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DETECTION AND CONTROL OF EPILEPTIFORM REGIME IN THE HODGKIN–HUXLEY ARTIFICIAL NEURAL NETWORKS VIA QUANTUM ALGORITHMS

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Abstract

The problem of detection and the following suppression of epileptiform dynamics in artificial neural networks (ANN) still is a hot topic in modern theoretical and applied neuroscience. For the purpose of such modeling, the Hodgkin–Huxley (HH) elements are important due to the variety of their behavior such as resting, singular spikes, and spike trains and bursts. This dynamical spectrum of individual HH neurons can cause an epileptiform regime originated in the hyper-synchronization of the cell outcomes. Our model covers the detection and suppression of ictal behavior in a small ANN consisting of HH cells. The model follows our approach [Borisenok et al., 2018] for the HH neurons as a classical dynamical system driving the collective neural bursting, but here we use a quantum paradigm-based algorithm emulated with the pair of HH neurons. Such emulation becomes possible due to the complexity of the individual 4d HH dynamics. The linear chain of two HH neurons is connected to the rest of ANN and works autonomously. The first neuron plays a role of the detecting element for the hyper-synchronization in the ANN and the quantum algorithm emulator; while the second one works as a measuring element (emulation of the quantum measurement converting the signals into the classical domain) and the trigger for the feedback suppressing the epileptiform regime. We use here the speed gradient algorithm for controling the emulating neuron and discuss its pros and cons to compare with our classical model of epileptiform suppression.

Key words

Speed gradient feedback control, classical emulation of quantum algorithms, small–scale ANNs, Hodgkin–Huxley neurons, epileptiform dynamics.

1 Introduction

The problem of detection and the following suppression of epileptic dynamics still is a hot topic in modern theoretical and applied neuroscience [Kim et al., 2020; Ikeda, 2022]. Being an extremely complex phenomenon, epilepsy should be studied at the different scales of brain dynamics: micro-scale (individual neurons and their small clusters), meso-scale (neural populations) and macro-scale [Kuhlmann et al., 2015; Depannemaecker et al., 2021], and each scale has its own specific, see, for instance, [Freestone et al., 2013; Medvedeva et al., 2020] for mesoscopic modeling and [Varsavsky et al., 2011] for the macroscopic level. Additionally, the macroscopic ictal patterns observed experimentally cannot be easily explained by the standard models of a single micro- or mesoscopic seizure focus triggering activity that spreads to uninvolved brain regions [Davis et al., 2021]. The detailed review on the mesoscopic models and their perspectives one can find in [Wendling et al., 2016].

The processes triggering the epilepsy regimes also are complex and can be caused by different factors: switching between different inner attractors in the system [Lopes da Silva et al., 2003; Suffczynski et al., 2004] and the effects of unstable transient processes [Medvedeva et

al., 2020], or stimulated by an external noise [Taylor et al., 2014]. The topology of the network is another important matter to be discussed in details [Kramer et al., 2008].

Thus, the successful modeling of real epileptic processes should be a matter of interdisciplinary collaboration for the specialists from different areas [Iasemidis et al, 2009]. Also, it has been demonstrated recently that, in general, the complexity in the neural networks can be drastically reduced by fast processes, organizing the elementary units of the system ('agents') into relatively small number of clusters [Proskurnikov and Granichin, 2018].

Here we focus on searching for a new theoretical approach based on the quantum mechanics paradigm to detect and suppress the hyper-synchronized dynamics in an artificial neural network (ANN) of a small (miscroscopic) scale, and we discuss the principal parts of the algorithm rather than the modeling real epileptic data.

There are many alternatives to chose the single neuron models: the Izhikevich [Izhikevich, 2003], FitzHugh–Nagumo (FHN) [FitzHugh, 1961; Nagumo et al., 1962], Morris–Lecar [Morris and Lecar, 1981], 'growth transform dynamical' systems [Gangopadhyay et al., 2020], and others. FHN artificial neural networks with empirical structural connectivity measured in human subjects are especially successful for computational mimicking the fine details on the appearing [Gerster et al., 2020] and absence [Medvedeva et al., 2020] of the epileptic seizures in humans.

