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STOCHASTIC MODELS OF THE SLOW/FAST TYPE OF ATRIOVENTRICULAR NODAL REENTRANT TACHYCARDIA AND TACHYCARDIA WITH CONDUCTION ABERRATION

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Models are proposed to describe the heart's action potential. A system of stochastic differential equations is used to recreate pathological behaviour in the heart such as atrioventricular nodal reentrant tachycardia (AVNRT) and also AVNRT with conduction aberration. Part of the population has abnormal accessory pathways: fast and slow. An additional pathway is not always induced, since the deterministic model is not proper due to a stochasticity in this process. Introduction of a stochastic term allows modelling a pre-excitation perturbation (such as unexpected excitation by premature contractions in atrium (PAC)) which triggers the mechanism of AVNRT. Also, a system of AVNRT with additional conduction aberration, which is a rare type of arrhythmia, is considered. The aim of this work is to propose a mathematical model superior to the deterministic one that recreates this disease better and allows understanding its mechanism and physical dependencies, which may help to propose a new therapy of AVNRT. Results are illustrated with numerical solutions.

Keywords: mathematical model, stochastic differential equations, action potential, atrioventricular nodal reentrant tachycardia, conduction aberration.

1. Introduction

Heart diseases are one of the leading causes of death worldwide, especially conduction diseases, which can lead to heart failure, such as supraventricular tachycardia. In the face of the coronavirus epidemic, patients with heart failure are at high risk. The data show that the highest risk of death among COVID-19 patients who have other conditions exists in the group of people with cardiovascular diseases (Downing *et al.*, 2022). This is why early diagnosis and appropriate treatment of cardiovascular diseases is so important. However, in the case of arrhythmias, such as atrioventricular nodal reentrant tachycardia (AVNRT), this is difficult. Although AVNRT is the most common regular arrhythmia, affecting 25/1000 adults and accounting for 50–60% of all regular arrhythmias of the heart (Małaczyńska-Rajpold *et al.*, 2012), it is not fully understood. For almost 60 years we have known that the atrioventricular node has complex structure where we have more conductivity pathways which can be classified as fast or slow; see Fig. 1.

The first pathway is built of α fibers characterized by slow conduction and a short refractory period, and the second pathway is built of the β fiber, with faster conduction and a longer refractory period. Such a system makes it possible to develop AVNRT. Necessary for its establishment is the trigger, which is usually premature atrial excitation. Electrophysiological evidence for the existence of two pathways with different conduction and refractive times is the presence of the features of two pathways through the AV node. It is present in the cardiac electrophysiology study (EP study) as a *jump* in the stimulation of the AV conduction curve (Małaczyńska-Rajpold *et al.*, 2012).

Although we try to understand the mechanism of this arrhythmia using an invasive method of therapy, we do not know the exact anatomy and physiology of this structure. What do we know? This arrhythmia is caused by reentry. It is a type of a supraventricular tachycardia (SVT) and appears above a His bundle (an element conducting an impulse from the atrioventricular node to the interventricular septum and further to the ventricular muscle). This tachycardia is paroxysmal and

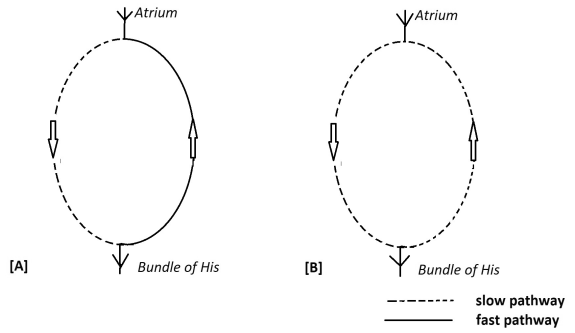

Fig. 1. Sketch of a typical location of slow/fast AVNRT (a), uncommon form of AVNRT: slow/slow (b).

rarely occurs for a long time. But when it lasts longer it can lead to heart failure.

We can distinguish different forms of AVNRT:

- typical (common form, called slow/fast)—about 77% of all AVNRT,
- atypical (uncommon form, also called fast/slow)—about 12% all of AVNRT,
- other forms of AV nodal reentrant arrhythmias (slow/slow type)—11%; we have three types of slow/slow AVNRT depending on where the slow pathway is located, which is reflected by the descending branch of the reentry loop, or more than two reentry waves, etc. (Mani and Pavri, 2014; Katrisis and Josephson, 2016; Kaneko *et al*., 2020).

These types depend on the location of the atrial deflection between consecutive QRS complexes. For simplicity we employ the combination of the Q, R and S waves (QRS complex) that represents ventricular depolarization. The form of AVNRT depends on the multilevel architecture of the atrioventricular node. The AVNRT circuit involves larger areas including the atrioventricular junction, adjacent atrial structures and, in particular, so-called atrial inputs, including at least anterior-superior and postero-inferior entries, sometimes also the left atrial entry.

In this paper, the research on modeling the pathology of AVNRT is presented. We consider the atrioventricular node (AV) as pacemaker centres made of special cells similar to embryonic cells (Konturek, 2001). For years, the most popular models of action potentials which occur in the heart have consisted of differential equations such as the van der Pol model. A syndrome of AVNRT is usually short-lived and the rhythm returns quite quickly to the heart's sine rhythm. Our model of the typical type of AVNRT and for the situation where we have additional pathways should consider randomness in generating paroxysmal arrhythmia of AVNRT. Deterministic models, even though numerically very effective, are not very suitable for studying the behaviour of such a system.

In this paper we propose a stochastic model of chosen types of AVNRT. The van der Pol model for description of the AVNRT pathology is considered (Jackowska-Zduniak and Foryś, 2016; 2018). It is a phenomenological model but without randomness. Jackowska-Zduniak and Foryś (2018) obtained interesting results for various types of AVNRT, but a given type of AVNRT is modelled using only an exact description of the existing pathology and there is no triggered source regarding physiological behaviour.

To begin further research we must understand also the sources of this problem and not only the behaviour observed while the arrhythmias last. We try to find the beginning of these symptoms, which has a stochastic character. We know that AVNRT has a sudden paroxysmal character so we need to add a stochastic term in our model. The coexistence of AVNRT with other conduction disorders is considered because then the clinical picture is not obvious and the disorders are often paroxysmal. When we understand complex physics of these pathologies, this will make it possible to propose a correct treatment of these types of AVNRT, based not only on invasive methods but also pharmacotherapy.

