*ELECTRONICS AND ELECTRICAL ENGINEERING*
*ISSN 1392-1215* *2006. Nr. 3(67)*
*ELEKTRONIKA IR ELEKTROTECHNIKA*

*MEDICAL TECHNOLOGY*
*T115*
*MEDICINOS TECHNOLOGIJA*

# The Dynamics of Extrasystolic Periods with Respect to Refractive Period in Mathematical Model of Parasystole

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## Introduction

The extrasystoles (ES) is most common form of heart arrhythmias, which appeared through of the recurrent excitation pulses (*re-entry)* or through of the ectopic beats going out from unusual regions of human heart. ES is called than premature contractions of the heart. Its can arise in atria, ventricles or in heart's conductive structures. ES can be solitary, cluster, recurrently or irregularly.

The functional premature isolate ES can be to provoke by the neuroses or by the pathological reflexes. Its is noticeable in sound hearts ECG of many examining patient's, but the being of these ES doesn't shown necessary in the heart disease [1]. ES can to make to 10% whole heart contractions, when the heart's tissues or his valves are affect. The danger rise only through much frequent ES, if its arise more frequently than 3-6/min., then appeared some thousand ES during twenty-four hours [2]. Every premature ES can trouble of the heart work. The pre-extrasystolic coupled interval ($T_{CI}$) before such ES in ECG is shorter, comparing as normal frequent R-R intervals. According to F. Sacher et al. [3] and S. H. Lee et al. [4], the premature ES on atria can be sometimes to initiate the atria fibrillation. Ventricular ES can be that triggers for the appearance of ventricular fibrillation [4]. A significance for the appearance of ES and for prognosis of heart rhythm restitution in clinic has a region of ectopic focus, functional conditions of heart beats, like as the deepness of heart's diseases. However, the establishment of the heart damages and location of the ectopic focus, which pulses competing with the beats of sinus node, out of ECG not is always a successful [5]. In addition to, a separation of functional ES from ES, arising by heart damaged, is difficult task.

Analysis of dynamics the parasystolic arrhythmias (PAR) in biomodel of rabbit's isolated right atrium [6] permit to hypothesize, that the frequent recurrence couplets of ES or single ES can will be also to appeare in ECG patient's on cases of parasystole in clinic. Recognition of this dynamics can help diagnose so far sparsely diagnosing the parasystole as result of the existence two independent beats oscillators. For to verify of this hypothesis and for the confidence of the truthfulness of effects, which we notice in biomodel, we created the mathematical-computer based PAR model. In model we establishe the regularity of appearance of arrhythmias in our setting conditions: the type of arrhythmias can be to change on conditions of stable duration periods of excitation pulses only the exchange of refractory period ($T_{ref}$), by the influence of antiarrhythmic drugs [7].. We selected a parameters of excitation pulses and the duration of $T_{ref}$ together estimating the possible heart rhythm variability.

Specifically, the purpose of our study was to find out the consistent pattern of the rising of couplets or single ES by means of mathematical-computer PAR model in wherein the duration of $T_{ref}$ and the parameters of the periods of excitation pulse can be selected changing.

## Object

Analysis of PAR dynamics using our created mathematical-computer model was performed. This model estimated to take into account the function of heart sinus node and heart cells refractoriness. In model the heart tissue that homogenous we keeping, in which the excitation beats spread what the plain valve without the obstacles. Because one heart cell is about $3x10^8$ once smaller, comparable with the all heart size, the tissues of the heart can interpret how the excitation medium for arousing stimulation. The model estimated, that after each excitation pulse, the new pulse is insensible will be for the some time. The $T_{ref}$ duration determined this insensible interval, begin at 100 ms.

