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Spontaneous Halt of Spiral Wave Drift in Homogeneous Excitable Media

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Abstract. In computer simulations, we found a new type of spiral wave drift in a homogeneous two-dimensional excitable medium, namely, a circular drift of the spiral wave with decrease of the drift velocity right up to its total cessation. We have investigated certain quantitative characteristics of the new spiral wave behavior. As a result, we have demonstrated that the new spiral wave behavior essentially differs from the types of its behavior that was known before. This discovery can improve comprehension of mechanisms of some potentially life-threatening cardiac arrhythmias.

Keywords: excitable media, spiral waves, mathematical modeling, cardiac arrhythmia

Excitation waves, a sort of autowave processes, are typical for many physical, chemical, and biological systems. Such systems are said to be excitable media. Important instance of biological excitable media is cardiac tissue. Normal regimes of excitation wave propagation provide for normal cardiac activity, while the other regimes result in heart disturbance and even in life-threatening cardiac arrhythmias. These considerations determine the importance of investigation of the excitation waves.

In two-dimensional excitable media, a typical autowave process is a spiral wave (alias rotor). Spiral waves appear as rotating phase waves of chemical or some other activity, which propagate through a stationary medium. In homogeneous media, rotor can typically be approximated by an Archimedean spiral, rotating with roughly constant speed [1].

Under some simplification, it is often useful to represent the spiral wave as a bowed halfwave. A break of the half-wave is called the tip of the rotor. Rotor behavior is commonly described in terms of rotor tip movement [2].

Until now, three types of rotor tip movement in two-dimensional homogeneous medium were known [3, 4]. These are 1) a uniform circular movement, 2) a meander, i.e. a two-periodic movement, with the tip moving along a curve similar to cycloid (whether epicycloid or hypocycloid), and 3) a 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 investigations, a replacement of the uniform circular movement of the rotor by the meander and a replacement of the meander by the hyper-meander are caused by an Andronov-Hopf bifurcation [1].

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We have described a new autowave regime in which the rotor tip moved along the curve similar to cycloid, but the rotor tip drift spontaneously decelerated and stopped [5]. As a result, spiral wave behavior transformed from meander into circular rotation. The new rotor behavior was found in homogeneous two-dimensional excitable medium with use of the Aliev-Panfilov model [6] in our simulation. Such a spontaneous halt of the rotor drift in homogeneous medium was called the *lacet* [5] to emphasize its difference from the types of rotor behavior that are well-known before. It has been also demonstrated in the computer simulation of cardiac arrhythmia [5] that, in the case of the lacet, a spontaneous transition from polymorphic to monomorphic arrhythmia is observed. Formerly, such a transition was considered to be possible only in the case of essential heterogeneity of the excitable medium.

However a question still remained whether the rotor drift deceleration would be observed in the case of the classic two-periodic meander if the time of observation were increased adequately. In this paper, we stated the quantitative method of rotor motion description as well as the results of comparative investigation of the rotor drift velocity in the cases of the meander and of the new rotor behavior. Some essential differences between the two-periodic meander and the lacet are described.

1. MATHEMATICAL MODEL

We used the mathematical model of excitable medium by Aliev and Panfilov [6], which is a modified version of the popular FitzHugh-Nagumo model [3]. Here are the equations of the Aliev-Panfilov model:

$$\frac{\partial u}{\partial t} = \Delta u - ku(u-a)(u-1) - uv,$$

$$\frac{\partial v}{\partial t} = \varepsilon(u,v)(-u - ku(u-a-1)),$$

$$\varepsilon(u,v) = \varepsilon_0 + \frac{\mu_1 v}{u+\mu_2}$$
(1)

where u(x,y,t) is a dimensionless function similar to the transmembrane potential in myocardial cells and $\mu v(x,y,t)$ is a dimensionless function similar to a slower recovery current. According to its authors, the Aliev-Panfilov model has some important differences from the FitzHugh-Nagumo model in order to reach a more adequate description of the cardiac tissue. The parameters in the equations (1) were adjusted [6] to reflect the properties of the normal cardiac tissue accurately (k = 8.0; $\varepsilon_0 = 0.01$; a = 0.150; $\mu_1 = 0.2$; $\mu_2 = 0.3$).

In our simulations, the parameters were the same as indicated above, except that the parameter *a* was varied from 0.1100 to 0.2300 by the step $\Delta a=0.005$. In addition, we carry out simulations with 0.1800<*a*<0.1803 varied by $\Delta a=0.001$ as well as with 0.1803<*a*<0.1804 varied by $\Delta a=0.0001$. Note that the parameter *a* specifies the threshold of excitation [7, 8]. The threshold of excitation essentially determines the type of rotor circulation as it has clearly been demonstrated in [3, 4].

