Neural network simulations of the primate oculomotor system
IV. A distributed bilateral stochastic model of the neural integrator
of the vertical saccadic system

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Abstract. The present report examines the performance of a distributed bi-directional neural network that simulates the vertical velocity to position integrator of the primate brain. Consistent with anatomy and physiology, its units receive stochastically weighted input from vertical medium-lead burst neurons. Also consistent with anatomy, units belonging to integrators with opposite on-directions (up or down) are interconnected via the posterior commissure (again in a stochastically weighted manner) and they can be excitatory or inhibitory. To demonstrate that integration can be a one-step process, the output of model units was routed directly to vertical motoneurons. Model units replicate the wide range of saccade-related discharge patterns encountered in the portion of the primate brain that is thought to house the vertical neural integrator (the interstitial nucleus of Cajal) while “lesions” of model units and/or their interconnections replicate the symptoms which follow insults to this brain area.

1 Introduction

Saccades are movements which rapidly redirect the eyes towards interesting features of the surrounding world. Their horizontal and vertical size is separately determined by horizontal and vertical central pattern generators (the so-called burst generators). The former is located in the paramedian reticular formation of the pons (PPRF) and the medulla (Luschei and Fuchs 1972), while the latter occupies the rostral interstitial nucleus of the medial longitudinal fasciculus (Büttner-Ennever and Büttner 1978; King and Fuchs 1979). The output of the burst generators is carried by medium-lead burst neurons (MLBs) to extraocular motoneurons (MNs), causing them to emit a burst of discharge proportional to the size of saccades in their preferred direction (left or right, up or down). At the end of each saccade, MN discharge settles into a tonic pattern proportional to the eye position reached due to the saccade (Robinson 1970). This tonic eye position signal is extracted from the phasic discharge of the burst generators via a process akin to mathematical integration and is also conveyed to MNs.

There is considerable evidence from lesion studies to suggest that the interstitial nucleus of Cajal (NIC) is part of the neural integrator of the vertical saccadic system as is the nucleus prepositus hypoglossi (NPH) for the horizontal system (for a review see Moschovakis 1997). Lesions of the NIC have been shown to cause vertical gaze holding failure in the cat (Le Taillanter 1991; Fukushima et al. 1995) the monkey (Crawford et al. 1991) and the human (Ranalli et al. 1988; Sharpe and Ranalli 1991) while lesions of the NPH have been shown to cause horizontal gaze holding failure in both the cat (Cheron and Godaux 1987) and the monkey (Cannon and Robinson 1987; Kaneko 1997). What biological mechanisms would enable a piece of brain tissue to engage in Newtonian calculus? Early efforts to answer this question (Kamath and Keller 1976) assumed that integrator units are endowed with positive feedback so that the firing rate of each one of them is described by an equation of the form

\[ y(t) + \tau \dot{y}(t) = x(t) + ky(t) \]  

(1)

where \( x(t) \) is its input, \( y(t) \) its output, \( \tau \) its time constant, and \( k \) the gain of the positive feedback. The gain of the closed loop system described by (1) is

\[ \frac{y(s)}{x(s)} = \frac{1}{s + 1/T} \]  

(2)

where \( s \) is the Laplace variable and \( T \) (the time constant of the system) is equal to \( \tau/(1-k) \). For the neural integrator to have a time constant equal to 20 s, \( k \) must equal 0.99975 if \( \tau = 5 \) ms. A value of \( k \) that is 10% lower than ideal results in an integrator time constant of 50 ms. This sensitivity to small changes of its feedback gain is one of the limitations of this model and was

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recognized early on. Moreover, in addition to modulated transient signals, its units would integrate the background discharge of their input. To address these shortcomings, Cannon and colleagues (1983) proposed a model which achieved positive feedback by means of a lateral inhibitory network of homogeneous neurons. This model integrated just the time-varying part of its input signals and because of its distributed nature, there was no need to precisely control the strength of any one of its feedback connections. Finally, the response of its units to pulses of input (such as provided by MLBs) is a step function of time. This is consistent with the existence of NPH (Lopez-Barneo et al. 1982; Delgado-Garcia et al. 1989; McFarland and Fuchs 1992), NIC (King et al. 1981; Fukushima et al. 1990; Dalezios et al. 1998) and PPRF (Keller 1974) units which discharge in relation to eye position and display no saccade-related bursts. Accordingly, such units have been given the role of carrying the output of the neural integrators to MNs (Escudero et al. 1992). On the other hand, tonic units are remarkable for their small encounter frequency. Neurons which display burst–tonic activity profiles predominate in both the NPH and the NIC (King et al. 1981; Lopez-Barneo et al. 1982; Delgado-Garcia et al. 1989; Fukushima et al. 1990; McFarland and Fuchs 1992; Dalezios et al. 1998) but are thought to participate in earlier stages of integration processing (Lopez-Barneo et al. 1982).

