

A Proposed Neural Network for the Integrator of the Oculomotor System

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Abstract. Single-unit recordings, stimulation studies, and eye movement measurements all indicate that the firing patterns of many oculomotor neurons in the brain stem encode eye-velocity commands in premotor circuits while the firing patterns of extraocular motoneurons contain both eye-velocity and eye-position components. It is necessary to propose that the eye-position component is generated from the eye-velocity signal by a leaky hold element or temporal integrator. Prior models of this integrator suffer from two important problems. Since cells appear to have a steady, background signal when eye position and velocity are zero, how does the integrator avoid integrating this background rate? Most models employ some form of lumped, positive feedback the gain of which must be kept within totally unreasonable limits for proper operation. We propose a lateral inhibitory network of homogeneous neurons as a model for the neural integrator that solves both problems. Parameter sensitivity studies and lesion simulations are presented to demonstrate robustness of the model with respect to both the choice of parameter values and the consequences of pathological changes in a portion of the neural integrator pool.

1 Introduction

For the past fifteen years, oculomotor neurophysiologists have postulated the existence of a pool of neurons that temporally integrates premotor neural commands¹ (Robinson, 1968, 1971). Cohen and Komatsuzaki (1972) were the first to provide physiological evidence. They found that stimulation of the paramedian zone of the pontine reticular formation

(PPRF) in monkeys caused conjugate, ipsilateral, horizontal eye movements. During constant stimulation the eyes deviated at a constant velocity, and at the end of the stimulus the eyes remained in the new position for several hundred milliseconds, the duration of natural periods of fixation. They concluded that activity induced by electrical stimulation appeared to be integrated with respect to time.

The next study to support the existence of the integrator was performed by Skavenski and Robinson (1973). These authors recorded eye movements and single-unit activity of motoneurons in the abducens nucleus of the alert monkey during sinusoidal rotation in the dark. From a frequency analysis of eye and head position, they demonstrated that the total phase lag could not be accounted for by a combination of semicircular canal dynamics and the muscle and orbital tissue lags alone. The single-unit study demonstrated a phase lag of almost 90° between the firing patterns of abducens motoneurons and primary vestibular neurons. This is the lag that would be produced by a neural integrator.

Subsequently it has been shown that the optokinetic system also provides an eye-velocity command that shares the integrator with the vestibular command (Waespe and Henn, 1977). Burst cells in the PPRF carry a signal proportional to eye velocity during a saccade (van Gisbergen et al., 1981) and it has been proposed that this too is integrated to provide the step change in motoneuron discharge rate that follows a saccade (Robinson, 1975). There are good physiological and theoretical reasons to suppose that all conjugate, eye-movement systems share a common neural integrator (ibid). The concept of a neural integrator in the premotor brain-stem pathways is widely accepted, but its anatomical location and method of operation remain to be elucidated.

Two previous attempts have been made to model the neural integrator (Rosen, 1972; Kamath and

¹ In this text the terms "commands" and "signals" are used interchangeably to designate neuronal discharge firing patterns which create the subsequent eye movements

Keller, 1976). Rosen's model was comprised of individual "neurons" that were in one of two states: either silent or firing maximally. Unfortunately, neurons in premotor, oculomotor areas are never seen to behave in this way. Kamath and Keller's model consisted of a lateral excitatory network of densely-packed, homogeneous neurons. The dynamics for an individual neuron were modelled by a first-order process with a time constant, τ , of 5 ms. This value is an upper limit for τ based on measurements of membrane potential transients induced by current injection (Rall, 1960). The lateral excitatory connections were reduced to a lumped parameter model of the above first-order pole and a positive feedback loop with a gain of K . The transfer function, $H(s)$, for such a configuration is:

$$H(s) = \frac{1}{s + 1/\tau - K} = \frac{1}{s + 1/T_n}; \quad T_n = \frac{\tau}{1 - K\tau}.$$

Becker and Klein (1973) showed, from measurements of the drift of the eye in eccentric positions in the dark, that the time constant, T_n , of the leaky, neural integrator in humans is on the order of 20 s. Thus in Kamath and Keller's model $K\tau$ equals 0.99975. If K were only 0.025% too large, the network would be unstable, and conversely if K were 0.4% too small, T_n would be 1.2 s, unacceptably small. Thus, as these authors pointed out, the model was unreasonably sensitive to the value of the gain of the feedback, K , – in other words the model was not robust. (Their solution to this problem – using two positive feedback loops instead of one – unfortunately does not solve the problem.) Nevertheless, their basic idea is sound and we will show that a system of reverberating collaterals can be made to work so long as one does not lump the distributed feedback into a single feedback path that requires unacceptably high tolerances.

There is an additional shortcoming of these previous models. All cells that carry an eye-velocity signal, many of which presumably serve as input to the neural integrator, have appreciable tonic or background firing rates and it is the modulation about this DC component that encodes eye movement commands. The modulated component is integrated with a gain of about 2 and a time constant of 20 s. [A typical neuron carries the eye-velocity signal at 1.0 (spikes/s)/(deg/s) and the eye-position signal at 2.0 (spikes/s)/deg.] If the neural integrator functioned as a simple first-order pole with the above properties, then the DC gain would be 40. However, cells that carry an eye-position signal, many of which may be part of the neural integrator, have background firing rates approximately equal to that of cells which serve as inputs to the integrator; in other words, the DC gain is about 1.0. Thus the model must be more sophisticated than a

simple first-order pole in that the gains of the background and integrated components of the input must be independently controllable.