2. Mathematical model

Deterministic models offer very good representations of naturally occurring phenomena (the double-fire phenomenon in the heart, tumor growth, hypothalamus-pituitary axis, etc.), but they do not represent everything. Stochastic representation takes into account randomness that is included in all real world events and thus represents more then its deterministic counterpart. Some additional random excitation can cause serious arrhythmias that may be even life threatening. We know that, in the conductivity system of the heart, there are a lot of chaotic behaviours; also physiological behaviour of our heart has some arrhythmias which are not a syndrome of a disease.

The first model of action potential in the heart appeared in early 1920s; see the articles by Mobitz (1924) as well as van der Pol and van der Mark (1928). In the early 1950s, when experimental methods became more advanced, Hodgkin and Huxley (1952) proposed a model (HH model) of action potential based on experimental results regarding the giant squid axon. The HH model took into account the presence of channels in the cell membrane and described in detail the formation of action potential. The results of that research were awarded a Nobel Prize in physiology and medicine in 1963. Jackowska-Zduniak and Foryś (2018) proposed a system of ordinary differential equations which is based on the Hodgkin–Huxley model and allows reconstructing

pathological behaviours in the heart conducting system, such as AVNRT. In this work, Hodgkin–Huxley type models with couplings and delays were considered. Semi-phenomenological ionic models were modified to cardiac action potential (AP) models in fundamental investigations accomplished by D. Noble (Di Francesco and Noble, 1985; Henggui *et al*., 2009). The Di Francesco–Noble model consists of voltage-gated ionic currents, ion pumps and exchangers, Ca2C-sequestration and Ca2C-induced Ca2C-release which can describe a Purkinje fiber (PF).

Tusscher and Panfilov (2006) proposed a new model based on resent experimental restitution data and developed dynamics of the Ca+ionic channel. The model is used to recreate a phenomenon of alternations in a single cell. Electrical alternans can be observed during narrow atrioventricular junctional reentry tachycardia with an additional pathway (e.g., Wolf–Parkinson–White syndrome). But we should underline that the list of default model parameter settings consists of 53 items. A large number of equations and a large space of parameters in HH-type models make us look for simplified models. This is how the FitzHugh model arose, further developed by Nagumo *et al*. (1962). The FitzHugh–Nagumo model is a simplified 2D version of the Hodgkin–Huxley model which models dynamics of action potential. This model contains the van der Pol oscillator as a special case, so it is also a relaxation oscillator. In literature, a mathematical model of pathological behaviour in the cardiac system is known, e.g., AVNRT.

Gamilov *et al*. (2019) proposed a mathematical model of coronary circulation, which is suitable for reconstruction of the myocardial blood flow change during cardiac pacing and tachycardia. This model is based on an unsteady viscous incompressible fluid flow through the 1-dimensional elastic tube network. Jackowska-Zduniak and Foryś (2018) described atrioventricular nodal reentrant tachycardia using modified coupled van der Pol models with delay. These models reconstruct exactly mechanisms of existence of AVNRT but not a source that triggers this pathology, while it is important to propose a therapy for such a problem. The results of numerical simulations show a physical side of this pathology and help to better understand differences and dependencies between different types of AVNRT. The results of these works are in agreement with further clinical experiments. Also in this paper mathematical analysis of proposed model is made.

A new trend of adding a stochastic term to ordinary differential equations can be observed in many papers. The difficulty of modelling and treating heart diseases arises with their complexity. The heart is regulated by many biological factors (e.g., AVNRT is triggered by stress or nicotine or unexpected premature contractions (PAC)), at various scales, and an abnormal electrical activity is a phenomenon emerging from dynamic instability. Also unexpected excitations by premature contractions such as PAC (in atrium) or PVC (in ventriculum) contribute to arrhythmias. The question doctors and researchers are asking is what is in PVC that often leads to death. We do not know when it will occur, it appears accidentally, it is unpredictable. This is where we see room for our stochastic component.

Qu *et al*. (2014) considered nonlinearity and stochasticity in a mathematical model of the heart. The HH model considered is used to describe a cardiac myocyte. Stochastic ion channel openings and closings are modelled using Markov transitions. The proposed complex model dynamics are dominated by microscopic random fluctuations. Zheng *et al*. (2013) analyzed RR intervals to the developed 1D model with stochastic parameters which can jump to another deterministic system within the same parameter family. The model complies with the 2D embedding of angles from heart rate data.

In many research works (e.g., Ghorbanian *et al*., 2015; Kussela, 2004) authors consider a stochastic modified van der Pol model to describe biological problems. Ghorbanian *et al*. (2015) proposed a new phenomenological model of the EEG. The model is based on stochastic coupled Duffing–van der Pol equations. Model parameters were optimized with respect to EEG data. The results showed that this model can reconstruct the frequency and entropy content of the EEG signal. Also, Kussela (2004) applies a stochastic model in biomedicine, to model the heart-rate fluctuations in a time scale from minutes to hours. In the paper, a one-dimensional Langevin-type stochastic differential equation with a Gaussian white noise is considered. Direct simulations of the stochastic model for normal and pathologic cases can produce statistical parameters similar to those of a real case. Leung (1998), Li *et al.* (2019a; 2019b) and Shenghong *et al*. (2018) make a mathematical analysis of a stochastic van der Pol model (stochastic bifurcations, asymptotic stability). We did not find a paper with a stochastic model to describe tachycardia.

2.1. Model construction. We start describing a van der Pol system which is used to recreate action potentials in our model. The van der Pol equation was constructed in the 1920s by the physicist Balthasar van der Pol as a description of nonlinear oscillations in a triode circuit (van der Pol, 1926). Relaxation is one of the most important features of this equation. It is the ability to adjust the frequency to that of the external inducement system. This feature makes relaxation oscillators suitable for modelling systems in which it is important to generate a response to stimulation, with a matching frequency and a constant amplitude. This property is important in creation

of action potential in the conductivity system of the heart.

