Cortical Potential Distributions and Information Processing

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The use of sets of spatiotemporal cortical potential distributions (CPDs) as the basis for cognitive information processing results in a very large space of cognitive elements with natural metrics. Results obtained from current source density (CSD) analysis suggest that in the CPD picture, action potentials may make only a relatively minor contribution to the brain’s code. In order to establish if two CPDs are close, we consider standard metrics in spaces of continuous functions, and these may be employed to ascertain if two stimuli will be identified as the same. The correspondence between the electrical activity within brain regions, including not only action potentials but all postsynaptic potentials (PSPs), and CPDs is considered. We examine the possibility of using the CSD approach to find potential distributions using the descriptive approach in which precise sets of times are ascribed to the occurrence of action potentials and PSPs. Using metrics in the multidimensional space of paths of collections of point processes, we show that closeness of CPDs is implied by closeness of sets of spike times and PSP times if a certain metric is used but not others. We also set forth a dynamical model consisting of a system of reaction-diffusion equations for ionic concentrations coupled with nerve membrane potential equations and active transport systems. Making the approximation of a descriptive approach, the correspondence between sets of spike times and PSP times and CPDs is obtained as with the CSD method. However, since it is not possible to ascribe precise times to the occurrence of PSPs and action potentials, the descriptive approach cannot be used to describe the configuration of electrical activity in cortical regions accurately. We also discuss how the CPD framework relates to the binding problem and submillisecond timing.

1 Introduction

Early theories of coding in the nervous system (Sherrington, 1906; Eccles, 1953) focused on rate coding in which the average frequency of action potentials carries information about the stimulus. This type of coding, which was established in the firing responses of such cells as motoneurons (Granit, Kerner, & Lamarre, 1966) and sensory receptors (Terzuolo & Washizu, 1962), has become associated with the integrate-and-fire mode of operation of a nerve cell (Konig, Engel, & Singer, 1996) where timing is not a key factor.
The idea has also been developed in the past few decades that time intervals between impulses in patterns of action potentials play a key role; this manner of information delivery has become known as temporal coding (Barlow, 1963; Villa & Fuster, 1992; Abeles et al., 1995; see Fujii, Ito, Aihara, Ichinose, & Tsukada, 1996, for a review). Nearly all theories of information processing thus focus attention on properties of trains of action potentials, which are usually considered as temporally discrete events. (McCulloch & Pitts, 1943; Hubel & Wiesel, 1962; Hopfield, 1982; Tuckwell, 1998). This includes synchronization, oscillation, correlation and repeating patterns (Toyama & Tanaka, 1984; Kreiter & Singer, 1992; Ghose & Freeman, 1992; Deppisch et al., 1993; Usher, Schuster, & Niebur, 1993; Hopfield & Herz, 1995; Maass, 1995; Bush & Sejnowski, 1996; Kempter, Gerstner, van Hemmen, & Wagner, 1998; Lestienne & Tuckwell, 1998; Singer, 1998; Golomb, 1998).

The approach in which attention is focused on these discrete events (times of occurrence of spikes) leads to difficulties in the construction of metrics for neocortical activity because common metrics for sequences (of time points) often give large distances if seemingly minor differences occur between spike trains. This can be seen by considering two finite sequences of spike times, \( s = \{s_k\} \) and \( t = \{t_k\} \), where \( k = 1, 2, \ldots, n \), and employing, for example, the standard metric

\[
\rho_2(s, t) = \left[ \sum_{1}^{n} |s_k - t_k|^2 \right]^{\frac{1}{2}}.
\]

Two spike trains can be very similar, and yet such a metric will return a large value for the distance between the sequences of spikes. To illustrate, with time in milliseconds, first let \( s = \{0, 5, 6, 10, 11, 15, 20, 21\} \) and let \( t = \{0, 5, 10, 11, 15, 21, 22\} \). Then the distance between the trains is \( \rho_2(s, t) = \sqrt{60} \). If now the second spike train is replaced by the similar one \( t = \{0, 5, 6, 10, 11, 15, 21, 22\} \), then the distance using this metric is only \( \rho_2(s, t) = \sqrt{2} \). Furthermore, focusing on spike trains as the carriers of information or the determinants of cognitive states appears to be an expedient approach, perhaps due to experimental emphasis on unit recordings. Since there is a large amount of electrophysiological activity in addition to the occurrence of spikes, it seems that this contribution from this other activity (mainly in the form of postsynaptic potentials) should be included in a description of cortical neurophysiological states and cannot be dismissed when considering cognitive information processing. That is, one has to admit the possibility that theories that concentrate only on the occurrence of action potentials might be omitting significant contributions from nonspiking neurophysiological activity. That is, action potentials constitute perhaps only part or even a small part of the picture as far as cognitive experiences are concerned. Action potentials are a means of transmitting a signal from one part of the nervous system to another (or other kind of organ), but their
arrival at a target manifests itself primarily as postsynaptic potentials, not further action potentials.