The qualities of this model already are detail described [8]. Model algorithm is different from other resembling models, because the excitation pulses of both oscillators randomly are generated, on limits variability,

determined taking into clinical data [9]. This variability we could to enlarge or to restrict along at the desire. $T_{ref}$ one can easily to choose. The initial means of the duration of excitation periods we also could be easily choosing - as the longer pulses ($T_l$) as shorter pulses ($T_s$). Every excitation pulses and the responses on these pulses are identifying. Other qualities of model: in this it is provide for different $T_{ref}$ the possibility to estimate the number of pulses from both excitation oscillators, which will suppress on some time of investigation, if responses on pulses does not receive, and if responses are receive on the presence. In model also is provided the possibility to analyse of the arrhythmias appearance, the duration of the recurring parasystolic cycles ($T_c$), as the duration of the $\boldsymbol{T_{CI}}$, as the duration of rhythmical and arrhythmic intervals in $T_c$.

## Results

Because the mathematical – computer used model in essence correspond with the dynamics of competition of sinus node and ectopic parasystolic focus in rabbit's isolate right atrium [6, 7], is important the establishment, in time changing $T_{ref}$ of the conditions, in which can arise the couplets or single individual ES and can be preserve the rhythmical intervals.

We investigate the situation of different regimes:

1. The dynamics of the responses on the excitation pulses investigate by changing the $T_{ref}$ and choosing excitation periods $T_l$ and $T_s$ (theirs variability $\sigma$=0,00160) on limits of clinical norm, when is the stable difference

$$\Delta T = T_l - T_s . \quad (1)$$

2. The dynamics of the responses on the excitation pulses investigate by changing the $T_{ref}$ or the $\Delta T$, when markedly shorting the pulse periods of both excitation oscillators - $T_l$ and $T_s$, for to imitate the episodes of tachycardia.

In first case, choosing $T_l$ =0,82 s, $T_s$ =0,8 s ($\Delta T$ =0,02 s), the $T_{ref}$ duration we changed at 0,1 s to 0,82 s (to $T_l$). A rhythmogram, which received in these conditions, when the $T_{ref}$ =0,37 s is presented in the Fig.1, a). On result, in every $T_c$ form two rhythmical intervals **I** and **II** (**I** are the responses to $T_s$ =0,82 s excitation pulses and **II** are the responses to $T_l$ =0,8 s pulses). Between its is found the arrhythmical interval **III**, which is composed of the "couplet" - of the some ES. When the $T_{ref}$ =0,37 s, **III** interval remain formed only out of 4-6 $\boldsymbol{T_{CI}}$, shorting to 0,37±0.04 s. Thus, the $T_{ref}$ =0,37 s in these conditions of excitation is the border limits of appearance of the couplets. When $T_l$ =0,82 s and $T_s$=0,8 s, but $T_{ref}$ =0,4 s ($T_{ref}$ =1/2 $T_c$) the situation is presented in the Fig. 1, b). Only one shorter to $\boldsymbol{T_{CI}}$ =0,4 s remain before one ES in every $T_c$ on these conditions. When $\boldsymbol{T_{CI}}$ =0,4 s, the duration of **I** intervals are the same what the duration of the **II** intervals. The $T_{ref}$ prolongation to 0,6 s result the duration of the $\boldsymbol{T_{CI}}$ - either is equal also 0,6 s – that is shown in Fig. 1, c). The prolongation of $T_{ref}$ to $T_{ref}$ =0,75 s, (to near to duration of the $T_s$) in the same excitation conditions, is present in Fig.1, d). The $T_{ref}$ is the border limit for disappearance for single ES, which are always the responses on $T_l$ pulses The further lengthening the $T_{ref}$ at $T_s$ to $T_l$, caused shortening of **I** intervals and accordingly the prolongation of **II** intervals, but whole duration of the $T_c$ not change. Our choosing of the variability of the statistics duration of pulses ($\sigma$=0,00166) in these conditions has not of the considerable influence – the scatter of $T_{CI}$ durations in separate $T_c$ amount only ±0,02 s.

