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PRINCIPLES OF EYE-HEAD COORDINATION

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Abstract

To explore the visible world, humans and other animals rapidly shift their line of sight to potential targets. These voluntary movements are executed by the eyes either alone, in which case they are called *saccades*, or in coordination with the head in which case they are called *gaze shifts*. Both of these movements serve the same goal reliably, accurately and fast while displaying highly stereotypical metrics and kinematics during movement execution. The strategy and mechanisms that are employed by the nervous system when planning gaze shifts are gleaned from two computational models that were formulated in this thesis and address the phenomenon of eye-head coordination at two different levels of abstraction.The first model used optimal control theory to discover the crucial variables and constraints that are important during motor planning of gaze shifts. This model accounts for the stereotypy that is observed in the psychophysics of head-fixed saccades and head-free gaze shifts. Results from these simulations suggest that the organization principle that guides these movements exploits a balance between effort and movement duration, thus implying that extraocular muscle tension and energy dissipation due to inertial effects of the head and movement duration are parameters that are collectively taken into consideration and minimized at the neural level. The second computational model simulates the neural circuitry that generates eye-head gaze shifts. The goal of these neural network simulations is to model the relevant neural processes starting from the spatial representation of the target (a neural map found in the superior colliculus) and ending with the set of requisite neuromuscular commands that drive the eyes and head. A control-theoretic systems approach is used to explore the computational repertory of the connectivity established by the model units and to explore if it generates results consistent with the experimental data obtained from neurophysiology, electrical stimulations, neuroanatomy, neurology and psychophysics. We conclude that minimum-effort is the movement organization principle of eye-head coordination which is implemented by the brain using a crosstalk mechanism between independently controlled head and eye motor pattern generators.

Περίληψη

Κατά την παρατήρηση του περιβάλλοντα κόσμου, άνθρωποι και άλλα έμβια όντα μετατοπίζουν το βλέμμα τους προς περιοχές ενδιαφέροντος στο οπτικό πεδίο τους. Αυτές οι εκούσιες κινήσεις εκτελούνται είτε μόνο με τα μάτια είτε σε συνδυασμό με το κεφάλι, και ονομάζονται ʹσακκαδικέςʹ και ʹμετατοπίσεις του βλέμματοςʹ αντίστοιχα. Και οι δύο αυτές εκούσιες κίνησης εξυπηρετούν τον ίδιο σκοπό αξιόπιστα, με ακρίβεια και ταχύτατα, παρουσιάζοντας στερεότυπα κινηματικά και μετρικά χαρακτηριστικά κατά την εκτέλεση της κίνησης. Η παρούσα διατριβή διαπραγματεύεται δύο υπολογιστικά μοντέλα που συμβάλλουν στην κατανόηση των αρχών και των μηχανισμών που χρησιμοποιεί το κεντρικό νευρικό σύστημα για το προγραμματισμό και την εκτέλεση των συντεταγμένων κινήσεων του οφθαλμού και του κεφαλιού. Το πρώτο από τα δύο μοντέλα βασίζεται στην θεωρία βέλτιστου ελέγχου για τον εντοπισμό των σημαντικών μεταβλητών και των περιορισμών που αξιοποιούνται κατά το σχεδιασμό αυτών των κινήσεων, με τρόπο τέτοιο που να εξηγεί τα στερεότυπα χαρακτηριστικά που παρατηρούνται στην ψυχοφυσική των σακκαδικών κινήσεων και των μετατοπίσεων του βλέμματος. Τα αποτελέσματα των εξομοιώσεων των υπολογιστικών μοντέλων προσδιόρισαν την αρχή λειτουργίας των κινήσεων αυτών, η οποία συνδυάζει ελάχιστη ʹπροσπάθειαʹ με ελάχιστη συνολική διάρκεια κίνησης. Γνώμονα αυτού αποτελεί η ελαχιστοποίηση τριών παραμέτρων: της εξοφθάλμιας μυϊκής τάσης, της έκλυσης ενέργειας που προκαλείται από τις αδρανειακές επιδράσεις των κινήσεων του κεφαλιού καθώς και του χρόνου διάρκειας της κίνησης. Το δεύτερο υπολογιστικό μοντέλο που βασίζεται στην θεωρία ελέγχου δυναμικών συστημάτων έχει σκοπό την εξομοίωση των νευρωνικών κυκλωμάτων που ευθύνονται για την παραγωγή των εντολών των μετατοπίσεων του βλέμματος, από το ανώτερο επίπεδο της χωρικής αντιπροσώπευσης του στόχου (που στον εγκέφαλο βρίσκεται στο άνω διδύμιο) μέχρι και τις νευρομυϊκές εντολές που τροφοδοτούν τον οφθαλμό και το κεφάλι. Το μοντέλο αυτό εξερευνά την υπολογιστική ευλογοφάνεια των υποθετικών συνδεσμολογιών του μοντέλου και παράγει αποτελέσματα τα οποία έρχονται σε συμφωνία με πειραματικά δεδομένα από νευροφυσιολογία, ηλεκτρικούς ερεθισμούς, νευρανατομία, νευρολογία και ψυχοφυσική. Συμπερασματικά, παρατηρήσαμε ότι οι συντεταγμένες κινήσεις του οφθαλμού και του κεφαλιού υπακούν στην αρχή της ελάχιστης προσπάθειας και επιπρόσθετα ότι υλοποιείται από τον εγκέφαλο χρησιμοποιώντας έναν μηχανισμό ανασταλτικής επικοινωνίας μεταξύ των γεννητριών κινητικών προτύπων του κεφαλιού και σακκαδικών κινήσεων των οφθαλμών.

Acknowledgments

Organization of this thesis

This thesis is organized into five chapters. Chapter 1 discusses the main concepts and theories that are encountered in the neural control and motor coordination literature. The next two chapters (2 & 3) are structured in such a way as to provide readers with the background needed to comprehend the stand-alone sections (2.4 & 3.4). These are essentially modified versions of the articles that are sent for publication and both consist of introductory, methodological subsections along with results and discussion. Chapter 2 introduces a theoretical framework based on optimal control theory that is used to study eye-head coordination. It describes how movements can be expressed in terms of optimality criteria and provides the mathematical tools that are required to understanding our model derivation for eye-head gaze shifts in section 2.4. Chapter 3 introduces the basic concepts of modeling neural systems. It analyzes the main components of the neural circuitry invoked by our gaze control model and discusses the main issues that are necessary for understanding the neural control of saccades and eye-head gaze shifts. Chapter 4 bridges the two modeling approaches that were presented in chapters 2 & 3 and then concludes this thesis with some final remarks. Finally, chapter 5 presents complementary work that was accomplished as part of the research work conducted for this thesis.

Contents

Chapter 1

Introduction

The ability to move is the essence of being alive. Biological movement is planned, coordinated and executed through the interaction between brain and body. A central goal in neuroscience is to explain how this is accomplished by the nervous system. Despite a century of research, understanding the neural basis of voluntary motor behavior still remains a challenge.

1.1 Neural Control of Biological Movement

Motor systems can execute skillful tasks automatically with ease and without the need to consciously decide the joint motions or the detailed sequence of muscle contractions. In an attempt to reduce the complex sequence of neural processes that deal with this problem, we can divide motor processes into three general categories: the process of deciding to act, the process of planning the act and the process of implementing the act (Kandel et al. 2000). Decision making processes that concern voluntary movements usually take place in higher brain centers, such as the motor and premotor cortex, where neural activity encodes information regarding the representation of the motor intent, which is shaped by the continuous flow of visual, somatosensory and postural information about the environment and self-position (Kandel et al. 2000). Once a decision is reached, commands are sent to downstream motor centres where neural processes take place to determine the specific muscle synergies that will carry out the task by converting aspects of the programmed movement, such as its desired amplitude and direction, into signals that coordinate and control the mechanical action of the muscles. Motor control ensures that purposive movement is sufficiently monitored to influence the system in a desired way and to ensure it reaches the desired goal. One of the long-standing questions is how the nervous system successfully coordinates and controls goal-directed tasks.

While tasks are specified in an abstract manner, motor systems must eventually work at a detailed level, specifying muscle activations that lead to accurate joint rotations which, in turn, will take the

body segment through a desired path. Motor control investigates the neural processes that are responsible for movement planning and movement execution (Bernstein 1967). A motor system acts by sending premotor commands to motoneurons that directly innervate muscle fibers causing them to contract thus generating force to enable the active rotations of joints and the acceleration/deceleration of body segments. However, making a movement is more than just sending motor commands. The brain also needs to decide if and how it will respond to sensory feedback during the movement. Servo strategies have traditionally inspired ideas aiming to account for the neuromuscular interactions responsible for the neural control of movements (Wiener 1965). For example, feed forward systems were adopted as candidate neural controllers in which sensory feedback from actual limb movement is ignored during displacement (Houk and Rymer 1981, Miall and Wolpert 1996). Even though these systems have the potential to provide perfect performance when they are equipped with perfect internal models of the mechanical plants that allow them to translate commands into desired states (Kawato 1999), they lack the ability to deal with unpredictable disturbances or perturbations thus compromising stability and accuracy. Since no biological system can be both perfectly accurate and perfectly free of external disturbances, error correction is usually necessary. This led to the formulation of controllers relying on closed-loop configurations and utilizing feedback loops to adjust incoming information during movement (Houk and Rymer 1981). The disadvantage of feedback circuitry is that no matter how high the feedback gains are, they can not account for the accuracy of fast movements and they tend to suffer from instabilities, largely due to the delays of feedback signals (Miall et al. 1993). This generated the idea that the nervous system might be evaluating the state of the system with the use of efferent copy signals [1] incorporated into local loops, thus enabling the system to deal with the delay issues encountered with reafferent input (Kawato 1999, Miall and Wolpert 1996). This raises the issue of hierarchy and the flow of information in the neural system. One idea would be to send movement plans through a large communication loop via the cortex. However, this was later reconsidered when central pattern generators were discovered in the spinal cord that controlled repetitive and reflexive movements, thus bypassing central brain circuitry (Kandel et al. 2000, Ijspeert 2008, Grillner 2006). Voluntary and skilled movements are usually associated with higher levels of motor intent, meaning that more information is necessary and must be integrated in order to shape motor commands. The problem is to determine what information is

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[1] The notion of an efference copy in the nervous systems dates back to the middle of the 19th century, where Hermann von Helmholtz suggested that the brain used these as specific motor commands controlling the eye muscles to determine the location of an object relative to the head.

used when and where and to discover the neural structures housing feedback loops. These challenges and ideas have shaped our understanding of how movements are monitored and controlled by the brain. For example, Bernstein's work has been an important source of inspiration for the study of complex and coordinated movements. One of his arguments was that our central nervous system is capable of processing many aspects in parallel due to the relatively autonomous 'storeys' in our brain which were created during evolution. Accordingly, each newly developed 'storey' took control over the phylogenetically older 'storey' and gave rise to a new and richer class of movements (Bernstein 1967). In fact, Bernstein's viewpoint has its roots in Sherrington's concept that movements result from combinations of low-level reflexes [2]. More recently, these 'reflexes' or 'storeys' have been commonly referred to as 'motor primitives' and represent the simpler elements or building blocks at different levels in the motor hierarchy. Therefore, several different movements can be derived from a limited number of these primitives through appropriate operations and transformations (e.g. by regulating the gain of the motor primitive or by scaling the amplitude and duration of basic movement patterns in task-dependent ways) and can be combined to form more complex actions (Grillner 2006, Flash and Hochner 2005, Mussa-Ivaldi and Solla 2004, Mussa-Ivaldi and Bizzi 2000).

Even though it is imperative to fully understand the control of single-segment movements, the traditionally focus of attention of motor physiologists, such movements fail to address the complexity of the control and coordination needed in multijoint movements (Bernstein 1967, Flash and Hogan 1985). Most animals, including humans, are gifted with bodies that posses several more degrees of freedom than are needed to carry out any particular task (Bernstein 1967). The ability to accomplish tasks reliably, rapidly, and gracefully relies, firstly, on the apparent redundancy of the musculoskeletal system that is engaged in the movement and, secondly, on the neural sophistication of the coordination strategies. So, it is reasonable to claim that motor planning in fact aims at solving the degrees of freedom problem, i.e. to identify one of infinitely many possible movements that will satisfy the desired goal (Jordan and Wolpert 1999, Todorov 2004). Attempts to explain the fact that coordinated movements, rhythmic and voluntary, display a wide variety of invariant features in their movement details has led to the postulation of several theories regarding the motor planning and kinematic redundancy of such movements. One way to deal with the problem of coordination

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[2]As a result of his intensive research and pioneering work on the mammalian central nervous system, Nobel laureate Charles S. Sherrington wrote his findings in the book titled 'The integrative action of the nervous system' published by the *Yale University Press* in 1906. At the time, his conception of motor behavior was based on the notion of the reflex. He states in p. 8 of the 1967 reprint : 'The main secret of nervous co-ordination lies evidently in the compounding of reflexes'.
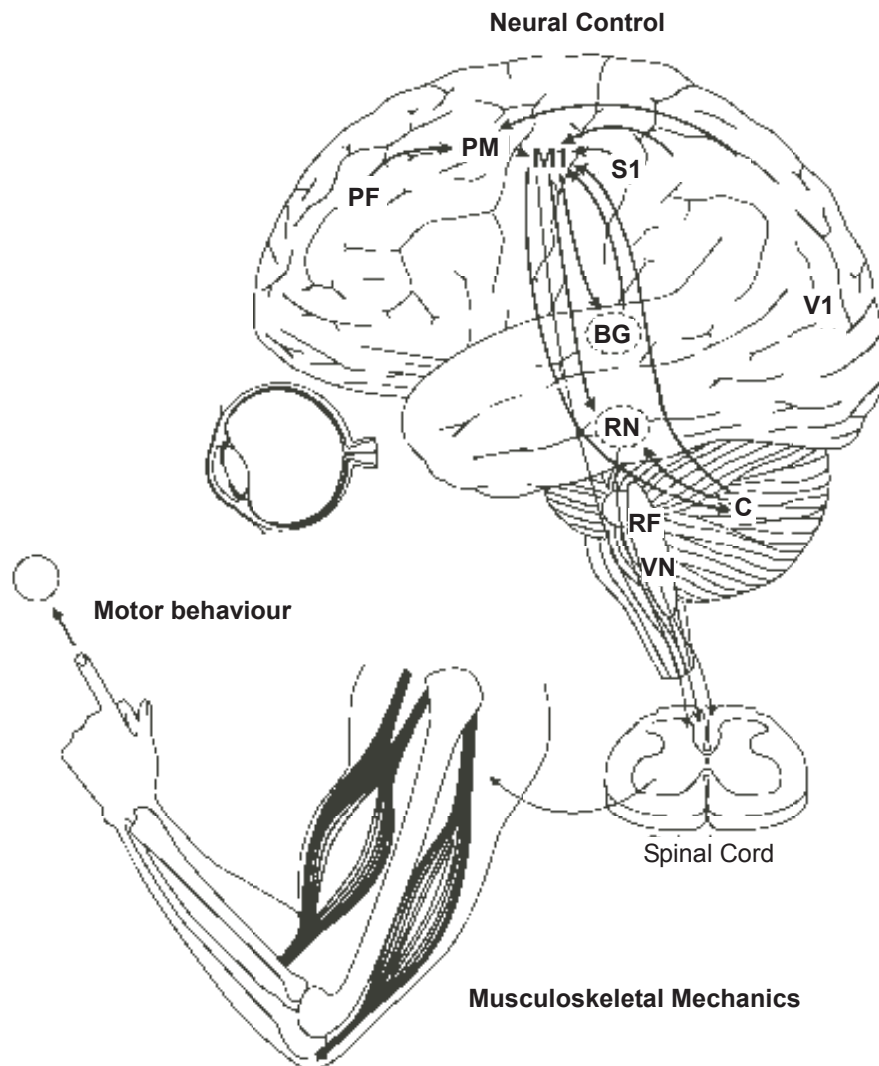
Neural Control

Figure 1.1: *Motor behaviour describes how our body moves during a motor task and is a product of the interaction between the brain and the musculoskeletal system. The central nervous systems issues the motor commands that produce the appropriate muscle activity that controls the mechanical components of the motor system. For simplicity, the brain can be classified into three levels of hierarchical organization: the spinal cord, the brainstem and the cortex. The spinal cord is the lowest in the hierarchy and is known to process peripheral sensory information from the skin, joints, and muscles of the limbs and trunk and to control movement of the limbs and the trunk. The brainstem is the lower part of the brain, adjoining and structurally continuous with the spinal cord. It contains regions such as the reticular formation (RF) and vestibular nuclei (VN) which are responsible for the control of eye and head movements, while providing modulatory information for downstream neural processes that deal with reflex and locomotor pattern generation in the spinal cord. The highest level of control is provided by the cerebral cortex, which supports a large and adaptable motor repertoire and plays a central role in higher cognitive functions such as memory, attention, perceptual awareness, language and consciousness (the prefrontal cortex is engaged in several of these functions; PF). This diagram illustrates some of the key regions that are involved in voluntary movements such as the two areas of the cortex more directly involved in motor planning, referred to as the primary motor cortex (M1) and the premotor cortex (PM). These cortical areas deal with the selection and execution of voluntary movements and directly contact the spinal cord and the brainstem. Sensory information that helps shape voluntary motor commands is available from the visual cortex (e.g. the primary visual cortex; V1) and through the primary somatosensory cortex (S1). Other brain areas that are involved in the motor planning of voluntary movements are subcortical regions, such as the basal ganglia (BG), the red nucleus (RN), and the cerebellum (C). This figure has been adapted from Figure 1 of S. H. Scott (2004), Optimal feedback control and the neural basis of volitional motor control,* Nature Reviews Neuroscience, *Vol. 5, p. 534-546.*

of kinematically redundant segments is using inverse methods. The idea behind an inverse computation is to identify a unique trajectory that will take the end-effector from its initial position to its end position such that there is a unique set of joint angles for each position of the end effector. Biological motor systems are vulnerable to the indeterminacy problem since joint torques can be realised by using an infinite combination of muscle forces (Schenau et al. 1995, Gielen et al. 1995). Even though neural systems inherit this computational risk, the brain still manages to efficiently plan and execute complex movements. Therefore, it is unlikely that such inverse computations take place. Another simple idea is to directly control main kinematic variables. A popular theory that is based on this notion is one that relies on point attractor dynamics and is known as the 'equilibrium point hypothesis' (Feldman 1966, Feldman 1986, Bizzi 1981). This hypothesis was born out of the observation that in a single-joint system, the length-tension properties of antagonist muscles interact to stabilize the limb at a desired joint angle by exploiting the spring-like biomechanical properties of muscles (Houk and Rymer 1981). In this framework, a movement is initiated by setting a stiffness level for the set of muscles that control the joint, i.e. the difference between the current and the desired stiffness level will drive the limb to an equilibrium point. An entire movement trajectory may be formed by shifting this equilibrium point along a virtual trajectory until the end-effector reaches its target (forward computation). While this theory of neuromuscular interaction simplifies motor execution, it remains unclear how appropriate stiffness levels are defined and how they are shifted in time to bring the system to its end-point. Moreover, this hypothesis does not specify how motor planning is accomplished (i.e, how central commands our converted into muscle inputs). Another way to solve the problem of redundancy in coordinated movements is to identify the constraints which reduce the number of degrees of freedom in the motor system (Nelson 1983). It is well accepted that a unique activation pattern is observed for every particular motor act (Bernstein 1967). However, it is not clear which constraints give rise to the unique activation patterns. Consistent with Bernstein viewpoint, behavioural stereotypy is clearly an indication of some kind of internal constraint that eliminates redundancy in a task-dependent way. To deal with this, several approaches employ optimization techniques to minimize some objective function in order to identify the muscle activation patterns that gives rise to the biological redundancy (Nelson 1983). However, this raises the question on whether the brain actually implements the particular criterion for the coordination of muscles. Although several controversial viewpoints do exist within the motor control community, it is generally agreed that the important challenge for understanding motor function is to connect these three levels

of the motor system: motor behavior, musculosketelal mechanics and neural control (Fig. 1.1). It is only when trying to duplicate motor skills with artificial systems that one discovers the complexity associated with the interaction of these levels, which so far, has prevented us from creating robots with a biological-level of movement skills. Using a reduced set of movements, control policies or motor synergies has attracted great interest in modern robotics research (Flash and Hochner 2005), especially to learn from the way organisms are constructed and controlled biologically, and to understand how this leads to complex and adaptive behaviors. The interplay between theories in computational neuroscience for motor control, robotics and artificial intelligence might advance our ability to develop adaptive robotic systems and to draw ideas from engineering disciplines for the understanding of strategies in biological motor control.

1.2   Eye-Head coordination

The control of combined eye and head movements can be considered as one of the simple multi-joint motor systems for the study of coordination. The mechanics of saccadic eye movements are relatively simple when compared to those of limb movements, which use multiple joints and operate with varying loads (Robinson 1981). Extensive research has been conducted for the study of saccades not only for the inherent interest of understanding how they are generated, but also as a simple way to more generally study motor and premotor mechanisms in the brain.

Saccades are used by species whose retinas have a central high-resolution region (the fovea) to explore visual scenes by redirecting their line of sight from one region of interest to another (Yarbus 1967). To enable them to extend shifts of the line of sight beyond the mechanical limits of the eyes and to explore wider regions, saccades are accompanied by rapid head movements and the combination of the two are called *gaze shifts* (Fig. 1.2). The gaze control system consists of three main components: the oculomotor system, which moves the eyes in the orbit, the head motor system, which moves the head by activating the neck muscles, and the vestibulo-ocular reflex, which stabilizes the retinal image by producing counter-rotations of the eye that compensates for the slower ongoing rotation of the head (Bizzi 1981). There is a huge amount of data available on each of these subsystems and allows us to put the pieces of the puzzle together and go a step closer to fully understanding gaze control.

This thesis is devoted to the computational study of the motor control of coordinated horizontal
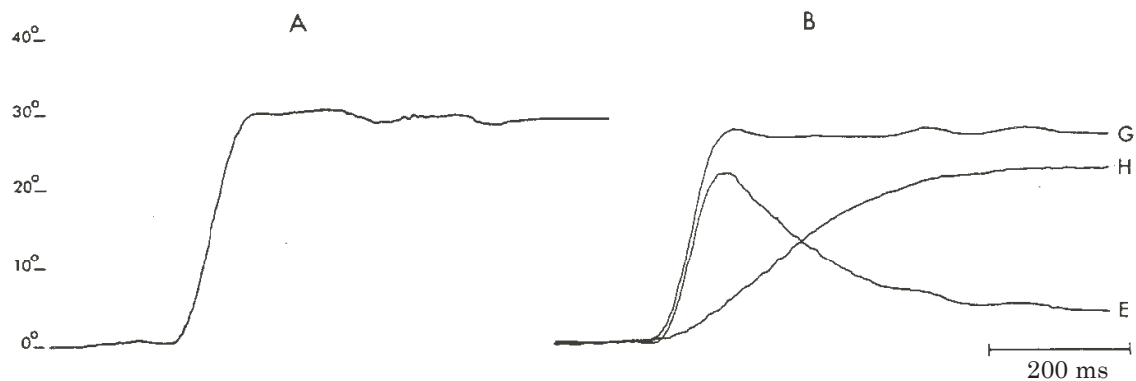
Figure 1.2: *Typical horizontal gaze shifts executed by a monkey to a visual target appearing $30°$ to the right of the fixation point. A: Eye saccade with the head-restrained. B: Gaze shift to the same target with the head free to move. Eye (E) and head (H) trajectories are shown along with the total gaze movement (G). Once the target is reached the eyes counter-rotate in their orbit to compensate for the ongoing head movement due to the operation of the vestibulo-ocular reflex. This figure has been taken from E.Bizzi (1981), Eye-head coordination, in V. B. Brooks (ed.), Handbook of Physiology., Vol. 3, American Physiological Society, Bethesda, MD, pp. 1321-1336.*

eye-head gaze shifts. Two sets of models of eye-head coordination have been formulated that address two different levels of abstraction. The first of the two modelling techniques adopts a phenomenological approach to offer insight into the crucial variables and constraints that are important during planning of gaze shifts. Optimal control theory is used to discover the organization principles that guide the generation of gaze shifts by specifying the underlying neural motor commands that are required to account for the stereotypy that is observed in the psychophysics of these movements (Chapter 2). The second of the two approaches models the neural circuitry that generates eye-head gaze shifts. The goal of these neural network simulations is to model the neural processes that take place downstream of the spatial representation of the motor goal all the way to the set of neuromuscular commands that drive the eyes and head. A control-theoretic systems approach is used to explore the computational power of the connectivity established by the model units and examine if is consistent with experimental data known from neurophysiology, electrical stimulations, neuroanatomy, neurology and psychophysics (Chapter 3). Finally, some concluding remarks on the convergence of the two modeling approaches are pointed out in the remaining section (Chapter 4). We show that the neural control model provides ideas about the neural mechanisms that could implement the principles elucidated through the optimal control approach, while the optimal control model provides an intuitive feeling about the principles that may be served by the neural circuitry that underlies eye-head coordination.

Chapter 2

Optimality in Eye-Head Coordination

2.1 Modeling Optimal Motor Behavior

Theoretically, almost any task can be achieved in infinitely many different ways. Despite this flexibility though, behavioural studies of coordinated movements reveal that most motor systems accomplish their tasks in a highly stereotyped manner on different repetitions of a task and when different individuals execute the same task. Why would the brain select a certain movement pattern rather than another? This stereotypy is a product of motor evolution and motor learning and is a strong indication that the brain exploits some sort of advantage when doing so. Motor planning can be, thus, considered as a computational process of selecting a single pattern of behavior from several alternatives. By assuming optimality, we are able to select the 'best' pattern that will satisfy the task in question by ranking different patterns according to a specific criterion. Optimization theory provides the tools to carry out such a selection by defining a 'cost function' or 'performance criterion' (Bryson and Ho 1969). This process is implemented by expressing a movement that obeys a particular motor plan in terms of a mathematical measure. An optimal movement would then be one that minimizes this chosen measure. By adopting this rationale, it is possible to translate any high level planning process into motor synergies without explicitly specifying the joint rotations and kinematics that are necessary for carrying out the task (Wolpert and Ghahramani 2000).

The challenge is to identify and quantify the physical parameters and constraints that are relevant to a skilled voluntary movement. To do so, we take advantage of the fact that all movements occur in the space-time continuum and involve forces and masses. In principle, any physical system can be modeled by a set of differential equations in time which relate body displacements to torques acting on the mass. The parameters specifying the mechanical features of the system depend on the inertial and viscoelastic properties of the limbs or segments participating in the movement. Once this is

accomplished, constraints affecting the neuromuscular control inputs (i.e. control magnitude limits) or the mechanical limits that may affect the potential movements metrics (i.e. constrained workspace) must be specified in terms of the boundary conditions of the system's differential equations. In addition to these constraints, the key to successful optimal control modelling lies in defining the performance objective(s). These are usually expressed in terms of minimizing some physical measure such as movement time (T), force ($\int_0^T |u(t)|\ dt$), effort ($\int_0^T u^2(t)\ dt$), jerk ($\int_0^T \dot{a}^2(t)\ dt$), etc., where u is the control action (e.g. torque) per unit mass and $\dot{a}$ is the rate of change of acceleration (Nelson 1983). A single criterion is generally insufficient to yield an optimal solution, i.e. one that reproduces realistic biological movement patterns, since it tends to push potential behavior to its limits. So, rather than forcing the system to operate at constraint limits, it is more reasonable to expect that it will operate as a compromise between more than one potential objective (Nelson 1983). In reality, motor systems probably do this by exploiting a combination of several criteria. However, the identification of a predominant cost or trade-off would give us an intuitive understanding of how the brain organizes goal-directed movements. So the challenge in optimal control modeling lies in reverse engineering the criterion(a) solely from the observed behavioural data.

Experimental evidence shows that coordinated eye-head movements to visual targets are characterized by a set of lawful relationships. Horizontal eye-head gaze shifts are stereotypical movements with heavily constrained metrics and kinematics. For example, the duration of head restrained saccades and head unrestrained gaze shifts depends linearly on their amplitude as does their peak velocity, known as the main sequence relationship (Bahill et al. 1975, Tomlinson and Bahra 1986). The slope of the amplitude-duration relationship is about three times steeper for head-free gaze shifts than for head-fixed saccades (Tomlinson and Bahra 1986, Freedman and Sparks 1997b, Freedman 2008, Phillips et al. 1995). Also, head-free eye velocity profiles are symmetric when they accompany small gaze shifts ($< 20°$) but become two-peaked for larger gaze shifts (Tomlinson and Bahra 1986, Freedman and Sparks 1997b, Freedman and Sparks 2000, Tweed et al. 1995, Roy and Cullen 1998), for a review see (Freedman 2008). On the hand, when the head is restrained, saccade velocity profiles display a short acceleration phase followed by a longer deceleration phase if the amplitude of the movement is greater than $20°$; in humans (van Opstal and van Gisbergen 1987, Collewijn et al. 1988) and monkeys (Freedman 2008). Moreover, larger gaze shifts rely on considerable head contributions whereas smaller ones are accomplished essentially by the eyes alone. Furthermore, the eyes do not contribute more than $30° - 35°$ to larger gaze shifts

(Freedman and Sparks 1997b, Stahl 1999, Volle and Guitton 1993). Finally, eye and head contributions to gaze shifts depend on initial eye position in the orbit (Freedman and Sparks 1997b, Volle and Guitton 1993).

