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Short communication

Origin of arrhythmias in a heart model

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ABSTRACT

An investigation of the nonlinear dynamics of a heart model is presented. The model compartmentalizes the heart into one part that beats autonomously (the x oscillator), representing the pacemaker or SA node, and a second part that beats only if excited by a signal originating outside itself (the y oscillator), representing typical cardiac tissue. Both oscillators are modeled by piecewise linear differential equations representing relaxation oscillators in which the fast time portion of the cycle is modeled by a jump. The model assumes that the x oscillator drives the y oscillator with coupling constant α. As α decreases, the regular behavior of y oscillator deteriorates, and is found to go through a series of bifurcations. The irregular behavior is characterized as involving a large amplitude cycle followed by a number n of small amplitude cycles. We compute critical bifurcation values of the coupling constant, α_n, using both numerical methods as well as perturbations.

1. Introduction

It is well known that heart arrhythmias are often characterized by an arterial pulse which consists of alternating strong and weak beats called alternans. Electrical alternans of the heart, defined as beat to beat variability in electrocardiogram (ECG) signal, have been associated with ventricular arrhythmias in many clinical settings [2]. In particular, a recent study has showed that alternans affecting the T-wave is common among patients at increased risk for ventricular arrhythmias [2], where the T-wave is the component of ECG associated with the repolarization phase of action potentials of the ventricular cells [1]. Ventricular heart cells are of the excitable type that possess an equilibrium membrane potential and will normally only fire upon receiving a strong enough electric signal. This signal is generated by the autonomously firing cells of the sinoatrial (SA) node, known as the pacemaker, and conducted to the ventricals through cardiac tissue.

The idea of this work is to model the heart as two oscillators, one for the SA node (call it x) and one for the rest of the heart (call it y), which could represent excitable ventricular cells. The x oscillator is modeled as beating autonomously when uncoupled from the y oscillator, while the y oscillator is modeled as not beating at all, but rather as staying fixed in an equilibrium position, when uncoupled from the x oscillator. Our goal is to describe the bifurcation sequence which occurs as the coupling constants vary.

The oscillators are modeled as relaxation oscillators with instantaneous jumps. This model of relaxation oscillators has been used previously in a model of a forced oscillator [3], two coupled limit cycle oscillators [4] and three coupled limit cycle oscillators [5].

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2. The uncoupled oscillators

The oscillators are modeled as relaxation oscillators with instantaneous jumps. Specifically we say that when x decreases to 1 it instantaneously jumps to -2, and when it increases to -1 it jumps to +2. Same goes for y.

The x oscillator is modeled by

$$\dot{x} = -\frac{x}{2} \quad \text{plus jumps from} -1 \text{ to } +2 \text{ and from } +1 \text{ to } -2 \tag{1}$$

The y oscillator is modeled by

$$\dot{y} = \begin{cases} -\frac{y}{2} & \text{for } y > 0 \\ -\frac{y}{2} - \frac{3}{4} & \text{for } y < 0 \end{cases} \quad \text{plus jumps from } -1 \text{ to } +2 \text{ and from } +1 \text{ to } -2 \tag{2}$$

Note that the y oscillator has a stable equilibrium point at $y = -3/2$.

3. Coupling

We seek to study the simplest possible model which captures the essential phenomenon of arrhythmia. For this model we assume that the coupling is one-way: the x oscillator forces the y oscillator, but not vice-versa. Thus the x oscillator still satisfies Eq. (1), whereas the y oscillator satisfies the equations:

$$\dot{y} = \begin{cases} -\frac{y}{2} + \alpha x & \text{for } y > 0 \\ -\frac{y}{2} - \frac{3}{4} + \alpha x & \text{for } y < 0 \end{cases} \quad \text{plus jumps from } -1 \text{ to } +2 \text{ and from } +1 \text{ to } -2 \tag{3}$$

where $\alpha > 0$ is a coupling parameter.

4. Behavior of the coupled system

For large enough α, the x oscillator entrains the y oscillator and y undergoes a series of "large oscillations", defined as motions which involve jumps from both -1 to +2 and from +1 to -2.