To understand how the neural integrator accomplishes its task(s), it is important to know the anatomical and physiological features of the cells it comprises. Over the past several years, work in our laboratory has focused on those of the vertical integrator in the NIC. Of the several efferent pathways that arise in the NIC, the one decussating in the posterior commissure (PC) and deploying dense terminal fields in the contralateral NIC and the oculomotor complex (Kokkoroyannis et al. 1996) is particularly relevant to the present report. Our data indicate that the integrity of this pathway is necessary for normal vertical velocity to position integration (Partsalis et al. 1994). Further, they indicate that fibers which originate in the NIC and course through the PC towards the oculomotor complex display burst–tonic activity profiles in that they burst (or pause) for vertical saccades and discharge tonically in relation to vertical eye position (Moschovakis 1995; Dalezios et al. 1998). Far from being stereotypical, the discharge parameters of these fibers vary broadly in relation to movement metrics and vertical eye position (Dalezios et al. 1998). Finally, preliminary data suggest that these fibers do not supply the NIC with recurrent collaterals (Moschovakis 1995).

In the light of this evidence, it is reasonable to ask whether it is possible to build a model of the vertical neural integrator that reflects the known anatomical and physiological properties of NIC neurons and relies on a single processing step. Here, we describe such a model and analyze its performance. Its verisimilitude is evaluated through a detailed comparison between: (a) the signals carried by model elements and the discharge of NIC neurons, and (b) model output following “lesion” of its elements and eye movements following lesions of the NIC and its efferents. A brief description of this model has appeared in abstract form (Sklavos and Moschovakis 2000).

2 Methods

Figure 1 is a block diagram of a lumped version of our model together with typical signals encountered at several of its stages for saccades of two different directions (up, blue; down, red). We assumed that the vertical neural integrator is made of at least two half-centers: one upward (UNI) and one downward (DNI). Further we assumed that each half-center is made of a mixed population of excitatory (UNIe, DNIe) and inhibitory (UNIi, DNIi) units. The existence of both excitatory and inhibitory vertical NI neurons is indicated by the enzymes expressed by commissural NIC cells retrogradely labelled after tracer injection in the contralateral NIC and the oculomotor complex of the rhesus monkey (Horn et al. 1999). Also consistent with known anatomy (Moschovakis et al. 1990, 1991a,b), we assumed that model units receive excitatory input from MLBs with similar on-direction. The weight of these connections (\(w_{ij}\) between the \(i\)th MLB and its target NI unit \(i\), contained in an \(n \times m\) matrix \(V\)) was assumed to vary stochastically around a mean value of 0.6 (Fig. 1). Given the magnitude of the SD of their distribution (equal to the mean), several of the weight coefficients had a sign opposite to that of the mean. These were about one-third of the theoretically maximum number of connections between MLB and NI units, and their value was set to zero. Also, consistent with known anatomy (Moschovakis et al. 1991a), inhibitory MLBs were assumed to establish symmetric connections (opposite in sign but varying in a similar manner) with NI units (Fig. 1, the stippled bars of the same histograms).

Each one of the NI units of our model established excitatory (NIe units) or inhibitory (NIi units) connections onto NI units with opposite on-direction. This is consistent with the fact that the neural integrators which are confined to opposite sides of the brain have opposite on-directions (Crawford et al. 1991) and the fact that the axons of the relevant NIC efferent neurons cross the midline with the PC to supply the contralateral NIC with terminal fields (Moschovakis 1995; Kokkoroyannis et al. 1996). The mean strength of connections between NI units was determined analytically from the system of differential equations describing our model. In vector notation these can be written as

\[
\tau \dot{y}(t) + y(t) = C y(t) + V x(t)
\]

(3)

where \(y(t)\) is the instantaneous discharge of \(n\) NI units, \(x(t)\) is the input they receive from \(m\) MLBs, \(V\) is the \(n \times m\) matrix containing the weights of connections \(v_{ij}\) between the \(j\)th MLB and the \(i\)th NI unit, and \(C\) the \(n \times n\) square matrix containing the weights of connections \(c_{ii}\) established by the \(i\)th NI unit onto the \(i\)th contraversive NI unit. Note that there are no connections between units with the same on-direction. In