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Can A Network of Chemical Oscillators Help to Diagnose Schizophrenia?

ASHMITA BOSE* AND JERZY GORECKI

Institute of Physical Chemistry, Polish Academy of Sciences
Kasprzaka 44/52, 01-224 Warsaw, Poland

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Schizophrenia is one of the most common mental disorders, however it is difficult to detect and can remain undiagnosed for years. It is believed that information if a patient is ill can be extracted from EEG signals recorded using electrodes located at the patient scalp. In the paper we postulate that a network of chemical oscillators can process recorded signals and help to diagnose a patient. In order to verify our approach we investigated the network functionality on a small dataset of EEG signals recorded from 45 ill and 39 healthy patients. We optimized a network formed by just six interacting oscillators using an evolutionary algorithm and obtained over 82% accuracy of schizophrenia detection on the training dataset.

Keywords: Schizophrenia, EEG signal, chemical computing, oscillators, network, Oregonator model, genetic optimization

1 INTRODUCTION

The semiconductor technology has dominated modern information processing. Its success is the consequence of highly efficient realization of semiconductor logic gates characterized by a long time of error-free operation. The gates can be assembled together making more complex information processing devices. The technology perfectly matches the bottom-up design strategy of information processing systems [1]. However, to use the bottom-up

* Contact author: E-mail: abose@ichf.edu.pl

approach we should KNOW FIRST how to combine together simple components to obtain the anticipated result.

There are many problems for which we can define the input variables and specify the set of anticipated outputs, but we do not know the algorithm that links the input with the output. For example, problems inspired by needs of medical diagnostic belong to such class. The input information is collected from a number of medical tests and on this basis we are expected to conclude if the patient is healthy or ill. But in many medically oriented problems we do not know the algorithm that produces the answer on the basis of the input data. Our knowledge on the relationship between input and output is based on previously accumulated examples. For such types of problem the top-down design strategy seems to be more appropriate than the bottom-up one.

To illustrate the top-down design of a computing medium let us consider a problem A for which we know the solution for a number of cases (records) that contain the set of input values $(p_1, p_2, ..., p_n)$ and the corresponding output $q = A(p_1, p_2, ..., p_n)$. Formally our knowledge on the algorithm A can be regarded as the database D_A containing records in a form of (n+1) tuples $(p_1, p_2, ..., p_n, q)$, where the first n elements are predictors (for example results of different medical tests) and the last element (q) is the discrete data type. In medically oriented problems the value of q estimates the patient state, like the NHS CORVID clinical frailty scale [2] or in the simplest case it is just a single bit saying if a patient is ill or healthy. The computing medium is supposed to return the correct data type if the predictor values are used as the input. Therefore, if we are able to define a good classifier of D_A using a computing medium then we obtain an instant machine that executes the algorithm A.

The basis assumption of this paper is that a classification problem can be approximately solved by a network of interacting chemical oscillators (cf. Figure 1). We assume that the network is formed of two types of oscillators [3–5]. There are input oscillators used to put the predictor values into the network. The activity of an oscillator assigned as the input of the i-th predictor is suppressed for time related to value of p_i. There are also so called normal oscillators that are inhibited for a fixed time that is not related to the predictor value. These normal oscillators moderate interactions in the medium and optimize them for a specific problem. We also assume that the output information is coded in the number of oscillation cycles observed on a given element of the network. As we show later, the choice of the output oscillator results directly from the network optimization. Therefore, the full definition of a computing network includes the number of oscillators in the network, their types and the interactions between them. For the schizophrenia diagnosis we use the network illustrated in Figure 1a. The number of oscillators m is fixed as $m = 6$. Also the illustrated geometry of interactions between

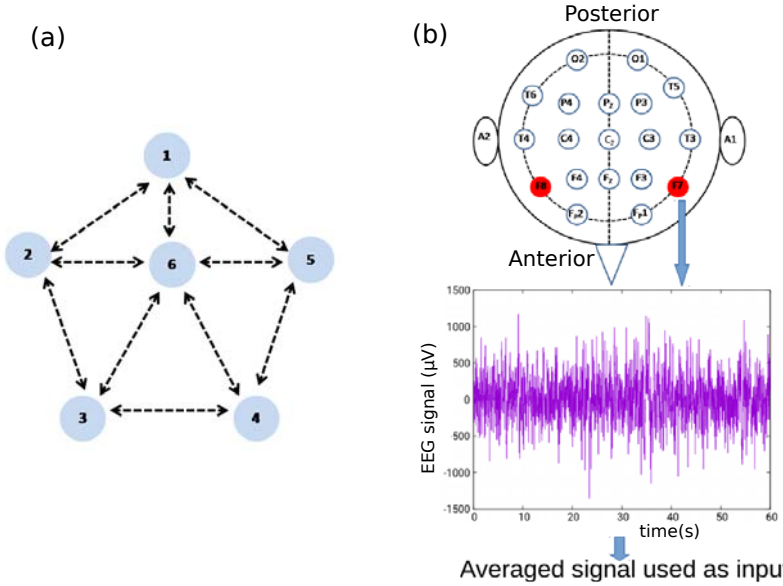

FIGURE 1
(a) The structure of chemical oscillator network assumed to diagnose schizophrenia. (b) Schematic representation of positions of different electrodes used for recording potential values. The potentials derived from the red marked channels are the ones that were used as inputs for the classifier described in this paper.