For small enough α, the x oscillator has small effect on the y oscillator, which undergoes a series of "small oscillations", defined as motions which do not involve any jumps. These may be thought of as vibrations about the equilibrium position $y = -3/2$.

We may abbreviate these limiting cases by the notation:

$$\begin{array}{ll} L, L, L, L, \ldots & \text{large enough } \alpha \\ S, S, S, S, \ldots & \text{small enough } \alpha \end{array}$$

where L stands for one cycle of large oscillations and S stand for one cycle of small oscillations.

Numerical integration shows that as α decreases we see a sequence of bifurcations which may be abbreviated as follows:

$$\begin{array}{ll} \alpha > \alpha_0 & L, L, L, L, L, \ldots \\ \alpha_0 > \alpha > \alpha_1 & L, S, L, S, L, S, \ldots \\ \alpha_1 > \alpha > \alpha_2 & L, S, S, L, S, S, L, S, S, \ldots \\ \alpha_2 > \alpha > \alpha_3 & L, S, S, S, L, S, S, S, L, S, S, S \ldots \\ & \ldots \\ \alpha_{n-1} > \alpha > \alpha_n & L, S, \ldots, S, L, S, \ldots, S, L, S, \ldots, S, \ldots \\ & (\text{where } S, \ldots, S \text{ stands for a string of } n\ S\text{'s}) \\ \alpha_\infty > \alpha > 0 & S, S, S, S, S, S, \ldots \end{array}$$

we will denote such sequences by L^s, for example, 1^3 corresponds to 1 large oscillation followed by 3 small oscillations [6].

We desire values for the bifurcation points α_n, $n = 0, 1, 2, 3, \ldots$ We start by finding the value of α_∞, see Fig. 1. Note that the motion of the x oscillator is not affected by the motion of the y oscillator, nor by the value of the parameter α. Assuming a jump from $x = -1$ to $x = +2$ has just occurred at $t = 0^-$, we have the initial condition $x(0) = 2$. Then one cycle of the x motion turns out to be given by

$$x(t) = \begin{cases} 2e^{-t/2}, & 0 < t < 2\ln 2 \\ -4e^{-t/2}, & 2\ln 2 < t < 4\ln 2 \end{cases} \tag{4}$$

The period of the x motion is $4\ln 2$. At time $t_1 = 2\ln 2$ the x motion jumps from +1 to -2. At time $t_2 = 4\ln 2$ the x motion jumps from -1 to +2.

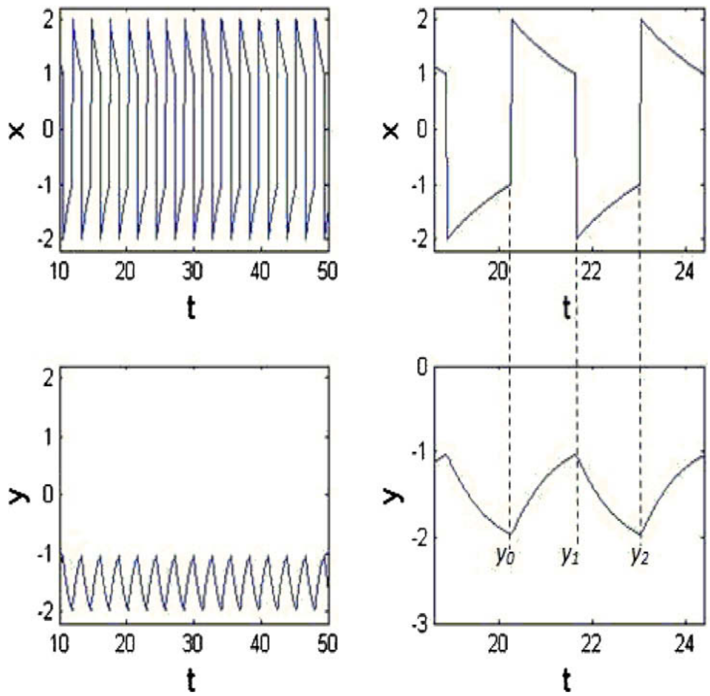

Fig. 1. Computation of α_∞. Plot corresponds to $\alpha = 0.5$. The right half of this Figure is an enlargement of the left half.

