

THE COVARIANT-ENHANCED-COUPPLING MODEL OF GLOBAL-ELECTRO-CORTICAL ACTIVITY[¶]

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ABSTRACT

Global-electrocortical activity is being modeled as a system of driven harmonic oscillators, considering telencephalonic structures as masses of linked oscillators generating activity at a number of resonant modes. This paper proposes the covariant-enhanced-coupling model of global-electrocortical activity of the human brain, which is a generalization of the covariant-generalized-coupling model. Enhanced coupling is dependent, not only, on the electrical potentials, but also, on their first and the second time derivatives. The signal equations, which were, originally, set up in the comoving frame, are transformed into the laboratory frame, expressed in the covariant notation using tensorial representation. This brings in the magnetic field in addition to the electric field.

Keywords: Magnetoencephalography, neuromagnetic response, covariant model, generalized-coupling model, mathematical definition of brain death

INTRODUCTION

Brain is a complex structure and theory of brain function is emerging as a most important and an interesting field. This topic has long attracted the attention of biologists and physicists, alike. One of the most challenging problems of neuroscience is working of the brain. Quantitative data regarding the nervous system, being much more sparse, pose great difficulties in attempts to build mathematical models of brain functioning. It is a very intricate system containing around the order of 10^{11} nerve cells with approximately 10^{15} interconnections. Necessary for the development of principles, able to connect brain-cell activities to the other psychological processes, will be a deeper comprehension of the phenomena describing bioelectrical and neuronal interactions.

This work reviews models of global-electrocortical activity. The activity is pictured as a system of driven harmonic oscillators, considering telencephalonic structures as masses of linked oscillators generating activity at a large number of resonant modes. This paper proposes the covariant-enhanced-coupling model of global-electrocortical activity of the human brain, which is generalized from the covariant-generalized-coupling model. Enhanced coupling depends on the electrical potentials as well as their time derivatives (the first and the second). The signal equations are, initially, set up in the comoving frame. They are, then, transformed into the laboratory frame and written in covariant notation employing tensorial representation. This introduces the magnetic field in conjunction with the electric field.

MODELING OF BRAIN ACTIVITY

Computational neuroscience is a discipline that traces its origins to the efforts of Hodgkin and Huxley, who pioneered quantitative analysis of electrical activity in the nervous system (Lytton *et al.*, 2017). Modeling of brain activity has been of interest to many researchers. Shine *et al.* (2016) described the dynamics of functional brain networks. Rouleau (2017) studied structures and functions of the post-mortem brain. Rouleau and Persinger (2017) investigated regional processing of induced current in *ex vivo* brain specimens. Shen *et al.* (2017) used connectome-based predictive modeling to determine individual behavior from brain connectivity. Breakspear (2017) reviewed dynamic models of large-scale brain activity. According to him, there is evidential support that collective, nonlinear dynamics are the base of adaptive cortical activity. Becht and Mills (2020) modeled individual differences in brain development. Donnelly-Kehoe *et al.* (2019) used whole-brain modeling of resting-state activity to reveal reliable local dynamics in the brain across sessions. Since discovered, the EEG of human brain has shown itself a vital tool in brain research. However, selecting the correct electroencephalographic reference still remains to be a challenge

[¶]The italic superscripts *a, b, c, ...*, appearing in the text, refer to endnotes given before references.

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(Vega *et al.*, 2019). Xu *et al.* (2018) studied global-signal-regression impact on characterizing dynamic functional connectivity and brain states. The study of Mesbah-Oskui (2016) indicate that alterations in thalamic spillover inhibition could underlie the changes in electrocortical activity that signal anesthetic-induced loss-of-consciousness. Grenier *et al.* (2019) are of the opinion that brain organoids models, improved with classical and emerging molecular and analytic tools, have the potential to unravel the opaque pathophysiological mechanisms of neurodegeneration and devise novel treatments for an array of neuro-degenerative disorders. Starting from a review of the basic principles of *in vitro* 'brain organogenesis', Quadrato and Arlotta (2017) discuss which aspects of human brain development and disease can be faithfully modeled with current brain organoid protocols, and discuss improvements that would allow them to become reliable tools to investigate complex features of human brain development and disease.

Of particular interest has been the study of global-electrocortical activity of brain. The author wrote his Ph. D. dissertation (Kamal, 1989) on generalization of model developed by Wright and Kydd (1984). The work was published as series of papers during 1989-1997 (Kamal *et al.*, 1989; 1992a; b; Kamal and Siddiqui, 1997). Study of group structure of covariant model of global-electrocortical activity provided a mathematical definition of brain death (Siddiqui *et al.*, 1993). Review presentations were given in national and international conferences on modeling (Kamal, 1993; Siddiqui, 1995; Siddiqui and Kamal, 1992; Siddiqui and Khan, 1993; Siddiqui *et al.*, 1990) and simulation (Khan and Siddiqui, 1993; 1995) of global-electrocortical activity.

Author's research students studied magnetobiology of the covariant and the generalized-coupling models (Naem, 1990), in particular, effects of weak gravitational field on the electrocortical activity of brain (Ahmed, 1990), published as a paper few years later as theoretical estimate of EEG in weightlessness (Ahmed *et al.*, 1997). More recently, Klein *et al.* (2019) attempted to identify a possible link between changes in brain blood flow and neuronal activity during microgravity. Bradford *et al.* (2016) investigated role of electrocortical activity in distinguishing between uphill and level walking in humans. Indahlastari *et al.* (2020) modeled transcranial electrical stimulation in the aging brain. Finkenzeller *et al.* (2018) studied Impact of maximal physical exertion on interference control and electrocortical activity in well-trained persons.