A quantification of global neurocognitive or brain states is considered to be an important component of a neurophysiological theory of information processing. Whether one focuses on spikes or broader classes of neurophysiological activity, it is important to be able to ascertain if two cognitive processes (assumed neurophysiologically based) are close to each other, not only from the point of view of a satisfactory theory but also with respect to neurophysiological activities themselves; that is, with such a quantification there must be a measure of distance between such states, which leads to the introduction of metrics. Without a suitable metric to ascertain if physiological brain states are similar, it is not possible to understand when and why similar states lead to similar perceptions or possibly more general cognitive (“mental”) processes. This is also motivated by the need to compare cognitive processes in different individuals between whom there must be considerable variability in anatomy, physiology, and chemistry. We adopt the viewpoint that collections of sequences of spike times in populations of neurons probably do not by themselves provide an accurate or complete basis for describing cognitive states, despite the fact that some models of discrete neural networks are capable of emulating features of gross cortical activity such as alpha rhythms (Liley, Alexander, Wright, & Aldous, 1999). This view springs from the observations that global or field potential distributions are only partially dependent on spikes and that they may also depend significantly on collections of sequences of postsynaptic potentials at various synapses. That is, many different types of ionic current within certain brain regions may contribute to some extent to the overall cognitive state of an individual. This idea leads naturally to the description of cognitive states by means of spatiotemporal distributions of field potentials. These are taken in what follows to be electrical potentials, although the role of magnetic fields is not negligible (Okada, Lauritzen, & Nicholson, 1988; Bowyer et al., 1999; Mackert et al., 1999), so that in a broader framework, one might use an electromagnetic field description for cortical states (classically, the pair \( \mathbf{E}(x, t), \mathbf{H}(x, t) \) of electrical and magnetic field strengths throughout the relevant time and space domains).

2 Potential Distribution Coding

Rather than focus on spikes and, in particular, their times of occurrence as a point process, we concentrate on the spatiotemporal distribution, stochastic or deterministic, of the electrical potential as it changes from instant to instant. A three-dimensional system of space coordinates with a fixed origin, and fixed axes can be chosen within a brain or brain region. Similarly an arbitrary but fixed time origin can be ascribed. At any space point \( x \) and time \( t \), there is an associated electrical potential, \( V(x, t) \), relative to that at some reference point. If \( M \subseteq \mathbb{R}^3 \) is a three-dimensional region of the cerebral
cortex or other brain region and \( T = [t_1, t_2] \subset R^+ \) is a time interval, then for fixed \( t \) and \( x \in M \), \( V(x, t) \) is a real-valued continuous function varying in space, or a spatial distribution of potential.

We wish to consider the set of actual electrical potential distributions \( V = V_{M, T} = \{ V(x, t), x \in M, t \in T \} \) throughout the space-time region. For convenience, only extracellular points of \( M \) may be considered; we will assume that measurements of (field) potentials are influenced only by ions and their associated currents in this extracellular compartment, which is a topologically connected region. Although only extracellular points of \( M \) will be considered, we will continue to use the same symbol \( M \) for the spatial region under consideration. (The amount of extracellular space within the cortex has been estimated as about 0.2 of the total volume; Lux & Neher, 1973.) Note that \( V \) can be considered as a four-parameter stochastic process \( \{ V(x, t; \omega), x \in M, t \in T \} \) in which the parameters are the three spatial coordinates and the time, the sample space variable \( \omega \) being usually suppressed. Different realizations correspond to different values of \( \omega \). (For further explanation, see Parzen, 1962, or Tuckwell, 1995.) For fixed \( \omega \), the sample paths of \( V \) are supposed to describe, or correspond to, the neurocognitive processes that occur within \( M \) in the time interval \( T \). Although \( M \) is not fixed during the life of an individual, it is convenient to regard it as fixed in this context in relatively small time intervals. We also note that the exact potential \( V(x, t) \) cannot be measured exactly but can be estimated by an approximate experimental field potential over a region \( A_x \) surrounding the space point \( x \) (and probably also a small time interval surrounding \( t \)),

\[
V_E(x, t) = \frac{1}{|A_x|} \int \int \int_{A_x} V(x', t)w(x', t)dx',
\]

where \(|.|\) denotes volume. The region \( A_x \) reflects the size of a recording electrode, and the weight function \( w(x, t) \) reflects its electrical properties.

### 2.1 Metrics.

The set of all possible potential distributions \( V(x, t) \) on \( M \times T \), which we denote by \( C_V(M \times T) \), is a set of bounded continuous functions and a subset of the space \( C(M \times T) \) of all bounded continuous functions on that product space. For such a space, there are suitable commonly used metrics (Simmons, 1963), or distance functions, which are natural and hence useful in describing the magnitudes of the distances between cortical states. Let \( V_1 \) and \( V_2 \) be two points in \( C_V(M \times T) \) (i.e., spatiotemporal potential distributions). One such metric is provided by the uniform or sup norm,

\[
D_1(V_1, V_2) = \sup_{M \times T} |V_1(x, t) - V_2(x, t)|.
\]

Alternatively and perhaps more satisfactorily, we may consider \( C_V \) as a subset of the space of square integrable functions on \( M \times T \), usually denoted
by $L_2[M \times T]$, in which case we may use the metric
\[
D_2(V_1, V_2) = \left[ \int_M \int_T (V_1(x, t) - V_2(x, t))^2 \, dt \, dx \right]^{\frac{1}{2}}.
\] (2.3)

However, if one is interested only in comparing spatial potential distributions at a given time $t_1$ and thus considered only to be functions of $x$, then the following corresponding metrics will be useful:
\[
d_1(V_1, V_2) = \sup_{M} |V_1(x, t) - V_2(x, t)|
\] (2.4)

and
\[
d_2(V_1, V_2) = \left[ \int_M (V_1(x, t) - V_2(x, t))^2 \, dx \right]^{\frac{1}{2}}.
\] (2.5)

$D_1$ and $d_1$ are volts, whereas $D_2$ is in volts sec$^{1/2}$ meters$^{3/2}$ and $d_2$ is in volts meters$^{3/2}$.

