

A Continuum Theory of Electro-Cortical Activity

David T J Liley^{1,2}, Peter J Cadusch¹ and James J Wright²

¹ *School of Biophysical Sciences and Electrical Engineering, Swinburne University of Technology, Hawthorn, Victoria 3122, Australia*

² *Brain Dynamics Laboratory, The Mental Health Research Institute of Victoria, Locked Bag 11, Parkville, Victoria 3052, Australia*

1 Introduction

The use of field equations to describe the spatio-temporal properties of neural activity has a relatively recent history. The works of Beaulieu [1], Wilson and Cowan [2] and Nunez [3] represent some of the earliest examples of such theories. However results and insights obtained by these methods were inevitably compromised by deficits in anatomical and physiological data, as well as the limited utility of their non-linear integro-differential formulations. Further such theories are incapable of dealing with a real inhomogeneities and anisotropies, between scale interactions and single

neuron stochasticity. Later workers have improved the specification and accuracy of anatomical and physiological parameterisation [4-6] and/or have introduced computationally more efficient partial differential formulations [7,8], yet all have retained some arbitrary or unphysiological properties. The theory presented here preserve the general mathematical form and specifics of cortical architectonics of the earlier advances [7,8,5,6,4], and by the introduction of realistic neuro-transmitter kinetics, ionic reversal potentials and a more complete partial-differential formu-

lation, remove many of their arbitrary features as well as suggesting a more veracious framework upon which notions of self-organizing dynamics may be developed. All parameters of the resulting equations are obtainable from independent experiment. The equations are now found to describe an increased range of experimentally observed macroscopic electro-cortical phenomena.

2 Integral Formulation

In order to avoid details of cellular and cortical geometry the state variable modeled is the *mean soma membrane potential*, h_j , which for excitatory neurons has been demonstrated to be proportional to the mir-

ror image of the extracellular local field potential in cortex with axially symmetric neurons oriented perpendicular to the surface [18]. Each neuron is considered as a single RC compartment into which all efferent

synaptic activity terminates. Synaptic activity is described in terms of the deviation of the mean soma membrane potential from the resting state.

$$\tau_j \frac{\partial h_j(r, t)}{\partial t} = -h_j(r, t) + \sum_{j'} \psi_{jj'}(h_j) \int dt' G_{jj'}(t, t') \left\{ \sum_k \int d\xi \int dv \int_{\mathbf{R}^2} d^2r' \rho_{jj'}(r') S_{jj'}(r', t', \xi, v) f_{jj'}^k(v) d_{jj'}^k(\xi) \eta_{jj'}^k(r, r') + p_{jj'}(r, t') \right\} \quad (1)$$

where $r', r \in \mathbf{R}^2$ and $\rho_{jj'}(r) S_{jj'}(r, t, \xi, v) f_{jj'}^k(v) d_{jj'}^k(\xi) \delta^2 r \delta t \delta \xi \delta v$ are the number of action potentials occurring between $t, t + \delta t$ within $\delta^2 r$ about r along conduction fibers of conduction velocity between $v, v + \delta v$ having combined synaptic delays between $\xi, \xi + \delta \xi$ from cells of type j' for fiber system type k . $h_j(r, t)$ is the deviation of the mean soma membrane potential from the resting state of neurons of type j at r at time t , ρ_{jj} is

the neuronal cell density, $G_{jj'}(t, t')$ is the post-synaptic response of a cell of type j at time t due to a single pre-synaptic action potential arriving at time t' from a cell of type j' , $\eta_{jj'}^k(r, r')$ is a function describing the expected number of axo-synaptic connections received by a neuron of type j at r from a neuron of type j' at r' for the k th fiber system, τ_j is the membrane time constant and $\psi_j(h_j)$ is a weighing function describing

the effects of the mean soma membrane potential on the magnitude and time course of dendritic activity due to pre-synaptic action potentials. To first approximation this can be calculated by assuming a linear I-V (Ohmic) relationship between post-synaptic current and membrane potential. Higher order expressions for the I-V relationship can be found by requiring a constant transmembrane electric field (zero membrane charge density) in the solution of the Nernst-Planck equation [9].

