EEG Generator—A Model of Potentials in a Volume Conductor

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INTRODUCTION

Existing models of EEG generation

Since the early days of clinical electroencephalography (EEG), it has generally been accepted that rhythmic electrical activity recorded from the human scalp originates within the cerebral cortex. The critical experimental evidence was reported in 1929 by Berger in his first three reports on human EEG. He noted on numerous occasions that the amplitude of the electrical potentials was considerably greater when electrodes were placed directly on the exposed cortex or on the scalp overlying bone defects. By recording simultaneously from a pair of electrodes located subcortically in the white matter, he determined that typical EEG activity was obtained only from the cortex and not from the white matter.

Many researchers have tried since that time to account for the mechanism of EEG generation. Early researchers favored the idea that the EEG represents summated action potentials of cortical neurons (Adrian and Yamsgiva 1935; Bishop 1936). In addition, an early description of a strong correlation of rhythmic single-unit activity in the pyramidal tract with rhythmic EEG waves suggested that cortical neurons are involved in EEG activity (Adrian and Moruzzi 1939). Further experiments corroborated the fact that extracellularly recorded action potentials of cortical cells often show a statistically significant relationship with EEG waves (Ajmone Marsan 1965; Creuzfeldt et al. 1957; Creuzfeldt and Meisch 1963). These relationships vary according to the type of EEG wave. Some wave types such as spindle waves or paroxysmal potentials show a close relationship to unitary activity, whereas for other wave types the relationship is looser.

However, the fact that EEG waves could also be observed in states when no action potentials were present, such as during deep anesthesia (Mountcastle 1957) or hypoxia (Creutzfeldt et al. 1957), demonstrated that action potentials could not be the only source of slow surface potentials. The existence of “dendritic potentials” (i.e., slowly propagating potentials in the superficial layers of the cerebral cortex) (Adrian 1936; Chang 1951) suggested a relationship between EEG waves and activity in the apical dendrites of cortical neurons (Chang 1951). However, the existence of activity in deeper layers of the cortex during certain EEG waves showed that deeper structures were also important (Bishop and Clare 1952; Calvet et al. 1964; Spencer and Brookhart 1961a,b; Von Euler and Ricci 1958). Other studies indicated that nerve cells may sustain wave activity similar to the EEG, thus suggesting that some EEG waves could ensue from the summation of synaptic potentials (Purpura 1959). The close relationship between postsynaptic potentials and surface EEG was later demonstrated by intra- and extracellular recordings from individual cortical cells (Creutzfeldt 1964; Jasper and Stefanis 1965; Phillips 1961). Later on some experimental studies provided an estimate of the size of unitary generators of the EEG and suggested that these generators must have cellular dimensions (Elul 1962). The theory that cortical slow waves are constituted primarily by postsynaptic potentials of cortical neurons is widely accepted today.

The processes of generation of the EEG signal in a large number of neurons forming a neural mass are complex. This led to both analytic and synthetic approaches to such processes. Freeman (1975, 1979, 1986) proposed a model describing the generation of the EEG of olfactory areas of the brain. He accounted for the interaction between structures in the olfactory area in terms of feedback loops. Freeman introduced the concept of sets that are “lumped” approximations of interactive aggregates of cells with different interconnection properties. He showed that the EEG signals simulated by a set of nonlinear coupled differential equations that describe groups of interacting populations of neurons approximate the experimentally recorded EEGs.

Most research on the generation of EEG has focused on models that attempt to determine the origin of certain types of rhythmic electrical activity seen in the EEG such as sleep spindles and alpha rhythms. Parallel to the analytic approach, Lopes da Silva (1974, 1976) proposed a model of the alpha rhythm of the thalamus and the cortex. In contrast to Freeman’s
“lumped dynamical” models of the olfactory system, this model is a distributed one in the sense that each neuron is modeled individually. The da Silva model consisted of a set of simulated neurons, thalamocortical relay cells, and interneurons. The model’s output signal was the sum of the membrane potential fluctuations of all the thalamocortical relay neurons. This output closely simulated an alpha rhythm. However, the main disadvantage of this type of model is that it is difficult to treat analytically. Van Rotterdam et al. (1982) suggested a more complex lumped model; they modeled the cortex as an infinite one dimensional chain of neurons consisting of two different kinds—main cells and interneurons. Although the model treated individual neurons, it was actually more valid as a mean field model where the main cells correspond to spatially localized homogenous excitatory neural masses and the interneurons to spatially localized inhibitory neural masses. They claimed that the source of alpha rhythm is some subcortical driving source that generates waves at a frequency that the brain can propagate with much less dumping than other frequencies.

A more general approach that accounts for the generation of alpha rhythms and its spread over the cortex was proposed by Liley and coworkers (Liley 1997; Liley et al. 1999, 2002, 2003). They considered the cortex to be an excitatory spatial continuum of reciprocally connected excitatory and inhibitory neurons interacting by way of short-range (intracortical) and long-range (corticocortical) connections. This approach showed that the strength and form of synaptic interactions between inhibitory interneurons constitute the most relevant determinants of the frequency and damping of alpha band oscillations. The input to the cortex can be assumed to be indistinguishable from band-limited white noise, while the cortex operates as a noise filter that preferentially passes frequencies between roughly 8 and 13 Hz.

Another set of models attempted to define the origin of oscillations in general, their propagation over the cortex, and their cortical dynamics. The lumped model was further refined by Nunez (1974, 1995). Nunez developed a mean field theory of the cortex split into “neural masses.” He derived an integral wave equation to describe the spatial and temporal variation of cortical electrical potential. He found that electrical oscillations could exist in the brain that are independent of the location and time history of subcortical inputs. He found that these oscillations depend on the relative number of excitatory and inhibitory connections between the neural masses and on the velocity distribution functions for action potential propagation. Wright and Liley (1996) showed that the wavelike processes revealed in the EEG exhibit linear and near equilibrium dynamics at the macroscopic scale despite extremely nonlinear, probably chaotic, dynamics at the microscopic scale. Their simulations were based on anatomical and physiological estimates of synaptic densities, coupling symmetries, synaptic gains, dendritic time constants, and axonal delays. They showed that the frequency content, wave velocities, frequency spectra, and responses to cortical activation of the ECoG can be reproduced by a “lumped” simulation treating small cortical areas as a single function unit. Describing the overall activity, Robinson et al. (1997, 1998, 2002) developed a model based on the model of Wright and Liley. They argued that the isolated cortex is relatively stable, leading to strongly damped waves and minimal influence of boundary conditions. When corticothalamic feedback is included, weakly damped waves become possible at low frequencies and near the alpha frequency.