The van der Pol (vdP) equation has the form

$$\frac{\mathrm{d}^2x}{\mathrm{d}t^2} + x - \mu(1-x^2)\frac{\mathrm{d}x}{\mathrm{d}t} = 0, \tag{1}$$

where $\frac{1}{2}\mu(x^2-1) = \alpha$ is a dumping constant, which is a function of x, α is negative for $|x| < 1$ and positive for $|x| > 1$ (on the assumption that $\mu > 0$). The model requires modifications to reflect the real properties of action potential. Postnov *et al*. (1999) introduced a nonlinear cubic term (Duffing term) into the equation in place of the harmonic force term, thus obtaining the expected phase space structure. The structure of the phase space preserves features of the neural model: saddle, node and focus. To make it easier to regulate the frequency, a pair of independent parameters was introduced instead of one parameter in the Duffing term, (Grudziński, 2007). Thanks to this change, we are able to separately manipulate the shape of the pulse and the times of the pulses, which was impossible in the case of the vdP oscillator, and it was not possible to enter the parameter in the modified van der Pol model (Jackowska-Zduniak and Foryś, 2018).

The modified van der Pol (mvdP) model takes the following form:

$$\begin{aligned} \dot{x} &= y, \\ \dot{y} &= -a(x^2-\mu)y - fx(x+d)(x+e), \end{aligned} \tag{2}$$

where we have control parameters and x is the description of action potential while y is the description of the current which is connected with the potential. The main property of the modified relaxation oscillator is the mutual interaction of a limit cycle which is presented around an unstable focus with a saddle and a stable node. This allows reproducing correctly the refraction period and non-linear phase sensitivity of the action potential of node cells (Grudziński, 2007).

The model above can be treated as an SA node or an AV node model. The reference values of parameters are given as $\mu = 1$, $a = 5$, $d = 3$, $e = 7$, $f = 3$ (Grudziński, 2007). Parameter values for the van der Pol model were chosen such that the oscillation's frequency corresponds to a real frequency of sinoatrial (SA) and atrioventricular (AV) nodes. The parameter a belongs to the interval $[0.5, 6]$, the parameter e is in the range $[4, 12]$ and the parameter f may change in the range $[2.5, 3]$. Parameter a influences time intervals between pulses. The parameters e and d play a major role in the validation process of the model; they regulate the location of steady states in the phase space. The independent coefficient f corresponds to a harmonic oscillator frequency. The selection of appropriate parameters was done after a verification of the model by Grudziński (2007).

2.2. First model construction. The first model consists of two coupled modified van der Pol models (it recreates slow/fast AVNRT), which were proposed by Jackowska-Zduniak and Foryś (2018), and an additional modified van der Pol model excited by some external excitation. For the slow/fast type of AVNRT, we model the fast pathway as the first modified van der Pol system and the slow pathway as a second one. The difference between these systems is related to the length of the period of oscillations. The slow pathway is modelled as slower, so we fit parameter e so as to be equal to 4.5 (three steady states of the type described above exist). In the first system all parameters are the same as the reference values; see (P0) in the sequel.

We introduce a feedback and time delay in order to reproduce the slow/fast type of AVNRT. Introducing feedback loops entails the creation of waves which can correspond to re-entry waves, which is presented in Fig. 1. The feedback is introduced to the third equation because the re-entry wave is from the slow pathway to the fast one. Moreover, small delay is observed in this type of AVNRT. The time when a wave goes along uncontrolled in order to return to the node is reflected by the delay added to the feedback part, which is presented by Jackowska-Zduniak and Foryś (2018). But to this model we add also one more modified van der Pol model which recreates the sine rhythm (such as the fast rhythm in the first equation of our model) but with additional external stimulation (noise, external period pulses).

We add this external stimulation because AVNRT is usually caused by premature excitations of atrial origin (PAC). PAC is not a guiding rhythm, but paroxysmal excitation of the system. The discharge interrupts the sine rhythm and eventually leads to tachycardia. In the literature (Brugada *et al*., 2019), three external excitations are needed to set off tachycardia. In this paroxysmal excitation or noise (two versions of external excitation) we have our random term which leads to stochastic differential equations.

Stochastic differential equations are not coupled with the AVNRT model because we trigger our AVNRT syndrome by performing switching when the period of our sine rhythm is significantly different from a reference one, which is $T \approx 1.37$. The trigger is realized in a computer code (Matlab) where the condition which compares the currently measured period with the reference one is used. If the obtained value is less or greater than the reference one, the system is switched.

The first of the proposed models has the following form:

$$\begin{aligned} \dot{x_0} &= y_0 + \text{`external\_excitation'}, \\ \dot{y_0} &= -a(x_0^2-1)y_0 - fx_0(x_0+d)(x_0+e_1), \end{aligned} \tag{3a}$$

mvdP submodel

$$\begin{aligned}
\dot{x_1} &= y_1 - k_1 x_2,\\
\dot{y_1} &= -a(x_1^2 - 1)y_1 - f x_1(x_1 + d)(x_1 + e_1),\\
\dot{x_2} &= y_2 - k_2(x_2 - x_2(t - \tau)),\\
\dot{y_2} &= -a(x_2^2 - 1)y_2 - f x_2(x_2 + d)(x_2 + e_2),
\end{aligned} \tag{3b}$$

slow/fast AVNRT submodel

where k_1 and k_2 denote coupling coefficients (describing interaction between nodes in the heart), and τ is time delay. The values of parameters are given as $k_1 = 0.75$, $k_2 = 0.2$, $a = 5$, $d = 3$, $e_1 = 7$, $e_2 = 4.5$, $f = 3$; we shall refer to this setting as (P0). Noise and external excitation are added only in the first equation because x_0 and y_0 are related to the voltage and current, respectively, which have a constant relationship for the given circuit.

Let φ_{x2} and φ_{y2} be arbitrary continuous functions defined on the interval $[-\tau, 0]$. Then there exists a unique solution of Eqns. (3b) (part of the model with delay) defined on $[0, +\infty)$. For the proof, see the work of Zduniak *et al*. (2014).

External excitation is defined as follows:

1. Gaussian pulses:

$$G(t) = \frac{A}{\sqrt{2\pi}\sigma} e^{-(t-t_p) - \left(\frac{L((t-t_p)) + \frac{1}{2\sigma^2} n_{\text{cycle}}}{n_{\text{cycle}}}\right)^2}, \tag{4}$$

where A is the amplitude of the pulse, t_p is the time of the first pulse, σ is the width of the pulse, n_{cycle} is the period between pulses. The reason to choose this form is that we need to start with a pulse which has a fixed spectral width. It is connected with the fact that regular excitation may evoke a regular answer. We know that the van der Pol system is phase sensitive, and that, depending on the phase, excitation may change the potential period length. This knowledge is our starting point in using external excitation.