3 Neurophysiological Activity

3.1 Stimuli. Consider a stimulus $S_0$, of extrinsic or intrinsic origin, or a combination of both. With this stimulus will be associated a set of spike trains, postsynaptic potentials, and other neurophysiological events that can be considered as constituting a point in a multidimensional metric space. There will also be an associated potential distribution, which we assume is defined in the region $M \times T$. However, it is very unlikely that the set of spike trains, postsynaptic potentials, or corresponding potential distribution are uniquely determined by $S_0$ because the response to the same stimulus is never exactly the same at different presentations. Thus, there will be an average potential distribution associated with $S_0$, which we denote by $\overline{V}_0$. If a stimulus $S$ occurs, it will be identified with $S_0$ if the potential distribution $V$, elicited, satisfies
\[
D_1(V, \overline{V}_0) < \epsilon_1,
\] (3.1)
or
\[
D_2(V, \overline{V}_0) < \epsilon_2,
\] (3.2)
where the positive constants $\epsilon_1$ and $\epsilon_2$ are measures of the discriminatory ability of neurocognitive processes.

Now $M$ may be partitioned into $w$ disjoint subsets $M_k$ such that
\[
\bigcup_k M_k = M, \quad M_j \cap M_k = \phi
\]
for \( j, k = 1, 2, \ldots, w \), where \( \phi \) is the null (empty) set. Then any potential distribution \( V \) can be decomposed into \( w \) subpotential distributions,

\[
V_k = \{V(x, t), x \in M_k, t \in T\}, k = 1, 2, \ldots, w,
\]

with a similar decomposition for \( V_0 \). Metrics \( D_{1,k} \) can be defined on \( C[M_k \times T] \), and \( S \) will be identified with \( S_0 \) if, for example,

\[
\max_k D_{1,k}(V_k, V_0) < \epsilon_3.
\]

3.2 General Neurophysiological Processes. The determinants of the electrical potential (or the entire electromagnetic field) throughout brain regions are the fixed distributions of charges and the currents due to the movements of charged particles, including various ions as they course into and out of neurons and glia and the extracellular compartment. Then, as a first approximation, one may assume that the methods of current source density (CSD) analysis (Rappelsberger, Pockberger, & Petsche, 1993, for example; see Mitzdorf, 1985, for a review) are valid, though the usefulness of this approach remains to be fully explored. This formalism, which is based on Maxwell’s equations, is usually expressed through the equation

\[
\nabla \cdot [\sigma \nabla V] = -I(x, t), \tag{3.3}
\]

where \( \sigma \) is the conductivity tensor and \( I(x, t) \) is the current density. Equation 3.3 is usually employed to determine the current density \( I \) from the measured field potentials, which may be an ill-posed problem. However, here we note that given \( I \), one may in principle solve equation 3.3 with appropriate boundary and initial conditions to determine the potential distribution throughout a brain region over a given time interval. It is possible to deduce from this that the potential distribution \( V \) should be uniquely determined by the current density. If, as hypothesized, \( V_{M,T} \) determines the cognitive processes in an individual over the time interval \( T \), then, on the assumption of the validity of equation 3.3, there is a one-to-one correspondence between such processes and current density distributions \( I = \{I(x, t), x \in M, t \in T\} \). One may assume also that \( I \) is in \( C[M \times T] \).

4 Spike Trains and Postsynaptic Potentials: A Descriptive Approach

It is important to relate the distance function in the cortical potential distribution (CPD) framework to the ongoing neurophysiological activity in the brain. In order to incorporate the contributions from spike trains and activated synapses within \( M \), we adopt a descriptive approach at first, attempt to develop a dynamical approach later, and also consider a combination of the two approaches. In the descriptive approach, we are given the sequences of firing times and times of activation of synapses. For simplicity,
it is assumed that the neurophysiological effects of an action potential or postsynaptic potential are always the same. This is clearly an approximation, as the effects of spikes and postsynaptic potentials depend on the previous history of events and more particularly on the immediate previous history. For example, after a rapid succession of spikes, there is often sufficient potassium accumulation in the extracellular space to cause a substantial shift in membrane potential, which can have a dampening effect on subsequent spiking (Lebovitz, 1970). Similarly, rapid volleys of impulses at a synapse can lead to a reduced postsynaptic potential amplitude (Curtis & Eccles, 1960). In addition, even in adult brains, the anatomy and physiology, including synaptic distributions and synaptic strengths at both pre- and postlocations are very susceptible to dynamical changes (Hess & Creese, 1987; Dawirs, Teuchert-Noodt, & Busse, 1991; Liao, Jones, & Malinow, 1992; Manabe, Wyllie, Perkel, & Nicoll, 1993).