The effect of anesthetic agents on cortical dynamics was modeled by the Steyn-Ross group (D. A. Steyn-Ross et al. 2001; M. L. Steyn-Ross et al. 1999, 2001, 2003, 2004). They used the Liley (Liley et al. 1999) model and incorporated the effect of a general anesthetic agent into the model by assuming that the effectiveness of inhibitory synaptic events increases as the concentration of the anesthetic increases. They showed that for certain ranges of anesthetic concentrations, the model predicts the existence of multiple steady states for brain activity, leading to the possibility that at a critical level of anesthetic, there would be a sudden switch-over from normal levels of cortical activity to a quiescent, low-firing state.

Models of membrane and synaptic properties of thalamic cells and circuits were designed to account for the generation of alpha spindle rhythmicity that occurs at the onset and in light stages of sleep reported by Steriade and colleagues. Models suggested for intrinsic oscillations were proposed by Wang (1994) and Destexhe (1996). Several other computational models have been used to explain the genesis of synchronized oscillations within the thalamic reticular nucleus (Golomb and Rinzel 1993, 1994; Wang and Rinzel 1992, 1993). Other models suggested that the oscillations were generated by thalamocortical-thalamic reticular networks (Golomb et al. 1996; Wang et al. 1995). The comprehensive work of Destexhe and Sejnowski (2003) drew on a computational model approach which is tightly linked to experimental data to provide insights into the dynamics of neural networks. They studied bursting neurons of the thalamus with a focus on thalamic and thalamocortical slow wave oscillations.

Current theories of epilepsy are closely linked to our understanding of the EEG. It is crucial to understand how the EEG arises to assess the relevant strengths and limitations of the EEG for providing information concerning the generation and spread of epileptic activity. At its most fundamental level, an epileptic seizure represents synchronization of a massively large population of neurons. Therefore it is important to understand how this synchronization is reflected by changes in the EEG, how neurons become synchronized, and how this synchronization can be altered with electrical stimuli.

The EEG is a measure of the degree of synchrony in a large population of oscillating dipoles. The time-averaged potential for parallel dipoles that oscillate in phase is of order of n, whereas if they oscillate out of phase the time-averaged potential is of order of √n (Nunez and Srinavasan 1981). Therefore the EEG reveals the contribution of synchronously oscillating dipoles. Because a spatially localized dipole layer can be approximated by a single dipole, this has led to the development of powerful methods to localize dipole sources and hence identify epileptic foci.

The propagation of epileptic activity from an epileptic focus involves synchronization of massive numbers of neurons. Changes recorded by the EEG during a seizure primarily reflect changes in neural synchrony. Thus measurements of EEG coherence between different cortical sites are useful for monitoring seizure evolution. High coherence has been interpreted as evidence of structural and/or functional connections between cortical areas (Fein et al. 1988). In addition to using EEG to characterize the generation of a seizure, detection of the occurrence of a seizure and estimation of epileptic foci...
location requires the ability to predict a seizure occurrence sufficiently far in advance. This provides a time window for aborting stimulus (by implanting electrodes or by activating an anticonvulsant drug delivery mechanism). Many analysis methods for seizure prediction have been suggested including the power spectrum, cross-correlation, principal component analysis, phase correlation, and mutual prediction (Schiff et al. 1996). For a comprehensive review of the work done in the field of EEG and epilepsy, see Milton and Jung (2002).

Models of generators

A number of hypotheses have been put forward over the years concerning the nature of the EEG generator and the mechanism of wave emergence. One suggestion for a generator was a vertically oriented cortical pyramidal neuron with a single apical dendrite extending toward the surface and branching horizontally in the superficial layers. The somatic and dendritic portions of the neuron are supplied with excitatory and inhibitory synaptic endings. In this model, EEG waves emerge from these excitatory or inhibitory synaptic inputs on the upper or lower portions of the neuron.

Alternatively, in other models, the EEG generator was defined as a pyramidal neuron but different mechanism for EEG wave emergence was put forward. In this case, EEG activity is considered to be primarily the result of three different generators. One generator is located within the superficial layers of the cortex (upper 500 μm) and underlies the purely surface-negative phenomena. The second generator is located within the intermediate layers (1,000 μm deep), and the third generator is located 1,000–2,000 μm below the upper surface (Calvét et al. 1964; Scherrér and Calvét 1972). Another model favored a scheme in which the unitary generator of the EEG was a single synapse or more likely a group of synapses rather than the entire neuron (Adyé and Elul 1965; Elul 1972; Elul and Adyé 1966).

These models also have drawbacks. In an idealized model, each generator can show various degrees of correlation with the others. In the extreme case, it may be completely uncorrelated. It is also desirable to have a generator that generates a fixed spatiotemporal activity pattern each time it is activated. This idealized concept permits groups of generators to be desynchronized, fully synchronized, or partially synchronized (with several subgroups of generators, each group of generators operates at a certain level of synchronicity, and there is a different level of correlation between generators from different groups).

Defining a generator as a pyramidal cortical neuron may negate the possibility of independent generators. Cortical pyramidal neurons receive their inputs from common sources; thus the activity of a specific neuron is correlated with the activity of another neuron that receives the same message from the same source.

Another difficulty in defining the pyramidal neuron as an EEG generator is the uniformity problem. Depolarization of the generator’s basal dendrite or depolarization of the apical dendrite of the same generator may cause similar intracellular potential deflections, but the contribution of these two activities to the EEG records is different in both cases. As for the depolarization of the generator’s basal dendrite, the EEG record shows a surface-positive wave as opposed to depolarization of the apical dendrite that leads to a surface-negative EEG wave. The reverse phenomenon is also not uniform; a surface-positive EEG wave may appear as a result of two different events in the same generator. Excitatory input to the basal dendrite or inhibitory input to the apical dendrite may produce the same contribution to the EEG recording, namely a surface-positive EEG wave.

