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A Neural Mass Model of Spontaneous Burst Suppression and Epileptic Seizures

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***Abstract*— The paper presents a neural mass model that is capable of simulating the transition to and from various forms of paroxysmal activity such as burst suppression and epileptic seizure-like waveforms. These events occur without changing parameters in the model. The model is based on existing neural mass models, with the addition of feedback of fast dynamics to create slowly time varying parameters, or slow states. The goal of this research is to establish a link between system properties that modulate neural activity and the fast changing dynamics, such as membrane potentials and firing rates that can be manipulated using electrical stimulation. Establishing this link is likely to be a necessary component of a closed-loop system for feedback control of pathological neural activity.**

I. Introduction

This paper introduces an augmentation to a neural mass model of a cortical column [1], such that the model can exhibit multiple types of neural behavior without changing parameters. The motivation for this extension to an existing model is to form a link between fast dynamics, of membrane potentials and neural firing rates, and slowly changing dynamics that may modulate networks and lead to pathological activity such as seizures.

To date, most neural mass models explain the transition from normal behaviour to paroxysmal activity by manually changing parameters (see [2], [3], for example). This approach is useful for generating hypotheses about the mechanisms of such events; however, it does not form a closed model of the phenomena of interest. Recently, a few examples of neural mass models have been developed that are capable of exhibiting spontaneous seizure-like events [4], [5] and burst suppression [6]. Models of this kind are capable of providing insights into the transitions from healthy to disease states in the brain, rather then just describing specific states by manually changing parameters. Furthermore, models of this type provide a link between aspects of physiology that vary slowly and influence excitability of cortical networks, membrane potentials, and firing rates.

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The neural mass model of Jansen and Rit [1] is one of the most popular descriptions of the mass action of cortical columns due to its balance between realism and parsimony. Augmentation of this model builds upon the existing literature to add an extra level of biological realism, further generalizing the model. In doing so, we can explain a richer repertoire of neural dynamics. The motivation is to use this model for feedback control, via electrical stimulation, of slowly varying parameters in order to prevent epileptic seizures.

II. A Standard Neural Mass Model

To derive a standard neural mass model, we begin by defining the post-synaptic potential of population n as a result of an input firing rate from population m as their convolution,

$$v_n(t) = v_{r,n} + \int_{-\infty}^{t} \frac{\alpha_{mn}}{\tau_{mn}} h_{mn}(t-t') g_m(v_m(t'))\,\mathrm{d}t' \tag{1}$$

$$v_n(t) - v_{r,n} = \int_{-\infty}^{t} \frac{\alpha_{mn}}{\tau_{mn}} h_{mn}(t-t') g_m(v_m(t'))\,\mathrm{d}t' \tag{2}$$

$$\tilde{v}_n(t) = \int_{-\infty}^{t} \frac{\alpha_{mn}}{\tau_{mn}} h_{mn}(t-t') g_m(v_m(t'))\,\mathrm{d}t', \tag{3}$$

where α_{mn} is the gain for the post-synaptic response kernel denoted by $h_{mn}(t)$, from neural population m to n, and τ_{mn} is the membrane time constant. Typically, $\alpha_{mn}(t)$ and τ_{mn} are constants (particularly for current-based synapses), but we will relax this assumption. Also, $g_m(v_m(t))$ describes the input firing rate as a function of the pre-synaptic membrane potential. The resting membrane potential of the post-synaptic population is denoted by $v_{r,n}$, $v_n(t)$ is the post-synaptic membrane potential, and $\tilde{v}_n(t)$ is the deviation of the membrane from the resting potential. For the model of a cortical column that we are considering, the index n (post-synaptic) may represent either the pyramidal (p), excitatory interneuron (spiny stellate) (e), inhibitory interneuron (i), fast inhibitory ($i1$), or slow inhibitory ($i2$) populations.

