ITHEA

International Journal INFORMATION TECHNOLOGIES & KNOWLEDGE

2009 Volume 3 Number 3

International Journal

INFORMATION TECHNOLOGIES & KNOWLEDGE

Volume 3 / 2009, Number 3

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International Journal "INFORMATION TECHNOLOGIES & KNOWLEDGE" Vol.3, Number 3, 2009

Edited by the Institute of Information Theories and Applications FOI ITHEA®, Bulgaria,
in collaboration with the V.M.Glushkov Institute of Cybernetics of NAS, Ukraine,
and the Institute of Mathematics and Informatics, BAS, Bulgaria.

Publisher: ITHEA®

Sofia, 1000, P.O.B. 775, Bulgaria. www.ithea.org, e-mail: info@foibg.com

Printed in Bulgaria

ISSN 1313-0455 (printed) ISSN 1313-048X (online) ISSN 1313-0501 (CD/DVD)

IMPROVING OF RECOGNITION ACCURACY OF ECG-SIGNAL IN VARIOS DISORDERS OF HEART AND OPTIMIZATION OF TREATMENT BY DRUGS

Nataliya Bilous, Elena Visotskaja, Olga Kozina,
Andrey Porvan, Gleb Kobzar, Alexey Krasov

Abstract: Application of ECG scale-space representation and its derivatives for clarification of point positions on results of wavelet detector for increase of boundary points determination accuracy in the automatic mode at higher rapidness while providing maximal reliability of recognition of ECG elements is offered. In addition, possibility of scale-space representation application is investigated for the selection of cardiac cycles for averaging signal. A new method of optimal drug selection is also proposed that reduces recipe space more than doubled taking into account required for treatment of patient symptoms pharmacological actions of drugs. Using the obtained function as function of goal for deterministic parametric model of optimal selection of multi-direction activity drugs allows adequately and systematically complete process of selecting of effective treatment of all symptoms of patient..

Keywords: electrocardiogram, ECG analysis, diagnostics, curvature, scale-space, dynamic programming, м-rate of curvature, optimal drug selection, coefficient of efficiency of impact.

ACM Classification Keywords*: I.5 PATTERN RECOGNITION and J.3 LIFE AND MEDICAL SCIENCES*

Introduction

Cardiovascular diseases are the leading cause of death in almost all developed countries. The absolute mortality rate in Ukraine from cardiovascular diseases in the 6-8 times higher than those in developed Western countries. It becomes clear to what extent is the issue of early diagnosis, prevention and treatment of cardiovascular diseases in our country.

Diseases of heart - a bright example of pathology, course and outcome of which is directly dependent on the timing of treatment to the doctor, timely diagnosis and start appropriate treatment. Many functions of cardiovascular system can be monitored by various devices and give important information about the status of the organism and the possible deviations from the normal regulation of functions. Electrocardiography - method for studying heart which does not lose its status over time. It remains one of the most common and integral methods of cardiac diagnosis and has continued to develop and improve. Achievements of recent years show that ECG provides information not only on the electrical and anatomical characteristics of heart, but also on changes in heart at the molecular level.

Modern possibilities of computer processing of signals enable rapid processing of large data sets. The combination of these capabilities and traditional methods of analysis of ECG allows to create computational cardiomonitory which complete automatic analysis of time and frequency parameters, storing electrocardiograms (including compression and transfer) during full cycle of the survey from accumulation of initial data to obtain a qualified medical decision.

Complication of automatic analysis of ECG consists in signal structure ambiguousness. Forms of ECG depends on both the using leads and the patients pathologies. In addition, ECG signal is exposed to baseline wander noise, electromyographic interference, electrodes pop or contact noise, patient-electrode motion artifacts and 50 or 60 Hz power line interference. Thus, the stage of contour analysis is critically important for the correct raising of diagnosis, as logic of diagnostic algorithms works exactly on the basis of recognized and measured parameters of ECG. That is why from 80th and till now automatic analysis of ECG is one of the most actual tasks in the area of biomedical technologies which not have a definite and complete decision. Moreover investigations in telemedicine, development of projects for remote processing of diagnostic data by modern communication means brings to forming new requirements into tasks of ECG automatic analysis (EAA). One most important requirement is an increase of rapidness of EAA for decreasing of a server's loading up to work in the mode of the real time.

The task of EAA has wide set of decisions: structural methods, correlation methods, Wavelet-transform approach, methods on the basis of analysis of derivatives. However, it will shown farther, methods which possess high recognition of ECG elements distinguishing, do not provide sufficient accuracy of elements boundaries determination. And on the contrary, methods providing high accuracy of elements boundaries determination on condition of correct detection of electrocardiosignal are less steady to the presence of noises and weakening of signal, i.e. do not possess sufficient ECG elements recognition reliability. These premises allow talking about the necessity of development of complex approach for recognition of ECG elements and determination of their boundaries.

At the calculation of basic ECG parameters with assistance of characteristic points inside 5-15 secs record arise up tasks of choice of informational cardiac cycle and construct of averaged signal. Providing of correct choice of informational cardiac cycle allows to avoid errors related to arising of high-peak interferences on frequencies of useful signal, and constructing of average signal - to reduce noise level without considerable distortions of initial ECG.

In this article the application of scale-space signal representation and its derivatives for clarification of end-points of characteristic elements positions by results of Wavelet-detector work is offered. Such approach provides maximal reliability of recognition of ECG elements and improves accuracy of characteristic elements end-points positions determination in the automatic mode with increased rapidness.

