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Original Contribution

EVIDENCE SUGGESTING INDIVIDUAL OCULAR MOTOR CONTROL OF EACH EYE (MUSCLE)

L. F. Dell'Osso

Ocular Motor Neurophysiology Laboratory, Veterans Affairs Medical Center; the Departments of Neurology and Biomedical Engineering, Case Western Reserve University and University Hospitals of Cleveland, Cleveland, Ohio
Reprint address: L. F. Dell'Osso, Ph.D., Ocular Motor Neurophysiology Laboratory, Veterans Affairs Medical Center (127A), 10701 East Boulevard, Cleveland, OH 44106

□ **Abstract—Current models of the ocular motor system are usually presented in their most reduced form, are unilateral in architecture, and precise yoking is presumed. Although this simplifies the models, it does not accurately simulate the actual neuroanatomy and limits the models to simple, stereotyped responses. Studies of normal humans and monkeys have demonstrated striking disconjugacies in normal responses. Normal saccades may be disconjugate, or 1 eye may exhibit a dynamic overshoot. Asymmetric vergence can result in disconjugate saccades, unequal magnification spectacles cause differential saccadic gain adjustment, and saccades to unequal disparities also cause unequal saccades in the 2 eyes. In strabismus, deviated eyes typically do not mimic the movements of the fixating eye nor do their latent or congenital nystagmus waveforms duplicate those of the fixating eye. In spasmus nutans, each eye oscillates independently of the other. In achiasmatic dogs, uni-ocular saccades and uni-ocular nystagmus waveforms are seen; the same may be true in human achiasma. These data from both normals and those with abnormalities suggest that current models for ocular motor control are inadequate representations of the actual system. The inability of unilateral, yoked control (or even bilateral, yoked control) system models to duplicate the ocular motor responses of binocular mammals suggests that their ocular motor systems evolved from the bilateral, independent control systems seen in chameleons. One need only postulate a yoking overlay superimposed on two independent control systems to achieve conjugacy (bilateral, yoked, independent control) of the eyes. Abnormalities producing grossly disconjugate eye movements may then be simulated using the independent control of each eye released by a deficiency in the yoking overlay. Independent control of each eye coupled with the essential bilateral brain stem architecture implies that each individual *muscle* is driven by independent populations of neurons (burst cells, neural integrator cells, etc.). The agonist muscles of each eye are usually coordinated (yoked) but may function independently if the task dictates or if binocularity did not develop. Models based on the above architecture would be robust and could duplicate the many responses (both normal and abnormal) possible from the neurophysiological system.**

□ **Keywords—ocular motor control; eye muscle control; models; yoking.**

Introduction

Understanding the neuroanatomical organization of the motor system controlling the movements of the two eyes in binocular animals has been the goal of numerous studies over the past two decades. One of the major approaches to this problem has been through the use of control system models of various functional parts (subsystems) of the overall control mechanism. One tendency of modelers is to reduce their model to the minimum model capable of duplicating the data. Such reductionism allowed simulation on early analog

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computers that were often limited to a relatively small number of operational amplifiers. It also simplified analysis of the system and avoided "unnecessary" redundancy of function. The latter was an engineering judgement, not meant to imply correspondence with the way nature evolved the ocular motor system. Nature appears to be more fond of functional redundancy, perhaps because of its survival value, than are engineers, whose training emphasizes efficient solutions to a problem.

As a result, there emerged unilateral, yoked control (UYC) models that produced both positive and negative signals despite both the bilateral nature of brain stem organization and the positive-only nature of neuronal signals; neurons cannot fire negatively. As Figure 1a shows, UYC models have only 1 eye, because perfect yoking is assumed; they are essentially monocular models. Such reductionism in modeling is not, in and of itself, a cause for concern. However, to the extent that it oversimplifies the system under study, it may tend to foster the impression that the neurophysiological system is also that simple. In addition, such models may fail to duplicate those properties of the actual system that are a function of the neuroanatomical interconnections. One of the basic tenets of control system theory is that the ultimate behavior of a system is more a function of its interconnections (feedback loops) than of the gains of particular elements. In cases where the bilateral nature of ocular motor control was under consideration, bilateral, yoked control (BYC) models were used. As Figure 1b shows, BYC models also have only 1 eye for output because perfect yoking is assumed. All signals are positive on either side of the brain stem. The steering diodes are included to illustrate the anatomical division of retinal error signals in each direction; they do not imply negative retinal error signals (e_l). Also, the neural integrators shown are the common integrators responsible for eye position; the local, resettable integrators (1) that determine pulse width are contained within the "FEM" boxes. The "push-pull" interconnections of the common neural integra-

