same direction, or in opposition to the ramp.

Response to pulse-step stimuli were correctly calculated, with the pulse being ignored if it lasted under 50ms, as shown in Figure 4, demonstrating the parallel-programmed nature of saccadic [25] programming, which allows new visual input to override previously programmed saccades.

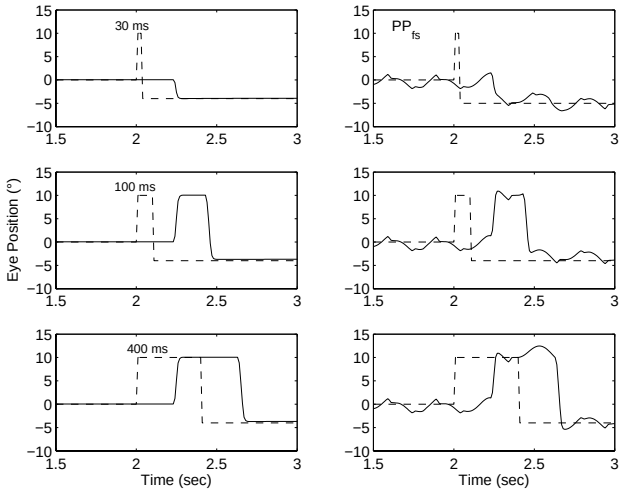

Figure 4. Pulse-step response. Targets that do not remain in place for more than 30 ms before jumping to a new location are properly ignored, even in the presence of nystagmus (right).

Generation of Nystagmus

FMNS–To simulate FMNS [26], we provided a constant input "tonic imbalance" to the IM, which in accordance with Alexander's Law, caused greater slow-phase drifts as eye position went further into abduction. Depending on the slope and magnitude we can generate left-/right-beating latent nystagmus (LN–one eye open) or manifest latent nystagmus (MLN–both eyes open).

INS–The pendular family of INS waveforms appear quite complex, but they can be generated by building upon some simple rules [27]. Once the SP system was induced to ring [11], the next step was to enable automatic braking and/or foveating saccade generation, to convert the pure pendular waveform to either pseudo-pendular (PP) or pendular with foveating saccades (P_{fs}) respectively, as seen in Figure 5. Note that PP remains centered around the fovea (the 0° line), whereas P_{fs} has been shifted so that one extreme is now aligned on the fovea, allowing the slowest portion of the waveform to be used for vision. P_{fs} is a waveform commonly seen in INS subjects, whereas PP is only seen transitionally, as they shift to a more visually useful waveform. We then added the ability to both forms of saccade, yielding the pseudopendular with foveating saccades waveform (PP_{fs}), which improves upon P_{fs} by limiting the runaway velocity of the eye, leading to a slight decrease in peak-to-peak amplitude, a quicker turnaround, allowing a few more cycles every minute and therefore potentially opportunities to foveate. To further increase potential visual acuity, we extended the periods following foveating saccades by canceling a fraction of the oscillation signal when foveation was attempted and the retinal error velocity was at or below 4°/sec. This strategy is utilized by subjects for both P_{fs} and PP_{fs} waveforms.

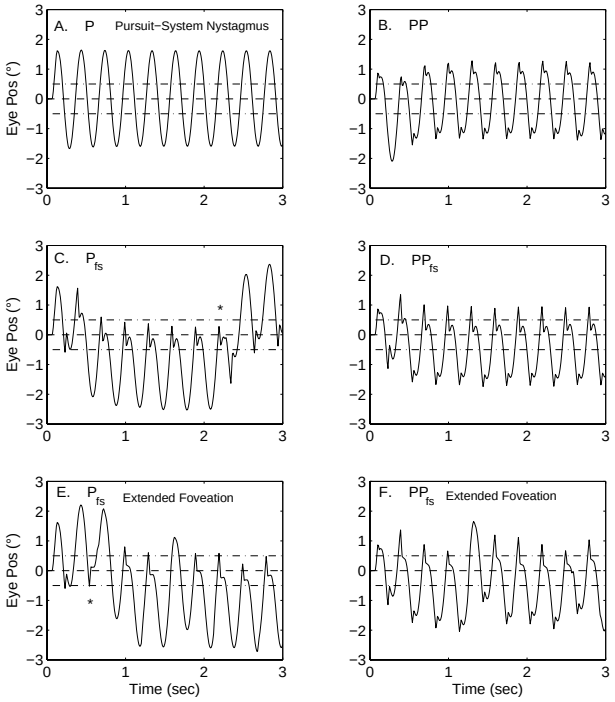

Figure 5. "Evolution" of the PPfs waveform. A) The pure pendular oscillation from the pursuit system. B) The addition of braking saccades reduces the peak-to-peak amplitude, while C) the addition of foveating saccades shifts the waveform so that the low-velocity portions lie on the target. D) PP_{fs} uses both braking and foveating saccades. E&F) Extending the foveation period following foveating saccades further increases potential acuity.