Starting at $t = 0$ with x given by Eq. (4), y is governed by the following:

$$\dot{y} = -\frac{y}{2} - \frac{3}{4} + 2\alpha e^{-t/2} \Rightarrow y = -\frac{3}{2} + e^{-t/2}\left(y_0 + \frac{3}{2} + 2\alpha t\right) \tag{5}$$

From (5) we find an expression for y_1 at $t_1 = 2\ln 2$ which is the time when x jumps from $+1$ to -2:

$$y_1 = \frac{y_0}{2} + 2\alpha \ln 2 - \frac{3}{4} \tag{6}$$

During the interval $t_1 < t < t_2 = 4\ln 2,\ y$ is governed by the following:

$$\dot{y} = -\frac{y}{2} - \frac{3}{4} - 4\alpha e^{-t/2} \Rightarrow y = -\frac{3}{2} + e^{-t/2}(2y_1 + 3 - 4\alpha t + 8\alpha \log 2) \tag{7}$$

and y_2, the value of y at $t_2 = 4\ln 2$, the time when x jumps from -1 to $+2$, is given by:

$$y_2 = \frac{y_1}{2} - 2\alpha \ln 2 - \frac{3}{4} \tag{8}$$

Combining (6) and (8), we obtain

$$y_2 = f(y_0), \quad \text{where } f(y_0) = \frac{y_0}{4} - \alpha \ln 2 - \frac{9}{8} \tag{9}$$

For periodic small oscillations, we have $y_2 = y_0$, in which case Eq. (9) gives

$$y_0 = f(y_0) \Rightarrow y_0 = -\frac{3}{2} - \frac{4}{3}\alpha \log 2 \tag{10}$$

Now at the point of transition from small oscillations to a large spike, $y_2 = y_0 = -2$. The corresponding value of α is α_∞:

$$\alpha_\infty = \frac{3}{8\ln(2)} \approx 0.541 \tag{11}$$

Note that this value of α with $y_0 = -2$ corresponds to $y_1 = -1$ from Eq. (6).

Next we compute the value of α_n. Consider the 1^n periodic motion shown in Figs. 2 and 3. It begins with n small oscillation cycles followed by one large oscillation cycle.

The small cycles are characterized by y_k, being values of y at the x jump times $t_k = 2k\ln 2$, that is $y_k = y(2k\ln 2)$. Each of these is governed by equations similar to (6), (8) so that we obtain, using the notation of Eq. (9)

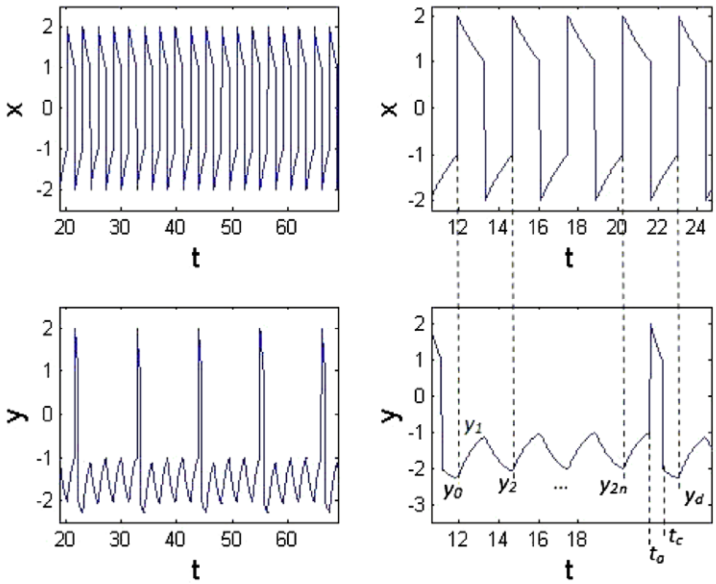

Fig. 2. Computation of α_n. Plot corresponds to $\alpha = 0.548$. The right half of this Figure is an enlargement of the left half.