oscillators does not change during optimization. The application of the top-down strategy to this network means that the other parameters such as locations of input and normal oscillators, inhibition times for the normal oscillators, method for inputing the predictor values or the type of interactions between oscillators undergo optimization to achieve the highest accuracy on a representative dataset of cases. Both systematic methods of optimization and random trial and error ones can be applied. We have found [3–5] that evolutionary optimization oriented on obtaining the best classifier for a representative training dataset of the problem can lead to a computing network, that performs the anticipated task with a reasonable accuracy.

Obviously one has to select the computing medium before starting to optimize the network. In our previous papers on chemical database classifiers [3–5] we used oversimplified event-based-model reflecting the basic features of the oscillator time evolution and of interactions between oscillators coupled by mutual activations. The event-based-model assumes sharp boundaries between three phases of the oscillation cycle: excitation, refractory and responsive phase. It takes interactions into account as the condition for excitation of an oscillator in the reponsive phase that is in contact with an excited

oscillator. Here we consider more realistic model. We represent the individual oscillator dynamics using the two-variable Oregonator model [6, 7] of the Belousov-Zhabotinsky(BZ) reaction [8, 9]. The interactions between individual oscillators are represented by reactions involving activators of individual oscillators. The choice of model has been motivated by the broad interest in applications of BZ-reaction for chemical information processing. The BZ-reaction is a complex, catalytic oxidation of an organic substrate (usually malonic acid) in an acidic environment [10, 11]. Two stages of BZ reaction can be identified. One is a fast oxidation of the catalyst and the other is a slow reduction of the catalyst by organic substrate. The solution color reflects concentrations of catalyst in the oxidized and reduced form, thus such nonlinear behaviour of the medium as oscillations, wave propagation or appearance of spatio-temporal patterns can be easily observed. If the ruthenium complex ($Ru(bpy)_3^{2+}$) is used as the reaction catalyst then BZ-reaction becomes photosensitive [12]. Oscillations can be inhibited by light. For the same initial concentrations of reagents the medium can oscillate at dark, show an excitable behaviour at low light intensity and has a steady state when it is strongly illuminated. The Oregonator model used below to simulate in-silico the time evolution of the medium (see Equations (1,2)) correctly describes this feature. At specific conditions a spatially distributed medium can be locally excited and the excitation can propagate in space. This type of behaviour resembles propagation of nerve impulse in living organisms. As the result, the BZ reaction has attracted attention as an inexpensive medium for experiments with neuron-like chemical computing [13, 14]. Moreover, a moving pulse of excitation can be interpreted as a propagating bit of information. Using this interpretation one can construct chemical binary logic gates [15, 16] and argument for universality of chemical reaction-diffusion computing [17]. However, such approach requires a spatially distributed medium with a complex structure and precisely controlled reaction parameters.

Our recent results have shown that implementation of BZ-oscillator networks leads to simple computing structures that are able to perform complex tasks [3–5]. Systems of interacting droplets containing reagents of BZ-reaction can be stabilized by solution of lipids in the organic phase [18]. If the photosensitive variant of BZ-reaction is used then oscillations in droplets can be individually controlled. For example the droplets acting as normal oscillators in the network can be inhibited by illumination within the time interval that does not depend on the input values. On the other hand the illumination times of input droplets can be related to the corresponding predictor value.

Computer simulations have shown that even a small network composed of a few oscillators, like the one shown in Figure 1a, with time evolution described by the event-based-model can be used to diagnose if a cancer cell is malignant or benign [4]. In this report we concentrate on designing of a

classifier that is supposed to determine if a patient has schizophrenia or not. Schizophrenia is the most common form of psychotic behavior where patients experiences hallucination, delusion, chaotic speech. However, schizophrenia is difficult to detect and easily go undetected for years. It is believed that information about schizophrenia can be extracted from the EEG signals recording brain activity [19]. Such signals are recorded from electrodes placed in different parts of the scalp (see Figure 1b). In order to reduce the amount of input data we assume that schizophrenia can be diagnosed using the time average signals. We postulate that the information extracted from the signal can be processed using a network of interacting chemical oscillators in the form presented in Figure 1a. The detailed model of the network and information about its optimization is introduced in the Section 2. The discussion of obtained results is presented in the following Section.

