

Tracking Parameters of a Neural Mass Model: A Method to  
Provide Insight into the Mechanisms behind Seizure

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# 1 Introduction

## Aims

**Estimate model parameters from a neural mass model of the hippocampus.** Epilepsy is not well understood. Approximately one third of patients with epilepsy are refractory to treatment, and not much is understood about the mechanisms underlying seizures. In this paper, a new method to image aspects of the brain is introduced. This method involves the application of a well known neural mass model with a relatively new estimation technique. In particular, the estimation of physiologically relevant parameters from a neural mass model of the hippocampus (Wendling et al., 2002) is considered, using an unscented Kalman filter (Voss et al., 2004).

**To improve the understanding of epilepsy and improve the outcome of epilepsy patients.** By estimating the physiologically relevant parameters from the neural mass model of the hippocampus, it will be possible to image the changes occurring in the brain prior to seizure. This will be achieved by estimating model parameters based on electrographic recordings of seizures recorded from the hippocampus. Further, this method can be applied to determine the effect that treatment has on the physiological parameters. Imaging the brain in this manner will make it possible to titrate therapies that are patient specific and therefore more efficacious. For example, if it is observed that the model parameter describing inhibition decreases prior to seizure, a treatment that has the opposite effect on the model parameter can be determined and used on the specific patient.

## How has this been achieved previously?

**Introduction to neural mass model, freeman, jansen etc** The original formulation of the neural mass model was in the early 1970's (Lopes da Silva et al., 1974; Freeman, 1963). The model was further developed in the mid 1990's. In this model, a cortical region of the brain is modeled as having a population of inhibitory and excitatory neurons, with the excitatory neurons being responsible for the production of the observed electrographic activity. This neural mass model was capable of replicating normal, or background, EEG as well as slow rhythmic activity, or alpha waves (Jansen and Rit, 1995). This description by Jansen and Rit was capable of replicating background and alpha rhythms observed in EEG by altering model parameters.

**Inadequacy of jansen model and intro to the wendling model** The model described by Jansen and Rit (1995) was shown to be capable of replicating other key features observed in EEG. However, the model was not able to replicate a key feature observed prior to seizure for recordings from the hippocampus, low amplitude high frequency EEG. A study performed by White et al. (2000) showed a possible reason for the models inability to replicate low amplitude high frequency EEG. They showed that within the hippocampus the inhibitory populations effect on excitatory

populations had two distinctly different propagation delays, and that both were significant for the reproduction of EEG. They hypothesised that the cause of the two different propagation delays were due to the location of the synapses connecting the inhibitory populations to the excitatory populations. With the longer propagation delay due to synapse connections far from the soma (peri-dendritic), and the shorter delay due to connections near the soma (peri-somatic). This effect was incorporated into the neural mass model by Wendling et al. (2002). In order to account for the two propagation delays observed the Wendling group described two different types of inhibitory populations. One fast (peri-somatic), and the other a slow (peri-dendritic) inhibitory population. In the same study, it was shown that the addition of the peri-somatic inhibitory population made it possible for the neural mass model to replicate the key characteristics of low amplitude high frequency EEG. This model is referred to as the neural mass model of the hippocampus.

**This model is capable of replicating key characteristics observed in EEG prior to and during seizure.**

The neural mass model of the hippocampus is capable of replicating key features observed in EEG prior to, during and post seizure. The model can replicate key features by altering parameters that describe the balance between excitation and inhibition in the modeled region of the brain. The model, although it is described in a neuronal sense, is not a model of the brain. However, it is a good descriptor of EEG recorded from the hippocampus. Due to its description of neuronal connections and systems in terms of populations the model is relatively uncomplicated. This is shown in Wendling et al. (2002) where key features observed prior to, during and post seizure can all be replicated by altering three model parameters, which describe the balance between excitation and inhibition. This ability of the model means that only three model parameters need to be estimated, and allow imaging of these unmeasured dynamics using estimation.

