Nonlinear and nonstationary ECG analysis of spontaneous transition from polymorphic to monomorphic arrhythmia in a mathematical model of cardiac tissue dynamics

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***Abstract*—Dependence of ECG dynamics on behavior of the excitation vortex in the myocardium was investigated in computational simulation by the example of the autowave lacet. The lacet, which seems to be a phenomenon of so called bifurcation memory, can lead in the heart to spontaneous transition from polymorphic to monomorphic arrhythmia. It was demonstrated that the information revealed in ECG with the normalized-value analysis of electrocardiographic variability corresponds sufficiently with the drift velocity of the excitation vortex.**

***Index Terms*—ANI-method, autowave, computational simulation, electrocardiographic variability, non-linear analysis, ventricular arrhythmia**

I. Introduction

Normalized-value analysis of electrocardiographic variability ('ANI-method' in Russian notation [1]) was proposed for studying nonstationary time series obtained as observed value of some cyclic (quasiperiodic) process. For example, the ANI-method could be useful for analysis of both normal and arrhythmic electrical cardiac activity. The current implementation of the ANI-method (ANI-2003, [2], [3]) was developed for ECG analysis of experimental polymorphic ventricular arrhythmia and ventricular fibrillation. The ANI-2003 maps an ECG fragment onto two real indices (arbitrary units). The indices provide a quantitative representation of polymorphism, which is one of the qualitative ECG features of potentially life-threatening reentrant arrhythmias.

The cardiac arrhythmias mentioned are life-threatening cardiac disorders [4]. In accordance with the recent multicentric investigations (CAST, ESVEM, CASCADE etc), treatment using antiarrhythmic drugs of all classes leads to positive results in 58.5% of cases. In other words, the antiarrhythmic treatment is commonly prescribed nearly at random. The situation indicates that investigation of ventricular arrhythmias must be continued in the most intensive manner, including the search for new diagnostically valuable ECG features.

The ANI-method seems to be most probably helpful for these tasks. For example, the ANI-2003 helped to ascertain in physiological experiments that the dependence of antiarrhythmic effect of the lidocaine, the Na-channel blockator, on its concentration have strongly pronounced nonlinear nature [5]. In this work, we demonstrate in the framework of computational biology that the ANI-2003 is effective for some characteristics of movement of the spiral wave of myocardial excitation to be traced.

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The spiral wave of excitation (alias reverberator) is a typical autowave phenomenon in two-dimensional excitable media. The reverberator can be described simplistically as a half of a plane wave curved around its break point. The break point is also called the tip of the reverberator. Reverberator behavior is commonly sketched in the terms of movement of its tip. Autowave reverberators are known to be main cause of different kinds of ventricular arrhythmia. As long as the dynamics of the reverberators rides on myocardium state, it can be theoretically estimated the myocardium state by details of their dynamics.

Recently we found [6] a new autowave behavior, which we called the lacet, — namely, the transformation of reverberator motion from a two-periodic meander into one-periodic circular rotation due to spontaneous deceleration of reverberator drift (see Fig. 1). Formerly, three types of reverberator tip movement in homogeneous two-dimensional medium were known [7]. These are 1) uniform circular movement, 2) meander, i.e. two-periodic movement, with the tip moving along a curve similar to cycloid (epicycloid or hypocycloid), and 3) hyper-meander, i.e. a 'complex' or maybe 'chaotic' movement whose wave tip trajectory could not be described in terms of two periods.

According to some investigators, a transfer from the uniform circular movement of the reverberator to the meander is caused by an Andronov-Hopf bifurcation [8]. The lacet is perhaps a phenomenon of so called bifurcation memory, detected in different fields of computational biology [6], [9] as well as in engineering sciences [10] in last decade. It was demonstrated in computational simulation [4], [11] that the lacet in the myocardium coincides with spontaneous transition from polymorphic to monomorphic arrhythmia in the ECG dynamics.

Here, we demonstrate in computational simulation by the example of the lacet that the information revealed in ECG with the ANI-2003 corresponds sufficiently with velocity of the reverberator drift.

