The Brain Wave Equation: A Model for the EEG

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ABSTRACT

Both spontaneous and evoked potentials measured on the surface of the head are believed due to postsynaptic potentials in vertically oriented neurons in the cortex. Potential differences between surface locations at any given time are due to the instantaneous difference in synaptic activity between the corresponding vertical regions. Because of the high correlation of activity between regions separated by distances large compared to the radius of influence of single neurons, communication between these locations must be by means of action potentials. In order to quantify the dynamics of interaction of 10^{10} cortical neurons, use is made of the concept of a neural mass. The neural mass consists of sufficiently large number of neurons so as to exhibit certain average properties which are independent of its exact inner circuitry. An integral wave equation is derived to describe the spatial-temporal variation of cortical potential. Solutions are obtained indicating that electrical oscillations, which are independent of the location and time history of subcortical input, can persist in the cortex. The nature of these oscillations depends on the relative abundance of excitatory and inhibitory connections between neural masses and on the physiological state of the brain. The latter is partially determined by velocity distribution functions for action potential propagation. A dispersion relation for brain waves is shown to exist for certain ranges of the connection parameters. In some limiting cases, weakly damped waves occur with $\omega = ck$, where c refers to a characteristic velocity for the distribution functions. Preliminary experiments indicate qualitative agreement with this result.

1. INTRODUCTION

It has been fairly well-established over the past several years that much of the spontaneous and evoked potentials measured on the head surface are due to postsynaptic activity on vertically oriented neurons in the cortex. Head surface potentials occur whether or not the local neurons fire action

potentials, and the action potentials themselves contribute little or nothing to the surface potentials. Whenever superficial apical dendrites are depolarized or when soma are hyperpolarized by synaptic potentials, the local surface potential becomes negative with respect to deep cortical locations on a line perpendicular to the surface. Alternately, the surface may become positive with respect to the depth by dendritic IPSP's or by somatic EPSP's. In either case transcortical current loops are set up around the neurons, with sources or sinks typically located near the somas of the large pyramidal cells approximately 10^{-1} cm. below the surface. Current sources are located indirectly from depth recordings of vertical second differences of potential, these quantities being related by Laplace's equation and Ohm's law [1]. The potential difference between any two surface points (or at any fixed cortical depth) at any time is due to the instantaneous difference in the degree of synaptic activity between the two vertical regions. A review of the experimental evidence supporting these findings is given by Creutzfeldt [2]. Theoretical arguments which indicate that realistic values of head surface potential differences ($\sim 100\mu$V) can easily be generated by synaptic potentials is given by Pollen [3]. Theoretical calculations of potential fields around single neurons due to spikes and EPSP's in the soma are also given by Rall [4] and by Bogdanov and Golovchinskii [5,6].

An EPSP across the soma of a pyramidal cell typically causes a current flow up through its dendritic tree, across the membrane, and back to the soma through the extracellular medium. The horizontal extent of this current loop depends on the width of the dendritic tree ($\sim 10^{-1}$ cm) and on the relative conductivities of the membrane and electrolyte. The spatial extent of the field generated by a neuron depends on the conductivity and volume capacitance of the cortex and probably on a variety of other properties which are unique to the inhomogeneous neural medium. A calculation which assumes a passive, homogeneous medium predicts an exponential fall off of potential with distance with a characteristic length equal to a fraction of a centimeter for frequencies near ten cycles/sec [7]. The active properties of adjacent cells may well dominate the spatial dependence and cause even stronger attenuation of potential with distance. Therefore, it is unlikely that widespread, spatially coherent EEG phenomena like the alpha rhythm can be generated by a small number of isolated generators, but must be due to the collective interaction of large numbers of neurons.

The spatial-temporal variation of head surface potentials may be represented by the Fourier series,

$$\phi(x,y,t) = \sum_{n=0}^{\infty} A_n(x,y)\sin(\omega_n t + \theta_n), \tag{1}$$

where x and y refer to a set of head surface coordinates. The human EEG spectrum often exhibits a peak in some frequency range characteristic of physiological state. In the case of the alpha rhythm, the power per unit frequency interval, $A_n^2/\Delta\omega$, in the 8 to 12 cycles/sec range is typically four times that in the 0–8, 12–20 cycles/sec range for "good alpha" subjects [8]. This peak in the spectrum usually occurs at all points on the upper portion of the head; however individual Fourier coefficients are highly dependent on both space and time (vary from epoch to epoch). The spectrum is often sufficiently peaked so that electroencephalographers easily identify the "alpha state" from the original EEG record. Sleeping subjects produce spectrums that are peaked in the low frequency range. In the case of stage 4 sleep, the power per unit frequency interval in the delta band (0–4 cycles/sec) may be as much as 30 to 40 times as large as that in the 4–20 cycles/sec range [8]. Another instance in which the human EEG spectrum often exhibits a well defined peak occurs when the subject's visual system is exposed to a periodic sequence of light flashes. In this case the spectrum is peaked at the flash frequency for frequencies below approximately 15 to 20 cycles/sec [9]. If the experiment is performed with closed eyes, the alpha peak may also be evident. There are, of course, a large number of periodic wave forms that are highly nonsinusoidal like the spike-wave complex characteristic of epileptic phenomena.