We consider a function of Gaussian pulses (see Fig. 2) with given parameters: $A = 5$, $t_p = 10$, $\sigma = 0.2$, $n_{\text{cycle}} = 15$; we shall refer to this setting as (P1).

2. Noise:
The Ornstein–Uhlenbeck process turns out to be central to the mathematical description of both white noise and Brownian motion.

   (a) Gaussian white noise.
   The most common is white noise. The most natural and simple generalization of Gaussian white noise is provided by exponentially correlated Gaussian noise, as generated by a stationary Ornstein–Uhlenbeck process. We assume that $\eta(t)$ is a stationary process obeying

$$\frac{\partial \eta}{\partial t} = -\frac{\eta}{\theta} + \frac{\text{GWN}(t)}{\theta},$$

   $\theta > 0$, where $\text{GWN}(t)$ denotes Gaussian white noise with $\langle \text{GWN}(t) \rangle = 0$ and $\langle \text{GWN}(t)\text{GWN}(t') \rangle = \delta(t - t')$. In the limit of $\theta \to 0$, the case of Gaussian white noise is recovered.

   Gaussian white noise is presented in Fig. 3.

   (b) Brownian motion.
   The Wiener process (standard 1D Brownian motion) of a random variable $W(t)$ is a real process and satisfies the following conditions: (i) $W(0) = 0$; (ii) the process $W(t)$ has stationary and independent increments on non-overlapping intervals; (iii) $W(t)$ is a Gaussian process with zero mean and variance of increments,

$$\langle [W(t_2) - W(t_1)]^2 \rangle = 2D(t_2 - t_1),$$

   where $t_2 > t_1$, D is a diffusion coefficient. In stochastic differential equations (SDEs) we use a random perturbation which is presented by $\mathrm{d}W_t$ with a small positive value (ϵ) in front of the perturbation term. The stochastic differential equation has the following form:

$$\mathrm{d}X(t) = f(X(t))\,\mathrm{d}t + g(X(t))\,\mathrm{d}W(t), \tag{5}$$

   where f is a drift function and g is a diffusion function (constant in our case).

   A sample of Brownian motion is presented in Fig. 4.

2.3. Second model construction. The second model consisting of two coupled modified van der Pol models (it reflects slow/fast AVNRT), which is proposed by Jackowska-Zduniak and Foryś (2018), and the first equation of this model is excited by external excitation. Now we add this external stimulation PAC to model slow/fast AVNRT. We have neither additional equations nor switching, but we have our additional source of trigger and we want to compare these results with the model with switching.

The second model has the following form:

$$\begin{aligned}
\dot{x_1} &= y_1 - k_1 x_2 + \text{`external_excitation'},\\
\dot{y_1} &= -a(x_1^2 - 1)y_1 - f x_1(x_1 + d)(x_1 + e_1),\\
\dot{x_2} &= y_2 - k_2(x_2 - x_2(t - \tau)),\\
\dot{y_2} &= -a(x_2^2 - 1)y_2 - f x_2(x_2 + d)(x_2 + e_2),
\end{aligned} \tag{6}$$

where parameters and external excitation are defined as in the first constructed model.

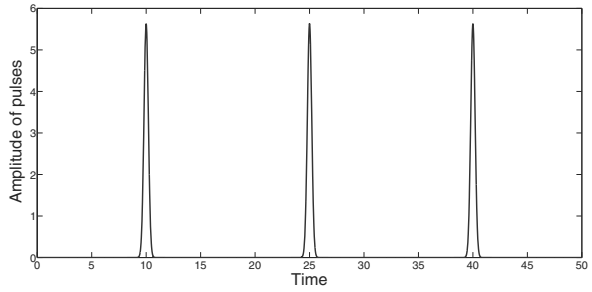

Fig. 2. Gaussian pulses (4) for parameter setting (P1).

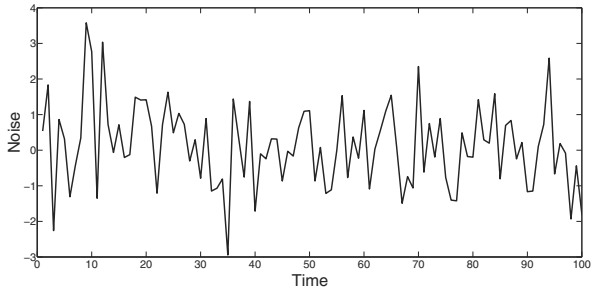

Fig. 3. Gaussian white noise.

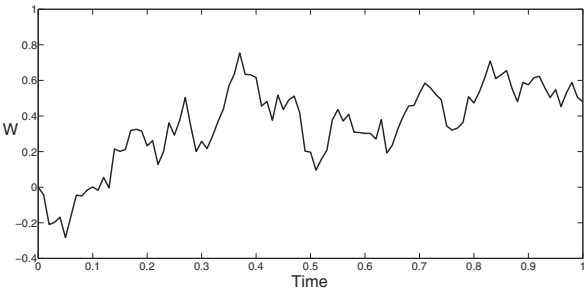

Fig. 4. Sample of Brownian motion.

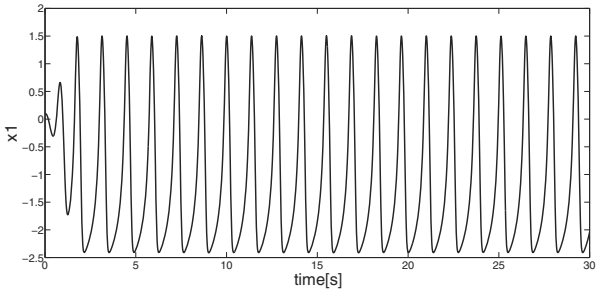

Fig. 5. Dynamics of action potential for the reference mvdP model, where the parameters are $a = 5$, $d = 3$, $f = 3$, $e = 7$.