In second case, when we choose the short periods of the excitation pulses, the influence of $\Delta T$ size on the appearance of arrhythmias, when $T_{ref}$ =0,4 s ($T_{ref} > T_s$) shown the Fig 2. The rhythmogram, presented in the Fig. 2, a), was received, when $T_l$ =0,52 s and $T_s$ =0,5 s (when $\Delta T$ =0,02 s, what in Fig.1, b). It is evident, that the $T_c$ is shortened, than in Fig.1, b) and in every $T_c$ the intervals **I** are shortened than the intervals **II**. However, and in this case in every $T_c$ remained only one $T_{CI}$ =0,4±0,01 s. The situation which modelled in the Fig. 2, b), was obtained, when $T_l$ =0,58 s and $T_s$ =0,5 s, ($\Delta T$ =0,08 s) and $T_{ref}$ =0,4 s. Comparing it case with the cases, presenting in the Fig. 1, b) and in Fig. 2, a), (when $\Delta T$ =0,02 s), we see, that lengthening of the $\Delta T$ to 0,08 s, caused shorter the $T_c$. However, in every $T_c$ in this conditions remained in one $T_{CI}$ =0,4±0,05 s. The model showed, that, when the excitations periods are short ($T_l$ =0,52 s and $T_s$ =0,5 s), lengthening $T_{ref}$ to $T_l$, or lengthening $\Delta T$ to 0,08 s, the means of $T_{CI}$ a little more "scatted", therefore individual $T_{CI}$ can some different at the $T_{ref}$ (to 0,05 s).

Situation, when periods of excitation are $T_l$ =0.58 s and $T_s$ =0,5 s, the $T_{ref}$ lengthened to 0,57 s, shown a rhythmogram in the Fig. 3, a). The lengthening of the $T_{ref}$ duration to near means $T_s$ determined the border limit of disappearance of single ES. At present the ES not appeared, remain solely the rhythmical responses to $T_l$ =0,58 s pulses. In this conditions $T_{ref}$ =0,56 s is the border limits of the appearance of ES. The increasing of $T_{ref}$ only 0,01 s at 0,57 s to $T_{ref}$ =$T_l$ =0,58 s), called out the chaotic alternation the responses by $T_l$ pulses and more length responses (see in Fig. 3, b). The periods of the responses can reach to 1,16 s., and responses shorter that 0,58 s, are disappeared.

## Discussion

Our investigation of the competition of two independent oscillators of the excitation pulses in biomodel [6, 7] showed, that in absence the variability of the pulse periods, can in two cases. 1) bigeminy appeared, when $T_{ref}$ =const and $T_l$ = $T_s$, but the pulses sending in different moments. While the $T_{ref}$ changing can appeare trigeminy or other allorhythmias. 2) When the periods of excitation pulses are unequal, the appearance of various class of arrhythmias depend on the $T_{ref}$. The $T_{ref}$ change can to call the various type of PAR – the episodes of tachycardia, the couplets of ES or recurrent single ES in every $T_c$. The criterions for separation of PAR or other arrhythmias is the dependence of the type of arrhythmia as from $T_{ref}$ duration, as from the conditions of excitation also the independence of the $T_c$ duration on $T_{ref}$.

The PAR aren't specific – the ektopic beats can to found in the heart on cases his organic diseases, electrolytic disturbance in myocardial cells, in a fever,

after influence of toxic factors and antiarrhythmic drug, used in bigger doses and through other causes [1]. When the ES, allorhythmias, paroxismal tachicardia, flutter and fibrillation atria caused the ectopic bearts, the arrhythmia not disappeared sending the artificial ES. The helping ectopic rhythms appeared when the function of the sinus node became weaken. If the ectopic focus is lower in the heart conductance system, the frequent of ectopic beats is smaller and more dangerous for the patient.

