A FIBRILLATION MODEL BASED ON NONINVASIVE OBSERVATIONS
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Abstract: - Ventricular fibrillation (VF) remains the most common cause of sudden death. Atrial fibrillation (AF), while not usually lethal, also causes significant fatality. Many attempts have been made towards the modeling of the fibrillation process, most of which are based on invasive observations. In our previous study, we used blind source separation (BSS) algorithm, and showed that the fibrillation process can be decomposed into two main independent components. We also showed that from the perspective of independent components, surface ECGs contain the same information as the electrogram. In this study, we use previous results and by the use of guinea-pig (GP) ventricular cell model, we make a single cell model of the fibrillation process. We adjust our model by the use of noninvasive observations from several patients with VF and try to extract general rules for model adjustment. We check the validity of our model by the use of power spectrum analysis and show that by appropriate adjustment, the model's output observation has the same power spectrum as VF observation and conclude that our model can simulate VF dynamics.

Key words: - fibrillation modeling, independent components, ionic currents, dynamical systems, power spectrum.

1 Introduction
Fibrillation is a dangerous episode in cardiac muscle. Ventricular fibrillation, (VF), is the most common arrhythmia, which directly leads to sudden cardiac death. Atrial fibrillation, (AF), while not usually lethal, also causes significant fatality. Therefore, any new work towards the understanding of this process may lead to the development of new methods in prevention, diagnosis, and therapy and save many people's lives.

Most studies in this context have been done by using invasive data from human or animal heart muscle. Invasive observations are burdensome and expensive and the required equipment is not available to every researcher especially biomedical engineers, therefore noninvasive methods are preferred.

In our previous work, we carried out an independent component decomposition method based on surface ECG and we concluded that our noninvasive method could be used instead of the invasive methods for fibrillation process identifications [1]. The surface ECG is an observation on a dynamical system; heart muscle. A dynamical system is a system that at each instance of time has a state and a rule that informs how the state changes in time. The state is generally written as a vector of state variables. The set of all such states is called the state space (or phase space). A sufficiently long time observation on a dynamic system contains enough information for its characterization [2]. A dynamic system is characterized by its state variables. State variables are independent variables, which combine to create the behavior of the system. The mechanical activity of heart results from the action potential and action potential occurs because of ionic currents so it is evident that state variables of heart i.e. independent dynamic variables can be linked to ionic currents.

Fig.1 illustrates the action potential and two main currents in the guinea-pig ventricular cell [3]. Arrhythmia in heart can be interpreted as changes in heart dynamics and so heart diseases could be called dynamic diseases [4]. The dynamics of a system is influenced by its state variables and so identification of state variables can lead to identification of normal
and abnormal behavior and better controlling of arrhythmia.

In [1] we showed that \( i_{NaCa} \) and \( i_{Ca} \) are the main state variables in fibrillating heart mussel, Fig.2 shows the typical behavior of these two ionic currents in guinea-pig ventricular cell, from which it is clear that they have tri and bi phasic profiles respectively and it is obvious that \( i_{NaCa} \) has a more complex dynamics than \( i_{Ca} \), therefore any process which is more influenced by \( i_{NaCa} \) has a more complex dynamics.

In this study we model the fibrillation process as a dynamical system with two state variables. These state variables being; \( i_{NaCa} \) and \( i_{Ca} \). This means that the dynamics of a fibrillating ECG observation can be modeled as a mixture of these two components.

2 Methods

Our independent component model for VF is depicted in Fig.3. Here \( S_1 \) is \( i_{NaCa} \) source, \( S_2 \) is \( i_{Ca} \) source, and \( a_1 \) and \( a_2 \) are mixing coefficients respectively. We use the Noble et al 1998 guinea-pig (GP) ventricular cell model for generating \( i_{NaCa} \) and \( i_{Ca} \) current sources [3]. The ventricular cell action potential and ionic currents of the guinea-pig are very similar to those of the human. The model shown in Fig.3 generates currents as shown in Fig.2 when \( S_1 \) and \( S_2 \) are stimulated by an atrial-ventricular (A.V) node stimulus. The stimulus must be sufficiently large in order to stimulate the cell, so any possible interventions which can disturb the amplitude or triggering intervals may affect the occurrence of action potentials.

Fig.4 illustrates the situation of a cell among its neighbors. A cell in ventricle heart muscle is surrounded by a large number of neighbor cells and each neighbor may send a current via the synaptic junction to it. This effect is very important because the sum of the currents from these neighbor cells may be sufficiently large enough to stimulate the cell or prevent it from normal stimulation by an A.V stimulus.

In VF ventricular cells lose their regular relations and we can assume that each neighbor current in Fig.4 is not only independent from but also has the probability distribution identical to the other neighbors. We can assume that the net current of the neighbor cells is equal to the sum of a large number of i.i.d (independent identically distributed) currents via synaptic dynamics.

The sum of sufficiently large number of i.i.d processes is a Gaussian process, this white Gaussian process passes through the dynamics of synapse which is a first order one[5] so the whole input currents from neighborhood synapses can be modeled by Ornstein-Uhlenbeck (OU) process[6].

In our VF model of Fig.3, we have modeled the whole stimulus currents from neighbors with source \( S_3 \) which is an OU process, \( a_3 \) is the weighing coefficient for this source.

Using our experience in [1], we know that \( i_{NaCa} \) is the main state variable in fibrillation dynamics Therefore we adjust \( a_1 = 1 \) and because \( i_{Ca} \) is the second component we adjust \( a_2 = 0.4 \) for the present.