Wright and Kydd's Linear Model

Their model rests on many simplifications and overlooks issues of cell-to-cell coupling as well as details of anatomy, *etc.* (Wright and Kydd, 1984). Essential theoretical features of this model may be summarized as:

- a. Electrocortical recordings represent the transformed spatial average of cortical potentials.
- b. The telencephalon is considered to be a wave medium, which is assumed to be linear, with regard to the gross wave potentials. It must be borne in mind that the underlying microscopic interactions turn out to be extremely nonlinear.
- c. Boundary conditions (closed and constant) cause the linear waves to produce activity at many resonant modes, each having a constant natural frequency.
- d. The values for the natural modes of the resonant frequencies are bunched about central values, in accordance with Cramer's Central Limit Theorem.
- e. Ascending inhibitory systems work in part to suppress resonant activity and in part as generators of noise-like driving signals.

A mass of unit sources, which are coupled to one another may be described by a set of n equations (n is the number of synaptic connections of the order of 10^{15}) representing driven-harmonic oscillators^a

$$(1) \quad \ddot{\phi}_i + D_i(t)\dot{\phi}_i + N_i^2(t)\phi_i = \sum_j K_i^j(t)\phi_j; \quad \ddot{\phi}_i = \frac{d^2\phi_i}{dt^2}, \quad \dot{\phi}_i = \frac{d\phi_i}{dt}$$

i, j run from 1 to n excluding $j=i$ (no self-coupling). The symbol, Σ , denotes summation, ϕ_i represent electrical potentials in sections of the dendritic tree and t is time in the laboratory frame. $D_i(t)$, $N_i(t)$, $K_i^j(t)$ are free parameters equivalent to damping coefficients, natural frequencies and coupling constants, respectively. These parameters are assigned physiological interpretation based on the assumptions:

i. All $N_i(t)[D_i(t), K_i^j(t)]$ have a finite variance $\sigma_N[\sigma_D, \sigma_K]$ about a mean $\bar{N}[\bar{D}, \bar{K}]$. No particular type of distribution for $N_i(t)$, $D_i(t)$, $K_i^j(t)$ is assumed.

ii. All $N_i(t)$, $D_i(t)$, $K_i^j(t)$ are stochastically independent, as each represents processes being perturbed by very complicated nonlinearities in the interactions of the linked oscillatory sources, with diverse input signals.

Based on the above-mentioned assumptions about the parameters, the Central Limit Theorem of Cramer is applicable as n tends to be a large number. Hence, it is justified to replace all $N_i(t)$, $D_i(t)$, $K_i^j(t)$ by their respective means

$\bar{N}, \bar{D}, \bar{K}$. The model system could be visualized as a linear system, which is time invariant. Equation (1) may be put in a different form by introducing a set of variables $\{z_k\}$, defined by

(2a) $z_k = \phi_k$, if k is an odd number
 (2b) $z_k = \dot{\phi}_{k-1}$, otherwise

This equation is expressed as

(3) $\frac{dz}{dt} = A_{WK}z$

where $z = [z_k]; k = 1, 2, \dots, m$ is an $m \times 1$ column vector A_{WK} is the Wright and Kydd's state-transition matrix, having the elements

$$\begin{bmatrix} 0 & 1 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ -N_1^2 & -D_1 & K_1^2 & 0 & K_1^3 & \text{-----} & K_1^n & 0 \\ 0 & 0 & 0 & 1 & 0 & \text{-----} & 0 & 0 \\ K_2^1 & 0 & -N_2^2 & -D_2 & K_2^3 & \text{-----} & K_2^n & 0 \\ 0 & 0 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ K_3^1 & 0 & K_3^2 & 0 & -N_3^2 & \text{-----} & K_3^n & 0 \\ 0 & 0 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ \text{-----} & \text{-----} \\ K_n^1 & 0 & K_n^2 & 0 & K_n^3 & \text{-----} & -N_n^2 & -D_n \end{bmatrix}$$

The elements in Wright and Kydd's state-transition matrix all have different dimensions, which is evident by looking at the units of $-D_1$ [dimension: (time)⁻¹] and $-N_1^2$ [dimension: (time)⁻²]. In the following section, the system of equations (3) is going to be re-written so that all the elements of the state-transition matrix are dimensionless. The transfer function comes out to

(4) $\frac{\phi_j}{\phi_i} = \frac{K_i^j(t)}{D^2 + D_i(t)D + N_i^2(t)}$, where $D^n = \frac{d^n}{dt^n}$

The Covariant Model

The covariant model introduces comoving frame of the signal for the purpose of writing equations describing the time variation of potential of a dendritic tree; the frame is strapped down to the potential wavefront of dendrite (Kamal, 1989; Kamal *et al.*, 1989). Upon transformation of this equation into the laboratory frame a magnetic vector potential appears along with the electrostatic potential. In the comoving frame, a mass of unit sources coupled to each other are described by the set of equations

(5) $\ddot{\Phi}_i + D_i(\tau)\dot{\Phi}_i + N_i^2(\tau)\Phi_i = \sum_j K_i^j(\tau)\Phi_j; \ddot{\Phi}_i = \frac{d^2\Phi_i}{d\tau^2}, \dot{\Phi}_i = \frac{d\Phi_i}{d\tau}$

where $D_i(\tau), N_i(\tau), K_i^j(\tau)$ being 4×4 matrices with eigenvalues $D_i^\mu(\tau), N_i^\mu(\tau), K_i^{j\mu}(\tau); \mu = 0, 1, 2, 3$, respectively, τ representing time in the comoving frame, t time as measured in the laboratory frame. In this covariant model