4.1 Impulsive Currents and Point Neurons and Synapses. The following approach is probably the simplest, but it can lead, as shown in the appendix, to problems with boundary conditions. As a first step, assume that all the currents associated with an action potential of a given neuron can be collected at a single space point and that the current flows are relatively rapid and can therefore be considered instantaneous. Let there be \( n \) neurons located at space points \( x_k, k = 1, 2, \ldots, n \), and let their corresponding spike times be \( t_{jk}, j = 1, 2, \ldots, n_k(t) \), where \( n_k(t) \) labels the largest spike time of neuron \( k \), which occurs in the time interval \((0, t]\). When neuron \( k \) emits a spike, suppose there are \( p_k \) contributions to the current density from the various ion species of amplitudes \( A_{ki} \), \( i = 1, 2, \ldots, p_k \). \( A_{ki} \) is actually the total charge delivered for ion species \( i \) whenever neuron \( k \) fires. Now let the synapses be localizable at the space points \( y_l, l = 1, 2, \ldots, m \), and assume again that their associated net current flows are impulsive and have times of occurrence \( s_{rl}, i = 1, 2, \ldots, m_l(t) \), where \( m_l(t) \) labels the largest postsynaptic potential (PSP) time of synapse \( l \), which occurs in the time interval \((0, t]\). The corresponding strengths of the currents generated are denoted by \( B_{lr} \), \( r = 1, 2, \ldots, q_l \). Thus, \( B_{lr} \) is the charge delivered for ion species \( r \) at an activation of synapse \( l \). \( A_{ki} \) and \( B_{lr} \) are not fixed; they may be random, time dependent, dependent on several state variables (ion concentrations, transmitter concentrations, etc.), or history dependent. For convenience we put

\[
\alpha_k = \sum_{i=1}^{p_k} A_{ki}, \quad \beta_l = \sum_{r=1}^{q_l} B_{lr}.
\]  

(4.1)

Then in this descriptive approach, we have

\[
\nabla \cdot [\sigma \nabla V] = - \sum_{k=1}^{n} \alpha_k \delta(x - x_k) \sum_{j=1}^{n_k(t)} \delta(t - t_{jk})
\]
Here distances are in meters, \( V \) is in volts, \( \alpha_k \) and \( \beta_l \) are in coulombs, and \( \sigma \) has units of [ohms meters]\(^{-1}\). Equation 4.2 may be written in another way. We let \( N_k(t) \) be the number of spikes of the neuron at \( x_k \) in the time interval \((0, t] \) and let \( M_l(t) \) be the number of postsynaptic potentials that occur at the synapse located at \( y_l \) in the same time interval. The quantities \( N_k = \{N_k(t), t \geq 0 \} \) and \( M_l = \{M_l(t), t \geq 0 \} \) are stochastic point processes, which leads to a stochastic partial differential equation for the cortical potential \( V(x, t) \):

\[
\nabla \cdot [\sigma \nabla V] = - \left[ \sum_{k=1}^{n} \alpha_k \delta(x - x_k) \frac{dN_k}{dt} + \sum_{l=1}^{m} \beta_l \delta(x - y_l) \frac{dM_l}{dt} \right]. 
\] (4.3)

The sample paths of the \( N_k \) and \( M_l \) are step functions, so their derivatives, as they appear in equation 4.4, are random sequences of impulse (Dirac delta) functions. The processes \( N_k \) and \( M_l \) are not in general Poisson processes, but sometimes they will be able to be approximated locally (in time) by temporally inhomogeneous Poisson processes.

**4.2 One Space Dimension.** In the case of one space dimension, assuming the conductivity does not vary with \( x \), we have, for a finite space interval \( 0 \leq x \leq L \),

\[
\sigma \frac{d^2V(x, t)}{dx^2} = - \left[ \sum_{k=1}^{n} \alpha_k \delta(x - x_k) \frac{dN_k}{dt} + \sum_{l=1}^{m} \beta_l \delta(x - y_l) \frac{dM_l}{dt} \right]. 
\] (4.4)

However, it is seen in the appendix that this leads to difficulties with boundary conditions. Hence we turn to spatially distributed neurons and temporally distributed spikes and postsynaptic potentials.

**4.3 Spatially Distributed Neurons and Synapses and Spatiotemporally Distributed Action Potentials and Postsynaptic Potentials.** Since neurons, and to a lesser extent synapses, and their corresponding current sources and sinks are distributed over nonnegligible spatial regions and the associated current flows have nonzero durations, we obtain a more realistic equation for \( V \) by taking these factors into account. We again let the neurons be labeled \( k = 1, 2, \ldots, n \) and the synapses carry indices \( l = 1, 2, \ldots, m \). The contribution to the current density per unit volume from the \( k \)th neuron for an action potential elicited at time \( t = 0 \) is \( u_k(x; t; x_k) \) and that for a PSP arising at the \( l \)th synapse is \( v_l(x; t; y_l) \). The emission of spikes and the activation of synapses is assumed to occur at the same times as above, so the equation
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for $V$ is

$$\nabla \cdot [\sigma \nabla V] = - \left( \sum_{k=1}^{n} \sum_{j=1}^{m_{k}(t)} H(t - t_{kj}) u_{k}(x, t - t_{kj}; x_{k}) \right. \right.$$ 

$$+ \left. \sum_{l=1}^{m} \sum_{i=1}^{m_{l}(t)} H(t - s_{li}) v_{l}(x, t - s_{li}; y_{l}) \right] . \quad (4.5)$$

Here $H(.)$ is a unit step function, being unity for nonnegative arguments and zero otherwise. $V$ is a random process, as the sequences of occurrence times of action potentials and postsynaptic potentials constitute random point processes.

