Closed-Loop Proportion-Derivative Control of Suppressing Seizures in a Neural Mass Model

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Abstract— **In this work, we present an analytical approach of closed-loop Proportional-Derivative (PD) control to determine the stimulation parameters for suppressing high-amplitude epileptic activity in a neural mass model. Closed-loop PD control to suppress epileptic activity in the Jansen's neural mass model (Jansen's NMM) has been studied. This work shows that the output signal of the Jansen's NMM model without the PD control feedback is high amplitude epileptic seizure activity which turns into low amplitude activity with the intervention feedback of a PD controller. A graphical stability analysis method was employed to determine the stability region of the PD controller in the gain parameter space. Therefore, this approach draws a region of PD controller parameters that is empirically chosen to stabilize epileptic seizure activities in the chosen NMM. Furthermore, this approach allows us to explore the relationship between the model parameters of inducing epileptic activity and the feedback controller parameters to foster a better understanding of the mechanism to suppress epileptic seizure activity by applying closed-loop stimulation (pharmacology stimulation, electrical stimulation or optogenetic stimulation etc.).**

Keywords—neural mass model, suppress seizures, closed-loop control, feedback stimulation

I. INTRODUCTION

Closed-loop feedback control stimulation holds great promise for treating neurological disorders (Parkinson's disease, epilepsy and psychiatric disorders etc.) [1-3]. Epilepsy has been widely recognized as an induction in normal brain activity under various trigger conditions in neural networks, in rats and humans [4], [5]. References [6-8] describe several neural mass network models for studying dynamic mechanisms of neocortical focal seizures from different perspectives of computational modeling and system theory. Wang et al [9] demonstrates that abnormal values of the external input can generate high amplitude epileptic activity in the Jansen's neural mass model (the Jansen's NMM).

Closed-loop controllers have been reported to connect stimulation input with correspondingly-generated local field potential (LFP) to achieve local suppression of epileptic activity in neural networks [10]. Over the last decade, researchers have made extraordinary progress in the development of PID type controllers to stabilize various epileptic seizure activities in neural mass models and brain tissue in the field of control engineering [11-13]. In this work, we apply a proportional-derivative controller to provide feedback for suppressing high amplitude epileptic activity in the Jansen's NMM. A graphical stability methodology has been applied to provide an analytical design approach for choosing proportional and derivative gain parameters to stabilize the high amplitude activity of the Jansen's NMM. Therefore, the analytical design approach of this research makes the closed-loop PD feedback control independent of a specific neural model, which can be applied to control methodology studies of other promising neural models in the future.
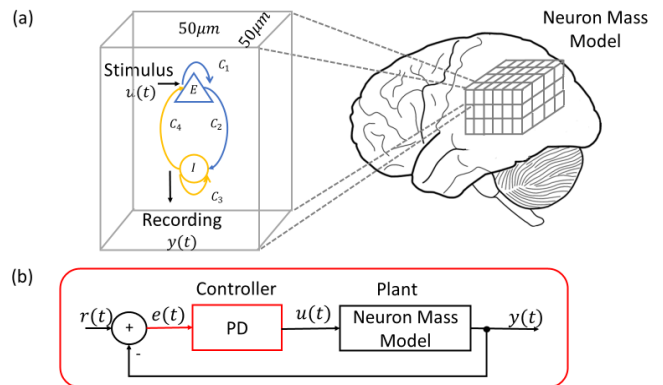
Fig. 1 Structure of the neural mass model. (a) An approximation of all minicolumns to be 50 μm * 50 μm in size where "E" and "I" mean excitatory and inhibitory subpopulations. Blue and yellow blocks mathematically detail excitatory and inhibitory subpopulations. (b) A simplified closed-loop scheme of feedback control of the neural mass model where the controller exhibits PD control and the plant represents the neural mass model.

Fig. 2 The proposed closed-loop PD scheme for suppressing epileptic seizures in the Jansen neural mass model: (a) Block diagram of the proposed PD control block diagram to suppress seizure in the Jansen's NMM. (b)Simplified equivalent form of the proposed closed-loop PD control scheme, in which $G_{pd}(s)$ represents the transfer function of the PD Controller, $G_{NMM}(s)$ represents the transfer function of the Jansen's NMM.

II. NEURAL MASS MODEL

In Fig. 1, a simplified closed-loop control scheme of the Jansen's NMM has been generalized. Fig. 1(a) describes each of the neuron populations as two blocks of 'E' and 'I' which represent excitatory and inhibitory subpopulations as minicolumns (50 um * 50 um in size) of brain dynamics. Fig. 1(b) shows a PD control scheme of the Jansen's NMM model as a closed-loop control model. For clarity, Fig. 2 shows the system in Fig.1 as a neuro-physiologically inspired mathematical model with a population of 'feed-forward' pyramidal neurons, receiving inhibitory and excitatory feedback from local interneurons.