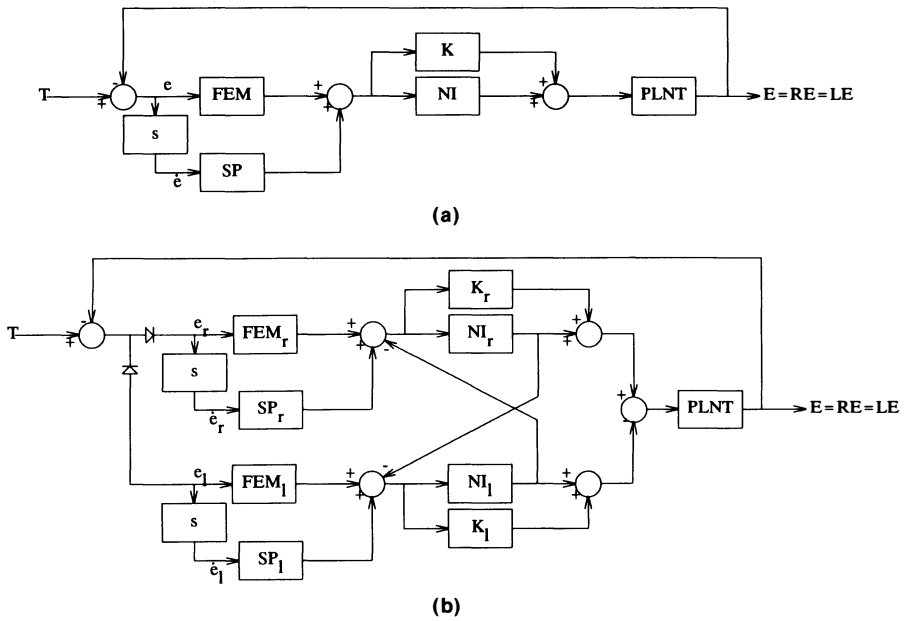


Figure 1. Illustration of (a) unilateral, yoked control architecture and (b) bilateral, yoked control architecture in models containing both the fast eye movement (FEM) and smooth pursuit (SP) subsystems. In this and following figures, T = target, e = retinal error position, ė = retinal error velocity, NI = neural integrator (common), PLNT = ocular motor plant, K = proportional (constant) pathway, E = eye, RE or re = right eye, LE or le = left eye, r = right, l = left, s = Laplace notation for differentiation.

tors allows integration of differential signals and preservation of common, tonic signals (2).

Two factors have combined to perpetuate the use of reductionist models of ocular motor control. The *first* is the recognition that unilateral models can be used to simulate most normal eye movements, and the *second* is the almost perfect yoking exhibited by normal humans and monkeys (the subjects of most eye movement research). This has led to the conceptualization that a single substrate is responsible for the generation of each type of eye movement in each direction. That is, one pulse generator connected to one common neural integrator produces unidirectional saccades in both eyes. Models containing such an architecture necessarily produce perfectly yoked outputs in both eyes. However, the limitations of such models emerge when studying patients with ocular motor deficits that produce eye movements that are not perfectly yoked; it can also be appreciated when one considers some responses of normals.

This paper will present observations from both normal and abnormal eye movement data that suggest a more complex ocular motor control architecture—*independent control of each eye*. Because of the inherent bilateral nature of brain stem organization, the latter directly implies independent control of each eye *muscle*. Taken individually, some of the observations are only mildly suggestive of independent control; others are strongly suggestive. None may, by itself, provide conclusive proof of independent control, although some appear to. However, taken together, they support a strong case for the hypothesis that the neuroanatomy of our ocular motor systems is basically configured for independent control of each eye (muscle) and it is binocularity that imposes the yoking normally seen.

Observations and Discussion

Studies of normal ocular motility have, on occasion, yielded data that call into question the assumption of obligate yoking produced by singular control of both eyes in binocular animals. Indeed, one early investigator (Bert Zuber) was led to exclaim, "the ocular motor system can make the eyes do anything it wants to." I presume this comment was prompted by the exasperation resulting from the occasional occurrence of eye movement data that did not conform to prevailing concepts of binocular control. In our laboratory, over 2 decades of study of pathological eye movements in human patients have produced enigmatic eye movements that defy our understanding of ocular motor control. They suggest that not only can the ocular motor system do with the eyes what it wants to, but also some things it may not have intended.