From a theoretical view point, the spatial distribution of potential over the head is equally as important as the temporal variation. However, technical problems associated with multichannel recording and data processing have severely limited the available spatial information. The Fourier frequency components of Eq. (1) may themselves be expanded in a double Fourier series, that is,

$$A_n(x,y) = \sum_{l=0}^{\infty} \sum_{m=0}^{\infty} B_{lmn} \sin(k_{xl}x + \theta_{xl}) \sin(k_{ym}y + \theta_{ym}). \tag{2}$$

Thus, each frequency component of the EEG is made up of a number of waves of different spatial wavelengths in the x and y directions on the head surface, given by $2\pi/k_{xl}$ and $2\pi/k_{ym}$, respectively. In a recent study, the average spatial distribution of a large number of single alpha waves over the back of the head was obtained in twenty "normal" subjects by Remond et. al. [10]. The average alpha potential forms a dome pulsating at the mean frequency of the alpha rhythm. The dome is centered on the midline about 6 or 8 cm above the inion. Thus, it appears that alpha waves have average wavelengths of the order of 14 cm, at least in the parieto-occipital region. The double sum in Eq. (2) then exhibits a peak when $k_{xl} \sim k_{ym} \sim 2\pi/14$ for values of n corresponding to the alpha frequency. EEG phenomena of very

short wavelengths must be studied by means of electrodes on the cortical surface since the scalp, being an electrical conductor, acts as an electroencephalographic averager [11]. It is the long wavelength activity due to the collective interaction of large numbers of neurons that is of interest here, however.

Because its spatial-temporal properties are fairly well-known, the alpha rhythm is a prime candidate for a theoretical model. However, since all EEG phenomena apparently have many common physiological contributions, any such model should be sufficiently general to account, at least qualitatively, for nonalpha phenomena. Current speculations on the physiological basis for the alpha rhythm are reviewed in a recent text [12]. These speculations, most of which lack any quantitative substance, are divided into two groups, the "reverberating circuit theory" and the "pacemaker theory." In the former case rhythmicity is assumed to be due to impulse traffic along a chain of neurons where the time for the volley to complete a cycle corresponds to the periodicity of the recorded rhythm. An apparent drawback of this theory is that it fails to explain how the striking regularity of the EEG can be maintained for long periods of time. The "pacemaker theory" assumes that rhythmic activity is an inherent property of group of subcortical cells, especially those in the thalamic nuceli. The rhythm is imposed upon the cortex in a topographical pattern determined by specific thalamocortical fibers. This explanation fails to explain the spatial coherence and spatial variability of the alpha rhythm, a difficulty that would seem to plague any theory based on isolated generators.

It has been established by a number of experimental investigators that rhythmic activity in the cerebral cortex can be generated within the cortex itself without benefit of rhythmic afferent volleys [12]. Most experiments have included lesions of the connection between the cortex and subcortical structures or complete neutonal denervation of a cortical area. The EEG, although rhythmic, may be quite abnormal, in such experiments. Of course, the wave generating ability of the cortex does not rule out the possibility that "normal" EEG activity is due mostly to subcortical rhythmic input.

2. THE BRAIN WAVE EQUATION

Although action potentials may not contribute to the measured EEG, it is strongly suggested by our previous arguments that potential field communication between distant locations ($> 10^{-1}$ cm) in the cortex must be by means of action potentials. Some of the action potentials travel on axons that directly connect two locations in the cortex. Others are transported through very complex subcortical circuits but finally return to the cortex at some later time, which depends on the geometry of the circuit and the

number of intervening synapses. In addition, the electrical behavior of the cortex is, in general, quite strongly influenced by subcortically originating input. In a number of experiments, for example, the cortical response to a periodic light flash, this afferent input is a dominant factor affecting the EEG. This analysis is, however, most concerned with EEG phenomena that exist because of cortical and subcortical circuits carrying action potentials that originate in the cortex. In this case, the afferent input acts as the initial impetus of cortical activity and is a continuing source of "noise" appearing in the EEG. Later a judgment can perhaps be made as to which EEG phenomena are correctly described in this manner.

The wide variety of observed EEG phenomena are apparently due to trans-membrane potentials at various vertical locations in the cortex. For example, some evoked potentials obtain their major contribution from synaptic activity on the somas of the pyramidal cells of layer V. Because of the reactive properties of the membrane, the vertical extent of extracellular potential adjacent to a pyramidal cell depends strongly on the duration of the transmembrane potential. Thus, theoretical studies indicate that the extracellular potential due to a somatic spike is negligibly small at distances much less than the membrane space constant. In contrast, the extracellular potential due to a somatic PSP is significant at distances above the soma equal to several space constants, with magnitude at any vertical location proportional to the magnitude of the PSP [1,6].