This uniformity problem derives from different positions of sources and sinks along the neuron. At the level of the synapse, there is an active sink in the case of excitatory postsynaptic potential (EPSP) or an active source in the case inhibitory PSP (IPSP). Along the cell and at a distance from the synaptic level, there is a distributed passive source in the case of an EPSP or a distributed passive sink in the case of IPSP. The extracellular potential at the sink is negative at the source it is positive. Sites of sources and sinks can be located by using current source density analysis (CSD). The CSD of field potential analysis identifies the sites of current flow that generate potential differences in neuronal tissues (for a review, see Mitzdorf 1985). This method has been used to reveal physiological and anatomic features of neuronal circuits (Aroniadou and Keller 1993; Lambert et al. 1991; Mitzdorf and Singer 1978) on the basis of the spatiotemporal distribution of sinks (inward membrane currents reflected in the extracellular space) and corresponding sources (outward membrane currents) that are generated when a circuit is activated. The method is based on cortical depth recordings as an input $a$. The method makes use of the second derivatives of potential in the direction of columnar axes (on the basis of experimental observations that derivatives in directions normal to columnar axes tend to be small).

The definition of a generator as a single synapse also presents some difficulties. Because every axon in the cortex generates thousands of synapses, a single synapse does not operate independently from the rest of the synapses lying on the same axon. Activation of an axon with its thousands of synapses means correlations in generators activity (the synapses) because all the generators receive their input from the same source.

We suggest a new definition of a generator that may overcome these difficulties. We define a generator as an axon and the cloud of synapses lying along its branches. That is, the unitary activity of the generator is a cloud of synapses lying along a specific axon activated each time an action potential is conducted along the axon. This definition of the axon and its cloud of synapses solves the problem of dependency between generator activity. The triggering event initiating generator activity is the action potential conducted along the axon, and firing trains that are conducted through the axons of two neurons sharing a common source may have a wide range of correlation values. Thus activity in adjacent generators may be independent.

In addition, by using this definition of a generator, we can directly estimate the rate of triggering events activating the generators by recording action potentials via extracellular microelectrodes. Furthermore, by analyzing extracellular recordings, we can estimate the correlation coefficients between driving forces and evaluate other activation statistic parameters of generator activation.

The definition of a generator as an axon and its cloud of synapses also overcomes the problem of uniformity because
each time an action potential is produced, it is conducted along 
the axon and its processes, and all the synapses lying along this 
axon and its processes are activated by that specific action 
potential. Thus the activity of the generator is uniform each 
time it is activated. However, it should be noted that this 
generator is not a point in space but rather a volume defined by 
the axon’s processes in space.

There are two issues that can complicate this definition. The 
first one is the fact that synaptic transmission itself is not 
guaranteed each time an action potential is propagated along 
the axon and its branches. Synaptic transmission is probabilis-
tic and depends on synapse activity history. The second issue 
is that in the case of extensive activity synaptic influence does 
not add up in a linear way.

In the study presented here, we examined the contribution of 
a single activated generator to the surface potential. We first 
modeled the contribution of a single synapse to the potential 
recorded on the surface by using the theory of potentials in a 
volume conductor. By analyzing the contribution of a single 
synapse, we can quantitatively assess the contribution of a 
single activated generator to the recorded surface potential. 
Furthermore, we can evaluate how the activity of a population 
of EEG generators is related to the surface potential and study 
the effect of several statistical and topographical organizations 
on the contribution to the surface potential as well.

The article proceeds as follows: in the next two sections, we 
review (in a tutorial fashion) the methods for estimating ex-
tracellular potentials. In the fourth section, we present our 
model based on one of the methods reviewed in the second 
section. Results are presented in the fifth section followed by a 
discussion of the results and the influence of the selected 
method on the results presented.

**Extracellular Potential**

**Introduction and problems in the field**

Extracellular potentials at a point in a volume conductor 
(recorded with respect to an electrode so distant that its 
potential is not related to brain activity) are difficult to inter-
pret. It is difficult to determine the location of the active 
processes because their currents spread throughout the volume. 
The size and time course of the potentials are uncertain because 
as the distance between the recording electrode and the active 
tissue increases, the recorded potential becomes smaller. The 
relationship between the changes in membrane potential and the 
resulting current flow in the volume conductor is quite 
complicated.

**General working assumptions**

Generally, the brain closely approximates an electrical me-
dium in which magnetic induction is negligible and Ohm’s law 
is valid. Thus the potentials generated in a volume conductor 
by known current sources depend on two conditions: the 
magnitude and locations of the current sources and the con-
ductivities and geometric shapes of various parts of the inho-
mogeneous and anisotropic medium.

In this section, we assume that the sources are positioned in 
an idealized infinite homogenous isotropic medium so that only 
the source issue applies. Thus the main factor that determines 
the potentials generated is the magnitude and location of the 
current sources. We define an “infinite medium” as a medium 
all of whose boundaries between regions with different con-
ductivities are far from all current sources and measuring 
points.