**Previous work on estimating the neural mass model of the hippocampus has been done using a genetic algorithm.**

The neural mass model of the hippocampus has previously been estimated using the genetic algorithm (Wendling et al., 2005). The genetic algorithm is capable of estimating model parameters using recursion. This makes the method accurate but time consuming. Therefore, results from studies using the genetic algorithm are often limited. The result of which is incomplete characterisation of EEG, with little to no evidence of the changes in model parameters observed during the transitions from normal to ictal EEG being unique.

**What is being done, and why is it better or different?**

In this paper, the accuracy of estimating the three model parameters describing the balance between excitation and inhibition using an unscented Kalman filter is determined. In order to achieve

this, artificial EEG is simulated using the neural mass model of the hippocampus. The artificial EEG is then considered to be the observations in the estimation procedure. Model parameters are then estimated, under the assumption that they were originally unknown.

**Why the Kalman filter** The filter, unlike the genetic algorithm, does not rely on recursion and is therefore less time consuming. This comes at the cost of accuracy. This paper looks at the accuracy of the filter under numerous conditions to determine how robust it is. If the unscented Kalman filter is accurate at estimating model parameters then this method could be used further to help characterise full EEG data sets, and allow for treatments to be evaluated and developed.

**Structure of the paper** In the methods section, a description of the neural mass model of the hippocampus is presented, as well as the equations used to simulate the model. Further, the formulation of the unscented Kalman filter for the neural mass model of the hippocampus is described. In the results section, the performance of the algorithm under numerous conditions are demonstrated. Lastly, in the discussion an evaluation of the performance of the filter is provided, discussing whether this method is a viable way forward to use model estimation to help image the effect that disorders and treatments have on the brain.

## 2 Methods

**What we are doing in this paper** The Wendling model is capable of replicating key features of observed in hippocampal EEG prior to, during and post seizure (Wendling et al., 2002). Here the estimation of physiologically relevant model parameters from the Wendling model is considered. An unscented Kalman filter is used to estimate the model parameters of interest. For this study the estimation procedure is tested using artificial EEG simulated using the Wendling model. By doing so it is possible to determine how robust the unscented Kalman filter is when estimating the Wendling model.

### Wendling model description.

The Wendling model describes the aggregate membrane potentials and firing rates produced by different neural populations. The populations are then excited or inhibited by other populations in the model. The net effect of one population on another is determined by a scaling constant termed the connectivity constant. A graphical representation of the model is shown in Figure 1. In the model four different neural populations are considered. The pyramidal neural population is the generator of the model output, and its aggregate membrane potential is the simulated artificial EEG. Excitatory interneurons excite the pyramidal neurons. Slow and fast inhibitory interneurons inhibit the pyramidal neural population. Further, the pyramidal neural population excites the excitatory, slow and fast inhibitory populations. Lastly, slow inhibitory interneurons inhibit the fast inhibitory neural population. The effect of each neural population on the other is scaled by a connectivity constant. This connectivity constant accounts for the number of neurons within each population. Lastly, a stochastic input to the model is added to account for the effect of afferent pyramidal neurons on the modeled neural mass.

**Mathematical functions used in the model** The Wendling model consists of two primary structures. The first structure is a sigmoid function which converts an aggregate membrane potential to an average firing rate (Equation 1). In equation 1  $g(v(t))$  is the firing rate,  $g_{max}$  is the maximum firing rate,  $r$  is the sigmoid gradient and  $v_0$  is the membrane potential at which  $0.5g_{max}$  is reached. The second structure is an average firing rate to aggregate membrane potential kernel (Equations 2-3). In equations 2-3  $v_k(t)$  is the aggregate membrane potential,  $h_k(t)$  is kernel which converts firing rates into membrane potentials,  $\theta_k(t)$  is the synaptic gain and  $\tau_k$  is the time