Eye Movements of Normals

In 2 of the earlier studies of human saccadic metrics, it was found that the saccadic trajectories of each eye might independently overshoot or undershoot the target during the pulse portion of the response, and the resulting "glissade" to the target was specific for the metrics of that eye's saccade (3,4). Such data from normal humans had an immediate impact on the methodology used to record eye movements; from that point onward, no serious investigator could present data using bitemporal EOG electrodes. However, it also provoked thought into ocular motor architecture. Were these differences in the saccadic response to purely horizontal targets due to differences in neural signals to each eye or different neuromuscular responses to the same neural signal?

The occurrence of uni-ocular dynamic overshoots (5) in normals is another instance of disconjugacy that suggests independent neural control signals to each eye. These movements are more common in small saccades and are thought to reflect activation of the antagonist burst neurons (active braking). They may, however, reflect pulse-slide-step innervational mismatches (6). Regardless of which of these mechanisms is responsible, their occurrence in 1 eye also raises the possibility of independent ocular control.

The saccades associated with asymmetric vergence may be of unequal amplitudes. These

have been shown not to be the result of simple superposition of a yoked, conjugate saccade and a slow vergence output (7–11). Enright concluded that the *step* of neural innervation was "generated separately for each eye" and independently of the pulse driving a saccade (12). Zee et al. (13) developed several models to simulate saccade-vergence interaction; two of them utilized independent burst neurons for each eye.

Experiments with spectacles of different magnifications, or prisms placed in front of the eyes produced unequal saccadic gain adaptations in each eye (8,13–18). Because such gain changes are accomplished by pulse-width modulation of the saccadic bursts, it is probable that they were produced within the saccadic pulse generator circuitry for each eye. Bains et al. (19) studied instantaneous velocity vectors of normal human saccades and found little inter-eye variation. They concluded that there was a single saccadic generator for both eyes, and adaptation occurred downstream from it. Another equally plausible explanation is that, in normals, the need for binocularity imposes a tight yoking that precludes significant inter-eye differences in saccadic trajectories.

Findlay and Harris (17) showed that saccades to unequal disparities may also be of unequal amplitude, suggesting different burst cells for each eye. A recent experiment conducted by F.A. Miles consisted of stimulating different-amplitude saccades in each eye by the use of either red-green or polaroid filters (personal communication). It was found that the ocular motor system produced saccades of the correct (different) amplitude in each eye without any training or adaptation. Thus, the substrate (saccadic generators) to make unequal saccades in the 2 eyes, each based on its own visual input signal, was present in normal humans; these movements would not result if there were a single saccade generator for both eyes.

Strabismus and Nystagmus

The deviated eye of subjects with strabismus and latent/manifest latent nystagmus (LMLN) or CN does not always follow the fixating eye accurately. The LMLN or CN waveforms of the fixating eye are closely locked into the target position. The deviated eye's oscillations are not well controlled in either waveform or position with respect to the target (that is, the strabismus angle is usually variable during any short period of fixation). This is thought to reflect a disturbance in yoking secondary to the visual suppression of the deviated eye necessary to prevent diplopia. It is not known whether the resulting differences reflect different control signals to the 2 eyes or differential responses to a common control signal.

Spasmus Nutans

The pendular nystagmus of spasmus nutans is of variable conjugacy in the 2 eyes (20). During the interval of a few seconds, it may vary from an in-phase nystagmus of the two eyes to 180° out of phase, taking on intermediate phase shifts continuously. Also, it sometimes appears uni-ocularly. It is difficult to attribute such behavior to anything other than independent oscillations of uncoupled (unyoked) control systems.

Eye Movements of Achiasmatic Dogs

Preliminary studies of the eye movements of achiasmatic mutant Belgian sheepdogs revealed the presence of uni-ocular, convergent and divergent saccades (21). Thus, the burst cells and neural integrator cells that drove one eye did not drive the other, which remained idle (uni-ocular saccades) or was driven in the opposite direction by *other* burst and neural integrator cells (convergent and divergent saccades). The lack of an optic chiasm in these dogs precludes binocular vision, and this congenital abnormality appears to have prevented development of the yoking mechanism present in normal, binocular dogs. As a result, each eye appeared to be independently controlled. In addition, these dogs have a nystagmus whose waveforms mimic those of human congenital nystagmus (CN) (21,22). One major

difference, however, is that the nystagmus in the dogs may appear in 1 eye only at any given time; human CN is a directionally conjugate oscillation, even in the presence of strabismus. This implies an ocular motor system oscillation that affects 1 eye only. In human CN, fixation attempt is responsible for the genesis and maintenance of the nystagmus oscillation. In these monocular dogs, the uni-ocular CN may reflect fixation by that eye and its subsequent appearance in the other eye uni-ocularly may reflect a change in the fixating eye.