**Calculation of extracellular potentials**

In an early study, Lorente de Nó (1947) calculated the field 
surrounding an axon undergoing an action potential. In essence 
the method consisted of approximating the cell by a series of 
point sources; the strength of each source was determined by 
the amount of current flowing across the surface of its corre-
sponding section of cell membrane. By calculating the extra-
cellular potential, he proposed mainly the closed field and the 
open field model. The closed field means that sources and sinks 
have a certain symmetric geometric relationship so that cur-
rents and potentials are nearly all confined to some local 
region. A brain structure that approximates closed field geom-
etry is the hippocampus. The hippocampus structure is folded 
onto itself in a peculiar shape that may substantially limit the 
spread of currents and potentials outside its boundaries. Unlike 
cells with radially symmetric dendrites such as aspiny stel-
late cells, which are also said to have a closed field config-
uration, cells with the dendrites along the predominant direction 
(i.e., longitudinal axis) are said to have an open field config-
uration because, theoretically, if one has a good enough pre-
amplifier and the noise level is sufficiently low, such dipole 
like can be recorded any distance from the neuron as long as 
the recording electrode stays in a conductive medium. The 
cerebral cortex can be thought of as an open field structure 
because of the pyramidal cells that are lined up and their 
dendrites that all point to the surface and are aligned similarly. 
Rall (1962) used the same method for calculating fields as 
Lorente de Nó and examined the distribution of extracellular 
potential due to synaptic input to the soma where the dendritic 
membrane was assumed to be passive. He initially used a 
simple model of a neuron consisting of a spherical soma and a 
cylindrical dendrite. He first found the transmembrane potent-
ial as a function of time and location along the dendrites due 
to soma depolarization. He calculated the current leaving the 
dendrite between any two points. These transmembrane cur-
tents were used to calculate extracellular potentials. The ex-
tracellular potential can be viewed as generated by a distribu-
tion of current sources in the dendrites with strength propor-
tional to the second derivative of the transmembrane potential 
with respect to the distance.

Based on the simple case of a single neuron, Klee and Rall 
(1977) computed the distribution of electric potential for se-
vcr specific cases of simplified neuronal populations arranged 
as idealized cortices. These included a closed spherical cortex 
composed of 50,000 synchronously active neurons and several 
related cases of open cortices.

Recent studies (Gold et al. 2006, 2007; Holt and Koch 1999; 
Pettersen and Einevoll 2008) examined the extracellular action 
potential in a morphologically reconstructed pyramidal cell. 
The neuron was considered to be a structure of multiple current 
point sources that combine linearly by superposition. The 
potential at any point was calculated based on current ampi-
tude and the distance from the source point to the measurement 
point. These studies simplified the structure of the neuron by 
using the line source approximation (Holt and Koch 1999).
This approximation makes the simplification of locating the transmembrane net current for each neurite using standard one-dimensional cable theory and volume conductor theory instead of treating a neurite as a three-dimensional cylinder.

Murakami and Okada (2006) attempted to determine the contribution of single neurons to the signal of EEG or magnetoencephalography (MEG). He constructed a realistically shaped multicompartiment three-dimensional single-neuron model for four principal cell types in the neocortex via NEURO. For each type of cell, the soma was stimulated by intracellular injection of a constant current, and the resulting intracellular current was used to compute the current dipole \( Q \) for the whole cell or separately for the apical and basal dendrites. The magnitude of \( Q \) was defined as proportional to the magnetic field and electrical potential far from the neuron. As expected, the pyramidal cells produced a stronger \( Q \) than the stellate cells. The \( Q \) for a population of stellate cells can be weaker than the linear sum of their individual \( Q \) values due to their variable dendritic geometry.

Bedard and Destexhe (2008) proposed a model of the genesis of local field potentials (LFPs). The model accounted the scaling of the power spectrum of LFPs as the inverse of the frequency, \((1/f)\). Starting from Maxwell’s equations, they introduced a macroscopic formalism in which macroscopic measurements are naturally incorporated, and also examined different physical causes for the frequency dependence.

**THEORY**

There are three main formulas for computing the extracellular potential. The first is the current density based calculation, as follows. Let us define \( J_\text{d}(\hat{r}) \) as the current density (in \( \text{Am}^{-2} \)) injected in the medium (for example, a transmembrane current density caused by synaptic activity in a neuron) at a given moment in time. The potential at a point \( \tilde{r}_0 \) in the volume conductor due to the injected current densities \( J_\text{d} \) at points \( \hat{r} \) lying at a distance \( R \) from \( \tilde{r}_0(R = |\hat{r} - \tilde{r}_0|) \) is the following

\[
V(\tilde{r}_0) = \frac{1}{4\pi\sigma} \int_{\text{surf}} \frac{\text{div} J_\text{d}}{R} d^3r
\]

where \( \sigma \) is the conductivity of the medium. The operator \( \text{div} \) indicates differentiation of a vector and it accounts for the total change of current (note that the divergence of the vector \( J_\text{d} \) gives a scalar quantity). The integral represents the summation over all current sources within the volume.

This approach has mostly been applied in its simplified version using point sources (Gold et al. 2006, 2007; Holt and Koch 1999; Pettersen and Einevoll 2008). The potential from a point current source \( I \) at time \( t \) is given by

\[
V(R, t) = \frac{1}{4\pi\sigma} \frac{I(t)}{R}
\]

where \( R \) is the distance from the point source (Nunez 1981). The extracellular potential sums up linearly when several point sources are present.

This general formula is not the only way to define \( V(\tilde{r}_0) \). There are two other formulas for the extracellular potential. These are more convenient because they relate the extracellular potential field directly to membrane processes of the individual neurons in the brain. One of these can be derived by assuming that the neuronal membrane can be considered as equivalent to a double layer with an inner (intracellular) membrane potential \( V_m \) and an outer (extracellular) potential \( V \). In these terms, \( V(\tilde{r}_0) \) is represented by the following expression

\[
V(\tilde{r}_0) = -\frac{1}{4\pi\sigma} \int_{\text{surf}} (\sigma_r V_m(\hat{r}) - \sigma_e V(\hat{r})) d\Omega(\hat{r} - \tilde{r}_0)
\]

where \( \sigma_r \) is the intracellular and \( \sigma_e \) is the extracellular conductivity and \( d\Omega(\hat{r} - \tilde{r}_0) \) is the solid angle subtended by an infinitesimal surface on the membrane surface \( S \) and seen from the extracellular point \( \tilde{r}_0 \). It must be emphasized that the expression of current density based extracellular potential, presented as formula 1, takes this form only when the injected current densities \( J_\text{d} \) originate at the cell membrane as derived by Plonsey (1969). Because the extracellular potential is very close to zero, Eq. 3 can be simplified to the following approximate expression

\[
V(\tilde{r}_0) \approx -\frac{\sigma_r}{4\pi\sigma} \int_{\text{surf}} V_m(\hat{r}) d\Omega(\hat{r} - \tilde{r}_0)
\]

(Niedermeyer and Lopes Da Silva 2004; Plonsey 1965).