In addition, using scale-space representation (SSR) of ECG for selecting both representative (informational) cardiac cycle and cardiac cycles at calculation of average signal is offered. Using of SSR allows to remove possibility of selecting of cycles with interferences and with single artefacts as informational cardiac cycle and also enables to find pathological rejections which can arise up in single cardiac cycle. In the article the developed methods of rapid construction and comparison of SSR for providing of increased rapidness during work with plenty of records of ECG are offered.

Adverse changes in the cardiovascular system require the adoption of preventive measures and mild correction.

The complexity of the processes that determine the optimal adaptation of heart to the needs of the organism is reason of not a simple choice of efforts for correcting the state of the organism even for qualified doctor. Drugs that can have a useful effect in one case may give the opposite effect with similar symptoms to cardiac irregularities in the other case, when the disruption of heart based on other causes. In addition, all drugs are affecting to more than one physiological mechanism. That is why the most effective means of improving the state of heart, correcting violations in its work is the optimum set of plant origin drugs.

In this paper, the using of linear and nonlinear programming methods to solve the problem of optimal selection of drugs is proposed. This approach allows to select adequate appointing due to effective treatment of all patient symptoms taking into account his individual characteristics of the organism and the pharmacological characteristics of using drugs.

Also the mathematical model of the theory of Markov chains and numerical methods for evaluating the judgments of experts to determine the severity of the state of the human body is invited.

Introduction

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1 Automatic Analysis Of ECG. Tasks And Problems

ECG are differed due to a large variety, which is conditioned by both distinction of the decided tasks and specific of the investigated parameters of signal. The automatic analysis of ECG is usually conducted in two stages: preprocessing and extraction of characteristic elements ECG. As marked above, the most essential stage of ECG signal processing is extract of its important elements by recognition a QRS- complex, by selecting of its characteristic points (tops of Q, R, S waves, end points of QRSb and QRSe complexes and Pb, Pe, Tb, Te characteristic elements), by determination of some supporting point for relative start of measuring of RR-intervals durations (Figure 1.1).

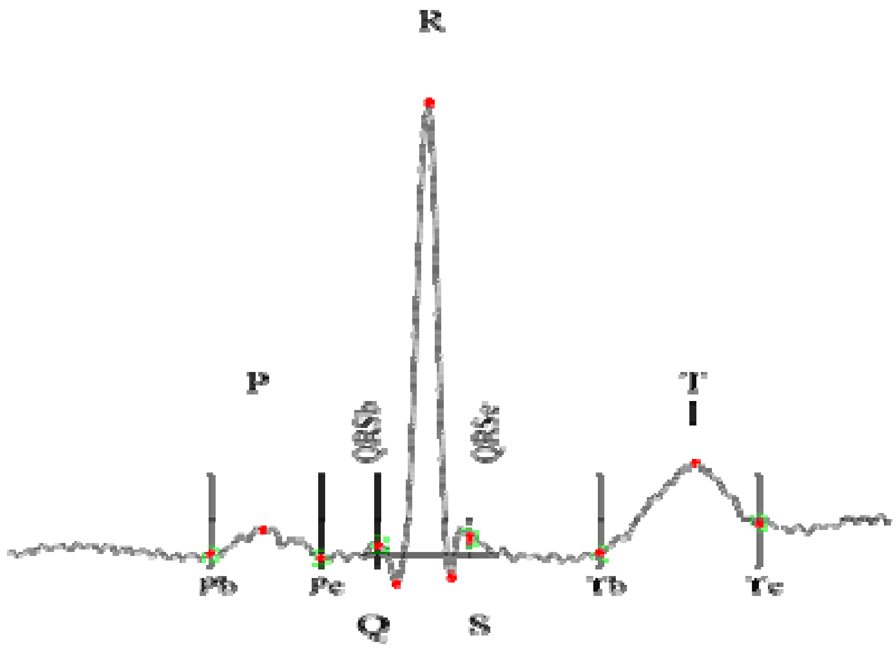


Figure 1.1 – characteristic points of ECG

It is possible to select a few groups of methods of EAA, basic from which are the followings:

–methods which use the analysis of derivatives of signal;

–structural methods that based on preliminary segmentation of signal, representation of signal as a sequence of the simplest elements and subsequent grammatical analysis of the received chain of characters;

–correlation methods which use the analysis of function of correlations between entrance ECG and by a severeal templates of ventricular complex;

- methods which based of wavelet transformations.

The most typical method of recognition of ECG elements is based on analysis of derivatives and consists of three stages: recognition of peaks with additional filtration for the removal of false peaks, a differentiating of peaks or in other words a finding of boundaries between real peaks, and also recognition of characteristic elements of ECG (complexes and waves).

Group of ECG derivative analysis methods is the most widespread as it was a starting point in AA of ECG. One of methods in the group of differentiating of peaks is based on the criterion of maximal curvature (which is formulated through the first and the second order derivatives). Due to this criterion, boundary points of peaks are points of maximal curvature. The other method uses derivatives in a different way analyzing the maximal slope of ECG curve which provides better result. The problem of this group of methods is low stability to the interferences and a necessity of preliminary filtration where authenticity of elements recognition will depend on the filtration efficiency. Nevertheless multidimensional analysis and more sophisticated rules for decision making provides here very good results [Laguna 1994].