A lateral inhibitory network of linear neurons is presented below as a plausible model for the neural integrator. The properties of such networks have been studied extensively; for example see Ratline and Hartliff's monograph (1974), but usually in the context of signal or feature extraction. To our knowledge such a network has not been used before in the more humble task of integrating a single variable. We demonstrate that such a network indeed functions as a leaky integrator, and furthermore, the model has the virtue of both having independent gains for the DC and modulated components of the input and being robust.

2 The Model

The neural integrator is formed from a pool of homogeneous neurons each of which inhibits the discharge rate of neighboring neurons in the pool. Most brainstem, oculomotor neurons have firing rates that are linearly related to eye position and/or eye velocity. Thus we propose that a neuron in the neural integrator pool operates in a linear range about its background firing rate. Therefore, the integrating nature, stability, and robustness of our model do not depend on threshold or saturating nonlinearities. The firing rate of each neuron is assumed to be proportional to its transmembrane potential at the axon hillock. This so-called generator potential is in turn determined by a first-order rate process with a linear combination of dendritic influences from presynaptic cells serving as the effective input. With these assumptions the firing rate of an individual neuron is modelled as

$$\tau \dot{x}(t) + x(t) = i(t),$$

where $x(t)$ is the firing rate, τ is the time constant of the first-order dynamics, and $i(t)$ is the net, effective, presynaptic input.

The response of the i^{th} neuron in a homogeneous pool of N such neurons is described by

$$\tau \dot{x}_i(t) + x_i(t) = \sum_{j=1}^M v_{ij} u_j(t) - \sum_{j=1}^N w_{ij} x_j(t), \quad (1)$$

where $u_j(t)$ is the firing rate of the j th input to the network, v_{ij} represents the weighting or strength of the influence of the j th input on neuron i ($v_{ij} > 0$ implies excitatory input, $v_{ij} < 0$ implies inhibitory input), and $w_{ij} \geq 0$ represents the weighting of the lateral inhibition exerted on the i th neuron by neuron j which is also a member of the homogeneous pool; j equal 1, 2, ..., N . Of course solutions to (1) may be negative, and one can interpret such negative firing rates as a decrease in

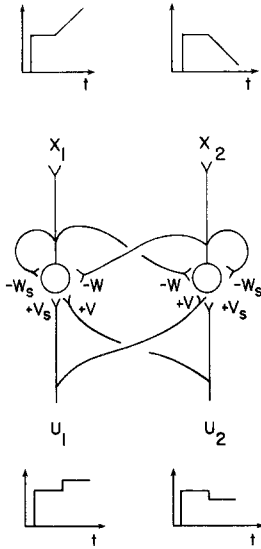


Fig.1. Schematic of a lateral inhibitory network with only two neurons. Insets depict qualitatively the inputs and responses for a step increase in background rate followed by a step input modulated in opposite directions. u_1 and u_2 represent input firing rates, w and w_s are lateral and self-inhibitory coefficients, v and v_s are input weighting coefficients, and x_1 and x_2 are the output firing rates

activity from some background rate; that is, $x(t)$ may be viewed as the perturbation in firing rate.

It should be noted that this type of model still relies inherently on positive feedback to persevere activity. If a cell inhibits its neighbor and is inhibited by it in turn, the net effect is positive feedback.

3 Properties of a Two-Neuron Network

The response of a reduced network with $N=2$ (Fig. 1) is examined to demonstrate that even this simple network behaves as two different low-pass filters; that is, the gain and pole characteristics can be independently controlled for the background vs the modulated component of the input signal. Suppose that w_{12} and w_{21} equal w , w_{11} and w_{22} equal w_s for self inhibition, and the inputs are weighted by v_{11} and v_{22} equal v_s , v_{12} and v_{21} equal v . The coupled, first-order, differential equation which describes this network is shown in matrix form in (2).

$$\begin{Bmatrix} \dot{x}_1 \\ \dot{x}_2 \end{Bmatrix} = \frac{-1}{\tau} \begin{bmatrix} (1+w_s) & w \\ w & (1+w_s) \end{bmatrix} \begin{Bmatrix} x_1 \\ x_2 \end{Bmatrix} + \frac{1}{\tau} \begin{bmatrix} v_s & v \\ v & v_s \end{bmatrix} \begin{Bmatrix} u_1 \\ u_2 \end{Bmatrix}. \quad (2)$$

It is a property of this network (shown below) that given u_1 and u_2 , the neurons will adopt a mean firing rate proportional to the mean of u_1 and u_2 plus the time integral of the difference between u_1 (or u_2) and that mean. Consequently one may consider the special case where δu_1 and δu_2 are equal but opposite deviations from a constant level. In this case the equations for δx_1 and δx_2 as functions of δu_1 (equal to $-\delta u_2$), which are in general fairly complex, second-order equations, reduce to a very simple first-order equation. For example, u_1 may be an excitatory vestibular input (Type I) from the right vestibular nucleus while u_2 is from the left. When the head is still u_1 and

u_2 are equal. During a head rotation to the right, u_1 would increase by δu_1 while u_2 would decrease by the same amount δu_2 . If we let δu equal the perturbation of the input, then δu_1 and $-\delta u_2$ equal δu . Under these circumstances the transfer function for each neuron can be shown to reduce to

$$\frac{\delta X_1(s)}{\delta U(s)} = \frac{-\delta X_2(s)}{\delta U(s)} = \frac{(v_s - v)/\tau}{s + (1 + w_s - w)/\tau} = \frac{(v_s - v)/\tau}{s + 1/T_n}, \quad (3)$$

where

$$T_n = \frac{\tau}{1 + w_s - w}.$$

If $w_s - w$ were, say, -0.99975 with τ equal to 5 ms and $v_s - v$ were 0.01, then the step response of neuron 1 is that of a simple, first-order, leaky integrator with a time constant of 20 s and a gain of 2.0, while δx_2 is minus this quantity.

