Relaxation oscillations in the atrium - a model

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Abstract— A one dimensional model of the atrium together with the sinoatrial node and the atrioventricular node is presented. The two nodes are each modeled by 15 element, diffusively coupled modified van der Pol oscillator chains while the atrium tissue is represented by a 90 element chain of diffusively coupled FitzHugh-Nagumo equations. The modified van der Pol oscillators are able to reproduce physiologically important properties such as the refractor period, modes of action potential frequency change and phase sensitivity. The activity of both branches of the autonomous nervous system may be introduced into the model in a simplified way. The model enables the study of the effect of the magnitude of the action potential conduction rate in the nodes on interspike intervals (equivalent of RR intervals) and explains the occurrence of RR interval alternans in certain patients. The effect of breathing modulation of heart rate and of a single deep breath can also be modeled. Finally, concealed conduction effects in the atrium are studied.

I. INTRODUCTION

Recently, a modified relaxation oscillator with a Duffing term was developed as a model of the sino-atrial (SA) and the atrio-ventricular (AV) nodes of the heart [1]-[3]. The properties of the modified relaxation oscillator are an interplay of a limit cycle with a hyperbolic saddle and a stable node. In effect the refractory period and the nonlinear phase sensitivity of the action potential of nodal cells were reproduced correctly. This allows to obtain several phenomena observable in animal experiments and in clinical setting. Even such a complex phenomenon as the vagal paradox [3]-[5], in which the effects of the activity of the sympathetic and parasympathetic branches of the autonomous nervous system have to be included, may be obtained from the modified relaxation model of the AV node.

Here, we present a one dimensional model of the atrium with both the SA and AV nodes included. These nodes were approximated by a 1-D chain of diffusively coupled modified relaxation oscillators [3]. The atrial muscle was modeled using a chain of modified FitzHugh-Nagumo (FHN) equations [6]. The FHN model captures the key features of excitable media and is widely used as a simple model of cardiac muscle electrical activity. The complete model consists of three segments: the SA node (15 elements), the atrial muscle (90 elements) and the AV node (15 elements) coupled diffusively at the interfaces and was solved numerically using the Euler method. Since the activation variables in the models of the nodes (on the one hand) and in the model of the atrium (on the other hand) had different ranges of variability, a normalization should be performed at the interfaces between them. Linear transformations were applied to the activation variable in the diffusion coupling part of the equations so that the variables of both systems have the same minimum and maximum values. The model is dimensionless but the parameters were set in such a way that the period of the oscillations was numerically of the order of the length of RR intervals in human heart rate variability recordings. The interspike intervals (ISI) of the calculated action potentials of the AV node of our model were compared with RR intervals obtained from selected 24-h Holter recordings of patients of the Institute of Cardiology at Warszawa.

II. MODEL OF THE ATRIUM

We divided our model of the atrium into three parts. For the SA and the AV nodes we used the following modified van der Pol oscillator [1]-[3]:

\[
\frac{d^2x}{dt^2} + \alpha(x-v_1)(x-v_2) \frac{dx}{dt} + f(x(x+d)(x+e) = 0
\]

\[\epsilon, d > 0, \quad v_1 > 0, v_2 < 0\]

where we set \(\alpha = 5, \quad d = 3, \quad v_1 = 1, \quad v_2 = -1, \quad \text{and} \quad f = 3\). To model the SA node we used \(\epsilon = 12\) and to model the AV node: \(\epsilon = 7\) in this way setting the proper physiological ratio of the intrinsic frequencies of the two nodes. The phase space of the oscillator (1) contains an unstable focus \(F\) at \(x = 0\), a hyperbolic saddle \(S\) at \(x = -d\), a stable node \(N\) at \(x = -e\) situated along the x-axis and a limit cycle (Fig.1).

![Fig. 1. Schematic of the phase space of the modified van der Pol oscillator. Symbol N – stable node, S – hyperbolic saddle, F - unstable focus](image)

The SA and AV nodes were approximated by a 1-D chain of diffusively coupled oscillators each described by (1). The atrial muscle was modeled using a modified 1-D FitzHugh-Nagumo (FHN) model. The FHN model captures the key
features of excitable media and is widely used as a simple model of cardiac muscle electrical activity [6]. The equations of the discretized FHN model are:

\[
\begin{align*}
\frac{dv_i}{dt} &= \frac{1}{\mu} (v_i - \frac{1}{3} v_i^3 - u_i) + D_i (v_{i+1} + v_{i-1} - 2v_i) \\
\frac{du_i}{dt} &= \mu (v_i + \beta - \gamma u_i)
\end{align*}
\]  

(2)

where \(v_i\) is the activation variable (basically equivalent to the action potential of the element \(i\)), \(u_i\) is the total slow current at that element, \(\beta = 0.7\), \(\gamma = 0.5\), \(\mu = 0.3\). The diffusion coupling coefficient \(D_i\) was set to values between 10 and 60.