2 NUMERICAL MODEL OF INFORMATION PROCESSING NETWORK AND PREPARATION OF INPUT DATA.

The network we proposed for distinguishing between schizophrenic and healthy patients was formed of just $m = 6$ oscillators arranged in geometry shown in Figure 1a. The broken arrows illustrate interactions between the oscillators. The time evolution of reactions proceeding in each oscillator were described by two-variable Oregonator model [6, 7]. If we neglect interactions with the other oscillators of the network and the decay of activator then equations describing the j^{th} oscillator are:

$$\frac{\partial u_j}{\partial t} = \frac{1}{\varepsilon}(u_j - u_j^2 - (f v_j + \phi_j(t))\frac{u_j - q}{u_j + q}) \quad (1)$$

$$\frac{\partial v_j}{\partial t} = u_j - v_j \quad (2)$$

where the variables u_j and v_j represent concentrations of an activator (U_j) and an inhibitor (V_j) for proceeding reactions. The parameter ε sets up a ratio of time scales of variables u and v, q is a scaling constant and f is the stoichiometric coefficient. In our simulations we used the following values of model parameters for all oscillators ($1 \leq j \leq 6$): $\varepsilon = 0.2$, $q = 0.0002$ and $f = 1.1$. The parameters of the Oregonator model were fixed and did not undergo optimization.

The time dependent function $\phi_j(t)$ describes the influence of illumination on a photosensitive BZ-reaction and it is proportional to light intensity. We considered $\phi_j(t)$ in the form:

$$\phi_j(t) = 0.1 \cdot (1.001 + \tanh(-10(t - t_{ilum}(j))) \quad (3)$$

In this definition $t_{ilum}(j) > 0$ defines illumination of the j^{th} oscillator. At the beginning the value of $\phi_j(t) \sim 0.2$ and the Oregonator model with parameters given above predicts a stable steady state corresponding to $u_j = 0.0002$ and $v_j = 0.0002$. For long times $\phi_j(t)$ approaches 0.0001 what corresponds to an oscillator with the period of approximately 10.8 time units. The values of $t_{ilum}(j)$ were subject of optimization for the normal oscillators. If the j^{th} oscillator functions as the input one for the predictor p_l then:

$$t_{ilum}(j) = t_{start} + (t_{end} - t_{start}) \cdot p_l \tag{4}$$

where the parameters t_{end} and t_{start} undergo optimization

The coupling between the oscillators #k and #j was described by additional reactions involving the activators U_k and U_j of these oscillators:

$$U_j + B_j \rightarrow U_k + C_k \tag{5}$$

$$U_k + B_k \rightarrow U_j + C_j \tag{6}$$

with the reaction rate β.

We also assume that the activator of each reaction can spontaneously decay with the reaction rate α:

$$U_j + D_j \rightarrow products \tag{7}$$

Here symbols B, C and D denote other molecules involved in these reactions. We assume their concentrations were high with respect to concentrations of activators involved. Therefore, the concentrations of B, C and D were assumed to be constant during the network evolution.

The values of Oregonator model parameters are similar to those given in the literature [20]. However, we did not know how to select the values of α and β, so they are also included into the optimization procedure.

Within our model the time evolution of the network is described by the following set of kinetic equations:

$$\begin{aligned} \frac{\partial u_j}{\partial t} &= \frac{1}{\varepsilon}(u_j - u_j^2 - (f v_j + \phi_j(t))\frac{u_j - q}{u_j + q}) \\ &\quad -(\alpha + \beta \sum_{i=1,m} s_{j,i})u_j + \beta(\sum_{i=1,m} s_{j,i} u_i) \end{aligned} \tag{8}$$

$$\frac{\partial v_j}{\partial t} = u_j - v_j \tag{9}$$

The last two terms in Equation 8 represent the coupling in between i^{th} and j^{th} oscillators and the activator decay. The symbols $s_{j,i}$ are defined as:

$s_{j,i} = 0$ if $j = i$ or if $j \neq i$ and oscillators $\#j$ and $\#i$ do not interact,
$s_{j,i} = 1$ if $j \neq i$ and oscillators $\#j$ and $\#i$ do interact.
In the considered network the interactions are fixed and illustrated in Figure 1a.

The set of equations (8,9) describes the network evolution after all parameters characterizing the medium are known.

We postulate that information necessary to detect schizophrenia can be extracted from the EEG signals recording brain activity [19]. Signals (the time dependent potential values) were recorded from electrodes located in different parts of the scalp (see Figure 1(b)). For the network optimization presented below we used signals received from F7 and F8 channels marked red in Figure 1(b). The dataset available on the web [21] containing signals recorded on $N = 84$ patients, out of which $N_h = 39$ were healthy and the other had symptoms of schizophrenia ($N_s = 45$).