Eye Movements of Achiasmatic Humans

Recently, the first humans with congenital achiasma were reported (23). Their clinical appearance, like that of the achiasmatic dogs, resembled that of humans with CN except they appeared to vary in conjugacy. The nystagmus waveforms were those of human CN. Further study of these unique cases will determine if they too exhibit uni-ocular eye movements; their videotaped eye movements suggest that they may. If so, this would suggest another instance where the absence of yoking releases the independent control systems that are apparently present in normal humans and dogs.

Evolution and the Chiasm

In the lower vertebrates (for example, fish, frog, lizard or bird), all fibers cross (total decussation) at the optic chiasm (Figure 2, "CHAMELEON"). In the higher vertebrates (eg., mammals), a percentage remain on the same side (partial decussation) (Figure 2, "HUMAN"). Only a small portion remain uncrossed in rodents but about 33% are uncrossed in carnivores and >40% in humans. In human albinos, many additional fibers (out to 20° temporally) cross at the chiasm (Figure 2, "ALBINISM"); the crossed and uncrossed temporal populations are intermingled, leaving no clear demarcation line between the two. Thus, although the exact number is unknown, and there is a dramatic intersubject variability, the percentage of crossed fibers far exceeds the <60% that cross in normal humans. In normal dogs, 85% of their optic nerve fibers cross at the optic chiasm. The total absence of an optic chiasm in the mutant dogs we tested, forced *all* optic nerve fibers to remain ipsilateral (Figure 2, "ACHIASMA"); "no such condition is on record in Vertebrates" (24). In terms of crossed and uncrossed optic fibers, achiasmatic dogs represent a condition opposite to chameleons and almost opposite to human albinos. In a sense, they are "anti-chameleons" and almost "anti-albinos."

The dog is an animal that evolved with an area centralis and optic fibers meant to partially decussate at the optic chiasm, synapse in specific layers of both the ipsilateral and contralateral lateral geniculate nuclei (LGN) and then project to the ipsilateral (vis-à-vis the LGN) visual cortex. This type of visual fiber organization produces a large binocular field of single vision in frontal-eyed animals. It is not immediately obvious what the visual world looks like to such an animal when a mutation prevents the partial decussation at the chiasm. One may safely presume that the fibers from the temporal retina of each eye correctly synapse in the LGN and then project to the ipsilateral visual cortex, producing a correct perception of the nasal visual field of that eye. However, the fibers from the nasal retina will incorrectly synapse in the ipsilateral LGN and incorrectly project to the ipsilateral visual cortex. If that is the case, and no adaptation takes place, each visual cortex will contain correct images of the nasal fields from their respective (ipsilateral) temporal retinas superimposed on horizontally reversed temporal visual fields from their respective nasal retinas. This would be similar to viewing two slides (one of the nasal visual field and one of the temporal field) simultaneously, where the temporal visual-field slide was reversed left-to-right before superimposing it on that of the nasal field. Without some form of selective suppression, such visual "noise" would prevent both accurate perceptual input and properly responsive motor output.

Implications for Modeling

The neuroanatomical architecture of the mammalian ocular motor system has been as-