(6a) $D_i^\mu(\tau) = D_i(\tau)$, if $\mu = 0$
 (6b) $= 0$, otherwise

Similar relations describe $N_i^\mu(\tau)$ and $K_i^{j\mu}(\tau)$. However, the eigenvalues for $\mu = 1, 2, 3$ may be nonzero (Kamal *et al.*, 1992a). The numbers, $D_i^\mu(\tau), N_i^\mu(\tau), K_i^{j\mu}(\tau)$ may be considered to be free parameters representing damping coefficients,

natural frequencies and coupling constants, respectively. Φ_i is a 4×1 column vector with the first entry as the only nonzero entry representing the electrical potential, φ . Using Lorentz transformation as a similarity transformation, with λ_i as the transformation matrix, the four-dimensional-spacetime-vector field Φ_i and the matrices $D_i(\tau)$, $N_i(\tau)$, $K_i^j(\tau)$ assume the following form

$$(7a) \quad \Phi_i \Rightarrow A_i = \lambda_i \Phi_i$$

$$(7b) \quad D_i(\tau) \Rightarrow \Delta_i(\tau) = \lambda_i D_i(\tau) \lambda_i^{-1}$$

$$(7c) \quad N_i(\tau) \Rightarrow \eta_i(\tau) = \lambda_i N_i(\tau) \lambda_i^{-1}$$

$$(7d) \quad K_i^j(\tau) \Rightarrow \kappa_i^j(\tau) = \lambda_i K_i^j(\tau) \lambda_i^{-1}$$

where $\lambda_i^{-1} = g \lambda_i g$, $g_{\mu\nu}$ is the metric tensor ($\mu, \nu = 0, 1, 2, 3$) with $g_{rr} = 1$; $r = 1, 2, 3$, $g_{00} = -1$, $g_{\mu\nu} = 0$, otherwise. Later on, equation (7e), which appears after equation (15), as well as equation (7f), which appears after equation (22), shall be added to this set. Equation (5), therefore, transforms as

$$(8) \quad \ddot{A}_i + \Delta_i(\tau) \dot{A}_i + \eta_i^2(\tau) A_i = \sum_j \kappa_i^j(\tau) A_j; \quad \ddot{A}_i = \frac{d^2 A_i}{d\tau^2}, \quad \dot{A}_i = \frac{dA_i}{d\tau}$$

A_i 's are in fact $A_i^{\mu} = (\varphi, \mathbf{A})$, the components of four-dimensional-spacetime-potential-vector field^b. A dimensionless parameter, $t_{\text{scale}} = \frac{\tau}{\Omega}$ (the scaling parameter Ω is introduced to make all the elements of the covariant-state-transition matrix dimensionless^c) and a set of new variables $\{Z_k\}$ are defined to construct the covariant-state-transition matrix, A_{COV} . The coördinates, therefore, become

$$(9a) \quad Z_k = A_k, \text{ if } k \text{ is an odd number}$$

$$(9b) \quad Z_k = \frac{dA_{k-1}}{dt_{\text{scale}}}, \text{ otherwise}$$

In terms of Z_k , the system of equations (8) may be written as

$$(10) \quad \frac{d\mathbf{Z}}{dt} = A_{\text{COV}} \mathbf{Z}$$

where $\mathbf{Z} = [Z_k]$ is a column vector. The covariant-state-transition matrix, A_{COV} , is a function of D 's, N 's, K 's and Ω . New variables are defined as $\mathbb{N} = \Omega \eta$, $\mathbb{D} = \Omega \Delta$, $\mathbb{K} = \Omega^2 \kappa$. The covariant-state-transition matrix, A_{COV} , is a linear transformation. In fact, it is a set of matrices. Different matrices could be generated by assigning different values to D 's, N 's, K 's.

$$\left[\begin{array}{cccccccc} 0 & 1 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ -\mathbb{N}_1^2 & -\mathbb{D}_1 & \mathbb{K}_1^2 & 0 & \mathbb{K}_1^3 & \text{-----} & \mathbb{K}_1^n & 0 \\ 0 & 0 & 0 & 1 & 0 & \text{-----} & 0 & 0 \\ \mathbb{K}_2^1 & 0 & -\mathbb{N}_2^2 & -\mathbb{D}_2 & \mathbb{K}_2^3 & \text{-----} & \mathbb{K}_2^n & 0 \\ 0 & 0 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ \mathbb{K}_3^1 & 0 & \mathbb{K}_3^2 & 0 & -\mathbb{N}_3^2 & \text{-----} & \mathbb{K}_3^n & 0 \\ 0 & 0 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ \text{-----} & & & & & & & \\ \text{-----} & & & & & & & \\ \mathbb{K}_n^1 & 0 & \mathbb{K}_n^2 & 0 & \mathbb{K}_n^3 & \text{-----} & -\mathbb{N}_n^2 & -\mathbb{D}_n \end{array} \right]$$

Each entry in this covariant-state-transition matrix, A_{COV} , is itself a 4×4 matrix. The transfer function comes out to

$$(11) \quad \frac{A_j^v}{A_i^u} = \frac{\sum [\kappa_i^j(\tau)]^\beta}{D^2 + \sum_\alpha \{ [A_i(\tau)]_\mu^\alpha D + [\eta_i^2(\tau)]_\mu^\alpha \}}$$

Group Structure of the Covariant Model

Siddiqui *et al.* (1993) studied group structure of the covariant model by considering symmetries of the covariant-state-transition matrix, A_{COV} . The matrix is neither symmetric nor hermitian. The matrix is transformed by interchanging alternate columns, bringing the first in place of second and so on. By block diagonalization, a nonsingular matrix, \mathcal{A} , is constructed. The determinant of \mathcal{A} is the negative of determinant of A_{WK} . One notes that each term is of degree $2n$ having a degree k in powers of N_i^2 and a degree $(2n-k)$ in powers of products of K_i^j , where k takes values from 0 to $2n$. A general determinant can be expressed as a polynomial in N 's and K 's with the coefficients K 's obtained by the irreducible representations of classes of the permutation group $S(2n)$. The class containing identity can be recognized as the positive term $\prod N_i^2$. The next term has a negative sign. The sign alternates with the classes with the exception that the last class, always, has negative sign. Therefore, one concludes:

a. A nonsingular matrix, \mathcal{A} , can, always, be constructed out of the covariant-state-transition matrix, A_{COV} .

b. The determinant does not depend on the damping coefficients, D 's. The determinant being the product of eigenvalues, these eigenvalues themselves do not depend on damping coefficients.