What would happen if u_1 and u_2 shifted in the same rather than the opposite directions? Suppose δu equals δu_1 and δu_2 . This “perturbation” of contralateral inputs in the same direction does not represent a response to natural stimuli, but is analogous to shifts in the background or DC component of the input. In this case the transfer function can be shown to reduce to

$$\frac{\delta X_1(s)}{\delta U(s)} = \frac{\delta X_2(s)}{\delta U(s)} = \frac{(v_s + v)/\tau}{s + (1 + w_s + w)/\tau} = \frac{(v_s + v)/\tau}{s + 1/T_0}. \quad (4)$$

Thus

$$T_0 = \frac{\tau}{1 + w_s + w}.$$

Recall that $w_s - w$ is -0.99975 and w and w_s are greater than or equal to zero. Therefore $w_s + w$ is greater than or equal to 0.99975. For example, if w_s were zero, and w were 0.99975, $1 + w_s + w$ would be close to 2.0. Thus T_0 is less than or equal to approximately 2.5 ms. For the integrated output to have a gain of 2.0 it was required that $v_s - v$ equal 0.01; if $v_s + v$ were about 2.0 then the DC gain for the background input would be 1.0 (for example, v_s equal to 1.0 and v equal to 0.99 would work). Thus we have shown that both the time constant and gain can be independently controlled for the DC vs. the modulated component of the input. Since the neural background rate normally changes very slowly with time, it is really only the DC gain of the background rate and not the pole location that is relevant.

If one imagined that the spontaneous component of the input were increased suddenly from zero to some finite value (Fig. 1), then over a matter of about 7.5 ms the output of the neural integrator would increase its

background rate exponentially from zero to an asymptote equal to this step size. In general any variations in u_1 and u_2 can be decomposed into one variation in their mean and another in their difference. The response to the former is quick and merely resets the background signals of the integrator. The response to the latter is integration with a large time constant. As a result the integration is independent of the background signal which normally changes very little and very slowly.

Of course this two-neuron network is no more robust than Kamath and Keller's (1976) model; the time constant of the network still depends on the precise value of the difference between w_s and w . However, this simple analysis demonstrates how a lateral inhibitory network with inputs modulated in opposite directions integrates the modulated component of the input, whereas the DC component common to both inputs merely establishes the operating level. It might be mentioned that a similar scheme has been utilized previously by Doslak et al. (1979) and in an equivalent form by Zee et al. (1974), to control background rate in two, push-pull, half-integrators that lie on either side of the brain stem but lateral inhibition had not been considered previously as a building block of the half integrators themselves.

4 Properties of an Infinitely Large Network

Although the integrator pool must contain a finite number of neurons, the qualitative response of a network containing a large number of neurons is often more easily appreciated by modelling the network as a continuum of infinitely many neurons. In particular the mechanism of the model's robustness can be conceptualized more easily in a continuous model before being tested in a discrete model. As argued by an der Heiden (1980), this transition is justifiable mathematically when the number N of neurons is very large and the difference in the parameters of adjacent neurons is small. Furthermore, on physiological grounds, one would expect the pool to consist of a large number of similar neurons such that some measure of the behavior of the entire pool is more relevant than that of an individual member. With these assumptions we can visualize the pool as a one-dimensional continuum or line of neurons where the "length" of this continuum is sufficiently large that edge effects are negligible. The firing rate, x , is now represented as a function of both space, k , and time, t ; that is, x is $x(k, t)$. We will also assume that the strength of lateral inhibition between two neurons is a function of the distance between them. Thus v_{ij} and w_{ij} from the discrete model of (1) become $v(k - k_0)$ and $w(k - k_0)$, respectively. The temporal dependence of (1) becomes

a partial derivative, and the summations over discrete spatial indices become convolution integrals in space. Thus the network description in the continuum is

$$\begin{aligned} \tau \frac{\partial x(k, t)}{\partial t} + x(k, t) \\ = \int_{-\infty}^{\infty} v(k - k_0) u(k_0, t) dk_0 - \int_{-\infty}^{\infty} w(k - k_0) x(k_0, t) dk_0. \end{aligned} \quad (5)$$

The behavior of this integrodifferential equation is best examined in the spatio-temporal frequency domain. Performing the Laplace transform in time and Fourier transform in space yields

$$\frac{X(P, s)}{U(P, s)} = \frac{V(P)/\tau}{s + (1 + W(P))/\tau}, \quad (6)$$

where s represents the complex temporal frequency and P denotes the spatial frequency. The spatial frequency of inputs to neural networks is a concept which is perhaps more familiar to those investigators studying sensory systems. In such analyses $U(P, 0)$ represents the spatial frequency content of an external stimulus that does not vary in time. In our analysis of a motor system, P represents the spatial frequency content of the incoming axonal projections to the integrator pool. That is to say, it represents an intrinsic "hard-wired" feature of the inputs projecting to the network. For example, if the integrator pool received projections from only one vestibular nucleus whose efferents were essentially identical, then the spatial content of the input is DC; that is, P equals zero. If, however, signals from the left and right vestibular nuclei, whose efferents are normally modulated in opposite directions, were interdigitated closely in space along the line of cells in the network, then P is a large, nonzero number which conveys the spatial frequency content of this interdigitated projection. In a discrete network the largest realizable P is π radians/neuron or 0.5 cycles/neuron, which corresponds to every other neuron receiving a projection from one vestibular nucleus while the remaining neurons receive an input from the other.

