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Research Article

Statistical Model for Excitation and Hypersynchronization in the Small Neural Populations

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Abstract

The mathematical modeling of epileptic seizures appearing in small neural populations can follow a few alternative ways: modeling of individual cells and their interaction vs. modeling groups and clusters on neurons. The purpose of this work is invention of a novel continuous (population-based) model for the appearance of the hyper-synchronized firing cells of the epileptiform type. In the same time, we use here the master equations based on the transition probabilities among different states of the cell excitation and hyper-synchronization. We developed an ODE model combining the dynamical equations for different sub-populations (unexcited, excited, and, as our novelty, hypersynchronized). Our model may serve as a simple but powerful tool to analyze the appearance and development of epileptiform dynamics in artificial neural networks. It can cover different cases of microepilepsy, and also may open the gate for studying drug-resistant epilepsy regime. Our dynamical set can be extended with the control inputs mimicking the external perturbations of the neural clusters with the electrical or optogenetic signals. In this case, the set of control algorithms can be applied to detect and suppress the epileptiform dynamics. Thus, the dynamic processes of epilepsy in small neural populations do not demand necessary the development of detailed models for individual neurons. Even the 'averaged' dynamical set for the unexcited, excited and hypersynchronized sub-populations can serve as an efficient tool for investigation and numerical simulations of microscopic seizures.

Keywords: Small neuron populations, Neural excitations, Master equation, Hypersynchronization, Epileptiform dynamics.

Küçük Nöral Popülasyonlarda Uyarma ve Hipersenkronizasyon için İstatistiksel Model

Öz

Küçük nöral popülasyonlarda ortaya çıkan epileptik nöbetlerin matematiksel modellemesi birkaç alternatif yol izleyebilir: tek tek hücrelerin modellenmesi ve bunların etkileşimi ile nöronlar üzerindeki grupların ve kümelerin modellenmesi. Bu çalışmanın amacı, epileptiform tipte hiper-senkronize ateşleyen hücrelerin ortaya çıkması için yeni bir sürekli (nüfusa dayalı) bir modelin icadıdır. Aynı zamanda, burada hücre uyarımının ve hiper senkronizasyonun farklı durumları arasındaki geçiş olasılıklarına dayanan ana denklemleri kullanmaktayız. Farklı alt popülasyonlar için dinamik denklemleri birleştiren bir ADD modeli geliştirdik (uyarılmamış, uyarılmış ve yeniliğimiz olarak hipersenkronize olmuş). Modelimiz, yapay nöral ağlarında epileptiform dinamiklerin ortaya çıkısını ve gelişimini analiz etmek için basit ama güçlü bir araç olarak hizmet edebilir. Farklı mikroepilepsi vakalarını kapsayabilir ve ayrıca ilaca dirençli epilepsi rejimini incelemenin kapısını açabilir. Dinamik setimiz, elektriksel veya optogenetik sinyallerle nöral kümelerin dış tedirginliklerini taklit eden kontrol girdileri ile genişletilebilir. Bu durumda, epileptiform dinamikleri saptamak ve bastırmak için bir dizi kontrol algoritması uygulanabilir. Bu nedenle, küçük nöral popülasyonlardaki epilepsinin dinamik süreçleri, bireysel nöronlar için gerekli ayrıntılı modellerin geliştirilmesini gerektirmez. Uyarılmamış, uyarılmış ve hipersenkronize alt popülasyonlar için 'ortalama' dinamik set bile, mikroskobik nöbetlerin incelenmesi ve sayısal simülasyonları için etkili bir araç olarak hizmet verebilir.

Anahtar Kelimeler: Küçük nöron popülasyonları, nöral uyarılmalar, ana denklem, hipersenkronizasyon, epileptiform dinamikler.

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1. Introduction

The mathematical modeling of epileptic seizures appearing in small neural populations can follow a few alternative ways: modeling of individual cells and their interaction vs. modeling groups and clusters on neurons (Kesmia et al., 2020).