The set of covariant-state-transition matrices, $\{\mathcal{A}_i\}$, satisfies all the conditions for forming a group under the binary operation of matrix multiplication:

Closure Property — Taking 2 matrices \mathcal{A}_1 and \mathcal{A}_2 and examining the product $\mathcal{A}_1 \mathcal{A}_2$ one notes that the elements of the first row are of the form 0, 1, 0, 0, ..., 0. In the second row, there appear D 's, N 's and zeros. The third row, then, contain 0, 0, 0, 1, ..., 0. Since the operation of matrix multiplication retains the form of \mathcal{A} , this set is closed under matrix multiplication.

Associativity — Since \mathcal{A} 's are $m \times m$ matrices, they must satisfy the properties of matrix algebra, in particular, the associativity property of matrix multiplication.

Existence of Identity — The identity is obtained by taking $N_i^2 = -1$, $D_i = 0$, $K_i^j = 0$.

Existence of Inverse — It was shown earlier that the matrix, \mathcal{A} , is nonsingular, implying existence of inverse. The inverse is, also, a member of the set of nonsingular matrices constructed from the covariant-state-transition matrices, A_{COV} .

Mathematical Interpretation of Brain Death

The identity of this group, obtained by taking $N_i^2 = -1$, $D_i = 0$, $K_i^j = 0$, could be identified with the physiological state of *brain death*. The first condition means that there is no interaction present among the neighboring neurons. In other words, the neurons are decoupled. The second condition states that there is no damping present. The condition on η_i^2 gives the eigenvalues of natural frequency as $N_i = \pm i$. In the solution of system of equations (8), the expression $\exp(iN_i\tau)$ with the eigenvalue of η_i as $-i$ does not represent a physiological situation (see the next section), whereas the eigenvalue $+i$ represents a decaying exponential. On the EEG this would correspond to brain death — a biological state manifested by absence of all muscle activity and absolute unresponsiveness to all stimuli, accompanied by an isoelectric electroencephalogram for 30 minutes, all in the absence of hypothermia or intoxication by central nervous system depressants.

Physical Interpretation of Brain Death

The rising exponential, with the eigenvalue of η_i as $-i$, cannot represent a physiological situation, as a rising exponential would imply that energy is supplied externally to the system, which is not possible in the situation under discussion. Physically, one may visualize identity of the group in the presence of a strong magnetic field. Such a field should decouple the neurons causing all K_i^j 's to vanish. The neurons, then, act independently and have zero interaction with the neighboring neurons. For such independent oscillators Cramer's Central Limit Theorem is not applicable. There'll be no resonance and the oscillations should die out quickly as suggested by the eigenvalue $+i$ in the expression $\exp(iN_i\tau)$. Damping may, also, be modeled by considering a single neuron in the temperature bath of

other neurons. In the absence of any nearest-neighbor interaction, one expects no damping indicated by vanishing of the coefficients D_i 's.

The Generalized-Coupling Model

In the linear model of Wright & Kydd (1984) the electrical potentials ϕ_i 's are coupled to ϕ_j 's through coupling parameters $K_i^j(t)$. However, one notes that a change in potential, $\dot{\phi}_i = \frac{d\phi_i}{dt}$, induces a magnetic field because of flow of current. A magnetic field shall, in turn, exert Lorentz force on a charged particle and hence, in general, $\dot{\phi}_i$, shall influence ϕ_i . In the covariant model (Kamal *et al.*, 1989) the dependence of A_i 's on \dot{A}_j 's was also suggested, when 2 covariant-state-transition matrices were multiplied, which generated nonzero coefficients for A_i 's (Kamal and Siddiqui, 1997).

Based on the above arguments, Wright & Kydd's damped-coupled-harmonic-oscillator equations are re-written to include generalized coupling, which, also, depends on $\dot{\phi}_i$'s.

$$(12) \quad \ddot{\phi}_i + D_i(t)\dot{\phi}_i + N_i^2(t)\phi_i = \sum_j [K_i^j(t)\phi_j + M_i^j(t)\dot{\phi}_j]$$

Compare this equation with equation (1). $M_i^j(t)$ are free parameters equivalent to generalized-coupling constants, which have a finite variance σ_M about a mean \bar{M} . No particular type of distribution for $M_i^j(t)$ is assumed. All $M_i^j(t)$ are stochastically independent. Hence Cramer's Central Limit Theorem is applicable and it is justified to replace $M_i^j(t)$ by \bar{M} . In terms of the variables defined in equations (2a, b), the system of equations (12) may be expressed as

$$(13) \quad \frac{dz}{dt} = A_{GC}z$$

Compare this equation with equation (3). A_{GC} is the generalized-coupling-state-transition matrix, whose elements are

$$\begin{bmatrix} 0 & 1 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ -N_1^2 & -D_1 & K_1^2 & M_1^2 & K_1^3 & \text{-----} & K_1^n & M_1^n \\ 0 & 0 & 0 & 1 & 0 & \text{-----} & 0 & 0 \\ K_2^1 & M_2^1 & -N_2^2 & -D_2 & K_2^3 & \text{-----} & K_2^n & M_2^n \\ 0 & 0 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ K_3^1 & M_3^1 & K_3^2 & M_3^2 & -N_3^2 & \text{-----} & K_3^n & M_3^n \\ 0 & 0 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ \text{-----} & \text{-----} \\ K_n^1 & M_n^1 & K_n^2 & M_n^2 & K_n^3 & \text{-----} & -N_n^2 & -D_n \end{bmatrix}$$

A_{GC} is a linear transformation and the set of all such matrices forms a group under the operation of matrix multiplication. The transfer function comes out to

$$(14) \quad \frac{\phi_j}{\phi_i} = \frac{K_i^j(t) + M_i^j(t)D}{D^2 + D_i(t)D + N_i^2(t)}$$

Compare this with equation (4).