In one space dimension, if one uses the CSD approach, the electric field is now given as

$$V_{x}(x, t) = - \frac{1}{\sigma} \int_{0}^{x} \left[ \sum_{k=1}^{n} \sum_{j=1}^{n_{k}(t)} H(t - t_{kj}) u_{k}(x_{1}, t; x_{k}) \right. \right.$$ 

$$+ \left. \sum_{l=1}^{m} \sum_{i=1}^{m_{l}(t)} H(t - s_{li}) v_{l}(x_{1}, t - s_{li}; y_{l}) \right] dx_{1} + f(t), \quad (4.6)$$

where the subscript notation has been used for a partial derivative with respect to the subscripted variable and $f(t)$ is a function to be determined from initial and boundary conditions. Another partial integration gives the potential, which we designate $V_{1}$:

$$V_{1}(x, t) = - \frac{1}{\sigma} \int_{0}^{x} \int_{0}^{x_{1}} \left[ \sum_{k=1}^{n} \sum_{j=1}^{n_{k}(t)} H(t - t_{kj}) u_{k}(x_{2}, t - t_{kj}; x_{k}) \right. \right.$$ 

$$+ \left. \sum_{l=1}^{m} \sum_{i=1}^{m_{l}(t)} H(t - s_{li}) v_{l}(x_{2}, t - s_{li}; y_{l}) \right] \times dx_{2} dx_{1} + g(x, t), \quad (4.7)$$

where $g$ is obtained from boundary and initial conditions.

Now consider possibly different sequences of spike times $\{t_{kj}^{*}\}$ and PSP times $\{s_{li}^{*}\}$ at the same neurons and synapses, which give rise to a potential $V_{2}$. Then using the metric $D_{2}$, we have for a measure of the distance between the corresponding space-time distributions of potential $V_{1}$ and $V_{2}$

$$D_{2}(V_{1}, V_{2}) = \frac{1}{\sigma} \left\{ \int_{M} \int_{T} \left( \int_{0}^{x} \int_{0}^{x_{1}} \left( \sum_{k=1}^{n} \sum_{j=1}^{n_{k}(t)} H(t - t_{kj}) u_{k}(x_{2}, t - t_{kj}; x_{k}) \right. \right. \right.$$ 

$$\left. \left. + \sum_{l=1}^{m} \sum_{i=1}^{m_{l}(t)} H(t - s_{li}) v_{l}(x_{2}, t - s_{li}; y_{l}) \right) \times dx_{2} dx_{1} + g(x, t) \right) \right\}$$
\[
- \sum_{j=1}^{n_k^*(t)} H(t - t_{jk}^*) u_k(x_2, t - t_{kj}^*; x_k)
+ \sum_{l=1}^{m_l(t)} \left\{ \sum_{i=1}^{m_i(t)} H(t - s_{li}) v_l(x_2, t; y_l) - \sum_{i=1}^{m_i(t)} H(t - s_{li}^*) v_l(x_2, t - s_{li}^*; y_l) \right\}
\left( dx_2 dx_1 \right)^2 \left( \frac{dt}{2^\frac{1}{2}} \right).
\]

(4.8)

Here, \(n_k(t)\) and \(n_k^*(t)\) are the indices of the largest spike times for neuron \(k\) in \((0, t]\), and \(m_l(t)\) and \(m_l^*(t)\) are the corresponding indices for the postsynaptic potential times at synapse \(l\).

### 4.4 Relation Between Spike and PSP Times and Potential Distributions.

We will show that if we adopt the CSD analysis approach, then certain standard distances between sets of spike and PSP times cannot be used to establish distances between potential distribution, whereas another finer metric can be so employed. Consider the number \(N_k(t)\) of spikes from neuron \(k\) in \((0, t]\) and the number \(M_l(t)\) of PSPs at synapse \(l\) in \((0, t]\) with corresponding quantities \(N_k^*(t)\) and \(M_l^*(t)\) for a second set of events. The functions (fixing the sample paths) \(N_k, M_l, N_k^*, M_l^*\) are all in the space \(D[0, t]\) of real-valued functions which are at each point of the interval \([0, t]\) possessing left-hand limits and right-continuous (cadlag—see, for example, Pollard, 1984). A standard metric for \(D[0, t]\) is the uniform metric, which gives the distance between \(N_k\) and \(N_k^*\) as

\[
\rho(N_k, N_k^*) = \sup_{0 \leq s \leq t} |N_k(s) - N_k^*(s)|, k = 1, \ldots, n,
\]