The character of the output of (6) depends on the assumed form of $v(k - k_0)$ and $w(k - k_0)$. Without loss of generality with respect to the integrating nature, stability, and robustness of the network, we can assume that each input projects to a single point or neuron in the integrator pool. Thus $v(k - k_0)$ is a delta-function distribution (1.0 at k_0 , zero elsewhere) and $V(P)$ equals 1 for all values of P . This assumption just simplifies (6) but, as mentioned, is not important for general integrator behavior; however, this assumption is relaxed below when we wish to adjust the gains of the background and modulated components independently. It is further proposed that the inhibitory

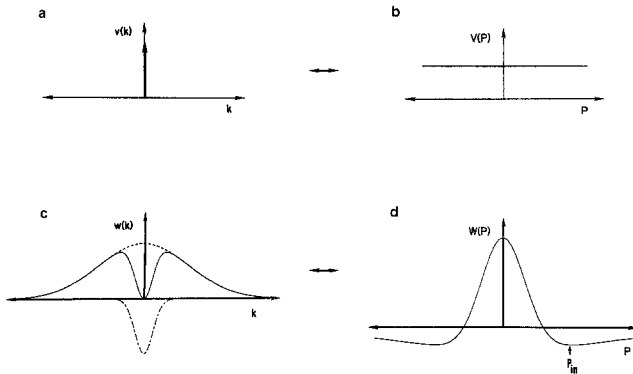


Fig. 2a-d. Assumed forms for the input projection and lateral inhibition profiles and their spatial frequency content. **a** $v(k)$ is a delta-distribution function. **b** The spatial frequency content of $v(k)$ is the constant 1.0. **c** One possible lateral inhibition profile computed as $w(k) = 2.5[\exp(-1/2(k/1.01)^2) - \exp(-1/2(k/0.202)^2)]$. The two individual Gaussian curves are indicated by dashed lines. **d** Spatial frequency content of the assumed lateral inhibitory profile.

$$W(P) = 2.5 \sqrt{2\pi} \{ 1.01 \exp[-1/2(1.01 P)^2] - 0.202 \exp[-1/2(0.202 P)^2] \}.$$

P_{in} indicates the spatial frequency of the modulated input projecting to the network. For the background component of the input, $P=0$

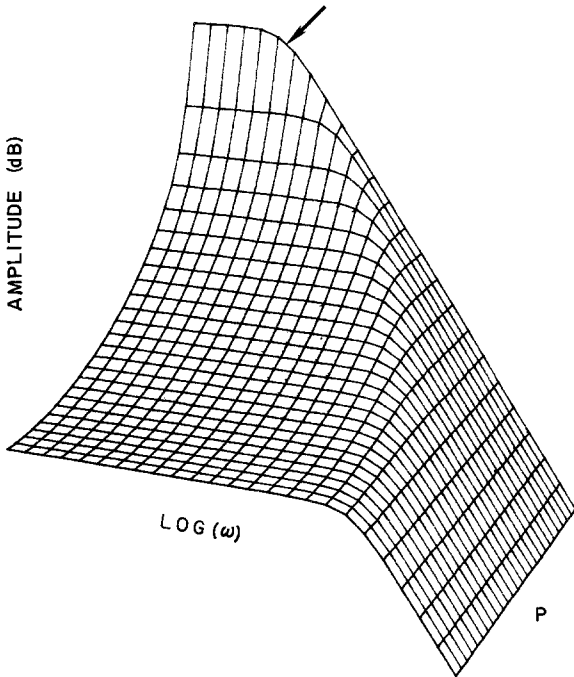


Fig. 3. A three-dimensional representation of the amplitude response of the transfer function $X(P, s)/U(P, s)$. Temporal frequency increases logarithmically from 10^{-3} to 10^{+5} rad/s along the axis marked $\log(\omega)$. Spatial frequency increases arithmetically from 0 to 0.5 cycles/neuron along the $+P$ axis. Amplitude, $X(P, s)/U(P, s)$ increases logarithmically along the vertical axis. The explicit forms of $W(P)$ and $V(P)$ are the same as those used in Fig. 2. The curve in the amplitude - ω plane corresponding to the spatial frequency of the modulated component of the input is indicated by the arrow. This curve has a corner frequency of 0.05 rad/s which corresponds to an integrator with a time constant of 20 s

influence of one neuron on another in the pool decreases as the relative distance between these two neurons increases. This need entail no anatomical restraints since the idealized pool can be topologically remapped to suit any anatomical observations such as the extent of axonal collateralization. Furthermore, we postulate that a neuron inhibits itself and some of its closest neighbors to a lesser degree than that of relatively distant neurons. Qualitatively one can envision such an inhibitory profile as a Gaussian distribution with a central dip. Figure 2 shows our assumed form of $v(k)$, $w(k)$ and their corresponding spatial frequency spectra $V(P)$, $W(P)$. In constructing these figures $w(k)$ was modelled as a Gaussian distribution with a large variance minus a second narrower Gaussian distribution with a smaller variance (dashed lines). Our assumed profile for $w(k)$ is not unreasonable physiologically and a similar profile has been observed in the compound eye of the horseshoe crab (Ratliff et al., 1969).