The post-synaptic response kernel, $h_{mn}(t)$, typically takes one of three different forms: one first order and two second order. The first-order form has an instantaneous rise and a decay defined by a single time constant. The second order kernels have a finite rise and decay time, with the difference being with one form having separate time constants (bi-exponential) for the rise (synaptic time constant) and decay (membrane time constant), whereas the other form is defined

using a single time constant (alpha function) by

$$h_{mn}(t) = \eta(t) t \exp\left(-\frac{t}{\tau_{mn}}\right), \tag{4}$$

where $\eta(t)$ is the Heaviside step function. Equation 4 is the form we shall use in this study; however, the framework holds for other forms.

This convolution can conveniently be written as

$$\mathrm{D}\tilde{v}_n(t) = \frac{\alpha_{mn}}{\tau_{mn}} g_m(v_m(t)), \tag{5}$$

where the linear differential operator, D, is

$$\mathrm{D} = \frac{\mathrm{d}^2}{\mathrm{d}t^2} + \frac{2}{\tau_{mn}}\frac{\mathrm{d}}{\mathrm{d}t} + \frac{1}{\tau_{mn}^2}. \tag{6}$$

This allows the dynamics of the neural mass to be described by the differential equation,

$$\frac{\mathrm{d}^2\tilde{v}_n(t)}{\mathrm{d}t^2} + \frac{2}{\tau_{mn}}\frac{\mathrm{d}\tilde{v}_n(t)}{\mathrm{d}t} + \frac{1}{\tau_{mn}^2}\tilde{v}_n(t) = \frac{\alpha_{mn}}{\tau_{mn}} g_m(v_m(t)). \tag{7}$$

This second-order ODE can be written as two coupled first-order ODEs by defining

$$z_n(t) = \frac{\mathrm{d}\tilde{v}_n(t)}{\mathrm{d}t}. \tag{8}$$

Recasting the system in this way allows formation of a state-space model in a canonical form. This gives the system,

$$\frac{\mathrm{d}\tilde{v}_n(t)}{\mathrm{d}t} = z_n(t) \tag{9}$$

$$\frac{\mathrm{d}z_n(t)}{\mathrm{d}t} = \frac{\alpha_{mn}}{\tau_{mn}} g_m(v_m(t)) - \frac{2}{\tau_{mn}} z_n(t) - \frac{1}{\tau_{mn}^2}\tilde{v}_n(t). \tag{10}$$

There is a sigmoidal relationship between the mean membrane potential and firing rate of each of the populations. This sigmoid nonlinearity may take different forms, for example, the cumulative density function (error function) or the logistic/hyperbolic tangent. Typically, the logistic function form is used, defined as

$$g\left(\tilde{v}_n(t)\right) = \frac{1}{1 + \exp\left(\varsigma_n(t)\left(v_{0n} - \tilde{v}_n(t)\right)\right)} \tag{11}$$

$$g\left(\tilde{v}_n(t)\right) = \frac{1}{1 + \exp\left(\varsigma_n(t)\left(v_{0n} + v_{rn} - v_n(t)\right)\right)} \tag{12}$$

$$g\left(v_n(t)\right) = \frac{1}{1 + \exp\left(\varsigma_n(t)\left(\tilde{v}_{0n} - v_n(t)\right)\right)} \tag{13}$$

where $\tilde{v}_{0n} = v_{0n} + v_{rn}$. Note that in this formulation, we are absorbing the maximal firing rate, which is typically a linear coefficient of the sigmoid, into the PSP gain (α_{mn}). This removes a redundant parameter that can not be recovered by estimation methods. The quantities ς_n and v_{0n} describe the slope of the sigmoid (variance of firing thresholds within the populations) and the mean firing threshold, respectively. These quantities are usually assumed to be constants, but this assumption will be relaxed. The parameter $\tilde{v}_{0n}$ describes the deviation of the mean firing threshold from the mean resting membrane potential, which becomes our lumped threshold parameter. For ease of notation, we can drop the *tilde* remembering that the resting membrane potential resides within this term.

This neural mass maps from a mean pre-synaptic firing rate to a post-synaptic mean membrane potential. The terms that are usually considered parameters of the model include τ, α, v_0, and ς. These can be set to model different neural populations, such as pyramidal neurons, spiny stellate cells, and fast and slow inhibitory interneurons ($\mathrm{GABA_a}$ and $\mathrm{GABA_b}$). The neural populations can then be configured to represent the circuitry of a cortical column and networks of cortical columns. Contributions in this regard have been made by [7], [2], [1], [8] and others. An illustration of the model of a cortical column is shown in Figure 1.