The Covariant-Generalized-Coupling Model

To set up a covariant formulation, one writes the electrical potential variation for a mass of unit sources coupled to each other in the comoving frame of signal passing through a segment of the dendritic tree as

$$(15) \quad \ddot{\Phi}_1 + D_1(\tau)\dot{\Phi}_1 + N_1^2(\tau)\Phi_1 = \sum_j [K_1^j(\tau)\Phi_j + M_1^j(\tau)\dot{\Phi}_j]$$

where $M_1^j(\tau)$'s are 4×4 matrices having eigenvalues $M_1^{j\mu}(\tau)$. Admissible values of μ are given after equation (7d). No particular type of distribution for $M_1^{j\mu}(\tau)$ is assumed. A similarity transformation under λ_i transforms the various spacetime vector fields and matrices as given in equations (7a-d). $M_1^j(\tau)$'s transform as

$$(7e) \quad M_1^j(\tau) \Rightarrow \mu_1^j(\tau) = \lambda_i M_1^j(\tau) \lambda_i^{-1}$$

Equation (15), therefore, becomes

$$(16) \quad \ddot{A}_1 + \Delta_1(\tau)\dot{A}_1 + \eta_1^2(\tau)A_1 = \sum_j [\kappa_j^1(\tau)A_j + \mu_j^1(\tau)\dot{A}_j]$$

Compare equation (16) with equation (8). Introducing the generalized coördinates defined in equations (9a, b), one obtains an eigenvalue equation

$$(17) \quad \frac{dZ}{dt} = A_{CGC} Z$$

Compare this equation with equation (10). A_{CGC} is the covariant-generalized-coupling-state-transition matrix, which is a function of D 's, N 's, K 's, M 's and Ω . If one introduces $M_1^j(\tau) = \Omega \mu_1^j(\tau)$ to make all the elements dimensionless, the covariant-generalized-coupling-state-transition matrix, A_{CGC} , becomes

$$\left[\begin{array}{ccccccccc} 0 & 1 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ -N_1^2 & -D_1 & K_1^2 & M_1^2 & K_1^3 & \text{-----} & K_1^n & M_1^n \\ 0 & 0 & 0 & 1 & 0 & \text{-----} & 0 & 0 \\ K_2^1 & M_2^1 & -N_2^2 & -D_2 & K_2^3 & \text{-----} & K_2^n & M_2^n \\ 0 & 0 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ K_3^1 & M_3^1 & K_3^2 & M_3^2 & -N_3^2 & \text{-----} & K_3^n & M_3^n \\ 0 & 0 & 0 & 0 & 0 & \text{-----} & 0 & 0 \\ \text{-----} & & & & & & & \\ \text{-----} & & & & & & & \\ K_n^1 & M_n^1 & K_n^2 & M_n^2 & K_n^3 & \text{-----} & -N_n^2 & -D_n \end{array} \right]$$

A_{CGC} is a linear transformation and the set of all such matrices forms a group under the operation of matrix multiplication. The transfer function comes out to

$$(18) \quad \frac{A_j^\nu}{A_1^\mu} = \frac{\sum\{[\kappa_i^j(\tau)]_\nu^\beta + [\mu_i^j(\tau)]_\nu^\beta D\}}{D^2 + \sum\{[\Delta_i(\tau)]_\mu^\alpha D + [\eta_i^2(\tau)]_\mu^\alpha\}}$$

Compare this with equation (11).

ENHANCED COUPLING IN GLOBAL-ELECTROCORTICAL ACTIVITY

In the generalized-coupling model, electrical potentials are coupled to other electrical potentials and their time rates of change. If this rate of change is uniform, this should produce a steady state, which is exhibited during regular operations of the brain. However, during epileptic seizures and such other phenomena, there is an avalanche of electrical activity and the rate shall not be uniform. To cover this situation, the second time derivative of electrical

potential is included in the model and the coupling is named as enhanced coupling. The model of global-electrocortical activity generated using this assumption is termed as the enhanced-coupling model.

The Enhanced-Coupling Model

Wright & Kydd's damped-coupled-harmonic-oscillator equations are re-written to include enhanced coupling, which depends on φ_i 's, $\dot{\varphi}_i$'s and $\ddot{\varphi}_i$'s.

$$(19) \quad \ddot{\varphi}_i + D_i(t)\dot{\varphi}_i + N_i^2(t)\varphi_i = \sum_j [K_i^j(t)\varphi_j + M_i^j(t)\dot{\varphi}_j + L_i^j(t)\ddot{\varphi}_j]$$

Compare equation (19) with equations (1) and (12). $L_i^j(t)$ are free parameters equivalent to enhanced-coupling constants, which have a finite variance σ_L about a mean \bar{L} . No particular type of distribution for $L_i^j(t)$ is assumed. All $L_i^j(t)$ are stochastically independent. Hence Cramer's Central Limit Theorem is applicable and it is justified to replace $L_i^j(t)$ by \bar{L} . In terms of the variables defined in equations (2a, b), the system of equations (19) may be expressed as

$$(20) \quad \frac{dz}{dt} = A_{EC}z$$

Compare this equation with equations (3) and (13). A_{GC} is the enhanced-coupling-state-transition matrix, whose elements are

$$\begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 & \dots & 0 & 0 & 0 \\ -N_1^2 & -D_1 & -1 & K_1^2 & M_1^2 & M_1^2 & \dots & K_1^n & M_1^n & L_1^n \\ 0 & 0 & 0 & 0 & 1 & 0 & \dots & 0 & 0 & 0 \\ K_2^1 & M_2^1 & L_2^1 & -N_2^2 & -D_2 & -1 & \dots & K_2^n & M_2^n & L_2^n \\ 0 & 0 & 0 & 0 & 0 & 0 & \dots & 0 & 0 & 0 \\ K_3^1 & M_3^1 & L_3^1 & K_3^2 & M_3^2 & L_3^2 & \dots & K_3^n & M_3^n & L_3^n \\ 0 & 0 & 0 & 0 & 0 & 0 & \dots & 0 & 0 & 0 \\ \hline K_n^1 & M_n^1 & L_n^1 & K_n^2 & M_n^2 & L_n^2 & \dots & -N_n^2 & -D_n & -1 \end{bmatrix}$$

A_{EC} is a linear transformation and the set of all such matrices forms a group under the operation of matrix multiplication. The transfer function comes out to

$$(21) \quad \frac{\varphi_j}{\varphi_i} = \frac{K_i^j(t) + M_i^j(t)D + L_i^j(t)D^2}{D^2 + D_i(t)D + N_i^2(t)}$$

Compare this equation with equations (4) and (14).