Do these patterns reveal anything about the rules underlying the organization of saccades and combined eye-head gaze shifts? Why do the eyes saturate at $30°$ during large gaze shifts when they can rotate up to their mechanical limit at $45°$? If the eye-head motor system aimed at minimizing movement time (which sounds reasonable since it would minimize the duration of our effective blindness), one would expect the eyes to exploit their full $45° - 50°$ limit of excursion. This might be an indication of some kind of performance trade-off. Moreover, why would the eyes accelerate, then decelerate, then reaccelerate (dual-peak velocity profile) for large gaze shifts? Why would the duration of shifts of the line of sight increase threefold when the head is free to move by comparison to those accomplished by the eyes alone (head-fixed)? Also, why does the position of the eyes at the beginning of the gaze shift modulate the eye and head contributions of constant-amplitude gaze shifts? Assuming that head-fixed eye saccades obey some optimal rule, would it also hold for coordinated eye-head gaze shifts? In this thesis, optimal control theory was used to model the eye-head motor system and to examine which, if any, criteria can predict this large set of psychophysics.

2.2 Background to Optimal Control

Optimal control is based on the calculus of variations and has a very long history of circa 350 years [1]. Consider a dynamic system described by a set of differential equations of the general form, $\dot{x} = f[x(t), u(t), t]$, where $x(t)$ is an n-dimensional state vector determined by $u(t)$, an m-dimensional control vector. $x(t)$ can be interpreted as the value of each state x at time t (usually two states - position, velocity- suffice for each degree of freedom). A movement is then a function $x(t)$ where $t \in [0, T]$ and T is the total duration of the movement. There is an infinite number of such curves, so an optimization process must be set up to choose one of these functions on the basis of a measure of cost. To accomplish this, we define a scalar performance index of the general form is,

$$J = \phi[x(t_f), t_f] + \int_{t_0}^{t_f} L[x(t), u(t), t]\, dt \tag{2.1}$$

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[1] A brief historical survey on the development of the calculus of variations and on optimal control theory can be found in R.W.H. Sargent, Optimal control, *Journal of computational and applied mathematics*, 124 (2000), p. 361-371.

where ϕ is a terminal accuracy constraint and L is often called the 'Lagrangian' and represents aspects of the movement that need to be minimized. t_0 and t_f indicates the the time of the onset and offset of the movement. The optimal control problem is to search for the $u(t)$ that minimizes J. Two fundamental strategies have been developed to confront this problem. The first is with the help of dynamic programming (DP), introduced by Bellman in the United States and the other is using the 'maximal principle' introduced by Pontryagin in the Soviet Union (commonly referred to as Pontryagin's Minimal Principle; PMP). Bellman's optimality principle considers every action $u(t)$ available at the current state x(t), then adds its immediate cost to the optimal value of the resulting next state, and chooses an action for which the sum is minimal. However, this takes on a partial differential form and requires the collection of local information. Optimal values are thus found with the help of dynamic programming that takes on a recursive form by performing backward passes in which every state can be visited after all its succesor states have been visited. While DP is robust in its numerical approximation of the optimal solution, it is also subject to the curse of dimensionality due to its iterative and greedy nature (Todorov 2006). Unlike DP, PMP avoids this problem by deriving expressions involving ordinary differential equations that lead to exactly the same solutions, provided that dynamics are deterministic. PMP employes the 'Hamiltonian' function H by adjoining the system differential equations $\dot{x}$ with L through the Lagrangian multiplier functions $\lambda(t)$ (also called *costate* vectors),

$$H[x(t), u(t), \lambda(t), t] = L[x(t), u(t), t] + \lambda^T(t)f(x(t), u(t), t) \qquad (2.2)$$

This is the function that is minimized with respect to $u(t)$. Instead of computing all possible gradients of δx with respect to δu, PMP uses multiplier functions $\lambda(t)$, $\dot{\lambda}^T = -\dfrac{\partial H}{\partial x}$ that are ordinary differential equations to reach stationary values in H. Extremal solutions are, thus, determined by identifying those values of $u(t)$ which will not cause any variations in δH, i.e. $\dfrac{\partial H}{\partial u} = 0$ for $t_0 \leq t \leq t_f$. In summary, to find a control vector $u(t)$ that yields a stationary value of J, one must simultaneously solve for $\dot{x}$ and $\dot{\lambda}$ by substituting for optimal u^*. Its boundary conditions are calculated in part from $\lambda(t_f) = \dfrac{\partial \phi}{\partial x}$ and from certain initial and final conditions imposed on some of the states of the system. Using PMP, the optimal control problem is reduced to a simple ordinary differential equation in the form of a *two-point boundary-value* problem. Its solution is obtained by solving the system of $2n_x$ ordinary differential equations subject to $2n_x$ boundary conditions. Therefore we can solve this system

with standard boundary-value solvers such as MatLab's 'bvp4c.m'. A more detailed description of the optimal control theory used in this work is provided in Bryson and Ho (1969) [2].

2.3   Optimal Motor Control

Over the past two decades, optimal control theory has proven to be a powerful mathematical tool by providing an elegant computational framework for the study of the neural control of movements. Most optimality models of biological movement that have been formulated assumed deterministic dynamics and imposed their objectives using either kinematic or dynamic variables (Jordan and Wolpert 1999). Kinematic objectives are used to guide trajectory formation by constraining the time course of movement variables such as limb position, velocity, and their higher derivatives, whereas dynamic objectives constrain the neuromuscular input to the system, i.e. applied forces and torques. If predictions are accurate, then the former set of objectives imply that the brain ignores nonkinematic factors in generating behaviour, while the latter imply that consideration is given to dynamic factors when selecting a course of action. For example, the minimum jerk (kinematic) rule proposed by Flash and Hogan (1985) and the minimum torque-change (dynamic) model proposed by Uno et al. (1989) belong to different objective classes but both successfully modeled multijoint arm movements. The strategy that the brain adopts is unclear. However, neural computations involved in producing movement probably take all relevant factors, kinematic and dynamic, into account simultaneously. This raises another issue, namely whether the control policy integrates online sensory feedback thus enabling mid-flight intervention of pre-programmed trajectories or whether it ignores it. Optimal control models that adopt an open-loop approach are used to predict average movement trajectories or muscle activity, whereas most closed-loop models accommodate cases where sensorimotor noise and/or perturbations are present to account for motor variability (Todorov 2004). Several existing models have been formulated along these lines to predict arm movements (Flash and Hogan 1985, Uno et al. 1989), hand and fingertip (Smeets and Brenner 1999) trajectories, grasping (Cole and Abbs 1986) and reaching (Haggard et al. 1995), jaw movements during speech (Nelson 1983), postural movements (Balasubramaniam et al. 2000) and so on. Besides the minimum jerk or minimum torque-change mentioned above, two well known optimal control models that have been proposed as generalizable motor planning principles of the central nervous system are the minimum

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[2]Section 2.4, *'Continuous systems; some state variables specified at a fixed terminal time'* of Chapter 2, *'Optimization problems for dynamic systems'* in Bryson, A. and Ho, Y. (1969) *Applied Optimal Control.* Blaisdell Publishing, Walthman, MA

variance model (Harris and Wolpert 1998) that relies on the existence of signal-dependent noise and the minimum intervention which is proposed as a theory of motor coordination in the context of optimal feedback control (Todorov 2004).

Interestingly enough, no earlier optimal control model has been shown to account for the psychophysics of eye-head coordination. However, two models have been proposed that attempt to predict the stereotypical velocity patterns and amplitude duration relationship of head-fixed saccades. Minimum time (bang-bang control) is one of them (Clark and Stark 1975, Enderle and Wolfe 1987). Even though this sounds very reasonable since it attempts to minimize the duration of ocular shifts, it is unable to reproduce realistic saccade velocity profiles. Another optimal control model that has been proposed is the minimum variance model, which was able to predict saccade psychophysics accurately. This model assumes that the brain chooses movements that minimize the endpoint variance in the presence of signal-dependent noise that increases with the magnitude of the control signal (Harris and Wolpert 1998). However, it has been argued that the oculomotor system contains a small fraction of noise and that inaccuracies with respect to target acquisition arise from errors in sensory processes (van Beers 2007). In our work, we demonstrate that head-fixed saccades are organized according to the minimum effort rule. This rule minimizes the squared sum of the motor commands while commands sent to the eye are scaled, based on eccentricity. By extending this rule to accommodate head motor commands, we were *also* able to account for the psychophysics of combined eye-head gaze shifts (section 2.4 provides a detailed analysis of our results).

Control policies implemented by optimal control methods are also widely-used in robotic applications. However, the complexity associated with learning a control rule is strongly reduced by providing a-priori information about the desired criteria of the controlled movement, which is usually hand-crafted by insights of a human expert. Nevertheless, it would be meaningful to examine whether or not, the 'minimum-effort' rule can generate typical patterns of eye-head movements in robotic anthropomorphic heads (e.g. Maini et al., 2008). One could then retrieve the optimal control signals on the basis of this criterion rather than design and implement a controller to generate primate-like eye-head gaze shifts.

These phenomenological theories shed light on behavioural data in that they indicate constraints and variables that the brain considers crucial during movement planning. However, optimal control modeling restricts itself to the behavioral level of analysis and treats the central nervous system as a black box (Flash et al. 2009). The 'optimal' control laws and motor commands that are obtained

using this method to predict action are mere mathematical functions without any obvious neural underpinning. In the past, efforts to relate optimal motor plans to neurobiological processes met little success. In the next section (Chapter 3), we model the neural mechanisms that give rise to the optimal eye and head commands during gaze shifts.

2.4 Optimal Control of Gaze shifts

This section describes how eye-head coordination is governed by a trade-off between effort and movement time and how this might be neurally implemented by the brain. The report of this section is a revised version of our original manuscript that was submitted and accepted for publication at The Journal of Neuroscience.

Optimal control of gaze shifts

A.A. KARDAMAKIS   A.K. MOSCHOVAKIS

Abstract

To explore the visible world, human beings and other primates often rely on gaze shifts. These are coordinated movements of the eyes and head characterized by stereotypical metrics and kinematics. It is possible to determine the rules that the effectors must obey to execute them rapidly and accurately and the neural commands needed to implement these rules with the help of optimal control theory. In this paper, we demonstrate that head-fixed saccades and head-free gaze shifts obey a simple physical principle, *'the minimum effort rule'*. By direct comparison with existing models of the neural control of gaze shifts, we conclude that the neural circuitry that implements the minimum effort rule is one that uses inhibitory crosstalk between independent eye and head controllers.

1 Introduction

To execute even the simplest action, animals resort to sophisticated neural control that takes into consideration the degrees of freedom and the dynamics of the effectors used to accomplish it. The computational complexity of the processes employed to establish the relevant muscle synergies is often reduced through simplifying brain mechanisms (Bernstein, 1967). Optimal control theory (Todorov, 2004; Wolpert and Ghahramani, 2000) exploits the kinematic and dynamic stereotypes of observed movements to gain insight into these mechanisms. To this end, the performance objective is usually expressed as minimization of a 'cost' function, where 'cost' can include time, force, impulse, energy, jerk, stability, and accuracy (Nelson, 1983). In the past, jerk (Flash and Hogan, 1985), torque change (Uno et al., 1989), and variance in the presence of signal dependent noise (Harris and Wolpert, 1998) are three of the physical measures of 'cost' that have been minimized to elucidate the principles of organization of arm reaching movements, while minimum-time (Clark and Stark, 1975; Enderle and Wolfe, 1987), and minimum-variance (Harris and Wolpert, 1998) have been used to predict the trajectories of rapid eye movements (saccades).

Both the difficulty of a task and the complexity of its neural control increase when two and more effectors must be coordinated. A case in point is the coordination of the eyes and the head during rapid gaze shifts. These are stereotypical movements with severely constrained metrics and kinematics. For example, the duration of head restrained saccades and head unrestrained gaze shifts depends linearly on their amplitude as does their peak velocity (known as the main sequence relationship, e.g., (Bahill et al., 1975; Tomlinson and Bahra, 1986)). Also, head-free eye velocity profiles are symmetric when they accompany small gaze shifts ($< 20°$) but become two-peaked for larger gaze shifts (Tomlinson and Bahra, 1986; Tweed et al., 1995). Moreover, larger gaze shifts rely on considerable head contributions whereas smaller ones are accomplished essentially by the eyes alone while eye and head contributions to gaze shifts depend on initial eye position in the orbit (Freedman and Sparks, 1997; Volle and Guitton, 1993).

The neural control of saccades and gaze shifts has attracted considerable experimental attention and several models have been proposed to account for the considerable body of evidence amassed. In their pioneering 'linear summation hypothesis', Bizzi and co-workers (Bizzi, 1979) proposed that saccades and the vestibulo-ocular reflex sum linearly, such that head contributions to gaze shifts are subtracted from ocular contributions. Alternatively, the brain has been thought to use 'gaze feedback control' (Guitton et al., 1990; Laurutis and Robinson, 1986). This scheme assumes that gaze (eye position in space) is the controlled variable and that a neural controller compares it to instantaneous eye position in space to create an internal representation of gaze-error which simultaneously drives the eyes and the head until the line of sight reaches the target. Finally, more recent models of eye-head gaze shifts (Phillips et al., 1995; Freedman, 2001; Moschovakis et al., 2008), assume the existence of cross-talk between their independent head- and eye-related circuits ('independent eye and head control'). Which of these models, if any, reflects reality remains a matter of debate.

In this paper, we use optimal control methods to understand the functional principles of eye-head gaze shifts. We assumed that eye and head motor commands keep movement duration as short as possible while minimizing the squared sum of the magnitude of the control signals that drive the eye and head plants. This is analogous to a minimum energy dissipation criterion and we refer to it as the minimum-effort principle. This assumption suffices to predict the major kinematic features of rapid horizontal eye-head gaze shifts over a wide range of amplitudes, including: 1) realistic single-peak eye velocity profiles of head-fixed saccades as well as small and centripetal head-free gaze shifts, 2) double-peak eye velocity profiles of large centrifugal gaze shifts, 3) ocular components that do not

exceed $35°$ even for large gaze shifts, 4) initial eye position dependent contributions of the eyes and the head. Minimum effort also provides insight into the interrelation between the duration and amplitude of head-fixed saccades and head-free gaze shifts. To explore possible neural mechanisms that could generate the optimal signals inferred from our model, we compared the commands generated by a 'gaze feedback' model to those of an 'independent eye and head' neural control model. We demonstrate that the latter can generate the commands needed to implement the herein proposed minimal effort rule, while the former cannot.
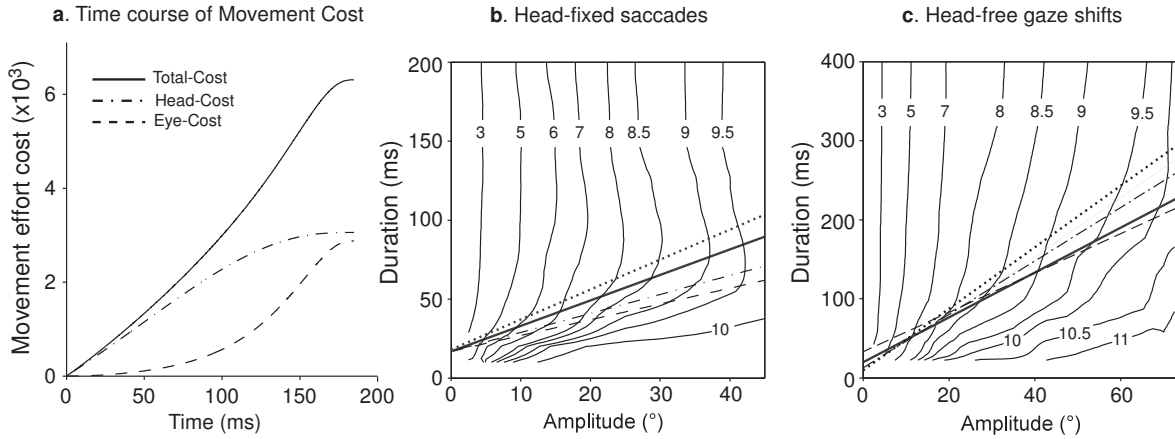

Figure 1: Effort and Movement Duration. a. Time course of effort for a medium-sized ($50°$) gaze shift. Solid line: Combined effort for both eye and head. Dashed line: Effort associated with eye component. Dashed-dot line: Effort associated with head component. Note that the total effort of the movement is the cost value of the combined effort at the end of the movement. b. Iso-effort contours for head-fixed saccades. Abscissa: saccade amplitude, ordinate: saccade duration. Lines indicate the amplitude-duration relationship obtained from: Fuchs et.al. (1967), King et.al. (1986), vanGisbergen et.al (1981) and the one used in our optimal control model (dashed line, stripped line, dashed-dot line and solid line, respectively). c. Iso-effort contours for head-free gaze shifts. Abscissa: amplitude, ordinate: duration. Lines indicate the amplitude-duration relationship obtained from: Tomlinson et al. (1986a), Philips et al. (1995), Freedman et al. (1997) and the one used in our simulations of eye-head gaze shifts. (dashed line, stripped line, dashed-dot line and solid line, respectively). Numbers indicate the total effort required to accomplish the movement (on the log-scale).

2   Methods

We formulated the model as an open-loop optimization one that attempts to recover the best sequence of muscle activations that will minimize a performance criterion. As our performance criterion, we adopted the minimum-effort rule as a two-component cost that depends on both the eye and head control signals. To compute the optimal trajectories of the eyes and the head during head-fixed saccades and head-free gaze shifts, we minimized the time-integral of the square of the eye (u_e) and

head (u_h) control signals (Eq. 1).

$$J = \min \int_{t_0}^{t_f} [a(x_e)u_e^2 + \beta u_h^2] \, dt \tag{1}$$

where $t_f - t_0$ is the movement duration, and a and β are weights that scale the eye and head commands, respectively. The state-varying penalty a acts as a weight parametrizing the eye control signal. It minimizes the forces associated with the eye as it moves into eccentric positions where an increasing amount of effort is required for the agonist extraocular muscle to contract progressively more. The eye weighting function is a differentiable second-order polynomial (of the form: $a = a_0 + a_1 x_e + a_2 x_e^2$) that approximates extraocular muscle tension as a function of eye position (Collins, 1975; Dean, 1996). Because of this term, the eye command that controls the agonist muscle causing the eye to move into eccentric positions are penalised by the state-dependent weight function. Weight β penalizes the head commands and is state invariant because we assume that the inertial forces are more prominent than neck muscle tension for head movements under $40°$. In the case of very large gaze shifts ($> 90°$), neck muscle tension and additional effectors, such as the trunk, may be incorporated into Eq. 1.

Equation 1 assumes that effort represents the control energy that is required to drive the eyes and the head and increases quadratically with the magnitude of the commands sent to these effectors. Rather than relate an optimality criterion with a physical state variable of the system, it is better to associate it with control variables by taking into account the dynamics of the mechanical components of the system (Uno et al., 1989). To account for the mechanical properties of the eye and the head, we used a second-order eye plant with time constants at 150 and 12 ms (van Opstal et al., 1985), and a second-order head plant with time constants at 182 and 105 ms (inferred from data presented in (Bizzi et al., 1978)). This results in a fourth-order state-space model of the gaze control system with two inputs and one output of the form, $d\mathbf{x}/dt = A\mathbf{x} + B\mathbf{u}$ and $y(t) = C\mathbf{x}(t)$ which is stated below:

$$\dot{x}_1 = a_{11}x_1 + a_{12}x_2 + b_1 u_e, \quad \dot{x}_2 = a_{21}x_1,$$
$$\dot{x}_3 = a_{33}x_3 + a_{34}x_4 + b_3 u_h, \quad \dot{x}_4 = a_{43}x_3, \tag{2}$$
$$\text{and} \quad y = c_2 x_2 + c_4 x_4,$$

The two first state-space equations x_1 and x_2 are the states of the eye plant, while the two next ones

x_3 and x_4 express the response of the head plant. The output equation y indicates gaze displacement, where the first term on the right hand side is the eye position with respect to the head (x_e) and the second term is the head position with respect to space (x_h).

Equation 1 does not include terms for online sensory feedback since experimental evidence suggests that the extraocular muscles are not endowed with a myotatic reflex (Guthrie et al., 1983) and vision is too slow to help in the control of saccades (Syka et al., 1979). To obtain the optimal control signals, we use Pontryagin's Minimum Principle (Pontryagin et al., 1962; Bryson and Ho, 1969) to derive analytical expressions for u_e and u_h and solve the problem as a two-point boundary value problem. According to Pontryagin's Maximum Principle, the Hamiltonian function H of the system is in the form of $H(\mathbf{x}, \mathbf{u}, t) = L(\mathbf{x}, \mathbf{u}, t) + \lambda^T(t) f(\mathbf{x}, \mathbf{u}, t)$, where function f is our state-space equation (Eq. 2), and L (the Lagrangian) occupies the integral part of the criterion function in Eq. 1 and λ are the set of lagrangian multipliers (costate vectors) which correspond to each of the states, respectively. In this formulation,

$$
\begin{aligned}
H(\mathbf{x}, \mathbf{u}, t) \quad = \quad & a u_e^2 + \beta u_h^2 + a_{11} x_1 \lambda_1 \\
+ \quad & a_{12} x_2 \lambda_1 + b_1 u_e \lambda_1 + a_{21} x_1 \lambda_2 \\
+ \quad & a_{33} x_3 \lambda_3 + a_{34} x_4 \lambda_3 + b_3 u_h \lambda_3 + a_{43} x_3 \lambda_4
\end{aligned}
\tag{3}
$$

The optimal controls $\mathbf{u}(t)$ can be derived semi-analytically by calculating the impulse response functions $\partial H / \partial \mathbf{u}$ and equating them to zero. This rule of stationarity would then result in the following expressions,

$$
u_e^* = -\frac{b_1 \lambda_1}{2 a(x_e)}, \quad \text{and} \quad u_h^* = -\frac{b_3 \lambda_3}{2\beta}
\tag{4}
$$

The costate differential equations are derived by substituting Eq.4 into the Hamiltonian in Eq.3 and by applying $\dot{\lambda}(t) = -\partial H / \partial \mathbf{x}$,

$$
\begin{aligned}
\dot{\lambda}_1 &= -a_{11} \lambda_1 - a_{21} \lambda_2, \\
\dot{\lambda}_2 &= -a_{12} \lambda_1 - \left(\frac{\partial a(x_e)}{\partial x_e} \cdot \frac{b_1^2 \lambda_1^2}{4 a^2(x_e)} \right), \\
\dot{\lambda}_3 &= -a_{33} \lambda_3 - a_{43} \lambda_4, \quad \text{and} \quad \dot{\lambda}_4 = -a_{34} \lambda_3
\end{aligned}
\tag{5}
$$

Boundary conditions need to be specified for $t = t_0$ and $t = t_f$ in order to fully define the two-point boundary value problem (refer to Fig. 1). Initial boundary conditions are given by path velocity constraints $\mathbf{x} : x_1(t_0) = x_3(t_0) = 0$. This implies that saccades and head movements start simultaneously with the gaze shifts they accompany as is the case in monkeys (Freedman and Sparks, 1997). Final boundary conditions are provided: 1) through $\lambda_f^T = \partial\phi/\partial\mathbf{x}$ (where $\phi = 0.5(y - \Delta G\prime)^2$) which is imposed on the costates λ and lead to the following boundary conditions: $\lambda_2(t_f) = 2c_2(y - \Delta G\prime)$, $\lambda_3(t_f) = 0$, and $\lambda_4(t_f) = 2c_4(y - \Delta G\prime)$, and 2) $x_1(t_f) = 0$, which implies that gaze shifts end together with ocular saccades as is the case in monkeys (Freedman and Sparks, 1997). Together with initial boundary conditions, the latter implies that the duration of gaze shifts equals the duration of the saccades that accompany them as is the case in monkeys (Freedman and Sparks, 1997). After the end of the gaze shift, the head continuous to move but does not alter the direction of the line of sight due to the operation of a fully functional vestibul-ocular reflex (Tomlinson and Bahra, 1986). For this reason, rather than simulate the complete trajectory of the head, we only consider the contribution of its movement until the end of the gaze shift.

Extremal trajectories are generated by simultaneously solving the sets of ordinary differential equations 2 and 5 subject to the boundary conditions with a standard boundary-value solver. Results were obtained by using the two-point boundary value problem solver function bvp4c.m available in MatLab. The following parameters were used in the simulation of the optimal control model (Eq. 1-5): $a_{11} = -90$, $a_{12} = -17.36$, $a_{21} = 32$, $a_{33} = -15$, $a_{34} = -6.54$, $a_{43} = 8$, $b_1 = 4$, $b_3 = 4$, $c_2 = 4.34$, $c_4 = 2.81$, $a_0 = 9.1$, $a_1 = 0.36$, $a_2 = 0.014$ and $\beta = 18$.

3   Results

The generation of saccades and eye-head gaze shifts is governed by an optimal balance between 'effort' and movement duration. We define 'effort' as the time-integral of the squared sum of the motor commands driving the relevant plants (see Eq. 1 in Methods) that represents the control energy required to efficiently displace an effector from one point in space to another. This movement effort cost is plotted as a function of time in Fig. 1a (solid) for a medium-sized ($50°$ in amplitude) centrifugal gaze shift. As shown here, the effort needed to execute the ocular component of such a gaze shift (dashed) grows parabolically as the eye moves into more eccentric locations and extraocular muscle tension increases quadratically (Collins, 1975; Dean, 1996). On the other hand, the initial part of the curve describing the cost of the head component (dash-dots) is linear and grows to an asymptote
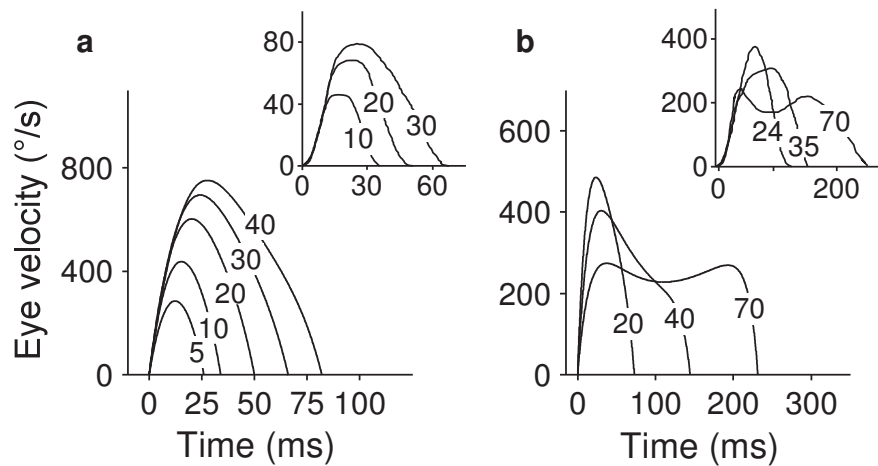
Figure 2: Eye velocity profiles. a: Time course of head-fixed eye velocity for saccades ranging from $5 - 40°$. b: Eye velocity profiles of head unrestrained gaze shifts of 20, 40, and 70° starting with the eyes centered in their orbit. c: Eye velocity profiles for two gaze shifts of the same size (40°) with the eye starting from positions 20° to the left (20L) and 10° to the right (10R) of straight ahead.

towards the end of the gaze shift as it enters into its deceleration phase.