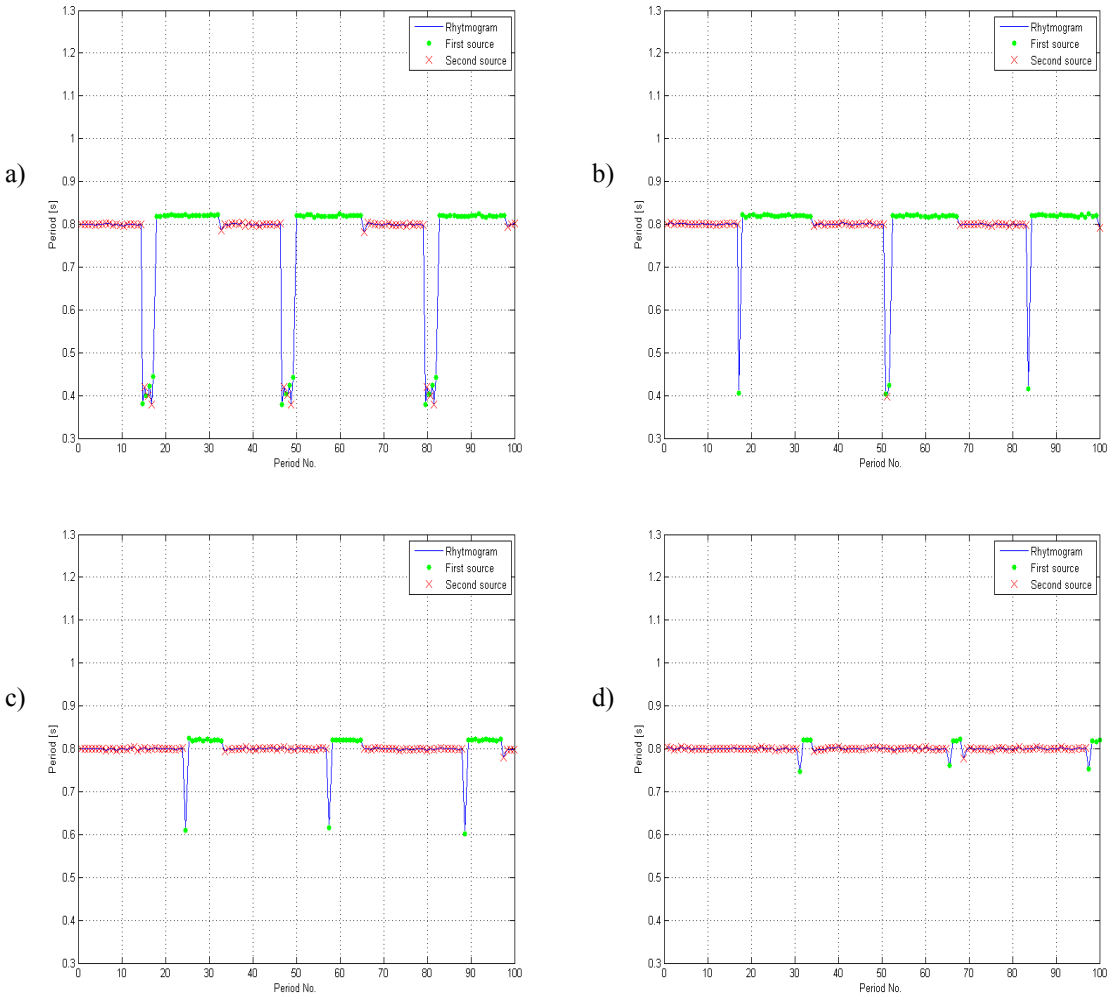


**Fig.1.** The rhythmograms of the responses on two competitive excitation focus pulses ($T_s$ =0,8 s, $T_l$ =0,82 s), by changing $T_{ref}$: a) $T_{ref}$ =0,37 s; b) $T_{ref}$ =0,4 s; c) $T_{ref}$ =0,75 s, d) $T_{ref}$ =0,79