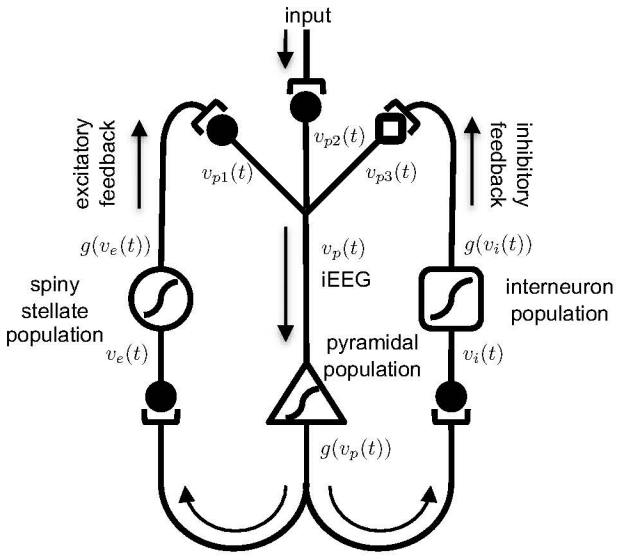

Fig. 1. **Model of a Cortical Column.** The model shows three interconnected neural masses, which are pyramidal neurons, excitatory spiny stellate cells, and inhibitory interneurons. The specific subtype of neural population is defined by the parameters that describe the post-synaptic response kernels.

The parameters of the neural masses define the population type and the behavior the model exhibits. For example, for a certain parameter combination, we obtain a model of a cortical column that will generate alpha-wave type activity, and for another set of parameters we obtain a different model that will exhibit epileptic behavior. Therefore, we consider this neural mass as a family of models, which we define as

$$\dot{\mathbf{x}} = f_\theta\left(\mathbf{x}, \varepsilon\right), \tag{14}$$

where $\mathbf{x} \in \mathbb{R}^2$ is a state vector representing the postsynaptic membrane potential and its derivative, ε represents system noise, which may be unmodeled inputs and model inaccuracies. The function $f_\theta(\cdot)$ describes the dynamics, where $\theta \in \mathbb{R}^4$ determines the mass type and the behavior it exhibits. An alternative way of describing the model is

$$\dot{\mathbf{x}} = f\left(\mathbf{x}, \theta, \varepsilon\right) \tag{15}$$

$$\dot{\theta} = 0, \tag{16}$$

where parameters are now modeled as states with trivial dynamics.

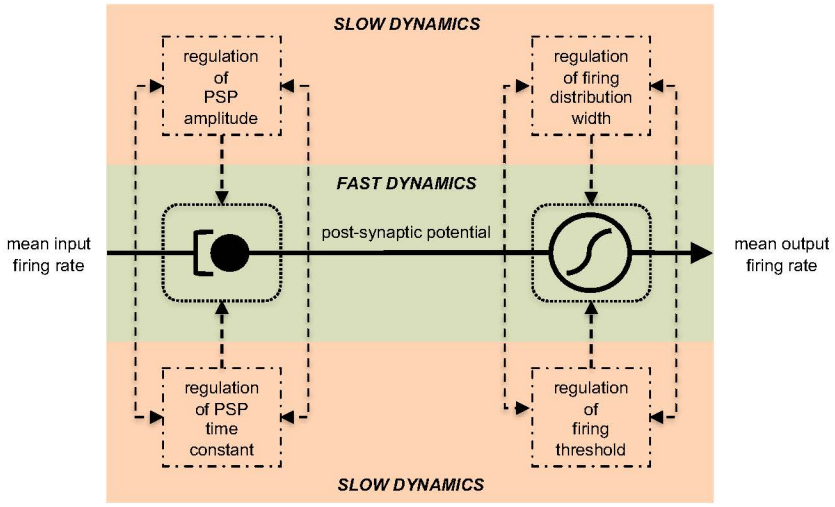

Fig. 2. **Neural Mass Model with Regulatory Mechanisms.** The augmented neural mass model shown in the figure has a regulatory system that uses feedback to slowly modify the post-synaptic response kernel and the properties of the activation function. This is known as a singularly perturbed system, since there is a clear separation of time scales between regulatory mechanisms and the firing and membrane potential dynamics.