The individual cell ('discrete') approach uses the 'first principles' for the intra- and extracellular processes forming the action potential in the axon and transferring the pulse to the next companion neurons (Izhikevich, 2003). Differential systems based on the axon membrane voltage and the gate variable(s) for the ion channels are capable to reproduce the complex combination of slow and fast dynamics triggering the epileptifom processes in the small clusters of such cells (Stefanescu et al., 2012).

The cell cluster-based ('continuous') approach deals with the average characteristics of neural groups and focuses on a certain small number of states occurring in the neural dynamical system (da Silva et al., 2003). The averaged continuous model for the neural population contains a set of attractors gradually deforming the system evolution from pre- and interictal to ictal phases and back (Namiki et al., 2020).

The purpose of this work is invention of a novel continuous (population-based) model for the appearing the hyper-synchronized firing cells of the epileptiform type. In the same time, we use here the master equations based on the transition probabilities among different states of the cell excitation and hyper-synchronization. We define three states of the small neural cluster: unexcited, excited and hypersynchronized. The variables related to the transitions among the states could be constants or functions of the state populations and the time. The principal feature of our model is satisfaction to the normalization properties.

Our approach can be extended with the control parameters. In the perspective it allows to investigate the appearance of epilepsy and its efficient detection and suppression in the frame of a relatively simple mathematical model.

2. Review of the Existing Models for Small Neuron Populations

In this section, we make a short review of two models which inspired our novel approach for the description of the excitation processes of neurons in the small clusters.

2.1. The Tomanik-Ahmed Model for Small Neuron Population

The 'continuous' Tomanik model for the epileptic seizures is based on the complex network approach (Tomanik, 2020). The neural population is divided according to three levels of the excitations for the cells participating in the seizure: the low (unexcited) population *L*, the medium excited population *M*, and the high (excited) population *H*. Their dynamics are described with the set of three ODEs.

$$\begin{aligned} \frac{dL}{dt} &= aL\cdot(1-L)-H\ ; \\ \frac{dM}{dt} &= bL-H\ ; \\ \frac{dH}{dt} &= cL+M-d\cdot H\ . \end{aligned} \tag{1}$$

There is a reduced version of this model without the medium variable *M* (Ahmed, 2020):

$$\begin{aligned} \frac{dL}{dt} &= aL\cdot(1-L)-H\ ; \\ \frac{dH}{dt} &= cL-d\cdot H\ . \end{aligned} \tag{2}$$

Model (1)-(2) has distinct disadvantages. It does not study the details the dynamics of the energy for the excitation processes and does not reflect the conservation laws. The model does not preserve the normalization: $L + M + H$ = const.

The Tomanik-Ahmed model also does not consider the hypersynchronization phase, it focuses only on the excitation processes of the cells without studying the collective effects.

2.2. The Buice-Cowan Model

At first, the dynamical model of Buice-Cowan considers three states of a single neuron spiking (Fig.1): *quiescent* state (q) when the neuron action potential rests at the level –70 mV; *activated* state (a), when the potential arises up to + 40 mV; and the *refractory* state (r), when it drops down up to the level –80 mV (Buice and Cowan, 2009).

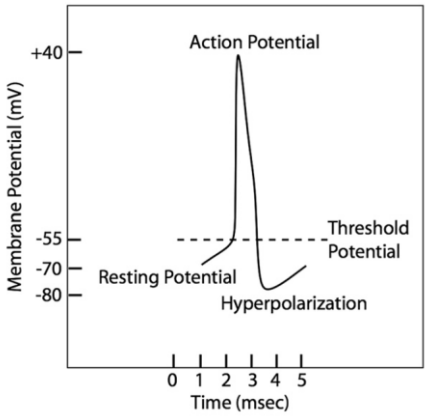

Figure 1. The dynamical phases of a single neural action potential (Buice and Cowan, 2009).

The neuron can follow the cyclic dynamics q → a → r → q → …, but the reverse transition process r → a is also allowed. In the last case, one observes the neuron producing a train of spikes due to the transitions a → r → a → r → …, see Fig.2.

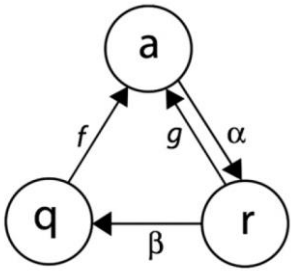

Figure 2. State transitions for a single neuron (Buice and Cowan, 2009).