The simulations were carried out in two-dimensional excitable media (with 128 as well as 200 elements along each dimension) with von Neumann boundary conditions. For calculation, we used a forward Euler numerical approximation ($\Delta t = 0.01 \text{ t.u.}$, $\Delta x = \Delta y = 0.50 \text{ s.u.}$).

A rotor was produced from a planar half-wave by a temporal impenetrable barrier (with no-flux boundary conditions), which separated the medium into two isolated rectangular areas and was removed at a suitable instant of simulation. In each case, the barrier position and the duration of its existence were chosen so that the rotation of the rotor tip when the rotor has reached its stationary circulation should occur approximately in the center of the medium. The planar half-wave was triggered along the medium boundary that was perpendicular to the temporal impenetrable barrier. The location of the rotor tip was defined as the point of intersection of the excitation and recovery state variables for their particular values (u = 0.89; v = 0.50).

All the computer simulations were carried out with use of the application developed by Yu.E.Elkin for investigation of autowave processes [9].

2. RESULTS OF COMPUTER SIMULATION

The classical meander is considered to be two-periodic motion of the spiral wave tip, with the tip uniformly moving along the circumference, the center of which uniformly moves, in its turn, along another circumference [1-4]. During the computer simulation carried out under conditions described above, we found a new type of rotor behavior on which the rotor tip trajectory appeared loops squeezed one after another. Because these trajectories show formal resemblance to carnival streamers of paper, such a spontaneous halt of the rotor drift in homogeneous two-dimensional medium we called the *lacet* (which means "carnival streamers of paper" in the translation from French into English) [5]. In this case, the center of the circumference, along which the rotor tip moves, does not move uniformly, but the rotor drift velocity decreases, i.e. the rotor drift has some deceleration. The deceleration occurs right up to total cessation of the rotor drift. After the rotor drift has halted, the rotor behavior appears similar to the uniform circular movement. Thus the lacet is characterized by spontaneous transformation of the rotor behavior from its motion similar to classical two-periodic meander into its uniform circular movement.



Fig. 1. An example of the rotor tip trajectory in the case of the rotor drift deceleration (the lacet type of the rotor motion). For the convenience, the trajectory is segregated into two pictures because some different parts of the trajectory overlap. Left side presents the rotor location at the moment t=979.87t.u. as well as the rotor tip trajectory within the term from t=100.00t.u to t=979.87t.u. Right side shows the part of the trajectory within the term from t=510.12t.u. to t=1510.12t.u.

Figure 1 demonstrates the lacet type of the rotor behavior with a=0.180. It is clearly evident from the picture that the distance between adjacent loops of the rotor tip trajectory decreased with time. After a time the rotor drift ceased, and then the rotor tip depicted a circle.

The results of the rotor drift deceleration are entirely identical for the media with size of 128x128 and 200x200. This reason excludes the supposition that the drift deceleration was caused by some boundary influence. The results were also repeated when the step of integration has been halved, that excludes the supposition that the drift deceleration was caused by the computing circuit.

We were successful in observing the lacet during the simulations with a>0.150, with the duration of the rotor behavior transformation into the uniform circular movement increasing monotonically with increasing the initial value of a.

With a < 0.150, the autowave turned from a planar half-wave to a rotor with its stable circular movement after two to three rotations.

With a>0.18035, we were not successful in observing either drift halt or any visual deceleration of the rotor drift during the time of observation. Figure 2 demonstrates two examples of the tip trajectories in the cases of a=0.190 and a=0.200.



Fig. 2. Examples of the rotor tip trajectory in the case of absence of visual deceleration of rotor drift (the case corresponds to the concept of the classical two-periodic meander). Left side presents the rotor location at the moment t=1213.18t.u. as well as a part of the rotor tip trajectory in the case of a=0.190. Right side shows the rotor location at the moment t=596.58t.u. and a part of the rotor tip trajectory in the case of a=0.200.

To solve a question whether the rotor motion with a>0.18035 occurs like the classical two-periodic meander or like the lacet, we determined to work out a quantitative description of the rotor drift velocity with different values of the parameter *a*.

In the following sections, the quantitative method of rotor motion description is depicted as well as the results of comparative investigation of the rotor drift velocity in the cases of the meander and of the lacet are presented.

3. APPROACH TO COMPUTING THE ROTOR DRIFT VELOCITY

For the trajectories obtained in this simulations in both cases, the meander and the lacet, the rotor 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 about some fixed center. To measure the velocity of the instant center, we evaluated the parameters of either circular movement (i.e., coordinates of the centers and the radiuses) utilizing the least-squares method (LSM). To reveal the fixed center we used the iterative procedure as following.

First, we chose an initial location of the fixed center. We sought the points of the trajectory in which the distance to the fixed center amounts to the local maximums. The envelope obtained in this manner was approximated with circumference by LSM, and the center of the circumference fitted was chosen as a location of the fixed center in the next step of iteration. The procedure was repeated until the location of the fixed center became steady.