III. Augmentation of the Neural Mass Model

This section describes a simple illustrative example of how to extend the model to capture dynamics that are important aspects of neurophysiology that are not adequately described in the existing formulation. For example, we expect the synaptic time constant to vary with changes in the firing rate of the respective neural population. This effectively changes the synapse from current-based to conductance-based. Furthermore, we expect the threshold parameter, v_0, to vary with the firing rate of the neuron, where a sustained high firing rate should increase the threshold and reduce excitability. This augmented neural mass is depicted in Figure 2. These modifications can be realized by the additional state variables

$$\dot{\zeta}_{mn}(t) = -\beta_{mn}\zeta_{mn}(t) + \phi_{1,mn}g_m(v_m(t)) + \phi_{2,mn}v_n(t) \tag{17}$$

$$\dot{v}_{0,m}(t) = -\gamma_m v_{0,m}(t) + \psi_m g_m(v_m(t)), \tag{18}$$

where β and γ are decay parameters and $\phi_{1,2}$ and ψ are weight parameters. Note that the new parameters are constants. The slow system can be written compactly as

$$\boldsymbol{\theta}(t) = \begin{bmatrix} \zeta_{mn}(t) & v_{0,m}(t) \end{bmatrix}^\top \tag{19}$$

$$\dot{\boldsymbol{\theta}}(t) = \mathcal{F}(\mathbf{x}(t), \boldsymbol{\theta}(t)). \tag{20}$$

Traditionally, investigators have been interested in the phenomenology (EEG), which is the fast system, but with the augmented model we can now describe the important regulatory systems and physiology.

IV. Simulation Example

The simulation results can be seen in Figure 3. For the simulation of the burst suppression activity, the parameters that control the feedback of the synaptic time constants were set to zero. Similarly, the parameters that control the feedback for the firing thresholds were set to zero when demonstrating the seizure-like events.

As seen in Figure 3(a), the burst suppression patterns occur at semi-regular time intervals, that follow the oscillations in the threshold. The bursts begin when the threshold is in a trough and subside when the thresholds peak.

Figure 3(b) shows an example of the epileptic-like events when feedback is added to the time constants. The spectrograms of the seizure-like waveform show the power is concentrated in a similar band to what is observed clinically.

V. Discussion and Conclusion

This paper has introduced an augmentation to the neural mass model of Jansen and Rit [1], such that it can exhibit spontaneous seizure-like waveforms and burst suppression activity. It is hoped that an augmentation of this form will facilitate a link between fast and slow systems in the brain. In doing so, we hope to enable closed-loop control of what was considered model parameters using electrical stimulation.

The dynamical mechanisms for the changes between different types of activity in this model are still unknown. However, it appears that by adding the feedback to the time constants we have introduced a form of bi-stability into the model, where transitions to seizure-like waveforms are driven by noise. This is akin to other work in the literature [9], [10]. In contrast to this, the simulation with feedback to the firing threshold appears to induced a regular oscillation of the parameters, which then makes the discharges occur at semi-regular intervals.

The burst suppression-like activity seen in our simulation is similar to observations in other recent work [11]. It is thought that this phenomenon is due to global processes that occur in the brain. Homogeneity of the patterns that appear across the cortex during burst suppression provides some indirect evidence of this conjecture. The parameter that would most likely reflect this in the Jansen and Rit model is the firing threshold (relative to the resting membrane potential), which would reflect ionic changes in the extra