The complete one dimensional model of the atrium consists of three segments: the SA node (15 diffusively coupled elements each containing the oscillator (1)); the atrial muscle (90 elements each described by (2)) and the AV node (15 elements as in the SA node but with a different value of the parameter \(e\)) coupled diffusively at the interfaces [3].

Linear transformations were applied to the activation variable in the diffusion coupling part of the equations so that the variables of both (1) and (2) attained the same minimum and maximum values. For example, the coupling term acting at an element of the interface on the SA side was:

\[
\text{coupling term} = D_{sa} (v^{SA}_{i+1} - v^{SA}_i) + D_{sa-a} (v^* - v^{SA}_i)
\]

\[
v^* = \frac{x^{KG}}{x^{KG}} (v^{FHN}_{i+1} - v^{FHN}_i) + x^{KG}_{min}
\]

where \(D_{sa} = 60\) and \(D_{sa-a} = 10\) are the diffusion coupling coefficient at the SA node and the SA-atrium muscle interface, respectively. The index \(i\) marks the position of an element in the simulation grid. \(v^*\) is the activation variable on the atrial side of the system. It is transformed linearly to fit the range of potentials within the node. Parameters \(x^{KG}_{max} = 1.56\), \(x^{KG}_{min} = -2.4\), \(v^{FHN}_{max} = 1.8\), \(v^{FHN}_{min} = -2.03\) are the extrema of the activation variables in both systems assessed numerically with the diffusion coupling set to zero. An analogical coupling method was used at atria-AV node interface.

The Euler integration scheme was used with a time step \(\Delta t = 0.0001\). We assumed zero-flux boundary conditions to minimize the effect of the chain ends. Note that following [6], we set the parameters of the FitzHugh-Nagumo equations in such a way as to provide a physiologically plausible time scale of the action potential duration.

### III. RESULTS

The structure of the phase space (Fig. 1) seems to be the minimum one which allows to model several properties of the conduction system of the heart observed experimentally. In particular, the model (1) is able to change its frequency in two out of three modes observed in the human heart: through a change of the spontaneous depolarization rate and through a change of the resting potential [3]. The period of oscillations saturates as the node moves away from the limit cycle; in our model this is due to a change of the parameter \(e\) which in this way may be associated with sympathetic activity [3]. Because the phase response curve of the oscillator (1) is highly nonlinear [3], a regular square wave drive results in an irregular response with an average period lower than the spontaneous one. This simulates how the vagal branch of the autonomous nervous system modulates the heart rate. The association of the properties of the model with the activity of both branches of the autonomous system allowed reproducing the vagal paradox [3]. From the point of view of the 1-D model of the atrium discussed here, the most important is the genesis of the refractory period obtained for (1) (note that the van der Pol equation does not exhibit a refractory period). The insensitivity of (1) to external perturbation (i.e. the refractory behaviour) occurs when the state point passes by the saddle point (Fig. 2).

![Fig. 2 The potential x(t) of (1) (part a) and the corresponding limit cycle (part b). y denotes the current variable.](image)

When the parameters of SA node and of the AV node are identical, then the specific set of these parameters used here yields a metronomic behavior of the model with a period of about 900 which corresponds to the limit cycle in Fig. 2. When the saddle in the AV node part of the model was shifted slightly closer to the limit cycle \((d = 2.88\) instead of 3.0), the trajectory took more time to pass by the saddle point which extended the refractory time in this area of the model. Effectively, this models a slower conduction rate of the AV node. The asymmetry of the nodes resulted in an alternans of the interspike intervals (ISI) period-2 orbit in phase space (Fig. 3).