3 Simplifications via assumptions

The previous defining equations are simplified by assuming

- two functionally distinct excitatory and inhibitory neuronal subpopulations
- two spatial scales of neuronal interaction - cortico-cortical [long-range] and intracortical [short-range] connectivity

- cortico-cortical fibres are exclusively excitatory and synapse on both excitatory and inhibitory cells
- local axonal propagation delays are considered negligible
- neuronal connectivity functions are isotropic and homogeneous

- relative refractory periods are ignored to first approximation
- synaptic and cortico-cortical conduction delays are assumed sharply peaked around a central value

It can be easily shown that the application of these assumptions gives rise to the following set of coupled non-linear integro-differential equations

$$\tau_e \frac{\partial h_{e,i}(r, t + \bar{\xi})}{\partial t} = h_{e,i}^* - h_{e,i}(r, t + \bar{\xi}) + \psi_e(h_{e,i}) \int_{-\infty}^t dt' G_{e,i}(t - t') \left[\rho_e \int_{\mathbf{R}^2} d^2r' S_e(r', t') \beta_{e,e,i}(\|r - r'\|) + \rho_e \int_{\mathbf{R}^2} d^2r' S_e(r', t' - \|r - r'\|/\bar{v}) \alpha_{e,e,i}(\|r - r'\|) + p_{e,e,i}(r, t') \right] + \psi_i(h_{e,i}) \int_{-\infty}^t dt' G_i(t - t') \left[\rho_i \int_{\mathbf{R}^2} d^2r' S_i(r', t') \beta_{i,e,i}(\|r - r'\|) + p_{i,e,i}(r, t') \right] \quad (2)$$

with $\psi_j(h_j) = (h_j^* - h_j)/h_j^*$ where h_j^* is the reversal potential associated with post-synaptic excitatory ($j = e$) or inhibitory ($j = i$) activity, h_j^* is the resting membrane potential and h_j is redefined as the *absolute* membrane potential. p_{ej}, p_{ij} represent local exci-

tatory and inhibitory input to each neural sub-population, respectively. $S_e(r, t) \delta t, S_i(r, t) \delta t$ are the fraction of excitatory and inhibitory cells becoming active between $t, t + \delta t$ at r , respectively. G_e, G_i ($G_{jj} \equiv G_j$) are now defined as the *time invariant post-synaptic impulse responses*, $\beta_{jj'}(r), \alpha_{jj'}(r)$ are functions describing the expected number of synapses

received by one cell, of type j , from another, of type j' , separated by a distance $\|r\|$ for short (intra-cortical) and long range (cortico-cortical) connectivity respectively. The formulation presented here differs significantly from that of Jirsa and Haken [8] in that inhibitory activity is *not* assumed to be a *linear* function of the extant excitatory activity.

4 Functional specifications

The effect of pre-synaptic activity on the post-synaptic cell's membrane potential is described for simplicity in terms of a source term driving a second order system with two real and equal eigenvalues. This corresponds to the "alpha" function of the dendritic cable theory of Rall [11] and can be justified in terms of the ensemble kinetic behaviour of transmitter-activated channels [12]. Under certain assumptions other kinetic schemes are easily incorporated [12]. The impulse response is then

$$G_j(t) = \Gamma_j t \exp[-\gamma_j t] \text{ for } t \geq 0, 0 \text{ otherwise} \quad (3)$$

where Γ_j is the peak amplitude of the post-synaptic potential, and γ_j is the associated rate constant. The values chosen for the post-synaptic time constants correspond approximately to "fast" excitatory (AMPA/kainate), $j = e$, and "fast" inhibitory (GABA_A), $j = i$, neurotransmitter kinetics [13].

5 Partial differential formulation

The previous non-linear integro-differential equations can be approximated by a coupled set of non-linear partial differential equations by determining the corresponding *Greens functions*. A typical time-retarded spatial integral based on equations (2) is

$$\phi_e(r, t) = \rho_e \int dt' \int d^2r' S_e(r', t') \alpha_{e,e}(\|r - r'\|) \delta(t - t' - \|r - r'\|/\bar{v}) \quad (7)$$

where ϕ_e is defined as a *pseudo-potential*. This equation identifies a Greens function as

$$G(r, t; r', t') = \alpha_{e,e}(\|r - r'\|) \delta(t - t' - \|r - r'\|/\bar{v}) \quad (8)$$

By taking the Fourier transform in space and time of this Greens function partial derivative terms can be identified, however the resulting equation is not analytically invertible. Therefore a first order in numerator and second order in denominator rational approximation [Padé] in frequency about a vanishing wavenumber, consistent with a *mixed order partial differential equation*, is used. Thus the integral equation (7) can be writ-