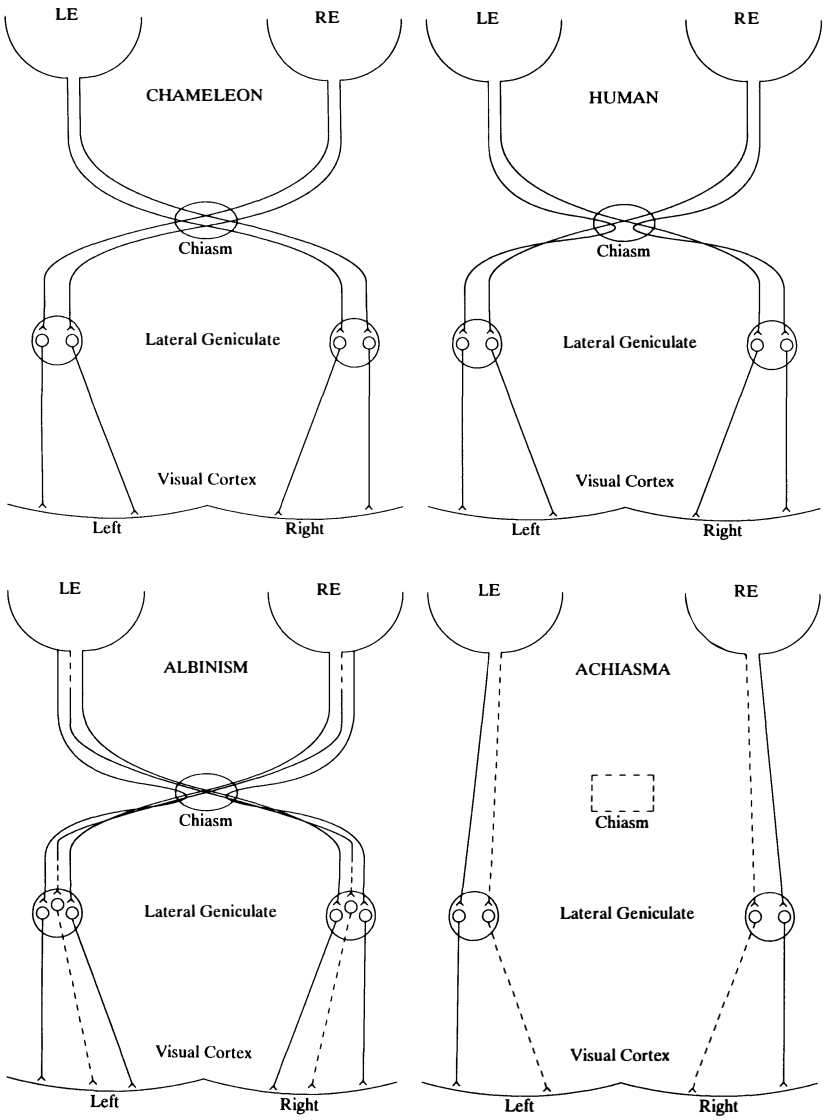


Figure 2. Illustrations of chiasmal connections in chameleon, human (dog/monkey), human albino, and achiasmatic dog (human). Misdirected pathways and absent structures contain dashes.

sumed to follow the "yoked" models, UYC or BYC. If, as the above observations suggest, it is closer to the chameleon system with independent motor control of each eye, some major changes are required. A model of the chameleon ocular motor system requires independent control of each eye. Figure 3 shows a bilateral independent control (BIC) model that approximates the chameleon's system. Each eye in the BIC model is driven by its own retinal input and, therefore, each muscle is driven by its own pulse generator-neural integrator combination. If mammalian ocular motor systems evolved from the chameleon, the same architecture should be preserved. Because binocularity imposes tight yoking, an overlay is needed to drive the independently controlled eyes in a conjugate manner. One way this could be accomplished is shown in Figure 4. This model contains bilateral, yoked,

