



**HAL**  
open science

# A thalamocortical feedback model to explain EEG during anesthesia

Meysam Hashemi, Axel Hutt

► **To cite this version:**

Meysam Hashemi, Axel Hutt. A thalamocortical feedback model to explain EEG during anesthesia. 2013. hal-00912405v1

**HAL Id: hal-00912405**

**<https://inria.hal.science/hal-00912405v1>**

Preprint submitted on 2 Dec 2013 (v1), last revised 23 Jan 2014 (v2)

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# A thalamocortical feedback model to explain EEG during anesthesia

Meysam Hashemi, Axel Hutt

INRIA CR Nancy - Grand Est, 54600 Villers-les-Nancy Cedex, France  
{meysam.hashemi, axel.hutt}@inria.fr

**Abstract.** General anaesthesia (GA) is a medical procedure which aims to achieve analgesia, amnesia, immobility and skeletal muscle relaxation. Although GA is commonly used in medical care for patients undergoing surgery, its precise underlying mechanisms and the molecular action of anaesthetic agents (AA) remain to be elucidated. A wide variety of drugs are used in modern anaesthetic practice and it has been observed that for many AAs, during the transition from consciousness to unconsciousness, the electroencephalogram shows biphasic effects in amplitude: an initial increase of the spectral power followed by a decrease at higher concentrations. Moreover during the administration of propofol, specific changes in EEG rhythms can be observed. The aim of this work is the extended discussion of a recent model by Hindriks and van Putten [10] that reproduces specific changes in EEG rhythms by the study of a neuronal population model of a single thalamocortical module. We illustrate specific features of the model, such as the physiological assumptions, the derivation of the power spectral density and the impact of the propofol concentration and of the stationary state. We show that the propofol-induced modification of the stationary state plays an important role in the understanding of the observed EEG.

**Keywords:** General anesthesia, Thalamocortical model, EEG, Power spectrum

## 1 Introduction

General anesthetics (GAs) include a large number of drugs which without them, modern medicine, especially surgery, would not have been possible. However, the mechanism underlying its anesthetic effects on human beings is not yet fully understood [1]. Besides the impressive effect of the loss of consciousness, general anaesthetics yield further phenomena such as analgesia, amnesia and muscle relaxation [2].

It has been observed that during the transition from consciousness to unconsciousness, by induction thipental, propofol, and sevoflurane, many derived EEG variables show biphasic effects, that is an initial increase of the spectral power followed by a decrease at higher concentrations [3]. Moreover, during the induction phase of propofol, enhanced oscillatory activity within several frequency

bands can be observed [4]. For clinically relevant concentration of propofol specific changes in EEG rhythms include an increase in alpha peak frequency, over frontal regions, accompanied by increase in delta and theta power [5,6].

Most of the previous studies on anesthetic phenomena have been done by considering a mean-field model to explain the biphasic behavior and describe some experimental feature of specific changes in electroencephalography (EEG) data recorded during anesthesia [7–11]. While some previous theoretical studies (Steyn-Ross 1999; Bojak and Liley et al. 2005; Hindriks and van Putten 2012) are based on the same type of continuous spatial mean-field model involving spatial partial derivatives [12], Hutt and Longtin have considered a neural populations model motivated by Wilson and Cowan [13] and Amari [14].

In this study we use a thalamocortical feedback model first developed by Rennie et al. [15] and recently extended to model general anaesthesia by Hindriks and van Putten [10] to reproduce the specific changes in EEG activity that can be observed during the propofol-induced general anesthesia. The present work reviews this latter model and points out the importance of stationary states to understand EEG power spectra during anaesthesia.

## 2 Methods

### 2.1 Model

The body of the model [10] is based on a population-level model of a single thalamo-cortical module consisting of four populations, namely an excitatory (E) and inhibitory (I) cortical population, a thalamic relay nucleus (S), and a thalamic reticular nucleus (R). The average soma membrane potential for  $a=E, I, S, R$  is modeled by

$$V_a(t) = \sum_{i=E,I,R,S} \bar{h}(t) \otimes K_{a,i} \phi_i(t - \tau_{a,i}), \quad (1)$$

where  $\phi_i$  is the pulse firing rate of the population  $i$  (in units Hz). The constants  $K_{a,b}$  are the strengths of the connections from population of type  $b$  to population of type  $a$  (in units mVs). The delay term,  $\tau_{a,b}$  is zero if the both populations are in the thalamus or in the cortex. For thalamocortical or corticothalamic pathway, the delay is nonzero [16]. We point out that this model does not distinguish excitatory and inhibitory synapses in contrast to other models for general anaesthesia as [7,9,11].