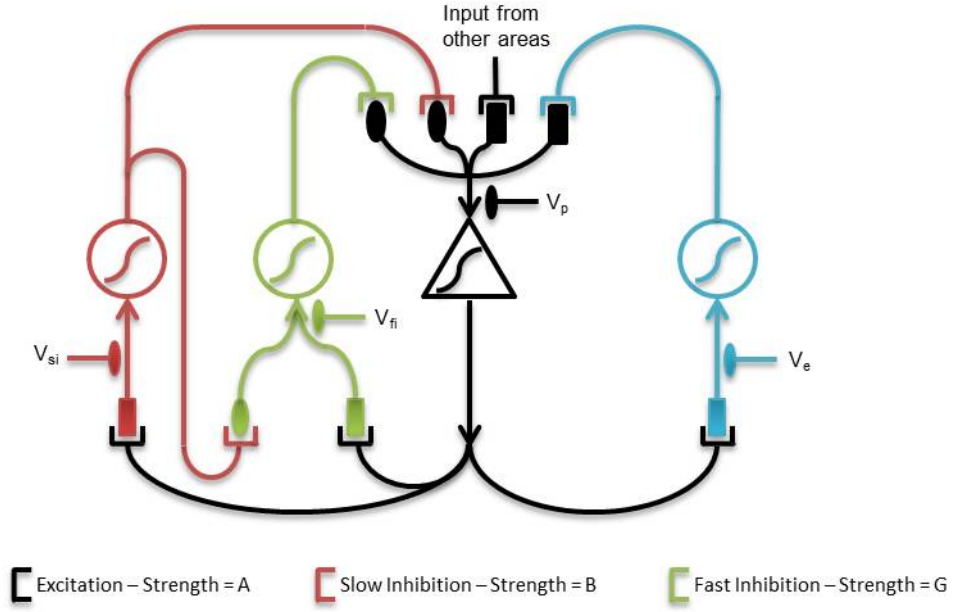


Figure 1: Graphical Description of the Wendling model.

constant.  $h_k(t)$  is a delayed exponential decay function (Figure 2).

$$g(v(t)) = \frac{g_{max}}{1 + \exp(r(v(t) - v_0))} \quad (1)$$

$$v_k(t) = h_k(t) * g(v(t)) \quad (2)$$

$$h_k(t) = \frac{\theta_k(t)t}{\tau_k} \exp\left(-\frac{t}{\tau_k}\right). \quad (3)$$

Here the subscript  $k$  is used to indicate that each neural population is described with a different synaptic gain and time constant. The synaptic gains are described by  $\theta_k$  as they are the parameters that are altered in order to simulate artificial seizure EEG (Figure 3). Further, the synaptic gains will be the variables that are estimated in this study. In this description of the Wendling model numerous model parameters are considered to be stationary, this includes the maximum firing rate ( $g_{max}$ ) and time constants ( $\tau_k$ ). Equations 2-3 can be converted into a set of two differential equations

$$\dot{v}_k(t) = z_k(t) \quad (4)$$

$$\dot{z}_k(t) = \theta_k(t)\tau_k n_k u_k(t) - 2\tau_k z_k(t) - \tau_k^2 v_k(t). \quad (5)$$

Here  $v_k(t)$  is the average membrane potential and  $z_k(t)$  is its derivative.  $\theta_k(t)$  and  $\tau_k$  are the specific neural populations synaptic gain and time constant. Lastly,  $u_k(t)$  is the firing rate to the specific neural population considered and  $n_k$  is a constant used to specify connectivity.

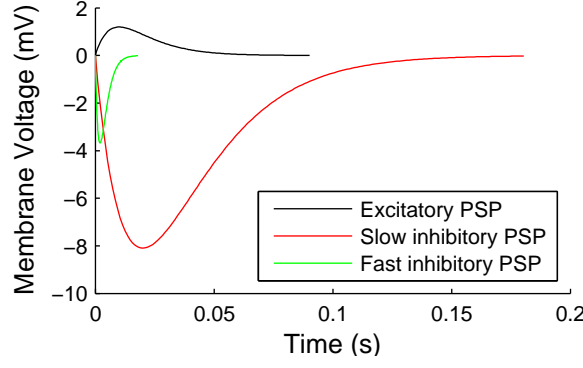


Figure 2: Firing rate to aggregate membrane potential converter.