Because of the extensive overlapping of the dendritic trees, many neurons apparently contribute to a wave observed on the cortical surface. The number of contributing neurons is even larger for potentials measured on the scalp because of its electroencephalographic averaging properties. These considerations suggest that gross surface potentials are roughly proportional to the degree of synaptic activity in the local neuron population, with only small contributions from small scale inhomogeneities. In order to quantify this suggestion, let the cortical region V be divided into volume elements, as indicated in Fig. 1. If dV is sufficiently large so as to contain a very large number of neurons, we expect the enclosed neural mass to exhibit certain average properties, which are independent of its exact inner circuitry [13]. Thus, long-wavelength EEG phenomena are assumed due to the dynamic interaction of these neural masses. Alternately, short wave fluctuations, which may be superimposed on the long wave activity, depend on anatomical and synaptic firing details inside each neural mass. This approach is, of course, analogous to that long used in the study of physical systems with large numbers of degrees of freedom. Some limitations are considered in a following section.

In order to relate surface potentials to synaptic activity, it is assumed that the cortex exhibits a gross homogeneity. In particular, the vertical

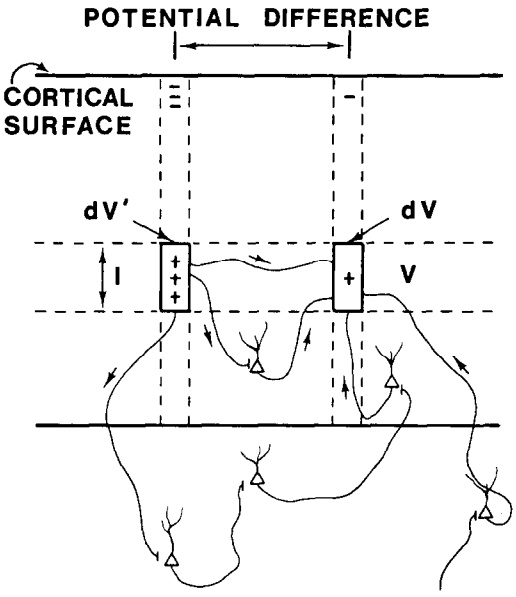

FIG. 1. Connections between volume elements in the cerebral cortex with different average horizontal velocities of action potential propagation.

distribution of synaptic activity, averaged over a volume element dV, is assumed to be the same in all parts of the cortex. In this case, the magnitude of the contribution of a PSP to the surface potential above dV is everywhere the same. The contribution to the surface potential at $\mathbf{r}$ comes mainly from the local cortical volume element, provided that volume elements are kept larger than the horizontal extent of the field generated in the element (as discussed in the introduction). Thus, these results are probably limited to relatively small potential gradients, that is, waves in $\phi(\mathbf{r},t)$ of wavelength greater than perhaps 1 cm. This limitation does not appear to effect the application here to long wave phenomena measured with macroelectrodes, however. If, for completeness, a contribution from spikes is included, the instantaneous gross potential at position $\mathbf{r}$ of the scalp or cortical surface is given by,

$$\phi(\mathbf{r},t)\sim\phi_1\eta_1 g(\mathbf{r},t)+\phi_0^+h^+(\mathbf{r},t)-\phi_0^-h^-(\mathbf{r},t). \tag{3}$$

Equation (3) follows directly from the following definitions:

ϕ_1 = Local surface potential generated by the firing of one cortical cell in dV.

$\phi_0^{\pm}$ = Local surface potential generated by a single EPSP (IPSP) in dV.

η_1 = The number density of cortical cells (length^{-3}).

$\eta_0^{\pm}$ = The number density of excitatory (inhibitory) connections to that part of the cells that are located inside dV (length^{-3}).

$g(\mathbf{r},t)$ = The fraction of cells inside dV that are firing at time t (dimensionless).

$h^{\pm}(\mathbf{r},t)$ = The number density of excitatory (inhibitory) synaptic firings on that part of the cells that are located inside dV (length^{-3}).

A further parameter of importance is $f_{\pm}(c,|\mathbf{r}-\mathbf{r}'|)$ = the number of excitatory (inhibitory) connections between the volume elements dV and dV' that have an average horizontal velocity of action potential propagation between c and $c+dc$ ($f_{\pm} \sim$ time/length^7). This definition implies that

$$l\int_{\text{cortical surface}} d^2\mathbf{r}' \int_0^{\infty} f_{\pm}(c,|\mathbf{r}-\mathbf{r}'|)\,dc = \eta_0^{\pm}. \tag{4}$$

The functional dependence of the $f_{\pm}$ is consistent with a homogeneous cortex. It is expected that the velocity dependence of $f_{\pm}$ varies with the physiological state of the subject. For example, the effect of sleep or drugs may be to block some of the cortical circuits which are normally open, thereby shifting the $f_{\pm}$ distribution towards smaller velocities.