Performance in the Presence of Nystagmus

Figure 6A shows a series of rightward and leftward saccades made while the model was simulating FMNS with a large gaze-angle effect. The amplitude of the nystagmus increases sharply the further the fixing right eye moves into abduction. For most gaze angles the slow-phase velocity exceeds the 4°/sec threshold, leading to defoveating fast-phases; foveating fast-phases are executed only when the fixing eye is maximally adducted. Figure 6B shows the model's output while simulating the INS waveform PP_{fs}. Note that the foveating saccades and the voluntary refixations do not interfere with each other; whichever one reaches the pulse generator first will be executed, followed by the other after the refractory period. Also of great interest is the model's behavior for the large (>20°) saccades; even though the initial saccade was not sufficient to bring the fovea on target, no corrective saccade was executed; the eye simply rode the slow phase toward the target and then calculated the necessary foveating saccade at the appropriate time in the cycle. Finally, note how the waveform direction shifts around the target on several instances, e.g., between 3 and 3.5 seconds for the 30° target. This is a *bias shift;* the waveform has transitioned from a leftward-beating foveating saccade to a rightward one, within the duration of one cycle without sacrificing target accuracy.

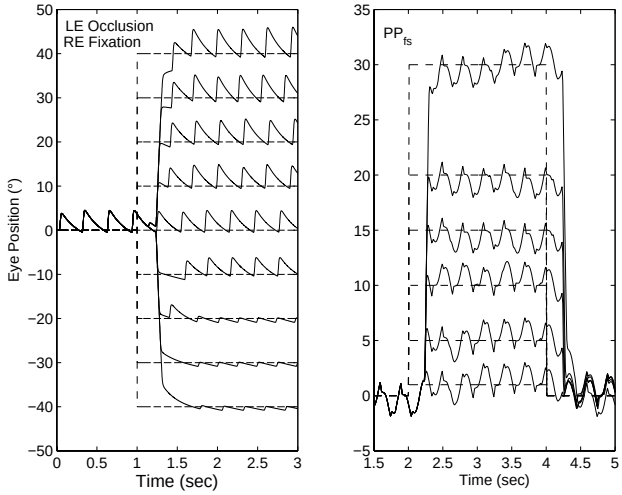

Figure 6. Performance of the saccadic system in the presence of nystagmus. Accuracy has not been impaired. A) FMNS. B) INS. In both cases, saccades and nystagmus fast-phases co-exist without interfering with each other. Also, when appropriate, the model will use a slow phase to reach the target.

Figure 3B shows that the model's ability to accurately pursue moving targets has not been compromised by the confounding oscillation of the nystagmus; the foveating periods simply lie along the line of pursuit and nystagmus quick phases do not interfere with catch-up saccades.

Other Disorders

By selectively "lesioning" the plant, the model simulated a paresis comparable to myasthenia gravis, where the affected eye responded insufficiently to saccadic commands, as compared to an unaffected eye. Making the common neural integrator leaky yields gaze-evoked nystagmus. Dysfunctions such as seen in cerebellar disorders could be modeled by changing the gain of the saccadic system, as shown in Figure 7; dropping it below 1.0 yielded hypometric saccades, while increasing it between 1.0 and 2.0 caused a converging series of hypermetric saccades. Gain greater than 2.0 resulted in sustained macrosaccadic oscillations.

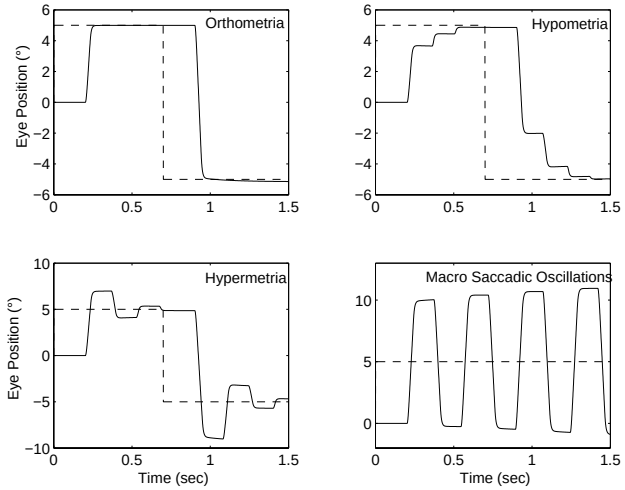

Figure 7. Proper saccadic system gain yields orthometric saccades. A gain <1.0 leads to hypometric saccades while hypermetric saccades are produced when the gain is between 1.0 and 2.0. Gains >2.0 lead to a continual saccadic oscillation.