Fig. 2(a) divides the Jansen's NMM into three interacting subpopulations: subpopulation 1 represents excitatory feedback subpopulations while subpopulation 2 represents inhibitory feedback subpopulations and subpopulation 3 is the main subpopulation. Fig. 2(b) demonstrates an equivalent closed-loop scheme of PD control of the Jansen's NMM, in which $G_{pd}(s)$ represents the transfer function of the PD Controller and $G_{NMM}(s)$ represents the transfer function of the Jansen's NMM. In Fig. 2(a), C_1 and C_2 of subpopulation 1 represent the average numbers of synaptic contacts in the excitatory feedback loop while in subpopulation 2, C_3 and C_4 are the average numbers of synaptic contacts in the inhibitory feedback loop. Excitatory synaptic dynamic function $h_e(t)$ and inhibitory synaptic dynamic function $h_i(t)$ linear systems transform the average post-synaptic membrane potential. $h_e(t)$ and $h_i(t)$ are defined as follows:

$$h_e(t) = \begin{cases} Aate^{-at} & t \geq 0 \\ 0 & t < 0 \end{cases} \quad (1)$$

$$h_i(t) = \begin{cases} Bbte^{-bt} & t \geq 0 \\ 0 & t < 0 \end{cases} \quad (2)$$

A and B in equation (1) and equation (2) describe the maximum amplitude of the excitatory and inhibitory population, while a and b are the lumped representations of the sum of the reciprocal of the time constant of the passive membrane and all other spatially distributed delays in the dendritic network.

As linear systems of $h_e(t)$ and $h_i(t)$ convert axonal pulses to postsynaptic potential, the impulse response $h_e(t)$ and $h_i(t)$ are shaped to resemble an excitatory postsynaptic potential (EPSP) and an inhibitory postsynaptic potential (IPSP), respectively. The input to these linear systems is pulse density which enables us to mimic the integrating action of the soma. Furthermore, in Fig. 2(a), u(t) is modelled as Gaussian noise. It serves as the input for triggering the Jansen's NMM while y(t) is the output of the Jansen's NMM model which can be interpreted as the local field potential of the NMM. The *Sigm* block in Fig. 2(a) converts the average membrane potential of a population of neurons into an average pulse density of action potentials fired by the neurons. Each postsynaptic potential (PSP) can be modelled by two differential equations as follows:

Parameters	Description	Standard Value
H_e	average excitatory synaptic gain	3.25mV
H_i	average inhibitory synaptic gain	22mV
τ_e	average synaptic time constant for excitatory subpopulation	0.0108s
τ_i	average synaptic time constant for inhibitory subpopulation	0.02s
C_1, C_2	average number of synaptic contacts in the excitatory feedback loop	$C_1=135, C_2=0.8$
C_3, C_4	average number of synaptic contacts in the inhibitory feedback loop	$C_3=0.25, C_4=0.25$
$v0, e_0, r$	parameters of non-linear S function	$v_0=6$mv, $e_0=2.5$, r $=0.56$mv

$$\frac{d^2y}{dt^2} = Aax(t) - 2a\frac{dy}{dt} - a^2y(t) \tag{3}$$

which can be rewritten as:

$$\frac{dy}{dt} = z(t) \tag{4}$$

$$\frac{dz}{dt} = Aax(t) - 2az(t) - a^2y(t) \tag{5}$$

x(t) and y(t) are the input and output signals of each postsynaptic potential, respectively. Hence, six different equations are derived as follows:

$$\frac{dy_0}{dt} = y_3(t) \tag{6}$$

$$\frac{dy_3}{dt} = AaSigm[y_1(t) - y_2(t)] - 2ay_3(t) - a^2y_0(t) \tag{7}$$

$$\frac{dy_1}{dt} = y_4(t) \tag{8}$$

$$\frac{dy_4}{dt} = Aa\{p(t) + C_2Sigm[C_1y_0(t)]\} - 2ay_4(t) - a^2y_1(t) \tag{9}$$

$$\frac{dy_2}{dt} = y_5(t) \tag{10}$$

$$\frac{dy_5}{dt} = Bb\{C_4Sigm[C_3y_0(t)]\} - 2ay_5(t) - b^2y_2(t) \tag{11}$$

where y_1, y_2, y_3 are the outputs of the three postsynaptic potential blocks (subpopulation 1, subpopulation 2 and subpopulation 3). The three differential equations are solved by applying an integration method of the Fehlberg fourth-fifth order Runge-Kutta method [14]. Table I shows the neural mass model simulation parameters.