For our purpose, an artificial neural network with the Hodgkin–Huxley (HH) elements [Hodgkin and Huxley, 1952] have been chosen due to the variety of their behavior such as resting, singular spikes, and spike trains and bursts [Bonabi et al., 2014]. This wide spectrum of the individual HH neuron dynamics can cause an epileptiform regime originated in the hyper-synchronization of the cell outcomes, and at the same time, it can be used for the efficient control algorithm over the collective dynamics. The important feature of the basic model (HH, FHN, or other) should be the existence of a threshold or a set of thresholds coming as inputs to drive the variety of the regimes in the system dynamics. Particularly, we demonstrated a similar 'quasi-quantum' approach for a searching algorithm with FitzHugh–Nagumo neurons [Borisenok, 2021a]. Our preference of HH neuron is based on our vision of the perspectives to emulate more complex quantum algorithms which may demand the developed set of the thresholds in the system (emulation analog of multi-qubit operations).

We also should emphasize that the type of neurons (HH in our case) used for the emulation is not necessary similar to the rest of the cells in the ANN which could be modeled with Izhikevich, Morris–Lecar, FitzHugh–Nagumo or any other appropriate alternative system.

Our basic model covers the detection and suppression of epileptiform pre-ictal and ictal behavior in a small ANN consisting of HH cells. The model follows our approach [Borisenok et al., 2018] for the HH neuron as a classical dynamical system driving the collective neural bursting, but here we use a quantum paradigm-based algorithm emulated with the special linear chain of two HH neurons. Such emulation becomes possible due to the complexity of the individual 4d HH dynamics [Borisenok, 2021b]. For the purpose of detecting and suppressing control we reserve two particular neurons in the given ANN, they are connected each to another into a linear chain, such that the second neuron has the only input from the first neuron. The control algorithm works autonomously. The first neuron gets inputs from many companion elements of the network, and it plays a role of the detecting element for the hyper-synchronization in the ANN and the quantum algorithm emulator; while the second neuron works as a measuring element (emulation of the quantum measurement converting the signals into the classical domain) and the trigger for the feedback suppressing the epileptiform regime via its multiple connections to other cells.

There are different control algorithms to drive the dynamics of Hodgkin–Huxley neurons [Borisenok and Ünal, 2017; Andreev and Maksimenko, 2019]. We use here the speed gradient approach [Fradkov, 2007] for controling the emulating neuron for its imitation of the Deutsch–Jozsa quantum procedure for a searching problem [Deutsch and Jozsa, 1992].

We define the 'states' of HH neuron in the manner of the pure qubit states, and propose a simple measurement procedure of resting or spiking in the following HH neuron of the chain to complete the searching problem in a single algorithmic cycle.

The algorithm presented in Section 2 develops our preliminary study for detecting the epileptiform dynamics in the small ANNs [Borisenok, 2021b]. For ANNs the epileptiform regime is based on hyper-synchronization of spiking dynamics coming from many neurons. After the formulation of our 'quasi-quantum' searching algorithm for the pair of HH neurons, in Section 3 we describe how to use the function classified by this algorithm for detecting the epileptiform dynamics, and how to imbed the control pair of HH neurons into a small ANN.

2 Hodgkin–Huxley Neuron Model Emulating Quantum Algorithm

Let us briefly formulate the ordinary differential (ODE) model of Hodgkin-Huxley single neuron and the signal transfer function for the linear HH chain. Then we describe the basic method how to emulate the quantum Deutsch–Jozsa algorithm with the pair of HH neurons.

2.1 Mathematical Model for Hodgkin-Huxley Neurons and Their Linear Chains

The Hodgkin-Huxley differential model has developed phenomenologically from the experiments with the stimulation of the giant squid axon with the external electri-

cal current. It has the set of four variables: the output membrane action potential $v(t)$ and three ion channels variables $m(t)$, $n(t)$, $h(t)$ related to the probabilities for the membrane gates to be open or closed [Hodgkin and Huxley, 1952]:

$$\begin{aligned} C_M \frac{dv}{dt} &= -g_{Na} m^3 h (v - E_{Na}) - g_K n^4 (v - E_K) - \\ &\quad - g_{Cl}(v - E_{Cl}) + I(t) \, , \\ \frac{dm}{dt} &= \alpha_m(v) \cdot (1 - m) + \beta_m(v) \cdot m \, ; \\ \frac{dn}{dt} &= \alpha_n(v) \cdot (1 - n) + \beta_n(v) \cdot n \, ; \\ \frac{dh}{dt} &= \alpha_h(v) \cdot (1 - h) + \beta_h(v) \cdot h \, ; \end{aligned} \tag{1}$$