4. DISCUSSION

We developed a rule-based, classic control system model to examine the operation of the OMS under both normal and nystagmus conditions. We chose this approach over methods such as neural networks, because we believe that it allows us more insight into the decisions that drive eye movements. Every design choice was a hypothesis to be tested and validated by the operation of the model and its ability to accurately operate under challenging conditions.

Since our primary hypothesis was that there is less difference than sometimes supposed between the OMS architecture of "normal" subjects and those with nystagmus, it was necessary that no extraordinary changes be made in the model for it to be capable of coping with the added difficulties of target tracking in the presence of a disruptive additional signal such as nystagmus. Such performance was achieved by simply using the basic necessary capabilities of the OMS, pushed beyond the normal demands of day-to-day function that provide the separation of volitional eye movement from the involuntary oscillation, and allow a stable perception of the world. In our model, this functionality resides in the proposed mechanism of the Internal Monitor, a grouping of several functions including, but not limited to: detection of when target position changes; reconstruction of eye position and velocity, and then target position and velocity based on the commands issued to move the eye and the detection of position and velocity errors; knowing when to generate a saccade, how large it needs to be, and whether or not to fully integrate the saccadic pulse. We do not propose that there is a specific neuroanatomical structure in the brain that is the IM; our grouping is merely functional, although there is some evidence that much of the necessary information (e.g., retinal position and error velocity, efference copy of commands issued) may be present in the paramedian tract [28]. Nevertheless, it is a large conceptual step between it and our IM.

We believe that the robust performance of this model, and its ability to simulate such a wide range of tracking behaviors, support our approach, especially since the model was capable of reproducing several complex human behaviors for which it was not explicitly programmed; they are examples of *emergent behavior,* the result of intimate interaction between the SP and saccadic systems, owing massive interconnection of many simple functions, such as those incorporated in the IM, leading to many unexpected capabilities.

This model will serve as the basis for future investigation into the OMS as we enhance current capabilities by, e.g., adding the ability to generate INS jerk waveforms and develop new functionality such as appending a vestibular system. This is an area where our approach has proven to be very beneficial: owing to the model's modular design, it is a simple matter to make substitutions for any given subsystem, because it is possible to examine the inputs, outputs *and* the internal state of the block under consideration, allowing for a more complete understanding of the operations of the OMS.

5. ACKNOWLEDGEMENTS

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6. REFERENCES

[1] L.M. Optican and D.S. Zee, "A hypothetical explanation of congenital nystagmus," **Biological Cybernetics**, vol. 50, 1984, pp. 119-134.

[2] R.J. Tusa, D.S. Zee, T.C. Hain, and H.J. Simonsz, "Voluntary control of congenital nystagmus," **Clinical Vision Science**, vol. 7, 1992, pp. 195-210.

[3] D.S. Broomhead, R.A. Clement, M.R. Muldoon, J.P. Whittle, C. Scallan, and R.V. Abadi, "Modelling of congenital nystagmus waveforms produced by saccadic system abnormalities," **Biological Cybernetics**, vol. 82, 2000, pp. 391-9.

[4] L.F. Dell'Osso and R.B. Daroff, "Nystagmus and saccadic intrusions and oscillations," in **Duane's Clinical Ophthalmology, Vol. II, Chap. 11**, W. Tasman and E.A. Jaeger, Eds. Philadelphia: Lippincott-Raven, 1997, pp. 1-33.

[5] R.D. Yee, R.W. Baloh, and V. Honrubia, "Study of congenital nystagmus: optokinetic nystagmus," **British Journal of Ophthalmology**, vol. 64, 1980, pp. 926-32.

[6] G. Kommerell and E. Mehdorn, "Is an optokinetic defect the cause of congenital and latent nystagmus?," in **Functional Basis of Ocular Motility Disorders**, G. Lennerstrand, D.S. Zee, and E.L. Keller, Eds.: Oxford, Pergamon Press, 1982, pp. 159-167.

[7] L.F. Dell'Osso, G. Gauthier, G. Liberman, and L. Stark, "Eye movement recordings as a diagnostic tool in a case of congenital nystagmus," **American Journal of Optometry and Archives of the American Academy of Optometry**, vol. 49, 1972, pp. 3-13.

[8] R.V. Abadi and R. Worfolk, "Retinal slip velocities in congenital nystagmus," **Vision Research**, vol. 29, 1989, pp. 195-205.