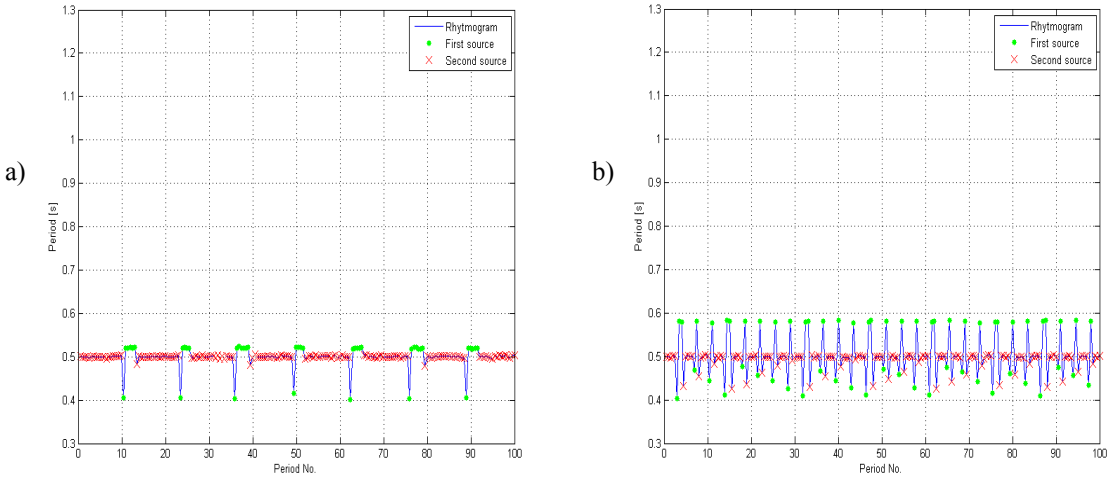


**Fig 2.** The rhythmograms of the responses on two competitive excitation focus, when $T_{ref}$ =0,4 s. a) $T_s$ =0,5 s, $T_l$ =0,52 s ($\Delta T$ =0,02 s); b) $T_s$ =0,5 s, $T_l$ =0,58 s ($\Delta T$ =0,08 s).

a) b)

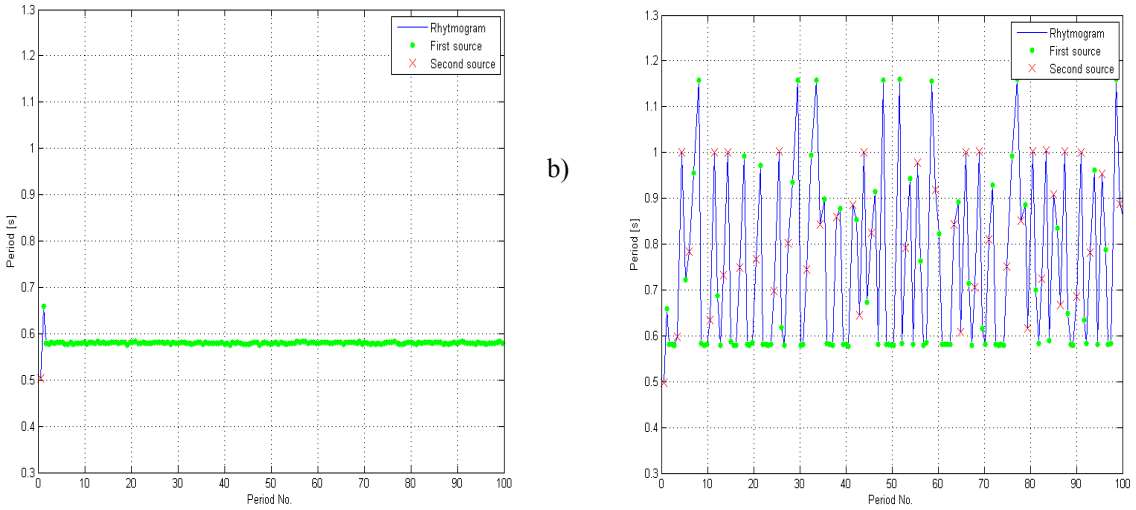


**Fig. 3**. Rhythmograms of two competitive excitation foci, when $T_{ref} > T_l$.and $T_s$ =0,5 s, $T_l$ =0,58 s.
a) $T_{ref}$ =0,57 s; b) $T_{ref}$ =0,58 s