To understand the interrelation between, movement duration, amplitude and effort these three quantities are simultaneously displayed as iso-effort contour plots for head-fixed eye saccades in Fig. 1b. Each contour line represents a constant level of effort for different combinations of amplitude and duration. For every movement amplitude, effort becomes almost movement size invariant beyond a critical duration, coincident with the inflection points of the iso-effort contours shown in Fig. 1b. Further decrease in duration beyond this critical value requires additional effort that increases exponentially in inverse proportion to duration. One would thus expect the amplitude-duration relationship of primate saccades not to venture far from these inflection points. An amplitude-duration relationship shallower than this would describe saccades that last less but at the cost of additional effort while a steeper one would characterize low-effort saccades that take a long time to complete. The amplitude-duration relationship of experimental subjects often passes through or very near these optimal points. For example, such a relationship (1.2 ms/deg, Fig. 1b, dashed-dots) is obeyed by the two monkeys of van Gisbergen et al. (van Gisbergen et al., 1981) and one of the monkeys (#1) of King et al. (King et al., 1986). Yet, the amplitude-duration relationships can differ a lot between subjects. Slopes as high as 1.9 ms/deg (Fig. 1b, stripped) were obtained from monkey #2 of King et al. (King et al., 1986) while slopes as low as 1 ms/deg (Fig. 1b, dashes) were found by Fuchs et al. (Fuchs, 1967). However, even in these somewhat extreme cases relationships experimentally

determined from monkeys do not depart much from the herein determined optimal one. To simulate optimal head-fixed saccades, a value of 1.6 ms/deg (Fig. 1b solid line) is used, which leaves the amplitude-duration relationship comfortably within the range of experimentally determined ones.
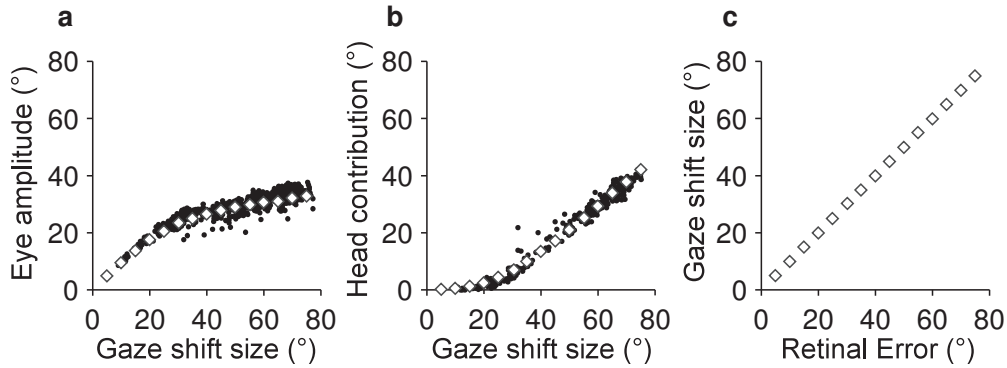

Figure 3: Metrics of gaze shifts with the eyes and the head facing straight ahead. Eye amplitude (a) and head contribution (b) as a function of gaze amplitude for gaze shifts ranging from 5 to 75°. c: Amplitude of head-unrestrained gaze shifts as a function of retinal error.

Similarly, Fig. 1c displays the iso-effort contours for head-free gaze shifts. Their inflection points are not as easily discernible and span a bigger region than those of the iso-effort contour plots of saccades and effort becomes invariant at much higher duration values. Experimentally determined gaze amplitude-duration relationships also intersect the iso-effort contours when the latter become size invariant. The dashed line of Fig. 1c illustrates a case in point documented by Tomlinson et al. (Tomlinson and Bahra, 1986) and characterized by a slope of 2.4 ms/deg. Other published gaze amplitude-duration relationships are even steeper. For example, a slope equal to 3.4 ms/deg (Fig. 1c, dashed-dot) was found in monkey *T* by Freedman et al. (Freedman and Sparks, 1997) and a slope equal to 3.7 ms/deg (Fig. 1c, stripped) was obtained from monkey (*RO*) by Philips et al. (Phillips et al., 1995). A value of 2.85 ms/deg (Fig 1c, solid line) is used to simulate optimal eye-head gaze shifts.

If the minimum effort principle holds, it should simultaneously apply to both saccade and gaze shift kinematics. To explore if this is the case, we first simulated a series of head-fixed saccades. Figure 2a shows the velocity profiles of five saccades ranging from 5° to 40° which obey the amplitude-duration relationship that follows the solid line of Fig. 1b. The velocity profiles of saccades smaller than 20° are symmetrical while larger saccades exhibit a short acceleration phase followed by a longer deceleration phase. Consistent with experimental observations in monkeys and humans (van Opstal and van Gisbergen, 1987), the skewness of the velocity profiles increases with movement size. Also consistent with experimental observations (Collewijn et al., 1988), the peak values reached by our

optimal velocity profiles display a soft saturation. Rather than having to explicitly constrain a model in order to reproduce them, several qualitative features of saccadic velocity profiles thus emerge from the application of the minimum effort rule.

After showing that the minimum effort rule provides an accurate account of saccade kinematics we explored if it also captures the main features of eye-head gaze shifts. To this end, we simulated a series of horizontal gaze shifts with amplitudes ranging from $5°$ to $75°$ and obeying an amplitude-duration relationship such as the one shown in Fig. 1c. No constraints were imposed on the sizes of the individual eye and head components of the gaze shifts. Instead their sum is constrained to equal retinal error ($\Delta G\prime$) for all gaze shifts spanning the entire range that was simulated (Fig. 3c). Figure 3b shows the relation between the size of the simulated gaze shift and the amplitude of the contribution of the head. As in experimental subjects (Freedman and Sparks, 1997; Stahl, 1999), small ($15-20°$) simulated gaze shifts are accomplished by the eyes virtually alone and the contribution of the head remains negligible (Fig. 3b). The contribution the eyes does not exceed $30-35°$ even for large gaze shifts. Beyond this point the head starts contributing progressively more (Fig. 3a). It should be pointed out that both the saturation of the ocular contribution for large gaze shifts and the negligible contribution of the head for small gaze shifts are not due to the imposition of additional constraints such as saturating and threshold nonlinearities but are instead emergent properties of the minimum effort principle.

The assumption that it underlies eye-head coordination also allowed us to reproduce the eye velocity profiles of gaze shifts widely ranging in size. Figure 2b shows three examples, the smallest one from a $20°$ movement, a medium-sized one from a $40°$ movement and the largest one from a $70°$ gaze shift. As the size of the gaze shift increases, peak velocity decreases and duration increases. Furthermore, the shape of the velocity profiles changes. It is almost symmetrical for the small one, skewed in the case of the medium-sized one, and dual-peaked for the biggest of the three. It would thus appear as if the eye must accelerate, subsequently decelerate and then reaccelerate whenever head-free gaze shifts are large enough, i.e. when they are accompanied by large head movements. Indeed, such twin peak eye velocity profiles have been documented by (Freedman and Sparks, 1997; Tweed et al., 1995; Roy and Cullen, 1998) for head-free gaze shifts of monkeys accompanied by large head contributions. To obtain these velocity profiles, we used the amplitude-duration relationship shown as solid line in Fig. 1c, as a boundary condition in the cost function we minimized. Use of a shallower amplitude-duration relationship (for example, one that lies below the slope obtained by

Tomlinson et al. (Tomlinson and Bahra, 1986) in Fig. 1c) leads to movements of shorter duration that are also characterized by the disappearance of the second peak in their velocity profiles.

The simulated movements we examined so far were assumed to start from straight ahead initial position of the eyes. Changing this initial condition allowed us to explore the interaction between eye and head contributions to gaze shifts. These are known to depend on the position of the eyes in the orbit at the onset of the gaze shift (Freedman and Sparks, 1997). To investigate the origins of this phenomenon, three gaze shift sizes, $30°$, $50°$ and $70°$ were simulated (Fig 4) while initial eye position varied between $30°$ to the left and $15°$ to the right of straight ahead. Although this was not imposed on our optimal control model through the adoption of any additional constraints, as shown in Fig. 4b, the size of the ocular contributions to the gaze shift is inversely correlated to initial eye position. To generate constant amplitude gaze shifts (Fig. 4c), the head contribution must exhibit the opposite relation (Fig. 4b), i.e. a positive slope with respect to initial eye position. A second emergent property of the minimum effort rule associated with position sensitivity of gaze shifts is the fact that the larger the size of the gaze shift the steeper the regression slope (Freedman and Sparks, 1997). Also consistent with experimental results, Fig. 9 of (Phillips et al., 1995), the shape of the eye velocity profile depends on the initial eye position. This is shown in Fig. 2c, which illustrates two examples, both from a $50°$ gaze shift, one of which started while the eyes were $20°$ to the left and the second when the eyes were $10°$ to the right of straight ahead. As shown here, centripetal gaze shifts (those starting from contralateral positions and passing through the midline) reach higher peak velocities than centrifugal ones.

4 Discussion

We used optimal control theory to disclose a principle of organization of eye-head gaze shifts, the minimum effort rule. Iso-effort contours reveal that the optimal performance of head-fixed saccades and head-free gaze shifts take advantage of a balance between effort and time. Every muscular system is subject to fatigue when used continuously and this is particularly true of the ocular muscles of primates and humans which are known to shift their gaze more than 10^5 times a day (Bahill and Stark, 1975). Once fatigued, saccades become slower with lower peak velocities that violate the main sequence relationship (Bahill and Stark, 1975). To reduce the risk of fatigue, the saccadic system could limit its operation to between 5 and 9.5 on the effort scale (Fig. 1), thus avoiding the use of excessive forces. This could be accomplished by increasing movement duration. However,
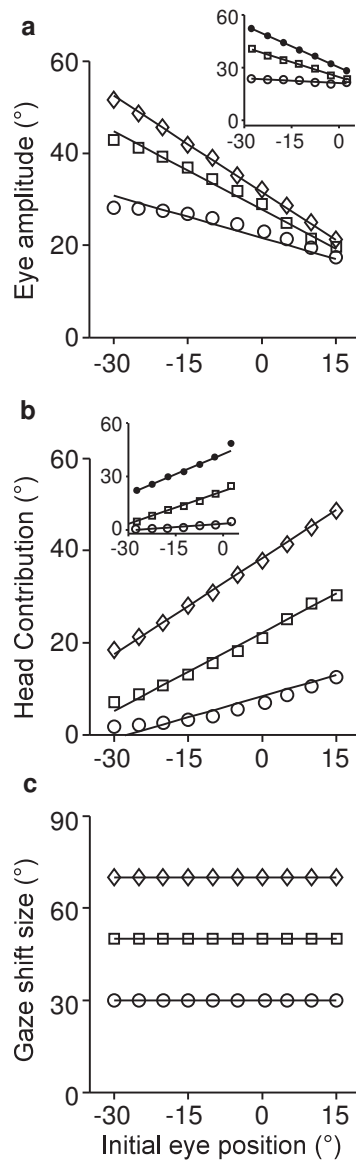
Figure 4: Metrics of gaze shifts with the eyes starting from different initial positions. Size of head (a) and eye (b) contributions to rightward head-free gaze shifts (c) of constant amplitudes equal to 30° (open circles), 50° (open squares) and 70° (dots), as a function of initial eye position (abscissa). Negative values indicate leftward initial eye positions. Data were fit with least-squares regression lines the slopes of which were the following: (a) 30°: -0.3; 50°: -0.5; 70°: -0.7 and (b) 30°: 0.3; 50°: 0.5; 70°: 0.7.

movements of the eyes compromise vision and thus their duration should preferably be kept to a minimum. One would thus intuitively expect optimal gaze shifts from the trade-off between effort and movement duration. As suggested before, extraocular muscles and the neurons that control them are endowed Ôwith one or more safety factors, which ensure accurate and consistent performance regardless of the demands placed on them' (Fuchs and Binder, 1983). Movement duration could be one such safety factor. In turn, eye and head contributions to gaze shifts are constrained by a trade-

28

off between the forces associated with the high inertia of head and the viscoelastic forces associated with rapid eye movements. Such a trade-off is reached at a point determined from the two weights (a and β) in the equation that describes the functionality of the system (Eq. 1) and penalize the size of the motor command sent to the eye (a) and to the head (β). Evidently one could generalize this argument to encompass additional effectors, such as the trunk and the lower body.

An inspection of optimal eye and gaze trajectories demonstrates their similarity to those executed by animals. Firstly, the velocity profiles of small head-fixed saccades ($< 20°$) are symmetrical while those of bigger movements are skewed with short acceleration and longer deceleration phases (Fig. 2) as in humans (van Opstal and van Gisbergen, 1987; Collewijn et al., 1988). Also, consistent with experimental observations (Freedman and Sparks, 1997; Stahl, 1999), smaller simulated gaze shifts ($< 20°$) are not accompanied by head movements and ocular components do not exceed $30 - 35°$ even for large ($40 - 90°$) gaze shifts (Fig. 3). Moreover, as in natural movements (Freedman and Sparks, 1997), the eye velocity profiles of relatively small gaze shifts ($< 15°$) are unimodal and rather symmetrical while larger ones are characterized by lower peak values and two-humped velocity profiles. Furthermore, the size of the contributions of the eye and the head depend on the initial orbital position of the eyes. The head contributes progressively less (and the eyes more) to gaze shifts of the same size as initial eye position is directed contralaterally to the impending gaze shift. The opposite is true when the eyes are directed ipsilaterally. The eye position dependence increases with the size of the gaze shift (Freedman and Sparks, 1997; Volle and Guitton, 1993). Comparison of Fig. 4 of this report to Fig. 15 of Freedman and Sparks (1997) demonstrates that our model reproduces quite well the overall features of this effect as determined experimentally for gaze shifts of 30, 50 and $70°$. For example, the slopes of the regression lines relating head amplitude to initial eye position increased from 0.3 to 0.7 as the size of the simulated gaze shift increased from 30 to $70°$. The same is true for the relationship between ocular contributions and initial eye position; for example, the slope (-0.7) we obtained for large gaze shifts ($70°$) lies in between the values determined experimentally (-0.43 and -0.85) in two monkeys executing $70°$ gaze shifts (Freedman and Sparks, 1997). Finally, comparison of Fig. 2c of this report to Fig. 9 of Philips (1995) demonstrates that, as in monkeys, the peak values and the velocity profiles of the ocular components of gaze shifts also depend of the initial position of the eyes.

Inspection of the optimal eye-head motor commands provides some insight into the signals driving the eyes and the head. Figure 5a illustrates the dynamic portion of the control signals leading to

head-free gaze shifts of three different sizes starting from straight ahead. These motor commands are velocity-dependent and compensate for inertial effects, and consistent with the separation principle (Guigon et al., 2007) they can be optimized independently from the static components reflected in the tonic activity compensating for gravitational and elastic restoring forces. The commands sent to the eye are tightly linked to eye velocity due to the fact that the eye is virtually inertia-less and is dominated by viscous elements. On the other hand, the head is dominated by its high inertial component and thus the agonist commands sent to it are tightly linked to the acceleration phase of its movement (Zangemeister et al., 1981). This is followed by antagonist commands applied by the opposing muscle to decelerate the head movement (Hannaford et al., 1986). For a certain amount of effort, the size of head contributions to gaze shifts increases when their acceleration phase coincides with the movement of the eye. This is due to the fact that signals conveyed to antagonist neck muscles (by convention these are considered to have a negative sign) induce the expenditure of effort (due to the quadratic form of the minimum effort performance criterion) and decelerate the head rather than assist agonist muscles in pushing it further in the same direction. Thus the present model provides an intuitive explanation for the fact that the duration of the ocular component of gaze shifts coincides with the acceleration phase of their head components (Guitton et al., 1990).

As shown in Fig. 5a, the signal controlling the head need not reach its peak value together with the signal controlling the eye. As the amplitude and duration of signals controlling the head increase, the shape of the eye commands change from single-peaked to two-humped profiles. Due to its rapid responsiveness, the velocity of the eyes can follow much faster control signals and distinct peaks can occur near the beginning and towards the end of large gaze shifts. On the other hand the head is a slower plant and slower signals suffice to drive it through realistic trajectories. The command signals sent to it display a single peak which often occurs approximately halfway through the activation of the agonist muscle. The aforementioned details concerning the waveforms of the optimal signals driving the eye and the head apply to gaze shifts of all sizes and emerge from the minimum effort rule.

What alternative optimality principles could govern gaze shifts? It has been argued that saccades are programmed such that their duration is kept to a minimum (Clark and Stark, 1975; Enderle and Wolfe, 1987). Assuming that the saccadic system is linear, the minimum-time requirement implies that it uses 'bang-bang' control, i.e., that its output is at its maximum force limits (positive or negative) over the entire movement. As argued before (Harris and Wolpert, 1998), adoption of the minimum time rule does not lead to realistic saccade velocity profiles. Moreover, minimizing
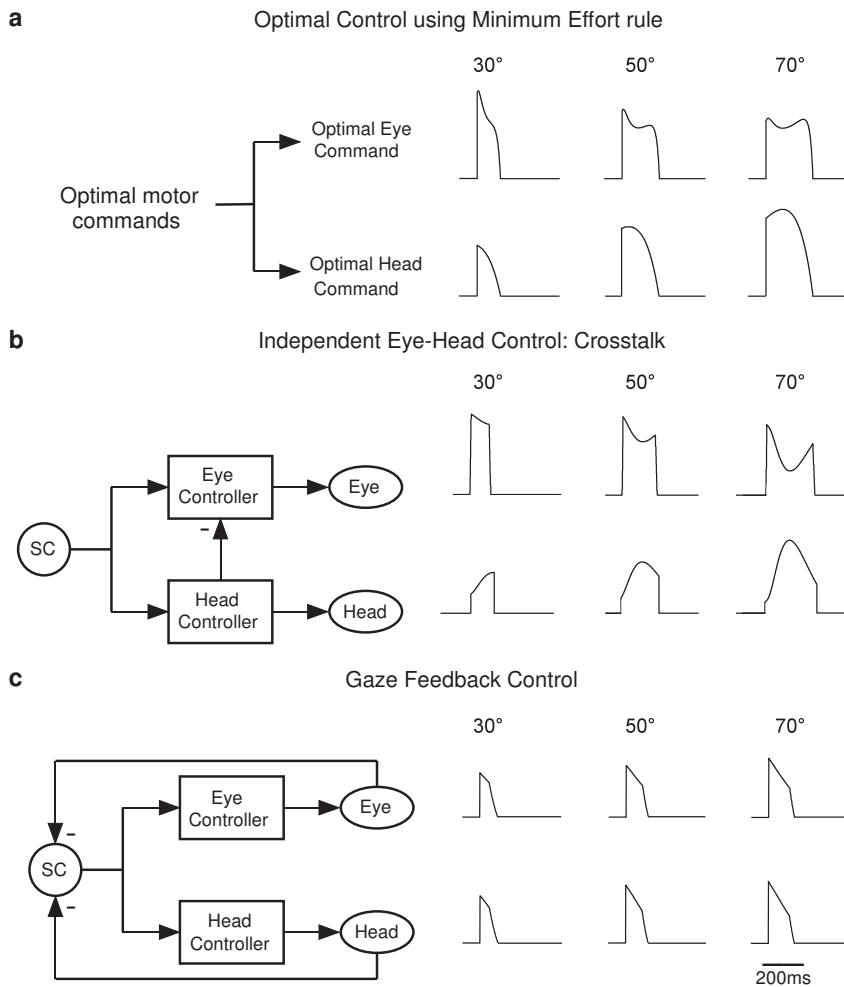
Figure 5: Motor commands controlling gaze shifts (ΔG) of 30, 50 and $70°$. (a) Signals derived from the minimum effort rule. (b) Left: Schematic illustrating the major building blocks of a neural model that assumes independent eye and head control and inhibitory crosstalk between the head related and eye related neural circuitry (Phillips et al., 1995; Freedman, 2001; Moschovakis et al., 2008). Right: The eye and head commands it generates for the gaze shifts illustrated in (a). (c) Schematic (left) illustrating the major building blocks of a neural model that assumes gaze feedback driving both the eye and head controllers (Guitton et al., 1990) and the control signals it generates (right). Negative signs next to the arrowheads indicate inhibitory connections. All other connections are excitatory. The VOR has been ignored due to its negligible role during the quick phases of gaze shifts. Both neural models (b) and (c) have been implemented in Simulink of the MatLab environment. Time bar (200ms) applies to all waveforms. The amplitude of the motoneuronal eye and head units (measured in sp/s) vary because of differences among the gains of their corresponding eye and head plants.

movement time leads one to expect larger contributions from the faster of the two effectors (the eyes) during coordinated eye-head gaze shifts. In fact, ocular contributions are smaller than expected from the oculomotor range since the eyes are known to reach eccentricities not exceeding $30-35°$ even when monkeys execute large eye-head gaze shifts and even though their oculomotor range is $45-50°$. Minimum jerk (rate of change of acceleration) or torque change models have been proposed

for arm movements, but are unlikely to provide the underlying principle of saccades and eye-head gaze shifts because they fail to account for important kinematic features of eye movements such as their skewed and dual peak velocity profiles (Harris and Wolpert, 1998). Finally, minimum variance in the presence of signal-dependent noise has been invoked to account for saccade trajectories (Harris and Wolpert, 1998). This is also unlikely since the signal dependent noise present in oculomotor commands accounts for only a small fraction of the variability of saccades (van Beers, 2007) nor can this principle account for the eye position dependence of ocular and head contributions to gaze shifts.

Our optimal control model describes eye-head coordination at the computational level and need not be relevant to the premotor circuits responsible for saccades and gaze shifts. The principles of operation of the system gleaned from such models are independent of brain structures and neural processes. It is however meaningful to ask what neural circuitry could generate motor commands consistent with those derived from the minimum effort rule. To answer this question, optimal control approaches must be supplemented with models of the neural control of gaze shifts that rely on systems theory to link neurophysiology (and neuroanatomy) to psychophysics (and neurology since the lesion of model units can be readily simulated).

Control systems theoretic approaches have been widely used to model the information flow and signal transformations in premotor circuitry controlling saccades and gaze shifts (Moschovakis et al., 1996). Models of the neural control of gaze shifts can be classified into two categories: a) gaze feedback control and b) independent eye and head control. These two classes of models differ in the control strategy they employ to accurately shift the line of sight. Gaze feedback models (Fig. 5c) are extensions of the eye position saccadic controller (van Gisbergen et al., 1981) and assume that desired gaze position is compared to current gaze position so that the resulting gaze-position-error signal drives both the eyes and the head (Guitton et al., 1990; Guitton and Volle, 1987; Laurutis and Robinson, 1986). In contrast, independent eye and head control models (Fig. 5b) assume that the SC command is decomposed into separate eye and head components driving their respective plants, independently. These models use an inhibitory interaction between the head portion and the eye portion of their circuitry, mediated by the VOR (Bizzi, 1979; Whittington et al., 1984) or an efference copy of the head command (Phillips et al., 1995; Freedman, 2001; Moschovakis et al., 2008).

To examine which gaze control model generates commands best resembling those inferred from

the present study, we simulated Freedman's (Freedman, 2001) as representative of the independent control models and Guitton's (Guitton et al., 1990) as representative of gaze feedback control models. For both of these models, there are parameter specifications allowing their numerical simulation. The right hand side of Figs. 5b and 5c, shows the phasic component of the commands sent to the eye (top rows) and the agonist neck muscle (bottom rows) obtained from the independent control (Fig. 5b) and gaze feedback model (Fig. 5c), respectively, for a 30, 50 and $70°$ gaze shift. As movement amplitude increases, the duration of the commands sent to the ocular plant of the independent control model increases and their shape displays a second peak (Fig. 5b) as do the waveforms produced by the minimum effort principle (Fig. 5a, top row). This is not the case for the signals produced by the gaze feedback model (Fig. 5c). Both eye and head signals appear to have a stereotypical waveform that is scaled in amplitude and in duration as a function of movement amplitude and there is no resemblance between these signals and the optimal eye and head controls in Fig. 5a.

We demonstrated that the minimum effort rule is an important design principle of eye-head motor coordination and that the central nervous system could implement it as an inhibitory crosstalk between independent eye and head controllers. Such an independent control strategy can generate motoneuronal discharges that match commands inferred from our optimal control model. While, this does not allow us to determine which of the independent control models is implemented in the brain, it provides good reasons to think that the eyes and the head are independently controlled during gaze shifts. Results from our optimal control and neural systems modeling converge towards a unified framework of eye-head motor coordination. We anticipate that the integration of optimal control and system identification of neural processes will prove decisive in efforts to understand the neural control of action.

5 Acknowledgements

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Chapter 3

Neural Control Modeling of Gaze Shfits

Brains process signals. Neural circuitry carries out specialized processes that deal with the analysis of sensory data, memory storage, the control of movements, etc, and is often located in distinct regions throughout the brain depending on the nature of the process. If we are to understand how the brain is able to accomplish all of these complicated tasks, we must understand the architecture of the brain itself and its underlying computations. Even though there are micro-scale and macro-scale levels of organization within the brain, i.e. from ions and molecules through synapses and neurons all the way up to local circuits and entire neural networks, knowledge of the connections between neurons and the signals they carry is the only way to thoroughly comprehend how a process is carried out by the central nervous system [1]. With this in mind, one is accustomed to think of brain function in terms of circuits and systems.

3.1 Background for Modeling Neural Systems

In a systems framework, theoreticians are tempted to use tools originating in mathematics and engineering, such as information theory and control theory, to analyze and interpret the computations that are executed by neural systems. A key concept in systems theory is the notion of an *operator* and of a *transfer function*. Examples of operations include addition, subtraction, multiplication, division, integration and differentiation, while transfer functions are mathematical representations of the dynamic relation between the input and the output of a system (Oppenheim et al. 1996). Any system can be viewed as a set of processes that operate upon input signals to transform them into output signals. Consequently, any physical process can be represented by an entire sequence of such

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[1]I quote the last two sentences from Lord E.D Adrian's Nobel Lecture in 1932 to emphasize the necessity for a system's view of the brain. '... Within the central nervous system the events in each unit are not so important. We are more concerned with the inter-actions of large numbers, and our problem is to find the way in which such interactions can take place.' From *Nobel Lectures*, Physiology or Medicine 1922-1941, Elsevier Publishing Company, Amsterdam, 1965.

elementary mathematical operations. Neural computations are no exception, and can potentially be represented by a complex combination and conjunction of simplified operations in the form of a mathematical model.

A model consists of a set of hypotheses that aim to describe how a system actually functions. Expressing models in mathematical terms may offer precise *and* concise knowledge and should yield important predictions on the performance of a system. Models can be formulated as single complex operations in the form of an equation (or set of equations) or they can be formulated as block diagrams that pictorially represent an entire sequence of mathematical operations (Houk and Rymer 1981). The former type of models use detailed equations to capture the important features of a system and are important since they encourage abstract thinking about a system, while block diagrams give graphical representations of mathematical models by demonstrating the explicit flow of information within the system. Entire networks can be built along these lines, which consist of several units and connections, where each unit represents a nerve cell and carries some kind of information. Connections communicate information from unit to unit and are characterised by a synaptic weight (or gain) which expresses how strongly the one is connected to the other. [2] The challenge here is to identify and set the parameters of such a network so that it matches those of the circuit it purports to simulate.

A great deal is known about the biophysical mechanisms responsible for generating neuronal activity, which provide the basis for constructing neuron models. Such models range from highly detailed descriptions involving thousands of coupled differential equations to oversimplified descriptions that are useful for studying large networks (Dayan and Abbott 2001). In fact, the most direct way to simulate neural networks is to connect model spiking neurons that generate and propagate action potentials to other interconnected units by simulating their biophysical mechanisms, e.g. membrane potentials, ion concentrations, conductances, propagations delays and synaptic transmissions (Dayan and Abbott 2001, Gerstner and Kistler 2002). This approach increases the realism in a neural simulation thus facilitating its comparison with electrophysiology (e.g., with raster scans or even neuron traces), but it suffers from the disadvantage of relying on large numbers of assumptions and from the need to do complex parameter tuning as well as the need to spend long periods of time for simulation and analysis (Dayan and Abbott 2001). On the other hand, firing rate models

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[2]*Note:* The goal of simulated neural networks are to model 'real' neural networks that are implemented by the brain and fundamentally differ from 'artificial neural networks' which are trained by means of a learning algorithm in order to minimize some sort of cost function (Robinson 1992).

limit their description of neurons to the average rate of action potentials they emit instead of directly computing membrane potentials as is the case for spiking neurons. Firing rate models tend to have smaller numbers of free tuning parameters than spiking models do and also tend to avoid the short time scale required to simulate action potentials and thus are much easier to simulate on computers (Dayan and Abbott 2001). In this formulation, interpretation of neural activity is done on the basis of spike averaging over small and finite time intervals and in some cases by averaging over equivalent neurons. Each model unit is described at a time t by a firing rate $v(t)$,

$$\tau \frac{dv_i(t)}{dt} = -v_i(t) + F(g \cdot u) \tag{3.1}$$

where the input from a presynaptic neuron is u, the strength of the connection is determined by gain g and τ is the time constant of the ith unit which determines how quickly the neuron responds to its input. The dot product between g and u indicates that the total input is the sum of input from all external sources. F is often called the activation function and usually takes a nonlinear form, e.g. sigmoid or threshold linear (Dayan and Abbott 2001). In our simulated network, activation is non-negative (half-wave rectified) and usually is not allowed to exceed a maximum discharge rate (saturation). Furthermore, inhibitory and excitatory connections are determined by the positive or negative sign of g. The state of the network is dynamic; it evolves in time and depends on the activation levels (instantaneous firing frequency) of all of the units in the system. To estimate the unit activations of such a neural network as a function of time, a system of nonlinear, coupled differential equations must be solved numerically.

The architecture of neural network models is shaped by information from psychophysical, neurophysiological, neurological and anatomical findings. Psychophysics offers us a documented relationship between stimulus and action by describing the physical quantities and limitations characteristic of a specific behavior, while neurophysiology offers insight into the response properties of neurons that are involved in generating the behaviour. Anatomy yields vital information on the connectivity between neurons. Furthermore, information obtained through neurological disorders and lesions gives us strong hints about the role of particular brain regions as judged from the behaviour deficit it causes. By gathering evidence from all these studies, well-founded models can be created that may hopefully provide an integrative understanding of a neural circuit, and if successful, it may constitute the working hypotheses for further experimentation until the neural circuits are correctly and fully

understood.