The form of the short (intra-cortical), β , and long range (cortico-cortical), α , connectivity functions are approximated for an isotropic cortex by [4,5]

$$\beta_{jj'}(r) = N_{jj'}^{\beta} \lambda_{jj'}^{\beta} \exp[-\lambda_{jj'} \|r\|] / (2\pi \rho_j) \quad (4)$$

$$\alpha_{e,j}(r) = N_{e,j}^{\alpha} \lambda_{e,j}^{\alpha} \exp[-\lambda_{e,j} \|r\|] / (2\pi \rho_e) \quad (5)$$

where $N_{jj'}^{\beta}$ is the total number of connections (synapses) that a cell of type j receives from cells of type j' via intra-cortical fibers and $N_{e,j}^{\alpha}$ is the total number of connections that a cell of type j receives from excitatory cells via cortico-cortical fibers. The functions $S_e(h_e)$ and $S_i(h_i)$ describing excitatory and inhibitory population pulse rates, as a function of the respective mean population membrane potentials, are in general non-linear. Based on the require-

ments of firing rate boundedness and monotonicity the general form for this non-linearity will be sigmoidal [2]. For instance $S_e(h_e)$ can be defined as [2]

$$S_e(h_e) = E_{max} (1 + \tau_{abs} E_{max} \exp[-g_e (h_e - \theta_e)])^{-1} \quad (6)$$

where g_e is proportional to the maximum slope which can be shown to be related to the reciprocal of the variance of firing thresholds in an homogeneous neural population [2]. θ_e represents a *population or aggregate firing threshold*, τ_{abs} is the absolute refractory period and E_{max} is the maximum fraction of excitatory neurons that can become active per unit time and will be related to the width of the action potential. The above expression can be defined such that $S_e(h_e^*) = 0$, however this will introduce a differentiable discontinuity that may be neither realistic or necessary. A similar expression applies to $S_i(h_i)$.

ten as the following *quasi-linear* hyperbolic partial differential equation

$$\left(\frac{\partial}{\partial t} + \bar{v} \Lambda_{ee} \right)^2 \phi_e(r, t) - \frac{3}{2} \bar{v}^2 \nabla^2 \phi_e(r, t) = N_{e,e}^{\alpha} \Lambda_{ee} \bar{v}^2 S_e(h_e) \quad (9)$$

where ∇^2 is the two-dimensional Laplacian. Robinson *et al* [7] derived a similar result. Because the Fourier transform of the one-dimensional time-retarded spatial integral contains only integer derivative terms in space and time the corresponding partial differential equation is *exact*

$$\left(\frac{\partial}{\partial t} + \bar{v} \Lambda_{ee} \right)^2 \phi_e(x, t) - \bar{v}^2 \frac{\partial^2 \phi_e(x, t)}{\partial x^2} = N_{e,e}^{\alpha} \Lambda_{ee} \bar{v} \left(\Lambda_{ee} \bar{v} + \frac{\partial}{\partial t} \right) S_e(h_e) \quad (10)$$

The above equation is similar in form to that obtained previously by Jirsa and Haken [8]. Similar results apply to the other time-retarded spatial integral in equation (2). Based on this result and under the restriction that S_i does not vary significantly over the characteristic scales of intra-cortical connectivity (*spatial coarse graining*), it can be shown that the following are

valid *mean field* dynamical equations

$$\tau_e \frac{\partial h(r, t + \bar{\xi})}{\partial t} = h^* - h(r, t + \bar{\xi}) + \Psi_e(h) I_e(r, t) + \Psi_i(h) I_i(r, t) \quad (11)$$

$$\left(\frac{\partial}{\partial t} + \gamma_e \right)^2 I_e(r, t) = \Gamma_e \gamma_e e \{ N_{e,e}^{\beta} S_e(h_e) + \phi(r, t) + p_e(r, t) \} \quad (12)$$

$$\left(\frac{\partial}{\partial t} + \gamma_i \right)^2 I_i(r, t) = \Gamma_i \gamma_i e \{ N_{i,i}^{\beta} S_i(h_i) + p_i(r, t) \} \quad (13)$$

$$\left(I \frac{\partial}{\partial t} + \bar{v} \Lambda \right)^2 \phi(r, t) - \frac{3}{2} \bar{v}^2 \nabla^2 \phi(r, t) = \Lambda^2 N^{\alpha} e^2 S_e(h_e) \quad (14)$$

where $h = (h_e, h_i)^T$, $h^* = (h_e^*, h_i^*)^T$, $I_e = (I_{ee}, I_{ei})^T$, $I_i = (I_{ie}, I_{ii})^T$, $N_e^{\beta} = (N_{ee}^{\beta}, N_{ei}^{\beta})^T$, $N_i^{\beta} = (N_{ie}^{\beta}, N_{ii}^{\beta})^T$, $N^{\alpha} = (N_{ee}^{\alpha}, N_{ei}^{\alpha})^T$, $\phi = (\phi_e, \phi_i)^T$, $\Lambda = \text{diag}[\Lambda_{ee}, \Lambda_{ei}]$, $\tau = \text{diag}[\tau_e, \tau_i]$, $\Psi_j(h) = \text{diag}[\Psi_j(h_e), \Psi_j(h_i)]$, $p_e = (p_{ee}, p_{ei})^T$, $p_i = (p_{ie}, p_{ii})^T$ and I is the identity matrix.