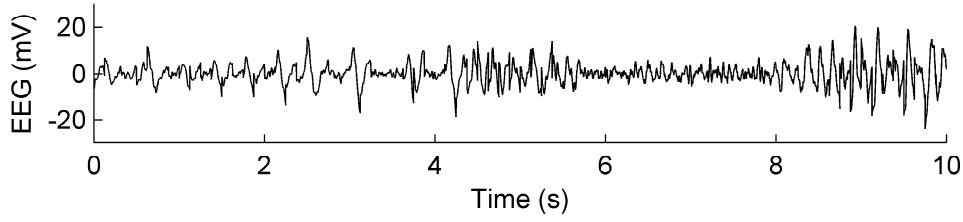


Figure 3: Artificial seizure simulated using the wendling model.

**Full mathematical description of the model** Using equations 4-5 the model can be described by a set of eight stochastic differential equations

$$dv_{po}(t) = z_{po}(t)dt \quad (6)$$

$$dz_{po}(t) = (\theta_p(t)\tau_p n_p g(v_p(t)) - 2\tau_p z_{po}(t) - \tau_p^2 v_{po}(t))dt \quad (7)$$

$$dv_{eo}(t) = z_{eo}(t)dt \quad (8)$$

$$dz_{eo}(t) = (\theta_e(t)\tau_e(\mu + n_e g(v_e(t)) - 2\tau_e z_{eo}(t) - \tau_e^2 v_{eo}(t))dt + \theta_e(t)\tau_e \epsilon(t)dW \quad (9)$$

$$dv_{sio}(t) = z_{sio}(t)dt \quad (10)$$

$$dz_{sio}(t) = (\theta_{si}(t)\tau_{si} n_{si} g(v_{si}(t)) - 2\tau_{si} z_{sio}(t) - \tau_{si} v_{sio}(t))dt \quad (11)$$

$$dv_{fio}(t) = z_{fio}(t)dt \quad (12)$$

$$dz_{fio}(t) = (\theta_{fi}(t)\tau_{fi} n_{fi} g(v_{fi}(t)) - 2\tau_{fi} z_{fio}(t) - \tau_{fi} v_{fio}(t))dt. \quad (13)$$

$dW$  represents a Wiener process and is required as  $\epsilon(t) \mapsto N(0, \sigma)$ . Here  $\sigma$  and  $\mu$  describe the mean and variance of the stochastic model input. Further,  $v_{ko}(t)$  and  $z_{ko}(t)$  represent the membrane potential produced by each neural population.  $v_k(t)$  and  $z_k(t)$  are the inputs to each neural population, and are considered to be the membrane potential of the specific population.  $k$  takes the values of  $p$ ,  $e$ ,  $fi$  and  $si$  representing pyramidal, excitatory, and slow and fast inhibitory populations, respectively. Therefore  $v_p(t)$  is the output of the model. All  $v_k(t)$  can be described

in terms of  $v_{ko}(t)$  as follows

$$v_p(t) = v_{eo}(t) - v_{sio}(t) - v_{fio}(t) \quad (14)$$

$$v_e(t) = c_1 v_{po}(t) \quad (15)$$

$$v_{si}(t) = c_3 v_{po}(t) \quad (16)$$

$$v_{fi}(t) = c_5 v_{po}(t) - c_6 v_{sio}(t), \quad (17)$$

where  $c_1$ ,  $c_3$  and  $c_5$  represent the connectivity strength from pyramidal to excitatory, slow inhibitory and fast inhibitory populations, respectively.  $c_6$  represents the connectivity strength from the slow to the fast inhibitory population. Lastly, all  $n_k$  can be defined as connectivity constants

$$n_p = 1 \quad (18)$$

$$n_e = c_2 \quad (19)$$

$$n_{si} = c_4 \quad (20)$$

$$n_{fi} = c_7. \quad (21)$$

Here  $c_2$ ,  $c_4$  and  $c_7$  represent the connectivity strength from excitatory, slow inhibitory and fast inhibitory to the pyramidal population.