The EEG signals were recorded with the sampling rate 128 Hz for 1 minute. Therefore, for each patient we have 16 data files corresponding to different electrodes and each data file contains $K = 7680$ values of recorded potential (in μV). The time between consecutive potential values is $\Delta t = 7.8125ms$. In order to reduce the amount of input data we characterized each data file by a single number. Let $V^l(n,k)$ denote the potential recorded for n^{th} patient, on the l^{th} electrode and at the time $t_k = k \cdot \Delta t$. For each patient we introduced 16 time averaged potentials defined as:

$$x_n^l = \sum_{k=1}^{K} V^l(n,k) \tag{10}$$

To proceed with the analysis we normalized the time averaged potentials over the set of patients. To do it we introduced:

$$\mu_l = \frac{1}{N} \sum_{n=1}^{N} x_n^l$$

and

$$\sigma_l = \sqrt{\frac{1}{N-1} \sum_{i=1}^{N} (x_n^l - \mu_l)^2}.$$

The value of l^{th} predictor for the patient n was defined as:

$$p_n^l = \frac{x_n^l - \mu_l}{\sigma_l} \tag{11}$$

Previous studies have shown that the signals obtained from the frontal lobe of the brain(F7,F8) clearly indicates the difference in the brain activity of a schizophrenic patient from that of a healthy subject [19]. Therefore, our problem of schizophrenia diagnosis is reduced to classification of the dataset: $D_S = \{(p_n^7, p_n^8, q_n), n = 1, N\}$ where the record type $q_n = 0$ for a schizophrenic patient and $q_n = 1$ for a healthy subject.

3 NETWORK OPTIMIZATION AND RESULTS

3.1 Network optimization

The time evolution of a network considered as the classifier of a schizophrenia database can be studied numerically if we decide about locations of the input and normal oscillators and if we define the values of t_{illum} for the normal oscillators, t_{end}, t_{start} for the data input, and α, β for the interactions between oscillators. Moreover we have to select t_{max} that defines the interval of time for which the network evolution is observed ($[0, t_{max}]$). We postulate that information about patient health can be extracted from the number of activator maxima recorded on a selected oscillator of the network, during the time interval $[0, t_{max}]$. In order to find which oscillator should be used as the output one we calculate the mutual information [22] between the set G of record types in the training dataset D_S ($G = \{q_n, n = 1, N\}$) and the sets of oscillation numbers $o_j(n)$ observed on the j^{th} oscillator in the network when the predictors of n^{th} database record are used as the network input ($O_j = \{o_j(n), n = 1, N\}$). The oscillator $\#i$ for which the mutual information between G and O_i is maximal is used as the network output. Therefore, if we know the network parameters we can locate the output oscillator and use the network for the diagnostic tasks. The mutual information calculated for the output oscillator was considered as the measure of network fitness. It can be expected that in the majority of cases the optimization based on the mutual information leads to a classifier with the highest accuracy [23]. But how to determine the network parameters?

Following the idea of cancer classification described in [4] we optimized the system parameters using an evolutionary algorithm. All previously mentioned parameters underwent optimization. The population of 200 networks were considered. At the beginning the population of networks was randomly generated. The fitness of each network was calculated using the whole training dataset. The next generation comprised of 2% of most fit networks of the previous population and of 98% offsprings generated by recombination and mutation operations applied to oscillators from top 40% networks of the previous population. To obtain an offspring we applied the following operations to the randomly selected networks:

1. Recombination operation in the network illumination characteristics:
   Another network selected from top 40% of the population was chosen to undergo parameter recombination and a new offspring was created with new values of t_{start} and t_{end}, forming a new set of parameters: $\{ t_{max}, t_{start}^{offspring}, t_{end}^{offspring}, \alpha, \beta \}$.
2. Mutation on the coupling factors and on rate of formation of products:
   The coupling factor(β) and the rate of formation of product(α) were mutated with mutation rate of 0.5. The mutated values of α and β were the sum of a fraction of their old values and a random number.
3. Modification on the illumination times of normal oscillators:
   Modification on the illumination times of normal oscillators was performed again by randomly selecting another parent from 40% of best fitted population and copying its values of t_{illum} to the next generation.
4. Recombination on oscillator type and on the time of simulation:
   The oscillator type, whether it will be an input oscillator or a normal one, also underwent recombination. The parents were again chosen randomly. The oscillator type can be altered or recombined. There were no constraints given among selecting the type of oscillator. There could be many or none input oscillators for a given predictor. There may be no normal oscillators if it optimizes the network. And an input oscillator was allowed to be the output one.

3.2 Results

At the beginning we considered the schizophrenia dataset classifier that processes averaged 60 s long signals. Considering the previous reports [19] we selected F7 and F8(frontal lobe) channels as these that bring the most relevant information about the patient state. In order to get information if a patient characterized by the predictors p^7 and p^8 is healthy or ill we simulated numerically the network evolution (Equations 8, 9) within the time interval [0, tmax] using Cash-Karp R-K45 method [18] with $h = 10^{-3}$ time step.