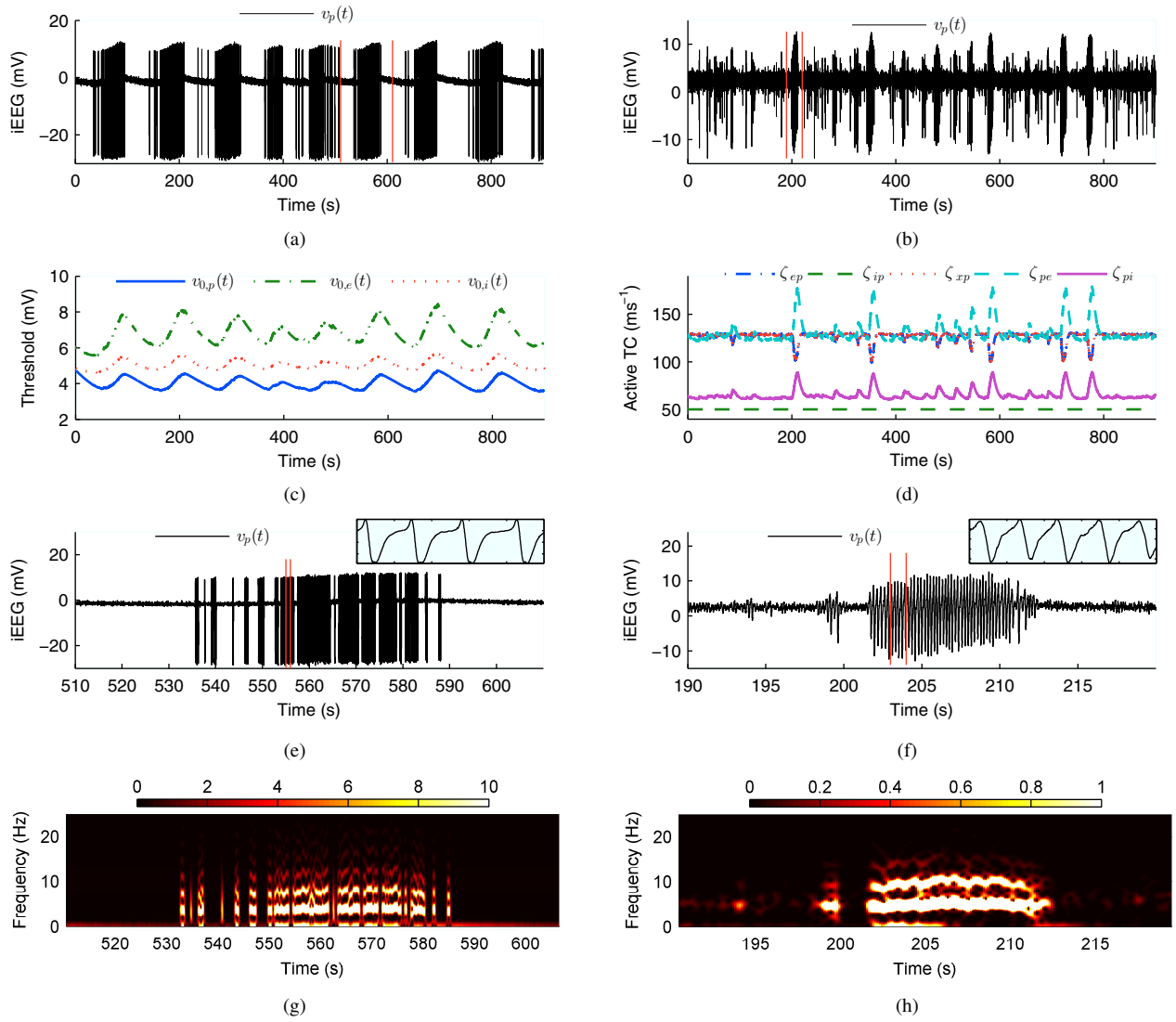

Fig. 3. **Simulation Results.** a) and b) simulated times series with feedback on the threshold parameters and time constant, respectively. The red vertical lines mark the intervals that are used in parts e) to h). c) and d) Slow dynamics of the parameters. e) and f) Zoomed versions of paroxysmal activity from panels a) and b), where e) resembles burst suppression as seen in anesthesia, and f) resembles a seizure recorded with intrancranial EEG. g) and h) Spectrograms of the paroxysmal activity.

cellular environment.

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