(4.9)

and similarly for the PSP sequences

\[
\rho(M_l, M_l^*) = \sup_{0 \leq s \leq t} |M_l(s) - M_l^*(s)|, l = 1, \ldots, m.
\]

(4.10)

The entire collection of spike trains from the \(n\) neurons and the PSP times from the \(m\) synapses is in the product space

\[
D^{m+n}[0, t] = D[0, t] \times \cdots \times D[0, t].
\]

By a well-known result in analysis, one possible metric for this (metric) product space is obtained by adding the individual metrics. Hence, a measure of the distance between the whole set of functions \(L = \{N_1, N_2, \ldots, N_n, M_1, M_2, \ldots, M_m\}\) and the corresponding starred quantity \(L^*\) is

\[
\rho_1 (L, L^*) = \sum_{k=1}^{n} \rho(N_k, N_k^*) + \sum_{l=1}^{m} \rho(M_l, M_l^*).
\]

(4.11)
Now if integrands are close, usually so too are the corresponding integrals. However, it may be concluded that
\[ \rho_1(L, L^*) \leq \delta \]  

(4.12)
does not imply that the corresponding space-time potential distributions satisfy
\[ D_2(V_1, V_2) \leq \epsilon, \]  

(4.13)
where the smaller \( \epsilon \) is, the smaller the corresponding value of \( \delta \) is. That is, closeness of the sequences of spike and PSP times does not imply that the integrands in equation 4.8 themselves are close if the metric \( \rho_1 \) is used. This can be established by an example such as the following. Suppose \( n_1 \geq 1 \) excitatory synapses are firing at a regular rate and that this is the only activity; let the corresponding potential distribution be \( V_e \). Consider also that \( n_1 \) inhibitory synapses are firing at that same rate with a resulting potential distribution \( V_i \). Then we have \( \rho_1(L_e, L_i) = 0 \), but \( D_2(V_e, V_i) \) is large.

On the other hand, if the set of all the individual distances \( \rho(N_k, N_k^*) \), \( k = 1, \ldots, n \) and \( \rho(M_l, M_l^*) \), \( l = 1, \ldots, m \) is uniformly small, which is gauged by the metric
\[ \rho_2(L, L^*) = \max_{k,l} \{ \rho(N_k, N_k^*) \cup \rho(M_l, M_l^*) \}, \]  

(4.14)
then when \( \rho_2 \leq \delta_1 \) for some small enough \( \delta_1 \), then the corresponding potential distributions will also be close.

5 A Dynamical Approach

One clear disadvantage of the CSD analysis method is that it is not evolutionary in the dynamical sense; that is, it does not provide a means of determining the future distribution of potential from a previous one in conjunction with data on external stimuli. In order to overcome this difficulty, one possibility is to turn to reaction-diffusion equations similar to those used to describe fluctuations of ionic concentrations around neurons and glia in the modeling cortical spreading depression (Tuckwell & Hermansen, 1981). Here we will sketch briefly a mathematical model for determining potential distributions using differential equations, with no claim to a complete model. The number of variables in such a construction is very large, as the following reduction to a one-space-dimensional consideration shows. The treatment is deterministic, but it is possible that fluctuations, whose origin is in the complexity of the connections and variety of nerve cells and synapses, will occur in the solutions and appear random. The latter two components will involve parameters that are probably reasonably fitted with normal distributions.
Let the concentration of the $v$th ion species be $C_v(x, t)$, its valence be $z_v$, $v = 1, \ldots, p$, and its effective diffusion coefficient be $D_v$. Assume that (space-clamped or point) neurons are located at single space points as above with the $k$th at $x_k, k = 1, \ldots, n$, having membrane potential $\phi_k$. Similarly, assume synapses are localizable at points $y_l, l = 1, \ldots, m$, with pre- and postsynaptic membrane potentials $\psi_{l1}$ and $\psi_{l2}$, respectively. As a starting point we use the equation of continuity (see, for example, Tuckwell, 1988, chap. 2),

$$\frac{\partial \rho}{\partial t} = -\frac{\partial j}{\partial x},$$

where $\rho(x, t)$ is the charge density and $j(x, t)$ is the current density. Allowing for diffusion, movement of ions due to the electric field, and the contributions to the current density from movements in and out of neurons during action potentials and postsynaptic potentials, we have, letting the electric potential be $V(x, t)$:

$$\frac{\partial^2 V}{\partial x^2} = -\frac{1}{\epsilon \epsilon_0} \sum_{v=1}^{p} z_v C_v \tag{5.1}$$

$$\sum_{v=1}^{p} z_v \frac{\partial C_v}{\partial t} = \sum_{v=1}^{p} \left\{ D_v \frac{\partial^2 C_v}{\partial x^2} + \frac{z_v D_v F}{RT} \frac{\partial}{\partial x} \left[ C_v \frac{\partial V}{\partial x} \right] \right\} + \sum_{k=1}^{n} \delta(x - x_k) F_v k(\phi_k, C) + \sum_{l=1}^{m} \delta(x - y_l) G_v l(\psi_{l1}, \psi_{l2}, C) + P_v(C) \tag{5.2}$$

$$\frac{\partial \phi_k}{\partial t} = \sum_{v=1}^{p} g_{vk}(V_{vk} - \phi_k) \tag{5.3}$$

$$\frac{\partial \psi_{lj}}{\partial t} = \sum_{v=1}^{p} g_{v, lj}(V_{v, lj} - \psi_{lj}), j = 1, 2. \tag{5.4}$$