The syntactic methods of automatic analysis of ECG are based on grammatical description of the segmented signal. Used segmentation has a few differences from offered Einthoven. Description of ECG is made from four characters — p, r, b, t each of which corresponds to the certain area of curve. In syntactic method, at first, localization of one R wave find by searching of simple maximum, then parametric description of QRS-complex (amplitude, duration of front and back front) create and after scanning of whole initial array of selections for localization of analogical alike areas which are other QRS-complexes is carried out. Methods of this group are showing good stability to the vibrations of baseline, however give errors at close amplitudes of R and T waves and at considerable noise level of initial signal of ECG.

A significant amount of research effort has been devoted to the automated detection of the fiducial (reference) points of the ECG characteristic waves [MINAMI 1992]. Most of these methods are filtering or adaptive thresholding based, which exhibit limitation in real application. Very few algorithms work well for the detection of all fiducial points such as the onsets and offsets of the P wave, T wave and the QRS complex (also known as the ECG wave boundaries). The main drawback of filtering-based approach is that frequency variations in the characteristic waves often adversely affect its performance. The frequency distribution of QRS complexes generally overlaps with that of the noise, resulting in both false positive and false negative detections. The main problems of the thresholding techniques are their high noise sensitivity and their low efficiency when dealing with odd morphologies. Therefore, more sophisticated signal processing techniques are needed to facilitate the development of new detection schemes with higher detection accuracy.

The other group of methods is based on the use of certain sequence of wavelet transformations for finding out complexes and waves. This group of methods appeared and developed comparatively recently – during last 10 years – however stability to noises and efficiency of finding out ECG elements had allowed the wavelet methods to take one of dominant places in the area of EAA [Al-Fahoum 1999]. Wavelet method, possessing most authenticity of ECG complexes recognition, waves and determination of their boundaries is based on consecutive application of CWT and FWT transforms which give abilities to separate noise and P, T waves from the QRS complex. This provides better results compared to one stage filtering of the QRS complex with only FWT or CWT transforms, if P and T waves are of high amplitude. The main advantage of the method is that it can be adjusted by varying the CWT transform frequency in the range of 1–3 Hz to particular T wave morphologies with clinically accepted precision which resulted in improvement of our score [Chesnokov 2006].

This method based on Wavelet transforms gained the lead on the official tests of methods of EAA in 2006 year by providing maximal authenticity of recognition and accuracy of measurings. However the necessity of the manual tuning of frequency for correct determination of P and T waves boundaries for most tasks of EAA allows to talk about the incomplete automatic work of the method and limits spheres of its application. In addition the fast-acting of method is not high because sequence of Wavelet transformations is used.

Thus, the method on Wavelet transforms provides maximal reliability of ECG complexes and waves recognition and determination of their boundaries. Demerit is only a semi-automatic process of measuring of P and T waves boundaries. The removal of this failing and increasing of rapidness will allow solving of given tasks.

2 Complex Approach Of ECG Elements Recognition And Boundary Determination Based On Wavelet Analysis And Scale-Space Representation of ECG

For increase of accuracy of boundary points determination with high reliability of ECG elements recognition the following complex approach is offered:

- QRS complex recognition by the method of wavelet transformations (WT).

- P and T waves recognition and determination of boundary points of QRSb, QRSe and Pb, Pe, Tb, Te characteristic elements by a method based on SSR of cardiosignal.

Thus, the method based on WT will provide maximal authenticity of recognition and the method based on SSR of cardiosignal will provide correct determinations of P and T waves and their boundaries in the fully automatic mode.

The method based on SSR of cardiosignal is offered for P and T waves recognition and determination of their boundaries in place of initial step of WT method.

We will consider formulation of scale-space representation for a continuous signal (in one-dimensional case).

Determination 2.1. For signal $f : \mathbb{R} \to \mathbb{R}$ scale-space representation $L : \mathbb{R} \times \mathbb{R}_+ \to \mathbb{R}$ is certain so, that reflection of signal at zero level is equivalent to the initial signal [6]:

$$L(x;0) = f(x),$$

and reflection on more wide scales is expressed by convolution of the initial signal and gaussian kernels with increasing width:

$$L(x;\sigma) = g(x;\sigma) * f(x).$$

By using integrals of implicit functions, the result of convolution «*» is like:

$$L(x;\sigma) = \int_{\xi=-\infty}^{+\infty} g(\xi;\sigma) f(x-\xi) d\xi,$$

where $g : \mathbb{R} + \mathbb{R}_+ \setminus \{0\} \to \mathbb{R}$ is the Gaussian kernel (one-dimensional):

$$g(x;\sigma) = \frac{1}{\sqrt{2\pi\sigma}} e^{-x^2/2\sigma}.$$

As known exactly Gaussian SSR - unique continuous linear SSR which satisfy to all necessary requirements: linearity (regarding to product), invariance to the change, scale invariance, property of semi-group, property of positivity.

For the construction of images of SSR of curvature for selected cardiac cycle the calculation of function of curvature is needed. The formula of curvature for the parametric given closed curve $\Gamma = \{(x(u), y(u) \mid u \in [0,1]\}$ has the following view:

$$k(u) = \frac{\dot{x}(u)\ddot{y}(u) - \ddot{x}(u)\dot{y}(u)}{(\dot{x}^2(u) + \dot{y}^2(u))^{3/2}}$$

Curvature Scale-Space (CSS) representation and existent algorithms of comparison of CSS is developed for closed curves and not used for the analysis of signals such as ECG before [Mokhtarian 1996]. However, it is possible to show that it is possible to adapt SSR for representation and comparison of ECG [[Belous 2008].