6 Numerical Solutions

Fourier-Laplace techniques have been previously applied to a linearized version of equation (2)[14]. Numerical solutions (phase-magnitude, root-loci and dispersion) reveal the presence of spatially weakly damped traveling waves at, or near, the frequencies of mammalian alpha (8 – 13 Hz). The emergence of such dynamics was dependent on the inclusion of long range excitatory connections. Further, increases in inhibitory interaction strength had the dominant effect in increasing the corresponding temporal frequencies, and decreasing their associated temporal dampings, of the mean soma membrane potential of excitatory and inhibitory neurons. Such results are consistent with the reported, paradoxical, effects of selective GABA_A agonists (benzodiazepines) in increasing beta power (13 – 20 Hz) and decreasing alpha power in mammalian EEG [15]. A one-dimensional von Neumann-Richtmyer finite difference solver [16] coupled with a fourth-order Runge-Kutta method was used for the numerical solutions of a one-dimensional version of equations (11)-(14).

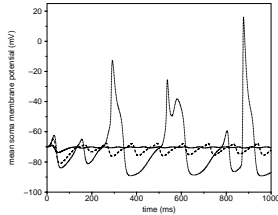


Figure 1: Illustration of three oscillatory modes of the mean soma membrane potential of excitatory cells at $x = 0$ in response to homogeneous driving of inhibitory and excitatory cells with spatio-temporally band-limited ($< 6.2 \text{ rad cm}^{-1}$, $< 620 \text{ rad s}^{-1}$) white noise: (i) $\langle p_{ij}(x,t) \rangle = 1.1 \text{ ms}^{-2}$ (solid line) (ii) $\langle p_{ij}(x,t) \rangle = 1.4 \text{ ms}^{-2}$ (dashed line) (iii) $\langle p_{ij}(x,t) \rangle = 1.5 \text{ ms}^{-2}$ (dotted line). Other parameters for the driving noise were $\text{var} p_{ij}(x,t) = 1.0 \text{ ms}^{-2}$, $\text{var} p_{ij}(x,t) = 1.6 \text{ ms}^{-2}$ and $\langle p_{ij}(x,t) \rangle = 1.6 \text{ ms}^{-2}$. Boundary conditions were null flux, simulation time step was 0.1 ms, $\tau_{ij} = 5 \text{ ms}$, $\Gamma_i = 0.18 \text{ mV}$, $\Gamma_j = 0.37 \text{ mV}$, $\gamma_i = 0.3 \text{ ms}^{-1}$, $\gamma_j = 0.065 \text{ ms}^{-1}$, $H_{ij}^e = -70 \text{ mV}$, $H_{ij}^i = 45 \text{ mV}$, $H_{ij}^e = -90 \text{ mV}$, $N_{ij}^e = 3034$, $N_{ij}^i = 536$, $N_{ij}^e = 4000$, $N_{ij}^i = 2000$, $A_{ij} = 0.4 \text{ cm}^{-1}$, $A_{ij} = 0.65 \text{ cm}^{-1}$, $\bar{v} = 0.7 \text{ cm ms}^{-1}$, $r_{\text{diff}} = 1 \text{ ms}$, $\theta_{ij} = -50 \text{ mV}$, $g_{ij} = 0.28 \text{ mV}^{-1}$, $g_{ij} = 0.14 \text{ mV}^{-1}$, $E_{\text{max}} = 1 \text{ ms}^{-1}$ and $\bar{\zeta} = 0 \text{ ms}$. Further details about the parameter values used can be found in [4] and [14].

7 Conclusions

The present theory thus embraces a wide range of the phenomena of electro-cortical activity to first approximation, and may be developed further to incorporate the complicated connectivity of real cortex. In-

Figure 1 illustrates three oscillatory modes for the mean soma membrane potential of excitatory cells in response to variations in the mean amplitude of an homogeneously applied spatio-temporally band-limited white noise driving excitatory cells - (i) low amplitude oscillation at 13 – 20 Hz (mammalian beta), (ii) moderate amplitude oscillation at 8 – 13 Hz (mammalian alpha) and (iii) high amplitude oscillations (analogous to epileptic spikes) associated with the regenerative spread of excitation.

