Are current-based synapses an accurate enough approximation? A homotopic mapping between current-based and conductance-based synapses in a neural field model of epilepsy

Andre.D.H. Peterson,1,2 H. Meffin,1 M.J. Cook,2 D.G. Grayden,1 A.N. Burkitt,1 and Iven.M.Y. Mareels1

1Neural Engineering Laboratory, DEEE, University of Melbourne, Australia
2Department of Medicine, St.Vincent’s Hospital, University of Melbourne, Australia

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The overwhelming majority of neural field and mass models use current-based synapses [1] unlike spiking models which typically use conductance-based synapses [2]. Although neural field models that employ conductance-based synapses have been studied [3–9], the functional effects on the neuronal dynamics have not been systematically analysed and compared to that of models with current-based synapses. This shortcoming is particularly apparent with respect to epileptic dynamics, where neural field models of epilepsy typically describe the transition to seizure-like activity as a bifurcation [10]. This letter examines and compares the differences between conductance-based synapses and current-based synapses by constructing a neural field model that encapsulates both through a homotopic mapping. The results demonstrate significantly different non-trivial effects of these synaptic mechanisms on the system dynamics, particularly with respect to the model’s bifurcation dynamics.

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I. INTRODUCTION

Modelling brain dynamics from a mesoscopic perspective typically employs the use of neural mass [1] or neural field models [11], the difference being that the latter incorporates information about spatial structure. This top-down phenomenological approach is based on subsequent modifications and derivatives of the canonical neural field equations [12–14]. A typical neural field or mass model of brain dynamics uses current-based synapses to approximate synaptic dynamics, as these are mathematically less complex to analyse due to lumping parameters. However, it has been shown through numerical simulations [6] and using spiking models [15] [16] that more biophysically realistic conductance-based synaptic mechanisms significantly effect the overall dynamics of the neural model. To our knowledge, this is the first analytical comparison of the dynamics between current-based and conductance-based synapses in a neural field model.

In this letter we use a mathematical technique called homotopic continuation theory that enables us to construct a general neural field model that encapsulates both current-based and conductance-based synapses. This is performed by introducing a new parameter $\kappa$ that interpolates between current-based ($\kappa = 0$) and conductance-based ($\kappa = 1$) synaptic mechanisms. In other words, we use numerical homotopic continuation to topologically deform the current-based synapses model into the conductance-based synapses model and vice-versa. The effect of the both synaptic mechanisms on the bifurcation structure is then comparatively examined, which has important consequences for modelling epilepsy.

Both neural mass and field models of epilepsy use bifurcation theory to explain the transition to seizure typically found in epileptic EEG recordings of brain electrical activity [17]. The most common type of bifurcation used to describe the transition to seizure is a Hopf bifurcation [10]. Although multi-stability and global bifurcations have also been used [18]. A Hopf bifurcation describes a mathematical transition from a linear steady-state or fixed point to nonlinear oscillatory activity. This reflects changes in linearity found in nonlinear time series analysis of EEG data [19].

The structure of this letter is as follows: first in section (II) we give a very brief background of the two synaptic mechanisms, their differences and the hypothesis which we mathematically prove. In section (III) a description of the main equations of a neural field model are given. Section (IV) presents the equation for the synaptic current that is constructed to encapsulate and interpolate between both current-based and conductance-based synapses using a homotopic continuation. The model’s dynamics are then analysed using methods from bifurcation theory (sections (V, VII)) to compare and contrast the subsequent change in dynamics. Finally, the results are interpreted physiologically in section (VIII).
II. BACKGROUND