After finding the location of the fixed center, every section of the trajectory between the adjacent local maximums of the distance to the fixed center was approximated with circumference by LSM. The center of this circumference was assumed to be the instant center

in the moment equal to average value of the time in which the rotor tip passed the corresponding section of the trajectory.

Using the location of the instant centers, we calculated the average speed of the instant center, which was assumed to be *the velocity magnitude of the rotor drift*.

4. COMPARISON OF ROTOR DRIFT AS MEANDER AND LACET

Figure 3 demonstrates dynamics of the rotor drift velocity in the cases of the meander and of the lacet. The velocity was calculated as it is described in Section 3 of this paper. In the case of the lacet (a=0.1803), the rotor made more than two rotations about the fixed center, performing approximately 50 rotations about the instant center, before it reached the final uniform circular movement. Note that no one would visually distinguish that rotor behavior from the two-periodic meander if the time of observation were less than about 2000 t.u.



Fig. 3. Comparison of dynamics of the rotor drift in the case of the meander (left side) and of the lacet (right side). Higher row of the graphs presents the dynamics of the space coordinates (x - blue line and y - red one). Lower row shoes the dynamics of the velocity magnitude of the rotor drift. All the graphs have the same scale for abscissa.

One should pay attention to an important difference in the rotor behavior in the case of the meander and of the lacet. In the case of the meander, the velocity magnitude of the rotor drift slightly increases verging towards some limiting value. In the case of the lacet, the velocity magnitude of the rotor drift is dramatically different. First it slightly decreases, then abruptly falls down and finally tends monotonically to zero. In other words, it is as if it were a spontaneous transformation of spiral wave behavior from the meander into the uniform circular rotation, with two phases of the drift deceleration being distinguished.

Therefore, this analysis of the instant center velocity enables one to distinguish the meander and the lacet types of rotor tip motion even in the case that the tip drift halt (in the case of the lacet) is not complete during the observation.

We suppose that the two-phase dynamics of the rotor drift deceleration in the case of the lacet is an interesting and important observation. But the cause of the effect stays incomprehensible.

5. APPROXIMATION OF DYNAMICS OF ROTOR DRIFT HALT IN THE CASE OF LACET

When the lacet occurred, we approximated the velocity magnitude of rotor drift by the function:

$$V(t) = V_0 \left(1 - \operatorname{th} \frac{t - \tau_1}{\tau_2} \right)$$
(2)

Here is used the least-squares method to obtain the values of τ_1 , τ_2 , V_0 . The parameter τ_I is the characteristic time of the first phase of rotor drift halt, which corresponds to the departure of rotor drift velocity from the pseudo-stationary value. And the parameter τ_2 is the characteristic time of the second phase of rotor drift halt, which corresponds to the fall of rotor drift velocity to zero.

Figure 4 shows an example of such approximation of the rotor drift velocity magnitude in the case of a=0.1803.



Fig. 4. Result of approximation of the velocity magnitude of rotor drift in the case of the lacet. Triangles show the velocities measured, the solid line is the approximation of these values by equation (2). The approximation performed by the application SigmaPlot.

6. DEPENDENCE OF CHARACTERISTIC TIMES OF ROTOR DRIFT HALT ON PARAMETER OF MODEL

We observed the lacet with different values of the parameter of the Aliev-Panfilov model, *a*, which controls the excitability of the medium. Both characteristic times, τ_1 and τ_2 , were measured for each case of our simulation when we observed the lacet. The results of the measurement were approximated with the following power dependence:

$$\tau_{1,2} = \frac{A}{(a_0 - a)^n}$$
(3)

The LSM is used to obtain the values of *A*, *n*, *a*₀. For τ_1 , the following values of the parameters in equation (3) were obtained:

 $A = 19 \pm 8,$ $n = 0.50 \pm 0.07,$ $a_0 = 0.18036 \pm 0.00007.$

For τ_2 , a similar procedure has given the following values of the parameters in equation (3):

 $A = 172 \pm 6,$ $n = 0.063 \pm 0.006,$

 $a_0 = 0.18038 \pm 0.00005.$

Fig 5 shows the measured values of τ_1 and τ_2 for different values of the *a* as well as the results of their approximation.



Fig. 5. Dependence of the characteristic times of the lacet drift halt, τ_1 and τ_2 , on the parameter of the Aliev-Panfilov model, *a*. Triangles show measured τ_1 and τ_2 , the solid lines are the approximations of these values by equation (3).

Note that, for either characteristic time, the value a_0 is the value of the model parameter a with which τ_1 or τ_2 tends to infinity. In other words, the lacet could be observed if $a < a_0$, while the classical two-periodic meander exists if $a > a_0$. One should pay attention for the fact that the values of a_0 are almost equal for τ_1 and τ_2 . Also one should note high accuracy of the measurement of the values.