The response of our network is illustrated for sinusoidal, temporal inputs qualitatively in Fig. 3. The height of the surface represents the amplitude response of the two-dimensional transfer function (6) while the two abscissas denote temporal, ω , and spatial, P , frequency. For sinusoidal temporal inputs s equals $j\omega$. For any fixed P , the amplitude - ω plane is the familiar Bode plot. As shown, it is that of a first-order, low-pass filter. This property is evident from the transfer function which is rewritten in (7) to emphasize its form of a simple low-pass filter with a time constant T_n .

$$\frac{X(P, s)}{U(P, s)} = \frac{V(P)/\tau}{s + 1/T_n(P)}; \quad T_n(P) = \frac{\tau}{1 + W(P)}. \quad (7)$$

As the spatial frequency, P , increases our assumed form of $W(P)$ decreases and approaches -1 at intermediate frequencies; whereas at very high spatial frequencies $W(P)$ asymptotically approaches zero (Fig. 2d). Thus on the transfer function surface (Fig. 3) the corner frequency ($1/T_n$) is large for small values of P and decreases for intermediate values. The highest spatial frequency shown in Fig. 3 (arrow) is 0.5 cycles/neuron, the highest spatial frequency in any discrete array of neurons. If the surface were extended to higher values of P , the corner frequency would increase asymptotically to $1/0.005$ or 200 rad/s. From an integrator viewpoint, the time constant is quite small for low spatial frequencies but becomes very large at intermediate spatial frequencies.

The property of integrating only the modulation of the input while the DC component of the output is proportional to that of the input was demonstrated for a two neuron network and can be seen again from the transfer-function surface in Fig. 3. Although the sig-

nals from push-pull, input structures are assumed to be interdigitated in space along the input to the network, the background component is the same for signals from the two sources. Thus P equals zero for the background component and, as Fig. 3 indicates, the output from this component has a high corner frequency; that is, it will not be integrated in the time domain. On the other hand, with the assumed interdigitated projections of the two inputs, the modulated component has a high, spatial-frequency content. If this P value is in the intermediate zone (P_{in} , Fig. 2d) where $W(P)$ is slightly more positive than -1 , then the amplitude response is large at low temporal frequencies and has a low corner frequency as shown in Fig. 3 by the arrow. Such a Bode plot is that of a leaky integrator with a long time constant. We shall assume that the spatial frequency of the input signal, P_{in} , is confined to this region.

One can note that in the region of spatial frequencies, P_{in} , where the network integrates best it is still necessary that $W(P)$ be -0.99975 . It would be impossible to build an integrator with a 20s time constant out of elements with 0.005s time constants without some global aspect of the network being held to a tight tolerance. We mean by robustness that the behavior of the model should not depend critically on any one connection or, in a model with thousands of connections, on even hundreds of connections. In particular, we consider the model robust if, in a given network, one can make significant alterations and lesions without losing the property of integration or becoming unstable. The proposed model does this as will be shown by a specific example in the next section.

In the continuum model considered here, this robustness can be seen by noting that $W(P)$ is formed by many connections and would change very little if a few of them changed by large amounts or many by small amounts. We can, for example, simulate the latter by changing all the connections in a random way. Let $w(k)$ be the sum of the ideal, deterministic inhibitory profile $w(k)$ (Fig. 2c) plus some random noise $n(k)$ which strengthens and weakens connections throughout the pool. Assume that $n(k)$ has a band-limited, white-noise power spectrum, $S_n(P)$

$$S_n(P) = \begin{cases} S_0 & |P| < P^* \\ 0 & |P| > P^* \end{cases}.$$

In a discrete model, P_{in} corresponds to the spatial frequency of every other neuron (0.5 cycles/neuron). If we prevent the noise from altering the strengths of connections alternately up and down the line (every other connection increased, every other decreased; at the spatial frequency P_{in}) we are, in effect, assuming that P^* is less than P_{in} . In that case the noise has no

effect on $W(P_{in})$ because P_{in} is above the noise cut-off frequency. Consequently T_n is unaffected by such noise. This means that T_n is independent of random fluctuations in synaptic connections between neurons provided that the alterations not have the periodicity of the input itself. The robustness of the network with respect to this general form of noise is demonstrated numerically for a finite network simulation in the Discrete Realization section. Of course this form of noise will affect the transmittance of the background rate or DC component of the input to the network. However, with the parameter values listed in the legend of Fig. 2, when P equals zero, $W(P)$ for the ideal deterministic case is 5.06 which is relatively large, so that even for a very liberal allowance of $S_n(0)$, $T_n(P)$ when P equals zero is orders of magnitude smaller than 20s so that virtually none of the DC component will influence the integrated output of the network.

The time constant of the integrator is primarily a function of the area of the central notch of $w(k)$. Recall that $w(k)$ is constructed from the difference between two Gaussian distributions, one with a large variance minus a second with a smaller variance (Fig. 2c). The contribution to $W(P)$ by the Gaussian with the larger variance approaches zero rapidly for increasing spatial frequencies. Therefore the value that $W(P)$ approaches near P_{in} in Fig. 2d is approximately proportional to the Gaussian component of $w(k)$ with the smaller variance. In other words the value of $W(P_{in})$ is related to an integral property of the central dip in $w(k)$. Thus, while T_n is not dependent on variations in general connectivity between more distant cells, and is still not dependent on variations in a few closer connections out of many, it is dependent on the average profile of close connections. From (6) it is evident that the model remains stable if and only if $W(P)$ is greater than -1 . The value of $W(P)$ as it approaches -1 is also determined precisely by the area of the central dip in $w(k)$. Thus by the same averaging argument just presented, the stability of the model is also dependent on the average profile of close connections. One suspects that this average profile is maintained by some sort of parametric-adaptive control system (e.g. Optican and Robinson, 1980) that monitors T_n and adjusts it. The most obvious way to detect changes in T_n is to use the exquisite sensitivity of the visual system to detect leakiness; that is, central drift of the eye on eccentric gaze. From the above analysis, one way to then control T_n is to modify, perhaps by a parallel circuit, the connectivity between cells and themselves and particularly their close neighbors. Again, any individual connection would be insignificant, only the overall result.