In a typical neural field model of epilepsy that uses current-based synapses, the synaptic input that arrives is linear and additive with no feedback or modulation. The synaptic current is linearly proportional to the incoming firing rate of action potentials entering the synapse. A typical bifurcation parameter is the external input, which when increased drives the neural model into an excited or seizure-like state. This can generate a bifurcation of the neural population dynamics, which is physiologically interpreted as a transition to a seizure-like state. When more biophysically realistic conductance-based synapses are incorporated in the same neural field model, as typically used in spiking neural models, a ‘feedback’ term from the membrane potential is introduced into the neuronal dynamics that multiplicatively modulates the synaptic input. This extra feedback term makes conductance-based synapses nonlinear and multiplicative compared to current-based synapses. The extra feedback term can be expressed as an active membrane time-constant [20] compared to a passive membrane time-constant used in current-based synapses. When the external input is increased in the neural field model with conductance-based synapses, a bifurcation is not generated for the same part of parameter space. We hypothesise that the multiplicative feedback from the membrane potential counteracts the excitability induced by increasing the external input. In this letter we perform a homotopic continuation between both models to mathematically prove this hypothesis. Specifically, we perform a bifurcation analysis where we use the homotopy parameter as a bifurcation parameter.

III. GENERAL FORMALISM OF MODEL

We use a modified cortical neural field model [21] with an input equation Eq.(1), an output equation Eq.(2) and a sigmoidal function to couple them Eq.(3):

\[
\frac{dV(t)}{dt} = -\frac{V(t)}{\tau_m} + I_{\text{syn}}(t), \quad (1)
\]

\[
\left[1 + \frac{d}{dt}\right]^{2} \phi(t) = Q(V(t)), \quad (2)
\]

\[
Q(V(t)) = \frac{Q_{\text{max}}}{1 + \exp[-(V(t) - \theta)/\sigma]}, \quad (3)
\]

Eq.(1) describes the change in membrane potential \(V(t)\), where the first term is the leak current and \(\tau_m\) is the passive membrane time constant. The second term is the synaptic current \(I_{\text{syn}}\) which contains the synaptic mechanism i.e., current-based or conductance-based synapses, that temporally filters the incoming firing rates \(\phi(t)\). The output wave equation Eq.(2) is derived from canonical neural field equations [21] [22] and describes the propagation of a spatially uniform scalar field of firing rates \(\phi(t)\) over an axonal range \(\gamma\), where the RHS is a sigmoidal function \(Q(V(t))\) defined in Eq.(3) which couples the input and output equations. Here \(Q_{\text{max}}\) is the maximum firing rate, and \(\theta\) and \(\sigma\) are the mean and standard deviation respectively of a distribution of threshold values over the neuronal population. We assume that the cortical area described is on a millimetric mesoscopic scale which is spatially homogeneous and isotropic [15] [23] [24].

IV. HOMOTOPIC MAPPING BETWEEN SYNAPTIC MECHANISMS

In this section we construct a neural field model that encapsulates both current-based and conductance-based synapses. This is performed by using homotopic continuation such that the synaptic current term contains a homotopy parameter, \(\kappa\), such that when \(\kappa = 0\), the model has current-based synapses, and when \(\kappa = 1\), it has conductance-based synapses. Homotopic continuation utilizes a continuous mapping between the two systems that continuously deforms one system into the other, even though they are not necessarily topologically equivalent i.e. they are homotopic but not necessarily homeomorphic. The general concept can be explained via a simple definition of a linear homotopic mapping \(H(x, \kappa)\) between functions \(g(x)\) and \(f(x)\) with homotopy parameter \(\kappa \in [0, 1]\)

\[
H(x, \kappa) = \kappa g(x) + (1 - \kappa)f(x). \quad (4)
\]

As can be seen from Eq.(4), as we continuously vary the parameter \(\kappa \in [0, 1]\) from zero to one, we deform the function \(f(x)\) into \(g(x)\). We now write the equations for a neural field model with an equivalent homotopic mapping between current-based and conductance-based synaptic mechanisms where \(f(x)\) is the change in the synaptic current due to current-based synapses and \(g(x)\) is the change due to conductance-based synapses. This enables us to compare and explain the key differences in dynamics caused by these different synaptic mechanisms. In particular we perform a bifurcation analysis using the homotopy parameter, \(\kappa\), as a bifurcation parameter to rigorously analyse the difference between the synaptic mechanisms.