7. CONCLUSION

It was shown in this work that the new type of the spiral wave behavior, which was discovered previously and named the *lacet* [5], have some essential differences from all type of the spiral wave behavior known before. The lacet is characterized by circular kind of the rotor drift with deceleration of the rotor drift velocity.

This work describes a method to compute the rotor drift velocity in the case, when the drift can be described as a superposition of two approximately circular motions. We measured the drift velocity in the case of different values of the model parameter a. Two-phase dynamics of the rotor drift deceleration in the case of the lacet was revealed, and the quantitative descriptions of the deceleration, a characteristic time of each phase of the rotor

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deceleration, was measured. The analysis of the instant center velocity is shown to enable one to distinguish the meander and the lacet types of rotor tip motion even in the case that the tip drift halt (in the case of the lacet) is not complete during the observation.

The lacet was observed in a sufficiently wide range of the parameter of the Aliev-Panfilov model a set as an initial condition. With increasing the initial value of a, each of the characteristic time increases monotonically and is power-behaved. They tend to infinity when the parameter approaches to some critical value. When the parameter a is set to a value higher than the critical value, the rotor behave as classical two-periodic meander.

Recently a phenomenon similar to the lacet was described in [10] for a simplest blood coagulation model consisted of a three-component set of differential equations of the reactiondiffusion type and observed in spatially one-dimensional systems. The authors of the paper indicated concluded that the origin of such transitional solutions of the system of differential equations was related to the so-called 'bifurcation memory'. It is interesting that, in all cases, the authors observed effects of 'bifurcation memory' only near those parts of the boundaries between parametric regions where bifurcation of merging occurred. It stays vaguely whether the observation is accidental or regular.

Though there is no general theory of active media yet, the available experience indicates that, once described, a new dynamic regime or bifurcation is thereafter found in other systems, even those that have been investigated for a long time. We suppose that the new type of rotor behavior that we found in one simple model of cardiac tissue, the Aliev-Panfilov model, is not unique, i.e. not specific for this model. Therefore it should be anticipated that the lacet will be find not only in classical and popular FitzHugh-Nagumo model, but also in realistic ionic models of myocardium such as described in [4, 11].

The disclosure of the lacet in the realistic models of cardiac tissue would be important, as lacet-like dynamics of an autowave can be critical in some cases of spontaneous transition from polymorphic to monomorphic arrhythmia [5]. Extending human knowledge about peculiar properties of cardiac arrhythmia will lead to more effective treatment of potentially life-threatening arrhythmia.

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REFERENCES

- 1. Biktashev V., Holden A., Nikolaev E. Spiral wave meander and symmetry of the plane. *Int. J. Bifurc. Chaos.* 1996. **6**(12A). 2433–2440.
- 2. Elkin Yu. Autowave processes. *Matematicheskaja biologija i bioinformatika*. 2006. **1**(1). 27-40. <u>http://www.matbio.org/downloads/Elkin2006(1_27).pdf</u> (in Russian)
- 3. Winfree A. Varieties of spiral wave behavior: An experimentalist's approach to the theory of excitable media. *Chaos.* 1991. **1**(3). 303-334.
- 4. Efimov I., Krinsky V., Jalife J. *Chaos, Solitons & Fractals*. Dynamics of rotating vortices in the Beeler-Reuter model of cardiac tissue. 1995. **5**(3/4). 513-526.
- 5. Moskalenko A., Elkin Yu. Is monomorphic arrhythmia monomorphic? *Biophysics*. 2007. **52**(2). 339-343.
- 6. Aliev R., Panfilov A. A simple two-variable model of cardiac excitation. *Chaos, Solitons & Fractals*. 1996. **7**(3). 293-301.
- Medvinsky A., Rusakov A., Moskalenko A., Fedorov M., Panfilov A. Autowave mechanisms of electrocardiographic variability during high-frequency arrhythmias: A study by mathematical modeling. *Biophysics*. 2003. 48(2). 297-305.
- Rusakov A. & Medvinsky A. Autowaves that Penetrate and then Circulate around an Array of Obstacles as a Mechanism of Arrhythmias in the Aging Heart. *Biophysics*. 2005. 50(1). 119-123.

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- 9. Application for simulation of the autowave processes, AWM, version 1.3 beta, *freeware*. http://www.maths.liv.ac.uk/~vadim/Elkin/AW/progs.htm
- 10. Ataullakhanov F., Lobanova E., Morozova O., Shnol' E., Ermakova E., Butylin A., Zaikin A. Intricate regimes of propagation of an excitation and self-organization in the blood clotting model. *Physics Uspekhi*. 2007. **50**(1). 89-94.
- 11. Noble D. Modelling the heart: from genes to cells to whole organ. *Science*. 2002. **295**. 1678-1682.

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