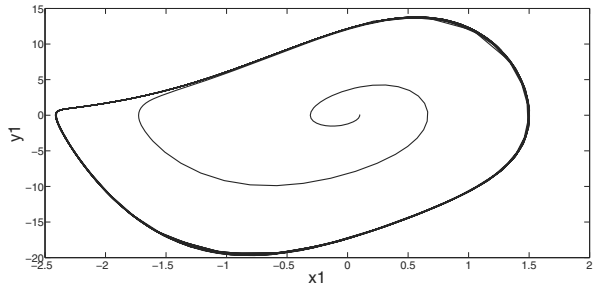

Fig. 6. Phase portrait of the reference vdP model, where the parameters are given as in Fig. 5.

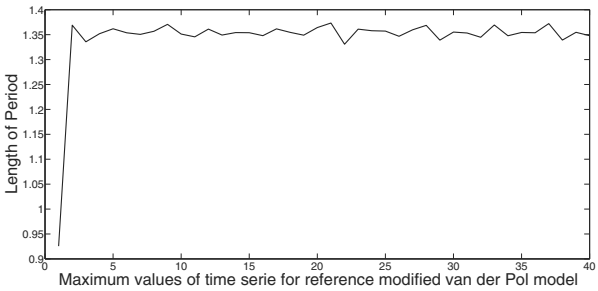

Fig. 7. Period length for the reference case.

3. Numerical analysis

In the first step we recall the behaviour of the reference van der Pol model without delay and couplings. We present a plot of time series which shows a periodic behaviour of our system; cf. Fig. 5. Figure 6 shows a phase portrait, which presents a very rich structure of the van der Pol oscillator—a limit cycle appearing in the phase space. In this system, there are three steady states: $x1 = 0$ (an unstable focus), $x2 = -d$ (a saddle) and $x3 = -e$ (a stable node). The period of our reference case is about 1.37, which is confirmed in Fig. 7.

The next model which we analyze is a slow/fast van der Pol model, but without external excitation and without switching. Now we observe only the behaviour of the main part of our models (submodels). We compare periodicity and also the behaviour of the phase portrait under delay and coupling in the van der Pol model. Also the main features of slow/fast AVNRT can be observed. This submodel consists two conductivity pathways (slow/fast) that coexist during tachycardia.

Numerical solutions of the slow/fast AVNRT submodel are in agreement with theory of the slow/fast type of AVNRT (Małaczyńska-Rajpold *et al.*, 2012). The length of the period ($T = 1.05$), after the initial time in which we can observe a temporary transient state, is about 35% shorter than the reference one (sine rhythm) and also variation in the action potential cycle length does not exceed 15% of the tachycardia cycle length, which is in Fig. 8. In a new report on tachycardia these guidelines are included in the diagnosis of this type of tachycardia (Brugada *et al.*, 2019). Also, we can observe in Fig. 9 a *jump*, which is a characteristic feature before

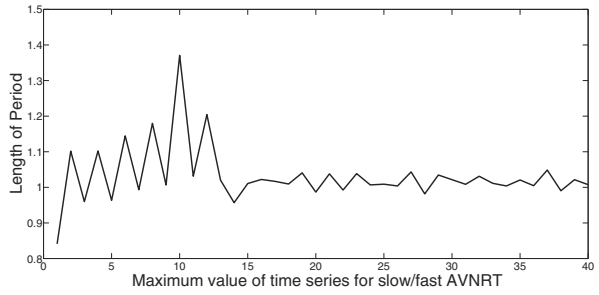

Fig. 8. Period length for a slow/fast AVNRT model.

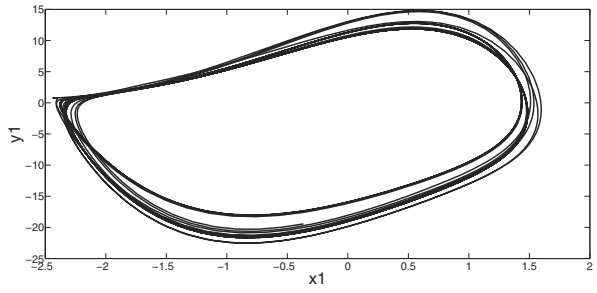

Fig. 10. Solution in the (x_1, y_1) plane for a slow/fast AVNRT model.

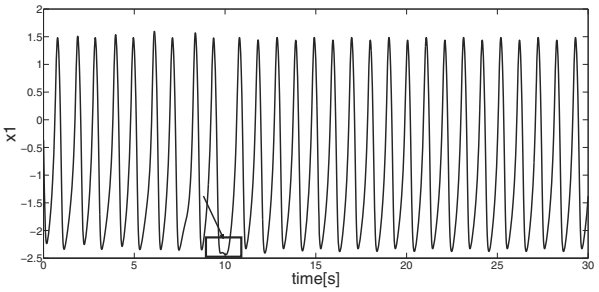

Fig. 9. Dynamics of action potential for the reference slow/fast AVNRT model, The arrow in a square shows a characteristic *jump* observed in this type of tachycardia as the first symptom of pathology.

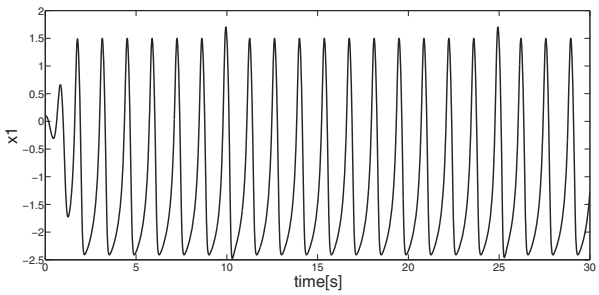

Fig. 11. Time series for a modified van der Pol model excited by Gaussian pulses.

the appearance of tachycardia (Małaczyńska-Rajpold *et al.*, 2012). A typical jump was defined as a sudden prolongation of an interval. After the *jump* the length of the period is stabilized in the phase portrait; cf. Fig. 10.

Now we consider the first proposed model which is given by Eqn. (3) and parameter setting (P0). Here external excitation is given as Gaussian pulses. There is no stochasticity, but in the beginning we compare the perturbation which is regular and observe the behaviour of our reference modified van der Pol model. Periodic excitation should trigger a regular response. Changes in the period in our first submodel of Eqn. (3) depend on the switching to a slow/fast AVNRT submodel. We expect three significant changes in the length (which reconstructs three PACs) of the reference period ($T \approx 1.37$) for the function to switch to the next submodel (slow/fast AVNRT submodel).