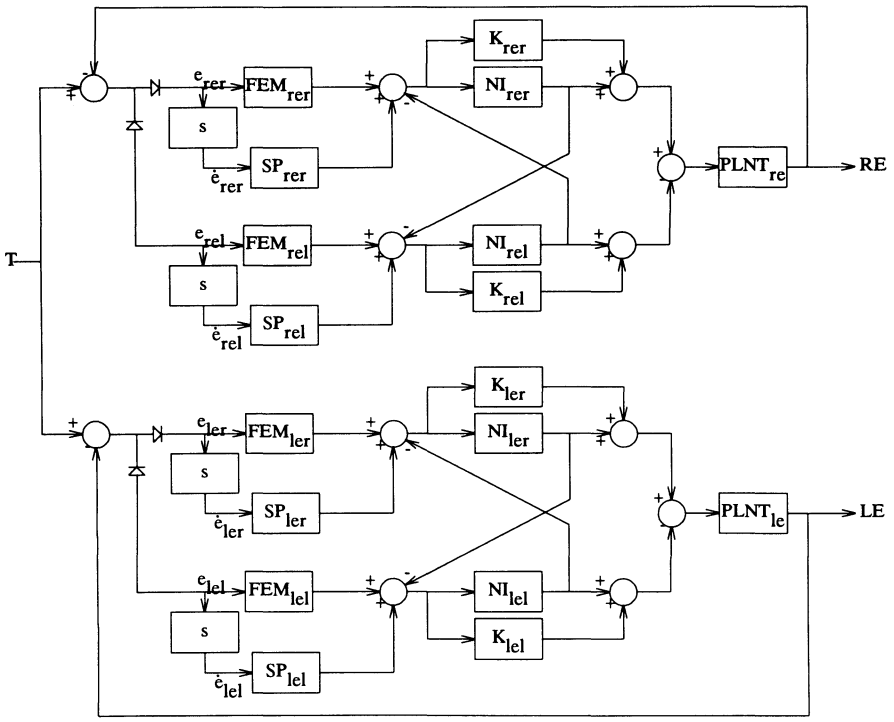


Figure 3. Illustration of bilateral, independent control architecture in a model containing both the fast eye movement (FEM) and smooth pursuit (SP) subsystems.

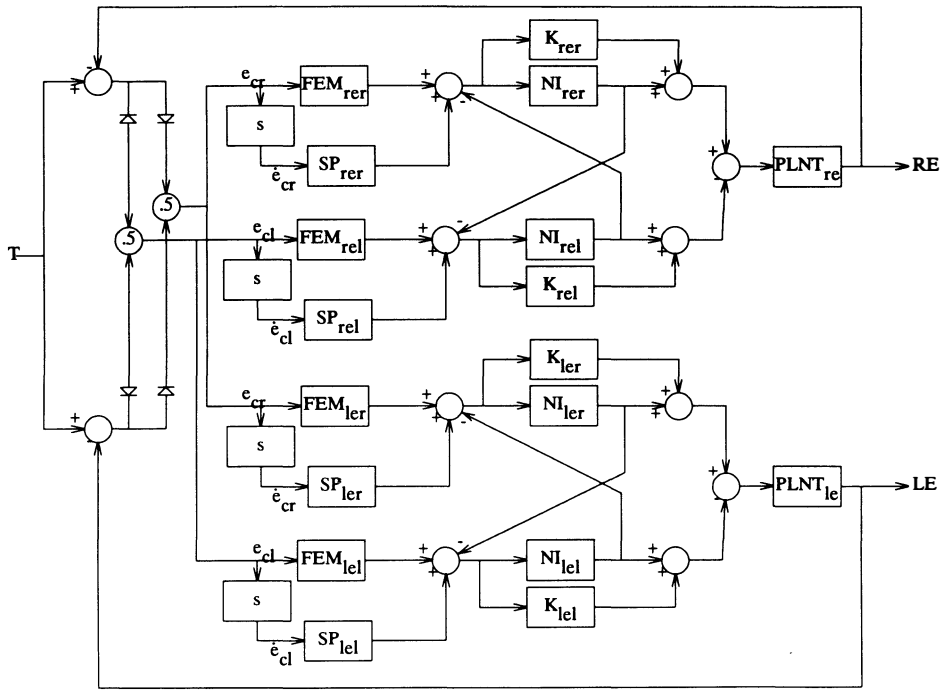


Figure 4. Illustration of bilateral, yoked, independent control architecture in a model containing both the fast eye movement (FEM) and smooth pursuit (SP) subsystems.

independent control (BYIC). Both eyes in the BYIC model are driven by a conjugate error signal derived from the errors seen by the individual eyes. The steering diodes in both Figures 3 and 4 indicate anatomical separation of retinal error signals in the two directions; all signals on both sides of the brain stem are positive. Models with the architecture of Figure 4 can produce the types of conjugate responses seen in most normals. The actual architecture of the yoking circuitry in binocular animals should allow the ocular motor system to function as either a BIC or BYIC system (or some combination of the two), depending on the type of input supplied. This architecture has yet to be worked out. Table 1 summarizes the inputs, outputs, and number and type of subsystems and common neural integrators for each type of ocular motor control.