II. Methods

Combination of computational simulation, which supply us with time series for subsequent analysis, and data processing was used. Formerly [1], [2], [3], the ANI-method was described in the mathematical form for discrete data. In this work, we present the generalized form of the ANI-method. The details of 2D simulations, the procedure for estimation of velocity of the reverberator drift, and the procedure for constructing the ECG in the simulations were described elsewhere [6], [11]. The main of them are mentioned briefly here.

A. Mathematical model of cardiac tissue dynamics

The mathematical model of excitable medium by Aliev and Panfilov [12], which is a modified version of the popular FitzHugh-Nagumo model [7], was applied. Here are the equations of the Aliev-Panfilov model:

$$\begin{aligned} \frac{\partial u}{\partial t} &= \Delta u - ku(u-a)(u-1) - uv \\ \frac{\partial v}{\partial t} &= \varepsilon(u,v)(-v - ku(u-a-1)) \\ \varepsilon(u,v) &= \varepsilon_0 + \frac{\mu_1 v}{u+\mu_2}\,, \end{aligned} \tag{1}$$

where $u(x, y, t)$ is a dimensionless function similar to the transmembrane potential in myocardial cells and $v(x, y, t)$ is a dimensionless function similar to a slow recovery current. According to the authors, the Aliev-Panfilov model is characterized by a strongly pronounced dependence of excitation duration on the time interval between consecutive excitation waves. This modification was developed in order to reach a more adequate description of the cardiac tissue in comparison with the original FitzHugh-Nagumo model. The parameters in the equations were adjusted [12] to accurately reflect the properties of the normal cardiac tissue ($k = 8.0$; $\mu_1 = 0.2$; $\mu_2 = 0.3$; $\varepsilon_0 = 0.01$; $a = 0.150$).

The simulations were carried out in 2D excitable media (128 elements along each dimension) with von Neumann boundary conditions. For calculation, we used a forward Euler numerical approximation ($\Delta t = 0.01$ t.u., $\Delta x = \Delta y = 0.50$ s.u.). A reverberator was produced from a planar half-wave by a temporary impenetrable barrier (with no-flux boundary conditions), which was removed at a suitable instant of simulation. In each case, the position of the barrier and the duration of its existence were chosen so that when the reverberator reached stationary circulation, the rotation of its tip occurred approximately in the center of the medium. The location of the reverberator tip was defined as the point of intersection of particular values of the excitation and recovery state variables: $u = 0.89$; $v = 0.50$.

The ECG at each instant, $U(t)$, was computed with

$$U(t) = \sum \left[\frac{\partial u}{\partial x}\frac{\partial}{\partial x}\left(\frac{1}{r}\right) + \frac{\partial u}{\partial y}\frac{\partial}{\partial y}\left(\frac{1}{r}\right) \right], \tag{2}$$

where summation is done over all points of the 2D excitable medium, u is the value of the recorded variable, r is the distance from the current point to the recording point. The position of the latter is set by the coordinates (x, y) of its projection on the plane of the medium and the distance d to this plane. Two virtual ECG recorders were placed at $d = 128$. One of them was over the center of the medium ($x = y = 64$), and the other was over its corner ($x = y = 0$)