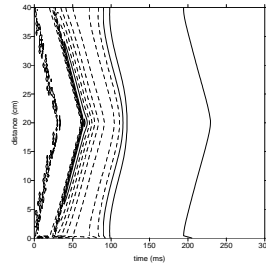


Figure 2: Contour plot [solid line $\leq H_i$, dotted line $> H_i$] of the spatio-temporal solutions for a one-dimensional version of equations (11)-(14) in response to an impulse of duration 10 ms and height 100 ms^{-2} at $x = 0$ for periodic boundary conditions. Note the annihilating regenerative waves of excitation (phase velocity $\approx 5.1 \text{ m s}^{-1}$). All simulation parameters are as for Figure 1.

The regenerative spread of excitation is further illustrated in Figure 2

homogeneities are easily added to the equations derived if gradient information is ignored and areal variations occur at characteristic scales large compared to numerical discretization. Further the issue of corti-

cal lamination can be most profitably addressed, within this theory, by considering more than two local neuronal populations.

cal lamination can be most profitably addressed, within this theory, by considering more than two local neuronal populations.

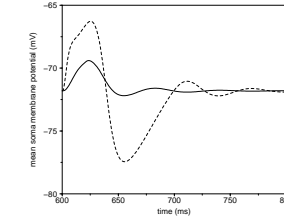


Figure 3: Temporal response, for a one-dimensional version of equations (11)-(14) of excitatory neurons at $x = 0$, to two different impulses applied at $x = 0$ - (i) 2 ms^{-2} [height], 29 ms (width) (solid line), and (ii) 40 ms^{-2} , 1 ms (dashed line). $g_{ij} = 0.28 \text{ mV}^{-1}$ otherwise all simulation parameters are the same as Figure 1.

Figure 3 illustrates the temporal response of excitatory neurons at $x = 0$ for two excitatory impulses of differing durations. The form of the damped oscillatory responses resembles the middle and late components found to exist in a variety of cortical event-related potentials (ERP). Of particular note is the notch on the first "wave" of excitation at about 25 ms. Such a notch is found in average evoked potential recordings from prepyriform cortex when the lateral olfactory tract is stimulated. Freeman explained this as the result of re-excitation of pyramidal cells by pyramidal cells [18]. This result is the first unequivocal replication of this phenomenon, which demonstrates the mutually excitatory connections that are crucial for learning in the olfactory system [19].

8 References

1. R. L. Beurk, *Trans. Roy. Soc. (Lond)* B **240**, 55 (1956).
2. H. R. Wilson and J. D. Cowan, *Kybernetik* **13**, 55 (1973).
3. P. L. Yuen, *Electric Fields of the Brain: The Neurophysics of EEG* (Oxford University Press, New York, NY, 1981).
4. D. T. J. Lilley and J. J. Wright, *Network* **5**, 175 (1994).
5. D. T. J. Lilley and J. J. Wright, *Network* **6**, 103 (1995).
6. J. J. Wright and D. T. J. Lilley, *Biol. Cybern.* **72**, 347 (1995).
7. P. A. Robinson, C. J. Rennie, and J. J. Wright, *Phys. Rev. E* **55**, (1997).
8. V. K. Jirsa and H. Haken, *Phys. Rev. Lett.* **77**, 960 (1996).
9. H. C. Tuckwell, *Introduction to Theoretical Neurobiology* (Cambridge University Press, Cambridge, 1988), Vol. 1.
10. H. A. Swadlow, D. L. Ruscen, and S. G. Waxman, *Exp. Brain Res.* **33**, 455 (1978).
11. W. Ball, *J. Neurophysiol.* **30**, 1138 (1967).
12. A. Destexhe, Z. F. Mainen, and T. J. Sejnowski, *J. Comp. Neurosci.* **1**, 195 (1994).
13. D. A. McCormack, *Progr. Neurobiol.* **39**, 337 (1992).
14. D. T. J. Lilley, in *Spatiotemporal Models in Biological and Artificial Systems*, edited by F. L. Silva, J. C. Principe, and L. B. Almeida (IOS Press, Amsterdam, 1997), pp. 89-96.
15. J. G. B. Sakets and L. Linnmayer, *Int. J. Clin. Pharmacol. Ther. Toxicol.* **27**, 51 (1989).
16. R. D. Richtmyer and K. W. Morton, *Difference Methods for Initial Value Problems*, 2nd ed. (Wiley-Interscience, New York NY, 1967).
17. J. J. Wright, *Biol. Cybern.* **76**, 181 (1997).
18. W. J. Freeman, *Mass Action in the Nervous System* (Academic Press, New York NY, 1975).
19. W. J. Freeman, personal communication.