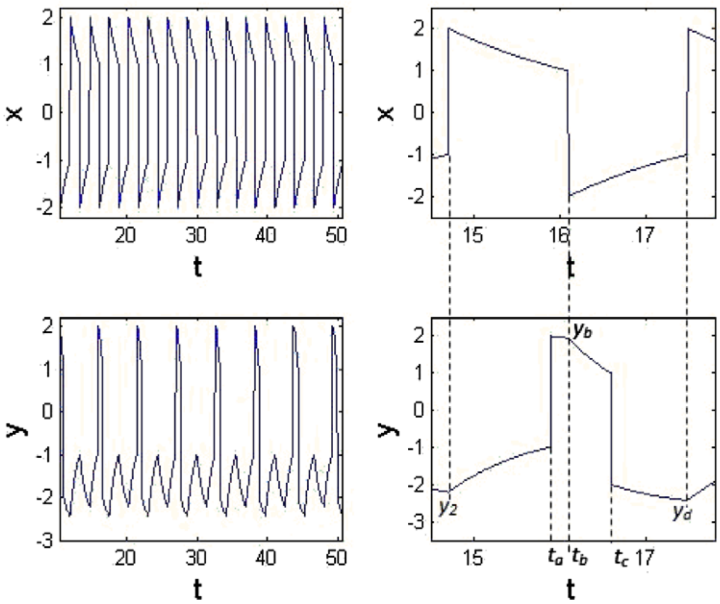

Fig. 3. Computation of α_n. Plot corresponds to $\alpha = 0.680$. The right half of this Figure is an enlargement of the left half.

$$y_2 = f(y_0) \tag{12}$$

$$y_4 = f(y_2) = f(f(y_0)) \tag{13}$$

$$\ldots$$

$$y_{2n} = f^{(n)}(y_0) \tag{14}$$

In order to compute a value for $f^{(n)}(y_0)$ we write $f(y_0)$ in the simplified form (cf. Eq. (9)):

$$f(y_0) = ky_0 - \lambda, \quad \text{where } k = \frac{1}{4}, \quad \lambda = \alpha \ln 2 + \frac{9}{8} \tag{15}$$

Then we find

$$f(f(y_0)) = kf(y_0) - \lambda = k(ky_0 - \lambda) - \lambda = k^2 y_0 - \lambda(k+1) \quad (16)$$
$$f^{(3)}(y_0) = k^3 y_0 - \lambda(k^2 + k + 1) \quad (17)$$
$$\cdots$$
$$f^{(n)}(y_0) = k^n y_0 - \lambda(k^{n-1} + k^{n-2} + \cdots + k + 1) \quad (18)$$
$$= k^n y_0 - \lambda \frac{(k^n - 1)}{k - 1} \quad (19)$$

From Eqs. (19), (14), (15) we obtain

$$y_0 = \beta_1 y_{2n} + \beta_2 + \beta_3 \alpha \ln 2 \quad (20)$$

where

$$\beta_1 = 4^n, \quad \beta_2 = \frac{3}{2}(4^n - 1), \quad \beta_3 = \frac{4}{3}(4^n - 1) \quad (21)$$

Following this sequence of n small oscillation cycles there is a single large oscillation cycle which consists of:

(a) growth of y from y_{2n} to -1 at time $4n \ln 2 + t_a$, followed by a jump to $y = +2$. Then,
(b) decay from $y = 2$ to y_b at time $(4n + 2) \ln 2$. Then,
(c) decay from y_b to $y = 1$ at time $4n \ln 2 + t_c$, followed by a jump to $y = -2$. Then,
(d) growth to y_d at time $(4n + 4) \ln 2$. Here $y_d = y_0$ for a periodic motion.