The number density of synaptic firings, $h^{\pm}(\mathbf{r},t)$, inside any volume element dV is due to the effect of action potentials, $g(\mathbf{r},t)$, that fire in surrounding cortical volumes dV' at earlier times, $t-(|\mathbf{r}-\mathbf{r}'|/c_i)$, plus the effect of afferent input, $h_0(\mathbf{r},t)$. That is,

$$h^{\pm}(\mathbf{r},t) = h_0^{\pm}(\mathbf{r},t) + l\int_0^{\infty} dc \int_{\text{cortical surface}} f_{\pm}(c,|\mathbf{r}-\mathbf{r}'|)\,g\left(\mathbf{r}', t-\frac{|\mathbf{r}-\mathbf{r}'|}{c}\right) d^2\mathbf{r}', \tag{5}$$

where this relation holds for both excitatory (+) and inhibitory (−) input. Here l relates surface and volume elements, that is, $dV = ld^2\mathbf{r}$. Equation (5) is quite general; however in order to proceed further, some relationship between $h^{\pm}(\mathbf{r},t)$ and $g(\mathbf{r},t)$ must be established. In some cases, this relationship may be nonlinear; however, it is postulated that a number of long-wavelength EEG phenomean are consistent with the following linearization:

$$B\eta_1 g(\mathbf{r},t) = h^{+}(\mathbf{r},t) - h^{-}(\mathbf{r},t). \tag{6}$$

That is, in any cortical volume element, the number of cells that are firing at any given time is proportional to the instantaneous difference between

the number of excitatory and inhibitory synaptic firings on cells inside the volume element. In Eq. (6), B is the average difference between the number of instantaneous EPSP's and IPSP's needed to make one cortical cell fire an action potential. The linear approximation is probably valid provided that cortical connections have a degree of randomness, and that the number of neurons in a volume element is sufficiently large. A similar relationship has been obtained in studies of input-output relations in a motoneuron pool [14]. Synaptic knob locations and neuron thresholds were assumed to be randomly distributed. The fraction of neurons firing in the pool was shown to be proportional to the fraction of afferent synaptic knobs activated by a shock stimulus. Subsequent experiments supported the prediction of linearity [15]. The limitations of the linear theory are further discussed in the final section. Define,

$$h(\mathbf{r},t) \equiv h^{+}(\mathbf{r},t) - h^{-}(\mathbf{r},t). \tag{7}$$

Combine Eqs. (5), (6), and (7) to obtain the linearized version of Eq. (5), that is,

$$h(\mathbf{r},t) = h_0(\mathbf{r},t) + \frac{l}{B\eta_1}\int_0^{\infty} dc \int_{\text{cortical surface}} h\left(\mathbf{r}', t - \frac{|\mathbf{r}-\mathbf{r}'|}{c}\right) \times [f_{+}(c,|\mathbf{r}-\mathbf{r}'|) - f_{-}(c,|\mathbf{r}-\mathbf{r}'|)]d^2\mathbf{r}'. \tag{8}$$

Equation (8) is an inhomogeneous Fredholm equation of the second kind for the space-time variation of the synaptic firing density. Inspection of Eqs. (3), (6), and (7) indicates that $h(\mathbf{r},t)$ is roughly proportional to the local surface potential for $\phi_0^{+} \approx \phi_0^{-}$. Thus, Eq. (8) is the fundamental equation used here to describe linear EEG phenomena. The presence of the retarded time, $t-(|\mathbf{r}-\mathbf{r}'|/c)$, on the right side of Eq. (8) suggests the likelihood that Eq. (8) exhibits oscillatory solutions for some values of the physiological parameters.

On the basis of histological evidence for the distribution of the basal dendrites of pyramidal neurons in the motor and visual cortices of the cat [16], the following form for the distribution of connections is taken,

$$f_{\pm}(c,|\mathbf{r}-\mathbf{r}'|) = \left(\frac{\eta_0^{\pm}\lambda_{\pm}^2}{2\pi l}\right)\exp(-\lambda_{\pm}|\mathbf{r}-\mathbf{r}'|)F_{\pm}(c), \tag{9}$$

where the above coefficient is chosen for proper normalization, Eq. (4). The results presented here are not expected to be critically dependent on the exact form of Eq. (9), but only that neural masses separated by distances large compared to the characteristic distances $\lambda_{\pm}^{-1}$, have very few connec-

tions. Of course, the neural system considered in this study includes subcortical circuits, so that widely separated cortical regions may contain a significant number of connections, in which case $\lambda_{\pm} \to 0$. With the use of Eq. (9), the integral equation for the synaptic firing density in the cortex, Eq. (8), is given by

$$h(\mathbf{r},t) = h_0(\mathbf{r},t) + \frac{\lambda_+^2 \eta_0^+}{2\pi B \eta_1} \int_0^\infty F_+(c)dc \int_{\substack{\text{cortical} \\ \text{surface}}} \exp(-\lambda_+ |\mathbf{r}-\mathbf{r}'|)$$