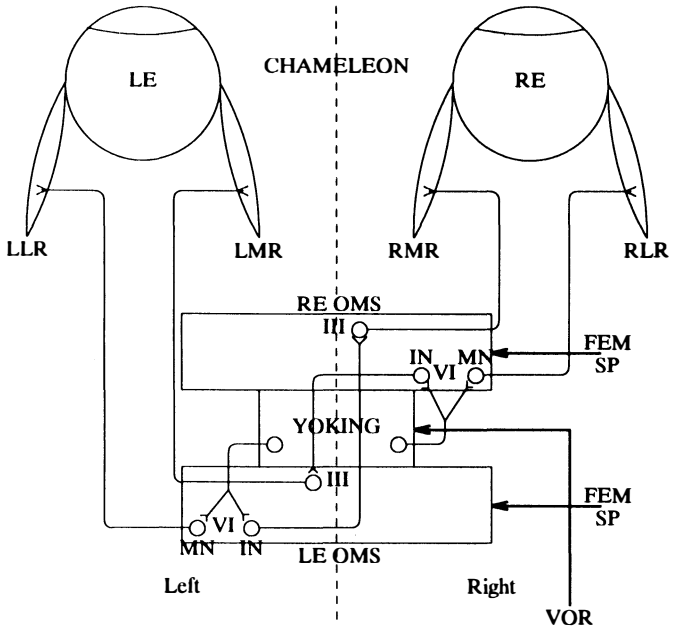
Finally, let us consider the question of where the yoking might be accomplished. Even in the chameleon, yoking is needed for the vestibulo-ocular reflex (VOR). Figure 5a shows a possible site for that yoking may be at the level of the interneurons of the VI Nerve. Because the VOR must produce a conjugate response to movement, its input is shown using a yoking circuit. Both the saccadic (FEM) and smooth pursuit (SP) subsystems act on monocular retinal inputs allowing uni-ocular responses. In mammals, the yoking also controls saccades and smooth pursuit, as is shown in Figure 5b. The vestigial monocular FEM and SP connections are shown dashed. Figure 5c, d attempts to diagram possible deficits in yoking that would exist in achiasmatic dogs and humans (5c), human infants with spasmus nutans (5c), and humans (monkeys) with strabismus (5d). The dashed neural connections indicate disturbed pathways, to both eyes in Figure 5c and to the nonfixating eye in Figure 5d. In achiasma (5c), the major inputs to both FEM and SP are presumed to be monocular (bold lines) while the VOR remains a yoked input. The dashed FEM and SP inputs to the yoking circuitry indicate the evolution of yoked eye movements that have been disturbed by the mutation of achiasma and, to a lesser extent, spasmus nutans. In strabismus (5d), the relative contributions of monocular and binocular inputs to FEM and SP are variable from subject to subject and may vary within a subject with variable strabismus; these inputs are shown dashed.

Before more specific neuronal connections can be hypothesized with confidence, anatomical data are required to answer several questions arising from the models in Figures 3 and 4. In the chameleon (and presumably higher mammals), is there a direct connec-

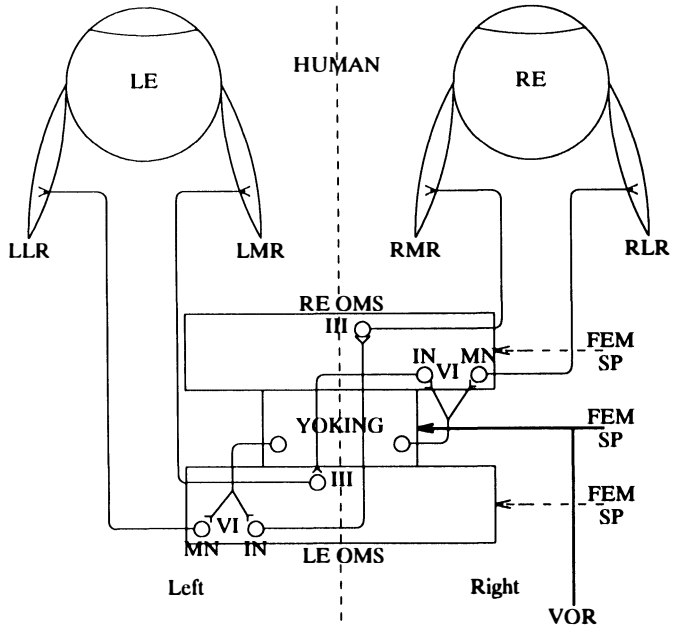
Table 1. Control system summary

Type of Control	Inputs		Subsystems		Common Neural Integrator	Outputs
	FEM (ϵ)	SP ($\dot{\epsilon}$)	FEM	SP		
UYC	Conjugate	Conjugate	1 Bidirectional Binocular	1 Bidirectional Binocular	1 Bidirectional Binocular	1 Conjugate E = RE = LE
BYC	Conjugate	Conjugate	2 Unidirectional Binocular	2 Unidirectional Binocular	2 Unidirectional Binocular	1 Conjugate E = RE = LE
UIC	Monocular	Monocular	4 Unidirectional Uniocular	4 Unidirectional Uniocular	4 Unidirectional Uniocular	2 Uniocular RE and LE
UYIC	Conjugate	Conjugate	4 Unidirectional Uniocular	4 Unidirectional Uniocular	4 Unidirectional Uniocular	2 Uniocular RE and LE

UYC = unilateral, yoked control; BYC = bilateral, yoked control; UIC = unilateral, independent control; UYIC = unilateral, yoked, independent control; FEM = fast eye movement; SP = smooth pursuit; ϵ = retinal error (position); $\dot{\epsilon}$ = retinal error (velocity).