3.2   Models of the Saccadic Burst Generator

The purpose of the saccadic system is to reorient the eyes quickly in space. The mechanics of saccadic eye movements are simple compared to other limb movements primarily because the eyeball may be considered as a constant and virtually inertialess load rotating around a fixed point. Moreover, only two muscles are engaged in rotating the eye in any one plane through reciprocal innervation, in a push-pull manner. Even though more complex models exist, the eyeball can at its simplest be modelled as a first-order plant with a time constant of 160ms (Robinson 1981). To drive this plant, a pulse of innervation is required to overcome the viscous drag of the orbital tissue and move the eye at a high speed. The pulse gradually declines to a final step of innervation that produces a sustained change in muscle tension that compensates for the elastic properties of the plant. In the oculomotor literature, this sequence of signals is widely referred to as the 'pulse-step' and it essentially ensures impedance matching between the output of the brain and the mechanical properties of the ocular plant (Robinson 1964). This is what ocular motor neurons (OMN) must discharge rapidly to create a burst of activity (the pulse) and gradually decay to a steady-state and position-related activity of tonic discharge (the step). The fundamental question that now arises is what premotor neural circuitry is needed to generate this requisite command that will ensure saccade execution?.

Numerous brain regions are involved in the generation of saccades from the cortex down to the brainstem (Moschovakis et al. 1996). One of the crucial brain regions causing saccadic eye movements and head movements, is the subcortical nucleus known as the Superior Colliculus (Sparks and Hartwich-Young 1989). The SC is a multi-layered structure and a place of convergence and intergration of information from several brain areas (Moschovakis et al. 1996). Several cortical areas such as the posterior parietal cortex, the frontal eye fields and the supplementary frontal eye fields provide input to the deeper layers of the SC with information encoding the selection of visual targets after being shaped by cognitive processes and by internal attentional states. The deeper layers of this midbrain region contain a topographically organized map where neurons discharge for gaze shifts which are directed to specific locations of the visual field (Robinson 1972). Recordings and electrical stimulations experiments show that neurons in the deeper layers of the rostral SC discharge before movements with small amplitudes, whereas those in the caudal SC discharge before larger move-

ments (Freedman and Sparks 1997a). Neurons in the deeper layers of the SC respond to visual, auditory and somatosensory stimuli (Sparks and Hartwich-Young 1989). They also project to downstream brainstem structures that generate combined eye-head movements. The SC is considered to be a nodal point for the dissemination of desired gaze displacement commands since it is the starting point of the final common pathway of saccade and gaze shift generation (Moschovakis et al. 1996). This midbrain region heavily projects to the saccadic burst generator (SBG) but also activates neck muscles and it is responsible for whole body rotations. Neural circuitry that lies downstream from the SC can therefore be regarded as structures that deal with the *motor planning of gaze shifts*.

Saccadic burst generators lie in the reticular formation (RF) of the brainstem and produce the precise bursts that gets the eye on target by transmission to vertical and horizontal ocular motoneurons (Moschovakis et al. 1996, Sparks 2002, Cohen and Henn 1972). Several types of neurons have been shown to participate in horizontal saccade-related activity (see Fig. 3.1). Omnipause neurons (OPNs) discharge at a relatively constant rate during fixation, but stop firing during saccade execution in all directions (Raybourn and Keller 1977). Other groups of neurons in the SBG include, the long-lead burst neurons (LLBNs) and medium-lead burst neurons (MLBNs) that are subdivided further into excitatory and inhibitory burst neurons (EBNs and IBNs, respectively) (Luschei and Fuchs 1972). BNs generate high-frequency bursts of activity slightly before the onset and throughout the duration of ipsilateral saccades (van Gisbergen et al. 1981). Properties of the neural discharge of these neural populations, such as the number of spikes, the burst duration and the peak firing rate are strongly correlated to movement parameters such as the amplitude, duration and velocity of saccades, undoubtedly suggesting that information encoding in SBG units are saccade-related. It is the excitatory burst neurons that are considered to be the output of the SBG and which issue the precise bursts that encode the eye velocity of the ongoing saccade (Igusa et al. 1980). EBNs project *directly* and *indirectly* to the ocular motoneurons (Fukushima et al. 1992, Moschovakis 1997). The direct path conveys the 'pulse' component required by the OMNs, while the indirect path via the nucleus prepositus hypoglossi (NPH) consists of cells that discharge in relation to horizontal eye position (also known as the 'neural integrator') which provide the excitation that is required for the 'step' portion of motor neuron activity (Kaneko 1997, Sparks 2002, Keller 1974).

Numerous computational models have been formulated for the core circuitry of the neural control of saccades. These intend to reproduce the functional characteristics and connectivity of neurons from the SC to the PPRF and to account for the dynamics of eye movements. It is widely thought
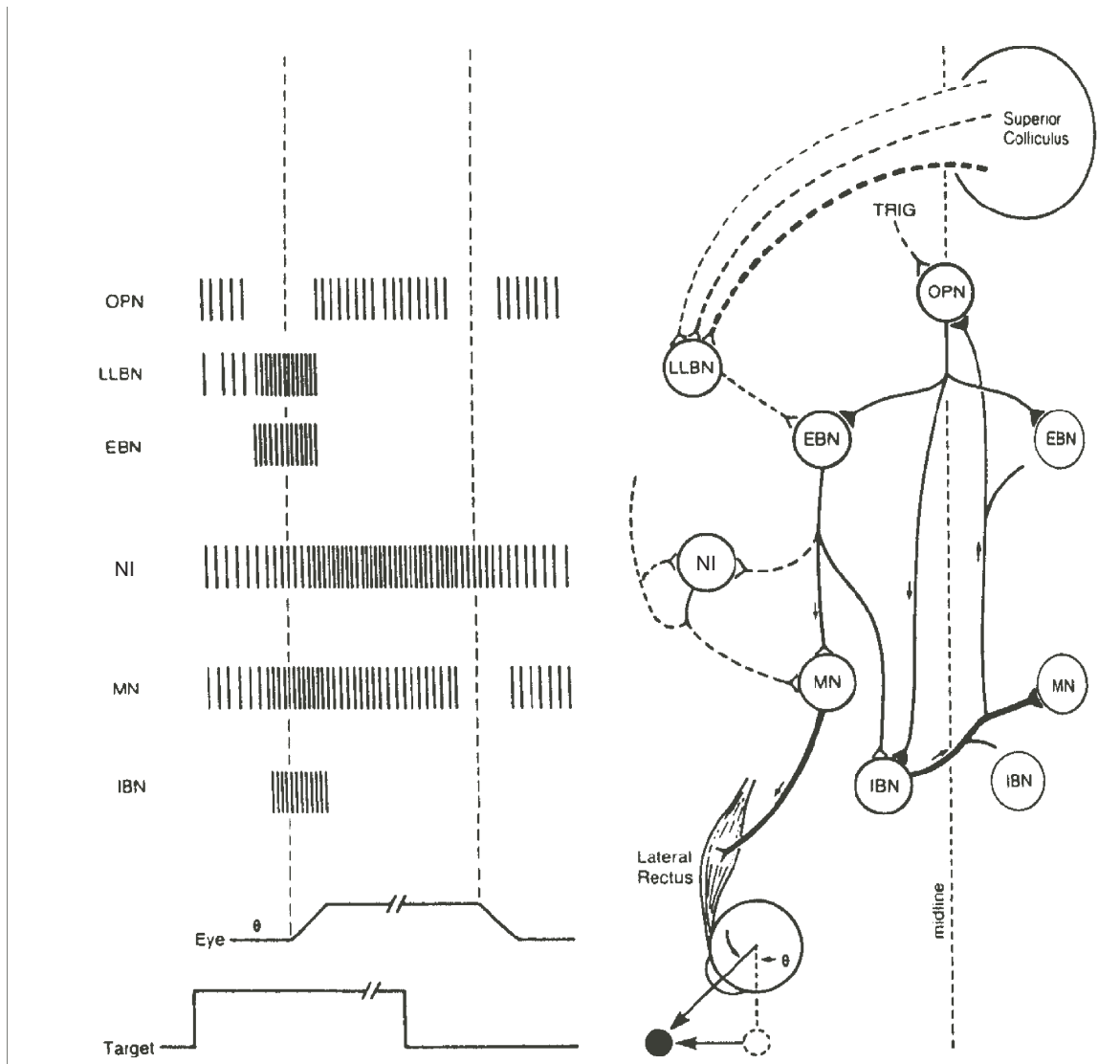
Figure 3.1: *A diagram of the connections of the cell types that are used in models of the horizontal burst generator (Right portion). SC, superior colliculus; LLBN, long-lead burst neuron; EBN, excitatory burst neuron; IBN, inhibitory burst neuron; OPN, omnipause neuron; NI, neural integrator cells in the nucleus prepositus hypoglossi; MN, ocular motoneurons. The SC is the input to the saccadic burst generator and projects to LLBN. It also provides the trigger signal (TRIG) that initiates saccades by inhibiting the OPNs for the duration of the saccade. OPNs inhibit the EBNs and the IBNs, which project to the motor neurons that innervate the agonist and antagonistic muscles, respectively. EBNs also project to the NI which then conveys eye position information to the MN. MNs innervate the lateral rectus extraocular muscle that pulls the eyeball towards its direction by an angle of ∂ (which is determined by the desired motor command issued by the SC). The empty dotted circle at the bottom is indicative of the initial fixation, while the solid circle shows the final destination of the saccade. Arrows illustrate the flow of information within the circuit. Solid and empty triangles accompanied by solid and dotted lines represent inhibitory and excitatory synapses, respectively. The left portion of the figure illustrates the discharge properties of the neurons in the circuitry displayed in the right portion of the figure. Vertical solid lines represent action potentials (or spikes). It can be seen that these neurons display a variety of spiking patterns, i.e. tonic, phasic, and phasic-tonic discharge. The two long dotted vertical lines show the onset and the offset of the saccade. The two bottom traces show the time course of the horizontal eye displacement in response to the appearance of a peripheral visual target at angle ∂ that eventually returns to the initial fixation point (pulse). This figure is a modified version of Fig. 3 in Fuchs, A. F., Kaneko, C. R. S. and Scudder, C. A. Brainstem control of saccadic eye movements. Ann. Rev. Neurosci. 8: 307-337, 1985.*

that the burst generator has the form of a closed loop controller that ensures saccade accuracy. Accordingly, local feedback mechanisms were incorporated in SBG models to understand how precise MLB discharge metrics are generated to guide the eyes to their final destination. Such a controller was originally proposed by Robinson in 1975. His model uses an efference copy of eye position for its feedback which is provided by the output of the neural integrator (note that visual or proprioceptive information are not used as sources of sensory feedback). This proposal has been the source of inspiration for many subsequent models of the brainstem saccadic generator. Models that rely on this eye 'position' information have been referred to as 'position' models and suggest that motor planning of saccades operate in craniocentric coordinates. Later on, Jurgens et. al. (1981) proposed a model whereby the burst generator operates in retinocentric coordinates, i.e. it issues commands indicative of desired eye displacement rather than desired eye position. This concept created a different class of SBG models which are referred to as 'displacement' models and were quickly justified as to their biological plausibility (see Moschovakis et al.; 1996). The introduction of some type of resettable or leaky integrator to the network was necessary to prevent accumulation of residual errors from previously integrated signals in order to ensure saccade accuracy. Models belonging to this class but assuming different neural architectures have been proposed by van Gisbergen et al. (1985), Scudder (1988), Moschovakis (1994), Nichols and Sparks (1995), Quaia and Optican (1997), Breznen and Gnadt (1997) and Gancarz and Grossberg (1998).

The performance of these models has been evaluated from their ability to reproduce a list of properties that are displayed by the saccadic system. For instance, a) generation of saccades belonging to the main sequence (psychophysics) (Bahill et al. 1975), b) eye velocity profiles (psychophysics) (Collewijn et al. 1988, van Opstal and van Gisbergen 1987), c) generation of straight oblique saccades (neurophysiology and psychophysics) (King et al. 1986), d) resumed saccades after interruption by OPN stimuation (neurophysiology) (Keller 1974, King and Fuchs 1977), e) generation of staircase saccades in response to continuous SC stimulation (neurophysiology) (Schiller and Stryker 1972), f) OPN lesion experiments (neurology) (Kaneko 1997) and g) realistic discharge profiles of unit activation functions (neurophysiology: e.g. LLBs; Moschovakis et al. 1988 and Waitzman et al. 1991, MLBs; van Gisbergen et al. 1981 and Moschovakis et al. 1991, OPNs; Strassman et al. 1987). After taking all of these constraints into consideration, it turns out that the 'most complete' model that can account for most of the data is the one proposed by Moschovakis (1994), which is also known as the

MSH model [3].

In brief, the MSH model operates in the following manner. SC activation excites the LLBN and 'latch' units causing 'latch' activity to build up, eventually reaching the point where it inhibits the OPN. Once OPN activity has ceased the inhibition on the RI and MLB units is lifted allowing for a saccade to begin. OPNs are considered to be gating neurons providing WHEN signals that actively suppress the saccadic system during fixation. To execute a saccade, disinhibition of OPNs is required which enables the rest of the circuitry to respond to the SC activation (WHERE signals) that specify the amplitude and the direction of movement. So, when OPNs are silenced, excitation from the LLBN causes EBN bursts which are conveyed to OMNs directly and indirectly via the NI, thus driving the extraocular muscles to produce saccades. Once the inhibitory feedback from the RI has quenched LLBN activity, the EBN activity decays since the excitatory input from the LLBN has been nulled. The latch activity also decays since the excitatory input from the EBN has been removed and so the OPN units reactivate and suppress the saccade system until a new command is issued by the SC. It is assumed that the LLBN and RI form the closed-loop configuration which make up the SBG. Strictly speaking, the MSH BG is a neural oscillator of the form $\frac{s}{s^2 + k^2}$, where k is the gain and s is the Laplacian operator (LLBN and RI are integrating units). Our neural network model of eye-head coordination uses a modified version of this motor pattern generator [4].

3.3   Models of the Gaze Control System

As with saccades, motor planning of gaze shifts starts at the SC where desired gaze displacement commands are issued to downstream premotor circuits controlling eye and head movement. Models for the neural control of gaze shifts are built around a core neural circuitry that generates saccades and are essentially extended versions of models of the saccadic burst generator with two additional components, the head controller and the vestibulocular reflex.

The vestibulo-ocular reflex (VOR) is crucial for gaze control. While the beginning of the gaze shift is tightly coupled to the beginning of the head movement, its end is not (Freedman and Sparks 1997b). To compensate for this ongoing movement of the head after the end of the gaze shift, the eyes counterrotate in their orbit so that gaze is stabilized in space allowing a stable perception of the environment despite ongoing movement of the head (Pelisson and Guillaume 2009). This is caused

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[3]For a full documentation and comparison of SBG models, refer to Benoit and Berthoz, 2008.
[4]For a detailed description of the MSH model, please refer to Moschovakis (1994).

by a VOR gain of unity that regulates eye velocity counterrotation to be equal to the continuing head movement (Tomlinson and Bahra 1986). However, to maximize its efficiency during the rapid reorientation of the line of sight, the gain of the VOR is close to zero, thus enabling the eyes to maximally cooperate with the head movement in shifting gaze (See Fig. 1.2). The vestibular apparatus receives input predominantly from the semicircular canals that detect angular acceleration of the head and signals how fast the head is rotating. For the horizontal canals, type I cells in the vestibular nuclei are excited during ipsilateral head turning both by excitation from ipsilateral canal afferents and by disinhibition from type II inhibitory cells (Robinson 1981). Saccade-related neurons in the vestibular nucleus pause for the duration of the saccade and carry eye position information and are referred to as 'position-vestibular-pause' neurons (McCrea et al. 1987, Tomlinson and Robinson 1984). The signal in the vestibular nucleus is amplified by a gain g and undergoes sign inversion, it becomes an eye velocity command (Robinson 1981). MNs combine the commands they receive from premotor neurons (such as VNs and BNs) and relay them to the eye muscles. Second-order vestibular neurons are gated during saccades and thus vestibular signals can not reach the oculomotor neurons. In reality, the gain of the VOR is close to zero (0.1-0.3) during saccades and close to unity (0.9) at all other times (note that $g = 1$ means perfect compensation). The VOR has been the topic of extensive research and is now a well-known system, rendering its computational modeling straightforward.

Conversely, the neural circuitry that controls the head during gaze shifts remains speculative due to the limited amount of information that is available regarding the discharge patterns and connectivity of head-related neurons. Electromyographic recordings show that neck muscles are activated in a biphasic manner, where an 'action' drives the agonist muscle in the direction of the gaze shift and is then followed by a 'brake' pulse that activates the antagonist muscle to quickly decelerate the head and bring the movement to an end (Hannaford et al. 1986, Ramos and Stark 1987). The pathway containing all relay stations between the output of the SC and the neck muscles is assumed to be part of the head controller. As a first approximation, the head related circuitry can be thought to operate as a simple differentiator that transforms the bell-shaped burst of neural activity transmitted from the SC into a biphasic signal, the two phases of which undergo separate amplification, and ensures impedance matching to the dynamics of the head plant. Moreover, the head is usually modelled as a second-order linear plant (time constants at 182 and 105 ms; inferred from Bizzi et al. 1978) that accounts for its viscoelastic and inertial elements which means the head controller must create a torque signal that will overcome these mechanical effects by accelerating and

decelerating the head in an realistic way. Hypothetically speaking, the head controller could adopt a closed-loop configuration (e.g. like a burst generator) regulating movement duration, amplitude and velocity as needs to be. However, due to lack of evidence, models of the gaze system adopt as simple a head controller as possible (e.g., the open loop throughput device we used) and ignore cortical control (to account for the higher volitional components associated with head movements) while only considering the direct involvement of the SC in generating movements of the head. However, models of the head controller usually incorporate a muscle stretch-reflex as a local loop to operate during external perturbations (Freedman 2001).

The neural network simulations of our gaze control model use a modified version of the MSH saccadic burst generator, a head controller in the form of a differentiator, and a straightforward model for the vestibul-ocular reflex. Even though several assumptions are required in order to construct these three individual components and put them together in a gaze control model, the focus of most computational models in this area are to identify the control strategy that the gaze system employs to accurately shift the line of sight. Two controversial views on the nature of the neural control of eye-head gaze shifts have led to extensive debate between two alternative positions on the subject: a) gaze feedback control and b) independent eye and head control. In brief, the first class of models assumes that desired gaze position is compared to current gaze position to estimate gaze position error, a signal that drives both the eye and head motor systems. In contrast, the second group of models assumes that a desired gaze displacement command is subsequently decomposed into separate eye and head commands that drive their respective motor systems independently. To ensure gaze shift accuracy, models belonging to class b) usually assume some type of downstream interaction between the eye and head controllers. Models belonging to class a) have been proposed by Laurutis and Robinson (1986), by Tomlinson (1990) and by Guitton et. al. (1990), whereas models using an independent eye and head control scheme were proposed in the pioneering work of Bizzi (1978), and later by Phillips et. al. (1995), Freedman (2001), Moschovakis et al. (2008) and by Kardamakis et. al. (pending revision; see Section 3.4 for manuscript details). Interestingly enough, a few of these neurophysiologic models have also been implemented to examine the effectiveness of achieving an appropriate control scheme for the generation of artificial eye-head gaze shifts on a robotic anthropomorphic head (Maini et al. 2008).

As with the case of models of the saccadic system, the performance of gaze control models should be evaluated on the basis of their ability to reproduce a list of properties that are displayed during
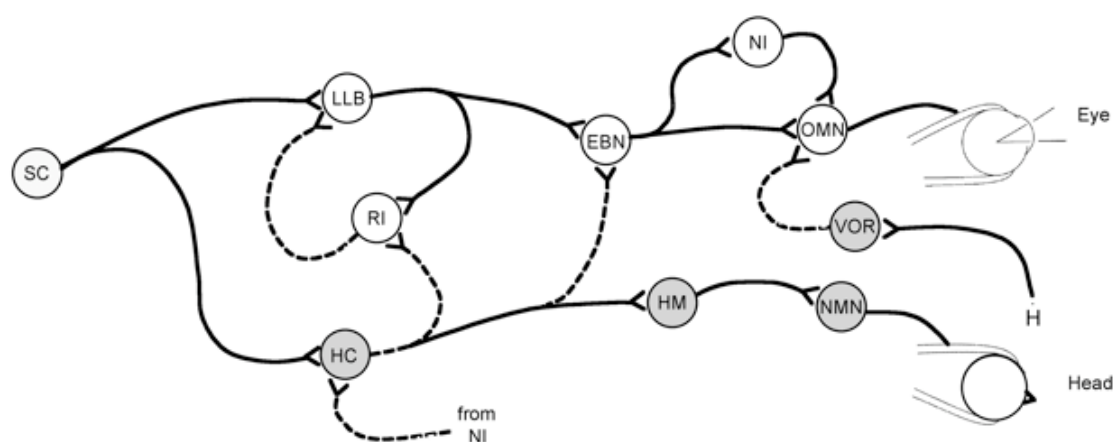
Figure 3.2: *This diagram shows the crucial connections between the head and eye motor pattern generators that are assumed by our neural network model of eye and head gaze shifts. SC, superior colliculus; LLB, long-lead burst unit; EBN, excitatory burst neuron; IBN, inhibitory burst neuron; NI, neural integrator cells; RI, resettable integrator; OMN, ocular motoneurons; NMN, neck motor neurons; HC, head motor command, HM, head mover; VOR, vestibulo-ocular reflex. The scope of this figure is to make clear the points of interaction between the head-related and eye-related circuitry and therefore other units that were mentioned in Fig. 3.1 (such as IBNs and OPNs) were excluded from the present diagram to avoid clutter. The LLB-RI cross-coupling is a neural oscillator that generates bursts when disinhibited by the OPNs during saccade generation. The HC-RI connection modulates the duration of the LLB burst, thus directly controlling the duration of the eye-head gaze shift and the HC-EBN inhibitory connection controls the amplitude and velocity of the eye. The last two connections are often referred to as the 'crosstalk'. Our models also assumes that initial eye position modulates the head motor commands through the NI-HC connection. The VOR is the last source of interaction between the head and eye motor system and relies on head velocity information which is made available by the vestibular sensory organs, namely, the semi-circular canals (not shown here). Note that the dashed lines indicate inhibitory connection. Grey-filled circles represent head-related units, while empty circles represent eye-related units (expect for the SC unit which is gaze-related). Units from only one hemisphere are shown.*

gaze shifts. Some of the issues involve: a) Identical gaze shift precision with the head fixed and the head free for targets within and beyond the oculomotor range (Bizzi 1981, Freedman and Sparks 1997b, Guitton and Volle 1987), b) peak eye and gaze velocity reduction for gaze shifts larger than $30°$ (Freedman and Sparks 1997b, Freedman 2008), c) two-peaked eye velocity profiles when the gaze shift is above $30°$ (Freedman and Sparks 1997b, Freedman and Sparks 2000, Tweed et al. 1995, Tomlinson and Bahra 1986), d) slope of the amplitude-duration relationship steeper for head-free gaze shifts than for head fixed saccades (Phillips et al. 1995, Freedman and Sparks 1997b, Tomlinson and Bahra 1986), e) slope of the amplitude-duration relationship invariant with respect to the starting position of the eyes (Freedman and Sparks 1997b), f) eye position saturation for larger gaze shift amplitude ($< 30 - 40°$) (Freedman and Sparks 1997b, Guitton et al. 1990), g) negligible size of head contribution to small amplitude gaze shifts (Stahl 1999, Freedman and Sparks 1997b), h) eye amplitude and head contribution depend on initial eye position (Becker and Jurgens 1992, Volle and

Guitton 1993, Freedman and Sparks 1997b), i) eye position sensitivity of saccades evoked in response to electrical stimulation of the Superior Colliculus (Segraves and Goldberg 1992, Azuma et al. 1996), and j) certain counterintuitive properties of gaze-related and eye-related burst neurons (Whittington et al. 1984, Tomlinson and Bance 1992, Sylvestre and Cullen 2006, Cullen and Guitton 1997). Additional behavioural observations that gaze control models may wish to account for are: 1) the so-called 'eye position plateaus', when instead of counter-rolling after the end a saccade the eyes remain stationary in the orbit and gaze is carried by the head (Phillips et al. 1995), 2) multi-saccadic gaze shifts, where a sequence of saccades separated by small periods of steady fixation accompany a head movement (e.g. Fig. 8B of Tomlinson86a), and 3) head perturbation experiments in which head motion is suddenly braked during a gaze shift (Pare and Guitton 1998). These last three points will be addressed in the near future by an extended version of our gaze control model.

3.4   Neural network simulations of gaze shifts

As mentioned previously, our gaze control model assumes independent control in that its SC commands are disseminated to the saccadic burst generator and to the head controller with different gains, and makes no use of signals to estimate a gaze error signal feedback, i.e. SC is outside the gaze control loop. Furthermore, it assumes downstream interactions between the head controller and the eye burst generator (see Fig. 3.2). Head commands are sent to the MSH control loop through an inhibitory connection to the RI units to adjust the discharge duration of the LLBN units. This actively controls the duration of the gaze shift. Another connection carrying the same head command then inhibits the EBN units and adjusts the amplitude and velocity profile of the saccades. A last connection is assumed from the NI (which carries eye position information) to the head controller to modulate the head command and depends entirely on the position of the eyes in the orbit at the beginning of the gaze shifts. To model these mechanisms, we adopt a rate coding scheme using a lumped representation of neurons and oculomotor operators (such as the NI, the RI, etc.). This section has been submitted for publication in Biological Cybernetics.

NEURAL NETWORK SIMULATIONS OF THE PRIMATE OCULOMOTOR SYSTEM. V. EYE-HEAD GAZE SHIFTS

A.A. KARDAMAKIS   A. GRANTYN   A.K. MOSCHOVAKIS

Abstract

We examined the performance of a dynamic neural network that replicates much of the psychophysics and neurophysiology of eye-head gaze shifts without relying on gaze feedback control. For example, it generates gaze shifts with ocular components that do not exceed $35°$ in amplitude, whatever the size of the gaze shifts (up to $75°$ in our simulations), and does not invoke ad hoc mechanisms (e.g., a saturating nonlinearity) to accomplish this. It reproduces the natural patterns of eye-head coordination in that head contributions increase and ocular contributions decrease together with the size of gaze shifts and this without compromising the accuracy of gaze shifts. It also accounts for the dependence of the relative contributions of the eyes and the head on the initial positions of the eyes as well as for the position sensitivity of saccades evoked by electrical stimulation of the superior colliculus. Finally, it shows why units of the saccadic system would seem to carry gaze-related signals even if they do not operate within a gaze control loop and even if they do not receive head-related information.

1 Introduction

To account for the fact that gaze shifts starting from the same position and reaching the same visual target remain the same despite considerable variability of their ocular and head components, in their pioneering studies Bizzi and his colleagues (e.g., Bizzi et al., 1978) proposed a hypothesis known as the 'linear summation hypothesis'. Besides assuming that the eyes and the head are driven by independent controllers (Fig. 1A), the summation hypothesis relies on three assumptions: 1) motor commands cause a saccade moving the eyes by $\Delta E'$ (equal to retinal error -Re, the distance between the fovea and the retinal image of the target), 2) the same commands are sent to the head, and 3) saccades and the vestibulo-ocular reflex (VOR) sum linearly, so that the contribution of the head is

51

subtracted from that of the eye movement. Remarkably, all three premises are debatable and maybe wrong. For example, the first one implies that the brain programs movements that the muscular apparatus cannot execute, such as eye movements beyond an animal's oculomotor range. As to the second one, head movements are better related to target position with respect to the head (Guitton et al., 1984; Volle and Guitton, 1993) rather than Re. Finally, whether the VOR works during gaze-shifts or not (and thus the truth content of premise #3) depends on the size of the movement. Although not equal to 1, the gain of the VOR is considerable when movements are relatively small ($< 40°$, Pelisson et al. (1988) and drops to zero for bigger movements (Tomlinson and Bahra, 1986b).

Rather than implement the summation hypothesis, the brain could be using an extension of the eye position saccadic controller (van Gisbergen et al., 1981) to program head-free gaze shifts (Laurutis and Robinson, 1986). Such a scheme (Fig. 1B), assumes that gaze (eye position in space, E/S) is the controlled variable. The comparator of this model receives feedback signals indicating the position of the eyes relative to the head (E/H) and of the head relative to space (H/S) to create an internal representation of gaze-error (Ge) which is used to drive both eye and head-related neural circuits so that inadequate contribution of one effector is compensated by the other. In this manner the accuracy of gaze shifts would be preserved regardless of the magnitude of the head components and of the gain of the VOR. On the other hand, not only is it unlikely that the brain implements gaze control (Moschovakis and Highstein, 1994; Moschovakis et al., 1996; Moschovakis, 1996), there are reasons to think that the eyes and the head do not receive the same drive. If they did, eye and head trajectories should differ only to the extent that they are executed by effectors that offer different loads. This is not true of either humans or monkeys. Instead of correlated metrics, the head and the eyes of human subjects can move in different directions and with different degrees of curvature (Tweed et al., 1995) while peak eye velocity is only weakly correlated with peak head velocity and acceleration in both humans and monkeys (Phillips et al., 1995; Tweed et al., 1995). All in all, theoretical considerations and psychophysics suggest that monkeys and humans control their eyes independently of the head.