In Figs. 11–13 we can observe a bi-periodical behaviour of mvdP with Gaussian pulses. A second rhythm is forced by external excitation but after the excitation the system tries to return to the previous state. The length of the basic period fluctuates within $T = 1.37$ and the second length of the period is between 0.8 and 0.9. In this case the system is stable and returns to the periodic behaviour.

The problem of the system given by Eqn. (3) with the excitation (4) is shown in Fig. 14. A switching between two submodels takes place when the period is dramatically shorter so T is less than 1.

Now we consider the same excitation which is given by (4) for the model given by (6). Numerical results for this case are presented in Fig. 15. The change in the length of the period is shown in Fig. 16. We observe a bi-periodic behaviour during which $T \approx 1$. It is a shorter period typical for tachycardia, but after each Gaussian pulse we observe one longer period between 1.3 and 1.4. After this the system returns to the previous state. It is true that the human heart rhythm with feedback on the AV node is low-variable and it is difficult to throw it out of balance. In this case we observe additional periods which are results of our external excitation, and this is not observed in clinical tachycardia. We should keep in mind that this is a phenomenological model, so the results are accurate as far as possible.

Deterministic theories assume that, in the case of perturbations, such as Gaussian noise added to the system, solutions of differential equations will leave the neighbourhood of a stable limit cycle. In practice, for some types of relaxation oscillators, it can be observed that stochastic trajectories remain in the neighborhood of a stable limit cycle (Dieci *et al.*, 2016), which can be seen in Fig. 17.

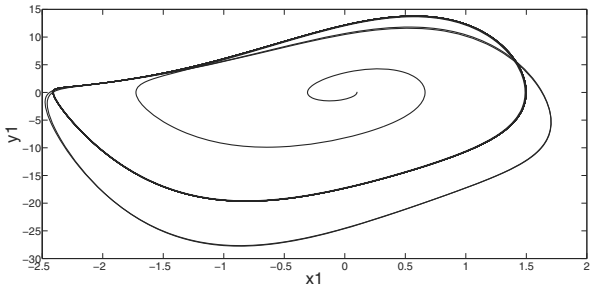

Fig. 12. Phase portrait of a modified van der Pol model excited by external excitation (Gaussian pulses).

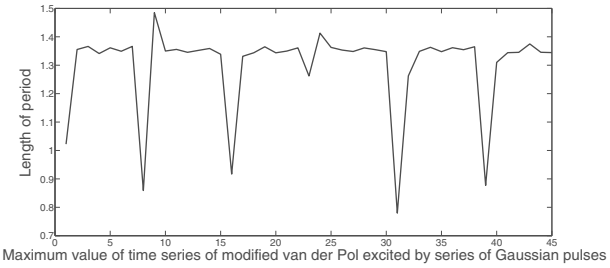

Fig. 13. Periods of a modified van der Pol model excited by a Gaussian function.

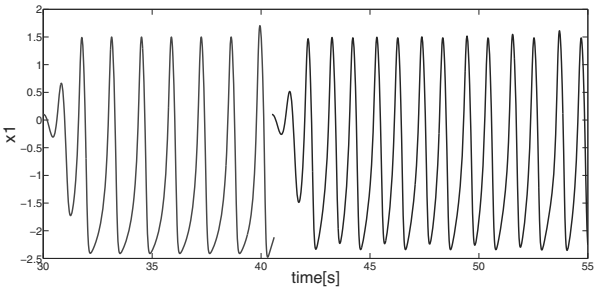

Fig. 14. Switching of an excited mvdP system to a slow/fast AVNRT system.

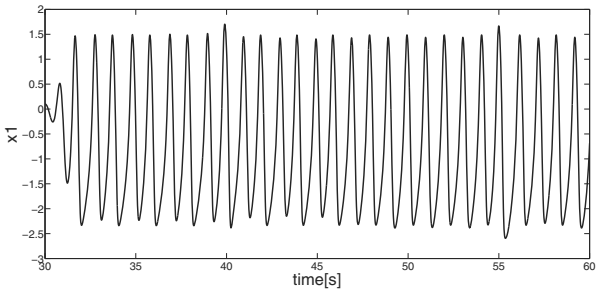

Fig. 15. Time series for a slow/fast AVNRT model excited by Gaussian pulses.

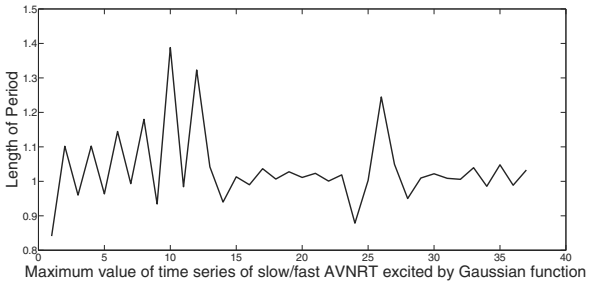

Fig. 16. Period length for slow/fast AVNRT with Gaussian pulses.

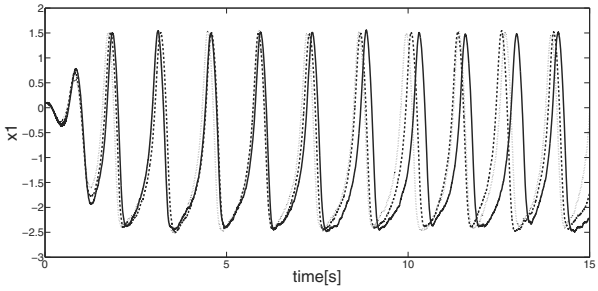

Fig. 17. Time series of an mvdP model excited by Gaussian white noise; three realizations of the trajectory.

We observe a reference modified van der Pol model excited by white noise; there are three realization of trajectories. The period is shorter than the reference mvdP, but the behaviour is bi-periodical, and we have some longer period. Around the local minimum of $x_1(t)$ for each path we can observe that there appear characteristic steps for additional excitation from SA. This is in agreement with our assumption that we have pre-excitation and it influences a modified van der Pol submodel. Switching this submodel to an s/f AVNRT one is possible if three longer periods appear; it is calculated for the chosen path (cf. Fig. 18). The mean value and variance function of x_1 of time over 200 realizations are shown in Figs. 19 and 20. In Fig. 19, we can observe global oscillations and also a regular shape. Also we observe a fluctuation of amplitudes in a stochastic waveform. Changes in the values of the amplitude are not essential. The key is the preservation of system vibrations and the change in the period length in relation to the reference period. In Fig. 20, we can observe strength synchronization of all paths but only at the beginning of the stochastic waveform and their subsequent desynchronization. This confirms the tendency of the system to stay around the stable limit cycle and an oscillatory character. The frequency of the peaks is similar from one realization to another, so the time of switching is similar for different paths of this model.