Here the membrane variables m, n, h are non-linear functions of the action potential v:

$$\begin{aligned} \alpha_m(v) &= \frac{0.1 \cdot (25 - v)}{\exp\left[\frac{25-v}{10}\right] - 1} \, ; \\ \beta_m(v) &= 4 \cdot \exp\left[-\frac{v}{18}\right] \, ; \\ \alpha_n(v) &= \frac{0.01 \cdot (10 - v)}{\exp\left[\frac{10-v}{10}\right] - 1} \, ; \\ \beta_n(v) &= 0.125 \cdot \exp\left[-\frac{v}{80}\right] \, ; \\ \alpha_h(v) &= 0.07 \cdot \exp\left[-\frac{v}{20}\right] \, ; \\ \beta_h(v) &= \frac{1}{\exp\left[\frac{30-v}{10}\right] + 1} \, . \end{aligned} \tag{2}$$

The control parameter in model (1) is represented by the external current $I(t)$ stimulating the axon. The set of the empirical constants includes the potentials E_{Na} (the equilibrium potential at which the net flow of Na ions is zero), E_K (the equilibrium potential at which the net flow of K ions is zero), E_{Cl} (the equilibrium potential at which leakage is zero) in mV, the membrane capacitance C_M and the conductivities g_{Na}, g_K, g_{Cl} (the conductivities for the sodium channel, the potassium channel and the leakage channel, respectively) in mS/cm^2:

$$\begin{aligned} g_{Na} = 120 \, ; \; E_{Na} = 115 \, ; \\ g_k = 36 \; ; \; E_K = -12 \, ; \\ g_{Cl} = 0.3 \, ; \; E_{Cl} = 10.36 \, . \end{aligned} \tag{3}$$

The dynamical system (1) demonstrates the variety of regimes: it can be in resting (the neuron does not show a sufficient activity), spiking (the neuron produces a single spike) or bursting (the neuron generates series of spikes). A particular regime depends on the control current I. If it is below a threshold level, then the HH neuron stays resting; if it overcomes the threshold level, the neuron generates a spike or a burst.

In a linear chain of HH neurons, the output action potential of the previous element defines the input of the following cell. We use here our gain model for the transfer of the output signal from k-th neuron via its synapse towards the dendrite/soma input of the l-th neuron [Borisenok et al., 2018]:

$$I_l(t) = \alpha [v_k(t) - v_{\rm rest}] \, , \tag{4}$$

with the phenomenological gain constant $\alpha > 0$. Here $v_{\rm rest}$ is the reference rest potential in the HH neuron ($v_{\rm rest} = -70$ mV).

Thus, the gain function (4) here serves for the coupling of two control HH neurons.

2.2 Emulation of Deutsch Algorithm with the Pair of Hodgkin–Huxley Neurons

Now let's prove that the quantum searching algorithm can be emulated with HH neurons.

The Deutsch–Jozsa quantum algorithm deals with a simple searching problem [Deutsch and Jozsa, 1992].

Suppose that we get a function f mapping $\{0,1\}^n$ into $\{0,1\}$ for an arbitrary natural n. The function f is chosen either as a constant: $f(x) = 0$ for all x from $\{0,1\}^n$ or $f(x) = 1$ all x from $\{0,1\}^n$, or as balanced: the number of inputs 0 for the mapping is equal to the number of inputs 1. The algorithm checks if the given function f is a constant. To do it for the classical approach we need $2^{n-1} - 1$ evaluations. Quantum algorithms, from another hand, can perform it much faster. Due to the so-called quantum phase kick–back effect in the algorithm, we need only a single measurement to distinguish between those two cases.

The circuit for the Deutsch–Jozsa algorithm contains three Hadamard gates, one multi-qubit block with the function f, and one measurement block [Aradyamath et al., 2019].

For instance, for the case $n = 1$ the result of the measurement is equal to:

$$\begin{aligned} |\text{output} > = \frac{1 + (-1)^{f(0) \bigoplus f(1)}}{2} |0> + \\ + \frac{1 - (-1)^{f(0) \bigoplus f(1)}}{2} |1> \, . \end{aligned} \tag{5}$$

Here the addition mod 2 denoted as $\bigoplus$. The output (5) solves the problem of searching. Indeed, if $f(0) \bigoplus f(1) = 0$, then the output is $|0>$, and the function f is constant. If $f(0) \bigoplus f(1) = 1$, then the output is $|1>$, and the function f is balanced. The same is valid for the case of n bits. If all n measurement results are $|0>$, we conclude that the function is constant. Otherwise, if at least one of the measurement outcomes is $|1>$, we conclude that the function is balanced.