Given these shortcomings, it is reasonable to ask if it might be possible to construct a model of eye-head coordination that does not rely on gaze feedback control and yet is consistent with presently available evidence. This was answered in the affirmative by Phillips et al. (1995) in a model of eye-head gaze shifts that reverted to the basic assumption of the summation hypothesis, that of independent controllers of the eyes and the head. Rather than assume that saccades and the VOR sum linearly,
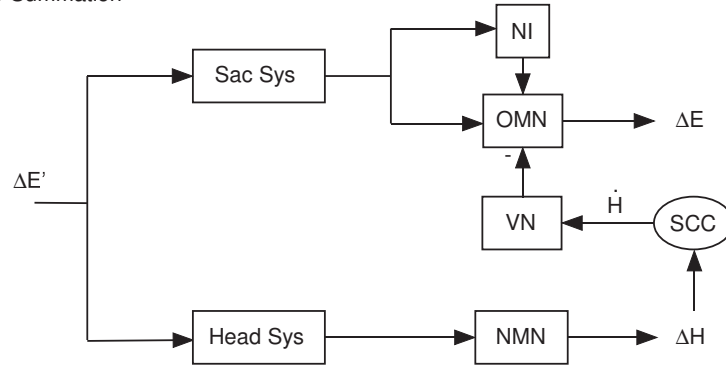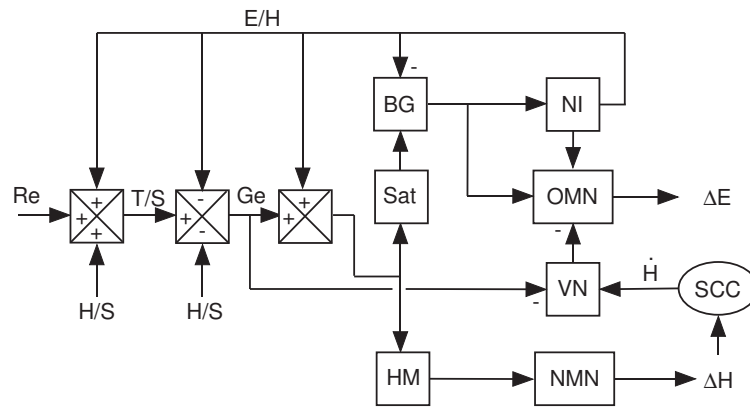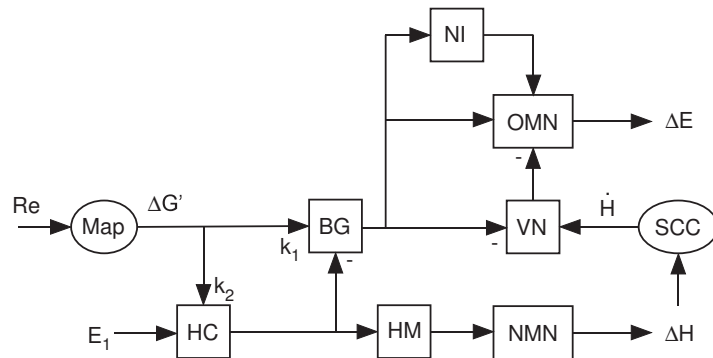
Figure 1: Comparison of the flow of information through three eye-head models. A. Linear summation hypothesis. B. Gaze control model. C. Cross-talk model. Inhibitory connections are indicated by minus sign next to the relevant arrowhead. All other connections are excitatory. Abbreviations: BG, burst generator of the saccadic system; $\Delta E'$, desired eye displacement; ΔE, eye displacement; $\Delta G'$, desired gaze displacement; ΔH, head displacement; E_1, initial eye position; E/H, eye position re head ; Ge, gaze error; $\dot{H}$, head velocity; HC, head movement command; HM, premotor circuits responsible for head movements; H/S, head position in space; Map, sensorimotor map of the superior colliculus; NI, neural integrator; NMN, neck motoneuron; OMN, extraocular motoneuron; Re, retinal error; Sat, saturation element; SCC, semicircular canals; T/S target position in space; VN, vestibular neuron.

these authors suggested a cross-talk between the head- and eye-related circuits of this model (Fig. 1C). To date, it is only an abstract version of this model that has been simulated (Freedman, 2001), a version that remains too schematic to allow an interpretation of its units and the signals they carry. For example, rather than use a circuit of interconnected units to generate the signals needed to drive the eyes during saccades, their time course is dictated by an equation. Also, instead of emerging from it, important features of eye-head coordination, such as the position dependence of the contributions of the eyes and the head, are included only as assumptions. One of the purposes of the present study is to remedy these shortcomings and propose a cross-talk model of primate gaze shifts that respects known anatomy, replicates known psychophysics and offers insight into the response properties of relevant neurons. A preliminary version of this work appeared in an abstract (Moschovakis et al., 2008).

2 Methods

Figure 2 illustrates, in block diagram form, the model we simulated and provides a pictorial summary of several of our assumptions. We simulated the eyes using a cyclopean version of a first order plant with a time constant equal to 160 ms (Robinson, 1981). Rotations in two directions (ipsiversive and contraversive) were due to inputs from two antagonistic groups of neurons (ocular movers; OMs). The ipsiversive ones (OMi) include the ipsilateral lateral rectus motoneurons, the ipsilateral abducens internuclear neurons and the contralateral medial rectus motoneurons as well as cells belonging to the ipsilateral neural integrators. The contraversive movers (OMc) include the contralateral lateral rectus motoneurons, the contralateral abducens internuclear neurons and the ipsilateral medial rectus motoneurons as well as cells belonging to the contralateral neural integrators. Saccade-related signals were produced by the burst generator (BG). To implement this, we chose the MSH BG, a pictorial description of which is enclosed by the stippled line in Fig. 2A. The original literature (Moschovakis, 1994) provides a description of its units (LLB, RI, MLB, OPN, latch) and a justification of their connections (LLB → MLB, MLB → latch, latch → OPN, LLB → RI, RI → LLB, OPN → RI, OPN → MLB).). Briefly, its output is carried to OMs by medium lead burst (MLB) units. Its feedback loop is made of long-lead burst (LLB) and resettable integrator (RI) units, and in contrast to other models of the BG, MLB units lie outside it. RI units are automatically reset at the end of each saccade due to the input they receive from OPNs. As shown below, the pause of the latter is strictly determined by gaze-related variables. Accordingly, and to distinguish them from the 'complex' OPNs (cOPNs; see

below), we refer to these units as 'saccade' OPNs (sOPNs; Petit et al. 1999). As in previous models of

eye head coordination (Whittington et al., 1984; Tomlinson, 1990; Phillips et al., 1995), two classes of

excitatory MLB units were included in our simulations: gaze-related (BN_G) and eye-related (BN_E) burst

neurons. Only the latter were assumed to receive input from the HC and to influence extraocular

MNs (Fig. 2A). Also, because the present implementation of the MSH model is two-directional, we

included inhibitory MLBs (IBNs), which were assumed to convey inhibitory replicas of BN_E and BN_G

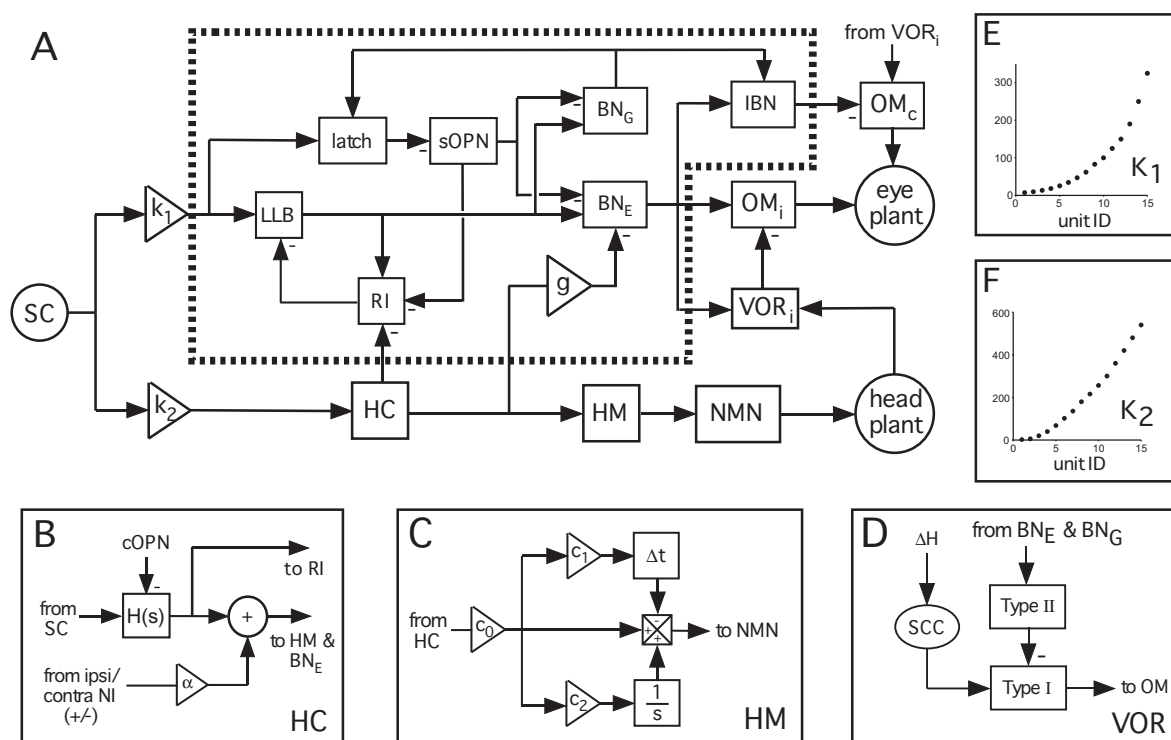discharges to the antagonist OMc.

Figure 2: A. Block diagrammatic illustration of the model we simulated. Stripped lines enclose a modified version of the MSH model of the saccadic burst generator (BG). Connections from sOPN to IBN, from BN_E to Latch and from BN_G to VOR units were not included to avoid clutter. B. Head command (HC) generator. C. Premotor circuits (HM) responsible for innervation of neck motoneurons. D. Vestibulo-ocular reflex (VOR) pathway. E. Synaptic weights of SC unit connections with the BG (K_1, ordinate) as a function of unit position in the SC array (abscissa, 1 is rostral, 15 is caudal). F. Synaptic weights (K_2, ordinate) of SC unit connections with the HC circuitry (layout as in E). Abbreviations: BN_E, eye related burst neuron; BN_G, gaze related burst neuron; cOPN, 'complex' omnipause neuron; IBN, inhibitory burst neuron; LLB, long-lead burst neuron; OMi, ipsilateral (agonist) ocular motoneurons; OMc, contralateral (antagonist) ocular motoneurons; RI, resettable integrator; SC, superior colliculus; sOPN, ÇsaccadeÈ omnipause neuron; Type I, Type II, secondary vestibular neurons; VORc, vestibulo-ocular reflex driving the eyes in the contralateral direction (leftward), opposite to that of head rotation (rightward in our simulations); VORi, vestibulo-ocular reflex driving the eyes in the rightward direction; a, c_0, c_1, c_2, g, variable gains. Other abbreviations and symbols as in Fig. 1.

The BG relied on the Superior Colliculus (SC) for its input signal, a Gaussian function of time (σ_t

= 15 ms). To generate eye-head gaze shifts, a copy of this signal was also sent to a head command generating circuit (HC, Fig. 2B). There it was low passed (through the filter marked H(s) that we used to prolong the SC signal) and gated by 'complex' OPNs (cOPNs), i.e., units pausing for durations poorly correlated with those of saccades which they outlast (Petit et al., 1999). Consistent with our model, the duration of cOPN pauses is equal to or a little longer than the duration of the head acceleration phases of head-free gaze shifts, and there is a significant positive correlation between the two (slopes: 0.99 - 1.21; r^2: 0.46 - 0.76; Grantyn et al. 2002). The gated HC signal is summed with the output of the oculomotor neural integrators (NI, see below) and then sent to the head premotoneurons (HM, Fig. 2C). We assumed that signals exiting the SC encode desired gaze displacement rather than desired instantaneous gaze position in space. To generate the desired gaze displacement signal, we did not assume that the SC employs a comparator that receives feedback signals indicative of target in space (T/S), eye in head (E/H) or head in space (H/S). Nor did we assume that the gaze displacement commands exiting the SC depend on the initial position of the eyes. Instead, we assumed that the SC receives a retinal error (Re) signal and transforms it into the activation of topographically arranged subsets of its output neurons. We further assumed (Fig. 2A) that the strength of the SC projections (k_1) to the BG is such that the drive arising from units responsible for bigger shifts is stronger than that for smaller shifts and that the same is true for the strength of the SC projections to the HC (k_2). Thus, to simulate gaze shifts of progressively bigger size, we systematically increased the synaptic weights k_1 (Fig. 2E) and k_2 (Fig. 2F) together with the size of the gaze shifts. The use of these synaptic weights can be thought of as a means to decompose desired gaze shifts into desired eye displacement and desired head displacement, respectively. A second important assumption of our model is that eye position (E_1) at the start of the gaze shift (t_{on}) modulates the head-related commands of HC units due to the excitatory (inhibitory) influences (scaled by a) they receive from the ipsilateral (contralateral) NI (Fig. 2B). To this end we passed the output of the NI through a sample-and-hold filter. Accordingly, the activation function of HC units is described by the expression

$$HC(t) = k_2 SC(t) + aNI(t_{on}) \tag{1}$$

In agreement with previous models (Ramos and Stark, 1987; Freedman, 2001), we simulated the head as a second order plant (with time constants equal to 105 and 181 ms). These were determined from the experimental data of (Bizzi et al., 1978). During gaze shifts, the head was driven by a dynamic circuit (HM) whose operations remain rather speculative due to the dearth of information

regarding the discharge pattern and connections of head-related neurons. As a first approximation, it can be thought of as a differentiator that transforms the bell-shaped inputs it receives from the HC into a biphasic signal, one of the phases of which corresponds to the 'action' and the other to the 'brake' pulses encountered in electromyographic records from neck muscles (Hannaford et al., 1986). After separate amplification, one of the phases is sent to neck MNs (NMNs) innervating muscles with a pulling direction similar (agonists) while the other is sent to NMNs innervating muscles with a pulling direction opposite (antagonists) to that of the movement. In this manner, the inputs to the head controller are converted into the torque signals needed to accelerate (through agonist MNs) and decelerate (through antagonist MNs) the head plant. Given its relatively short time constants, the head would not remain at the position reached by movements unless a tonic position signal is also fed to the head plant. We assumed that this tonic signal is obtained through integration (in the sense of Newtonian calculus) of the head displacement command exiting the HC. To ensure that they obey the amplitude-duration relationship of primate head movements (Freedman and Sparks, 1997), the relative strength of the 'action' and 'brake' pulses, as well as the delay between the two (Δt in Fig. 2C) and the gain of the position signal were determined through optimization with the help of a genetic algorithm (from the 'Genetic algorithm and direct search toolbox' of MatLab, The MathWorks Inc.).

In addition, HC units were assumed to project to eye-related units (BN_E) and to the resettable integrator (RI), but not to the gaze-related units (BN_G). Taken together, the first two can be thought of as a cross-talk between the head motor system and the saccadic system in that they carry an efference copy of head velocity to be subtracted from the BG. The connection to the RI prolongs saccades because it forces the BG to work longer till the LLBs are silenced and the prolongation scales with cross-talk signal amplitude and thus head component size. To estimate the gain of the connection to the BN_E units (g in Fig. 2A), we found the slope of the relationship between the amplitude of saccades and the number of spikes in their burst. Similarly, we found the slope of the relationship between the amplitude of the head component of gaze movements and the number of spikes in the burst of the head-related units of our model. The number of spikes of the HC and BN_E units ([HC], [BN_E]) were found by taking the time integral of their firing frequency between the start (t_{on}) and the end (t_{off}) of their respective bursting activity, as

$$[HC] = \int_{t_{on}}^{t_{off}} HC_{(t)}\, dt \qquad (2)$$

57

and

$$[BN_E] = \int\limits_{t_{on}}^{t_{off}} BN_E(t)\, dt - g[HC] \tag{3}$$

To ensure that the ocular components of gaze shifts are curtailed by an amount equal to the head components (at least for movements within the oculomotor range of the animal), the value of g was chosen such that the size of the gaze shift in response to a certain SC command is constant whether or not the head is restrained or free to move. Due to the small non-linearity of the relationship between [HC] and head component size, the cross-talk was set to a value equal to the ratio of the two slopes evaluated at $45°$ (the limit of the oculomotor range of the monkey).

Our model also includes a vestibuloocular reflex (VOR) to stabilize the visual world on the retina during head movements following and sometimes preceding rapid gaze shifts. We assumed that its gain equals Đ1 thus generating eye movements equal in amplitude and opposite in direction to those of the head. To model the VOR, we lumped the semi-circular canals and the primary vestibular afferents into a single unit that differentiates the head position signal and projects to neurons of the vestibular nuclei. These in turn send excitatory projections to the contralateral and inhibitory projections to the ipsilateral, extraocular MNs. Because their activity is gated by the output of the burst generators (through BN_E and type II vestibular neurons; Fig. 2D) these units pause (and thus the gain of the VOR of our model drops to zero) during ipsiversive saccades. Since we made no effort to have them interact with the NI, the secondary vestibular units of our model carry no eye position information and thus could be more appropriately thought of as vestibular-pause (VP) neurons (Tomlinson and Robinson, 1984) rather than position-vestibular-pause (PVP) neurons (McCrea et al., 1987).

Numerical simulations were run on a Pentium IV personal computer with a clock frequency of 2.8 GHz with MatLab/Simulink version 6.0 (The MathWorks Inc.). They were left to run for 1 s with a time step of 0.12 ms. The time constant of the integrators was assumed to be infinite (perfect integrators). With the exception of these and the oculomotor plant, the impulse response of all units was a Dirac δ function. In addition, their input-output characteristic was nonlinear. A threshold equal to zero ensured that units did not display negative firing frequencies. For inputs greater than zero, the input-output characteristic was linear for most of the units we simulated. However, consistent with known physiology, LLB and MLB units did not follow frequencies >1100 Hz (Moschovakis et al., 1996) and primary vestibular units head velocities $>350°/s$ (Pulaski et al., 1981).
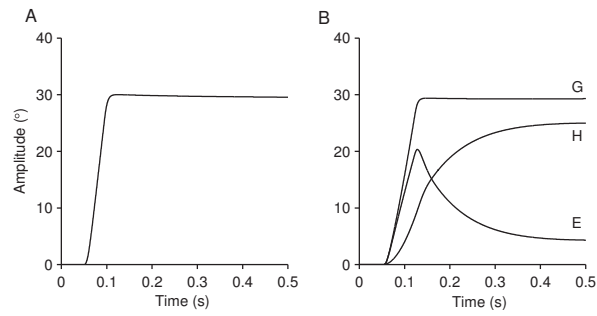
58

Figure 3: Typical gaze shifts generated by our model to a visual target appearing 30° to the right of the fixation point. A: Eye saccade with the head-restrained. B: Gaze shift to the same target with the head free to move. Eye (E) and head (H) trajectories are shown along with the total gaze movement (G).

3 Results

Our model replicated several psychophysical observations in primates. Firstly, it generated eye-head gaze shifts with realistic time-course. An example is shown in Fig. 3B which illustrates a 30° rightward eye-head movement in response to activation of the SC unit responsible for 30° movements (in this example, the 6th unit in the array we used). This movement consisted of a 20° saccade while the head contributed about 10° to the gaze shift. Upon its conclusion, which coincided with the end of the saccade, the eye counter-rotated (due to the VOR) to compensate for the continued movement of the head. Figure 3A illustrates a saccade executed with the head 'fixed', due to activation of the same SC unit, responding to the appearance of the same target at the same retinal eccentricity (30°). Despite the fact that in this case the 'head' part of the circuit did not work, the line of sight was displaced appropriately (by 30°) with the eyes alone.

To generate gaze shifts of different sizes, our model assumes that each SC unit projects to the BG and simultaneously to the head controller with synaptic weights (k_1 and k_2) the values of which depend on the size of the gaze displacement that the unit encodes. Thus, as shown in Fig. 2E, F, gains k_1 and k_2 increased progressively from the 1st to the 15th units of our SC array. With the appropriate parameterization, these 15 units could generate gaze shifts ranging from 5° to 75° (in increments of 5°). For movements up to about 40°, activation of each unit in the SC array led to gaze shifts of the same size whether 'head-free' or 'head-fixed'. This is illustrated in Fig. 4, which compares the size of head-fixed saccades (open squares) to that of head-free gaze shifts (open circles) directed to targets at the same eccentricities. The same figure also shows a plot of the amplitude of the ocular saccades (crosses) generated by our model during combined eye-head movements. As shown here,

for gaze shifts larger than about 30°, the contribution of ocular saccades is a decreasing function of the amplitude of the gaze shift. This decrease is compensated by the increasing contribution of head movements, such that the size of the gaze shift matches the eccentricity of the target.
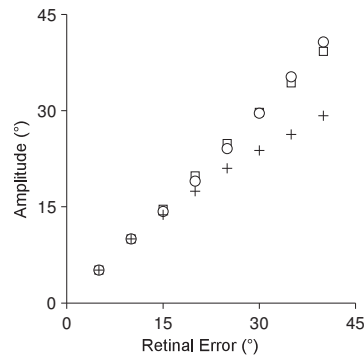

Figure 4: Plots of the size (ordinate) of simulated head-fixed saccades (open squares), total head-free gaze shifts (open circles) and saccadic components (crosses) of head-free gaze shifts. Gaze shifts are initiated when the eyes are in primary position and their size remains within the oculomotor range of monkeys.

When the head is free to move, gaze can be redirected to large target eccentricities, with shifts exceeding the oculomotor range. Our model accurately reproduces the relative contributions of eye and head movements for gaze shifts of 40-75° as well, i.e., beyond the oculomotor range of monkeys. This is illustrated in Fig. 5, where we plotted the amplitude of the eye (Fig. 5B) and the head (Fig. 5C) components at the end of the gaze shift. Figure 5A shows the relation between retinal error and the amplitude of the gaze shift. As expected of normometric movements the data lie on a line of unity slope passing through the origin of the axes. As in monkeys (Freedman and Sparks, 1997), model-generated gaze shifts smaller than about 15° were accomplished by the eye essentially alone without any significant contribution of the head (Fig. 5C). Gaze shifts larger than 45° and starting from straight ahead were accompanied by saccades that did not exceed 35° (Fig. 5B). It is important to note that this result is obtained without endowing the model with an *ad hoc* processing step, such as a saturating nonlinearity.

Movements generated by our model obeyed amplitude-velocity (Fig. 6A, B) and amplitude-duration (Fig. 6C, D) relationships that were consistent with the kinematic properties of gaze shifts observed in animals. To some extent, these were built into our model as assumptions. For example, we adjusted the parameters of the BG we employed so that the relationship between the duration and the amplitude of head-fixed saccades would be linear (Fig. 6D, solid) with a slope equal to 1.2 ms/deg. All other curves of Fig. 6 illustrate emergent properties of our model. Eye velocity increased
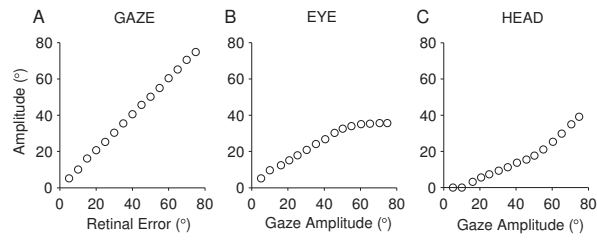
Figure 5: Amplitude of simulated head-unrestrained gaze shifts as a function of retinal error (A), and the corresponding contributions of eye (B) and head (C) displacements, as a function of gaze amplitude. All movements are initiated with the eyes centered in the orbits and their size is measured at gaze end.

with the size of head-fixed saccades (solid) and saturated at $700°/s$ for head-fixed saccades larger than $20°$ (Fig. 6B). In contrast, and in agreement with experimental data from monkeys (Freedman and Sparks, 1997), when the amplitude of head-free saccades increased beyond 15-20°, their peak velocity dropped (open circles). For example, the peak velocity of a simulated $30°$ head-fixed saccade was equal to $700°/s$ (Fig. 6B, solid), while it did not exceed $350°/s$ when the head was free to move (Fig. 6B, open circles) even though it accompanied an eye movement of the same size as before. As a consequence, it took longer for relatively large simulated eye movements ($20°$) to reach the end of their excursion when the head was free (Fig. 6D, open circles) than when it was fixed (Fig. 6D, solid). Also consistent with experimental data in the monkey (Phillips et al., 1995), the amplitude-duration relationship of simulated gaze shifts (Fig. 6C) was steeper (3.0 ms/deg) than that of simulated head-fixed saccades (Fig. 6D, solid).
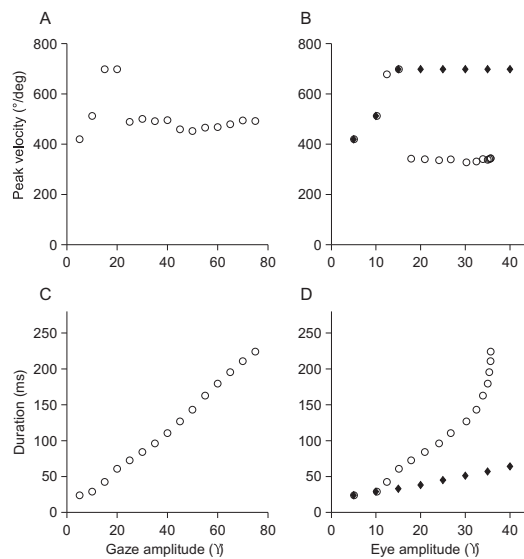

Figure 6: Amplitude-velocity (A, B) and amplitude-duration (C, D) relationships displayed for gaze (A, C) and eye (B, D) movements during head-fixed (solid) and head-free (open) gaze shifts.

The reduction of eye velocity documented in Fig. 6B is due to the inhibitory cross-talk signal that the head-related circuitry of our model sends to its saccadic burst generator (BG). This signal is derived from the head command and is sent to the BG where it is subtracted from the BN_E and RI units (Fig. 2A). This mechanism accounts not only for the reduction of eye velocity but also for the fact that its time course depends on the size of the gaze shift. As shown in Fig. 7, the eye velocity profile of the saccade that accompanies a $20°$ gaze shift has a single and nearly symmetrical peak. On the other hand, the eye velocity profile of the $40°$ gaze shift lasts longer and exhibits a dual peak. The same is true of the $60°$ gaze shift that is accompanied by an eye movement whose peak velocity did not change but whose duration increased considerably. The eye velocity traces reflect the activation functions of the BN_E units (Fig. 7, middle row) which also display dual-peak firing rate for saccades accompanying large enough gaze shifts. This is due to their inhibition by cross-talk signals which are negligible when the gaze shift is small and become progressively bigger (Fig. 7, bottom row) in direct proportion to the size of the gaze shift and the contribution of the head to it. Additionally, the duration of the eye velocity traces is progressively prolonged in direct proportion to the size of the gaze shift and the same is true of the activation functions of the BN_E units. This is due to the subtraction of the cross-talk signals from the RI units as well, thus forcing the closed loop to work for a longer period of time before the LLB units of the MSH BG would be silenced.