III. MODEL OF FEEDBACK CONTROL

Epileptic activity in a neural mass model can be categorized as high amplitude limit cycle oscillation born in Hopf bifurcation [5], which indicates the fixed point of the Jansen's NMM will lose its stability. In Fig. 2, closed-loop controllers have been proposed to provide feedback stimulations to stabilize the unstable fixed point of a neural mass model. This action prevents the generation of Hopf bifurcation to suppress high amplitude epileptic activity. To achieve this goal, a closed-loop proportional-derivative feedback controller is proposed in this work as a comparison to previously published work by Wang et al [1].

Fig. 2 (a) shows the interaction between the PD controller and the Jansen's NMM where u(t) is the output of the PD controller (stimulation signals) and y(t) is the output of the Jansen's NMM model (local field potential recordings in real neuroscience experiments). To define the stabilization area of proportional-derivative gain parameters, a graphical stability analysis method has been applied by using the following four steps:

Step 1: Derive Laplace Transform of the Jansen's NMM:

$$G_{NMM}(s) = \frac{H_e(s)}{1 + H_i(s)Ks^2[H_i(s)C_3C_4 - H_e(s)C_1C_2]} \tag{12}$$

Step 2: Derive Laplace Transform of PD Controller

$$G_{pd}(s) = K_p + K_d s \tag{13}$$

Step 3: Derive the characteristic equation of PD-Jansen's NMM closed-loop control system shown in Fig. 2(b)

$$\Delta(s) = 1 + G_{pd}(s)G_{NMM}(s) = 0 \tag{14}$$

$$(r(t) = 0,$$
$$G_{pd}(s)G_{NMM}(s) = \frac{U(s)}{E(s)} * \frac{Y(s)}{U(s)} = \frac{Y(s)}{E(s)},$$
$$R(s) - Y(s) = E(s),$$
$$1 + G_{pd}(s)G_{NMM}(s) = 0)$$

Step 4: Make variable substitution:
$$s = jw$$
The characteristic equation of the PD-Jansen's NMM closed-loop control system defines the stability space boundary of the PD-Jansen's NMM feedback control system. Supposing

$$|G_{NMM}(j\omega)| = \sqrt{\delta_{I_{NMM}}^2(\omega) + \delta_{R_{NMM}}^2(\omega)} \tag{15}$$

the characteristic equation of the PD-Jansen's NMM control system can be rewritten as:

$$\begin{cases} K_p = \frac{-\delta_{R_{NMM}}(\omega)}{\delta_{I_{NMM}}^2(\omega) + \delta_{R_{NMM}}^2(\omega)} & (16) \\ K_d = \frac{\delta_{R_{NMM}}(\omega)}{\omega[\delta_{I_{NMM}}^2(\omega) + \delta_{R_{NMM}}^2(\omega)]} & (17) \end{cases}$$

where

$$|G_{NMM}(j\omega)| = \sqrt{\delta_{I_{NMM}}^2(\omega) + \delta_{R_{NMM}}^2(\omega)}.$$

IV. RESULTS AND DISCUSSION

Simulation results plots the stabilization relationships in equations (16) and (17) of K_p and K_d with respect to two cases: hyper-excitation He = 5, 7, 9 and low inhibition Hi = 15,17,19 are shown in Fig. 3(a) and Fig. 3(b) respectively.

After examining the stabilization area in Fig. 3, two sets of experiments suppressing Jansen's NMM (hyper excitation: He=7 and Hi=22 and low inhabitation: He=3.25 and Hi=17) were chosen for further simulations.
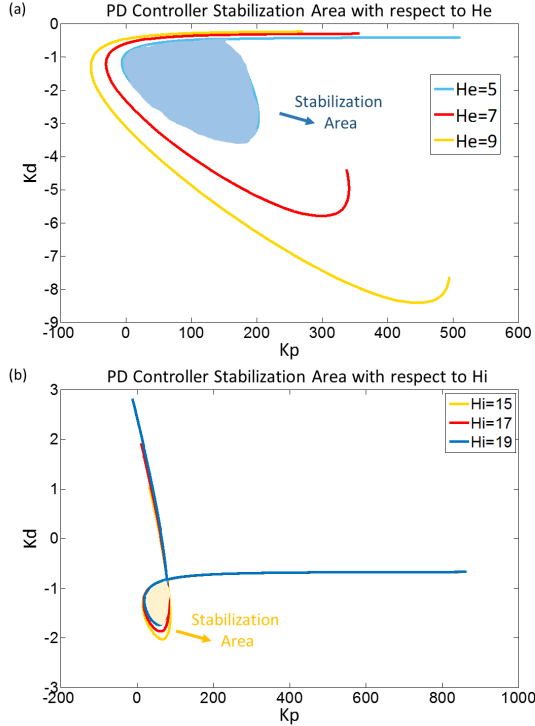