The physical constants $F, R, T, \epsilon$, and $\epsilon_0$ have their usual meanings, and the vector $C$ represents not only the collection of extracellular ionic concentrations $C_v$ but also intracellular concentrations, including those of pre- and postsynaptic elements. $V_{vk}$ is the Nernst potential for ion species $v$ at the $k$th neuron, $g_{vk}$ is the conductance of ion species $v$ at neuron $k$, and $g_{v, lj}, j = 1, 2.$ is the conductance for ion species $v$ at the pre- and postsynaptic membranes of synapse $l$ with $V_{v, lj}$ as the corresponding Nernst potentials. $P_v$ is the ionic
pump or active transport rate for ion species $v$, usually operating to restore resting conditions. $F_{vk}$ gives the contribution to current density through ion species $v$ due to the action potentials in neuron $k$, whereas $G_{vl}$ gives those contributions arising due to activity at synapse $l$. Here equations 5.3 and 5.4 are based on standard “conductance-based” models similar to the Hodgkin-Huxley model with appropriate modifications for the neurons in the cortical region under consideration, such as pyramidal cells (see, for example, Mainen & Sejnowski, 1995). Subsidiary equations for the ionic activation and inactivation variables are omitted for brevity. Included in the conductances $g_{vk}$ are contributions from synaptic activation due to all neurons that connect with neuron $k$. The network details have also been omitted for simplicity. Furthermore, there may be synaptic inputs from cells outside the cortical region under consideration. Equation 5.2 does not imply (except when there is only one species of ion present) the following set of equations, which can, however, be employed if it can be assumed that ions of each species are independent:

$$\frac{\partial C_v}{\partial t} = D_v \frac{\partial^2 C_v}{\partial x^2} + \frac{z_v D_v F}{RT} \frac{\partial}{\partial x} \left[ C_v \frac{\partial V}{\partial x} \right] + \sum_{k=1}^{n} \delta(x - x_k) F_{vk}(\phi_k, C) + \sum_{l=1}^{m} \delta(x - y_l) G_{vl}(\psi_{l1}, \psi_{l2}, C) + P_v(C), \quad v = 1, \ldots, p. \quad (5.5)$$

These equations, in conjunction with equations 5.1, 5.3, and 5.4, are more amenable than equations 5.1 through 5.4 to numerical solution by implicit schemes for parabolic systems. The parameters required to obtain solutions for the concentrations of the ions and the potential are obtainable from known anatomical and physiological data on cortical systems. We shall present numerical solutions in a later publication. It is also possible to use the descriptive approach, in which occurrence times of action potentials and postsynaptic potentials are considered to be given, in conjunction with the dynamical approach of this section. This would lead to a simplification of the above system in that we would retain equation 5.1, dispense with the systems 5.3 and 5.4, and replace equation 5.2 by

$$\sum_{v=1}^{p} z_v \frac{\partial C_v}{\partial t} = \sum_{v=1}^{p} \left\{ D_v \frac{\partial^2 C_v}{\partial x^2} + \frac{z_v D_v F}{RT} \frac{\partial}{\partial x} \left[ C_v \frac{\partial V}{\partial x} \right] \right\} + \sum_{k=1}^{n} \delta(x - x_k) \frac{dN_k}{dt} a_{kv} + \sum_{l=1}^{m} \delta(x - y_l) \frac{dM_l}{dt} b_{lv} + P_v(C),$$

where $M_k(t)$ is the number of action potentials issuing forth from neuron $k$ in $(0, t]$ and $M_l(t)$ is the corresponding number of postsynaptic potentials from
the $l$th synapse. The quantity $a_{kv}$ is the contribution to the current density through ion species $v$ when an action potential is emitted by the $k$th neuron and $b_{lv}$ is the corresponding quantity for activation of the $l$th synapse. Spatially and temporally distributed current waveforms can be used to replace these impulsive forms, as was done in equation 4.5. Furthermore, it is clear but not so immediately provable that if one uses the descriptive approach to obtain the nonhomogeneous terms as in equation 5.6, then the same results will obtain as in section 4 on the correspondence between spike and PSP time sequences and potential distributions.

6 Discussion

We have suggested that the mammalian brain operates in a space of potential distributions that constitute a subset of the space of continuous functions of three space variables and one time variable. That is, neither rate codes nor temporal coding provide a complete description of the ongoing information processing by the central nervous system. The concept is not far removed from that of distributed or vector coding (Churchland & Sejnowski, 1992, Ch. 4). Stimuli are identified with the potential distributions they elicit in space-time, and closeness of stimuli can be established using certain standard metrics for continuous function spaces. Such metrics seem natural and may coincide with the manner in which a brain distinguishes different perceptual or cognitive states. It is argued that since CSD analysis has purportedly demonstrated that action potentials contribute to a minor extent to CPDs, it follows that if one adopts the CPD coding picture, then spikes per se make a lesser contribution to the brain’s code than in either the rate coding or temporal coding pictures. We note that such conclusions from CSD analysis cannot be used to establish that the brain is using a CPD code. To establish the latter, experimental observations of potential distributions would have to be found to correlate strongly with cognitive states, and perhaps more strongly than spatiotemporal patterns of action potentials alone. There is already some evidence for this from electroencephalogram studies (attention, desynchronization, and sleep-related phenomena), evoked potentials, event-related potentials, and readiness potentials (Eccles, 1984; Hiraiaawa, Shimohara, & Tokunaga, 1990).