The Covariant-Enhanced-Coupling Model

To set up a covariant formulation, one writes the electrical potential variation for a mass of unit sources coupled to each other in the comoving frame of signal passing through a segment of the dendritic tree as

$$(22) \quad \ddot{\Phi}_i + D_i(\tau)\dot{\Phi}_i + N_i^2(\tau)\Phi_i = \sum_j [K_i^j(\tau)\Phi_j + M_i^j(\tau)\dot{\Phi}_j + L_i^j(\tau)\ddot{\Phi}_j]$$

where $L_i^j(\tau)$'s are 4×4 matrices having eigenvalues $L_i^{j\mu}(\tau)$. Admissible values of μ are given after equation (7d). No particular type of distribution for $L_i^{j\mu}(\tau)$ is assumed. A similarity transformation under λ_i transforms the various spacetime-vector fields and matrices as given in equations (7a-e). $L_i^j(\tau)$'s transform as

(7f) $L_i^j(\tau) \Rightarrow \ell_i^j(\tau) = \lambda_i L_i^j(\tau) \lambda_i^{-1}$

Equation (22), therefore, becomes

(23) $\ddot{A}_i + \Delta_i(\tau)\dot{A}_i + \eta_i^2(\tau)A_i = \sum_j [\kappa_j^i(\tau)A_j + \mu_j^i(\tau)\dot{A}_j + \ell_j^i(\tau)\ddot{A}_j]$

Compare equation (23) with equations (8) and (16). Introducing the generalized coordinates, defined in equations (9a, b), one obtains an eigenvalue equation

(24) $\frac{dZ}{dt} = A_{CEC}Z$

Compare this equation with equations (10) and (17). A_{CEC} is the covariant-enhanced-coupling-state-transition matrix, which is a function of D 's, N 's, K 's, M 's, L 's and Ω . If one introduces $\mathcal{L}_i^j(\tau) = \Omega \ell_i^j(\tau)$ to make all the elements dimensionless, the covariant-enhanced-coupling-state-transition matrix, A_{CEC} , becomes

$$\begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 & \dots & 0 & 0 & 0 \\ -N_1^2 & -D_1 & -1 & K_1^2 & M_1^2 & L_1^2 & \dots & K_1^n & M_1^n & L_1^n \\ 0 & 0 & 0 & 0 & 1 & 0 & \dots & 0 & 0 & 0 \\ K_2^1 & M_2^1 & L_2^1 & -N_2^2 & -D_2 & -1 & \dots & K_2^n & M_2^n & L_2^n \\ 0 & 0 & 0 & 0 & 0 & 0 & \dots & 0 & 0 & 0 \\ K_3^1 & M_3^1 & L_3^1 & K_3^2 & M_3^2 & L_3^2 & \dots & K_3^n & M_3^n & L_3^n \\ 0 & 0 & 0 & 0 & 0 & 0 & \dots & 0 & 0 & 0 \\ \dots & \dots \\ K_n^1 & M_n^1 & L_n^1 & K_n^2 & M_n^2 & L_n^2 & \dots & -N_n^2 & -D_n & -1 \end{bmatrix}$$

The transfer function comes out to

(25) $\frac{A_j^\nu}{A_i^\mu} = \frac{\sum \{ [\kappa_i^j(\tau)]_\nu^\beta + [\mu_i^j(\tau)]_\nu^\beta D + [\ell_i^j(\tau)]_\nu^\beta D^2 \}}{D^2 + \sum \{ [\Delta_i(\tau)]_\mu^\alpha D + [\eta_i^2(\tau)]_\mu^\alpha \}}$

Compare this with equations (11) and (18).

Group Structure of the Covariant-Enhanced-Coupling Model

The covariant-enhanced-coupling-state-transition matrix, A_{CEC} , is a linear transformation. If one considers the set of covariant-enhanced-coupling-state-transition matrices, $\{A_{CEC}\}$, one finds out that it forms a group under the binary operation of matrix multiplication. The group identity corresponds to the physiological state of *brain death*. The mathematical working is similar to the one presented in Siddiqui *et al.* (1993) — see the section ‘Group Structure of the Covariant Model’.

Magnetobiology

In this section, the effects of a uniform weak magnetic field B_{ext} ($\sim 10^{-16}$ tesla) are considered. Since the ambient magnetic field noise is much greater than 10^{-16} tesla, a magnetically shielded room is required to perform any measurement related to these weak fields. The magnetic field, not varying with time, is generated by a vector potential such that $B_{ext} = \nabla \times A_{ext}$. In order to calculate the shifts in frequencies based on a certain form of magnetic-vector potential, a magnetic field corresponding to that potential can always be determined using the above equation^d. The four-dimensional-spacetime-vector-potential field is A_{ext} . In the presence of this field the natural frequencies $N_i^\mu(\tau)$ are

modified to $N_i^{\mu}(\tau)$. However, the damping coefficients and couplings of the individual A_i 's, \dot{A}_i 's and \ddot{A}_i 's remain unchanged. Klitzing (1989) has shown that the effects of weak magnetic fields on the EEG of man are large enough to be measured. Therefore, equation (23) takes the following form in the laboratory frame

$$(26) \quad \ddot{A}_i + \Delta_i(\tau)\dot{A}_i + \eta_i^2(\tau)A_i = \sum_j [\kappa_j^i(\tau)A_j + \mu_j^i(\tau)\dot{A}_j + \ell_j^i(\tau)\ddot{A}_j]$$

where $A_i' = A_i + A_{\text{ext}}$. Since the signal velocities are very small as compared to the velocity of light, c , in free space, one is safe to take $t \approx \tau$. The external field $A_{\text{ext}}(x, y, z)$ is time independent, which gives $\ddot{A}_i' = \ddot{A}_i$, $\dot{A}_i' = \dot{A}_i$. Subtracting equation (23) from equation (26) and introducing, $\eta_i'^2 = \eta_i^2 + \delta\eta_i^2$, one gets

$$(27) \quad \delta\eta_i^2 A_i' = -(\eta_i^2 - \sum_j \kappa_i^j) A_{\text{ext}}$$