In our final discussion we will see that these parameters can be adjusted by the use of an experimental rule.

We set \( a_3 = 0 \) for the moment. Fig.4 shows an ECG observation from a patient in VF and Fig.5 shows the equivalent power spectrum with a peak around 10 HZ. This signal has no certain pattern but seems oscillatory. We measure the time between successive peaks and calculate the mean period of the signal (here we have a mean period of 0.12 sec), then we adjust the period of A.V stimulus; \( T_{AV} \) in Fig.3 to this value, The model output is shown in Fig.6 and the equivalent power spectrum in Fig.7. It is clear that Fig.6 and Fig.7 have no similarity with Fig.4 and Fig.5 respectively. Now we adjust the gain and time constant (\( T_{OU} \)) of OU process to 1 and 0.68 respectively (see Appendix A) and set \( a_3 = 3 \), we start our model again and look at output, as shown in Fig.8. It is clear that it looks more like Fig.4. The power spectrum of Fig.8 is shown in Fig.9. Now the question arises; how similar are the dynamics of Fig.8 and Fig.4? Alternatively, how can the model shown in Fig.3 simulate the observation shown in Fig.4? In this study, we have used Power spectra as a criterion for comparison i.e. we adjust our model so that not only the output of model appears like Fig.4 but also its power spectrum resembles Fig.5. Generally, this can be done by adjusting the OU time constant (\( T_{OU} \)). This is what we have done for the observation of Fig.4 and the results are shown in Fig.8 and Fig.9. We have repeated our study for the ECG records of several patients in VF[7] and have adjusted the \( T_{OU} \) so that the power spectrum of the model's output is like that of the patient. The best adjustments for 15 patients of 40, is summarized in Table 1. We have done these adjustments by the use of [1] and some trial and error. The main conclusion from the results in Table 1 is that it seems that there is some relation between mean periods of observed
ECG signal (T_{AV}) and T_{OU}. In order to justify this result, we fit a polynomial to the data of Table 1 for describing the relation between T_{AV} and T_{OU} (see Table 2), then we try to predict T_{OU} for a new VF observation. The results are acceptable and generally we can adjust our model so that its output spectrum has the general profile of a VF output spectrum shape and in the most cases the peak of the spectrum is around the real value. In Table 2 we have summarized our rule for adjusting our proposed model of Fig 3. The observation shown in Fig 4 has been made by the use of this rule.

3 Conclusions
In this study, we presented a new single cell model for VF. Our model is based on noninvasive observations. In this model, we have used iNaCa and iCa as two independent components (state variables), which have been generated by the Noble et al, 1998 guinea-pig ventricular cell model. First, we have adjusted our model experimentally by the use of several observations from patients and then we have extrapolated rules from the experimental results. We have justified our model by the use of power spectrum. The results are acceptable and the output of the model has a power spectrum like that of VF. Hence we can conclude again that iNaCa and iCa are two main state variables in VF.

Table 1 Model adjustments for 15 patients

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<th>Patient No</th>
<th>T_{AV}(sec)</th>
<th>T_{OU}(sec)</th>
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<th>a2</th>
<th>a3</th>
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<td>1</td>
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Table 2 General rules for model adjustments

<table>
<thead>
<tr>
<th>a1</th>
<th>a2</th>
<th>a3</th>
<th>T_{OU}</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>0.4±0.02</td>
<td>3</td>
<td>f(T_{AV})</td>
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</table>

\[ f(x) = 14.2x^2 - 0.3810x + 0.2050 \]

References:
[7] Physionet, Physiobank, Sudden Cardiac Death Database, and Tachyarrhythmia Database.
Fig. 1 General morphology of the action potential and two main ionic currents in the guinea-pig ventricular cell[3].

Fig. 2 iNaCa and iCa in GP cell. illustrating the tri- (iNaCa) and biphasic (iCa) morphologies.

Fig. 3 Independent component model for VF.

Fig. 4 a cell receives a net noise current as an O.U process from its neighbors.
Fig. 5. An ECG observation of a patient with VF.

Fig. 6. General Morphology of the power spectrum of the VF signal in Fig. 5.

Fig. 7. Model output for \( a_1=1, a_2=0.4, a_3=0, T_0=0.12 \). Clearly, this output cannot simulate observation of Fig. 5.

Fig. 8. Power spectrum of the observation of Fig. 6.

Fig. 9. Model output after inserting OU process; \( a_3=3, T_0=0.42 \).

Fig. 10. Power spectrum of model output when we insert OU process, clearly it is like VF one.
Appendix (A)

Consider the following first order dynamical system:
\[
\frac{dx(t)}{dt} + bx(t) = v(t)
\]
Where the input \( v(t) \) is white Gaussian noise, the steady state output of system; \( x(t) \) is a stationary response with the following autocorrelation function and power spectrum:
\[
R_x(\tau) = \frac{1}{m} e^{-\frac{b}{m} |\tau|}, \quad S_x(\omega) = \frac{1}{m^2 \omega^2 + b^2}
\]
which are shown respectively in the following figures:

We call this process Ornstein-Uhlenbeck (OU).

The synaptic dynamics are approximately driven by Gaussian white noise, synapses also have their own first-order dynamics, and then the synaptic current is an OU process.

An OU process has two parameters; \( b, m \).

\[
\frac{1}{b} \quad \text{is the gain of process, in this study we set } b = 1
\]

and \( T_{OU} = \frac{m}{b} \) is the time constant so we can adjust OU's spectrum by means of \( T_{OU} \).