To emulate the Deutsch–Jozsa quantum algorithm, we use a linear chain of two sequent HH neurons. The first neuron plays the role of the computational element. It works with the information about the function f; and it is driven by a certain feedback algorithm towards the goal action potential. The resulting potential of the first

neuron with the dendrite/soma model enters the second neuron, which plays the role of the measuring element.

For the transfer signal between two neurons we define the threshold (tr) level:

$$I_{\rm tr} = \alpha \cdot (v_{\rm tr} - v_{\rm rest}) \, . \tag{6}$$

The output of the first neuron stimulates the particular regime of the second measuring element. If the first HH neuron produces the acting potential below the threshold level $v_{\rm tr}$, the second neuron does not spike. If the output action potential of the first neuron v overcomes slightly the threshold level, the second one produces a single spike.

To emulate the Deutsch algorithm, let's define the 'pure quantum states' for the HH neuron: the resting $|0>$ and the single spiking $|1>$:

$$\begin{aligned} |0> &= 0 \cdot I_{\rm tr} \, ; \\ |1> &= 1 \cdot I_{\rm tr} \, , \end{aligned} \tag{7}$$

which correspond to the action potentials:

$$\begin{aligned} v_{|0>} &= v_{\rm rest} + 0 \cdot \frac{I_{\rm tr}}{\alpha} \, ; \\ v_{|1>} &= v_{\rm rest} + 1 \cdot \frac{I_{\rm tr}}{\alpha} \, . \end{aligned} \tag{8}$$

To unify both cases, the goal potential is expressed via the CNOT logical operator over the function f:

$$v_* = v_{\rm rest} + {\rm CNOT}\{f(0), f(1)\} \cdot \frac{I_{\rm tr}}{\alpha} \, . \tag{9}$$

The symbol $*$ stands here for the potential v (the output of the first neuron) which should be the goal of our control signal I in (1).

To achieve the goal (1), let's use Fradkov's speed gradient algorithm [Fradkov, 2007], with the non-negative differentiable goal function:

$$G(t) = \frac{1}{2}[v(t) - v_*]^2 \, . \tag{10}$$

The control signal in the HH neuron is one-dimensional. Therefore the speed gradient in the control space is reduced to the partial derivative:

$$\begin{aligned} &I = -\Gamma \frac{\partial}{\partial I} \left(\frac{dG}{dt} \right) = -\frac{\Gamma}{C_M} \left(v - v_* \right) \, ; \\ &\Gamma = {\rm const} > 0 \, . \end{aligned} \tag{11}$$

The control current (11) drives the system (1) towards the minimization of the control goal (9). The achievability of the stabilization/tracking goal in the HH dynamical system for the speed gradient algorithm has been discussed in [Borisenok and Ünal, 2017].

Now suppose that we drive the first neuron towards the goal potential (9). Then via the gain (4) it stimulates the second measuring element with two possible options: the second neuron will stay in rest or will generate a single spike. Just based on that we can conclude if the function f is constant or not:
If $f(0) = f(1)$, then $v_* = v_{\rm rest} = v_{|0>}$, and f is constant.
If $f(0) \neq f(1)$, then $v_* = v_{\rm rest} + I_{\rm tr}/\alpha = v_{|1>}$, and f is balanced.

Thus, we proposed the classical analog of the Deutsch–Josza algorithm.

3 Inhibitor Pair of HH Neurons for Detecting and Suppressing Epileptiform Dynamics

The first version of the algorithm has been proposed in [Borisenok, 2018] based on the classical algorithms. Here we will use the emulation of quantum Deutsch–Josza procedure [Borisenok, 2021b] to construct the complex control element of two HH neurons for detecting and suppressing the epileptiform dynamics in the small ANNs.

3.1 Function f for Detecting the Epileptiform Regime

To formulate an analog of Deutsch's algorithm for the hyper-synchronization detection, we need to define the function f to distinguish between the regular and epileptiform (i.e. hyper-synchronized) regimes. Let's define the spiking function for the n-th neuron as:

$$f_n = \begin{cases} 0 \;\; \text{if} \;\; v_n = v_{\rm rest} \, , \\ 1 \;\; \text{if} \;\; v_n > v_{\rm rest} \, . \end{cases} \tag{12}$$

The function (12) is non-zero for the spiking state, and it is equal to 0 for the resting. It is a straight analog of the function $f(x)$ for the Deutsch–Josza algorithm (Section 2).