According to V.Schulte-Frohlinde et al. [10], the human heart displays an extraordinarily large range of complex rhythm, in both health and disease. The sporadic appearance of ectopic beats is common and is not necessarily a cause for concern. However, an increased number of ES has been associated with an increased risk of sudden cardiac death. Therefore the number of ventricular ectopic beats to try reduced using a medication in clinic. However, when clinical trials were carried out in patients treated with drugs, the results surprisingly and dismayingly showed an increased rate of sudden death in the patients who received the medication compared to those who received *placebo*.

PAR model, our created including a possible variability of the pacemaker and ectopic focus pulses, showed the conditions of appearance of ES in time changing of $T_{ref}$ duration, and also the possibility of ES preservation in some diapason of the $T_{ref}$. In model the single, recurrent ES appeared in every $T_c$, if the $T_{ref}$ is equal or more length that $T_s/2$. The ES remain, while the $T_{ref}$ duration approach to the $T_s$ duration. General scheme in the Fig. 4 shown that the rhythm change and number of responses on the excitation pulses, when the $T_{ref}$ was lengthened in stable frequent of excitation pulses of both oscillators. In this scheme the diapason a) shown the changes of the durations of rhythmical and arrhythmical intervals A line 1 show, that the duration of arrhythmical intervals shorter, the line 2 show, that the duration rhythmical intervals elongate. The diapason b) is short. It reflected the shorting of the arrhythmical intervals to some couplets of ES. The diapason c) is long – recurrent single ES appeared changing of $T_{ref}$ at $T_s/2$ to $T_s$. In diapason at $T_s$ /2 to $T_s$ choosing duration of $T_{ref}$ predetermine the $T_{CI}$ duration. The line 3 shown remain only one short $T_{CI}$ in every the $T_c$ The line 4 shown of the changes of the number of responses on the $T_s$ pulses, and the line 5 shown the changes of number of the responses on the $T_l$ pulses. The short diapason d) composed only rhythmical responses on $T_l$, and on $T_s$ pulses. The diapason e) form the arrhythmia when the response periods are lengthen than $T_l$. In points A and B the number of responses are same as on $T_l$ as on $T_s$ pulses. In the scheme of Fig. 4 the possible variability of periods duration is not included. The concrete situation can be little different from general scheme in cases of very frequent or very sparse excitation pulses.

That the $T_{ref}$ duration determine the $T_{CI}$ duration, therefore its can be the reading parameter for prognosis of the ES appearance or disappearance. In model in time reduce of variability of the responses periods, approximating the $T_{ref}$ duration to $T_l$ duration, to the possible danger arrhythmia can be called. Exist the opinion, that reduce of rhythm variability can be danger [11]. It is estimated, that the heart rhythm variability biggest belong to the regulation of heart autonomic nervous system [11] and that can be even desire, if the fluctuation of periods not exceed 20% [9, 12].

The aim of treatment of arrhythmias is not only the maintenance for some time the rhythm on desirable diapason of frequent, but and the assurance that new rhythm disease not will be to rise. Many of antiarrhythmic drugs prolonged the $T_{ref}$. In our previously experiments we established, that effects of antiarrhythmic drugs influence upon the of Na ions current channels of myocites. According to Roden D.M. [13], the Na ions currents determine of the cells refractoriness. Model shown, that $T_{CI}$ lengthener together witch the $T_{ref}$ lengthening, if the ectopic focus will be existed in heart tissues. ES can attribute to PAR if concrete means of $T_{CI}$ duration is equal or bigger than $T_s/2$, but if is smaller than $T_s$. Is are importance to estimate, which out of many different periods is $T_l$, and which is $T_s$ if in ECG the variability of R-R periods exists. We established that first period after ES correspond the $T_l$ periods, when the frequent of excitation is in limits norm. The $T_s$ duration correspond which the duration of periods before $T_{CI}$. If the periods $T_s$ through variability is different, we propose calculate the arithmetical mean of near some periods. In addition, can be the $T_s$ duration calculate along formula (2)