In the optimization procedure we considered the population of 200 classifiers and evolved it for 740 generations. The optimization progress is illustrated in Figure 2(a). When the optimization ended the fitness of the best classifier was 0.416. Figure 2(b) presents the mutual information between the patient state and the number of activator maxima recorded on all oscillators of the most fit network. The oscillator #2 produced the maximum value of the mutual information and it was selected as the output one. The optimized network is characterized by: $t_{max} = 79.5$, $t_{start} = 72.1$, $t_{end} = 4.9$, $\alpha = 0.46$, $\beta = 0.65$, $t_{ilum}(1) = t_{ilum}(5) = 52.3$. The structure of the most fit network is shown in Figure 3(a). The circles with black rings are the normal oscillators.

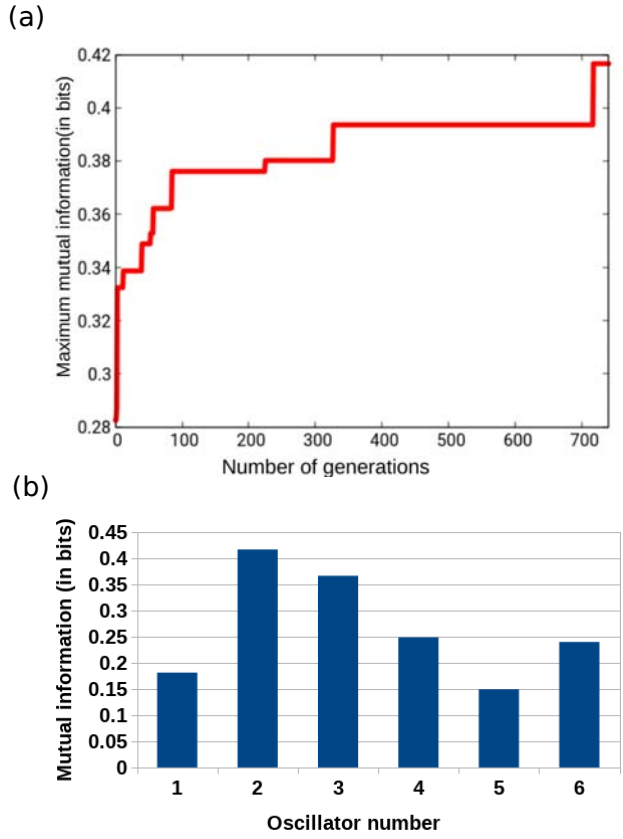

FIGURE 2
The optimization of the schizophrenia classifier processing the averaged 60 s long signals. (a) The fitness value as a function of the number of evolutionary steps. The maximum value of fitness obtained after 740 generations was 0.416 bit. (b) The mutual information between the patient state and the number of activator maxima recorded on all oscillators of the optimized network (cf. Figure 1a). The oscillator #2 produced the maximum value of the mutual information and it was selected as the output one.

The ratio between the surface of the red area and the area of disk representing an oscillator is the ratio between $t_{ilum}(j)$ and t_{max}. The circles with blue rings mark locations of the input oscillators (In_1 represents the input from F7 channel thus the predictor p^7, In_2 represents the input from F8 channel - predictor p^8). The circle with a double ring is the output oscillator. As seen the highest values of mutual information between the patient state and the number of activator maxima was observed for an oscillator that was also the input of predictor p^8.

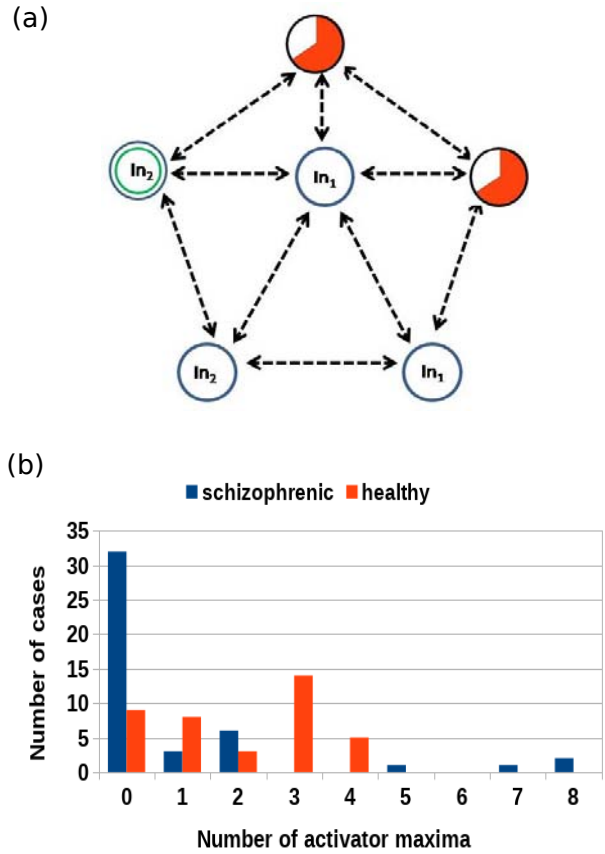

FIGURE 3
The structure and function of the schizophrenia classifier processing the averaged 60 s long signals. (a)The structure of optimized schizophrenia classifier. The circles with black rings are the normal oscillators. The red shaded parts of the piecharts represent the ratio between $t_{ilum}(j)$ and t_{max}. The circles with blue rings mark input oscillators (In_1 represents the input from F7 channel, In_2 represents the input from F8 channel). The circle with a double ring shows the output oscillator. (b) The relationship between the number of activator maxima recorded on the output oscillator and the patient health. The blue bars correspond to schizophrenic cases and the orange ones to the healthy ones.