The eye and head contributions to gaze shifts of the same amplitude and direction are known to depend on the position of the eyes in the orbit at the onset of the gaze shift (Freedman and Sparks, 1997). To examine this phenomenon, we simulated gaze shifts of two different amplitudes, a relatively small one ($30°$) and a large one ($70°$) generated in response to the activation of the 5th and the 14th unit in the SC array, respectively. Figure 8 illustrates the effect of varying the initial eye position between $-25°$ and $15°$ (in $5°$ increments) on the amplitude of head (Fig. 8A) and eye (Fig. 8B) contributions to gaze shifts of different sizes. The amplitude of the eye movement increased (and head contribution decreased) with initial eye positions progressively more eccentric in the direction opposite to that of the gaze shift. The effect was more pronounced for larger gaze shifts, as shown by the steeper slopes of their amplitude-position curves (Fig. 8A, B). Despite large variations of the eye and head contributions, the total amplitude of the gaze shift remained roughly constant (Fig. 8C). To illustrate the signal flow responsible for the position sensitivity of saccades during simulated head-free gaze shifts, the BN_E and head command signals are shown in Fig. 9 together with the movements they generate. The bottom traces display $50°$ rightward gaze shifts generated in response
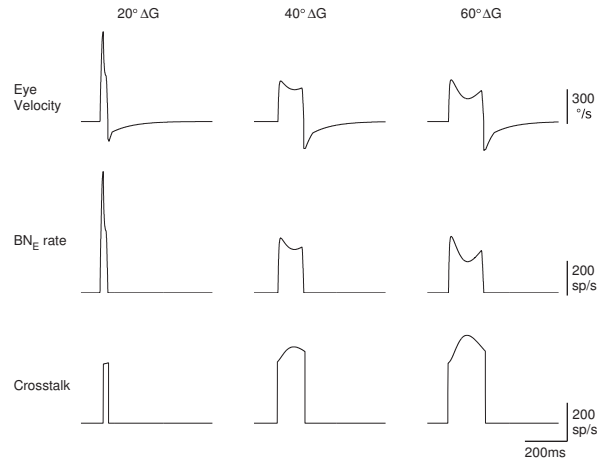
Figure 7: Time course of the eye velocity and of the firing rates of BN_E and cross-talk units during simulated head-free gaze shifts of increasing size (20, 40 and 60°). Negative values (those below the initial part of the velocity trace) are due to counter-rotations generated by the vestibulo-ocular reflex. Time scale applies to all traces.

to activation of the 9th unit of the SC array while initial eye positions varied from -25° to 15° in 10° increments (arranged in columns from left to right). With the progression of initial eye position from left to right, the amplitude of the head movement increased together with the amplitude of the signal generated by the head command (HC) unit of our model. The eye position related modulation of this signal arises from influences that HC units receive from the neural integrators (Fig. 2B), inhibitory from the contralateral and excitatory from the ipsilateral sides of the brain. Due to the cross-talk between the eye and head portions of our model, this eye-position dependent HC signal is also subtracted from the BN_E activity, which, as a consequence, becomes inversely proportional to the initial position of the eyes, and therefore generates position dependent ocular contributions to gaze shifts. The bottom trace of Fig. 9 documents the fact that despite the large position-dependent variability of the contributions of both the eyes and the head, the amplitude of the resulting gaze shifts remains constant.

The relationship between the number of spikes in BN bursts and the amplitude of gaze and saccade shifts has been employed before to distinguish gaze-related cells from eye-related cells (e.g., Whittington et al. 1984). Bearing in mind our assumption that BN_E, but not BN_G, units receive cross-talk signals from the HC, we used the same approach to compare their model-generated discharges. In Fig. 10A (open circles) we plotted the number of spikes in the burst (N_B) of the BN_E units versus the size of head-fixed saccades. Due to the constraints we imposed upon the burst generator, the slope of this relationship was equal to 1.2 spikes/deg. It was identical to that for head-free eye

saccades (dots) and shallower (0.7 spikes/deg) when N_B was plotted against the amplitude of the total gaze shift (crosses). Despite the fact that the BN_E units of our model receive information about head movements (via the cross-talk), they would be classified as eye-related cells according to the study cited above because the linear regression line between N_B and saccade size is the same for both head-free and head-fixed saccades. Figure 10B illustrates the results of a similar analysis, this time applied to the BN_G units of our model. Due to the constraints we imposed upon the burst generator, the slope of the relationship between N_B and the size of head-fixed saccades (Fig. 10B, open circles) was equal to 1.5 spikes/deg. It was steeper (2.5 spikes/deg) for the relationship between N_B and the size of head-free gaze shifts (crosses) and much steeper (4.1 spikes/deg) when N_B was plotted against head-free saccades (dots). Because the linear regression line between N_B and the size of head-fixed saccades is closer to that for head-free gaze shifts rather than head-free saccades, the BN_G units of our model would have been classified as gaze-related, despite the fact that they do not receive information about head movements and their discharges do not influence circuitry controlling the head.

It has been argued that the standard metric analysis based on N_B is not appropriate in studies of combined eye-head gaze shifts (Cullen et al., 2000). Therefore, we subjected the activation functions of our model units to system identification techniques to better understand the physical meaning of the signals they carry. To this end we fit the activation functions of certain model units (e.g., BN_E, BN_G and cross-talk) to quantities describing the eye and head trajectories (e.g., eye position, head position and their derivatives). The estimation of the parameters that optimally reconstruct the model unit activation functions was accomplished with the 'prediction error minimization' routine (pem.m) available in the System Identification Toolbox of MatLab. Examples of such fits to the instantaneous rate of BN_E, BN_G and cross-talk signals for gaze shifts of two different sizes (40 and 60°) are illustrated in Fig. 11. In the case of BN_E units (top row), the firing frequency ($f(t) = 1.2\dot{e}$) calculated from the 1d model (thick solid line) offers an almost perfect fit ($r = 0.999$) to the data from both small and large movements. The discharge reaches its peak value early in the movement and is followed by a transient decrease of the firing rate matching the two-peaked velocity profile of eye saccade during a 60° gaze shift. A 3d model ($45 + 0.06\dot{h} + 0.003\ddot{h}$) was needed to fit the cross-talk signal ($r = 0.997$). Because the cross-talk signal does not influence BN_G units, their firing rate does not display the two peaked frequency profile shown by BN_E units. We had to resort to a 4d model ($200 + 2.0\dot{e} + 0.9\dot{h} + 0.03\ddot{h}$) to account for the firing rate of BN_G units ($r = 0.874$). Evidently, their discharge reflects gaze- (i.e., eye-
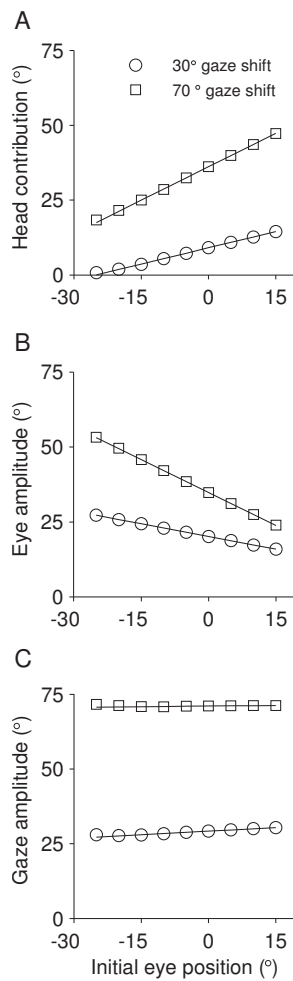
Figure 8: Size of head (A) and eye (B) movements during rightward head-free gaze shifts (C) of roughly constant amplitudes equal to 30° (open circles) and 70° (open squares), as a function of initial eye position. Negative values indicate leftward initial eye positions. Data were fit with least-squares regression lines the slopes of which were the following: (A) 30°: 0.36; 70°: 0.75; (B) 30°: -0.3; 70°: -0.74; (C) 30°: 0.06; 70°: 0.01.

plus head-) related physical quantities despite the fact that they do not receive head-related signals (Fig. 2A) nor do they operate within a gaze control loop. The source of the gaze-relatedness of such units is explored in the Discussion section.

The position sensitivity of the eye and head components of simulated gaze shifts encouraged us to examine if our model could also reproduce the well documented position sensitivity of head-fixed saccades evoked in response to electrical stimulation of the SC (McIlwain, 1986; Grantyn et al., 1996; Moschovakis et al., 1998). To this end, the activation function of one of the units (the one responsible for 30° head-free gaze shifts) of the left SC of our model was held at a constant value (300Hz) for the duration of the stimulation (100 ms) as would be the case if a pulse train were employed. The size of
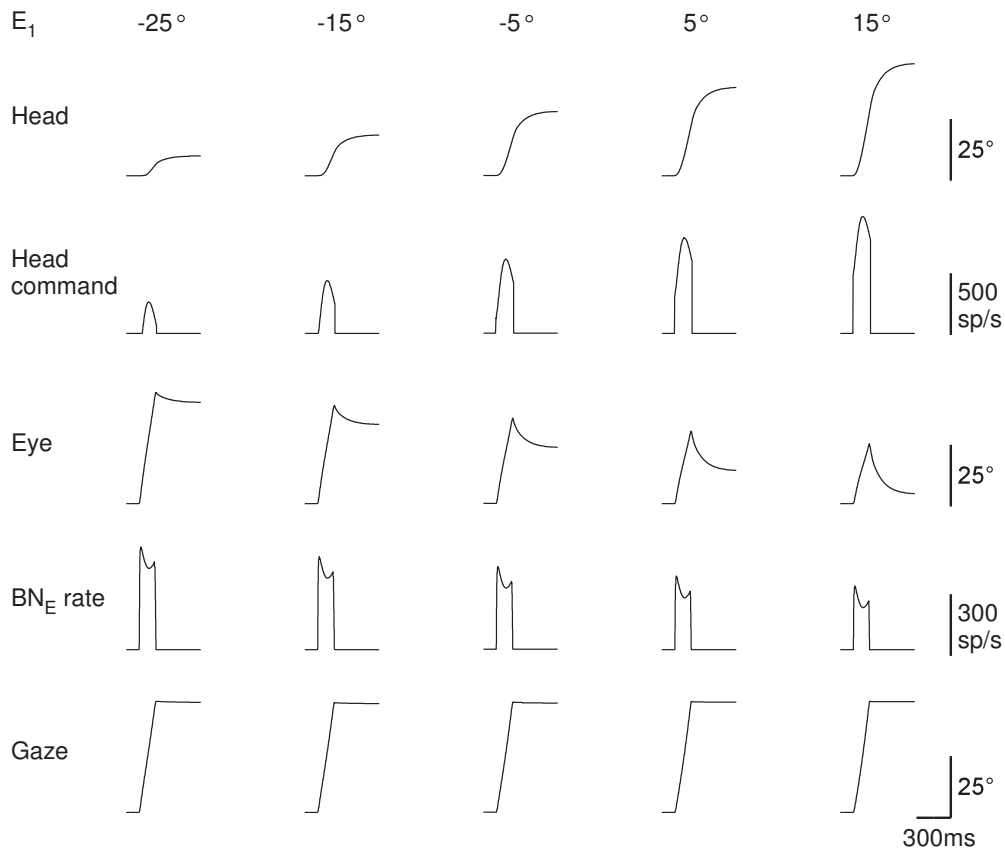
Figure 9: Time course of the eye, head and gaze trajectories along with the discharges of BN_E units and the head commands associated with gaze movements of the same amplitude (50°) and starting from different initial eye positions (varying from -25° to 15°). The time scale applies to all traces.

evoked rightward saccades was equal to 23° when the eyes started from straight ahead, bigger than 23° when the eyes started from contralateral (leftward) initial positions and smaller than 23° when they started from ipsilateral (rightward) initial positions (Fig. 12, open circles). The linear regression line relating the size of evoked saccades (ΔE) to the initial position of the eyes (E_1, varying from -20° to 20° in 5° increments) obeyed the equation:

$$\Delta E = 23 - 0.32 E_1 \qquad (4)$$

'Activation' of the unit responsible for 50° head-free gaze shifts evoked bigger saccades (37° when the eyes started from straight ahead - Fig. 12, solid). Their size also depended on the initial position of the eyes, but in this case the slope of the linear regression line through the data was steeper as it obeyed the equation:

66

$$\Delta E = 37 - 0.55E_1 \tag{5}$$

The fact that the slope and the intercept of Eq. 5 are bigger than those of Eq. 4 is reminiscent of the relationship between the size of the characteristic vector and the position sensitivity of saccades evoked in response to the electrical stimulation of the SC. This issue is further considered in the Discussion section in the light of several alternative mechanisms that could account for the position sensitivity of electrically evoked saccades.

Records of the discharge of BN_E and BN_G units might also help us decide which of these alternative mechanisms is implemented in the brain. This is suggested by the prediction that the BN_E and BN_G units of our model do not discharge in the same manner during gaze shifts accompanied by saccades starting from initial positions other than straight ahead. To illustrate this point we plotted the N_B of BN_E (Fig. 13A) and BN_G (Fig. 13B) units against the size of rightward head-free saccades starting from $20°$ to the left (crosses) or $20°$ to the right (dots) and head-fixed saccades starting from straight ahead (open circles). We limited our test to movements evoked in response to activation of the nine first units of our SC array because, as shown in Fig. 5B, saccade size does not increase with gaze amplitude when the latter is bigger than about $45°$ (i.e., the size of the gaze shift evoked by the ninth unit of the SC array). Note that the linear regression lines through the data for saccades starting from primary positions are reproduced from Fig. 10 (open circles). In the case of BN_E units (Fig. 13A), all three linear regression lines are identical (with a slope equal to 1.2 spikes/deg) thus indicating that their discharge (at least as determined by N_B) does not depend on initial eye position. This is not the case for BN_G units since the slope of the linear regression line for saccades starting from rightward positions (5.6 spikes/deg), is steeper than that of saccades starting from leftward positions (3.4 spikes/deg) and much steeper than that of saccades starting from straight ahead (1.5 spikes/deg).

4   Discussion

The present report demonstrates that a neural network model that assumes independent control of the eyes and the head and relies on subtractive cross-talk between the premotoneuronal circuits of these two effectors can account for much of the psychophysics and neurophysiology of eye-head coordination. For example, it replicates the realistic time-course and the accuracy of gaze shifts to

targets at several eccentricities both head-fixed and head-free, as well as the fact that gaze shifts of any size can be accomplished with varying combinations of ocular and head components. It also replicates the fact that the size of eye movements saturates at values equal to 35° and that the size of the ocular and head components of gaze shifts depends on the initial position of the eyes. Moreover, it provides a novel account of the position sensitivity of saccades evoked in response to the electrical stimulation of the superior colliculus in head-fixed animals. Finally, it suggests a pattern of connectivity that would explain why some neurons of the saccadic burst generator carry gaze-related signals even if they do not to receive head-related information and do not operate within a gaze control loop. Before comparing its performance to that of previous models, we examine how well its output reflects psychophysics and if the activation functions of its units resemble the discharge pattern of primate neurons known to participate in shifts of the line of sight.
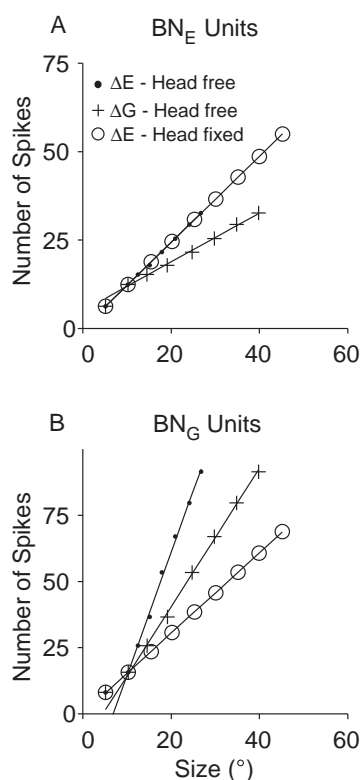
Figure 10: Plots of the number of spikes in the burst of the BN_E (A) and BN_G (B) units of our model (ordinate) versus the size (abscissa) of head-fixed (open circles) and head-free (dots) saccades and head-free gaze shifts (crosses). The lines through the data are the linear regression lines.

Psychophysics The rightmost column of Table 1 allows a point by point comparison, and demonstrates the remarkable similarity, of the performance of our model to the behavior of primates. Firstly,

movements of the head do not compromise the accuracy of shifts of the line of sight to an eccentric visual target in primates (e.g., Fig. 2A of Bizzi 1981) and the same is true of our model (Fig. 4 of this report). Secondly, the time course of simulated eye-head gaze shifts is virtually indistinguishable from those produced by monkeys (compare Fig. 3 of this report to Fig. 1 of Bizzi 1981). Also, the relative contributions of ocular and head movements to simulated gaze shifts of different sizes are realistic (compare Fig. 5 of this report to Fig. 6 of Freedman and Sparks 1997b). Ocular components of natural gaze shifts do not exceed 30-40° even during large (40-90°) gaze shifts (Freedman and Sparks, 1997) and this is reproduced qualitatively by our model (Fig. 5) despite the fact that it does not include a saturating non-linearity (further considered in the last section of the Discussion). Increasing (decreasing) the gain of the cross-talk would enable our model to also match the smaller (10 - 20°) and larger (45°) ocular contributions to gaze shifts found in the cat (Fig. 5 of Guitton et al. 1990) and the human (Figs. 5, 6 of Guitton and Volle 1987), respectively.
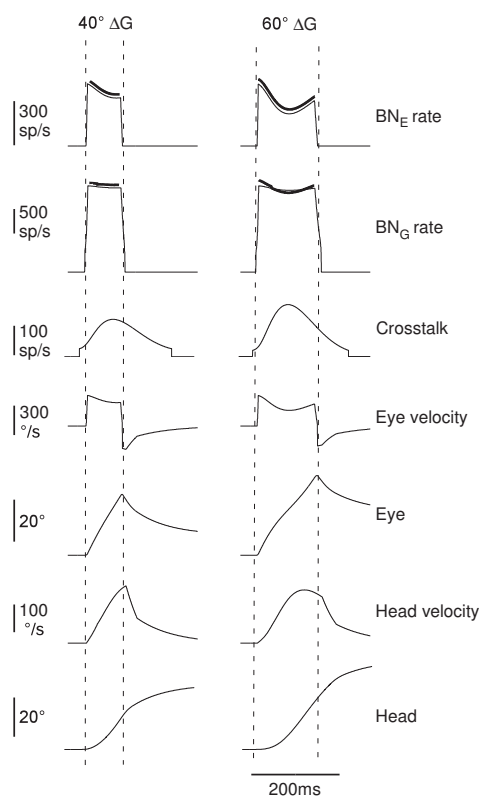
Figure 11: Time course BN_E, BN_G and X-talk signals together with instantaneous position and velocity of the eye and the head for a 40° (left) and a 60° (right) gaze shift. Thick solid lines are the best fits obtained with a prediction-error minimization technique (see text for analytical expressions).

The similarity between experimentally observed and model-generated gaze shifts extends to the amplitude-velocity and amplitude-duration relationships of ocular components (as seen for example

69

when Fig. 6 of this report is compared to Fig. 7 of Freedman and Sparks 1997b). Indeed, head-free saccades are smaller, slower and often last longer than head-fixed ones to the same targets both in monkeys (Bizzi, 1978; Freedman and Sparks, 1997; Tomlinson and Bahra, 1986a) and in the present model. Subtraction of cross-talk signals from BN_E units suffices to account for these observations as it leads to the reduction of saccade size without commensurate shortening of saccade duration. For example, the duration of a $30°$ head-fixed saccade is equal to 50 ms (from the amplitude duration relationship shown in Fig. 6D). Upon freeing the head, its duration increases considerably (by 60%), to 80 ms, i.e., the duration of the $60°$ gaze shift it accompanies, even if we assume that the amplitude-duration relationship of head-free gaze shifts is identical to that of head-fixed saccades. This seems to be the case in humans (Becker and Jurgens, 1992; Collewijn et al., 1992) but not in macaques, whose head-free gaze shifts obey amplitude-duration relationships with slopes steeper than those of head-fixed saccades. For example, slopes equal to 3.9, 4.2 and 3.7 ms/deg were determined for the head-free gaze shifts of monkeys CG, BW and RO, respectively, of Phillips et al. (1995) as opposed to 2.2, 2.8 and 2.5 ms/deg when the head of the same animals was fixed. The steeper slope of the amplitude duration relationship of simulated head-free gaze shifts is due to the subtraction of the cross-talk signals from the RI units of our model. In this manner the closed loop of the MSH BG we employed was forced to work for a longer period of time before its LLB units were silenced. The similarity between simulated and primate gaze shifts applies even to the velocity waveforms of individual simulated movements, in particular large ones which are characterized by very long durations and two-humped velocity profiles (compare Fig. 7 of this report to Fig. 8 of Freedman and Sparks 1997b).

We also examined if our model replicates the influence of orbital eye position on the pattern of eye-head coordination. As shown in humans (Becker and Jurgens, 1992; Volle and Guitton, 1993) and monkeys (Freedman and Sparks, 1997), the contributions of the eyes and the head to constant amplitude shifts of the line of sight do not remain the same if, instead of being centered, the eyes occupy an eccentric position relative to the head at the time when the gaze shift is initiated. When the eyes are initially deviated in the direction opposite to that of the impending gaze shift, eye movement amplitude increases and head movement amplitude decreases in proportion to the angle of the deviation. Opposite changes of eye and head contributions occur when eyes are initially deviated in the ipsilateral direction. The dependence on the initial eye position is stronger for gaze shifts of larger amplitudes (Volle and Guitton, 1993; Freedman and Sparks, 1997). As shown in

Fig. 9 of this report, our model reproduces quite well the overall features of the effect as determined experimentally for gaze shifts of constant (45°) amplitude. Comparison of Fig. 8 of this report to Fig. 15 of (Freedman and Sparks, 1997) demonstrates that there is a reasonable quantitative agreement as well between the results of our simulation and experimental data. For example, the slopes of the regression lines relating head contribution to initial eye position increase from 0.36 to 0.75 as the size of the simulated gaze shift increased from 30 to 70°. Considering the experimental differences between the two monkeys of Freedman and Sparks (1997b), which displayed slopes of 0.79 and 0.42 for fairly large gaze shifts (70°) and dropped to 0.11 and 0.09 for 25° gaze shifts, the performance of our model is quite realistic. The same is true for the relationship between ocular contributions and initial eye position; for example, the slope (-0.74) we obtained for large gaze shifts (70°) lies in between the values determined experimentally (0.43 and 0.85) in two monkeys executing 70° gaze shifts (Freedman and Sparks, 1997).
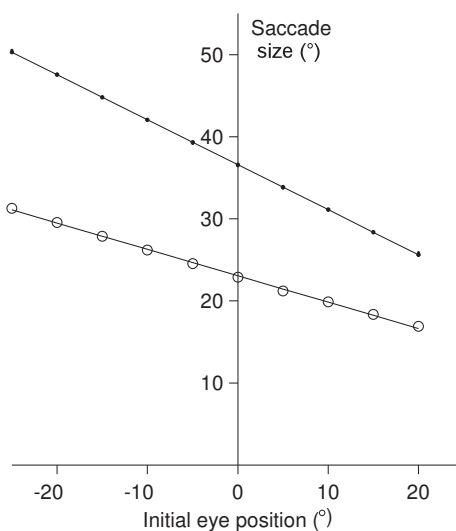
Figure 12: Plots of the size of simulated head-fixed saccades evoked in response to stimulation of SC units for 25° (open circles) and 45° (solid circles) gaze shifts (ordinate) as a function of initial eye position (abscissa). The lines through the data are the linear regression lines.

Our model also reproduces the position sensitivity of saccades evoked in response to the electrical stimulation of the primate superior colliculus (Segraves and Goldberg, 1992; Azuma et al., 1996) and the correlation between the size of the characteristic vector and the position sensitivity of evoked saccades (Azuma et al., 1996; Grantyn et al., 1996). Previous accounts for this phenomenon include the 'cerebellar' (Russo and Bruce, 1993), 'gaze' (Guitton et al., 1980) and 'superposition' (Moschovakis et al., 1998) hypotheses. Their merits and weak points were discussed in detail by Moschovakis et al. (1998) and will not be further considered here. The herein invoked mechanism, namely, the link

between the oculomotor NI and the head-related command generator (HC) as well as the cross-talk between the latter and the saccadic BG, offers a new plausible explanation for the position sensitivity of electrically evoked saccades.

Neurophysiology Comparisons between the activation functions of our model units and the discharge patterns of eye movement related cells have so far been limited to units of its MSH BG (LLBN, MLB, sOPN, RI and latch) during head-fixed movements (Moschovakis, 1994). The present model extends this comparison to the discharge of eye- and gaze-related neurons during head-free gaze shifts.

The relationship between the number of spikes in the bursts (N_B) of bursting cells and the amplitude of gaze and saccade shifts has been used to distinguish gaze-related cells from eye-related cells (e.g., Whittington et al. 1984). Because the linear regression line between N_B and the size of head-fixed saccades is closer to that for head-free gaze shifts rather than head-free saccades, the BN_G units of our model would be classified as gaze-related according to the aforementioned criteria (compare Fig. 10B of this report to Fig. 6 of Whittington et al. 1984), despite the fact that they receive no information about head movements, nor does their discharge influence the head. Similarly consistent with the aforementioned criteria it is the BN_E units of our model that would be classified as eye-related cells because the linear regression line between N_B and saccade size is the same for head-free and head-fixed movements (compare Fig. 10 A of this report to Fig. 5 of Whittington et al. 1984) despite the fact that they receive information about head movements from head premotor circuits via the cross-talk. These relationships are also reminiscent of those between the N_B of primate long-lead burst neurons and the size of saccades and gaze shifts head-free and head-fixed (Cullen and Guitton, 1997a). If BN_E units encode the amplitude of rapid eye movements in both head-free and head-fixed animals and because $\Delta G = \Delta E + \Delta H$ it is logical to expect shallower slopes for the relationship between N_B and total gaze amplitude ΔG (at least for gaze shifts large enough for $\Delta H > 0$). The experimental results of Whittington et al. (1984) meet this expectation and are reproduced by our model. Further, our model predicts that the slope of the linear regression line between the N_B of some MLB units of our model (the gaze-related ones) and saccade size should depend on the initial position of the eyes. The experimental demonstration that this is not the case would refute our model.

In our model we assumed that the inhibitory cross-talk signal arising from the head command generating circuit (HC) is directed selectively to BN_E units and does not influence the bursts of BN_G units. In addition, we assumed that BN_E units cause the movement of the eyes while the BN_G units do
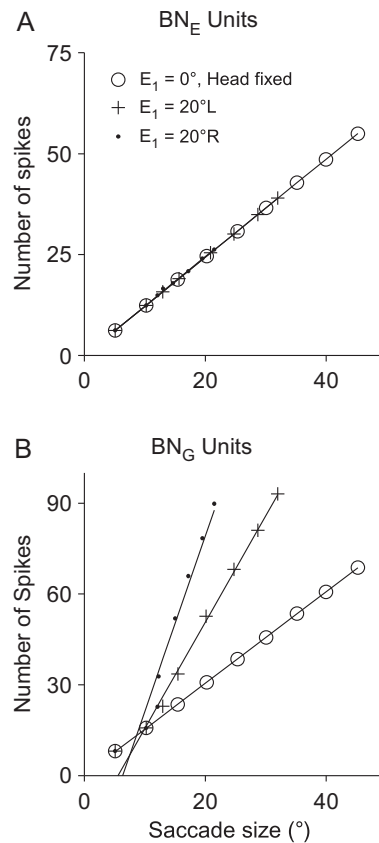
Figure 13: Plots of the number of spikes in the burst of the BN_E (A) and BN_G (B) units of our model (ordinate) versus the size (abscissa) of head-fixed saccades starting from straight ahead (open circles) or of the saccadic components of head-free gaze shifts starting from initial positions $20°$ to the left (crosses) and $20°$ to the right (dots). The solid lines through the data are the linear regression lines.

not. As shown here, these two assumptions lead to a clear distinction between the firing properties of BN_E and BN_G units, and to their classification as eye-related and gaze-related neurons, respectively, thus justifying the choice of terms when referring to them. However, some studies (Cullen and Guitton, 1997b; Sylvestre and Cullen, 2006) indicate that all horizontal MLBs behave as gaze- and not as eye-related cells during head-free gaze shifts. On the other hand, the distinction between eye-related and gaze-related MLBs appears convincing in the study of Whittington et al. (1984) while no MLBs were found to operate in gaze coordinates by Tomlinson and Bance (1992). Our modeling results are not meant to imply that we consider some of this conflicting evidence as more convincing. Our intent is to demonstrate that even if it exists, the gaze-relatedness of MLB discharge need not be due to the operation of a gaze control loop.

This conclusion is strengthened when we consider the results of the dynamic analysis of the signals carried by our model units. If extraocular premotoneurons encode gaze-related signals one is

led to the 'illogical conclusion that eye motoneurons encode eye-position-in space' (Ling et al., 1999). To counter this objection, it has been argued that the head velocity information carried by burst units does not reach the oculomotor plant because it is offset at the level of extraocular motoneurons by head-related vestibular signals (Cullen and Guitton, 1997b; Sylvestre and Cullen, 2006). The dynamic analysis of the signals carried by our model units provides an alternative, more plausible explanation. Indeed, we were able to demonstrate that the instantaneous discharge (f_{BN_E}) of the BN_E units is best related to eye velocity and is shaped by the LLB (f_{LLB}) and cross-talk (f_{Xtalk}) signals they receive. In more compact form,

$$af_{LLB} - gf_{Xtalk} = f_{BN_E} \propto A\dot{e} \tag{6}$$

where a and g are the gains associated with the LLB and cross-talk signals, respectively, $\dot{e}$ is eye velocity, and A equals 1.2 spikes/deg (determined from the dynamic analysis of the activation function of BN_E units). On the other hand, cross-talk signals can be written as,

$$f_{Xtalk} = B + C\dot{h} + D\ddot{h} \tag{7}$$

where $\dot{h}$ is head velocity, $\ddot{h}$ head acceleration, B is a bias term (equal to 45 spikes/s) and C, D coefficients of proportionality equal to 0.06 spikes/deg and 0.003 spikes/deg/s, respectively (again determined from the dynamic analysis of the cross-talk signals). Also, the discharge of the BN_G units is determined by the discharge of the LLB units they receive input from,

$$f_{BN_G} = \beta f_{LLB} \tag{8}$$

where β is the gain of the connection between LLB and BN_G units. Substituting into Eq. 6 and rearranging, we obtain,

$$f_{BN_G} - g(B + C\dot{h} + D\ddot{h}) \propto A\dot{e} \Rightarrow f_{BN_G} \propto A\dot{e} + g(B + C\dot{h} + D\ddot{h}) \tag{9}$$

It should thus hardly come as a surprise to see the gaze-relatedness of the discharge of BN_G units which, as shown by their dynamic analysis, is related to eye velocity, head velocity and head acceleration. In a similar manner, the discharge of interneurons of the saccadic system could be gaze-related even if they do not receive head-related signals and do not operate within a gaze control

74

loop.