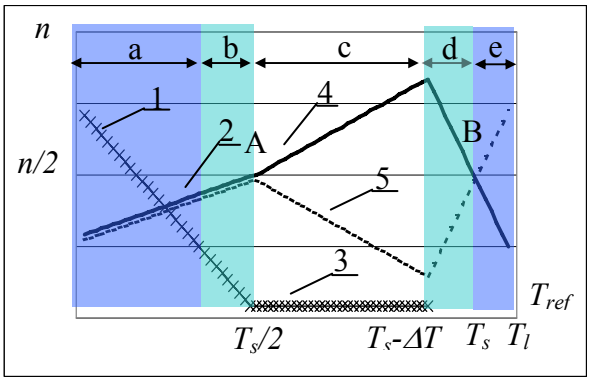


**Fig. 4.** The general scheme, showing the possibility of ES appearance, changes of rhythm and number of responses on excitation pulses in PAR model, on time changing of the $T_{ref}$. The detailed explanation is in text.

$$T_s = (T_l \times T_c)/(T_c + T_l). \qquad (2)$$

The period $T_c$ (or some periods $T_c$, if its are not equal) is necessary measure on ECG. Because on the influence on antiarhythmic drug can to change not only $T_{ref}$, but and together and $T_l$, $T_s$, $T_c$, therefore evaluating the changed situation, is necessary after that still calculate $T_s$. Ordinary for patients is registrate of short ECG, in which not always can to appearr some $T_c$, because $T_c$ duration can be too length. We believe, that in this cause has the basic that the PAR in clinic was sparsely diagnosed. Lately for the investigate of heart rhythm diseases are use the monitoring systems, witch permit at 24 h time registration the ECG and obtain data in shape of plates or graphic [14]. At long time registration of ECG can permit the our results compare with ES dynamics, that can be serve for facilitation of diagnosis of the heart rhythm disease. Thus, the consistent pattern, notice in PAR model, by changing the $T_{ref}$ and the dependence of class of the arrhythmias from $T_{ref}$ can be useful for prognosis of ES in clinic and for estimate of the efficiency of medication reduce using length time observation of ECG.

## Conclusions

Using our mathematical model of PAR are assessed that refractoriness of excitation medium, given low variability, determines type of recurrent ES and the duration of pre-extrasystolic periods.

The type of ES and alternation of per-extrasystolic periods, as observed during log-term ECG monitoring, may be helpful defining efficacy of the antiarrhythmic treatment.

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Presented for publication 2006 02 09

**M. Skučas, I. Grigaliūnienė, V. Barauskienė, R. Labrencas, D. Eidukas. The Dynamics of Extrasystolic Periods with Respect to Refractory Period in Mathematical Model of Parasystoles // Electronics and Electrical Engineering. – Kaunas: Technologija, 2006. – No. 3(67). – P. 81–86.**

To verify the hypothesis that many frequent extrasystoles (ES) can appeare throug the competition of ectopic excitation with pulses of sinus node, we created the mathematical computer-based model of parasystolic arrhythmias, taking into account possible variability of pulses of these pacemakers. We investigated the conditions of appearance of recurrent ES and subsequent dynamics of the ES dependent on the duration of refractory period ($T_{ref}$) in this model.