To detect the hyper-synchronization, let's choose arbitrarily the action potentials of some small number of n neurons. Thus, the first inhibitor neuron collects the information on the network state from the set of n arbitrary chosen cells in the form of binary signals (12). This set of n inputs can be changed for each next cycle of the detection, i.e. the connectivity matrix for that element is dynamically changes. The collected set $\{f_n\}$ serves for the following definition of the function f:

$$f = \prod_n f_n \, . \tag{13}$$

We are interested only in the detection of hyper-synchronization, when the product of the spiking function is equal to 1:

$$\prod_n f_n = 1 \, . \tag{14}$$

In the absence of hyper-synchronization among the chosen n neurons, the RHS(14) is equal to 0. One can easily check that the definition (13)-(14) corresponds to two

cases of f: it is either always 1 (the function f_n is constant), or the output consists of '0's and '1's (but in our case the function is not necessary balanced). Thus, two possible cases are:

– Epileptiform regime: $f = 1$ always; the function f_n is constant.

– Regular regime: $f = 0$, i.e. the function f_n is not constant.

Eq.(14) serves for the definition of the goal potential in the axon of the first neuron:

$$v_* = v_{\rm rest} + f \cdot \frac{I_{\rm tr}}{\alpha} \ . \qquad (15)$$

which is analog of (9). This goal potential must be substituted into the SG feedback (11), which works as an autonomous algorithm driving the first neuron towards the target state (15). Thus, for each working cycle of the detection the goal is stabilization, but it depends on the binary set of the spiking functions f_n, which is different for each working cycle. The output action potential (15) via the transfer function (4) creates the input current in the second neuron, and only for $f = 1$ this 'measuring' element produces a spike. The resting ($f = 0$) means the absence of hyper-synchronization.

Thus, the classical analog of the quantum searching algorithm uses the effects which are similar to the 'phase effects' for quantum systems, and it serves for the classification of the ANN dynamical regimes.

3.2 Finalization of the Control Algorithm

Now we can present the final form of the algorithm for detecting and suppressing the epileptiform dynamics.

Among all the neurons of the given population, we should choose arbitrarily n neurons (they are enumerated with the numbers from 1 to n). Based on their outputs the function f is defined similarly to (13)-(14). This function is analyzed with the complex control element consisting of the pair of the emulating HH neuron and the 'measuring' HH neuron.

The emulating neuron driven with the speed gradient method (11) classifies the regime (the epileptiform dynamics vs the regular one) and transfers the result of the classification for the second companion which produces or not produces a spike. The measuring element triggers the feedback control loops towards the initial set of HH neurons to suppress epileptiform regime in the form described in details in [Borisenok, 2018; Borisenok, 2021b].

To conclude, the finalized algorithm consists of the following steps:

1. Form the function f over the action potentials of arbitrary numbers of n neurons in the population.
2. Make the Deutch-type measurement of the function f with the pair of control neurons using the SG stabilization algorithm (15) for the first neuron.
3. If the function $f = 0$, there is a normal regime in the population dynamics.
4. If the function $f = 1$, there is an epileptiform regime in the population dynamics.
5. If the epileptiform regime is detected, trigger the feedback suppressing control signal from the inhibitor control HH pair to the neurons of the population.
6. Repeat the algorithm for the next cycle of the detection.

The cycle repetition time is based on the single spiking temporal intervals, and for the set (3) it can be chosen between 20 and 50 ms.

4 Conclusions

The pair of 4d Hodgkin–Huxley neurons is capable of emulating successfully the effects similar to the kick-back contributions to the Deutch–Josza quantum algorithm.

Such a pair of HH neurons acting as an autonomous control element could be used for detecting and suppressing the ictal phase of the epileptiform regime in the small population of HH or other types of neurons. The algorithm of the detection works more efficiently compared with the standard classical detection algorithms due to the influence of the phase 'kick-back effect' analog on the detection of the hyper-synchronized ANN behavior.

Our algorithm can be extended to model different forms of control: driving individual neurons vs control over the group of the cells in the population; to different physical realizations: electrical stimulations of the individual cells and the group of cells, optogenetic fields, and others. We strongly believe that the proposed approach can be extremely useful for modeling micro-scale epilepsy, for control over the microscopic instability residing in given stable macroscopic dynamics [Yamanaka et al., 2015], and for many other applications to ANNs. The adaptation of our approach for real epilepsy modeling will be a matter of our further research.

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