The cross-talk between its head and eye premotor circuits of our model is also largely responsible for the accuracy of the eye-head gaze shifts it generated, as well as for the fact that the contribution of the eyes to such gaze shifts saturates at values that fall far short of the oculomotor range. Further, it accounts for the reduced velocity of the ocular components of large simulated gaze shifts as well as for their twin peaked velocity profiles. The existence of a cross-talk such as the one we employed was experimentally corroborated by Freedman and Quessy (2004) who stimulated electrically the gigantocellular reticular nucleus to evoke head movements unaccompanied by saccades. Then they applied the same stimulus trains soon after the onset of behaviorally conditioned, natural eye-head gaze shifts and demonstrated that during such trains saccadic eye velocity is reduced. The neuronal mechanism underlying such an inhibitory cross-talk remains unknown. In any case, it cannot be implemented directly either by eye-neck reticulospinal neurons in the pons, which are excitatory (Grantyn and Berthoz, 1987), or by the head movement-related burst neurons in the gigantocellular nucleus, which make no connections with preoculomotor structures in the brainstem (Grantyn et al., 1992; Sasaki, 1992).

The eye position sensitivity of head contributions to gaze shifts reflects the influence of the oculomotor neural integrator upon the HC units of our model. The existence of a processing step that is sensitive to the initial position of the eyes and intervenes between the SC and neck motoneurons is consistent with the position sensitivity of the phasic responses of feline (Hadjidimitrakis et al., 2007) and primate (Corneil et al., 2002) neck muscles to electrical stimulation of the SC. The intensity of the bursts of eye-neck reticulospinal neurons accompanying ipsiversive saccades and activation of the ipsilateral neck muscles of head-fixed cats has been shown to increase when initial eye position is shifting in the same direction (Grantyn and Berthoz, 1987). Anatomical connections of the prepositus hypoglossi nucleus, the site of the horizontal NI, with the pontobulbar reticular formation have also been documented (McCrea and Baker, 1985; Hartwich-Young et al., 1990). These data are suggestive of the neural substrate that could underlie increases in head contributions to gaze shifts starting with the eyes deviated in the direction of the movement.

Comparison to previous models As shown in the first two rows of Table 1, the present model is not the first to account for the accuracy of gaze shifts both head-fixed and head-free. However, existing models rely on different mechanisms to accomplish this. The linear summation hypothesis works because it assumes that the VOR operates normally during rapid gaze shifts thus subtracting from

75

the eye the contribution of the head (Bizzi, 1978). Thus, the sum of eye and head excursions head-free is equal to that of the eyes alone head-fixed. However this can hold only for target eccentricities within the oculomotor range. The gaze control hypothesis assumes that gaze shifts are driven by a gaze controller, i.e., a feedback loop that compares the desired direction of the line of sight to the sum of eye position (re head) and head position (re body). With the head-fixed, the comparator continues to emit an error signal and drive the eyes until the line of sight reaches the target. With the head-free, it is the sum of eye and head position signals on its feedback path that must again equal desired gaze direction before the comparator is silenced (Guitton et al., 1990; Tomlinson, 1990; Prsa and Galiana, 2007). Both Freedman's (2001) and the present model work because the cross-talk that connects their head and eye premotor circuits, subtracts from the latter a signal proportional to the contribution of the head.

	Experimental Data	Gaze Feedback Control		Independent Eye-Head Control		
		Tomlinson	Guitton et al.	Bizzi et al.	Freedman	Present
1	Accuracy (<OMR)	Y	Y	Y	Y	Y
2	Accuracy (>OMR)	Y	Y	N	Y	Y
3	Main sequence	Y*	N*	Y*	Y	Y
4	Eye velocity profiles				Y	Y
5	Amplitude-Duration	N*	N*	N*	Y	Y
6	Position invariance of Amplitude-Duration				N	Y
7	Eye saturation	Y*	by assumption		Y	Y
8	ΔH of small ΔG	N*	N*		by assumption	Y
9	ΔE & $\Delta H = f(E_1)$	N*	N*	N*	by assumption	Y
10	ΔE stim. SC = $f(E_1)$	N*	N*	N*	by assumption	Y
11	Gaze/Eye bursters	Y	N	Y	N	Y

Table 1: Point by point comparison of eye-head models. 1. Identical gaze shift precision with the head fixed and the head free for targets within the OMR. 2. Identical gaze shift precision with the head fixed and the head free for targets beyond the OMR. 3. Peak eye and gaze velocity reduction for gaze shifts larger than $30°$. 4. Two-peaked eye velocity profiles. 5. The slope of the amplitude-duration relationship is steeper for head-free gaze shifts than for head fixed saccades. 6. The slope of the amplitude-duration relationship is invariant with respect to the starting position of the eyes. 7. Eye position saturation for larger gaze shift amplitude (<30-40°). 8. Size of head contribution to small amplitude gaze shift. 9. Eye amplitude and head contribution depends on initial eye position. 10. Eye position sensitivity of saccades evoked in response to electrical stimulation of the Superior Colliculus. 11. Presence of gaze-related and eye-related burst neurons. (Y) Model prediction consistent with experimental data. (N) Model not consistent with experimental data. (*) The experimental result was not explicitly simulated but should be (Y*) or cannot be (N*) explained by the model.

Guitton's version of the gaze control hypothesis cannot account for the slower velocity of head-free saccades because the head-related part of the circuit does not interact with its eye-related part during eye-head gaze shifts. The remaining models considered in row 3 of Table I invoke different mechanisms to account for the fact that head-free saccades are smaller and slower (Bizzi, 1981; Tomlinson and Bahra, 1986a; Freedman and Sparks, 1997) than head-fixed ones of the same amplitude. The linear summation hypothesis relies on a VOR that operates at a gain almost equal to 1 during the entire gaze shift (Bizzi, 1978). In order not to violate the persaccadic suppres-

sion of the VOR, the output of the semicircular canals is subtracted from the burst generators in a later version of the model (Whittington et al., 1984). Both Freedman's and the present model use cross-talk between their head and eye controlling circuits. This also allows them to replicate the two-peaked velocity profiles of sufficiently large gaze shifts observed in the monkey (Phillips et al., 1995; Freedman and Sparks, 1997). The linear summation model cannot account for the steeper slope of the amplitude-duration relation of primate head-free gaze shifts (Phillips et al., 1995) when compared to that of head-fixed saccades in the same animals (Table I, row 5) and neither can Tomlinson's and Guitton's models. The same is true of Phillips' model because in it the cross-talk signal is subtracted only from BN_E units (Phillips et al., 1995). Our model reproduces this phenomenon, because it assumes that cross-talk signals are subtracted from its RI units as well, thus forcing them to work longer to silence LLB units. Freedman's model also works due to the multiplicative cross-talk that its head controller uses to influence the BG (Freedman, 2001). However, precisely because of its multiplicative cross-talk, this model leads to erroneous predictions, namely that the duration of gaze shifts should increase when head contribution increases due to the deviation of initial eye position in the direction of the movement (Table I, row 6). Instead, as shown in Fig. 13 of Freedman and Sparks (1997a), the contribution of the head to gaze shifts of the same amplitude can increase by 100% depending on whether the eyes start $30°$ or $10°$ away from the direction of the movement without affecting in the least the duration of the gaze shift. In contrast, our model accurately predicts the initial eye position invariance of gaze durations despite large changes in the size of head contributions to these shifts (Fig. 9).

The models considered in Table I display mixed results when it comes to accounting for changes in the contribution of the eyes and the head that depend on the size of the gaze shift (rows 7 and 8). Guitton's model employs a saturating nonlinearity (e.g., the SAT box of Fig. 11 in Guitton et al. 1990) to constrain saccade size to some small value, certainly smaller than the oculomotor range of the animal. In contrast, the saturation of saccade sizes is an emergent property of both the present and Freedman's models and, in both, this is due to the cross-talk between their head and eye premotor circuits. It is also an emergent property of Tomlinson's model, because it employs a cross-talk signal (the ungated VOR path) in addition to the saturating nonlinearity on its eye burst-neurons. The present model may be the only one to account for the fact that the head contributes little to small gaze shifts (Table I, row 8) by assuming weaker projections (i.e., small values of k_2) of the rostral SC to head-moving circuits which must also overcome the inhibition of cOPNs. Freedman's model

77

replicates this finding only by assumption (Eq. 1 of Freedman 2001). In contrast, a recent version of the gaze feedback hypothesis (Prsa and Galiana, 2007) fails completely, because the head is driven by an amplified replica of the signal driving the eyes and the added gaze motor error signal is negligible.

Our model is also the only one of Table I to account for the fact that the relative contributions of the eyes and the head to gaze shifts of a certain size depend on the initial position of the eyes (row 9). The same is true of the position sensitivity of saccades evoked in response to the electrical stimulation of the SC (Table I, row 10). Both are due to the modulation of head commands with signals from the oculomotor neural integrator as well as the cross-talk between its head and eye circuits. Freedman's model also generates position sensitive contributions but it does so only by assumption (Eqs. 2, 3 of Freedman 2001).

Models of eye-head coordination also differ in terms of the role they assign to saccade- and gaze-related burst neurons found in the brain stem (Table I, row 11). As already discussed in the previous section, the linear regression line between the N_B of eye-related cells and movement size is the same for saccades whether head-free or head-fixed, whereas N_B and the size of head-fixed saccades is closer to that of head-free gaze shifts rather than head-free saccades in the case of gaze-related cells (Whittington et al., 1984). The linear summation hypothesis accommodates both of these cell classes in that it assumes that the saccade-related cells receive the output of the gaze-related cells after vestibular signals have been subtracted from it (Fig. 8 of Whittington et al. 1984). The same wiring is employed in Tomlinson's model (Fig. 14 of Tomlinson 1990). On the other hand proponents of gaze feedback control have repeatedly argued that the whole saccadic system uses gaze (rather than eye) coordinates (Guitton et al., 1990; Prsa and Galiana, 2007) and thus assume the existence of a single burst neuron type, gaze-related neurons. Freedman's model (Freedman, 2001) does not explicitly use gaze- and eye-related burst neurons unlike the model of Phillips et al. (1995) which employs several classes including eye- and gaze-related ones. However, instead of reflecting the operation of the local loop of the saccadic system, as is the case in the present model, the gaze-related units of Phillips model (1995) compare desired gaze direction to actual gaze direction to compute gaze motor error. The present model assumes that eye-related burst neurons are influenced by the cross-talk from the head premotor circuit and in turn contact extraocular motoneurons whereas gaze-related cells do not. Moreover, the dynamic analysis of their signals demonstrated that small changes in their connections would allow interneurons of the saccadic system to display gaze-related discharges even if they do not receive head-related signals and do not operate within a gaze control loop.

5 Acknowledgements

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Chapter 4

Concluding remarks

This thesis provides a unified framework of eye-head motor coordination. Computational analysis of gaze shifting was undertaken with the help of optimal control theory to investigate the internal constraints that are imposed on the nervous system during motor planning of coordinated eye-head movements. Our results suggest that head-fixed saccades (one degree-of-freedom) *and* head-free gaze shifts (two degree-of-freedom) maintain a balance between effort and movement duration. Moreover, head-free gaze shifts exploit a trade-off between inertial forces encountered with the head movement and extraocular tension caused by the viscoelastic forces exerted on the eye. By incorporating these criteria into our optimal control model, we were able to simulate realistic eye-head gaze shifts that are in good agreement with known psychophysics. This, however, is not a surprising conclusion. Even though it might seem far-fetched to expect such a simple concept to give rise to a rich variety of behavioral observations, with hindsight such an energy-based principle would appear natural for a physical system such as the eye-head motor system which must execute over a million saccades/gaze shifts a day. For this reason, muscle tension, energy dissipation due to inertial effects, and movement duration are all factors which the nervous system seems to minimize when planning the reorientation of our line of sight in space.

An enormous amount of data has been collected over the past few decades through continuous experimentation on head-free primates and other animals during eye-head coordination. Often, data collected from one research team contradicts data collected from another research team. Unfortunately, this leads to misinterpretations or even worse multiple interpretations of the same data inevitably causing confusion in the literature. The need to formulate plausible computational models is crucial in this field so that the data is organized in a solid and unique framework. A fundamental question that has bothered the oculomotor community from the early 80's is to fully understand the architecture of the neural machinery that is responsible for gaze shift accuracy. This has led

to controversy regarding their neural control: does the brain implement a gaze feedback loop or does it independently control gaze shifts by exploiting localized eye and head control loops? This is not as trivial as it might appear. If we can not agree on the neural control of gaze shifts after spending several decades collecting relevant data, the prospects for understanding higher level processes such as attention or emotion are slim. Both of the afore mentioned gaze control schemes are efference-based with the gaze feedback one relying on a large communication loop that controls both eye and head segments simultaneously, while the independent eye and head control scheme assumes separate local loops that communicate information to each other downstream. The former can be viewed as a *direct* version of an end-effector controller, while the latter as an *indirect* one. In this thesis, we adopted a systems-based control-theoretic approach to demonstrate how an independent eye-head control strategy that uses inhibitory crosstalk from the head controller to the eye controller can realistically reproduce the vast majority of the available data that has been recorded during eye-head coordination experimentation and published over the period of several years. This model is particularly appealing because it is simple with straightforward computations and involves a small number of assumptions along with a set of predictions that can be experimentally tested to examine the model's plausibility. The fact that such quantitative models, as the herein proposed one, can incorporate anatomical and physiological constraints, they have the potential to provide a step forward in elucidating the mechanisms that underlie this phenomenon by going beyond simple correlation studies and proposing explicit causal and plausible neural mechanisms (Fetz 1992).

An unexpected result of our simulations property of our simulations is that both our neural control model and our optimal control model are consistent with each other even though they radically differ in terms of assumptions. One notices the high degree of similarity between the patterns of the eye and head motor commands inferred by the optimal control model to those which are generated by simulating our neural network model (Fig. 5 of Section 2.4). It appears that the neural network modeling approach agrees well with the optimal control modeling at the level of the motor neurons. This is a nodal point for both modeling approaches especially since it is these neurons that provide the interface between brain and body. We conclude that minimum-effort is the movement organization principle of eye-head coordination which is implemented by the brain using a crosstalk mechanism between head and eye motor pattern generators.

Chapter 5

Complementary Journal and Conference Publications

This last section of the thesis consists of a collection of three relevant manuscripts:

1) The first article is titled 'Implications of interrupted eye-head gaze shifts for resettable integrator reset' by A. A. Kardamakis and A. K. Moschovakis was published in 'Brain Research Bulletin' (Vol. 70 in 2006, p. 171-178). The target of this article was to investigate the role of saccade-related units when subjects are engaged in gaze shifts that are interrupted in mid-flight. Psychophysicists often take advantage of this target-distractor paradigm in hope to better understand the neural control of gaze shifts. In fact, the claim was originally made that if the brain were to adopt a saccade burst generator that used displacement information (see Section 3.2) rather than position, then it would not account for the fact that mid-flight gaze shifts are accurate. The claim was based on the argument that residual signals present in the resettable integrator units (which are mandatory for displacement class of SBG) would be a source of inaccuracy during target acquisition with interrupted gaze shifts. We created a gaze control model to investigate if the activation functions of our RI units interfere in any way with the accuracy of movement to such targets. Our paper provides disproof of this claim by counterexample through neural network simulations of our gaze control model.

2) This is a one-page conference abstract of a paper presented in the Computational and Systems Neuroscience (Cosyne) annual meeting that took place in Salt Lake City, Utah (28 Feb - 2 Mar, 2008). It describes a preliminary version of work shown in Section 2.4 of this thesis and is titled 'Eye-head coordination obeys minimum-effort rule'.

3) This is another one-page conference abstract that was published in the Society of Neuroscience Abstracts after the 38th annual meeting that took place in Washington D.C. (Nov. 15 - 19, 2008). This is a preliminary version of our neural network gaze control model described in Section 3.4 of this thesis and is titled 'A new model of primate eye-head gaze shifts'.

Implications of interrupted eye-head gaze shifts for resettable integrator reset

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Abstract

The neural circuit responsible for saccadic eye movements is generally thought to resemble a closed loop controller. Several models of the saccadic system assume that the feedback signal of such a controller is an efference copy of "eye displacement", a neural estimate of the distance already travelled by the eyes, provided by the so-called "resettable integrator" (RI). The speed, with which the RI is reset, is thought to be fast or instantaneous by some authors and gradual by others. To examine this issue, psychophysicists have taken advantage of the target-distractor paradigm. Subjects engaged in it, are asked to look to only one of two stimuli (the "target") and not to a distractor presented in the diametrically opposite location and they often generate movement sequences in which a gaze shift towards the "distractor" is followed by a second gaze shift to the "target". The fact that the second movement is not systematically erroneous even when very short time intervals (about 5 ms) separate it from the first movement has been used to question the verisimilitude of gradual RI reset. To explore this matter we used a saccade-generating network that relies on a RI coupled to a head controller and a model of the rotational vestibulo-ocular reflex. An analysis of the activation functions of model units provides disproof by counterexample: "targets" can be accurately acquired even when the RI of the saccadic burst generator is not reset at all after the end of the first, interrupted eye-head gaze shift to the distractor and prior to the second, complete eye-head gaze shift to the "target".
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Keywords: Saccades; Oculomotor system; Burst generator; Computational model

1. Introduction

Rapid shifts of the line of sight (gaze shifts) are often accomplished with rapid displacements of the eyes (saccades) with respect to the head accompanied by movements of the head with respect to the body. The execution of rapid gaze shifts is due, at least in part, to the activation of a layered midbrain nucleus, the superior colliculus (SC). Electrical stimulation of its deeper layers produces combinations of eye and head movements in the cat [11,36] and the monkey [5,9]. Also, the discharge of primate SC movement cells encodes the amplitude of gaze shifts rather than their eye or head components at least in the caudal SC [7]. Desired gaze shift commands are presumably decomposed downstream of the SC into separate commands to eye and head movers. While information about the response properties and connections of neurons that intervene between the SC and

neck motoneurons is at present rather sketchy, there is considerable information about the neurons intervening between the SC and the extraocular motoneurons [32]. Of particular importance for the purposes of the present report are the burst generators of the saccadic system. These neural circuits are responsible for generating the transient discharges of extraocular motoneurons (MNs) that accompany saccades [14] and are made of several classes of neurons. Their output is conveyed to MNs by cells that display a brief burst of discharge before saccades of particular directions, the medium lead burst neurons (MLBNs, [45,30]). Other neurons also emit bursts of discharge before saccades of particular directions but their latency is longer (long-lead burst neurons—LLBNs, [23]) and still others pause during saccades of all directions (OPNs, [19]). In general, the parameters of discharge of the neurons that comprise the burst generators bear a close relationship to the metrical and often the dynamical characteristics of the saccades they accompany [16].

Following the neurophysiological and psychophysical demonstration that saccades can be modified in mid-flight [49,20], burst generators have been generally thought to resem-

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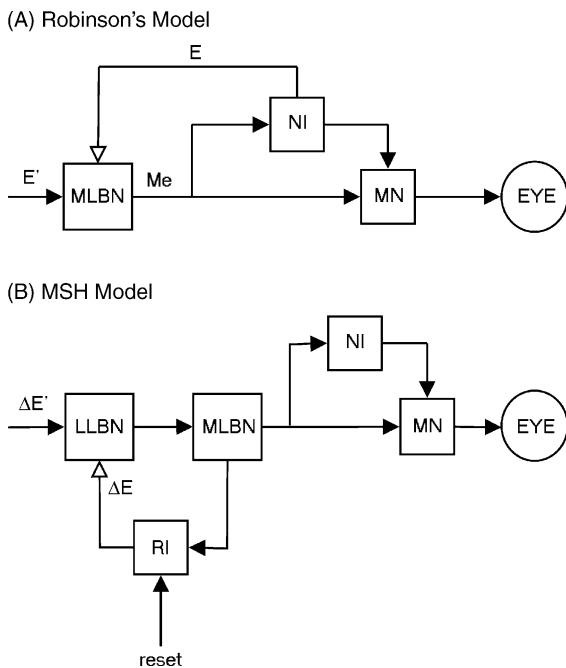
(A) Robinson's Model

(B) MSH Model

Fig. 1. Schematic illustration of the flow of information in Robinson's (A) and the MSH (B) model of the burst generator. Solid and open arrowheads indicate excitatory and inhibitory connections, respectively. Abbreviations: ΔE, eye displacement; $\Delta E'$, desired eye displacement; E, eye position; E', desired eye position; LLBN, long-lead burst neuron; MLBN, medium lead burst neuron; Me, motor error; MN, motoneuron; NI, neural integrator; RI, resettable integrator.

ble closed loop controllers. The feedback loop of such a controller automatically adjusts the intensity and the duration of MLBN bursts to fit the size of the saccades they accompany thus obviating the need to preprogram them. This requirement is rather permissive in that there are several ways to connect known saccade related cells into a closed loop saccadic burst generator [25]. For example, the early model of Robinson [39] illustrated in Fig. 1A assumes that MLBNs compare an internal feedback signal of eye position (E; supplied by the neural integrator, a neural network that integrates the bursts of MLBs to generate the sustained, eye position related discharges encountered in MNs during intersaccadic intervals) to a command signal of desired eye position (E'; equal to target position in space presumably originating in higher order structures). The instantaneous difference between E' and E can be thought of as a motor error (Me) signal which drives MLBNs until E matches E', the bursts stop and the eyes are on target.

To obviate the need for eye position feedback, later models assumed that it is a signal proportional to eye displacement (ΔE) that is fed back to the comparator to automatically adjust the intensity and duration of MLB bursts [18]. This created the need for a displacement integrator that would estimate the instantaneous displacement of the eyes and would be automatically reset at the end of each saccade. To address these issues, Moschovakis [25] proposed a model (MSH) that uses a copy of the output of its comparator (the LLBNs) to feed a resettable integrator (RI) that then projects back to LLBNs (Fig. 1B). When the estimate of distance travelled (the instantaneous value of the signal carrier by the RI) equals the desired eye displacement signal ($\Delta E'$)

presumably sent to LLBNs by higher order structures, LLBNs and MLBNs stop discharging and the eyes land on target.

The speed with which the RI is reset to zero has been the subject of some debate. For example, the first computer model of a burst generator to employ a resettable integrator assumed that the RI resets because of the inhibitory projections it receives from OPNs [25]. Because OPNs quickly reach presaccadic levels of discharge when they resume firing, this model's RI was reset almost instantaneously. The consequences of employing a gradually resetting RI have also been explored after assuming that the RI is a "leaky" integrator [25]. Besides making the activation function of RI units resemble more closely the discharge pattern of the neurons that could play this role [31], use of a leaky RI would render the "active" OPN-based resetting mechanism redundant, in particular if the time constant (T) of the RI is short enough. In the absence of a fast resetting mechanism, one would expect saccade size to be influenced by preceding saccades in particular for intersaccadic intervals that are insufficiently long ($<3T$) to allow for complete decay of the RI signal. Because such closely spaced gaze shifts do not constitute a sizable fraction of the normal gaze shifts of humans and other animals, the target-distractor paradigm has been used to elicit them more frequently and address the issue of instantaneous versus gradual RI reset [4]. In this paradigm subjects are instructed to look to only one of two stimuli (the "target") and not to a distractor presented in the diametrically opposite location. While attempting to comply with the instruction, subjects sometimes generate a movement sequence in which the first gaze shift is in the direction of the "distractor" followed by a second gaze shift to the "target". In such cases, the second movement is not systematically erroneous even when very short time intervals (as short as 5 ms) separate it from the first movement [4]. On the basis of these results, the validity and existence of a gradually resetting displacement integrator in the gaze shifting system was questioned [4]. Here, we disprove this claim by using an extension of the MSH model to simulate closely spaced eye-head gaze shifts such as those generated in the target-distractor experiments. We demonstrate that "targets" can be accurately acquired in simulations of target-distractor experiments even if RI units are not reset at all until after the second gaze shift (to the target) reaches completion.

2. Methods

Fig. 2, is a block diagram of the ipsiversive half of the one-dimensional, two-directional neural network we simulated. Its top part is an expanded version of the MSH model whose units and the connections they establish have been described in detail before [25]. Briefly, the front stage of the MSH burst generator is the long-lead burst (LLBN) unit that receives a desired eye displacement command from the superior colliculus (SC). LLBNs integrate (positive feedback) the difference between the inputs they receive from the SC and the feedback they receive from the resettable integrator (RI) and contact both the MLBN units and the RI. The short loop through RI units bi-directionally connected with LLBNs is the characteristic feature of the MSH model and is consistent with the axonal terminations of putative upward RI units [31] and the location of upward LLBNs [2,34]. Consistent with their axonal terminations in the monkey [45,46,33,31], the excitatory (EBNs) and inhibitory (IBNs) MLBN units are shown to project to ipsilateral and contralateral motoneurons (MNs), respectively, both directly and through a neural integrator (NI). Similar evidence [45,15,32] supports the existence of EBN projections to OPNs through sign inverting local circuit neu-
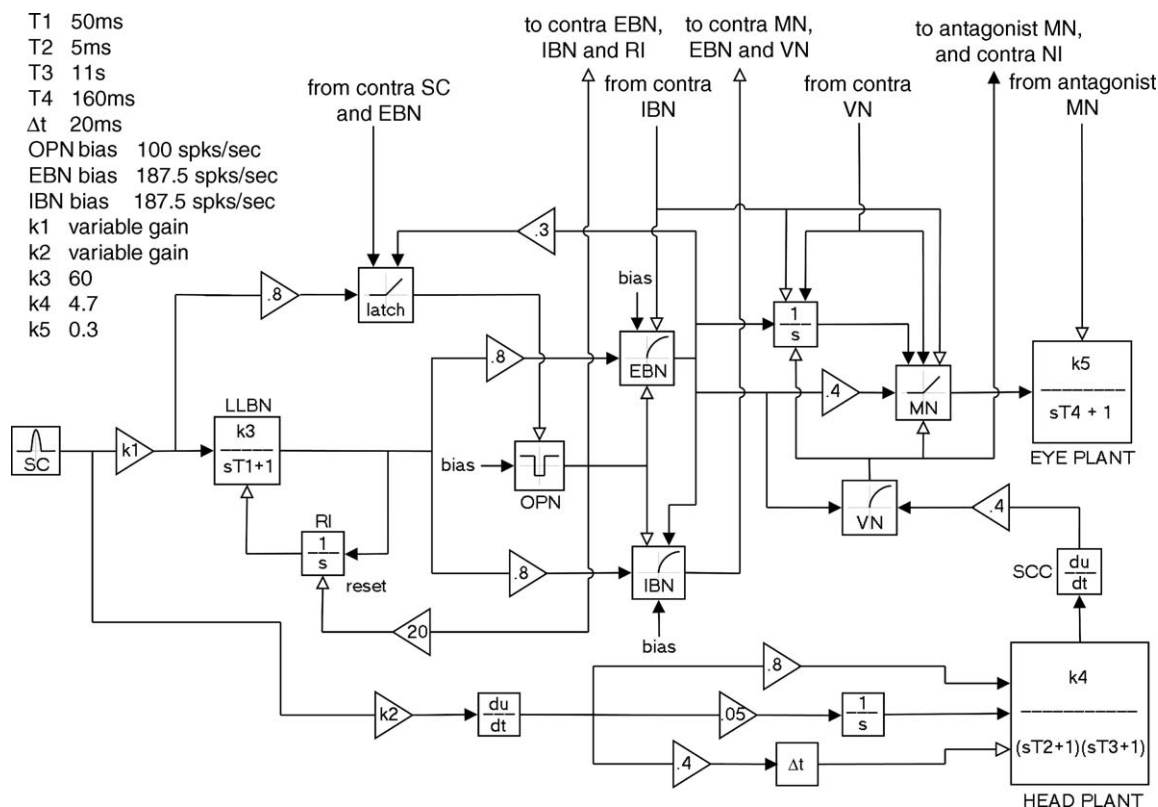
Fig. 2. Block diagrammatic illustration of the model we simulated. Abbreviations: EBN, excitatory burst neuron; IBN, inhibitory burst neuron; OPN, omni-pause neurons; SC, superior colliculus; SCC, semicircular canal; VN, vestibular nuclei. Other abbreviations and symbols as in Fig. 1.

rons (the "latch" unit of Fig. 2). Also in agreement with known anatomy [3,22], OPNs are shown to inhibit the MLBNs and the RI.