Woodbury (1960) presented the calculation of potential due to a dipole layer for the case where the internal and external cellular conductivities are equal. He stated that at any point, the potential attributable to the dipole layer of constant moment is proportional to the solid angle subtended by the surface at the point; \( \psi(\tilde{r}_0) = (e_m/4\pi) \Omega \), where \( e_m \) is the transmembrane potential (Fig. 1). The sign of the potential is the same as the sign of the charge on the face of the dipole layer nearest to the measuring point \( \tilde{r}_0 \). The solid angle is a measure of the apparent size of an object as viewed from a particular point. An object looks larger as it is brought nearer to a particular point even though the dimensions of the object do not change.

Figure 2 illustrates the fact that the membrane potential of a quiescent cell does not influence the potential at an external point. Any point outside the cell is faced by two equally but oppositely charged surfaces of the same solid angle. Because the membrane potential everywhere is constant in a quiescent cell (charge per unit area is constant in a quiescent cell), the

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**FIG. 1.** Dipole layer. A dipole layer or surface is formed by separating + and charges across a layer of thickness \( \delta \). The potential at point \( \hat{r} \) is proportional to \( \Omega \), the solid angle subtended at \( \hat{r} \) by the dipole layer.
potential due to a quiescent cell. Axial section of a closed cylindrical cell drawn to illustrate that the potential outside a quiescent cell is 0. A: from point \( \mathring{r} \), the electrode "sees" 2 equally and oppositely polarized cell membranes subtending the solid angle \( \Omega \). B: calculation of potential at point \( \mathring{r} \) due to the near membrane; potential is \( e = +(e_m/4\pi \Omega) \) because the positive side of membrane faces \( \mathring{r} \). C: potential due to the far membrane is \( e = -(e_m/4\pi \Omega) \) because the negative side of the membrane faces \( \mathring{r} \). The total potential is the sum of the individual potentials \( e = (e_m/4\pi \Omega) - (e_m/4\pi \Omega) = 0 \).

The third formula for calculating extracellular potential is based on solid angle and current dipole. For more details see Niedermeyer and Lopes Da Silva (2004).

**MODEL**

As discussed in the preceding text, we define a generator as an axon and its cloud of synapses. It is highly desirable to be able to quantitatively assess the contribution of a single generator to the surface potential. Because a generator activates thousands of synapses scattered along its processes, there is a need to assess the contribution of a single synapse (lying on all possible positions along the axon) to the surface potential. Assuming that the contribution of a synapse to the surface potential is additive, we evaluate the contribution of a single generator by summing the contribution of all its synapses. By obtaining the contribution of a single generator to the surface potential, we can analyze how the activity of populations of generators with certain levels of synchrony within the populations and across the populations is related to the recorded surface potential.

**Model of a neuron**

We used a very simplified and idealized compartmental model of a neuron. The neuron consisted of a cylindrical soma (10 micrometers in diameter, height of 10 \( \mu m \)), long cylindrical apical dendrite (1 \( \mu m \) diam, height: 1,440 \( \mu m \)), and three equally spaced cylinders representing basal dendrites extending from the bottom of the soma cylinder (1 \( \mu m \) diam, height: 480 \( \mu m \)). Figure 3A shows the schematic morphology of the neuron where each compartment (cylinder) is represented by a line that is the main axis of the cylinder it represents. The schematic morphology consists of a long apical dendrite, soma, and three basal dendrites forming a symmetric structure. Figure 3B shows the structure of three basal dendrites as though we were looking from a surface point on top of the apical dendrite.

We assigned standard passive electric properties obtained by the Neuron package to each of the compartments described above and divided each compartment into 20 isopotential segments using the program Neuron. For the dendritic compartments, we used NEURON’s passive mechanism (\( g_{\text{pas}} = 0.001 \) S/cm², \( e_{\text{pas}} = -65 \) mV), the membrane capacitance was set to \( C_m = 1 \mu F/cm² \), the membrane resistance was set to \( R_m = 15 \) kΩcm², and the axial resistivity was set to \( R_i = 150 \) Ωcm. We used NEURON’s Hodgkin-Huxley mechanism for the soma compartment. Every segment of the apical or the basal dendrites was defined as a potential location for termination of a synapse. A single synapse was activated each time on a different segment of the modeled neuron. For each activation of a synapse, we had all the segments’ membrane potentials as a function of time. We used a synapse from the NEURON package that produced a synaptic current by conductance change. The synapse can be described by rise time and decay time constants (we used NEURON’s Exp2Syn synapse). The postsynaptic potential amplitude depends on the position of the activated synapse along the neuron and on the position of the point we are measuring this amplitude. Figure 3 shows membrane potential deflections in several points (segments) along the neuron due to activation of an apical synapse located in the middle of its length.

By activating any synapse on the modeled neuron and having its effect on the transmembrane potential, we can assess the potential each activated synapse contributes to the surface potential.

**Model of surface potential**

Two hundred micrometers above the idealized neuron presented in the preceding text, we set an array of virtual points organized topographically in circles above the neuron where the neuron’s soma is located beneath the center of the circles. These virtual points represent recording electrodes located on the surface of the cortex (Fig. 4).
For each position of an electrode and each activated synapse, we computed numerically the potential due to the activation of the synapse on the neuron \[ s(d, s_i) \] based on the membrane potential of each segment obtained by the Neuron program and the solid angle the electrode "sees" for each segment. The computation of the surface potentials consisted of the following phases.

**Triangulation of the Neuron’s Membrane Surface Area.** As mentioned in the preceding text, each dendrite was divided into 20 small cylinders called segments. We first started with an approximation of the neuron’s membrane surface area by using cylindrical hexagons instead of circular cylinders. Thus we had six rectangles of membrane for each segment. We continued with a procedure of triangulation of the approximated membrane surface area. Each rectangle was divided into two triangles; therefore at the end of the triangulation process we had 12 triangles of membrane for each segment (Fig. 5).