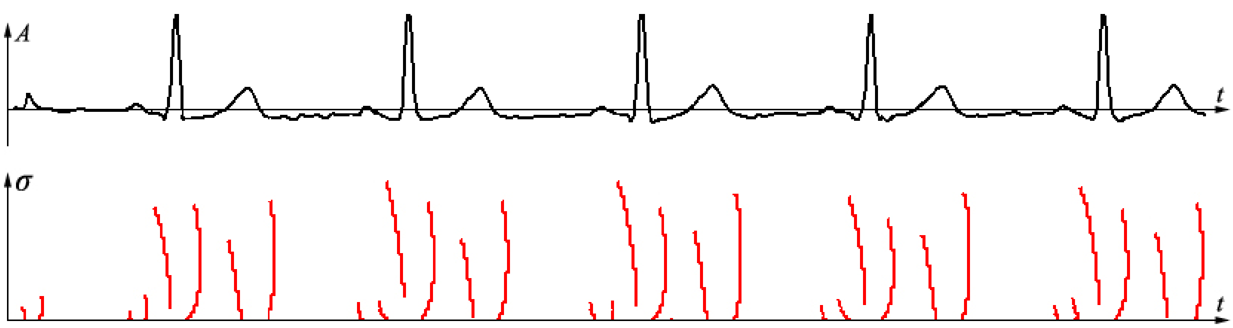
As a round of closed curve can be begun from any point, then CSS is cyclic. Representation of ECG begins and finishes in a certain point, therefore images of CSS of cardiosignal and, accordingly, set of maximums do not require shifting during construction and comparison. The other obvious problem is that curvature scale-space in its initial formulation do not provide convergence. That is why the other SSR is proposed to represent ECG – tangent angle SSR:

$$\begin{gathered}\alpha_i^\sigma = arctg\left(\sum_{k=i-3\sigma}^{i+3\sigma} \alpha_i \cdot g(i-k,\sigma)\right) \\ g(x,\sigma) = \frac{1}{\sqrt{2\pi\sigma}} e^{-\frac{x^2}{2\cdot\sigma}} \\ \alpha_i^\sigma \geq 30°, \alpha_{i-1}^\sigma < 30° \\ \alpha_i^\sigma < 30°, \alpha_{i-1}^\sigma \geq 30°\end{gathered} \tag{2.1}$$

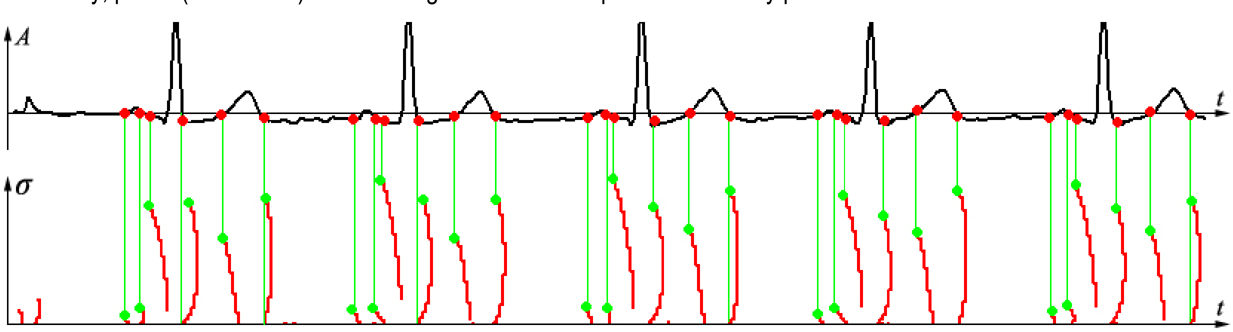
where α_i - tangent angle on the lowest scale, which can be simply calculated having curvature,

α_i^σ - discrete tangent angle representation on the σ -th scale.

As a result of SSR of ECG we get the next image of SSR:



Obviously, peaks (maximums) of SSR image of ECG correspond to boundary points of ECG elements:



3 Selection Of Informative Cardio Cycle, Construction Of Averaged Signal By Comparisons Of ECG Scale-Space representations

The task of informative cardiac cycle selection in the process of EAA appeared as a result of program realization of manual and development of semi-automatic systems of ECG analysis. In the similar systems the operator himself selects most informative cardiac cycle in which parameters of ECG are being calculated (manually or automatically). Operator follows next rules for selection of cardiac cycles:

a) cardiac cycle must be minimum exposed to high-frequency distortions;

b) cardiac cycle must not contain high amplitude interferences on the useful signal frequency (usually, reason of appearance of such interferences is motion of electrodes);

c) cardiac cycle doesn't have to differ on duration, intensity and also on wave shape from the other ECG cardiac cycles.

The observance of these rules provides the most exact measurings. However with development of the systems of EAA, process of forming of average cardiac cycle begins to replace process of choice of informative cardiac cycle in some systems. Averaging of signal which possible due to periodicity of ECG, provides suppression of noises without distortion of initial signal, especially in small details.