As the result of optimization procedure we obtained the most fit network for schizophrenia diagnosis. But we do not know how to read out the information coded in the number of the activator concentration maxima at the oscillator #2. Figure 3(b) shows the relationship between the number of activator maxima recorded on the output oscillator and the patient health. To translate this result into classification algorithm we used the majority rule. If for a

given observed number of activator maxima the number of ill patients in the training dataset is larger than the number of healthy one than we assume that all cases in which such number of maxima is observed diagnose schizophrenia. Therefore, we postulate the classification rule: if 1,3 or 4 maxima of activator concentration are observed during the time evolution at the oscillator #2 then the patient is healthy. If the number of observed maxima is different then the patient is schizophrenic. For the considered database this rule gives 82% accuracy in schizophrenia determination. The accuracy was calculated as the ratio between correctly diagnosed cases to all cases of the training dataset D_S. It is also interesting to notice that for 12 of 39 healthy patients were diagnosed incorrectly. On the other hand the diagnosis of schizophrenic patients was more accurate as there were only 3 mistakes for 45 cases.

The classifier described above have shown 82% accuracy in schizophrenia diagnosis. But can it be improved? The obvious approach is to use a larger network that would allow to consider a dataset with a larger number of predictors. However, such approach can be strongly biased by a limited number of cases in the training dataset. We would like to present another approach. Each 60 second signal $V^l(n,k)$ for n^{th} patient, on the l^{th} electrode at time $t_k = k \cdot \Delta t$ is composed of $K = 7680$ values of recorded potential. We divide this signal into signals:

$$V1^l(n,k) = V^l(n,k) \quad for \quad k = 1, 2560$$

$$V2^l(n,k-2560) = V^l(n,k) \quad for \quad k = 2561, 5120$$

$$V3^l(n,k-5120) = V^l(n,k) \quad for \quad k = 5121, 7680$$

It means that instead of one 60 s long signal we considered 3 signals $V1$, $V2$ and $V3$ recorded during the time intervals $[0, 20s]$, $[20s, 40s]$ and $[40s, 60s]$ respectively. The signals $V1, V2$ and $V3$ were averaged and normalized using the same algorithm as applied to the signal V (Equations 10,11). As the result we obtained three datasets D_{S1}, D_{S2} and D_{S3}, where the averaged, normalized potentials observed in subintervals of time were matched with the parameter describing the patient health. Next we performed the optimization procedure to obtain oscillator networks that classify the datasets D_{S1}, D_{S2}, D_{S3}. For each case we considered population of 100 classifiers and optimized it for 500 generations. The progress of optimization is illustrated in Figure 4. Subfigures (a), (b) and (c) correspond to datasets D_{S1}, D_{S2} and D_{S3} respectively. We can see that in all cases the fitness of the best classifier (0.33 bit, 0.323 bit and 0.371 bit, respectively) was lower than that achieved within 500 generations for the network classifying the dataset D_S.