In this model, only the axons of excitatory cortical neurons are long enough to emit propagating pulses along axons and the  $\phi_E$  obeys the damped oscillator equation

$$D\phi_E = S(V_a), \quad (2)$$

in which the operator  $D$  is defined as

$$D = \left( \frac{1}{\gamma} \frac{\partial}{\partial t} + 1 \right)^2, \quad (3)$$

where  $\gamma$  is the ratio of propagation velocity to mean axonal length. It is assumed that the spatial spread of activity is very fast in other populations and the activity variable can be approximated by a sigmoidal function as

$$\phi_a = S(V_a) = S_{max} [1 + \exp(-\frac{V_a - \theta}{\sigma})]^{-1}, \quad (4)$$

in which  $S_{max}$  is the maximal firing rate (in unit Hz),  $\theta$  is the average activation threshold (in units mV), and  $\sigma$  is proportional to the standard deviation of activation thresholds over the populations (in units  $\text{mV}^{-1}$ ).

In Eqs. (1),  $\otimes$  denotes the convolution operator and  $\bar{h}(t)$  denotes the mean synaptic response function

$$\bar{h}(t) = \frac{\alpha\beta}{\beta - \alpha} (e^{-\alpha t} - e^{-\beta t}), \quad (5)$$

where  $\alpha$  and  $\beta$  are the synaptic decay and rise rate of synaptic response function, respectively.

External input to the system can be considered as a non-specific input to relay neurons as

$$K_{S,N}\phi_N = \langle \phi_N \rangle + \sqrt{2\kappa}\xi(t), \quad (6)$$

where  $\langle \phi_N \rangle$  indicates its mean value,  $\xi(t)$  is a Gaussian white noise with average zero and a  $\delta$  correlation in time

$$\langle \xi(t) \rangle = 0, \quad \langle \xi(t)\xi(t') \rangle = \delta(t - t'), \quad (7)$$

and  $\kappa$  is the intensity of the driving noise. For more details of model and the nominal parameter values see [10].

## 2.2 Effect of propofol on populations

It is accepted that anesthetics act by binding directly to sensitive target proteins. Until now, many receptors, molecular targets and neuronal transmission pathways have been shown to contribute to general anesthesia. There have been a large number of studies linking the effect of many GAs to altered function of the GABA<sub>A</sub> receptors. All of them agree on one point: GAs at clinical concentrations are without effect unless GABA<sub>A</sub> is also present [17].

Recent clinical findings have revealed possible sites of elicited anaesthetic action of the anaesthetic propofol in the human brain. In vivo extracellular recordings have demonstrated that propofol suppresses field potentials in the rat thalamus and cortex [18]. Moreover it has been reported that thalamic and corticothalamic neuronal circuits are important targets for propofol [19]. Therefore, clinical observations strongly suggest to use a model including of cortex and thalamus to reach more precise elucidation of physiological mechanisms [20].

It has been shown that propofol increases the decay time constant of GABA<sub>A</sub> synapses, and hence increases the total charge transfer in these synapses but not that of excitatory synapses [21]. Interestingly propofol has been shown to have

a negligible effect on the amplitude synaptic receptors in cortical neurons, it markedly increases amplitude, decay time, and charge transfer of GABA<sub>A</sub> inhibitory postsynaptic currents evoked in relay neurons in the ventrobasal complex (VB) [22].

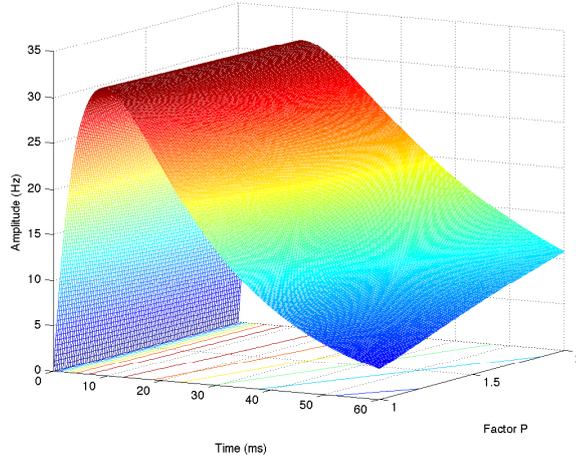
To integrate physiological observations into the model, the potentiation of synaptic receptors in anaesthesia condition can be modelled by  $\alpha \rightarrow \alpha/p$  with  $p \geq 1$ , which leads to a decrease in the decay rate constant  $\alpha$  or equivalently, an increase in decay time constant of GABA<sub>A</sub> receptors. The factor  $p$  indicates the target concentration of propofol in the neural populations. We take  $p = 1$  for zero concentration i.e, baseline condition. Then we could replace the synaptic response  $h(t)$  by