[9] A. Yamazaki, "Abnormalities of smooth pursuit and vestibular eye movements in congenital jerk nystagmus," in **Ophthalmology**, K. Shimaya, Ed. Amsterdam: Excerpta Medica, 1979, pp. 1162-1165.

[10] R. St. John, J.D. Fisk, B. Timney, and M.A. Goodale, "Eye movements of human albinos," **American Journal of Optometry and Physiological Optics**, vol. 61, 1984, pp. 377-385.

[11] D.A. Robinson, J.L. Gordon, and S.E. Gordon, "A model of smooth pursuit eye movements," **Biol Cyber**, vol. 55, 1986, pp. 43-57.

[12] L.F. Dell'Osso, S. Traccis, and L.A. Abel, "Strabismus - A necessary condition for latent and manifest latent nystagmus," **Neuro ophthalmol**, vol. 3, 1983, pp. 247-257.

[13] L.F. Dell'Osso, D. Schmidt, and R.B. Daroff, "Latent, manifest latent and congenital nystagmus," **Arch Ophthalmol**, vol. 97, 1979, pp. 1877-1885.

[14] L.F. Dell'Osso, "Congenital, latent and manifest latent nystagmus - similarities, differences and relation to strabismus," **Jpn J Ophthalmol**, vol. 29, 1985, pp. 351-368.

[15] L.F. Dell'Osso, "Congenital and latent/manifest latent nystagmus: Diagnosis, treatment, foveation, oscillopsia, and acuity," **Jpn J Ophthalmol**, vol. 38, 1994, pp. 329-336.

[16] L.F. Dell'Osso, R.J. Leigh, N.V. Sheth, and R.B. Daroff, "Two types of foveation strategy in 'latent' nystagmus. Fixation, visual acuity and stability," **Neuro Ophthalmol**, vol. 15, 1995, pp. 167-186.

[17] D.M. Erchul, L.F. Dell'Osso, and J.B. Jacobs, "Characteristics of foveating and defoveating fast phases in latent nystagmus," **Invest Ophthalmol Vis Sci**, vol. 39, 1998, pp. 1751-1759.

[18] L.F. Dell'Osso and R.B. Daroff, "Clinical disorders of ocular movement," in **Models of Oculomotor Behavior and Control**, B.L. Zuber, Ed.: West Palm Beach, CRC Press Inc, 1981, pp. 233-256.

[19] S. Ishikawa, "Latent nystagmus and its etiology," in **Strabismus, Proceedings of the Third Meeting of the International Strabismological Association**, R.D. Reinecke, Ed.: New York, Grune and Stratton, 1979, pp. 203-214.

[20] L.A. Abel, L.F. Dell'Osso, and R.B. Daroff, "Analog model for gaze-evoked nystagmus," **IEEE Trans Biomed Engng**, vol. BME, 1978, pp. 71-75.

[21] L.F. Dell'Osso and R.B. Daroff, "Braking saccade--A new fast eye movement," **Aviat Space Environ Med**, vol. 47, 1976, pp. 435-437.

[22] J.B. Jacobs, L.F. Dell'Osso, and D.M. Erchul, "Generation of braking saccades in congenital nystagmus," **Neuro Ophthalmol**, vol. 21, 1999, pp. 83-95.

[23] J.B. Jacobs, L.F. Dell'Osso, and R.J. Leigh, "Characteristics of braking saccades in congenital nystagmus," **Doc Ophthalmol**, vol. 107, 2003, pp. 137-154.

[24] J. Epelboim and E. Kowler, "Slow control with eccentric targets: evidence against a position-corrective model," **Vision Research**, vol. 33, 1993, pp. 361-380.

[25] W. Becker and R. Jürgens, "An analysis of the saccadic system by means of double step stimuli.," **Vision Research**, vol. 19, 1979, pp. 967-983.

[26] L.F. Dell'Osso and J.B. Jacobs, "A robust, normal ocular motor system model with latent/manifest latent nystagmus (LMLN) and dual-mode fast phases," in **Neuro-ophthalmology at the Beginning of the New Millennium**, J.A. Sharpe, Ed. Englewood: Medimond Medical Publications, 2000, pp. 113-118.

[27] J.B. Jacobs and L.F. Dell'Osso, "Congenital nystagmus: hypothesis for its genesis and complex waveforms within a behavioral ocular motor system model," **JOV**, vol. 4, 2004, pp. 604-625.

[28] K. Nakamagoe, Y. Iwamoto, and K. Yoshida, "Evidence for brainstem structures participating in oculomotor integration," **Science**, vol. 288, 2000, pp. 857-859.