In order to adjust the background level and the integrator gains to realistic values, it is useful to have a mechanism for controlling them independently. The

background rates of vestibular afferents and central neurons carrying the eye-position signal are similar (about 100 spikes/s) so gain between the background rates of the input $U(0,0)$ and output $X(0,0)$ should be around 1.0. Since $W(0)$ is 5.06, the DC gain from (6), $1/(1+W(0))$, is 0.16. On the other hand, at P_{in} , (6) becomes approximately $1/(\sigma\tau)$. Since τ is 5 ms, the integrator gain is 200. This is much too large since most brain-stem, oculomotor neurons have a gain around 2.0. The necessary gain changes can be effected by altering $V(P)$. If $v(k)$ is fit by a Gaussian curve, for example, instead of a delta function, it could have a value, $V(0)$, near 6.06 for low spatial frequencies and a small value, e.g. 0.01, at high spatial frequencies such as P_{in} .² Thus, the gain of the integrator and the gain of the background can be adjusted independently.

5 Discrete Realization

While the previous section may help some to see the importance of spatial frequencies in the model – a concept perhaps unfamiliar to some oculomotor theoreticians – it hardly satisfies the more realistic neurophysiologist who wants to see, by specific example, what comes out for a given input and how sensitive that is to variations in the neural connections. Consequently randomness in $w(k)$ and lesions in a portion of the network were simulated for a discrete model of 32 neurons. Thirty two, from experience, was felt to be a minimum required to simulate effects both near and relatively far from a lesion. Edge effects were eliminated by configuring the neurons in a circle so that neuron 32 was an immediate neighbor of neuron 1. Instead of performing matrix manipulations, we computed responses with the aid of an electrical-circuit, simulation package, SPICE, on a digital computer (Nagel, 1975). The net input to each neuron was computed according to (1) by a buffered voltage summer. The neuron was a low-pass, RC filter with a time constant of 5 ms, and the output of each neuron was also decoupled electrically from other loads. The frequency response for sinusoidal inputs and transient response for finite-duration, pulse inputs were computed. A variance of 1.5 was used for the wide Gaussian component of $w(k)$ (see legend, Fig. 4), and the area of the dip in $w(k)$ was chosen such that at P_{in} (0.5 cycles/neuron), $T_n(P_{in})=20$ s. This meant limiting self-inhibition so that $w(0)$ was 0.00014. For simplicity we continued to use a delta function for $v(k)$ even though this produces an integrator with a high gain. We felt that the added complexity in the simulation was not justified.

² For example, if $v(k)$ has the form $2.03 \exp[-1/2(k/1.14)^2]$, $V(P)$ will produce the desired gains at P equal 0 and P equal P_{in} .

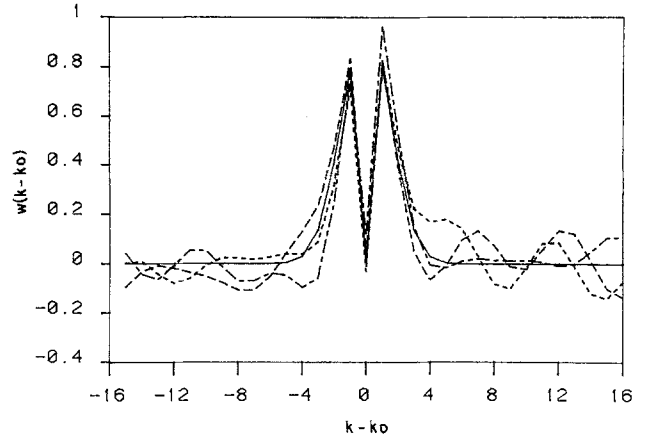


Fig. 4. The deterministic lateral-inhibitory profile for a discrete network is shown as a solid line. The discrete values were computed as $w(k) = \exp[-1/2(k/1.5)^2] - 0.99986 \delta(k)$ and these values are connected by straight line segments. The dashed lines illustrate three of the 32, discrete, independently-noisy distributions used to demonstrate robustness of the model with respect to band-limited spatial noise introduced in the inhibitory coefficients. For this distribution $T_n(0.5)$ was still 20 s

In the robustness argument for the continuous network, the noise was random, but all neurons had the same, (noisy), lateral-inhibitory profile. With the discrete model it is possible for each neuron to have independent, band-limited, random noise superimposed on the deterministic value of its lateral-inhibitory profile. The band-limited noise was computed as a summation of the first six harmonics of the fundamental frequency of a 32 neuron network (0.031 cycles/neuron). Thus P^* , the frequency band-limit for the noise is 0.19 cycles/neuron. The phase of each harmonic for a particular profile was randomly selected from a uniform distribution in the interval $[0, 2\pi]$ and the power of each harmonic was 0.5. In Fig. 4 three of the 32, noisy, inhibitory profiles (broken lines) are superimposed on an ideal deterministic profile (solid line) to illustrate the severity of the distortions introduced in $w(k)$ by the noise. If all of the neurons were to have just one of these distorted profiles, then one could predict from the continuum analysis that $T_n(P_{in})$ would still be 20 s. However, if each neuron's profile is independently random, it is not as obvious intuitively that $T_n(P_{in})$ will be unaffected by the noise. Nevertheless a frequency response simulation of the model verified that $T_n(P_{in})$ is still 20 s for independent, randomly-distorted, inhibitory profiles while $T_n(0)$ was 1.3 ms.³ Thus, even with grossly-distorted, lateral-