The matrices $\eta_i'^2 = \eta_i^2 + \delta\eta_i^2$'s are 4×4 matrices having eigenvalues δ_i^{μ} representing the shifts in frequencies. It is assumed that $\delta\eta_i$, κ_i^j and η_i can all be simultaneously diagonalized, *i. e.*, their commutators vanish

$$[\delta\eta_i, \kappa_i^j] = 0, [\delta\eta_i, \eta_i] = 0$$

Applying the transformation $\delta\eta_i \Rightarrow \lambda_i^{\sim} \delta\eta_i \lambda_i = \delta N_i$ *etc.* to write equation (27) in the comoving frame of the signal, one gets

$$(28) \quad \delta N_i^2 A_i^{\sim} = -(N_i^2 - \sum_j K_i^j)(A_{\text{ext}})_{i}^{\sim}$$

where $A_i^{\sim} = A_i + (A_{\text{ext}})_{i}^{\sim}$; $(A_{\text{ext}})_{i}^{\sim} = \lambda_i^{\sim} A_{\text{ext}}$. The matrices δN_i , N_i and K_i^j are, already, diagonalized. Equation (28) shall yield four equations each one sufficient to determine eigenvalues δ_i^{μ} . The results are

$$(29) \quad (\delta_i^{\mu})^2 = [\sum_j K_i^{j\mu} - (N_i^{\mu})^2] \Theta_i^{\mu}$$

where

$$\Theta_i^0 = -\frac{\gamma_i \mathbf{v}_i \cdot \mathbf{A}_{\text{ext}}}{\varphi_i - \gamma_i \mathbf{v}_i \cdot \mathbf{A}_{\text{ext}}}, \quad \Theta_i^f = 1, \quad \gamma_i = \frac{1}{\sqrt{1 - \frac{v_i^2}{c^2}}} \quad (\mathbf{v}_i \text{ 's are signal velocities})$$

Admissible values of r are given after equation (7d). The symbol c is explained after equation (26).

The same result was obtained in the covariant model (Kamal *et al.*, 1992a) and the covariant-generalized-coupling model (Kamal and Siddiqui, 1997). One notes that all the factors related to enhanced coupling with \dot{A}_i and \ddot{A}_i have canceled out. Therefore, it is concluded that a weak, uniform, stationary magnetic field shall give the same first-order shift in frequencies in the presence of enhanced coupling.

DISCUSSION AND CONCLUSION

Amrose Bierce, in *The Devil's Dictionary*, gave the following definition of 'mind':

MIND, n. — A mysterious form of matter created by the brain. Its chief activity consists in the endeavour to ascertain its own nature, the futility of the attempt being due to the fact that it has nothing but *itself* to know *itself* with.

This is the challenge! Despite the scale and the complexity of the problem, there have been attempts to understand function of the mind and, eventually, the brain. To give a little idea of the complexity handled by the power of mathematics, in the year 1987 the author started modeling global-electrocortical activity (when he enrolled for his PhD in Neurophysics) and set up the problem as an eigenvalue problem, with the covariant-state-transition matrix as a matrix of the order of $10^{16} \times 10^{16}$, ^e this giant matrix could not even be read (forget about processing) by the fastest supercomputer available in the world at that time in Los Alamos National Laboratory, New Mexico, United States. Of course, the problem can be handled using cloud computing, shared memory, *etc.*, these days. Now, we are at such a stage, where we can construct simple mathematical models and test their predictions, sometimes even in humans.

Our brains could be visualized as great supercomputers, arranging and organizing our daily activities. Neurons in a given layer transmit signals, as electrical impulses, to the next layer. These signals are of two types — signals, which activate downstream cells, are called *excitatory signals*; signals, which suppress their activity, are termed as *inhibitory signals*. In this paper, various models of global-electrocortical activity are described. These include Wright and Kydd's linear model, the covariant model, the generalized-coupling model and the covariant-generalized-coupling model, which are explained from the perspective of a mathematical physicist turned computer scientist. In this exercise, a mathematical definition of *brain death* has been obtained by studying the group structure of the covariant model. It is of interest that the first magnetoencephalogram was obtained in the Johns Hopkins Hospital, Baltimore, Maryland, United States, by Dr. Fowzia Siddiqui, currently working at the Aga Khan University Hospital, Karachi, Pakistan. The first theoretical explanation of magnetoencephalogram (the covariant model) was, also, given by a Johns Hopkins graduate (the author). A new model, the covariant-enhanced-coupling model of global-electrocortical activity, was put forward in this work, in which the electrical and the magnetic potentials in a synaptic connection, not only, depend on potentials from neighboring connections, but also, on the first and the second time derivatives of these potentials. Researcher of the future should be able to generalize this model to include contributions from the n^{th} derivative of the electrical and the magnetic potentials by employing mathematical identities. These efforts may, not only, be able to improve health care through efficient and effective treatment of nervous and psychiatric disorders, but also, lead us towards intelligent computing machines. The future of neuroscience, therefore, seems to be very promising.

KEY POINTS

- Global-electrocortical activity of the human brain was modeled as a system of driven harmonic oscillators; the equations were written in a covariant form using tensorial notation, in the commoving frame of the signal and transformed back to laboratory frame, which introduced magnetic fields along with electric fields.
- Group structure of the covariant model suggested link between identity of the group and the phenomenon of brain death.
- The generalized-coupling model employed generalized coupling dependent on both the electrical potentials and their time rates of change.
- The enhanced-coupling model incorporated enhanced coupling dependent on the electrical potentials, their rates of change as well as second (time) derivatives of the electrical potentials.
- The covariant versions of generalized-coupling and enhanced-coupling models had dependence of the magnetic vector potentials and their time rates of change, in addition to the electrical potentials.