The four quantities t_a, y_b, t_c and y_d satisfy the following equations:

$$y_{2n} = \frac{e^{t_a/2}}{2} - 2\alpha t_a - \frac{3}{2} \quad (22)$$
$$y_b = e^{t_a/2} - \alpha t_a + 2\alpha \ln 2 \quad (23)$$
$$y_b = \frac{e^{t_c/2}}{2} + 2\alpha t_c - 4\alpha \ln 2 \quad (24)$$
$$y_d = -\frac{e^{t_c/2}}{8} + \alpha t_c - 4\alpha \ln 2 - \frac{3}{2} \quad (25)$$

Now Eqs. (14), (22)–(25), plus the periodicity condition $y_d = y_0$, represent six equations in the six unknowns $y_0, y_{2n}, t_a, y_b, t_c$ and y_d. We handle these as follows. First we eliminate the exponential terms in Eqs. (22)–(25), respectively, to obtain:

$$t_a = \frac{1}{3\alpha}[y_b - 2y_{2n} - 2\alpha \ln 2] - \frac{1}{\alpha} \quad (26)$$
$$t_c = \frac{1}{6\alpha}[y_b + 4y_d + 20\alpha \ln 2] + \frac{1}{\alpha} \quad (27)$$

Now if (26) and (27) are substituted into (22) and (24) using $y_d = y_0$ and (20), we obtain two equations in the two unknowns y_{2n} and y_b. The resulting two equations can be treated numerically using Newton–Raphson methods for given α. By varying α we obtain the bifurcation values α_n, see Table 1.

In addition, and as a check, we present a perturbation solution. We set:

$$\alpha_n = \alpha_\infty + \epsilon = \frac{3}{8 \ln 2} + \epsilon \quad (28)$$
$$y_{2n} = -2 + \mu\epsilon \quad (29)$$

Table 1
Values of α_n obtained by Newton–Raphson methods and by perturbations.

n	Newton–Raphson	Perturbations
1	0.577	0.575382
2	0.5499	0.549603
3	0.5432	0.543158
4	0.5416	0.541547
5	0.54115	0.541144
6	0.54105	0.541044
7	0.54103	0.541018
8	0.54102	0.541012

with the additional knowledge that $y_b = 2$ at the point of transition from one 1^n state to another. The result is two equations in the two unknowns ϵ and μ. We then approximate each of these two equations by a first order Taylor series about $\epsilon = 0$, and solve for ϵ and μ. This results in the following approximate expression for the values of α_n at the bifurcation points:

$$\alpha_n = \frac{3}{8\log 2} + \frac{27\left(2^{2/3}-1\right)}{8\log 2\left(\left(82^{2/3}\log 2+12\right)4^n + 42^{2/3}\log 2 - 3\right)} + \cdots \tag{30}$$

For large n this may be approximated by the simpler expression:

$$\alpha_n = \frac{3}{8\log 2} + \frac{27\left(2^{2/3}-1\right)}{8\log 2\left(\left(82^{2/3}\log 2+12\right)4^n\right)} + \cdots \tag{31}$$

which may be written in the numerical form:

$$\alpha_n = 0.541010640 + \frac{0.137489383}{4^n} + \cdots \tag{32}$$

As shown in Table 1, this approximation gives excellent agreement with the previously obtained numerical results.

To obtain an approximation for α_0, we base a calculation on Fig. 4, which corresponds to $\alpha = \alpha_0$.

In region I, we have the ODE

$$\dot{y} = -\frac{y}{2} - \frac{3}{4} + 2\alpha_0 e^{-t/2} \tag{33}$$

with the side conditions

$$y = y_0, \quad t = 0 \quad \text{and} \quad y = -1, \quad t = 2\ln 2 \tag{34}$$