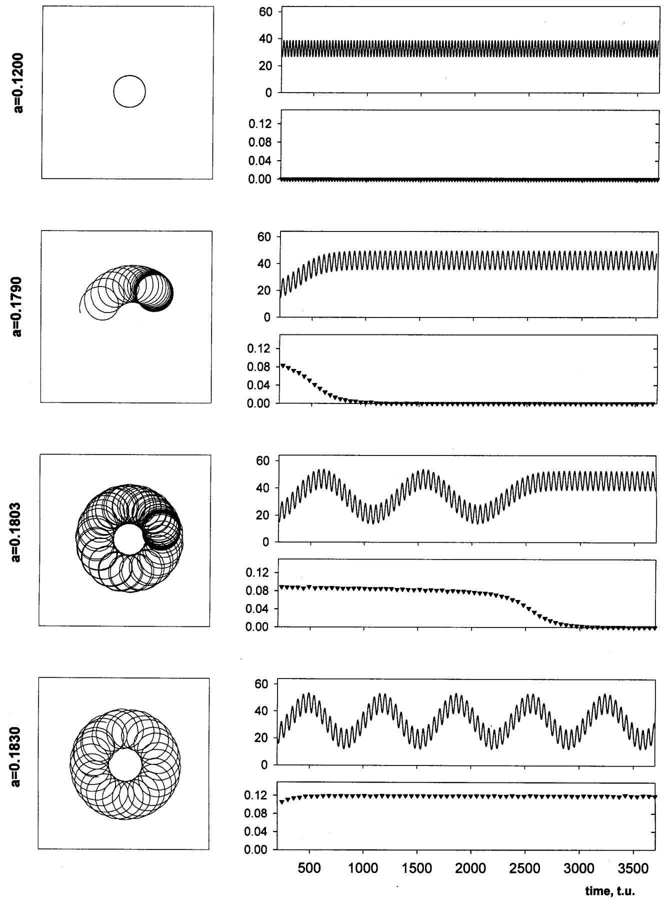

Fig. 1. Trajectories of the reverberator tip at different values of the parameter a of the Aliev-Panfilov model: the uniform circular movement at $a = 0.1200$, two examples of the lacet at $a = 0.1790$ and $a = 0.1803$ and the classic two-periodic meander at $a = 0.1830$. For each value of a, a group of three graphs is presented: the left graph for the tip trajectory; the right upper graph for the dynamics of the x coordinate of the tip and the right lower graph for the dynamics of speed of the instant center of the spiral wave. All the graphs on the right have the same horizontal scale.

B. Velocity of the reverberator drift

In the cases of both the meander and the lacet, the reverberator tip motion can be described as a superposition of two approximately circular motions: a rapid motion of the tip about an instant center, which in its turn slowly drifts in a circle about some fixed center. We supposed that the movement of the instant center is a good description of the reverberator drift.

To measure the speed of the instant center, we evaluated the parameters of either circular movement (i.e., coordinates of the centers and the radii) utilizing the least-squares method. We used an iterative procedure for revealing the fixed center.

C. ANI-method

ANI-method produces two indices. Index V_1 represents an average evaluation of the unlikeness of data segments inside the studied fragment of the data series and the index V_2 is its variation. To calculate the indices, we compare an arbitrary segment of an data series with another segment, which is considered to be a reference sample. The comparison procedure is described with the functional:

$$R(t,T) \equiv \frac{1}{S(t)} \left[\int_t^{t+T_{SW}} (\varphi(\tau+T) - \varphi(\tau))^2 \, d\tau \right]^{1/2},$$

where T_{SW} is the sampling window width and $S(t)$ is the peak-to-peak amplitude of the signal in the sampling window corresponded to time t. T_{SW} is the constant value inside the studied fragment of the data series. It is important that the compared segments are assumed to correspond to similar intervals of two adjacent cycles, therefore we chose T_{SW} to be comparable with the shortest duration of the cycle.

The procedure of searching for the similar interval of the next adjacent cycle is executed in the time interval (scanning window, T_{ScW}) confined with the domain of anticipation of the next adjacent cycle. Therefore, for each instant t, it is admitted that the similar segments of adjacent cycles of the data series are away from each other in the time interval $T_0(t)$, called quasiperiod, such as

$$R(t, T_0(t)) = \min_{T_{SW} \le T \le T_{ScW}} R(t,T).$$

The comparison procedure is carried out at each moment of time yielding the local characteristic of the data series variability (instant variability index, I):

$$I(t) \equiv R(t, T_0(t))$$

To monitor the time series changes with time, we calculate the variability indices V_{1i} and V_{2i} for the segment in some fixed-width window, that is called the averaging window, T_{AW}. The V_{1i} and V_{2i} is produced from $I(t)$. V_{1i} is the average $I(t)$ inside some short time interval $t_i \le t \le t_i + T_{AW}$, and V_{2i} is V_{1i} divided by the standard deviation of $I(t)$ inside the same interval. Shifting T_{AW} along the time axis, we obtain $V_1(t)$ and $V_2(t)$.