The corresponding probabilities of the transition processes (per unit of time) are denoted as f, g, α, and β, see Fig.2. Then from a single neuron one can come to the total number of neurons Q, A and R in the quiescent, activated and refractory states, such that $Q + A + R = N$, with N for the total number of cells in the population.

The probabilities to find a certain neuron from the population at the moment t in the states (q), (a) and (r) are: $P(q,t)$, $P(a,t)$ and $P(r,t)$. They satisfy the Buice-Cowan master equations (Buice and Cowan, 2009):

$$\begin{aligned} \frac{dP(q,t)}{dt} &= \beta \cdot P(r,t) - f \cdot P(q,t)\,; \\ \frac{dP(a,t)}{dt} &= f \cdot P(q,t) + g \cdot P(r,t) - \alpha \cdot P(a,t)\,; \\ \frac{dP(r,t)}{dt} &= \alpha \cdot P(a,t) - \beta \cdot P(r,t) - g \cdot P(r,t)\,. \end{aligned} \tag{3}$$

Set (3) has the normalization:

$$P(q,t) + P(a,t) + P(r,t) = 1\,. \tag{4}$$

In the simplest version of the Buice-Cowan model, the transition probabilities f, g, α, β are constant parameters.

3. New Statistical Model for Small Neuron Population

Our task is to reformulate the Buice-Cowan model adopting it for the excitations of the neuron populations in the small groups rather than the spiking of single cells, in the manner of the Tomanik-Ahmed system (1)-(2).

Let's define three sub-groups of the small neuron population:

1. The lower level of excitation L (virtually not-excited neurons);
2. The high level of the excitation H (excited neurons);
3. The hyper-synchronized part of the population S.

These three sub-groups are functions of time t, but the total number of neurons N in all three phases must be conserved:

$$L + H + S = N\,. \tag{5}$$

Let's define now the transitions between the sub-populations L, H and S, see Fig.3.

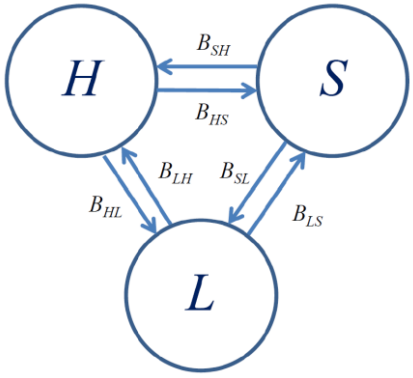

Figure 3. Transitions among different sub-groups L, H, and S in the small neural population.

In Fig.3 the positive parameters B_{ij} stand for the transition coefficients from i to j per unit of time ($i, j = L, H, S$).

The transition processes presented in Fig.3 can be written in the form of the master equation for the population sub-groups:

$$\begin{aligned} \frac{dL}{dt} &= B_{HL} \cdot H - B_{LH} \cdot L + B_{SL} \cdot S - B_{LS} \cdot L\,; \\ \frac{dH}{dt} &= B_{SH} \cdot S - B_{HS} \cdot H + B_{LH} \cdot L - B_{HL} \cdot H\,; \\ \frac{dS}{dt} &= B_{HS} \cdot H - B_{SH} \cdot S + B_{LS} \cdot L - B_{SL} \cdot S\,. \end{aligned} \tag{6}$$

Model (6) satisfies the normalization (5).

In the general case, the coefficients B_{ij} may depend on the time t and on the populations L, H, S as well.