Fig. 3 The effect of excitatory parameters H_e and the inhibitory parameters H_i on changing the stabilizing area within the PD Controller. (a) shows how the stabilizing area of the PD Controller differs with H_e = 5, 7, 9 respectively. (b) shows how the stabilizing area of PD Controller differs with H_i = 15,17,19 respectively.
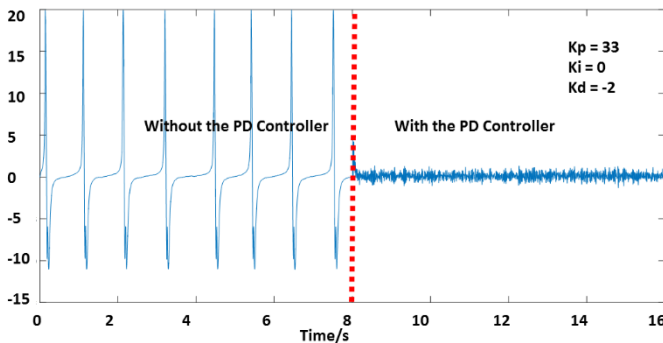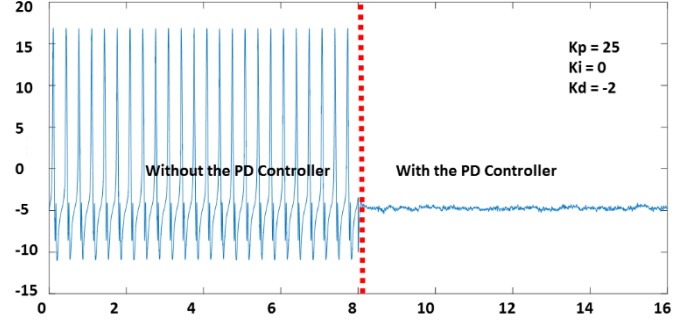

Fig. 4 Output comparison of the Jansen's NMM model. The first eight seconds of simulation were performed without the PD controller, and the second eight seconds simulation with stimulation feedback were performed with the PD controller (K_p = 33, K_i = 0 and K_d = -2) during hyper-excitation (H_e = 7 and H_i = 22).

A. Hyper Exciation

In Fig. 4, K_p = 33 and K_d = -2 have been picked from Fig. 3(a) to provide feedback stimulation under the circumstance of hyperexcitation simulations of the Jansen's NMM (H_e = 7 and H_i = 22) scenario.

B. Low Inhibitaion

To generate the results in Fig. 5, PD gain parameters K_p = 25 and K_d = -2 were chosen from Fig. 3(b) to provide feedback stimulation to intervene with the Jansen NMM model under the circumstance of low inhabitation neural mass model simulation of (H_e = 3.25 and H_i = 17).

Fig. 5 Output comparison of the Jansen's NMM model. The first eight seconds of simulation were performed without the PD controller, and the second eight seconds simulation with stimulation feedback from the PD controller (K_p = 25, K_i=0 and K_d = -2) during low inhibition (H_e = 3.25 and H_i = 17).

The above two experiment sets show how the PD controller can provide stimulation feedback to intervene with the Jansen's NMM model for suppressing high amplitude epileptic seizures successfully. The output of the Jansen's NMM was high amplitude activity which was clearly demonstrated in the first eight seconds. Then, under the intervention of PD controller feedback, the seizure network was stabilized into low amplitude activity in comparison to a system between without control feedback. Therefore, in this specific neural mass model simulation, high amplitude epileptic activity has been successfully suppressed by applying a closed-loop PD controller to deliver feedback stimulation using appropriate parameters to set up proportion and derivative gains.

V. CONCLUSION

This work shows that the output signal (local field potential) of the Jansen's NMM model without PD control feedback was high amplitude epileptic seizure activity. Low amplitude activity subsequently resulted from feedback stimulation of the PD controller. A graphical stability analysis method was employed to determine the stability regions of the PD controller within the stabilized parameter space. Under this circumstance, stabilized regions of the PD control parameters were derived which can provide proportion and derivative gain selection that can be used to stabilize epileptic seizure activity in the Jansen's NMM. The same control approach can also be applied to other closed-loop control schematics by replacing the plant with other neuron mass models or replacing the controllers with other control methodologies.

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