At the choice of cardiac cycles for averaging, algorithms of EAA systems use rules (a) and (b), but don't take into account that ECG signal is not fully periodic. In addition, published methods of averaging are based on the calculation of correlation on existent cycles which give EAA slower considerably [Strik 1988]. On fig. 3.1 cardiosignal is showed. It contains three cardiac cycles (PP1, PP3, PP4) which will be summarized and one cadiac cycle (PP2) which can result in two possible errors of averaging:

- inclusion of high amplitude interference with useful signal frequency in averaged signal;

- inclusion of two false cardiac cycles FPP2b and FPP2a in averaged signal that will result in considerable distortions.

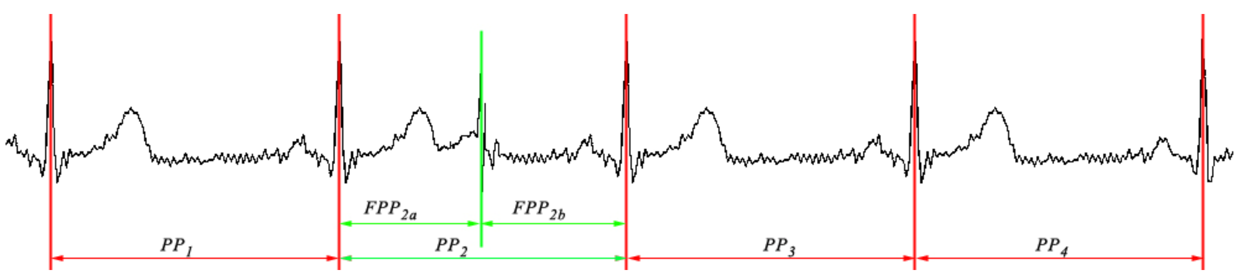


Figure 3.1 Cardiac Cycle Distortion and Results

A method which allows finding the most informative waves in the automatic mode based on comparison of scale-space representations of different cardiac cycles of one signal is considered in this section.

Definition 3.1. Let A - is a set of SSR (maximums of arcs). Then every point $\grave{a} \in A,\ i = 1,...,N$ are put in accordance two real numbers $u(a) \in \mathbb{R}$ – position of maximum on a curve - and $\sigma(a) \in \mathbb{R}$ is scale level which in pair determine position of point a in scale space.

Comparison of point images or, that equivalence, points set recognition (PSR), is one of the most fundamental problems in area of structural pattern recognition. It arises up in many areas such as 2D and 3D images analysis, treatment of documents, biometric authentication, databases of images, analysis of video, and also biological and biomedical applications. To the same task, obviously, comparison of PSR is related.

A task consists in finding of such accordance between every point of one set and points of other set for which some limitations are carried out, and also some global measure of likeness is optimized. Types of limitations and measures of likeness are determined due to according concrete problem.

Task 3.1 Accordance of two well-organized curve sets A and B of points of PSR can be found in a numeral kind by finding of one-power well-organized subsets $A' \subseteq A$ and $B' \subseteq B$ sets A and B and reflection $f(A'): A' \to B'$ which minimize the following function:

$$P(A,B,f) = \sum_{i=2}^{|A'|} \sqrt{(|u(a'_i) - u(a'_{i-1})| - |u(b'_i) - u(b'_{i-1})|)^2 + (\sigma(a'_i) - \sigma(b'_i))^2} + \\ + \sum_{a \in A/A'} \sigma(a) + \sum_{b \in B/B'} \sigma(b) = P^{ex}_{dp}(A', f(A')) + P^{inex}(A/A' \cup B/B'), \quad (3.1)$$

where $P^{ex}(A', f(A'))$ - is a cost of complete comparison of subsets A', B':

$$P^{ex}(A', f(A')) = \sum_{i=2}^{|A'|} \sqrt{(|u(a'_i) - u(a'_{i-1})| - |u(b'_i) - u(b'_{i-1})|)^2 + (\sigma(a'_i) - \sigma(b'_i))^2} \quad (3.2)$$

$P^{inex}(A/A' \cup B/B')$ - is a cost of eliminate of elements of sets A, B at comparison (analogical to the formula 4.3).

Formulation $P^{ex}(A', f(A'))$ in (4.5) requires one clarification. At comparison it is necessary in the beginning to select the first pair of points (a_0, b_0) in relative to which formula (3.2) calculates.

This task may be solved efficiently using dynamic programming [Belous 2008]. Thus, rapid and exact finding of accordance of not signals of cardiac cycles but their scale-space representations is available. This provides a choice only signals with similar form while averaging or selecting informative cycle. Result of ECG averaging that was presented on fig.3.1 is shown on fig 3.3

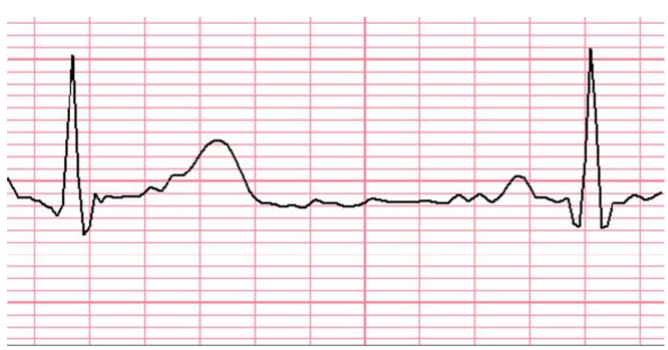


Figure 3.3 Averaging cardiac cycle

4 Method Of Rapid Forming Of Scale-Space Representations Of ECG

As it was mentioned to build SSR of ECG curvature estimation is neded.