$$\times h\left(\mathbf{r}', t - \frac{|\mathbf{r}-\mathbf{r}'|}{c}\right) d^2\mathbf{r}' - \frac{\lambda_-^2 \eta_0^-}{2\pi B \eta_1} \int_0^\infty F_-(c)dc \int_{\substack{\text{cortical} \\ \text{surface}}} \exp(-\lambda_- |\mathbf{r}-\mathbf{r}'|)$$

$$\times h\left(\mathbf{r}', t - \frac{|\mathbf{r}-\mathbf{r}'|}{c}\right) d^2\mathbf{r}'. \tag{10}$$

In order to obtain solutions to Eq. (10), use is made of the Fourier-Laplace transform:

$$h(k_x, k_y, p) = \int_{-\infty}^{\infty} dx \int_{-\infty}^{\infty} dy \int_0^\infty dt\, h(x,y,t) \exp(ik_x x + ik_y y - pt). \tag{11}$$

We neglect the effects of boundary conditions, that is, let the cortical surface area approach ∞. Boundary effects can be determined by means of a numerical solution of Eq. (10) for the spatial-temporal variation of the synaptic firing density. However, dispersion relations for a finite cortex can probably be adequately determined from the infinite cortex equation for waves of wave number $k \geqslant \pi/L$. In general, the mathematical complexities prevent the Fourier inversion of Eq. (11) even if $h(\mathbf{k},t)$ is known for all $\mathbf{k}$. However, in some cases, we can Laplace invert Eq. (11), in which case, the $\mathbf{k}$'th Fourier component of the synaptic firing density is given by

$$h(\mathbf{k},t) = \frac{1}{2\pi i} \int_{Br} h_0(\mathbf{k},p) H(\mathbf{k},p) \exp(pt) dp, \tag{12}$$

where the path of integration is along a vertical line in the p plane to the right of all singularities of the integrand. Here $h_0(\mathbf{k},p)$ is the Fourier-Laplace transform of the afferent cortical input and $H(\mathbf{k},p)$, which depends only on

the properties of the cortex and its subcortical circuits, is determined by Eq. 10). If $h_0(x,y,t)$ is oscillatory in time, as in the case of photic driving, $h(\mathbf{k},t)$ has an oscillatory solution of the same frequency; however it is the oscillations that occur independently of the afferent input that are of interest here. The existence and nature of these inherently cortical oscillations depends on the location and nature of the singularities of $H(\mathbf{k},p)$ in the p plane. In the unusual case when the only singularities of $H(\mathbf{k},p)$ are simple poles, the homogeneous solution of Eq. (12) is given by

$$h(\mathbf{k},t) = \sum_i R_i \exp[p_i(\mathbf{k})t], \tag{13}$$

provided that $h_0(\mathbf{k},p)$ satisfies the usual weak conditions so that the contour may be closed in the negative p plane. Here R_i is the residue of the ith pole of $H(\mathbf{k},p)$. In general,

$$p_i(\mathbf{k}) = \gamma_i(\mathbf{k}) + i\omega_i(\mathbf{k}), \tag{14}$$

so that the synaptic firing density is given by a sum of exponentially damped or growing sinusoidal oscillations. Of course, $h(\mathbf{k},t)$ can grow only to some finite maximum, at which time nonlinear effects invalidate Eq. (8). Of special interest to the theory of cortical oscillations are the weakly damped waves that occur due to poles p_j such that,

$$|\omega_j| \gg |\gamma_j|. \tag{15}$$

In this case, the oscillations will persist for times long compared to ω_j^{-1}, a property consistent with much of the observed EEG phenomena studied here.

In order to determine $H(\mathbf{k},p)$ for use in Eq. (12), substitute Eq. (11) into Eq. (10). Symmetry considerations of the infinite cortex allow setting $k_x = k$ and $k_y = 0$, with k interpreted as $(k_x^2 + k_y^2)^{1/2}$. Use is made of the following relations:

$$\int_0^\infty \exp(ikr\cos\theta)\,d\theta = 2\pi J_0(kr), \tag{16}$$

and

$$\int_0^\infty rJ_0(ar)\exp(-br)\,dr = \frac{b}{(a^2+b^2)^{3/2}}, \qquad \mathrm{Re}(b) > 0. \tag{17}$$

Thus,

$$[H(k,p)]^{-1} = 1 - \frac{\eta_0^+}{\eta_1 B}\int_0^\infty (\lambda_+^3 c^3 + p\lambda_+^2 c^2) \times [(k^2+\lambda_+^2)c^2 + 2\lambda_+ pc + p^2]^{-3/2} F_+(c)dc + \frac{\eta_0^-}{\eta_1 B}\int_0^\infty (\lambda_-^3 c^3 + p\lambda_-^2 c^2) \times [(k^2+\lambda_-^2)c^2 + 2\lambda_- pc + p^2]^{-3/2} F_-(c)dc. \quad (18)$$

For nearly all forms of the action potential velocity distribution function, $F_\pm(c)$, the singularities of H include branch points. In this case, Eq. (13) is not valid and a dispersion relation, $\omega = \omega(k)$, may not even exist except perhaps in some approximate sense. However, Eq. (12) may still have oscillatory solutions which exhibit many of the properties of "waves" [17, 18].