We now define a synaptic current term \(I_{\text{syn}}\) that encapsulates both current-based and conductance-based synaptic mechanisms with \(\kappa\) as the homotopy parameter:

\[
I_{\text{syn}}(t) = - \sum_{b = e,t, x} N_{b} g_{b}(t)[\kappa(V(t) - \bar{V}) + \bar{V} - E_{b}], \quad (5)
\]

where \(g_{b}(t)\), \(N_{b}\), and \(E_{b}\) are the conductances, synaptic connectivities and reversal potentials for the excitatory, inhibitory and external populations, \(b = e, i, x\) respectively. The conductance \(g_{b}(t)\) is modelled as a decaying
exponential from a maximal conductance $G_b$ over a synaptic time-constant $\tau_s$ with firing rate input $\phi_b$ as $\dot{g}_b(t) = -g_b(t)/\tau_s + G_b\phi_b$.

We have described the feedback from the membrane potential as fluctuations about a mean $(V(t) - \bar{V})$ so that when $\kappa = 0$ then these fluctuations are negligible and the mean membrane potential value, $\bar{V}$, is a constant and the synaptic mechanism is equivalent to current-based synapses. However, when the fluctuations are taken into account with $\kappa = 1$ then the constant mean membrane potential terms, $V$, cancel leaving the state variable $V(t)$ as a feedback term. Consequently, this makes the conductance-based synaptic current term $I_{syn}(t)$ with $\kappa = 1$ bilinear, which yields qualitatively different dynamics.

We combine Eq.\{1\} and Eq.\{5\}, and because the synaptic dynamics are an order of magnitude less than the membrane dynamics, we use time-scale separation to take the steady-state of the conductance $\dot{g}_b(t) = \tau_s G_b \phi_b(t)$. We can then express an operator acting on the membrane potential $V(t)$. This equation has an active time-dependent time constant, $\tau_c(t)$, that is inversely proportional to the input compared to the usual passive static one $\tau_m$:

$$
\left[ \tau_c(t) \frac{d}{dt} + 1 \right] \left[ \tau_s \frac{d}{dt} + 1 \right] V(t) = \sum_{b=e,i,x} \mu_b E_b \phi_b(t),
$$

$$
\frac{1}{\tau_c(t)} = \frac{1}{\tau_m} + \kappa \sum_{b=e,i,x} \mu_b \phi_b(t),
$$

where $\mu_b$ and $\phi_b$ are the synaptic gains (which include the synaptic connectivities $N_b$) and the incoming firing rates from population $b$ where $\phi_e = \phi_i = \phi$ and $\tau_c$ is the synaptic time-constant. The feedback from the membrane potential found in Eq.\{6\} can now be found in the form of an active time-constant \[20\] in Eq.\{7\} where $\tau_c(t)$ varies inversely with the external input $\phi_e(t)$. When the homotopy constant is $\kappa = 0$, then the active time-constant equals the passive time-constant, $\tau_c = \tau_m$, as in current-based synapses. Whereas for $(\kappa = 1)$, then the equation is for conductance-based synapses. This is the key difference between the two synaptic mechanisms.

V. BIFURCATION AND NONLINEAR DYNAMICS METHODS

We very briefly describe the mathematical methods used that are standard tools in nonlinear dynamics and bifurcation theory. First we calculate the fixed points for the system of Eqn’s $2, 3, 6, 7$ using a modified Newton-Raphson algorithm. We then linearise these equations around the fixed points to construct a 4th order Jacobian. A local bifurcation analysis is performed and the eigenvalues $\lambda$ of the Jacobian are computed. These eigenvalues $\lambda$ determine the local stability of the full nonlinear system from the the local neighbourhood of the fixed points of the linearised system, as ensured by the Hartman-Grobmann lemma [25]. However, as a consequence of this our results cannot be guaranteed for any global bifurcations.