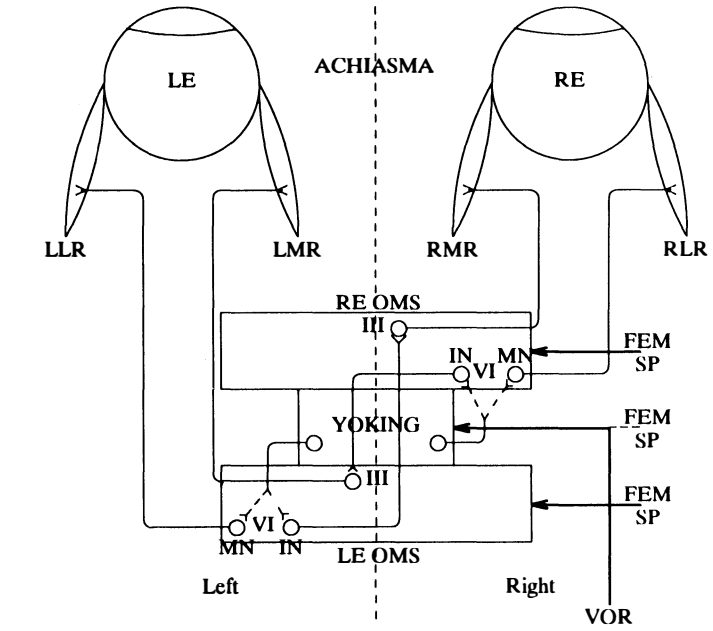


(a)

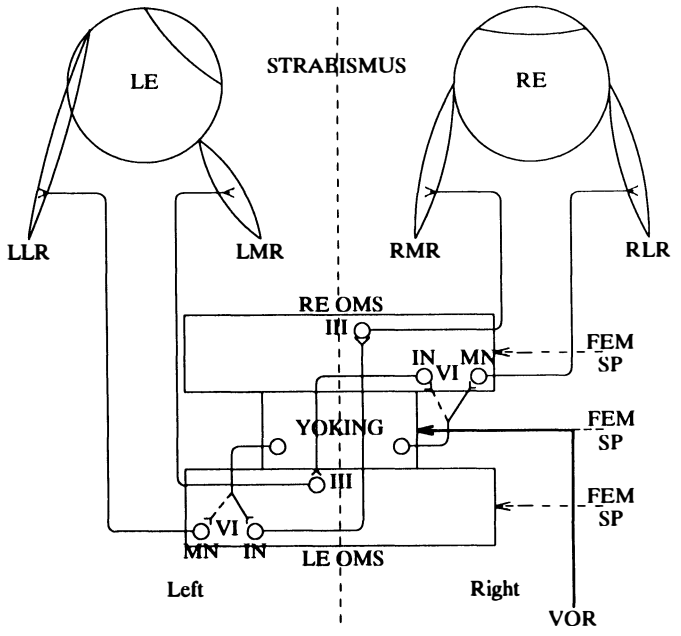


(b)

Figure 5. Illustrations of possible yoking sites in (a) chameleon, (b) human (dog/monkey), (c) achiasmatic dog (human) and (d) strabismic human (monkey). Bold lines indicate predominant subsystem inputs. Dashed lines indicate disturbed pathways of subsystem inputs. OMS = ocular motor system, R(L)LR = right (left) lateral rectus, R(L)MR = right (left) medial rectus, III = third nerve nucleus, VI = sixth nerve nucleus, MN = motoneuron and IN = internuclear neuron. (*Figure continues on following page.*)



(c)



(d)

Figure 5 continued.

tion for FEM (that is, burst neurons and common neural integrator neurons) and SP to the III Nerve or is the internuclear neuron pathway used? Are there connections between the motoneurons and internuclear neurons in the VI Nerve nucleus? The block diagrams provided suggest possible architectures from which working models of various subsystems

can be made. Their redundancy and specificity of function should allow demonstration of a wide range of behavior with minimal adjustment.

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