3. APPROXIMATE SOLUTIONS

In order to extract some of the essential properties of the cortical wave equation with a minimum of computational difficulties, consider the case of waves propagating in a narrow strip of cortex, which has connections only to other locations in the strip. The one dimensional version of Eq. (18) is readily obtained from Eq. (8), that is,

$$[H(k,p)]^{-1} = 1 - \frac{\eta_0^+}{\eta_1 B}\int_0^\infty (\lambda_+^2 c^2 + p\lambda_+ c) \times [(k^2+\lambda_+^2)c^2 + 2\lambda_+ pc + p^2]^{-1} F_+(c)dc + (+ \to -). \quad (19)$$

Our solutions are further restricted to waves propagating in a "cold" brain. That is, a brain in which horizontal action potential velocities connecting cortical locations are narrowly distributed about characteristic velocities $c_0^\pm$ so that the approximation, $F_\pm(c) \approx \delta(c - c_0^\pm)$, is valid. Of course, in all cases of physiological interest, $F_\pm(c)$ will have a nonzero "temperature," i.e., be distributed over a range of width $\bar{c}_\pm$. The condition for the validity of the cold brain approximation, which depends on the magnitudes of $\bar{c}_\pm$ is given at the end of this section. In the cold brain approximation and for waves in one dimension, all the singularities of $H(k,p)$ are poles; therefore the

homogeneous solution to the cortical wave equation is a sum of damped or growing oscillations, Eq. (13). In general, the dispersion relation depends on the relative magnitude of the excitatory and inhibitory connections. Consider then the following cases:

(1) *Similar excitatory and inhibitory circuits*, $\lambda c_0 \equiv \lambda_+ c_0^+ \approx \lambda_- c_0^-$. Equation (19) yields,

$$H(k,p) = [p^2 + 2\lambda c_0 p + (k^2+\lambda^2)c_0^2]$$

$$\times \{p^2 + 2\lambda c_0(1-D)p + [k^2 + (1-2D)\lambda^2]c_0^2\}^{-1}, \tag{20}$$

where

$$D = \frac{1}{2\eta_1 B\lambda}(\eta_0^+ \lambda_+ - \eta_0^- \lambda_-).$$

The dispersion relation is obtained by setting the terms in the curly bracket to zero. In order for oscillatory solutions to exist p must have an imaginary part, therefore wave solutions only occur for waves of sufficiently small wavelength, that is,

$$k > \lambda |D|. \tag{21}$$

For $k \gg \lambda |D|$, these waves have a frequency,

$$\omega = \pm c_0 k, \tag{22}$$

and a growth or damping constant,

$$\gamma = -\lambda c_0 (1-D). \tag{23}$$

(2) *"Slow" inhibitory and "fast" excitatory circuits*, $\lambda_- c_0^- \ll \lambda_+ c_0^+$. In this case, the inhibitory connections are largely subcortical and connect widespread regions of cortex; whereas excitatory connections are mainly cortical. We look for waves such that,

$$\lambda_- c_0^- \ll |p| \ll \lambda_+ c_0^+. \tag{24}$$

With this approximation and $F_-(c) \approx \delta(c - c_0^-)$, the following approximate dispersion relation is obtained from Eq. (19),

$$1 = \frac{A_+ \lambda_+^2}{k^2 + \lambda_+^2} - A_- \lambda_- \frac{p c_0^-}{p^2 + c_0^{-2} k^2}, \tag{25}$$

where $A_\pm \equiv \eta_0^\pm / \eta_1 B$. Oscillations occur if

$$k > \lambda_- |R_-|, \tag{26}$$

where

$$R_- = \frac{\frac{1}{2}A_-}{[A_+\lambda_+^2/(k^2+\lambda_+^2)]-1}. \tag{27}$$

For $k \ll \lambda_+$, R_- is roughly the ratio of the number density of inhibitory connections to excitatory connections. For $k \gg \lambda_- |R_-|$, these waves have a frequency,

$$\omega \equiv \pm k c_0^-, \tag{28}$$

and a growth or damping coefficient,

$$\gamma \equiv c_0^- \lambda_- R_-. \tag{29}$$

Because of the restriction of Eq. (24), these waves must have wave numbers in the range

$$\lambda_- |R_-| \ll k \ll \lambda_+ \frac{c_0^+}{c_0^-}. \tag{30}$$

(3) *"Slow" excitatory and "fast" inhibitory circuits*, $\lambda_+ c_0^+ \ll \lambda_- c_0^-$. The procedure is like that in (2). We look for waves in the range