**Simulation of model** This set of continuous stochastic differential equations is discretised using Euler-Maruyama's method, to simulate the artificial EEG.

$$v_{po,t+T} = v_{po,t} + T z_{po,t} \quad (22)$$

$$z_{po,t+T} = z_{po,t} + T(\theta_{p,t} \tau_p n_p g(v_{p,t}) - 2\tau_p z_{po,t} - \tau_p^2 v_{po,t}) \quad (23)$$

$$v_{eo,t+T} = v_{eo,t} + T z_{eo,t} \quad (24)$$

$$z_{eo,t+T} = z_{eo,t} + T(\theta_{e,t} \tau_e (\mu + n_e g(v_{e,t}) - 2\tau_e z_{eo,t} - \tau_e^2 v_{eo,t})) + \sqrt{T} \theta_{e,t} \tau_e \epsilon_t \quad (25)$$

$$v_{sio,t+T} = v_{sio,t} + T z_{sio,t} \quad (26)$$

$$z_{sio,t+T} = z_{sio,t} + T(\theta_{si,t} \tau_{si} n_{si} g(v_{si,t}) - 2\tau_{si} z_{sio,t} - \tau_{si} v_{sio,t}) \quad (27)$$

$$v_{fio,t+T} = v_{fio,t} + T z_{fio,t} \quad (28)$$

$$z_{fio,t+T} = z_{fio,t} + T(\theta_{fi,t} \tau_{fi} n_{fi} g(v_{fi,t}) - 2\tau_{fi} z_{fio,t} - \tau_{fi} v_{fio,t}). \quad (29)$$

Here  $T$  is the period between solutions. The static parameter values are demonstrated in Tables 1-2. The variance of the input ( $\sigma$ ) is specified such that 99.7% of realisations drawn from the Gaussian distribution fall within the specified maximum and minimum firing rate. In this case,



Table 1: Static Model Parameters

| MODEL PARAMETER | PHYSICAL DESCRIPTION                      | VALUE | UNITS     |
|-----------------|---|-------|-----------|
| $\tau_p$        | Time constant for pyramidal neurons       | 100   | $s^{-1}$  |
| $\tau_e$        | Time constant for excitatory neurons      | 100   | $s^{-1}$  |
| $\tau_{si}$     | Time constant for slow inhibitory neurons | 35    | $s^{-1}$  |
| $\tau_{fi}$     | Time constant for fast inhibitory neurons | 500   | $s^{-1}$  |
| $c$             | Connectivity constant                     | 135   | NA        |
| $g_{max}$       | Maximum firing rate                       | 5     | Hz        |
| $v_0$           | PSP for which 50% firing rate is achieved | 6     | $mV^{-1}$ |
| $r$             | Gradient of sigmoid function              | 0.56  | NA        |
| $\mu$           | Input mean firing rate                    | 90    | Hz        |
| $\sigma$        | Variance of input firing rate             | 15    | Hz        |

Table 2: Static model parameters: Connectivity.  $C$  is the connectivity constant specified in Table 1. Terms in brackets indicate the direction in which the constant affects the system. Here P, E, SI and FI represent populations of pyramidal neurons and excitatory, slow inhibitory and fast inhibitory interneurons, respectively.

| MODEL PARAMETER | PHYSICAL DESCRIPTION              | VALUE   |
|-----------------|-----------------------------------|---------|
| $c_1$           | Connectivity constant (P - E)     | $C$     |
| $c_2$           | Connectivity constant (E + I - P) | $0.8C$  |
| $c_3$           | Connectivity constant (P - SI)    | $0.25C$ |
| $c_4$           | Connectivity constant (SI - P)    | $0.25C$ |
| $c_5$           | Connectivity constant (P - FI)    | $0.3C$  |
| $c_6$           | Connectivity constant (SI - FI)   | $0.1C$  |
| $c_7$           | Connectivity constant (SI - P)    | $0.8C$  |

the firing rate limits are set to 30 and 150. For the cases where the realisations from the Gaussian distribution are not contained within the limits specified, the specific sample of interest is redrawn from the same Gaussian distribution until the firing rate falls within the specified range. In Table 1 the parameters  $\theta_{p,t}$ ,  $\theta_{e,t}$ ,  $\theta_{si,t}$  and  $\theta_{fi,t}$  are not specified as these parameters will vary for different simulations. However, for this simulation it is assumed that

$$\theta_{p,t} = \theta_{e,t}. \quad (30)$$

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