We established that the duration of the $T_{ref}$, approaching to $T_{ref} = T_s/2$ ($T_s$ – shorter periods of excitation pulses), predetermine the moment of appearance of the recurrent ES. The duration of $T_{ref}$ predetermined shortening of pre-extrasystolic periods. Groupes of ES remain as long as the duration of $T_{ref}$ remains close to $T_s/2$. Changes in the length of $T_{ref}$ trigger appearance of sporadic ES when $T_{ref} = T_s/2$, and these remain as long as $T_{ref} < T_s$. Based on long-term monitoring of ECG, our model may be helpful to evaluate effectiveness of medical treatment of arrhythmias. Ill. 4, bibl. 14 (in English; summaries in English, Russian and Lithuanian).

**М. Скучас, И. Григалюнене, В. Бараускене, Р. Лабренцас, Д. Эйдукас. Динамика экстрасистолических периодов в математической модели парасистолии при изменении рефрактерного периода // Электроника и электротехника. – Каунас: Технология, 2006. – № 3(67). – С. 81–86.**

Для проверки гипотезы, что многие часто на ЭКГ пациентов обнаруживаемые экстрасистолы (ЭС) являются формой редко диагнозируемой парасистолии, создана математическая компьютерная модель парасистолических аритмий. В этой модели учтено влияние рефрактерности среды возбуждения и наличие вариабельности периодов возбуждения. Проанализированы условия появления и динамики повторяющихся ЭС путем изменения периодов возбуждения и продолжительности рефрактерного периода ($T_{ref}$).

Установлено, что, при незначительной вариабельности периодов импульсов возбуждения, продолжительность $T_{ref}$ обусловливает появление повторяющихся ЭС и продолжительность предэкстрасистолического периода. Групповые ЭС наблюдаются при $T_{ref} < T_s/2$ ($T_s$ – периоды более коротких вожбуждающих импульсов). Единичные ЭС появляются при $T_{ref} = T_s/2$ и сохраняются, пока продолжительность $T_{ref} < T_s$. Приведенные данные могут быть важными для оценки эффективности медикаментозного лечения парасистолических аритмий во время мониторирования ЭКГ пациентов. Ил. 4, библ. 14 (на английском языке; рефераты на английском, русском и литовском яз.).

**M. Skučas, I. Grigaliūnienė, V. Barauskienė, R. Labrencas, D. Eidukas. Ekstrasistolinių periodų dinamika matematiniame parasistolijos modelyje, keičiant refrakterinio periodo trukmę // Elektronika ir elektrotechnika.– Kaunas: Technologija, 2006. – Nr. 3(67). – P. 81–86.**

Patikrinti hipotezei, kad pacientų EKG-se daugelis dažnai aptinkamų ekstrasistolių (ES) gali būti parasistolinės aritmijos, atsirandančios dėl ektopinio židinio impulsų konkurencijos su širdies sinusinio mazgo impulsais, sukurtas matematinis kompiuterinis parasistolinių aritmijų modelis. Šis modelis įvertina sužadinimo terpės refrakteriškumo įtaką ir galimą sužadinimo impulsų kintamumą. Modelyje ištirta, kokiomis sužadinimo sąlygomis ir kokiai refrakterinio laikotarpio ($T_{ref}$) trukmei esant pasirodo pasikartojančios ES ir kokia jų tolesnė dinamika, keičiant $T_{ref}$ .

Nustatyta, kad, esant nedideliam sužadinimo impulsų periodų kintamumui, pasikartojančių ES atsiradimą ir priešekstrasistolinių periodų trukmę modelyje lemia $T_{ref}$ trukmė. Grupinės ES išlieka, kol $T_{ref} < T_s/2$ ($T_s$ – trumpesnių sužadinimo impulsų periodų trukmė). Kai $T_{ref} = T_s/2$, atsiranda pavienės ES, kurios išlieka kol $T_{ref} < T_s$. Šie duomenys gali būti svarbūs parasistolinių aritmijų medikamentinio gydymo efektyvumui įvertinti klinikoje, pacientų EKG ilgalaikės stebėsenos metu. Il. 4, bibl. 14 (anglų kalba; santraukos anglų, rusų ir lietuvių k.).