Basing on the definition of ventricular tachycardia, we chose $T_{AW} = 6T_{SW}$. For successive ECG fragments of fixed length, a sequence of the indices draws a trajectory in the index space. The trajectory drawn in (V_1, V_2) index space enables one to visualize the detailed ECG dynamics.

III. Results

In our simulations, the parameters of (1) were the same as indicated above, except that the parameter a, which is similar to the threshold of excitation, was varied from 0.1500 to 0.2300. The dynamics of velocity of the reverberator drift as well as the ECGs were calculated for each parameter set, and each ECG was quantitatively evaluated by the ANI-2003. Some of our results were presented elsewhere [3], [4], [6], [11].

The comparison the velocity of reverberator drift and ECG dynamics described with $V_1(t)$ shows (Fig. 2) that there is perfect coincidence between them.

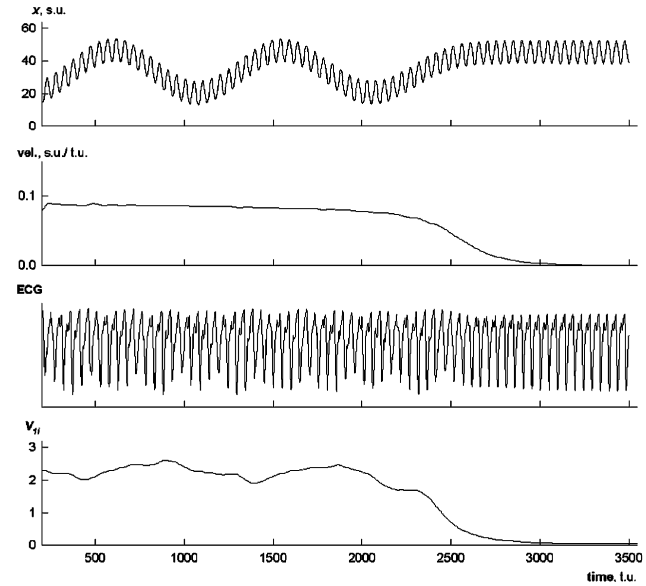

Fig. 2. The transition from polymorphic to monomorphic arrhythmia in the Aliev-Panfilov model at $a = 0.1803$. From top to bottom: the dynamics of the x coordinate of the reverberator tip, the dynamics of speed of the instant center of the autowave vortex, the ECG, and index of the ECG variability, $V_1(t)$. All the graphs have the same horizontal scale.

IV. Conclusion

In this study, we have shown that the technique for ECG analysis referred to as ANI-2003 could provide cardiologists with sensitive clinical tool for identifying life-threatening arrhythmias. The estimates derived from virtual ECGs in this study reveal some unexpected details of ventricular arrhythmia dynamics, which probably will be useful for diagnosis of cardiac rhythm disturbances.

ANI-method was developed for monitoring the stability of quasiperiodic processes. It could be anticipated different types of instability to effect different types of results obtained with ANI-method. In the example discussed in this work, two quasiperiodic processes interact with each other. One of them is rotation of the autowave vortex about the instant center and the other is the drift of the instant center. The rotation is stable and so it has nearly no effect on ECG. But the drift of the vortex changes its velocity in some specific manner, and one can see the similar changes in the index produced by ANI-2003.

In the heart, the autowave lacet, which is cardiac states conditioned by the bifurcation memory, requires to be distinguished from the other types of transition from polymorphic to monomorphic ventricular tachycardia. We demonstrated possibilities of the ANI-2003 for ECG diagnostics of spiral wave behavior like the autowave lacet. Should future studies confirm the existence of the lacet in the myocardium, the ANI-method shall be helpful in recognition of the autowave regime when visual analysis of ECG is insufficient.

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