**Triangle Solid Angle.** Every planar triangle projected on the surface of a sphere creates a spherical triangle. A solid angle of a triangle is a spherical triangle, which is the figure formed on the surface of a sphere by three circular arcs intersecting pair-wise in three vertices. The spherical triangle is the spherical analog of the planar triangle, and is sometimes called a Euler triangle (Harris and Stocker 1998).

Let a spherical triangle have angles \( A, B, \) and \( C \) (measured in radians at the vertices along the surface of the sphere) and let the sphere on which the spherical triangle sits have a radius \( R \) (Fig. 6). Then the surface area \( \Delta \) of the spherical triangle is: 

\[
\Delta = R^2 \left( A + B + C - \pi \right)
\]  
(Zwillinger 1995).

**Segment Effective Solid Angle.** As mentioned in the preceding text, the sign of the potential at a specific point due to a patch of membrane (in this case, a triangle) depends on the sign of the charge on the face of the dipole layer nearest that point. For each triangle, we assigned the sign of the potential to the solid angle value. The segment effective solid angle was defined as the sum of solid angles of all triangles composing the segment.

**Segment Surface Potential.** Based on the segment effective solid angle that is the apparent size of the segment in the “eyes” of the electrode point, and the membrane potential of a segment over time due to activation of a single synapse on the neuron, we calculated the potential at the electrode point (Eq. 4).

The segment surface potential was calculated for all segments comprising the modeled neuron; 20 segments of the apical dendrite, 20 segments for each of the basal dendrites, 1 segment of the soma.
CONTRIBUTION OF ADDITIONAL PATCHES OF MEMBRANE SURFACE. As discussed in the preceding text, each patch of charged membrane contributes to the potential recorded at a certain measuring point. Beside the membrane surface area composing the segments, other patches of membrane of the neuron contribute to the surface potential. We calculated the solid angle of the tip of each dendrite. The tip of each dendrite forms a disk that was divided into six triangles. The solid angle of each triangle was calculated, and the tip disk solid angle was defined as the sum of all six triangles composing it. Having the solid angle of this patch of membrane, we calculated the potential contributing to the surface by the disk. The contribution of all disks (1 of the apical dendrite and 3 of the basal dendrites) was added to the surface potential calculated in Segment surface potential. Two additional disks, those covering the soma cylinder, were treated. The treatment of these two disks was different because unlike the disks covering the tip of the dendrites, which were full disks, these two disks were not full. The upper soma disk has a hole that is the point where the apical dendrite is connected to the soma, so the solid angle of this disk was calculated treating only the membrane areas of the disk. The same treatment was also applied to the lower soma disk. In this disk, there are three elliptic holes, each connecting a different basal dendrite. Thus the solid angle of the lower disk treated only the membranous part of the disk.

RESULTS

Surface potentials calculated for an array of electrodes due to activation of a single synapse

We computed the surface potential due to activation of a single synapse lying on top of the apical dendrite at several surface points. The potentials shown in Fig. 7A are the potentials computed from a set of surface electrode points with gradually increasing distances from the soma of the activated neuron. As expected we obtained a negative wave due to activation of the top apical synapse. The peak amplitude of the waves decreased as the electrode was moved farther away from the neuron.

Similarly, we computed the surface potential due to activation of a basal synapse using the same array of electrode points as before (Fig. 7B). The potentials showed positive waves. As seen in the potentials, due to activation of the apical synapse, the decrease in amplitude as the surface electrode moved farther from the neuron can again be seen.

In addition, the wave amplitudes due to activation of a basal synapse were two orders of magnitude smaller than the amplitudes computed for the apical synapse (Fig. 7A). This difference in order of magnitude between potentials due to activation of an apical synapse and potentials due to activation of a basal synapse emerges from the differences in distance between the location of the electrode and the most active segments of the neuron. In the case of the apical synapse, the electrode was relatively close to the most active segments; thus the effective solid angles of the most active segments were larger. As a result, the contribution of these segments to the surface potential was greater, by contrast with the basal synapse, where the distance between the position of the electrode and the active segments was much larger, and the effective solid angles of these segments were much smaller. Thus the contribution of the most active segments to the surface potential was very small. As seen in the potentials, due to activation of the apical synapse, the decrease in amplitude as the surface electrode moved farther from the neuron can again be seen.

Surface potentials calculated for a single electrode due to activation of a single synapse located in several positions on the neuron

Using the model we can show the potentials a certain electrode point records as the position of an activated synapse on the apical dendrite is moved down along the apical dendrite toward the soma. The calculated potentials show the transition from a negative to positive wave as the synapse descends along the dendrite (Fig. 8A).

We used the same position of the electrode to calculate the potentials due to activation of a basal synapse the position of which was moved down along the basal dendrite (Fig. 8B).

As we moved down the location of the synapse along the basal dendrite the time of the peak amplitude was delayed. This is due to the fact that the electrode “sees” more from the upper segments of the neuron that change their membrane potential with a greater delay as the position of the activated synapse is moved down. This type of delay also exists in the case of apical synapses but it is much less apparent.

Radial symmetry in calculated surface potentials

The potentials due to activation of an apical synapse showed symmetry around the neuron. Figure 9A shows potentials recorded at 19 points; each point was positioned 300 μm from the neuron with a different angle from the soma (0–180°). Due to the symmetrical structure of the neuron, the potentials at the other angles (190–360°) are the same as the potentials calculated. The results for activation of an apical synapse show that the potentials were identical for all points around the neuron at a certain radius from it.

Figure 9B shows potentials due to a basal synapse for a set of electrodes positioned 300 μm from the neuron with different angles from the axis of the basal dendrite. In the basal synapse case, there is a radial symmetry relative to the axis of the activated basal dendrite.

Synapse contribution as a function of distance from the electrode

There are thousands of synapses activated in a given time bin and a certain brain volume. Because it is unfeasible to obtain the activation time of every single synapse, it is much more useful to describe their contribution to the surface potential in terms of variance. We calculated the surface potential in every simulated electrode position due to activation of a synapse on every segment possible along the modeled neuron. For every surface potential calculated, we calculated the variance contribution to the surface potential. Having the variance contribution, we calculated the mean contribution of a synapse to the variance of the surface potential measured as a function of distance from the recording electrode, syn_contribution

\[ \text{variance contribution to the surface potential measured as a function of distance from the recording electrode, } \text{syn_contribution} \]

\[ = \text{Var}(\rho(r, \alpha, s) V_{S_0}, \alpha) \]  

(mean over all synapse locations and all angles of a specific radius).