³ If there were a random, independent, DC component of the noise, then the background rate of each neuron would be different and depend on the particular form of the noise. However, the spatial DC component of the output (i.e. the equally-weighted mean over all the neurons) is still a first-order pole with a time constant of about 1.3 ms

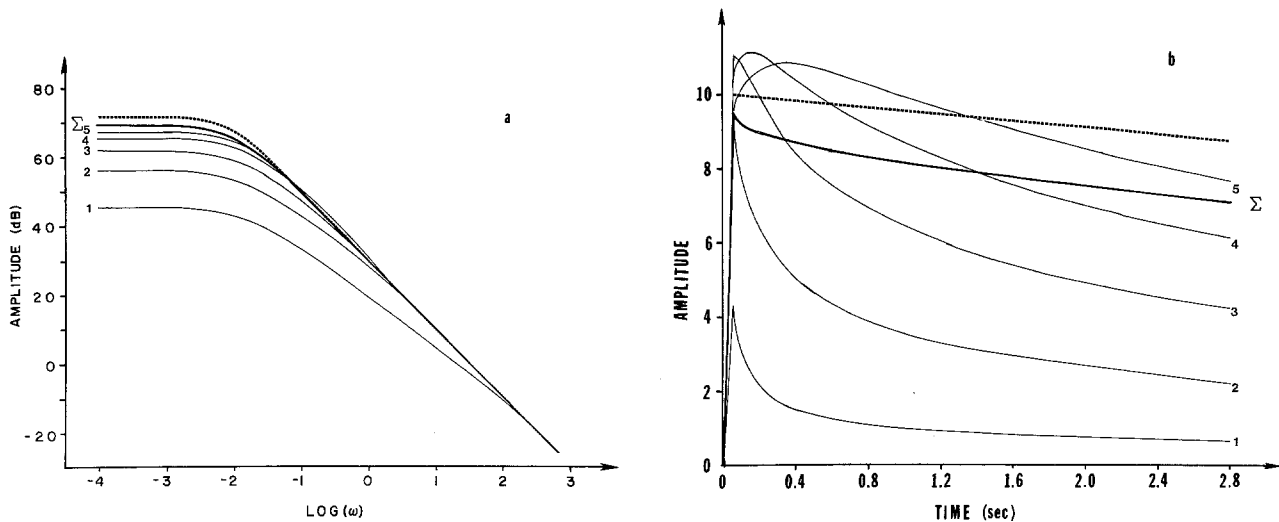


Fig. 5a and b. Response to sinusoidal (a) and pulse (b) inputs of a 32-neuron discrete model when one neuron has been destroyed. **a** Bode plot of the amplitude response for $P=0.5$ cycles/neuron. The heavy solid line is the response of an equally weighted sum of the 16 neurons receiving an increase in the modulation of their input (the corresponding summed amplitude response for the other half of the network is identical). The dashed line represents the response of the intact model with a time constant of 20s. The light, continuous lines show examples of the input/output amplitude ratios for individual “neurons” and the curve number indicates distance (in neurons) away from the lesion. **b** Model response to a 50ms pulse input of amplitude 1. The heavy, light, and dashed lines have the same meanings as in **a**

inhibitory profiles, the network still integrates the modulated component of its input well and independently of the background component.

A pathological lesion of the integrator pool was modelled by eliminating the lateral inhibition from one of the 32 neurons. This is equivalent to the cell death of $1/32$ (3%) of the integrator pool. This discontinuity in the network cuts a hole in the distribution $w(k)$ over the missing neuron and this sharp spatial transient causes effects to be exerted at all spatial frequencies. Thus even at an input frequency P of 0.5 cycles/neuron, the response of all of the neurons is no longer identical. Therefore we must choose some measure of the response of the whole network to characterize the performance of the integrator. We used the simple assumption that the outputs from all of the neurons receiving inputs that modulate in the same direction are summed with equal weights. A similar summation for neurons that modulate in the opposite direction constituted a second output. The transfer function between an input and its corresponding output is now no longer that of a simple first-order filter. The amplitude ratio of this input-output mapping is shown as a Bode plot in Fig. 5a and the transient response to a pulse with a duration of 50ms is shown in Fig. 5b. The response of the intact network that behaves like a simple first-order filter with a time constant of 20s is shown by the dashed line for comparison. The summed output of the lesioned integrator is no longer a single exponential decay. Just after the pulse the response falls off rapidly, by about 15% of the normal response

in this case, and then resumes a decay rate similar to the prelesion rate. The reason is easy to see. Cells adjacent to the lesion have lost much of their positive feedback through the lateral inhibitory pathways and they integrate very poorly (Fig. 5a and b, light lines). Cells further away leak less rapidly while cells quite far away are hardly affected. Thus the response in Fig. 5b (solid line) may be thought of as the sum of 16 leaky integrators all leaking at different rates. The response is obviously complicated but one can conceptually simplify it by regarding it as the sum of a small exponential with a short time constant (about 2s) and a larger one with a long, or normal, time constant. If a larger portion of the network were “lesioned”, the initial decay would be larger and faster and the amplitude of the slower component would be less. Not surprisingly the background rates of cells near the lesioned cell are different from the group mean.