To give an example, we discuss here a particular choice in the form:

$$\begin{aligned} \frac{dL}{dt} &= a \cdot H \cdot L - b \cdot L^2\,; \\ \frac{dH}{dt} &= b \cdot L^2 - a \cdot H \cdot L + \alpha \cdot H \cdot S - \beta \cdot H^2\,; \\ \frac{dS}{dt} &= \beta \cdot H^2 - \alpha \cdot H \cdot S\,. \end{aligned} \tag{7}$$

Model (7) corresponds to the following set of the transition parameters:

$$\begin{aligned} &B_{HL} = a \cdot L\,;\ B_{LH} = b \cdot L\,;\ B_{SL} = B_{LS} = 0\,; \\ &B_{SH} = \alpha \cdot H\,;\ B_{HS} = \beta \cdot H\,. \end{aligned} \tag{8}$$

In (8) the probability to make a forward transition $L \to H \to S$ and back is proportional to the number of cells in the 'lower' state of excitation. The transitions between states L and S are forbidden.

Numerical simulations for the system (7) are presented in Fig.4.

The total population $N = 100$, and the initial conditions are: $L(0) = 100$, $H(0) = 0$, $S(0) = 0$, i.e. the neurons in the system initially are not excited. The transition coefficients are chosen as: $a = b = 1$, $\alpha = \beta = 0.1$. That means that the transitions between the states L and H are more probable than the transitions between the states H and S.

In Fig.4 one can easily observe the developing of the excited (blue) and hypersynchronized (red) phases from the unexcited (green) phase. For the case (8) the asymptotic dynamics lead to the stabilization of all three phases.

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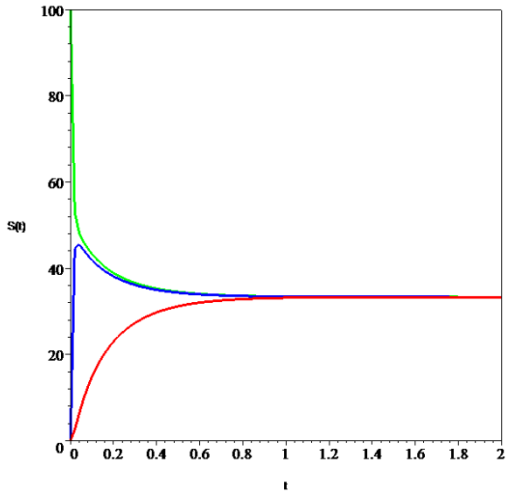

Figure 4. Dynamics in the small neural population: unexcited phase L (green), excited phase H (blue) and hypersynchronized phase S (red) for model (7).

Thus, in model (7) each phase will be stabilized asymptotically as time $t \to 0$ at the level:

$$L_\infty = \frac{\frac{a}{b}}{\frac{a}{b}+1+\frac{\beta}{\alpha}} \cdot N \; ;$$
$$H_\infty = \frac{1}{\frac{a}{b}+1+\frac{\beta}{\alpha}} \cdot N \; ; \qquad (9)$$
$$S_\infty = \frac{\frac{\beta}{\alpha}}{\frac{a}{b}+1+\frac{\beta}{\alpha}} \cdot N \; ,$$

i.e. $L_\infty = H_\infty = S_\infty = N/3$ for our particular choice of the transition parameters.

4. Results and Discussion

4.1. Results

We developed an ODE model combining the dynamical equations for different sub-populations (unexcited, excited, and, as our novelty, hypersynchronized). The dynamical system satisfies the normalization property, and it includes the details of the transitions between different subpopulations of the cells in a small neural cluster.

4.2. Discussion

Our model may serve as a simple but powerful tool to analyze the appearance and development of epileptiform dynamics in artificial neural networks. It can cover different cases of microepilepsy, and also may open the gate for studying drug-resistant epilepsy regime (Kwan et al., 2011).

The dynamical set (6)-(7) can be equipped with the control inputs mimicking the external perturbations of the neural clusters with the electrical (Rattay, 1999) or optogenetic (Joshi et al., 2020) signals. In this case, the set of control algorithms can be applied to detect (Borisenok and Ünal, 2017; Borisenok, 2021) and suppress (Borisenok et al., 2018; Borisenok, 2022) the epileptiform dynamics.

5. Conclusion

The dynamic processes of epilepsy in small neural populations do not demand necessary the development of detailed models for individual neurons. Even the ‘averaged’ dynamical set for the unexcited, excited and hypersynchronized sub-populations can serve as an efficient tool for investigation and numerical simulations of microscopic seizures.

6. Acknowledge

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