$$h(t) = \frac{H}{\eta(\alpha, \beta)} \bar{h}(t), \quad (8)$$

in which

$$\eta(\alpha, \beta) = \frac{\alpha\beta}{\beta - \alpha} \left[ \exp\left(-\alpha \frac{\ln(\beta/\alpha)}{\beta - \alpha}\right) - \exp\left(-\beta \frac{\ln(\beta/\alpha)}{\beta - \alpha}\right) \right], \quad (9)$$

and where the constant  $H$  indicates the synaptic efficacy [10]. The maximum height of  $h$  indeed is  $H$  and hence is independent of the rate constants  $\alpha$  and  $\beta$ . The baseline value chosen for  $\alpha$  and  $\beta$ ;  $\alpha=50$  Hz,  $\beta=200$  Hz leads to the value  $\eta(\alpha, \beta) = 31.5$ Hz .



**Fig. 1.** The temporal synaptic response function  $h(t)$  of inhibitory GABA<sub>A</sub> synapses subject to  $p$ . Parameters are set to  $\alpha=50$  Hz,  $\beta=200$  Hz

### 2.3 Theoretical power spectrum

The stationary state of Eqs. (1) obeys  $dV_a(t)/dt = 0$ . We could linearize the Eqs. (1) about the stationary state and write them in a general matrix form of a linear DDE as

$$\hat{\mathbf{L}} \left( \frac{\partial}{\partial t} \right) \mathbf{X}(t) = \mathbf{A}\mathbf{X}(t) + \mathbf{B}\mathbf{X}(t - \tau) + \mathbf{I}(t). \quad (10)$$

with matrices  $\mathbf{A}$ ,  $\mathbf{B}$ , the system activity vector  $\mathbf{X}$  and the external input  $\mathbf{I}$ . The solution of system can be written as

$$\mathbf{X}(t) = \int_{-\infty}^{\infty} \mathbf{G}(t - t') \mathbf{I}(t') dt', \quad (11)$$

and substitute Eq. (10) into Eq. (9) leads

$$\hat{\mathbf{L}} \left( \frac{\partial}{\partial t} \right) \mathbf{G}(t) = \mathbf{A}\mathbf{G}(t) + \mathbf{B}\mathbf{G}(t - \tau) + \mathbf{1}\delta(t), \quad (12)$$

in which  $\mathbf{1}$  is unitary matrix and

$$\delta(t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} e^{-i\omega t} d\omega. \quad (13)$$

In addition, it can be shown that

$$\hat{\mathbf{L}} \left( \frac{\partial}{\partial t} \right) e^{i\omega t} = \hat{\mathbf{L}}(\omega) e^{i\omega t}. \quad (14)$$

By applying the Fourier transform

$$\mathbf{G}(t) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} \tilde{\mathbf{G}}(\omega) e^{i\omega t} d\omega \quad (15)$$

and substituting Eq. (12)-(14) into Eq. (11), the Fourier transform of the Greens function of the system (9) can be written as

$$\tilde{\mathbf{G}}(\omega) = \frac{1}{\sqrt{2\pi}} [\hat{\mathbf{L}}(\omega) - \mathbf{A} - \mathbf{B}e^{-i\omega\tau}]^{-1}. \quad (16)$$

The power spectral density matrix  $\mathbf{P}(\omega)$  of  $\mathbf{x}$  is the Fourier transform of the auto-correlation function matrix  $\langle \mathbf{X}(t)^t \mathbf{X}(t - T) \rangle$  (Wiener-Khinchine Theorem) leading to

$$\mathbf{P}(\omega) = 2\kappa\sqrt{2\pi} \tilde{\mathbf{G}}(\omega) \tilde{\mathbf{G}}^t(-\omega).$$

where the high index t denotes the transposed vector or matrix [23].