Now we analyze the model which is given by (6) with the same noise as given above.

There are oscillations around the stable point, but they are irregular for each path (see Figs. 21 and 22). There is a *jump* characteristic for tachycardia

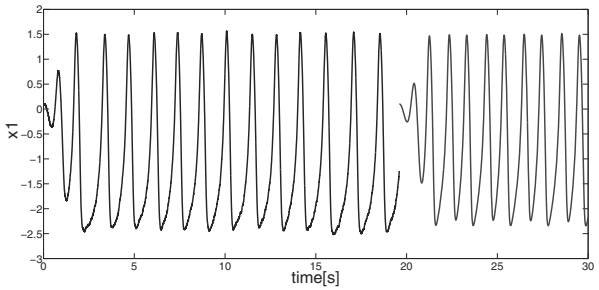

Fig. 18. Time series for the switching of a noisy mvdP system to a slow/fast AVNRT system.

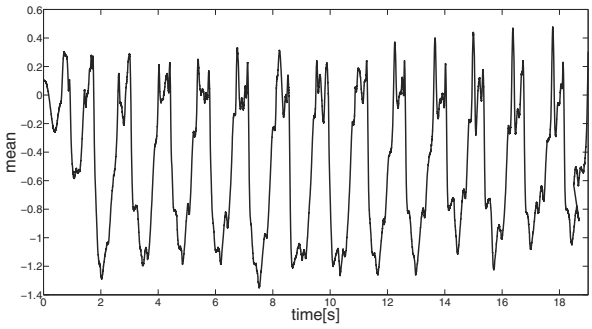

Fig. 19. Mean value of a noisy mvdP system for 200 paths.

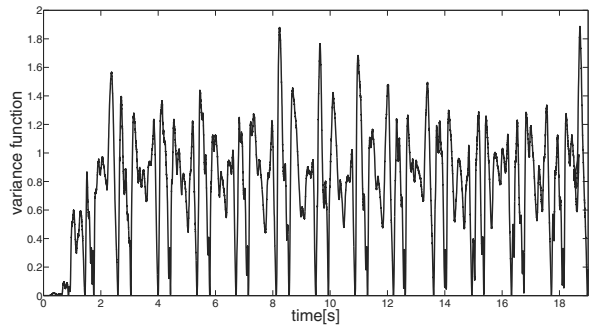

Fig. 20. Variance function of a noisy mvdP system for 200 paths.

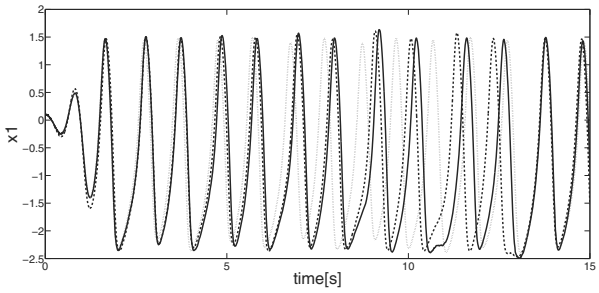

Fig. 21. Time series of slow/fast AVNRT with GWN for three paths.

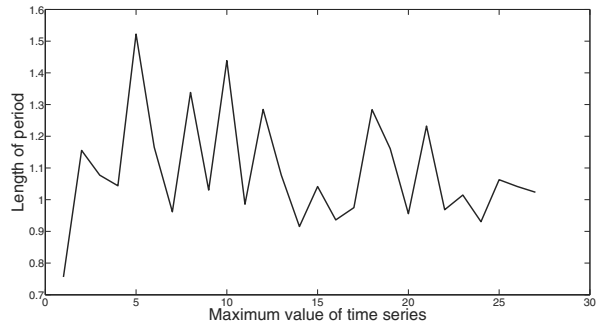

Fig. 22. Period length for slow/fast AVNRT with GWN.

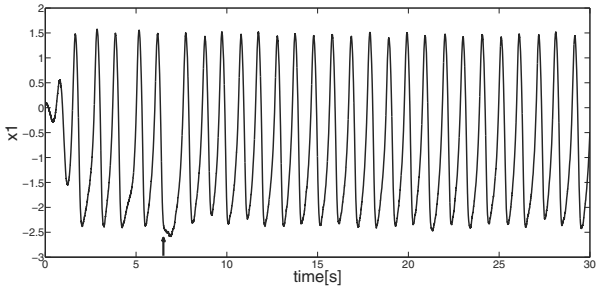

Fig. 23. Time series of slow/fast AVNRT with GWN; the arrow shows a *jump*.

at the beginning of this arrhythmia cf. Fig. 23. In this case arrhythmia depends on the presence of a conduction aberration, and then the fragment responsible for depolarization lengthens; thus the tachycardia period becomes unnaturally lengthened, as described by Brugada *et al*. (2019). It happens that tachycardia overlaps with the already existing agitation, which disturbs its clinical picture. At the same time, white noise added to the fast path included in the reentry acts more as an additional stimulus than a trigger.

The mean value of Eqn. (6) excited by GWN over 200 realizations is similar to that for modified van der Pol with GWN but the frequency of the peaks is bigger, while the variance function plots are very similar for both models excited by Gaussian white noise.

The last type of excitation discussed in this section is a Wiener process (Brownian motion). In the first step, we consider a modified van der Pol submodel excited by a Wiener process. In Fig. 24 we can observe a periodical behaviour with a longer period $T \approx 1.75$ than in the reference model for two realizations of trajectories. One path has no periodical behaviour, but intervals are also longer than in the reference model, so the switching is also present. Again, we can observe characteristic steps around the local minimum of $x_1(t)$. The switching between submodels is possible after three initial periods because they are significantly longer than in the case of the reference submodel. It is our trigger now. As in

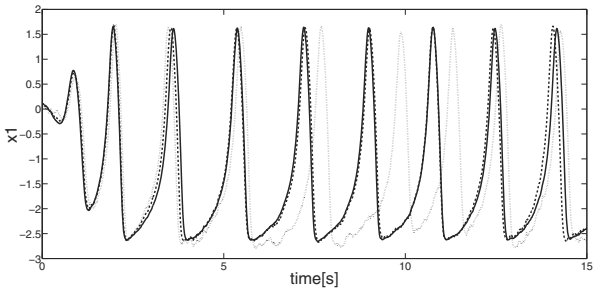

Fig. 24. Model mvdP perturbed by a Wiener process for three paths.