Assuming no correlation between different synapses terminating on a given cell, the contribution of all synapses to the variance is additive. The contribution of a single cell activated in a certain time bin to the variance of the surface potential is simply the variance of the sum of the activated synapses. Furthermore, we can assess the variance of an electrode listen-
According to a population of desynchronized synapses simply by summing the variance of every single generator listened to. Based on the mean variance contribution for each radius, Fig. 10 shows the relative contribution of a single synapse to the surface potential as a function of distance from the electrode. This curve actually describes the weight density function of a synapse so that the area of the region bounded by the curve is 1. The relative synapse variance contribution as a function of distance from the electrode obtained by the simulation is shown in red circles. The weight density curve can be approximated by the derivative of hyperbolic tangents as shown by the fitted blue line. It should be noted that the hyperbolic tangent was the function that exhibited good fit to the simulated curve and there was no theoretical reason for selecting this specific function.

**Contribution of an activated single generator and a population of generators to the variance of the surface potential**

The model presented in the preceding text can explain the contribution of a synapse to the surface potential as a function of time. In real life, an electrode does not listen to a single synapse but to a population of synapses activated by a population of neurons. Experimental studies have shown that in unsynchronized population of neurons; i.e., neurons firing at a constant low rate independently (~2 Hz), the measured root mean square (RMS) of the recorded surface potential is below the resolution of the electrodes. We applied this condition on the model to attempt to validate it.

**FIG. 7.** Surface potentials recorded by an array of electrodes. **A**: negative potentials calculated for a set of electrodes with increasing distance from the neuron due to activation of an apical synapse. The activated synapse was located on the apical dendrite 1.4 mm from the soma. The peak amplitude decreases as the electrode moves away from the neuron. Inset: absolute value of peak amplitude calculated for the set of electrodes with increasing distance from neuron. **B**: positive potentials calculated for a set of electrodes with increasing distance from the neuron due to activation of a basal synapse. The synapse was located on a basal dendrite 350 µm from the soma. The peak amplitude decreases as the electrode moves away from the neuron. Inset: peak amplitude calculated for the set of electrodes with increasing distance from neuron.
Let us consider a real life scenario of recording. Electrode that is positioned on the surface of the cortex listening to a 1-mm diam cylinder of cortex. The neurons lying in the recorded cylinder show spontaneous activity; that is, the neurons fire at a rate of 10 \(-2\) Hz independently. Let us define the recorded surface potential over time as \(f(t)\); thus the variance of the surface potential is defined as

\[
\text{Var} = \int_{0}^{T} f^{2}(t) \, dt - \left( \int_{0}^{T} f(t) \, dt \right)^{2}/T.
\]

Because the EEG/ECoG is a filtered signal above a certain low frequency, \(\int_{0}^{T} f(t) \, dt = 0\), the RMS measure is simply the square root of the variance.

We calculated the contribution of a single generator (a cloud of \(10^{5}\) synapses activated simultaneously) to the variance of the surface potential. We analyzed a single generator positioned along the main axis of the cylinder having \(10^{5}\) synapses scattered throughout the volume of the cylinder with a uniform density \(\rho\). The synapse density is defined as the ratio of the number of synapses lying along a single generator to the volume treated \(\rho = 10^{3}/\pi R^{2}h\), where \(h\) is the height of the cylinder, i.e., the depth of the cortex, and \(R\) is the radius of the cylinder analyzed, which is 0.5 mm. The 1-mm diam cylinder of cortex was divided into several smaller cylinders defined by an array of radii starting from a \(r_{1} = 20 \mu m\) radius to \(r_{2} = 0.5\) mm. We

FIG. 8. Potentials computed from a surface point due to activation of a synapse descending along a dendrite. A: potentials due to activation of a single synapse on every segment possible of the apical dendrite. The transition from negative potentials for the upper synapses to positive potentials for the lower synapses can be seen. The time of the peak amplitude is delayed as the activated synapse descends along the apical dendrite. The electrode is positioned 300 \(\mu m\) from the neuron. (The segment closest to the soma is labeled segment 1 and the most distal segment from the soma is labeled segment 20). B: potentials calculated due to activation of a single synapse on every segment possible of the basal dendrite. The time of the peak amplitude is delayed as the activated synapse descends along the basal dendrite. The electrode was positioned 300 \(\mu m\) farther away from the neuron. (The segment closest to the soma is labeled segment 1 and the most distal segment from the soma is labeled segment 20).
looked at each of the cylindrical rings defined by radius $r$ and thickness $dr$. The number of synapses in this cylindrical ring ascribed to a single generator is $\int_0^\infty \int_0^r a(r, x, t) r dr dx$, where $a(r, x, t)$ is the amplitude as a function of time of the recoded potential due to activation of a single synapse at depth $x$ by an electrode distant $r$ microns from the generator. We defined the distance between the electrode and the generator as a tangential distance; i.e., we projected the position of the soma on the surface and measured the distance between the two points on the surface. Having obtained the amplitude of the surface potential due to activation of a single generator as a function of time, we calculated the variance of this generator activity in time.

Given the variance contribution of a single generator to the variance of the surface potential in 1 s of time, we can calculate the variance due to activation of a totally unsynchronized
population of generators positioned in the analyzed cylinder. The number of generators in the cylinder is \( h \pi R^2 \rho \), where \( R \) is the cylinder radius, \( h \) is the cylinder height and \( \rho \) is the density of cells (we used \( \rho = 2 \times 10^9/\text{mm}^3 \)). Analysis of the desynchronized activity of the generators positioned in the treated cylinder firing at a rate of \( \sim 2 \) Hz independently, the variance of the activity is the sum of variances of all generators activated in the analyzed cylinder multiplied by 2 Hz. The RMS is simply the square root of the variance and it turns out to be \( 1 \times 10^{-3} \) mV. Clearly, this is an upper bound of RMS because the cloud of synapses of some of the cells may be positioned only partially inside the volume of the cylinder treated. This result is congruent with the experimental findings of a very low RMS value due to completely desynchronized activity.