$$\lambda_+ c_0^+ \ll |p| \ll \lambda_- c_0^-. \tag{31}$$

Oscillatory solutions occur if

$$k > \lambda_+ |R_+|, \tag{32}$$

where

$$R_+ = \frac{\frac{1}{2}A_+}{[A_-\lambda_-^2/(k^2+\lambda_-^2)]+1}. \tag{33}$$

For $k \ll \lambda_-$, R_+ is roughly the ratio of the number density of excitatory connections to inhibitory connections. These waves have frequency and damping decrements given by

$$\omega = \pm k c_0^+, \tag{34}$$

and

$$\gamma = -\lambda_+ c_0^+ R_+. \tag{35}$$

This dispersion relation is valid for waves of wave number,

$$\lambda_+ |R_+| \ll k \ll \lambda_- \frac{c_0^-}{c_0^+}. \tag{36}$$

(4) *Validity of the "cold" brain approximation,* $F_{\pm}(c) \cong \delta(c - c_0^{\pm})$. If $F_{\pm}(c)$ is highly peaked about $c = c_0^{\pm}$, the integral in Eq. (19) may be approximated by Taylor expanding the left side of the integrand about $c = c_0^{\pm}$. With the definition,

$$\bar{c}_{\pm} \equiv \int_0^{\infty} (c - c_0^{\pm}) F_{\pm}(c) dc, \tag{37}$$

the condition for validity of the cold brain approximation for the weakly damped waves of (1) through (3) is then given by,

$$\frac{k}{\lambda_{\pm}} \frac{\bar{c}_{\pm}}{c_0^{\pm}} \ll 1. \tag{38}$$

4. DISCUSSION

It has been shown that potential oscillations, which are independent of the location and time dependence of subcortical input, may persist in the cortex. The nature and existence of these oscillations depends on the relative distribution and abundance of excitatory and inhibitory connections between neural masses, and on the physiological state of the brain. The latter is partially determined by the velocity distribution functions for excitatory and inhibitory action potential propagation. The quantitative predictions of the cortical wave equation are dependent on several physiological parameters. In particular, $\eta_0^{\pm}/\eta_1$ is roughly the average number of excitatory (inhibitory) synapses on a single pyramidal cell body in the cortex; this parameter may be as high as 10^4. The discharge of a typical synapse may cause a $1/2$ mV depolarization in the cell body, whereas 10–25 mV is needed for an action potential to fire. Thus, the parameter B defined by Eq. (6) is typically in the range 10 to 10^2, [19].

The parameters $\lambda_{\pm}$ have small values if remote cortical regions are densely connected by cortical and subcortical excitatory (inhibitory) circuits, but are large if cortical neurons have significant connections only to others in the immediate vicinity. In the latter case, the value obtained by Sholl [16] $\sim 200\text{cm}^{-1}$ is a reasonable estimate, although generally, $\lambda_+ \neq \lambda_-$.

The characteristic horizontal velocities for excitatory and inhibitory action potential propagation $c_0^{\pm}$ are critically dependent on circuit configurations and are clearly very small compared to action potential velocities. In one experiment stimulation of the olfactory cortex in cats with a single shock results in a surface wave of potential moving with a velocity of approximately 200 cm/sec along the cortex [20]. In another, cortical wave propagation velocities of 100 cm/sec for cats and 60–70 cm/sec for

monkeys were reported [21]. These experiments provide a reasonable estimate for the wave group velocity, which is equal to $c_0^{\pm}$ in the special cases of Part 3.

The physiological parameters of this study are not known with sufficient accurracy to obtain a close quantitative check. However, we note that the experimental investigations cited in the first section indicate that the alpha rhythm has a wave number $k \sim 0.44$ cm^{-1} and frequency $\omega \sim 60$ rad/sec. Equations (22), (28), and (34) indicate that these quantities are linearly related by a characteristic horizontal velocity for inhibitory or excitatory action potential propagation. The value $\omega/k \sim 134$ cm/sec is therefore in the right neurophysiological range. Also, the experimental alpha wave number appears to be not inconsistent with the allowable range of persistent oscillations as indicated by Eqs. (21), (26), and (32). The moderately damped oscillations of the previous section are qualitatively similar to potentials evoked by single shocks [22]. The general dispersion relation may be obtained from the quartic Eq. (19), with $F_{\pm}(c) = \delta(c - c_0^{\pm})$. Weakly damped oscillatory solutions occur for certain ranges of wave number and connection parameters, $\lambda_{\pm}$ and $A_{\pm}$, defined under Eq. (25). Once these parameters are measured, the dispersion relation can be compared directly with the known frequency and wave number of the alpha rhythm.