As differential characteristic, curvature is very unsteady to discretisation and noising of images. Therefore, for providing of acceptable noise immunity at construction scale-space representations the function of curvature must be estimated indirectly.

Next formulation of m-weight of curve by which it is possible to formulate the estimation of curvature and satisfying to the requirement $\lim_{m \to +0} k_m = k$ (requirement for all estimations of curvature) is offered. For the calculation of such m-weight of curve the points of curve are needed only. The initial geometric curvature estimation method was proposed in [Karkischenko 1998].

It is proposed to use m-estimation of curavature to build curvature base scale-space representations to increase the rapidness of such representation construction. Proposed m-estimation is given in 2-dimentional parametric form of curve representation because it is easily converted to 1D form of ECG but may have a lot of other application in 2D.

Lemma 1. Let m is neighbourhood of point $\gamma(u) = (x(u), y(u))$, into which m-weight of curve given in parametrical view $\Gamma = \{(x(u), y(u) \mid u \in [0, L]\}$ is estimated. Then the following asymptotic formula $v_m = v_m^o + O(m), m \to 0$ takes place, thus v_m^o calculated on the following formula:

$$v_m^o = \left| S_m^o - \overline{S}_m^o \right| \Big/ \max(S_m^o, \overline{S}_m^o) \qquad (4.1)$$

where $S_m^o, \overline{S}_m^o$ – are areas of sectors of circumference with a radius $\triangle u$:

$$\begin{aligned} S_m^o &= \pi m^2 \angle(\overrightarrow{v^-}(u), \overrightarrow{v^+}(u)) / 360^o \\ \overline{S_m^o} &= \pi m^2 \angle(\overrightarrow{v^+}(u), \overrightarrow{v^-}(u)) / 360^o \end{aligned} \qquad (4.2)$$

where $\overrightarrow{v^-}(u)$ - a vector connecting the point of curve $\gamma(u) = (x(u), y(u))$ and $\gamma^-(u) = (x(u-m), y(u-m))$;

$\overrightarrow{v^+}(u)$ - a vector connecting the point of curve $\gamma(u) = (x(u), y(u))$ and $\gamma^+(u) = (x(u+m), y(u+m))$ (fig.4.1).

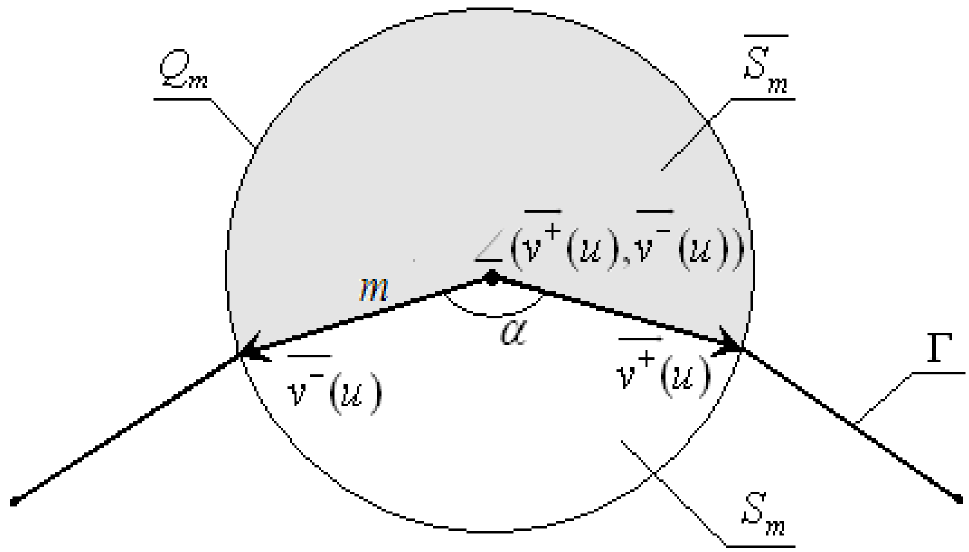


Figure 4.1 Neighbourhood for m-rate of function of curvature of contour curve

Lemma 2.. Let $m = \vartriangle u$ is Neighbourhood of point into which curvature of curve Γ given in parametrical view $\Gamma = \{(x(u), y(u) \,|\, u \in [0, L]\}$ is estimated. Then the following asymptotic formula takes place:

$$k = 3\pi v_m^o / (4m) + O_m^o(m),\ m \to 0 \tag{4.3}$$

Lemma 3. It is possible to assert that it is possible to obtain finding of estimation k_m^o with required accuracy at *estimating of curvature to sectoral method by introduction of the following limitation:*

$$v_m^o < \xi_m^o \tag{4.4}$$

where ξ_m^o is some cut-off of m-weight.