VI. PARAMETER VALUES

We use parameter values from [26] supplemented by $\tau_m=12$ ms, $\tau_s=1.3$ ms, $\gamma=300$ s$^{-1}$, $E_e=0$ mV, $E_i=-75$ mV, $\bar{V}=-62.5$ mV, $G_b$ and $\mu_b$ are computed from values of $s_b$ from [26].

VII. RESULTS

We find that the conditions under which bifurcations take place are quite different for each synaptic mechanism i.e., $\kappa = 0$ for current-based and $\kappa = 1$ for conductance-based synapses respectively. The feedback term from the membrane potential found in the active time-constant, which makes conductance-based synapses nonlinear, has a significant effect upon the neural dynamics in contrast with the linear current-based counterpart, $\kappa = 0$. In the current-based model, $\kappa = 0$, increasing the drive of the external input parameter $\phi_e(t)$ generates a Hopf bifurcation, which is typically interpreted as a transition to a seizure-like state. In comparison, increasing the external input in the conductance-based model $\kappa = 1$, has no effect due to the feedback from the membrane potential.

To investigate this property further we perform a bifurcation analysis of the homotopic continuation between the two synaptic mechanisms with Eq.\{6\}, using the homotopy parameter as a bifurcation parameter. Although these two systems are not topologically equivalent, they are locally homotopically equivalent. This enables us to perform a bifurcation analysis, as we homotopically deform one model into the other, by continuously varying the homotopic parameter $\kappa \in [0, 1]$. At each value of $\kappa$, the fixed points and their local stability is calculated. We are particularly interested in the point where there is a change in stability, which is indicative of oscillatory behaviour being suppressed, by the bilinear feedback term from the membrane potential by conductance-based synapses.

First we choose a section of parameter space where the current-based model oscillates by tuning the external input $\phi_e$ and the network balance, which is the ratio of inhibition to excitation as defined by Meffin et al [15]. Usually, these are additional bifurcation parameters that are typically used in current-based neural model to generate bifurcations [9, 13, 23].
continuation is performed and the current-based model is deformed into the conductance-based model. We analyse the conductance-based model for the same bifurcation values i.e., the same part of parameter space except the homotopy parameter, and find that the oscillations are suppressed at a critical value of the homotopy parameter $\kappa = \kappa_c^*$.  

FIG. 1: The fixed points are plotted as a function of the homotopy parameter, $\kappa$. The red fixed points are unstable and represent oscillatory behaviour. At a critical value of $\kappa = \kappa_c = 0.408$, the system switches from an unstable red fixed point to a stable non-oscillatory blue fixed point.

FIG. 2: A plot of the real part of the largest eigenvalue, $\lambda_{\text{max}}$, associated with the fixed points in Figure 1, versus the homotopy parameter, $\kappa$. As in Figure 1, at a critical homotopy value of $\kappa = \kappa_c = 0.408$, the positive unstable eigenvalues in red, cross the zero real line (black), and become stable eigenvalues shown in blue as their real part becomes negative.

As we can see from the bifurcation analysis in Figures 1, 2 of the fixed point and the real part of the largest eigenvalue, there is a critical value of the homotopy parameter, $\kappa = \kappa_c = 0.408$. At this point the feedback from the membrane potential term in the conductance-based synapses suppresses the oscillatory activity produced by the current-based synapses. This can be more clearly seen on the argand plane in Figure 3, where there is a Hopf bifurcation. The largest eigenvalues go from right to left through the imaginary axis i.e., from an unstable conjugate pair to a stable conjugate pair. This is indicative of a change of state from a limit cycle to a steady-state activity i.e., a transition from seizure-like behaviour to normal or resting state behaviour. The value of the critical point at which this takes place, $\kappa_c$ is also dependent upon the other parameter values such as the reversal potentials $E_b$, external input $\phi_s$, and network balance $\Psi$.

FIG. 3: The eigenvalues in Figure 2 plotted on an Argand plane. It shows an unstable conjugate pair in red, crossing the imaginary axis, from right to left, to become a stable conjugate pair, shown in blue. The eigenvalues cross the imaginary axis at the critical homotopy parameter value, $\kappa = \kappa_c = 0.408$, at which point a Hopf bifurcation occurs.