![Fig. 3 Period-2 limit cycle induced by an asymmetry of the SA and AV node conduction.](image)

The interspike intervals which were obtained from the period-2 behavior (left panel of Fig. 4) can be compared with an RR interval alternans which was obtained in the heart rate variability of a hypertrophic cardiomyopathy patient (right panel of Fig. 4) in the early morning hours. The patient had only sinus rhythm and no arrhythmia. Note that the RR...
interval alternans exhibits an additional, irregular modulation which is missing in the precisely periodic results of the model.

The average frequency of this modulation was estimated from the heart rate variability recording and found to be about 0.008 Hz which is possibly due to slow breathing. We then added a sinusoidal modulation term with this frequency with an amplitude of 0.15 to the each element of the SA node in our model. The phase portrait for the AV node is shown in Fig. 5 while the ISI interval alternans is depicted in Fig. 6. It can be seen that the result now resembles the RR interval alternans depicted in Fig. 4.

In the same heart rate variability recording, but just a few minutes later, an abrupt, short time decrease of the heart rate was obtained (right panel of Fig. 7). A similar behavior of the model was obtained when the amplitude of the modulation was increased to 0.3 (left panel in Fig. 7). In the model, a functional block occurs so that the ISI at the maxima corresponds to the natural frequency of the AV node which is, of course, lower than that of the SA node (i.e. in effect this is an escape beat). Note that, in the model, the modulation amplitude is constant while the single rapid decrease of the heart rate visible in the right panel of Fig. 7 may be explained as the result of a single deep breath. Every person once in a while takes a single, deep breath – a well known physiological effect.

Another group of results obtained is related to concealed conduction effects in the atrium [7]. As mentioned above, our model of the atrium with symmetric node properties and without a breathing modulation yields a series of constant ISI. We added a single ectopic source within the atrium and studied the effect of its location with respect to the nodes and of its frequency. The ectopic source was modeled by an additional activation of a single site in the model for only two time steps. A variety of complex rhythms resulted – including escape beats and escape rhythm.

The escape sequences was not due to a modification of the AV node properties but resulted from the interaction of the ectopic wave passing through the atrium with both the SA node and the AV node. Some of ISI rhythms obtained in this way were directly comparable with heart rate variability found in different patients. In particular, the assumption of a supraventricular ectopy with a specific ratio of its frequency to the average heart rate (30%) and a specific location (midway) was able to explain a curious feature of heart rhythm in a patient with very low heart rate variability and no noted supraventricular or ventricular arrhythmia in this part of the ECG (Fig. 8).

It can be seen in part a) of Fig. 8 that once a certain time the heart rate would decrease for a single beat and then sharply increase only to relax back to the average value. The effect occurred more often in the calculation then it did in the actual heart rate variability recording but the essential
features are recognizable in both tachograms in Fig. 8. Note
that this behavior is exactly opposite to what happens when
ventricular arrhythmia occurs.

Finally, we found that an ectopic source located closer to
the SA node (but not directly by it) has a much stronger
effect on the ISI pattern obtained than a source close to the
AV node.

IV. CONCLUSION

We combined a model of the SA and AV nodes of the
heart consisting of two modified van der Pol oscillators with
a one dimensional model of the atrium simulated by a chain
of FitzHugh-Nagumo equations. All elements of the model
were coupled diffusively. Our simple model allows to relate
the local dynamics of the activation wave in the atrium with
the RR intervals found in clinical heart rate recordings. In
particular, the model of the atrium recreates the effect of
breathing modulation which, in reality, is mediated by the
vagal nerve. We showed also that a slower conduction rate
through the AV node may lead to RR interval alternans.

We studied the effect of concealed conduction in the
atrium. When an ectopic source within the atrium is small or
very weak it may not be visible in the ECG. However, such
an ectopic source may still affect heart rate variability. We
studied the effect of such an ectopic source depending on its
frequency and location between the nodes. We were able to
explain unusual oscillations or short perturbations of the
heart rate of several patients. Our study shows that the effect
of concealed conduction is stronger when the source is
located near the SA node rather then the AV node.

The main advantage of our approach is that the kind of
information yielded by our model is very difficult to measure
given the current limitations of clinical and experimental
electrophysiology. The knowledge gained through the study
of our model should allow to enhance the diagnosis of both
heart rate variability and of pathology of conduction within
the atrium.

ACKNOWLEDGMENT

This paper as a project of the ESF Programme "Stochastic
Dynamics: fundamentals and applications (STOCHDYN)"
was supported by Polish Ministry of Science and Higher
Education, Grant No. ESF/275/2006.

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