At the end, the model assumes that excitatory activity generates the EEG and by virtue of the specific choice of external input the power spectrum of the EEG depends just on one matrix component of the Greens function by

$$P_E(\omega) = 2\kappa\sqrt{2\pi}\tilde{G}_{1,3}(\omega)\tilde{G}_{1,3}(-\omega) = 2\kappa\sqrt{2\pi}\left|\tilde{G}_{1,3}(\omega)\right|^2. \quad (17)$$

The stationary state of Eqs. (1) is given by

$$\begin{aligned} V_{0E} &= K_{EE}S(V_{0E}) + p_1K_{EI}S(V_{0I}) + K_{ES}S(V_{0S}), \\ V_{0I} &= K_{IE}S(V_{0E}) + p_2K_{II}S(V_{0I}) + K_{IS}S(V_{0S}), \\ V_{0S} &= K_{SN}\langle\phi_N\rangle + p_3K_{SR}S(V_{0R}) + K_{SE}S(V_{0E}), \\ V_{0R} &= K_{RS}S(V_{0S}) + K_{RE}S(V_{0E}), \end{aligned} \quad (18)$$

where  $K_{SN}\langle\phi_N\rangle = 1\text{mV}$  and we take three different impact factors for the anaesthetic effect of propofol as

$$\frac{H}{\eta_{ei}} = p_1, \quad \frac{H}{\eta_{ii}} = p_2, \quad \frac{H}{\eta_{sr}} = p_3,$$

in which we parametrize  $\eta_{ei}$ ,  $\eta_{ii}$  and  $\eta_{sr}$  by

$$\eta_{ei} : \alpha \rightarrow \frac{\alpha}{p_1}, \quad \eta_{ii} : \alpha \rightarrow \frac{\alpha}{p_2}, \quad \eta_{sr} : \alpha \rightarrow \frac{\alpha}{p_3}.$$

This assumes a complete insensitivity of synaptic receptors located on cortical pyramidal neurons and reticular nucleus.

For the linearization of Eqs. (1) one obtains

$$\mathbf{X} = \begin{pmatrix} \phi_E \\ V_I \\ V_S \\ V_R \end{pmatrix}, \quad A = \begin{pmatrix} K_1 & K_2 & 0 & 0 \\ K_4 & K_5 & 0 & 0 \\ 0 & 0 & 0 & K_8 \\ 0 & 0 & K_{10} & 0 \end{pmatrix}, \quad B = \begin{pmatrix} 0 & 0 & K_3 & 0 \\ 0 & 0 & K_6 & 0 \\ K_7 & 0 & 0 & 0 \\ K_9 & 0 & 0 & 0 \end{pmatrix}, \quad I(t) = \begin{pmatrix} 0 \\ 0 \\ \sqrt{2\kappa}\xi(t) \\ 0 \end{pmatrix},$$

with

$$\begin{aligned} K_1 &= K_{EE}, \quad K_2 = p_1K_{EI} \frac{\partial S[V]}{\partial V} \Big|_{V=V_{0I}}, \quad K_3 = K_{ES} \frac{\partial S[V]}{\partial V} \Big|_{V=V_{0S}}, \\ K_4 &= K_{IE}, \quad K_5 = p_2K_{II} \frac{\partial S[V]}{\partial V} \Big|_{V=V_{0I}}, \quad K_6 = K_{IS} \frac{\partial S[V]}{\partial V} \Big|_{V=V_{0S}}, \\ K_7 &= K_{SE}, \quad K_8 = p_3K_{SR} \frac{\partial S[V]}{\partial V} \Big|_{V=V_{0R}}, \quad K_9 = K_{RE}, \\ K_{10} &= K_{RS} \frac{\partial S[V]}{\partial V} \Big|_{V=V_{0S}}, \quad K_{11} = \frac{\partial S[V]}{\partial V} \Big|_{V=V_{0E}}, \end{aligned}$$

and

$$\hat{\mathbf{L}}(\omega) - A - Be^{-i\omega\tau} = \begin{bmatrix} \mathbf{L} \frac{\mathcal{D}}{K_{11}} - K_1 & -K_2 & -K_3 e^{-i\omega\tau} & 0 \\ -K_4 & \mathbf{L} - K_5 & -K_6 & 0 \\ -K_7 e^{-i\omega\tau} & 0 & \mathbf{L} & -K_8 \\ -K_9 e^{-i\omega\tau} & 0 & -K_{10} & \mathbf{L} \end{bmatrix} \quad (19)$$

where  $\mathbf{L} = (1 + i\omega/\alpha)(1 + i\omega/\beta)$  and  $\mathcal{D} = (1 + i\omega/\gamma)^2$ .