which gives

$$y_0 = -\frac{1}{2} - 4\alpha_0 \ln 2 \tag{35}$$

In region II, we have the ODE

$$\dot{y} = -\frac{y}{2} - 4\alpha_0 e^{-t/2} \tag{36}$$

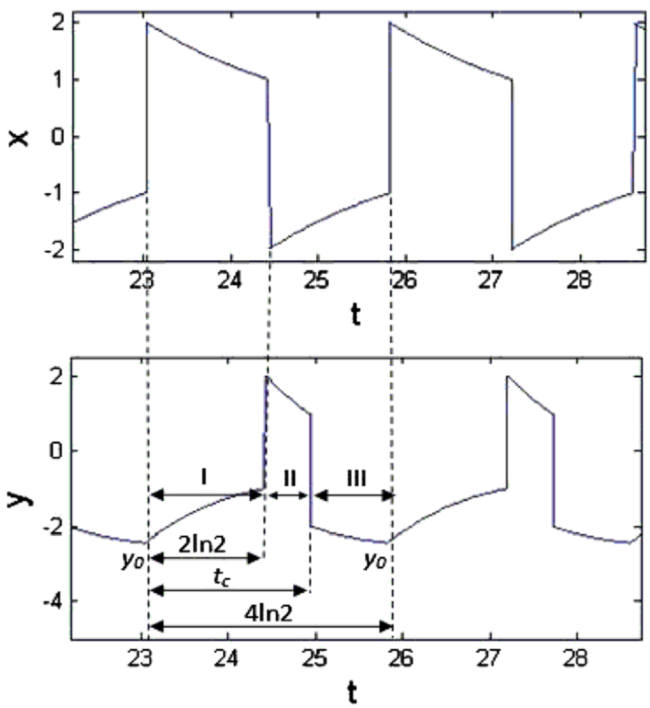

Fig. 4. Computation of α_0. Plot corresponds to $\alpha = 0.710$.

with the side conditions

$$y = 2, \quad t = 2\ln 2 \quad \text{and} \quad y = 1, \quad t = t_c \tag{37}$$

which gives

$$\alpha_0 = \frac{4 - e^{t_c/2}}{4t_c - 8\ln 2} \tag{38}$$

In region III, we have the ODE

$$\dot{y} = -\frac{y}{2} - \frac{3}{4} - 4\alpha_0 e^{-t/2} \tag{39}$$

with the side conditions

$$y = -2, \quad t = t_c \quad \text{and} \quad y = y_0, \quad t = 4\ln 2 \tag{40}$$

which gives

$$y_0 = -\frac{3}{2} - 4\alpha_0 \ln 2 + \alpha_0 t_c - \frac{e^{t_c/2}}{8} \tag{41}$$

Eqs. (35) and (41) together give

$$\alpha_0 = \frac{8 + e^{t_c/2}}{8t_c} \tag{42}$$

Eqs. (42) and (38) give:

$$e^{t_c/2} = \frac{16\ln 2}{3t_c - 2\ln 2} \tag{43}$$

Substituting (43) into (42) permits one to solve for t_c:

$$t_c = \frac{3 + 2\alpha_0 \ln 2}{3\alpha_0} \tag{44}$$

Finally, substituting (44) into (42) gives the following equation on α_0:

$$\frac{1}{2\alpha_0} - \ln \alpha_0 = \ln 2 + \ln\frac{16}{3} - \frac{1}{3}\ln 2 \tag{45}$$

Application of Newton–Raphson to Eq. (45) gives $\alpha_0 \approx 0.69778$.

5. Conclusion

This work has investigated the nonlinear dynamics of a heart model that compartmentalizes the pacemaker or SA node, and a second part that beats only if excited by a signal originating outside itself (the y oscillator), representing typical cardiac tissue. The model assumes that the x oscillator drivesheart into one part that beats autonomously (the x oscillator), representing the y oscillator with coupling constant α. As α decreases, the regular behavior of y oscillator deteriorates, and is found to go through a series of bifurcations. The irregular behavior can be characterized as involving a large amplitude cycle followed by a number n of small amplitude cycles, a behavior designated 1^n after [6]. We obtained the critical bifurcation values of the coupling constant, α_n, using both numerical methods as well as perturbations.

The model's behavior is interesting for what it does *not* contain, namely periodic motions of the form L^n. For example, these motions (which do not occur in the present model) would involve a sequence of L large amplitude cycles followed by n small amplitude cycles. By contrast, in the present model we see only periodic motions of the form 1^n.

The importance of this work lies in the simplicity of the model. Thus although we have omitted nearly every anatomical and physiological feature of the heart, we nevertheless see the kind of arrhythmicities which occur in mammalian hearts, and which represent illness in humans. Thus we may conclude that one source of arrhythmatic alternans, which through bifurcation lead to deadly ventricular fibrillation, lies in the relative ineffectiveness of the pacemaker cells, represented by a decrease in coupling constant α in the model.

Extensions of this work could include additional y oscillators representing the spatial distribution of cardiac cells. It is expected that such a model would exhibit spatial dependence of the various periodic motions. In real hearts such motions have been identified with spiral waves and ectopic heartbeat.

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