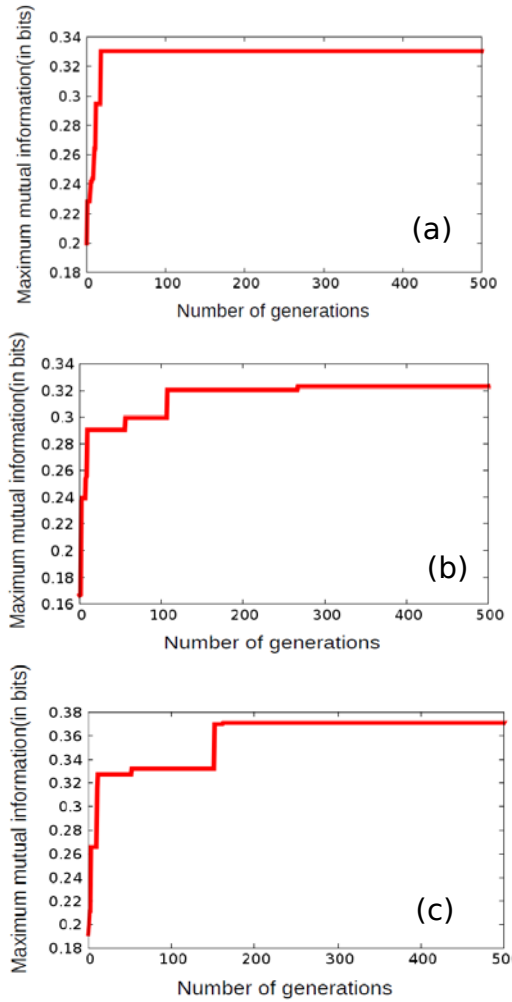

FIGURE 4
The progress of optimization of the schizophrenia classifiers processing the averaged 20 s long signals. Subfigures (a), (b) and (c) correspond to datasets D_{S1}, D_{S2} and D_{S3} respectively. The maximum values of fitness obtained after 500 generations were 0.33 bit, 0.323 bit and 0.371 bit.

The structures of the most fit classifiers are shown in Figure 5 (subfigures (a), (b) and (c) represent D_{S1}, D_{S2} and D_{S3} respectively). Like in Figure 3a the circles with black rings are the normal oscillators. The red shaded parts of the piecharts represent the ratio between $t_{ilum}(j)$ and t_{max}. The circles with blue rings mark input oscillators (In_1 represents the input from F7 channel, In_2 represents the input from F8 channel). The circles with a

double ring shows the output oscillator. The values of parameters describing the classifiers were:

1. For the classifier of D_{S1}:
   $t_{max} = 85.8$, $t_{start} = 12.5$, $t_{end} = 79.3$, $\alpha = 0.71$, $\beta = 0.52$, $t_{ilum}(3) = t_{max}$.
2. For the classifier of D_{S2}:
   $t_{max} = 89.6$, $t_{start} = 94.6$, $t_{end} = 10.1$, $\alpha = 0.38$, $\beta = 0.11$, $t_{ilum}(2) = 24.4$, $t_{ilum}(6) = 56.8$.
3. For the classifier of D_{S3}:
   $t_{max} = 77.9$, $t_{start} = 28.1$, $t_{end} = 78.6$, $\alpha = 0.76$, $\beta = 0.17$, $t_{ilum}(1) = 31.2$, $t_{ilum}(3) = t_{ilum}(5) = 9.37$, $t_{ilum}(6) = t_{max}$.

Therefore, both structures and parameters describing the classifiers of signals coming from different subintervals are very different. This may suggest insufficient optimization (but still optimization with a similar size of population and number of generations led to reasonable results for other problems [4, 5]), or, more likely too small and too divergent training dataset. Despite the differences it is interesting that in all cases the output droplet is also the input of a predictor. It is p_7 for the classifier of $D_{S2}$and p_8 for classifiers of D_{S1} and D_{S3}. Not surprising the relationships between the number of activator maxima recorded on the output oscillator and the patient health are different for D_{S1}, D_{S2} and D_{S3}. They can be extracted from results illustrated in Figure 6. For the classifier of D_{S1} a patient is schizophrenic if the number of activator maxima recorded on the output oscillator $o_4 \in \{0, 3, 5, 6, 8\}$. For the classifier of D_{S2} a patient is schizophrenic if $o_3 \in \{0, 5, 9\}$ and for D_{S3} a patient is schizophrenic if $o_2 \in \{0, 2, 6, 7, 9\}$. The accuracy of such classifiers were 77%, 75% and 79.7% for D_{S1}, D_{S2} and D_{S3} respectively. Now we can combine the expertise of all three classifiers together and postulate the a patient is ill if at least two of three classifiers predict schizophrenia. The accuracy of such classification increases to 90% and there were 7 healthy patients and only a single ill patient that were incorrectly diagnosed.

4 CONCLUSIONS AND DISCUSSION

In the presented study we assumed that schizophrenia can be detected by a chemical oscillator network that analyses EEG signals recorded from electrodes located on a patient scalp. We have introduced a more realistic model of the oscillators and of interactions between them, than rather crude event-based-model [3–5] used in a series of previous papers on database