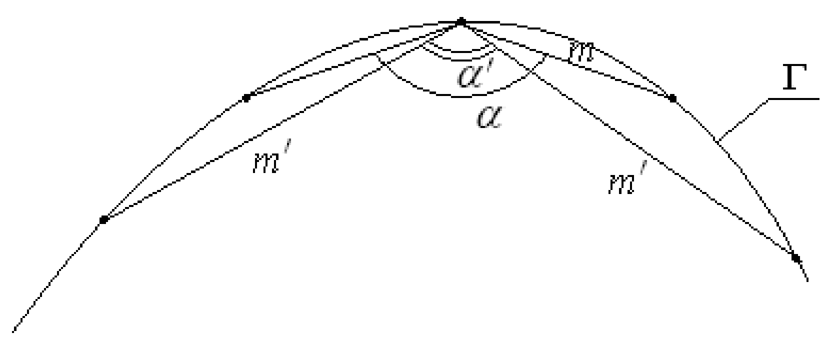


Figure 4.2 Neighbourhood of sectoral m-rate of function of curvature of contour curve

Lemma 3 has a double value for the construction of SSR of curvature and proper handle. At first, changing of neighbourhood m it is possible to check accuracy of m-rate of curvature in points of contour curve.

Secondly, as at $k \to 0$ error of sectoral rate $O_m^o \to 0$, it is possible to assert that for finding of transit points of curvature through a zero it is possible initially to take minimum size neighbourhood m. In addition, for points with small curvature it is possible to take small neighbourhoods m with guaranties here finding of estimation of curvature with given accuracy and fast-acting.

For receiving of rapid estimation of curvature with given accuracy it is possible to link neighbourhood of m and step $\triangle u$ of discretisation of contour curve $\Gamma = \{(x(u), y(u) \mid u \in [0, L]\}$.

A curve is presented like set of points $\Lambda = \{(x_i, y_i) \mid i \in [0, M_u]\}, M_u = L_u / \triangle u$, distance between any two points λ_i and λ_{i+1} of set Λ is equal thus

$$\left\| \lambda_i - \lambda_{i+1} \right\| = \triangle u = 1,$$

where $\|\cdot\|$ is the Euclidean metrics.

For the construction of discrete scale-space representation with invariant to scaling, ration the amount M_u of points of curve Λ with losing or adding new points to some general value M, I.e. lead $|\Lambda| = M$ [85, 86]. Thus, accept $L = M$ as new length of contour.

In addition, choose the step of discretisation on a scale $\triangle\sigma$. Then representation of points of curve Λ on a scale σ, such that $\sigma(\mathrm{mod})\triangle\sigma \equiv 0$ (or $\sigma = \triangle\sigma \cdot j, j \in N$), can be easy found on the following formula of the discrete approaching of Gaussian convolution:

$$x_i^\sigma = \sum_{j=-[M/2]}^{j<[M/2]} x_{i-j} g(i-j, \sigma), \quad y_i^\sigma = \sum_{j=-[M/2]}^{j<[M/2]} y_{i-j} g(i-j, \sigma),$$

4

$$g(x;\sigma) = \frac{1}{\sqrt{2\pi\sigma}} e^{-x^2/2\sigma} \tag{4.4}$$

Thus, $x_{i-j}^0 = x_{i-j}, \ \ y_{i-j}^0 = y_{i-j}$.

For the construction of SSR of curvature it is necessary to find the values of function of curvature in all M points of discrete curve for each of N_σ levels of scale. The calculation of position of some λ_i point on the levels of scale $\sigma > 0$ according (4.4) requires $O(M^2)$ operations, while due to rule 3σ only points in neighbourhood 3σ bring in a meaningful contribution to the sums (4.4). It is possible to transform formulas (4.4) to the following kind for considerable decreasing of amount of operations, that is ordinary practice at the use of Gaussian convolution in discrete spaces:

$$x_i^\sigma = \sum_{j=-[3\sigma]}^{j<[3\sigma]} x_{i-j} g(i-j,\sigma),\ \ y_i^\sigma = \sum_{j=-[3\sigma]}^{j<[3\sigma]} y_{i-j} g(i-j,\sigma) \tag{4.5}$$

Thus, at the maximal amount of levels on which the calculation of curve points is needed (and this amount in practice depends on how quickly on a curve will be not a single zero transit point of curvature) $\sigma = M/3$ for some $\triangle\sigma$ middle complication of calculations of every level will be order $O(M^2/2)$.

As for the exposure of maximums of SSR of curvature all levels of scale are needed, it is possible to apply another property of Gaussian convolution:

$$(f(x) * g(x,\sigma_1)) * g(x,\sigma_2) = f(x) * g(x, \sqrt{\sigma_1^{\ 2} + \sigma_2^{\ 2}}).$$

Let σ_i is a level of scale for which the discrete curve $\Lambda^{\sigma(i)}$ of which is already calculated. For the calculation of curve $\Lambda^{\sigma(i+1)}$ of the following level of scale in accordance with chosen $\triangle\sigma$ it is necessary to execute gaussian convolution of curve $\Lambda^{\sigma(i)}$ with a kernel σ^+ size of which can be calculated on the following simple formula:

$$\sigma^+ = \sqrt{\sigma_{i+1}^{\ \ 2} - \sigma_i^{\ 2}} \tag{4.6}$$

It allows to take middle complication of calculations of every level to the order $O(M \cdot \sqrt{M})$ at the maximal amount of levels (till to $\sigma = L/3$) on which the calculation of points of curve is needed.