To obtain two-directional gaze shifts, we replicated this circuit to obtain contraversive saccades and connected the two sides of the brain via axons of IBNs and OPNs (contacting the targets indicated in Fig. 2). We also added a head controller and supplied it with a replica of the commands sent to the burst generator. Given the dearth of information regarding the discharge pattern and connections of relevant neurons the head controller is the most speculative portion of our model. Nevertheless, our assumptions regarding this part of the gaze shifting circuit are rather minimal. Firstly, we assumed that it is a differentiator that transforms the input it receives into a biphasic signal, the two phases of which correspond to the "action" and "braking" pulses encountered in electromyography records from neck muscles [13]. After separate amplification they were sent to motoneurons innervating muscles with a pulling direction similar (agonists) or opposite (antagonists) to that of the movement, respectively. In this manner, the SC signal was converted into the torque signals needed to accelerate (through agonist motoneurons) and decelerate (through antagonist motoneurons) the head plant, a second order system such as previously used to model movements of the head [6]. Our model also includes a vestibulo-ocular reflex (VOR) to generate eye movements equal in amplitude and opposite in direction to those of the head and thus stabilize the visual world on the retina during head movements. To this end, we lumped the semicircular canals and the primary vestibular afferents into a single unit that differentiates the head position signal and projects to the vestibular nuclei (VN). We also lumped type I and II units into the VN unit of our model. Consistent with presently available evidence (reviewed in [46]) type II units receive input from the BG and inhibit type I units. In turn, type I units receive input from the semicircular canals and send excitatory projections to the contralateral, and inhibitory projections to the ipsilateral, extraocular MNs. Because their activity is gated by the output of the burst generators these units pause during saccades. Since we made no effort to have them interact with the NI, the secondary vestibular units of our model carry no eye position information and thus, strictly speaking, cannot be thought of as the position-vestibular-pause (PVP) neurons [24]. Instead, they resemble

vestibular-pause (VP) neurons [48]. They carry a head velocity signal except during saccades, and thus the gain of the VOR of our eye–head model is 0 during saccades and 1 at all other times.

Numerical experiments were carried out using Simulink version 6.0 (The MathWorks Inc.) on a Pentium IV personal computer with a clock frequency of 2.8 GHz. All numerical experiments simulations were left to run for 1 s with a time step of 0.12 ms. Nevertheless, other time steps were tried (1.0–0.1 ms) and produced identical results. The oculomotor plant we used is a single pole model of the eye and orbital tissues with a time constant of 160 ms [40]. The time constant of the integrators was assumed to be infinite (perfect integrators). With the exception of these and the oculomotor plant, the impulse response of all units was a Dirac δ function. In addition, their input–output characteristic was non-linear. A threshold equal to zero ensured that negative firing frequencies were cut-off. Except for the LLBNs and saturating units, the input–output characteristic of the units we simulated was linear. Consistent with known physiology, LLBN and EBN units were set to saturate at frequencies <1100 Hz [32] and the primary vestibular afferents at 300 Hz [38].

3. Results

Fig. 3 provides examples of the time course of leftward and rightward gaze shifts generated by our model. The left column (Fig. 3A), illustrates an 80° leftward gaze shift (top) composed of a 60° saccade (middle) and a 20° head movement (bottom; measured at the end of the gaze shift) following activation of the right SC. After the end of the rapid eye movement, gaze is stabilized onto the stationary target (Fig. 3A, top) despite the fact that the head continues to move. Gaze stabilization is due to the engagement of the vestibulo-ocular reflex (VOR); because its gain was assumed equal to 1 before and after saccades, it generated eye movements of the same
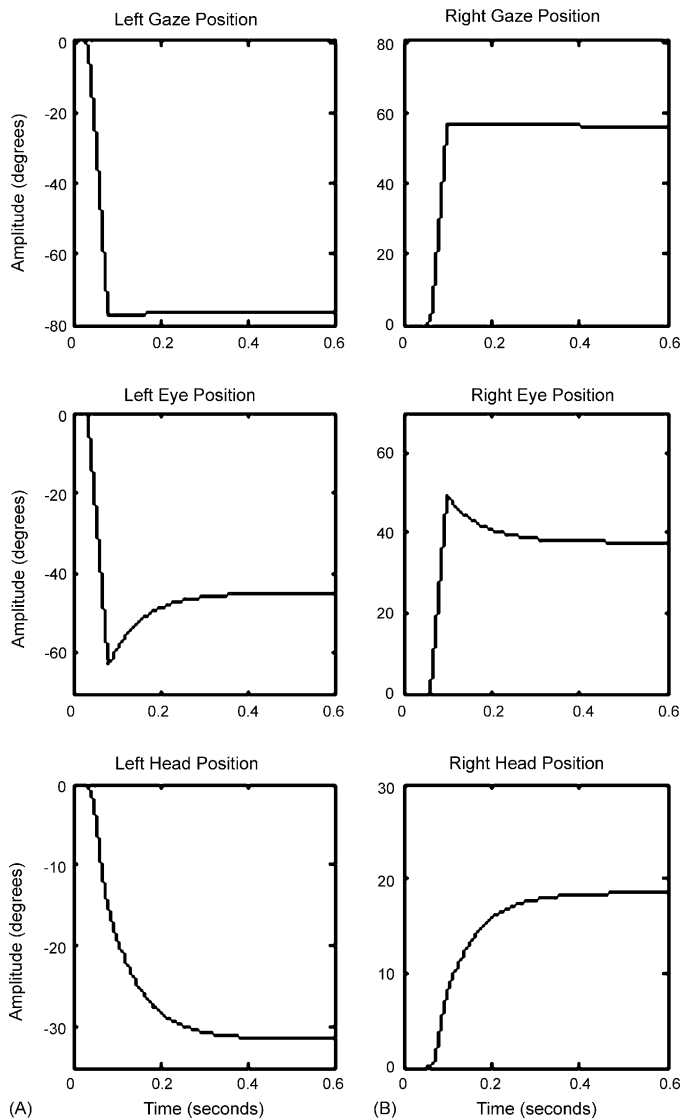
Fig. 3. Simulated eye-head gaze shifts to the left (A) and to the right (B). Panels from top to bottom illustrate instantaneous gaze, eye and head position, respectively.

velocity and opposite in direction to the continuing head movements.

Consistent with known neurophysiology, activation of SC units progressively more distant from the rostral edge of the SC led to progressively bigger gaze shifts [9]. We parametrized our model in such a way that activation of neighboring SC units led to the generation of gaze shifts that differed by about $7.5°$. Also consistent with neurophysiology [44], we did not assume that neurons preferring bigger gaze shifts display higher maximal frequency or longer discharge duration. In fact, we made the simplifying assumption that all SC units display the same bell-shaped frequency profile (Fig. 2, SC) irrespective of the size of the movement evoked when they are activated. We also assumed that the gains k_1 and k_2 (Fig. 2) of the connections between SC units and their targets increase or decrease together with the size of the movements they prefer. For example, Fig. 3B illustrates a $60°$ rightward gaze shift composed of a $50°$ eye displacement

and a $10°$ head displacement (again measured at the end of the gaze shift) which was evoked after activating a unit with gains k_1 and k_2 that were lower by 25% when compared to those of the unit responsible for the movement shown in Fig. 3A. The notion that the strength of connections between SC neurons and their targets is proportional to the size of the movements that the cells prefer has been used before to model the spatiotemporal transformation (STT) of the output of the SC (where desired eye displacement is place coded) into the rate code that is used by LLBNs [42,25]. It is also consistent with known neuroanatomy at least as concerns SC projections to the saccadic burst generator in the paramedian pontine reticular formation [29]. Here, we assumed that such a mapping device also applies to SC projections to the head controller. The latter was endowed with rather rudimentary processing power; in particular, it could not convert input signals of higher frequency into output signals of longer duration.

The movements illustrated in Fig. 3 are typical of the gaze shifts generated by our model and will be used to illustrate how it behaves during "interrupted" eye-head gaze shifts. Let us assume that two targets appear simultaneously, the first one $80°$ to the left and the second $20°$ to the right of straight-ahead. Had the first target appeared in isolation, activation of the right SC would evoke a completed gaze shift such as that of Fig. 3A leading to accurate target acquisition. However, the appearance of the second target $20°$ to the right of straight-ahead is presumably responsible for the interruption of the first gaze shift. To compensate for the excursion of the line of sight by $35°$ due to the first, interrupted movement, we assumed that the second command issuing from the left SC with a delay equal to 20 ms would dictate a gaze shift of $55°$ ($20° + 35°$). This second command cancels the first one, truncates the first leftward movement and generates a second rightward gaze shift roughly similar that of Fig. 3B directing the line of sight to the second target (Fig. 4A). As argued in the Section 4 (below), the point of our simulations is not to examine how and where commands issuing from the ipsilateral and contralateral SC interact with each other such that the first command is cancelled in mid-flight. Instead, it is to examine the signals carried by the resettable integrators and whether they interfere with the accuracy of gaze shifts in particular when these are closely spaced in time. As shown in Fig. 2, the RI units are assumed to work as perfect integrators (with infinite time constants) and to integrate the output of the long-lead burst neurons (to provide a neural estimate of actual eye displacement). Taking into consideration its transfer function and the inputs it receives, the instantaneous firing rate (f; in spikes/s) of the rightward RI unit of our model, as a function of time, is described by the expression:

$$f_{RI_r}(t) = + \left\langle \alpha \int f_{LLB_r}(t)\,dt - \beta f_{OPN}(t) \right\rangle \tag{1}$$

where $f_{LLB_r}(t)$ is the activation function of the ipsilateral LLB unit, $f_{OPN}(t)$ the activation function of the OPN unit, $+\langle\ \rangle$ indicates that only non-negative values of the argument are passed at the output of the unit and α, β are gains. Similarly, the instantaneous firing rate of the leftward RI unit of our model is described
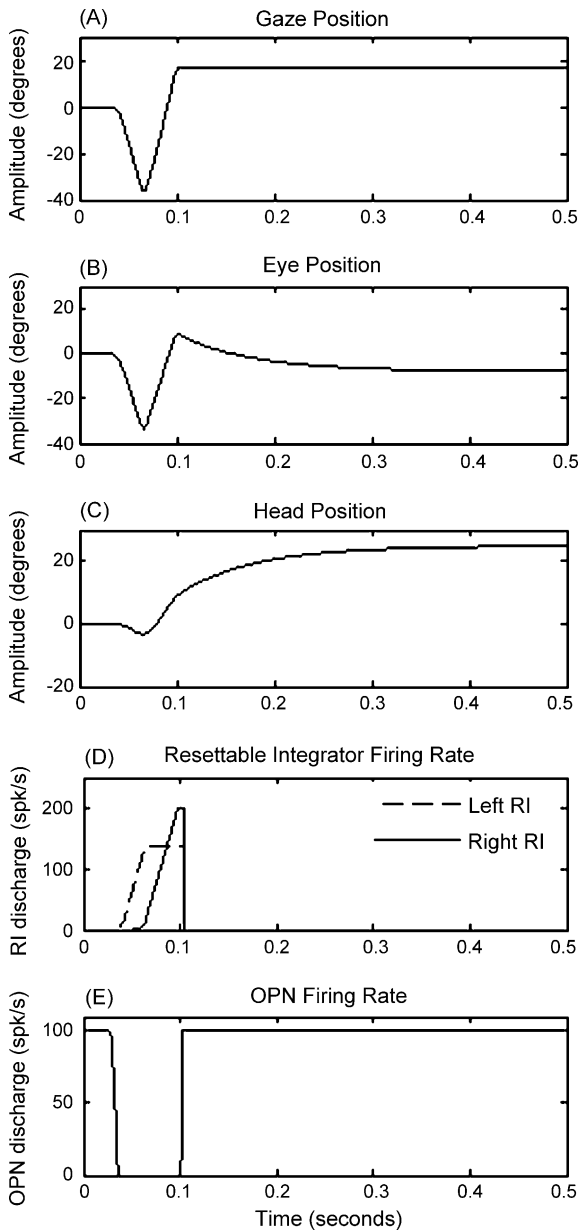
Fig. 4. Simulated leftward gaze shift that was interrupted in mid-flight and the line of sight redirected to the right. The top three traces illustrate instantaneous eye, head and gaze position, respectively. The bottom two traces illustrate the signals carried by the left (solid) and right (stippled) RI units and the OPNs.

by the expression:

$$f_{\mathrm{RI}_\mathrm{l}}(t) = + \left\langle \alpha \int f_{\mathrm{LLB}_\mathrm{l}}(t)\,\mathrm{d}t - \beta f_{\mathrm{OPN}}(t) \right\rangle \qquad (2)$$

LLBN units (f_{LLB}) integrate the difference between the input from the SC (f_{SC}) and the output from the RI units (f_{RI}), with a time constant T_1 of 50 ms. Omni-pause (OPN) units receive bilateral input from EBNs and the SC via the 'latch units'. Because the gain of the latter is 1, the activation function of OPNs (f_{OPN}) can be simply expressed as

$$f_{\mathrm{OPN}}(t) = + \langle \mathrm{BIAS} - (f_{\mathrm{SC}_\mathrm{r}}(t) + f_{\mathrm{SC}_\mathrm{l}}(t) + f_{\mathrm{EBN}_\mathrm{r}}(t)$$
$$+ f_{\mathrm{EBN}_\mathrm{l}}(t)) \rangle \qquad (3)$$

where $f_{\mathrm{SC}_\mathrm{r}}(t)$ is the activation function of the right SC (which controls leftward gaze shifts) and $f_{\mathrm{SC}_\mathrm{l}}(t)$ is the activation function of the left SC (which controls rightward gaze shifts). The sum of the activation functions of the right ($f_{\mathrm{EBN}_\mathrm{r}}$) and left ($f_{\mathrm{EBN}_\mathrm{l}}$) EBNs operates simply as a gate that determines the duration of OPN pauses. The activity of EBNs also governs the accuracy of ipsiversive saccade metrics and is dictated by the activity of ipsilateral LLBNs that is in turn controlled by the 'closed-loop'.

We further define t_l and t_r the onset times of a leftward and a rightward gaze shift, respectively, and Δt_l (Δt_r) the duration of the leftward (rightward) eye saccades which accompany them. The duration of those produced by our model is correlated with their amplitude, ΔE_l and ΔE_r, through amplitude–duration relationships similar to that found in primates (not shown). For $t_\mathrm{l} < t < t_\mathrm{l} + \Delta t_\mathrm{l}$, $f_{\mathrm{EBN}_\mathrm{l}}(t) > 0$ (leftward gaze shift) and for $t_\mathrm{r} < t < t_\mathrm{r} + \Delta t_\mathrm{r}$, $f_{\mathrm{EBN}_\mathrm{r}}(t) > 0$ (rightward gaze shift), and since the negative sum in Eq. (3) is greater than the bias, $f_{\mathrm{OPN}}(t) = 0$ and thus Eqs. (1) and (2) are dominated by the activation functions of LLBNs. When $t = t_\mathrm{l} + \Delta t_\mathrm{l}$, $f_{\mathrm{EBN}_\mathrm{l}}(t)$ becomes zero and the same is true of $f_{\mathrm{EBN}_\mathrm{r}}(t)$ when $t = t_\mathrm{r} + \Delta t_\mathrm{r}$. Because of the descent of $f_{\mathrm{SC}_\mathrm{l}}(t)$ and $f_{\mathrm{SC}_\mathrm{r}}(t)$, which occurs in parallel, the activation of OPNs increases towards the bias (Eq. (3)). Because of the large value of the gain β, Eqs. (1) and (2) are dominated by the second term of their right hand side and the RI is reset instantaneously.

Neurally programmed gaze shifts are completed when there is enough time for each of them to reach its respective target (i.e., for $t_\mathrm{r} > t_\mathrm{l} + \Delta t_\mathrm{l}$, when, for example, a leftward gaze shift is followed by a rightward one). In cases such as this, the actual gaze shifts, ΔG_l and ΔG_r equal the desired gaze shifts ($\Delta G'_\mathrm{l}$ and $\Delta G'_\mathrm{r}$). If as in the example illustrated in Fig. 4A, the second, rightward gaze shift interrupts the earlier leftward one (i.e., for $t_\mathrm{r} < t_\mathrm{l} + \Delta t_\mathrm{l}$), $f_{\mathrm{SC}_\mathrm{r}}$ is truncated and brought to zero instantaneously (at t_r). As a consequence, ΔG_l is smaller than $\Delta G'_\mathrm{l}$ by an amount that depends on the value of $|t_\mathrm{l} + \Delta t_\mathrm{l} - t_\mathrm{r}|$ (this value is indicative of the proportion of the motor command that passed through the neural network prior to its truncation). The waveforms of both the RI_l and the RI_r units (located in opposite sides of the brain) are shown in Fig. 4D (dashed and solid lines, respectively) for a case such as this. The right RI (RI_r), which participates in the control of the second gaze shift (to the "target"), reaches a peak value that corresponds to the excursion of the eyes that actually took place (from $-35°$ to $+20°$; Fig. 4D, solid). Its contents are cleared (i.e., it is reset) at the end of the rightward (second) saccade due to the inhibitory connection between the OPNs and the RI (Fig. 2) and the fact that OPNs resume firing at the end of the second movement (to the "target"; Fig. 4E).

The activation function of the left RI (RI_l) unit (Fig. 4D, dashed), which participates in the generation of the interrupted gaze command to the "distractor", is more interesting. It has been claimed that in circumstances such as that illustrated in Fig. 4, the gaze shift directed to the "target" should be systematically hypometric unless the resettable integrator is instantaneously reset [4]. Fig. 4 disproves this claim, in that it demonstrates that

the RI_l continues to discharge after the end of the movement to the "distractor" and through the movement to the "target" and yet the latter is accurate. The failure of the RI_l unit of our model to reset upon gaze redirection is due to the fact that the OPNs remain silent (Fig. 4E). This is in turn due to the fact that the second command exiting the SC (f_{SC_l}) increases rapidly obeying a bell-shaped curve. Rather than silence the ongoing tonic discharge of OPNs, as is the case for the similarly shaped f_{SC_r}, the rapid ascent of f_{SC_l} helps maintain the OPNs in a state of inactivation (i.e., in this case Eq. (3) continues to be dominated by the activation of "latch units"—the term in parentheses on the right hand side of Eq. (3)). The RI_l is reset together with the RI_r (in the opposite side of the brain), only after the movement to the target is also complete [$f_{RI_l}(t_r + \Delta t_r) = f_{RI_r}(t_r + \Delta t_r) = 0$] and the OPNs resume firing (Fig. 4E). The fact that RI_l holds a value proportional to the displacement feedback generated during the first leftward gaze shift to the "distractor" does not interfere in the least with the accuracy of the second rightward gaze shift to the "target".

4. Discussion

Our intention is not to present a model that accounts for all facets of eye-head coordination but rather to provide disproof by counter-example. The claim disproved is that because eye-head gaze shifts to a "target" are accurate even when they follow immediately after an interrupted gaze shift to a "distractor" the validity and existence of a gradually resetting displacement integrator in the gaze shifting system is questionable [4]. Our simulations demonstrate that eye-head gaze shifts to a "target" can overlap previous gaze shifts and remain accurate even if the displacement integrator is not reset at all. The reason is that the displacement feedback signals carried by the RI in one side of the brain need not interfere in the least with the accuracy of motor commands prepared by the burst generator located in the opposite side.

Our model is an extension of the MSH model to control eye-head gaze shifts. Accordingly, it inherits its plausibility as regards numerous psychophysical, anatomical, neurophysiological, lesion and microstimulation data [25]. Nevertheless, our model has considerable limitations. Firstly, its head controller is a fairly abstract one and its operation is limited to differentiation and scaling of the signals it receives from the SC. Nor does our model include cross talk from the head to the eye controllers that would enable it to account for the dependence of eye velocity profiles on the size of accompanying head movements [8]. Finally, it does not include proprioceptive input that would allow it to account for the accuracy of gaze shifts following head perturbation experiments [47]. More detailed elaboration of this part of the model will have to wait the collection of additional information about the discharge patterns and projections of the premotoneurons that contact neck MNs. Although it will be important to address these issues in future models of eye-head coordination, they do not affect the ability of our model to simulate "target-distractor" experiments or our conclusions regarding the involvement of the RI in their execution.

The "target" oriented movements that we simulated were in a direction opposite to that of the truncated "distractor" oriented movements that preceded them. Accordingly, we assumed that the two movements are executed in response to commands successively emitted by the two colliculi located in opposite sides of the brain. Further, we assumed that units carrying the SC commands driving the eyes and the head towards the target directly inhibit neurons of the opposite SC carrying commands driving the eyes to the "distractor" thus truncating them. This is consistent with the fact that the dynamics of the gaze, eye and head movements during the first, erroneous movement fit those of gaze shifts that had been programmed for much bigger amplitudes but were truncated [4]. The truncation of distractor oriented movements could be implemented through the well known commissural path that originates from tectal long-lead burst neurons [28] and is consistent with the fact that tectal cells which burst before saccades in one direction are inhibited during saccades in the opposite direction [17,37].

Consistent with the discharge pattern of SC neurons [7] our model assumes that each SC issues commands coding the metrics of gaze shifts contraversive to the activated SC. Although not tested in circumstances identical to the herein simulated ones (i.e., when the line of sight shifts towards a distractor before its redirection to the "target"), this is true even when the line of sight shifts in the interval between presentation of a target and execution of a saccade towards it (e.g., "double-step" stimulation experiments [12]). The neural processes needed to account for the accuracy of saccades in double-step stimulation experiments are thought to be complete by the time commands exit the SC (reviewed in [43,26]) and are therefore beyond the scope of the present model. Suffices to say that a model that is consistent with subject performance and relies on signals indicative of eye displacement rather than eye position has been proposed for the SC in the form of the "vector subtraction hypothesis" [28,26]. Moreover, a biologically plausible neural network model of the vector subtraction hypothesis that makes use of machinery that is known to exist in the SC has been proposed [1]. Its use as a sensorimotor interface in the present model would account, at least in part, for the generation of SC commands that would compensate for the excursion of the eyes due to the interrupted gaze shifts and drive the line of sight to the target.

Our model uses an MSH BG to control the ocular portion of the simulated eye-head gaze shifts and thus assumes that a RI generates the displacement feedback signals its local loop needs to function properly. It also assumes that each BG is endowed with a RI that estimates the instantaneous displacement of the eyes along the cardinal direction that the BG prefers. Taking into consideration the preferred directions of presaccadic neurons it is possible to delineate at least four burst generators in the primate brain [27]: (1) leftward, (2) rightward, (3) upward and (4) downward. The notion that the brain contains separate resettable integrators for each one of these cardinal directions is consistent with presently available evidence. For example, the interstitial nucleus of Cajal is known to contain cells that could embody the downward RI in that they emit bursts of discharge

shortly before the onset of downward saccades and their axonal terminations target the rostral interstitial nucleus of the medial longitudinal fasciculus, an area known to contain long-lead burst neurons [33]. As expected of cells that could embody a unidirectional RI (such as those simulated in the present study), the number of spikes in the bursts of such cells is well correlated to the amplitude of downward, and not upward, saccades [33]. Similarly, the number of spikes in the bursts of neurons that have been found in the nucleus of posterior commissure and could embody the upward RI is well correlated to the amplitude of upward, and not downward, saccades [31]. The existence of RI neurons that prefer a particular cardinal direction and help a BG prepare commands associated with movements in the same direction implies that the signals they carry need not interfere with the commands prepared by another BG for movements in the opposite direction.

Our simulations disprove the claim that the accuracy of closely spaced eye-head gaze shifts in "target-distractor" experiments questions the validity and existence of a gradually resetting displacement integrator in the gaze shifting system [4]. These authors also argued that their results are not "consistent with an alternative proposal of an instantaneous reset of the displacement integrator linked to the end of a saccade" given that the hypometric movements to the distractor "are essentially truncated and hence never reached completion" [4]. The accuracy of the target directed movements we simulated disproves this claim as well, in particular since as expected of Corneil et al. [4] failure to reach movement completion would prevent our model RI units from being reset. In both cases, the accuracy of the simulated movements is due to the fact that the displacement feedback signals carried by the RI in one side of the brain need not interfere in the least with the accuracy of motor commands prepared by the burst generator located in the other side. Although we simulated the RI units as perfect integrators that reset instantaneously as soon as the OPNs resume firing (i.e., at the end of the second movement, to the "target"), the same result would obtain had we used a gradually resetting RI, and for the same reason. Actually, the existence of a gradually resetting mechanism with a time constant roughly equal to 45 ms has been inferred from SC stimulation experiments demonstrating that the size of evoked saccades is an exponentially declining function of the time that elapses from a previous natural saccade [35,21]. However, we do not wish to argue in favor of a gradually resetting mechanism, in particular since there are reasons to doubt that the SC stimulation results elucidate properties of the RI. Firstly, the size of SC evoked saccades depends on the time that elapses from the beginning of a previous natural saccade, and not, as expected of a process that follows the saccade (such as the decay of the RI signal), its end [41]. Also, judging from the accuracy of closely spaced gaze shifts of the same direction that are evoked in "double-step" stimulation experiments and can be separated by intervals as short as 40 ms, the time constant of the resetting mechanism cannot be much longer than about 10 ms [10]. All in all, our modeling study emphasizes the need for caution when neural processes are deduced from psychophysics alone.

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Eye-Head Coordination Obeys Minimal-Effort Rule

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Gaze shifts are combined eye-head movements consisting of coordinated eye saccades and rapid head movements. These two-segment movements have an extra degree of freedom that allows the gaze system additional flexibility when programming eye and head commands for reorienting the line of sight. However, behavioral observations show that the eye and head contributions are systematically constrained in that larger gaze shifts rely on larger head components, whereas smaller ones consist mainly of eye movements. Furthermore, eye contributions do not exceed amplitudes of 30-35° even for gaze shifts as large as 75° and eye velocity profiles are less and less symmetrical as the amplitude of the gaze shifts increases. Optimal control theory suggests that these data could be accounted for if the brain followed the principle of minimal effort to program horizontal gaze shifts. The optimal set of control signals is obtained by relating the dynamics of the controlled eye/head components to the criterion function. The performance objective is to minimize the squared sum of eye/head torque signals, integrated in time for each coordinated movement (minimal-effort). By applying Pontryagin's Maximum Principle, we obtained analytical expressions for eye/head control signals and from these we acquired the optimal trajectories of the eyes and the head by solving the deterministic two-point boundary-value problem. To qualitatively represent extraocular muscle length-tension curves we introduced an eye position-varying weight expressed as a polynomial function. This accounts for the active elastic restoration forces that pull the eye towards the central position. A second weight corresponding to the optimal head control signal was used to express the large inertial difference relative to the eye. In this context, eye/head commands are programmed to follow a performance trade-off between viscoelastic and inertial forces.

Optimal trajectories were obtained for rightward horizontal centripetal and centrifugal gaze shifts ranging from 5° to 75° while initial eye positions varied from 30° to the left to 10° to the right of straight ahead. Our model accurately predicted the amplitude of eye and head components relative to the amplitude of the gaze shifts as well as the fact that ocular movements do not exceed 30°. Furthermore, the model accounts for the quantitative relationships between eye and head contributions as a function of initial eye positions. The head contributed progressively less (and the eyes more) to gaze shifts of the same size as initial eye position deviated further in the contralateral direction. The greater the size of the gaze shift, the steeper the slope of these relationships. Perhaps the most striking feature of the model is its ability to generate eye velocity profiles that closely match those of animals. Lower peak velocities and dual-peak velocity profiles emerge as a result of the minimal-effort principle. Simulations of optimal head-restrained saccades also show realistic unimodal velocity profiles with shorter acceleration and longer deceleration phases, and provide an explanation of the main sequence relationship. Reproduction of the major kinematic features of head-fixed and head free movements implies that the time course of force development was successfully modelled. Ultimately, the motoneuronal commands sent to the eye and the head must in turn be consistent with the signals predicted by the minimal-effort rule. Our results suggest that the minimal-effort rule provides a rationale for the adoption of the cross-talk mechanism between eye and head control signals, which belongs to the independent eye/head control class of neural models.

A new model of primate eye-head gaze shifts.

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Abstract:

We present a neural network that simulates the portion of the primate brain responsible for eye-head gaze shifts and evaluate its performance. Although it assumes that it is the eyes and the head that are controlled independently rather than their sum (gaze), our model replicates the psychophysics of eye-head gaze shifts and is consistent with neurophysiology. Firstly, it replicates the accuracy and the time course of gaze shifts to targets at several different positions both head free and head fixed as well as eye plateaus and the results of head perturbation experiments. Secondly, it replicates the relative contributions of the eye and the head such that the latter increases and the former decreases together with the size of the gaze shifts while the absolute size of eye movements saturates at about 30 deg. Thirdly, it replicates the fact that the relative contributions of the eye and the head depend on the initial positions of the eyes as well as the position sensitivity of electricaly evoked head-fixed sacades. Moreover, it demonstrates that EBN units would be classified as eye-related cells and IBN units as gaze related cells on the basis of the linear regression line between NB and saccade size despite the fact that the former receive information about head movements and the latter do not. Finally, our model makes a number of predictions. For example, it predicts that the slope of the linear regression line between NB and saccade size should depend on the initial position of the eyes.

Theme and Topic (Complete): D.06.c. Eye and head control
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