We point out that the new constants  $K_i$ ,  $i = 2, 3, 5, 6, 8, 10, 11$  are proportional to the nonlinear gain  $\partial S/\partial V$  computed at the stationary state. With Eq. (16) and (19), it turns out that the stationary state and the corresponding nonlinear gain play in important role in the power spectrum.

### 3 Results

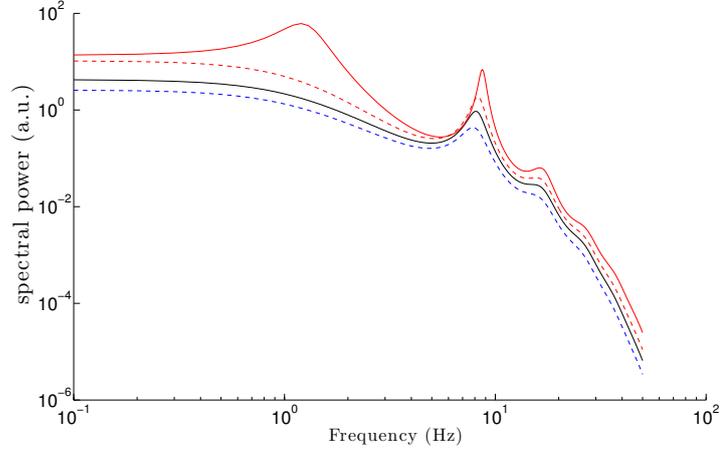
This section shows results on the power spectrum and show that the model under study reproduce the specific changes observed in EEG data during the propofol-induced anesthesia including enhancement of delta and theta bands accompanied by shifted alpha oscillation while increasing anesthetic concentration.

Figure 2 shows the theoretical EEG power spectrum in the baseline condition and after the administration of propofol. The spectrum resembles well experimental observation in EEG power spectrum, i.e. increases in delta and theta power as well as more pronounced alpha oscillations with increased peak-frequency. The dynamical analysis of the thalamo-cortical system has been done by Hindriks and van Putten (2012). They have shown that there exist three resonances in the baseline condition, consisting of an oscillatory resonance corresponding to the peak in the alpha-band and a pair of zero-frequency resonance. With increasing propofol concentration, the damping rate of alpha resonances weakens the oscillation while its frequency increases. These modulations indicate the increase in alpha power and its peak-frequency, respectively. Moreover, the zero-frequency resonance collides and gradually increases in frequency manifesting increases in delta and theta power accompanied by the appearance of a peak in the delta frequency (solid red line in Fig 2.)

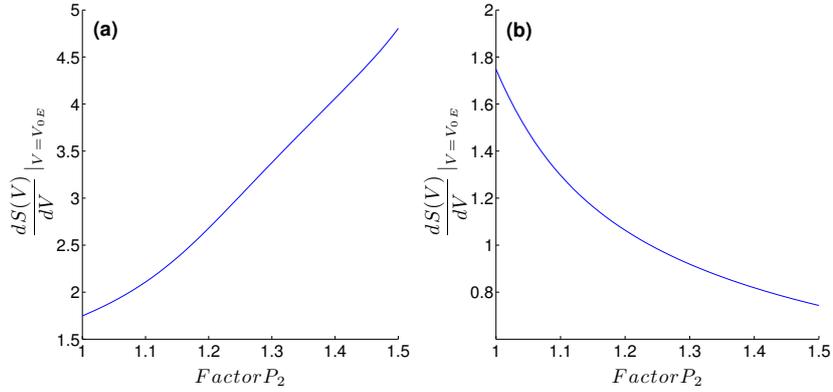
Finally, Hindriks and van Putten have discussed the differential role of potentiation of synaptic receptors located on the dendrites of different neural types. They have found that synaptic potentiation within local cortical inhibitory neurons suffices to reproduce experimental observation in EEG during anesthesia [10].