For the cases of waves in a two dimensional cortex or brains with action potential velocity distribution functions that are not highly peaked, the cortical wave equation does not have simple sinusoidal solutions. The solution for a single spatial wavelength may itself consist of a number of complicated wave forms. The replacement of damped sine waves by Bessel functions (for example) does not, however, alter the essential validity of these arguments and may merely result in a broadening of observed frequency spectra [23].

Most of these theoretical results are, of course, dependent on the validity of the linear cortical wave equation, Eq. (8). By inspection of Eq. (6), it is clear that the cortical wave equation can only be valid if the difference between the number density of excitatory and inhibitory synaptic firings lies in the range,

$$h_{\min} \leqslant h(\mathbf{r}, t) \leqslant B\eta_1, \tag{40}$$

where $h_{\min}$ is the neural mass threshold, below which no action potentials fire. The inhomogeneous part of the $h(\mathbf{r}, t)$ can, of course, become negative, but solutions with amplitudes that grow in time are valid only as long as the above relation is satisfied. Such unstable waves may be characteristic of epileptic phenomena. In addition to the above limitation, the differential volume elements dV must contain a sufficiently large number of neurons so

that the linear approximation, Eq. (6), is valid. Thus the results are restricted to waves in $h(\mathbf{r},t)$ of wave number,

$$k \ll (\eta_1)^{1/3}, \tag{41}$$

where, $\eta_1 \sim 10^6$ cm^{-3} [24]. This relation is roughly $k \ll 10^2$ cm^{-1}, which is probably only a significant restriction for potentials measured in the cortex with microelectrodes. Such short wavelength EEG phenomena must be treated through a consideration of the interaction of individual neurons as has been accomplished in the olfactory bulb, for example [25]. Since the number of neurons is a volume element is large, the refractory property of neurons does not invalidate the linear theory for the low frequency ($< 10^2$ cycles/sec) waves characteristic of the EEG. It has been assumed that the action potential velocity distribution function is independent of time; therefore the results presented here are valid provided that $F_{\pm}(c)$ vary on a time scale that is long compared to $((1/h)(\partial h/\partial t))^{-1}$.

This study has some similarity to the mathematical considerations of the stability of brain-like structures by Beurle [26] and Caianiello [27]. In addition, an analysis of richly connected regenerative firing "units" with both excitatory and inhibitory connections has been made by Griffith [28]. These networks have the ability to exhibit sustained oscillations. The approach here differs in several respects. In particular, the mind-brain identity problem has been completely avoided in order to develop a theory of observable EEG phenomena. In this analysis, both space and time are independent variables. In contrast to previous work, signals are transported over distances up to the size of the cortex with finite velocity, thus the presence of the retarded time in Eq. (8). As the distance between neural masses, $|\mathbf{r}-\mathbf{r}'|$, approaches zero, a time delay for signal propagation still occurs due to synaptic delay and to the rise times of the PSP and action potential. If a fixed delay, t_0, is included in Eq. (8), the right side of Eq. (19) is modified by the factor e^{pt_0}. Thus, the neglect of the effect of this delay is valid for waves with frequency $\omega \ll t_0^{-1}$. Since t_0 is of the order of a few msec [19], this condition is satisfied by the low frequency EEG of interest here, but evidently not by the localized neural interactions considered in the earlier studies cited above.

This theory suggests quantitative explanations for several observed EEG phenomena, including the existence (for certain ranges of "physiological state"), frequency, and spatial wavelength of the alpha rhythm. In addition, it is suggested that continuous alpha frequency spectra corresponding to wavelengths roughly between 15 and 1 cm progressively shift towards

higher frequencies at the shorter wavelengths. The exact nature of this shift depends, of course, on the dispersion relation, which contains parameters that are not presently known. However, preliminary experiments by this author, in which spatial-temporal Fourier analyses of alpha rhythm recorded along the midline have been obtained, have shown a consistent relationship between frequency and wave number as suggested by this theory. The experimental results are presented in a subsequent paper [29].

Patients under the influence of halothane anesthesia exhibit an EEG remarkably similar to the alpha rhythm (except that it is mostly in the frontal regions). Furthermore, the frequency of the halothane rhythm is an accurate measure of doseage. A minimum dosage results in a rhythm of roughly 13 cycles/sec, whereas frequencies as low as 6 cycles/sec occur at higher dosages [30]. These observations are consistent with the speculation that low concentrations of halothane act to synchronize the EEG by "balancing" excitatory and inhibitory processes (as in the special cases considered in Sec. 3). Higher concentrations may lower average horizontal signal propagation velocities by altering the functioning neural pathways. The cortical "resonant" frequency is roughly a characteristic velocity/characteristic length.

It might be speculated that abnormal slow waves in the vicinity of a cortical lesion are due to the blockage of superficial cortical circuits thereby shifting the local distribution functions, $f_{\pm}$, towards smaller velocities. An EEG can be simulated by means of numerical solutions of Eq. (8), with solutions dependent on the size, horizontal location, and depth of the lesion. Perhaps a comparison with clinical evidence could be made.

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