6 Discussion

The goal of this study is to propose a hypothetical network of neurons that operate in a linear range, consistent with observed, brain-stem, single-unit activity, and that function *en masse* as a leaky integrator with a time constant on the order of 20s. As an improvement over previous models, we impose two further constraints on our network. **First, it must be capable of integrating only that component of its input which encodes the motor command**; that is, the modu-

lation superimposed on the background firing rate. Second, the network must be both stable and robust with respect to variability of the parameter values and the possibility of lesions within the network. Our analysis demonstrates that these goals are achieved by a lateral-inhibitory network of homogeneous neurons.

The lesion simulation suggests a mechanism for a variation of the common, clinical observation of gaze-evoked nystagmus. In this syndrome a patient's eyes drift centripetally on the attempt to maintain eccentric gaze, and at large angles of gaze corrective, rapid eye movements (saccades) are required repeatedly to recapture the visual target. This produces a saw-toothed, jerky eye movement called nystagmus. If the integrator became leaky through a decrease in T_n , the eyes would, between saccades, drift toward the rest position (straight ahead) with a single exponential time course and this is often the case [see Robinson (1974) or Zee et al. (1981) for examples of experimentally-induced, gaze-evoked nystagmus]. In other cases, however, the eye begins to drift centrally rapidly but quickly slows down to a much slower rate. If the latter rate is consistent with a time constant of 10–20 s, it is barely discernable and the eye appears to come to rest. The puzzle has been, if the integrator is just leaky, why does the eye slip back only part way? Abel et al. (1978) proposed that the integrator should be divided into parts so that only part of it could be made leaky and we basically agree. Figure 5b shows that our model simulates this waveform nicely after a loss of one cell out of 32. The virtue of our model is that it is not necessary to decouple the integrator into separate parts (Abel et al., 1978) to get the result; the distributed model does this naturally since it permits the behavior of some cells (those near the lesion) to be quite different from others (those far away). Thus, this particular variety of gaze-evoked nystagmus is simulated well by partial lesions of our neural network.

Cerebellar lesions, especially of the flocculus, are known to decrease T_n from 20 to 1.3 s (Robinson, 1974; Zee et al., 1981) and it has been proposed that there exists a rather leaky integrator pool in the brain stem with the latter time constant and that some sort of feedback loop mainly through the flocculus, increases this time constant to 20 s. If this escalation were done by a lumped, positive feedback, the gain of that pathway would be 0.935 and would require that fluctuations be maintained within 7%. This is not unreasonable, especially if this parameter is under feedback control, but it seems more likely to us that the transcerebellar pathway forms a parallel pathway by which brain-stem cells can influence their neighbors. By manipulating the distribution $w(k)$, the time constant T_n can easily be controlled in a way that does not depend on individual connections.

Because of midline symmetry, the neural integrator must consist of two groups of cells, one in each half of the brain stem. Each could consist of inhibitory neurons driven in push-pull by Type I, excitatory, so-called pure-vestibular cells in the left and right vestibular nuclei. (A Type I neuron increases activity with ipsilateral head rotation; a Type II neuron is just the opposite.) The activity of half the cells in each pool would increase while that of the other half would decrease. Thus the pool would be a mixture of Types I and II cells. Alternatively, all the cells driven from one vestibular input could be segregated on one side of the brain stem; their activity would all increase or decrease with increased activity of the vestibular input. This arrangement causes the two half integrators to operate in push-pull; all the cells would be of the same type, I or II. They would be joined across the midline by lateral inhibitory connections.

Since Types I or II, excitatory or inhibitory vestibular neurons are abundant in the vestibular nuclei, there is no difficulty providing the vestibular inputs for either of these arrangements. Unfortunately, there is not enough physiological or anatomical data on cells that might be part of the integrator to form any opinion now about which arrangement might be more realistic; although, so far, no areas of the pons have been found that contain cells carrying the eye-position signal that are not mixed, some increasing their activity in one direction, others in the opposite direction. This tentative finding suggests the former rather than the latter alternative. The choices are not mutually exclusive and several or all could be operating at once. There are also double-layer models for neural networks in which half the cells are excitatory, half inhibitory (Ermentrout et al., 1980). Such a model could also, no doubt, be made to integrate. A virtue of it would be that in coupling the integrator output to ocular motoneurons in a push-pull manner, that will also maintain a reasonable background rate on the latter, it is awkward if only inhibitory cells are available and quite easy to do if both excitatory and inhibitory cells are available.

There are two quite unrealistic aspects of the cells in the model: they are all alike and they carry the eye-position signal but not a velocity signal. Neurons in the brain stem that carry the eye-position signal have a broad distribution of background rates and sensitivities to changes in eye position. Much of this inhomogeneity is probably brought to the pool on the vestibular input fibers themselves that also have a wide distribution of background rates and gains. Also, as the simulations with noisy connections and lesions show, these manipulations also create inhomogeneity in the pool. The missing velocity signal is a more serious problem. Cells without them are called pure-

tonic, or pure-position, and very few of them have been observed in the brain stem (Keller, 1974). Most cells also carry a signal proportional to eye velocity during vestibular, pursuit, or saccadic movements or some combination of them. Thus, the next step in making the model more realistic would be to find a way to make its cells respond to the modulated input itself as well as its integral.

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