The descriptive approach has been presented as that in which it is assumed that there are well-defined time points at which action potentials and PSPs commence and that the current flows associated with them have well-defined functional forms, approximated, possibly by impulsive functions, in space-time. Using this descriptive approach in conjunction with either the CSD analysis method or a dynamical system obtained from the equation of continuity and involving ion concentrations and nerve membrane potentials along with subsidiary variables, the use of certain metrics has been considered. This was done to see how closeness of potential distributions corresponded with closeness of sets of spike trains and times of
occurrence of PSPs. PSPs have been included because they make the greatest contribution to cortical potentials. It was found when employing a standard metric in multidimensional event-time space, closeness of spike trains and PSP times does not imply closeness of potential distributions. However, this could be remedied if a metric was employed that measured the simultaneous closeness of all components of the multidimensional event-time paths.

However, the assumption that action potential activity and PSPs can be described by sets of single time points is clearly not valid because there are always (relative) continua of graded potential changes preceding, leading into, and following both action potentials and postsynaptic potentials. Thus, whether one adopts the CSD analysis method or the dynamical systems approach of equations 5.1 through 5.4, it is not possible to obtain a complete description of CPDs using the descriptive approach.

It might be questioned, in the climate of current theories of information processing, with their emphasis on spikes, why a seemingly more complicated scheme might be needed in which regional space-time potential distributions constitute the elements of the brain’s code. However, the exclusive use of action potentials has probably been partially fortuitous because these are the most noticeable and easily observed electrophysiological events in the brain. Sampling field potentials over wide regions should be feasible experimentally at the same time as unit recordings are made. It is unlikely that the myriad of other ongoing electrophysiological processes is ignored in taking into account an individual’s cognitive state, and these are reflected in the overall space-time distribution of potential. The use of CPDs seems also to contribute to providing a solution to the binding problem that addresses the issue as to how activities in diverse structures are woven together to obtain a global picture (Engel, Fries, Konig, & Singer, 1999). This is because, in the suggested framework, a cognitive state is determined by the global distribution of potential, and a metric that operates on such global distributions automatically takes into account the various components from disparate regions or activities.

Furthermore, changes in a $V$-distribution can occur rapidly, and if the distribution at time $t$ is noticeably different from the distribution at time $t + \Delta t$, an informational change will occur that is in the spirit of quests to demonstrate submillisecond timing (Singer, 1999). That is, if the CPD determines the cognitive state, the latter may change in time faster than the limits imposed by the frequencies of action potentials. To illustrate, consider $T_1 = [0, \delta t]$ and $T_2 = [\delta t, 2\delta t]$ so that $T_1$ and $T_2$ are disjoint successive small time intervals. Then define $V_1 = \{V(x, t), x \in M, t \in T_1\}$ and $V_2 = \{V(x, t + \delta t), x \in M, t \in T_1\}$. The distance between these two potential distributions in the same region over successive time intervals may be quantified as

$$D_2(V_1, V_2) = \left( \int_M \int_{T_1} (V_1(x, t) - V_2(x, t))^2 \, dtdx \right)^{\frac{1}{2}}.$$
As long as $D_2$ is large enough to lead to a perceived change in cognitive state, there is no limit as to how small $\delta t$ may be.

**Appendix**

An integration in equation 4.4 gives

$$\sigma[V_x(x, t) - V_x(0, t)] = - \left[ \sum_{k=1}^n \alpha_k H(x - x_k) \frac{dN_k}{dt} \right. + \left. \sum_{l=1}^m \beta_l H(x - y_l) \frac{dM_l}{dt} \right] + f(t), \quad (A.1)$$

where $f(t)$ is a function of time to be determined by boundary and initial conditions. A zero electric field condition at $x = 0$ and at $x = L$ gives

$$\sigma V_x(x, t) = - \left[ \sum_{k=1}^n \alpha_k H(x - x_k) \frac{dN_k}{dt} + \sum_{l=1}^m \beta_l H(x - y_l) \frac{dM_l}{dt} \right]. \quad (A.2)$$

Since this gives in fact the electric field strength on $[0, L]$, we see that this quantity has impulses at the times of occurrence of action potentials and postsynaptic potentials. For example, if there is an action potential in neuron $k$ in the interval $(t, t + \delta t)$, then the electric field impulsively jumps for all $x \geq x_k$ at time $t$ and returns instantaneously to zero. The potential, obtained by another integration, also clearly acts anomalously. This seems to point to a general deficiency in the CSD method or indicates that the use of impulsive current densities is not suitable with that method.

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**References**


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