Figure 3 shows how the nonlinear gain dependent on the propofol concentration. We observe that the nonlinear gain may increase (a) or decrease (b) with increasing propofol dependent on the synapses that are modified. If the inhibitory synapses at excitatory neurons ( $p_1$ ) and at relay neurons ( $p_3$ ) respond identically to a change of the propofol concentration in a specific relation to the response of synapses at inhibitory neurons ( $p_2$ ), then the nonlinear gain increases (Fig. 3(a)) reflecting an increased excitability and the power values increase as well (Fig. 2, red curves). In contrast, if the response of all three synapse types respond identically (as assumed in previous studies such as [11]), then the nonlinear gain decreases (Fig. 3(a)) and the decreased excitability diminishes the power spectrum values (cf. Fig. 2, blue curve).

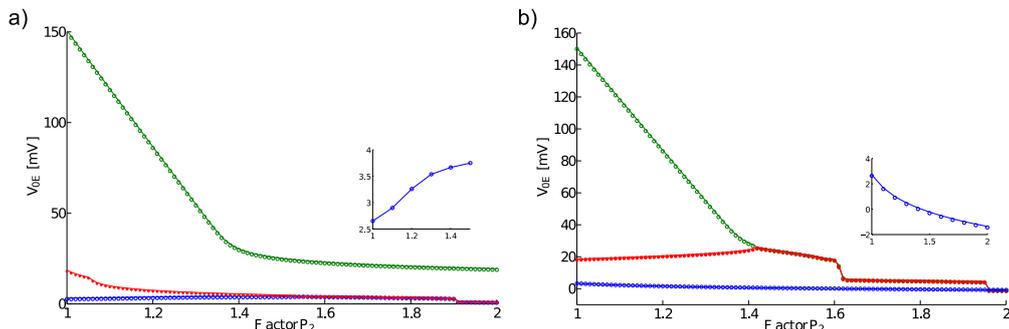
Moreover, the stationary states behave differently in the two cases, cf. Fig. 4. Increasing (decreasing) the nonlinear gain is accompanied by an increasing (decreasing) value of the corresponding stationary state, see panels (a) and (b). It is also remarkable that in (a) the two lower stationary states collide to a single state whereas in (b) the two upper states collide. This difference indicates two fundamentally different mechanisms which may yield the different dynamics observed in the power spectrum. This link will be a research topic of future work.



**Fig. 2.** Theoretical power spectrum of EEG in the baseline condition (solid black line) and three different set of factor  $p$  in the anaesthesia condition;  $p_1=p_3=1+0.5(p_2-1)$ ,  $p_2=1.1$  (dashed red line),  $p_2=1.25$  (solid red line) and  $p_1=p_2=p_3=1.05$  (dashed blue line).



**Fig. 3.** The nonlinear gain  $dS/dV$  computed at the lowest stationary state of pyramidal neurons  $V_{0E}$  as function of factor  $p_2$ . **a)**  $p_1=p_3=1+0.5(p_2-1)$ , **b)**  $p_1=p_2=p_3$ . Results are the same for other stationary states.



**Fig. 4.** The stationary states  $V_{0E}$  subjected to the factor  $p_2$ . **a)**  $p_1=p_3=1+0.5(p_2-1)$ , **b)**  $p_1=p_2=p_3$ . We observe three states for  $p=1$  where (a) the two lower states collide or (b) the two upper states collide. The center branch (red) is linearly unstable, whereas the other branches are linearly stable.

## 4 Discussion

In the recent study of Hindriks and van Putten the authors have considered a high-dimensional mean field model to reproduce observed EEG changes during general anesthesia. The present work illustrates this work in some detail and highlights the important assumptions. We have extended the previous work by investigating the effect of the stationary state and have revealed the the increase or decrease of power seems to be strongly related the the increase or decrease of the stationary state of the system. This new finding proposes a more detailed study of the stationary state of neural population activity under anaesthesia.

## Acknowledgments.

The authors acknowledge funding from the European Research Council for support under the European Union's Seventh Framework Programme (FP7/2007-2013) ERC grant agreement No.257253.

## References

1. Alkire, M., Hudetz, A., and Tononi, G. (2008). Consciousness and anesthesia. *Science* 322, 876–880.
2. Franks, N., and Lieb, W. (1994). Molecular and cellular mechanisms of general anesthesia. *Nature* 367, 607–614.
3. Kuizenga, K., Wierda, J., and Kalkman, C. (2001). Biphasiceegchanges inrelation to loss of consciousness during induction with thiopental, propofol, etomidate, midazolam or sevoflurane. *Br. J. Anaesth.* 86, 354–360.
4. Cimenser, A., Purdon, P. L., Pierce, E. T., Walsh, J. L., Salazar-Gomez, A. F., Harrell, P. G., et al. (2011). Tracking brain states under general anesthesia by using global coherence analysis. *Proc. Natl. Acad. Sci. U.S.A.* 108, 8832–8837.