**DISCUSSION**

Two methods for calculation of an extracellular potential created by membrane potential deflections of a cell were presented here. The first method (Eq. 1) was based on current source density, and the second was based on the cell membrane potential itself (Eqs. 3 and 4). In our model, we calculated extracellular potential using the second method (Eq. 4). In addition, we assumed that the conductivities of the intracellular medium (\( \sigma_i \)) and the extracellular medium (\( \sigma_e \)) were equal (\( \sigma_i/\sigma_e = 1 \)). The inequality of \( \sigma_i \) and \( \sigma_e \) affect the potential variation by a multiplicative ratio \( \sigma_i/\sigma_e \) (Plonsey 1965).

There is an alternative way of calculating the extracellular potential using Eq. 4 without treating the whole membrane surface area as was done in the model showed here. The main idea is that the dendrites of the modeled neuron are divided into isopotential cylindrical segments. Hence the contribution to the surface potential emerges only from the cross segment areas (where there is a difference in membrane potential between segments). The electrode sees a given cross segment area (which form a circular disk) with a certain solid angle and the membrane potential on the two sides of the cross-section is different; thus there is a contribution to the surface potential. We compared the potential computed using Eq. 4 with this alternative method. The potentials were identical. In line with this alternative method, Pettersen and Einevoll (2008) showed that a neuron’s extracellular spike amplitude is approximately proportional to the sum of the dendritic cross-sectional areas of all dendritic branches connected to the soma.

In the basic model presented in MODEL, we calculated the contribution of a synapse activation terminating on a large pyramidal neuron to the surface potential (see specifications of the neuron size in MODEL). Then we presented an extension of this model from a surface electrode listening to the activation of a single synapse terminating on a single cell to an electrode listening to a population of synapses terminating on a population of neurons lying in a certain brain volume (a cylinder). This extension assumed that the volume of the treated cylinder only consists of large pyramidal cortical neurons (as in the model). Clearly, this would lead to a larger RMS than if we replaced some of the large pyramidal neurons by smaller ones representing layer II and III pyramidal neurons.

In addition, during activity as described in the extended model, i.e., neurons firing at a constant low rate independently \( \sim 2 \) Hz, there is leakage in the dendrites emerging from the spontaneous activity. We modeled this leakage by tuning the conductance parameter \( \text{mho/cm}^2 \) of the modeled neuron.

The results shown in the preceding text imply that distal current sources on the apical dendrite (those positioned closer to the surface and far from the soma) make the greatest contribution to the ECoG recorded and the smallest contribution to variation in soma membrane potential. Indeed when referring to a single synapse, there is greater electrical contribution to the surface potential by an apical superficial synapse than by a deeper basal synapse. These results may not get along with other typical theoretical macroscopic modeling studies that make use of mean soma membrane potential. It has to be noted that the number of synapses close to the surface is much smaller than the number of synapses located on the basal dendrites. In addition, the soma is not the compartment with the major contribution to the ECoG. Regarding scalp EEG, the electrode is positioned very far from all synapses relative to the size of a cell. Thus the difference between the contribution of apical superficial synapse and deeper basal dendrites is less prominent than that presented by the model that is applicable to ECoG.

We showed earlier that low RMS values are obtained because of completely desynchronized activity. The same analysis can be applied to any population of generators having a certain level of synchrony. Buxhoeveden (2002) presented the minicolumn as the smallest level of vertical organization in the cortex (80–100 neurons depending on cortical area). This structure can be thought of as a population of generators which are synchronized to a certain extent. He also presented the macrocolumn, which consists of minicolumns (60–80) bound together by short-range horizontal connections that cooperate in a given functional state. This structure can be thought of as a population of generators that is divided into subpopulations with a certain degree of synchrony within each subgroup and between all pairs of subgroups.
For a first order of approximation and under the assumptions mentioned in the preceding text regarding the medium, the amplitudes obtained by the model seem correct. Such approximations provide important intuitive insights into tissue volume conduction and provide a necessary step to the more accurate description required for inhomogeneous media. As the extended model for desynchronization activity showed, we obtained very low values that are expected and in agreement with experimental results obtained by Elul (1972). As first order of approximation, we used a very simple and idealistic model of a neuron without any dendritic trees. On one hand, branches of apical dendritic tree that are close to the surface contribute considerably to the surface potential. On the other hand, our modeled apical dendrite has a constant diameter along its length, thus its distal segments (those distant from the soma and closer to the surface) contribute more to the surface potential than if they were modeled with smaller diameter.

In this paper, we presented a new definition for the term EEG generator. This definition makes it easy to find the activity rate of a generator and the correlation between given generators simply by using multiple parallel recordings of single-unit activity. Relying on this new definition, we can examine the relation among generators activity, generators statistics, and the EEG/ECoG signal recorded in the preceding text. In this study, we calculated the contribution of a single generator to the variance of the recorded signal and showed that under the condition of completely unsynchronized activity, we obtained low values of RMS as expected. This calculation for the RMS value can be made for any statistical organization of generators, from completely unsynchronized to fully synchronized populations.

We can further use the weight function in additional analysis. This function assigns each synapse a weight factor as a function of distance from the electrode. We can use the weight function obtained here to assess the contribution of an activated generator as a function of distance from the recording electrode. Second, we can evaluate the effect of a group of generators (many clouds of synapses) on the variance of the recording electrode. This information is crucial for understanding an electrode’s record as a weighted mixture of the generator’s population activity.

Avitan et al. (2007) described a model for extracting statistical parameters of a population of generators from multi-channel recordings. The analysis assumed that a recording electrode simply averages the activity of all generators lying below it. Having a weight function of generators as a function of distance from the recording electrode means we can treat recordings as a weighted mixture of a population of generators. This will enhance the model and make it applicable to real life scenarios. This is our next step in research on the EEG as a function of the dynamics of its generators.

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REFERENCES