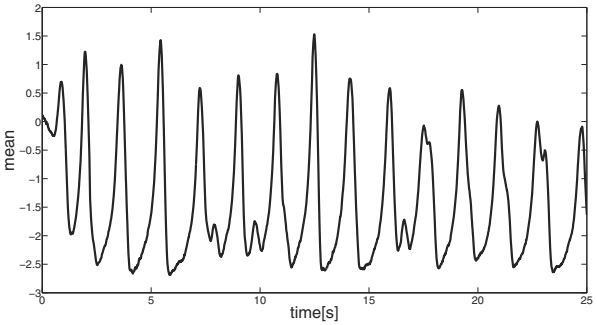

Fig. 25. Mean value of a noisy mvdP system for 200 paths.

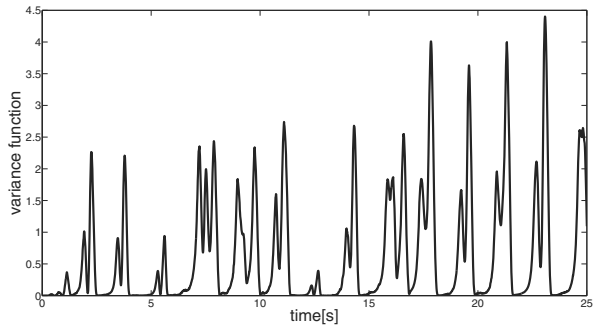

Fig. 26. Variance function of a noisy mvdP system for 200 paths.

the previous behaviour, we have a switching between subsystems: the modified van der Pol model with the Wiener process and a slow/fast atrioventricular model with feedback and delay. In Fig. 25, the plot of the mean has an oscillatory character with smaller frequency than in the model with additional white noise, which we can observe also in Fig. 27. The simulated variance is more slowly varying than for the excitation by GW; see Fig. 26. The oscillatory character of these realizations and similar features allows us to obtain a trigger in the form of three elongated or shortened pulses to induce tachycardia, i.e., to switch our model.

Now we consider Eqn. (6) with the noise given above. For simplicity, in Eqn. (6) with Brownian motion we assume that τ is zero. In Fig. 27, we observe a multi-periodic behaviour for each path. But this periodical behaviour is present all the time in the neighbourhood limit cycle. Along with the stochastic disturbance of the trajectory, the shape of the limit cycle slightly changes, which we can see in Fig. 28 in the rectangle window (the arrow indicates the alternation). This is related to getting the trajectory closer to the saddle. Stable and unstable manifolds of the saddle have influence on the shape of the limit cycle, a recently slightly rounded *spout* is now sharpened. This model can be interpreted as tachycardia with an additional partial aberration of conduction. It is caused by additional excitation with these coupled models. As in the case of white noise, this excitation is not a trigger but an additional perturbation which is known in physiology and can be interpreted. Also for this case the mean value and the variance function are similar as in Figs. 25 and 26. A variability between realizations for given stochastic noise is a valuable result, which shows that even the feedback model is sensitive in each phase to excitation, which tends to change the period, and to pathological behaviour.

4. Conclusions

The analysis showed that the proposed switching model is more suitable for modeling the AVNRT triggering mechanism and tachycardia itself. Also, a stochastic perturbation is more appropriate for modeling sudden premature PAC excitation than a periodic one. Most of the tachycardia features are reproduced in the proposed model, starting with PAC excitations, and the *jump* preceding the AVNRT arrhythmia phenomenon. It also quantitatively correctly reproduces the range value of the period length during tachycardia, which is 35% shorter than the reference period (sine rhythm) and rhythm variability during arrhythmia does not exceed 15%, as confirmed in the medical literature (Brugada *et al.*, 2019).

However, it is worth emphasizing that the model given by Eqn. (6) recreates the actual conduction aberrations that may coexist with tachycardia. The model results are consistent with ECG traces where AV dissociation occurs (quite rarely) but may do so neither atria nor ventricles are part of the reentry (Brugada *et al.*, 2019). In this way, the additional stimulation of the already coupled model modelled a more complex arrhythmia phenomenon.

In further research a more effective algorithm to calculate a stochastic problem as well as a therapy model will be proposed. The author will consider also a mathematical analysis of the proposed stochastic models.

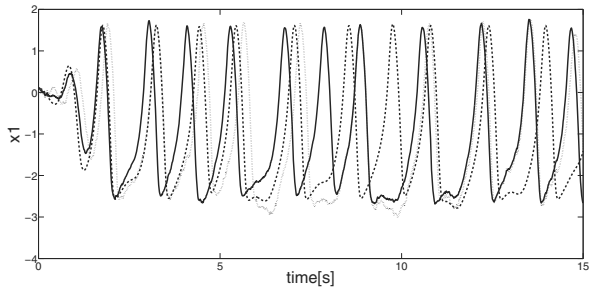

Fig. 27. Time series for a slow/fast AVNRT model (Eqn. (3b)) with noise (Brownian path); three paths.

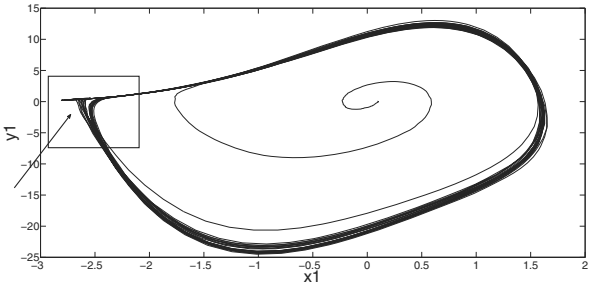

Fig. 28. Phase portrait for a slow/fast AVNRT model (Eqn. (3b)) with Brownian motion. Along with the stochastic disturbance of the trajectory, the shape of the limit cycle slightly changes; see the rectangle window (the arrow indicates the alternation).

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