5. Murphy, M., Bruno, M. A., Riedner, B. A., Boveroux, P., Noirhomme, Q., Landsness, E. C., et al. (2011). Propofol anesthesia and sleep: a high-density EEG study. *Sleep* 34, 283–291.
6. Ching, S., Cimenser, A., Purdon, P. L., Brown, E. N., and Kopell, N. J. (2010). Thalamocortical model for a propofol-induced rhythm associated with loss of consciousness. *Proc. Natl. Acad. Sci. U.S.A.* 107, 22665–22670.
7. Bojak, I., and Liley, D. (2005). Modeling the effects of anesthesia on the electroencephalogram. *Phys. Rev. E* 71:041902. doi: 10.1103/Phys Rev E. 71.041902.
8. Liley, D., and Bojak, I. (2005). Understanding the transition to seizure by modeling the epileptiform activity of general anaesthetic agents. *J. Clin. Neurophysiol.* 22, 300–313.
9. Steyn–Ross, M., Steyn–Ross, D., Sleigh, J. W., and Liley, D. T. J. (1999). Theoretical electroencephalogram stationary spectrum for a white-noise-driven cortex: evidence for a general anesthetic-induced phase transition. *Phys. Rev. E* 60, 7299–7311.
10. Hindriks, R., and van Putten, M. J. A. M. (2012). Meanfield modeling of propofol-induced changes in spontaneous EEG rhythms. *Neuroimage* 60, 2323–2344.
11. Hutt, A., and Longtin, A. (2009). Effects of the anesthetic agent propofol on neural populations. *Cogn. Neurodyn.* 4, 37–59.
12. Liley, D., P. J. Cadusch and J. J. Wright (1999). A continuum theory of electrocortical activity. *Neurocomputing* 26-27:795-800.
13. Wilson H. R. and Cowan J. D. (1973). A mathematical theory of the functional dynamics of cortical and thalamic nervous tissue. *Kybernetik*, 13,55-80.
14. Amari S (1977). Dynamics of pattern formation in lateral inhibition type neural fields. *Biol. Cybern.* 27,77-87.
15. C. J. Rennie, Robinson P. A. and Wright J.J. (2002). Unified neurophysical model of EEG spectra and evoked potentials. *Biol. Cybern.* 86 (6), 457-471.
16. Jonathan D. Victor, Jonathan D. Drover, Mary M. Conte, and Nicholas D. Schiff (2011). Mean-field modeling of thalamocortical dynamics and a model-driven approach to EEG analysis, *PNAS* 118:15631–15638 .
17. Rudolph, U., Antkowiak, B (2004). Molecular and neuronal substrate for general anaesthetics, *Nat. Rev. Neurosci.* 5(9):709–720.
18. Antkowiak B: In vitro networks: cortical mechanisms of anaesthetic action. *Br J Anaesth* 2002, 89(1):102–111.
19. Ying SW, Goldstein PA: Propofol effects on the thalamus: Modulation of GABAergic synaptic inhibition and suppression of neuronal excitability. Program No 411 2002 Abstract Viewer/Itinerary Planner Washington, DC: Society for Neuroscience, 2002 Online 2002.
20. Ying, S., and Goldstein, P. (2005). Propofol suppresses synaptic responsiveness of somatosensory relay neurons to excitatory input by potentiating GABA<sub>A</sub> receptor chloride channels. *Mol. Pain* 1:2. doi:10.1186/1744-8069-1-2.
21. Kitamura, A., Marszalec, W., Yeh, J., and Narahashi, T. (2002). Effects of halothane and propofol on excitatory and inhibitory synaptic transmission in rat cortical neurons. *J. Pharmacol.* 304, 162–171.
22. Ying, S., and Goldstein, P. (2005). Propofol-block of SK channels in reticular thalamic neurons enhances GABA<sub>A</sub>ergic inhibition in relay neurons. *J Neurophysiol* 93: 1935-1948.
23. Hutt, A. (2013) The anesthetic propofol shifts the frequency of maximum spectral power in EEG during general anesthesia: analytical insights from a linear model. *Front. Comput. Neurosci.* doi:10.3389/fncom.2013.00002.