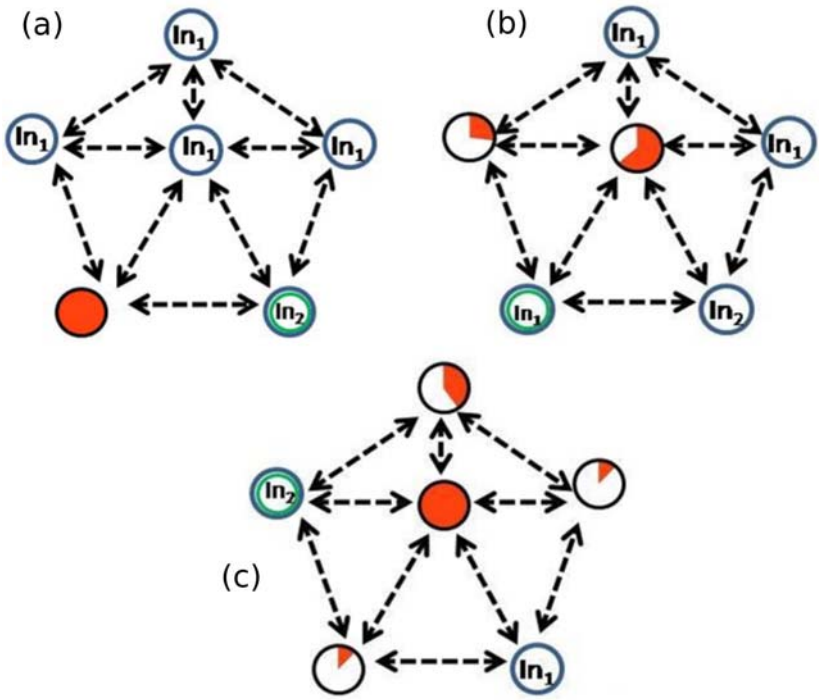

FIGURE 5
The structures of the schizophrenia classifiers processing the averaged 20 s long signals. Subfigures (a), (b) and (c) correspond to datasets D_{S1}, D_{S2} and D_{S3} respectively. The circles with black rings are the normal oscillators. The red shaded parts of the piecharts represent the ratio between $t_{ilum}(j)$ and t_{max}. The circles with blue rings mark input oscillators (In_1 represents the input from F7 channel, In_2 represents the input from F8 channel). The circles with a double ring show the output oscillators.

classification using interacting oscillators. The application of the new model does not change the main conclusion of previously reported results: optimized networks of chemical oscillators can be successfully applied for classification problems. In our case a network of 6 coupled oscillators gave 82% of correct diagnosis for cases in the considered dataset. Its modification based on three stage diagnosis on parts of recorded signal produced even higher, 90% accuracy of diagnosis.

Although the presented results are encouraging the access to data for larger number of patients seem important for the further studies. We think our results can be strongly affected by a small size of available data. It can be seen when we divided the recorded potentials into three time sub-intervals and optimized the classifiers separately for each sub-interval (cf. Figure 5). Seeing a typical randomness of recorded signal (cf. Figure 1) it is hard to

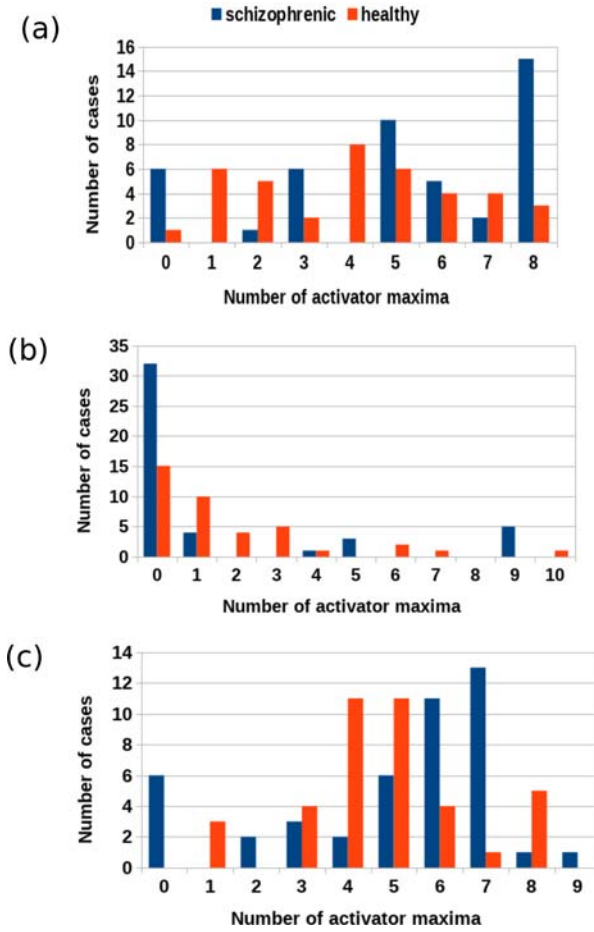

FIGURE 6
The relationship between the number of activator maxima recorded on the output oscillator and the patient health for of the schizophrenia classifiers processing the averaged 20 s long signals. The blue bars correspond to schizophrenic cases and the orange ones to the healthy ones. Subfigures (a), (b) and (c) represent D_{S1}, D_{S2} and D_{S3} respectively.

expect that results measured for the first 20 s sub-interval are qualitatively different than those for the next one. Nevertheless, we obtained significantly different networks for the diagnosis in different subintervals. It can happen that there are many local maxima of optimization, but we believe that the difference in our optimization comes from a small sample of test cases. We believe, that for unbiased set of data the results of each 20 s interval belonging to healthy and ill patients should be similar, because the signals should be independent on the time when they are measured. Therefore, the difference

between classifiers optimized for different time intervals illustrates the randomness in the considered dataset.

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