VIII. DISCUSSION AND CONCLUSION

This research provides an explicit and rigorous examination of the exact differences between the current-based and conductance-based models in a neural field model. The analysis is performed by formalising a relationship between the two models in the form of a homotopic continuation.

The homotopic continuation was performed between the synaptic mechanisms by varying a homotopy parameter, $\kappa \in [0, 1]$, which continuously deforms one synaptic mechanism into the other and vice-versa. After re-calculating the fixed points each time we varied the homotopy parameter, we performed a stability and bifurcation analysis. We found that there is a critical value of the homotopy parameter, $\kappa_c = 0.408$, where the oscillatory activity from the current-based model was suppressed by the feedback from the conductance-based model. This explicitly shows how the feedback from the fluctuations of the membrane potential added by conductance-based synapses gives a qualitatively different behaviour for the same parameter space. These results highlight the role that the fluctuations of the membrane potential
play in significantly affecting the network stability, and consequently epileptic transitions.

The fluctuations of the membrane potential in a population of neurons are largely proportional to the synaptic background activity [27,28]. This is reflected as an increased leakiness of the membrane or a contraction of the active time-constant. When there is a constant noisy input that is both inhibitory and excitatory, then the contracted time-constant is indicative of a ‘high conductance state’ [29]. This is where the total conductance received is higher than then resting or leak conductance [30]. In this state, the variability of neuronal firing and response to background input as well as dendritic integration is different. Hence, the homotopy parameter $\kappa$ can be interpreted physiologically as a change in the synaptic background activity that affects the conductance state of the network.

The homotopy parameter, $\kappa$, interpreted as a change in the synaptic background activity affects the conductance state of neurons and results in fluctuations of their membrane potentials [28]. It is the multiplicative effect of these fluctuations that suppress the transition to seizure-like activity and need to be taken into account in more accurate neural models. If these fluctuations are of reasonably small amplitude, for example, as in resting state behaviour, then current-based synapses can be an adequate approximation. However, if these fluctuations are larger in amplitude, for example, as occurs in oscillatory or seizure-like activity, then they need to be included to provide an accurate description of the dynamics [33].

This type of feedback process from the synaptic background activity that manifests as fluctuations of the membrane potential is dependent upon the network balance. For an excitatory dominated network this would be a form of positive feedback. Whereas for an inhibitory dominated network such as ours, the feedback will be negative. Bifurcations that go from a linear steady-state to a nonlinear oscillatory state as found here, can occur when the strength of a feedback process reaches a critical value [19]. Our results show that when the strength of a negative feedback process reaches a critical value, then there is a bifurcation from a nonlinear oscillatory state to a linear steady-state. These complimentary ‘phase transitions’ highlight the fundamental importance of endogeneous regulatory mechanisms that modulate cortical excitability at multiple scales.

It should also be noted that the parameter values have been chosen such that the suppression of seizure-like behaviour is explained by the feedback from the membrane potential. It is also possible to choose parameter values for the reversal potentials for example, where both models have the same oscillatory behaviour. Hence, the critical value of the homotopy parameter $\kappa_c$ is dependent on the various parameters of the model.

To our knowledge this is the first demonstration of a homotopy between current-based and conductance-based synaptic mechanisms. It clearly highlights the difference between the additive effects of current-based synapses and the multiplicative effects of conductance-based synapses. This is particularly so when the synapses receive noisy input from the background synaptic activity of the network. The neuronal response to effects of additive noise and multiplicative noise is significantly different [32,34].

Essentially, we have constructed a mathematical mapping between two different synaptic mechanisms (additive-linear and multiplicative-nonlinear) and examined their effects on the dynamics of a typical neural field model. This calls into question previous results of neural field models that use current-based synapses, including those used to model epileptic seizures, since using a more biophysically realistic synaptic mechanism yields significantly different results for network behaviour.

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