DEDICATION

This paper is dedicated to the loving memory of my most revered teacher and mentor **Professor Dr. S. A. (Shaikh Ansar) Husain** (1933-2011). Professor Husain earned his B. Sc. from Lucknow University, India (1952), M. Sc. from University of Karachi (1955), another M. Sc. (1965) and Ph. D. (1968) from University of Alberta, Canada. His Ph. D. dissertation was entitled, 'Sulfur Isotope Exchange Reactions'.

He joined Department of Physics, University of Karachi in 1955 and retired in 1993 after reaching the age of superannuation (Lecturer 1955-1958; Assistant Professor 1958-1969; Associate Professor 1969-1979; Professor 1979-1993; Chairman during 1970s, 1980s and 1990s; Secretary, Affiliation Committee 1979-1987).

A poet and a very dynamic personality, he was author of physics textbooks for Class XII and B. Sc. As a young 22-year old faculty member, he arranged visit to Department of Physics of Nobel Laureate Arthur Holly Compton (shared 1927 Physics Nobel Prize 'for his discovery of the effect named after him' with Charles Thomson Rees Wilson) during his stopover in Karachi in 1955. Among the many awards and honors he received, I'll mention Gold Medal (1973), Scientist for 1988 (Forum of the Old Karachi University Social Students) and inclusion of name in 5000 *Personalities of the World*, the American Bibliographical Institute, 2nd Edition, 1988-1989. He was President of the Karachi Physics Society and the Albert Einstein Society (Karachi) as well as Member of the American Physical Society, the Pakistan Association of Scientists and Scientific Professions and Board of Advanced Studies and Research of University of Karachi.

Title of a paper, presented in 1986 (Siddiqui and Kamal, 1986), was taken from a lecture of the legendary professor in 1974, when the author was a student of B..Sc. (Honors), First Year in University of Karachi. During *the International Conference on Physics and the World of Today in the Memory of Professor Dr. Shaikh Ansar Husain* held in Department of Physics, University of Karachi, the author delivered **Professor Dr. Shaikh Ansar Husain memorial lecture** (Kamal, 2011).



SAK had the honor to share authorship with his beloved teacher in 7 peer-reviewed journal papers (2 of them Springer Nature Journals, having Thomson-Reuters Impact Factor — Kamal *et al.* 1989; 1992b) and 7 conference presentations^f. The author had the good fortune to complete his masters' thesis (Kamal, 1978) and doctoral dissertation (Kamal, 1989) under the guidance and supervision of this torchbearer of learning.

ENDNOTES

^aEquations (1) are given in Wright and Kydd (1984) as

$$\ddot{x}_1 + D_1(t) \dot{x}_1 + N_1^2(t) x_1 = K_1^2(t) x_2 + .K_1^3(t) x_3 + \dots + K_1^n(t) x_n$$

$$\ddot{x}_2 + D_2(t) \dot{x}_2 + N_2^2(t) x_2 = K_2^1(t) x_1 + K_2^3(t) x_3 + \dots + K_2^n(t) x_n$$

to

$$\ddot{x}_n + D_n(t) \dot{x}_n + N_n^2(t) x_n = K_n^1(t) x_1 + K_n^2(t) x_2 + \dots + K_n^{n-1}(t) x_{n-1}$$

The expressions on the right-hand side of the equations (as given in paper of Wright and Kydd)

$$K_2^1(t) x_2 + .K_3^1(t) x_3 + \dots + K_n^1(t) x_n$$

$$K_1^2(t) x_1 + .K_3^2(t) x_3 + \dots + K_n^2(t) x_n$$

to

$$K_1^n(t) x_1 + .K_2^n(t) x_2 + \dots + K_{n-1}^n(t) x_{n-1}$$

seem to have typos, since indices appearing as superscript (contravariant indices) are summed with indices appearing as subscript (covariant indices), according to the rules of tensor analysis. In this work, these equations are written in compact form as equations (1) using sigma notation, x 's replaced by φ 's, common notation to represent electrical potentials in electromagnetism. In the tensorial notation, used in differential geometry, equations (1) are written in Einstein convention (in which sigma is avoided) as

$$\ddot{\varphi}_i + D_i(t) \dot{\varphi}_i + N_i^2(t) \varphi_i = K_i^j(t) \varphi_j$$

In this convention, it is understood that repeated indices (also called dummy indices) denote summation. Such a representation is ideal for advanced computational neuroscience, where covariant models have to be developed based on the tensorial representation, which should be invariant under the scaled-Poincaré transformations, the most general coordinate transformations put forward 11-year ago (Kamal, 2009).

^bThe components of A_i contain both the electric potential and the magnetic-vector potential.

^c Ω has the unit of time, its value is taken as the average time of travel of a signal between two neurons.

^dAlthough the EEG sources are not equivalent to isolated oscillating charges in a dielectric medium, an equivalent potential in four-dimensional-spacetime-vector-field formulation can be found out for the electric fields in the brain. In fact, EEG gives the average effect and hence the effects of interaction of an external magnetic field with this equivalent potential field could be computed.

^eThe average number of synaptic connections 10^{15} are obtained by multiplying the number of neurons 10^{11} with the connections emanating from each neuron 10^4 ; another factor of 10 introduced because the problem was formulated in the commoving frame with 4 components of the generalized potential — 1 component as the electrical potential + 3 components of the magnetic vector potential

^fThose related to neuroscience appear in reference section of this paper (Ahmed *et al.*, 1997; Kamal *et al.*, 1989; 1992a; b; Siddiqui *et al.*, 1993); complete list is included in the memorial lecture (Kamal, 2011).

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