After the calculation of curve of every scale, directly the estimation of curvature can be expected by proposed sectoral m-weight of curve. Corner α_i^σ for the point $\lambda_i \in \Lambda^\sigma$ of curve at some level of scale $\sigma = \triangle\sigma \cdot j, j \in N$ it is possible to calculate as:

$$\alpha_i^\sigma = \arccos\big((x_i^\sigma - x_{i-1}^\sigma)(x_{i+1}^\sigma - x_i^\sigma) + (y_i^\sigma - y_{i-1}^\sigma)(y_{i+1}^\sigma - y_i^\sigma)\big) / |\overrightarrow{v_+^\sigma}||\overrightarrow{v_-^\sigma}|, \tag{4.7}$$

where $\overrightarrow{v_+^\sigma} = \lambda_{i+1}^\sigma - \lambda_i^\sigma$;

$\overrightarrow{v_-^\sigma} = \lambda_i^\sigma - \lambda_{i-1}^\sigma$.

After this it is simple to receive sectoral m- weight v_m^o and estimation of curvature k_m^o of point λ_i^σ due to formulas (4.3) and (4.4).

The next method of construction of images of SSR of curvature on the basis of adaptive binary simplification of contour curve and calculation of sectoral m- weight neighbourhood m of which can be related to the level of simplification of curve is offered.

For finding of estimations of curvature of contour function at all levels of scale on the first step it is required to ration the contour curve so that length of discrete curve and amount of points were multiple 2: $L = M = 2^N, \triangle u = 1$.

Determination 4.2.. Binary simplification of discrete curve is an operation of exception of every second point from set Λ^σ of points of curve at some level of scale σ . In other words set Λ_η^σ of points of simplified curve can be found as:

$$\begin{gathered}\Lambda_\eta^\sigma = \{\lambda_i \in \Lambda_{\eta-1}^\sigma \mid i = [0, M_{\eta-1}], i(\mathrm{mod}2 \equiv 0\} \\ \Lambda_0^\sigma = \Lambda^\sigma\end{gathered} \tag{4.8}$$

Determination 4.3. The level of simplification η of discrete curve Λ_η^σ on a scale σ is equal to the amount of simplifications in accordance with (4.8) created for receiving of curve Λ_η^σ from a curve Λ at all levels of scale $\sigma' < \sigma$. Obviously $\eta \le \log_2(M)$.

It is suggested to calculate the curves of the followings levels depending on the level of simplification, using for development of curve only those points which was saved after binary simplifications on previous levels:

$$x_i^\sigma = \sum_{i \in \{\lambda_j \in \Lambda_\eta^{\sigma-\triangle\sigma} \| \|x_i^{\sigma-\triangle\sigma} - x_j\| < 3\sigma^+\}} x \cdot g(\|x - x_i^{\sigma-\triangle\sigma}\|, \sigma^+), \tag{4.9}$$

where x_i^σ is the first coordinate of finded point $\lambda_i \in \Lambda_\eta^\sigma$ of curve on a scale σ at the level of simplification η;

σ^+ - kernel of convolution which necessary for receiving of curve Λ_η^σ from curve $\Lambda_\eta^{\sigma-\triangle\sigma}$ calculated due to formula (4.8).

By analogy y_i^σ can be calculated .

We will enter cut-off ξ_m^o for m- weight of curves. We will simplify a curve each time during iterative development in accordance with a formula (4.9), when maximal weight of points of curve appears below than some cut-off :

$$\max_{\lambda_i \in \Lambda_\eta^\sigma} v_m^o(\lambda_i) < \xi_m^o + \triangle\xi, \tag{4.10}$$

where $v_m^o(\lambda_i)$ is a value of m- weight of curve Λ_η^σ in a point λ_i ;

$\triangle\xi$ - additional element which guarantees implementation of condition $v_m^o(\lambda_i') < \xi_m^o, \lambda_i' \in \Lambda_{\eta+\Delta\eta}^{\sigma+\Delta\sigma}$ on the curve of next scale and level of simplification.

Due to Lemma 3 it guarantees the calculation of estimation of curvature by sectoral m- weight of curve Λ_η^σ with given accuracy level. Actually, simplification of curve takes place when a curve is smoothed out so that the maximal estimation of curvature $v_m^o(\lambda), \lambda \in \Lambda_\eta^\sigma$ of points of discrete curve decreases to some apriory given level $C \cdot \xi_m^o$ and simplification of curve does not bring to the increase of maximal estimation of curve curvature $v_m^o(\lambda), \lambda \in \Lambda_{\eta+\Delta\eta}^{\sigma+\Delta\sigma}$ higher than some other level $C \cdot (\xi_m^o + \triangle\xi)$, $C = 4m/3\pi$ on next scale.

Application of method of adaptive discretisation allows to considerably accelerate the process of construction of scale-space representations, that will influence on increasing of velocity of as process of recognition of ECG elements and determination of their boundaries so and the process of forming of average signal which was offered in this work.

5 Experiments

For experimental verification of the developed methods selection of control ECG of healthy people, selection of ECG from patients by the heart attack, cardiomiopathy, arrhythmia of different kinds and other of diseases was formed. General amount of records is equal 30 containing on average for 6 leads. Thus amount of records – 180.

3 types of measuring of basic parameters of ECG (determined due to positions of boundary points and peaks of ECG elements) inside every selection, necessary for further diagnostics were conducted: manual measuring by specialists-cardiologists, measuring by the method of WT and offered method. The next tables are got.

Comparing of the automatic and manual measuring:

automatic measuring / manual measuring

	Автоматический										Ручной									
№ П	L(P)	A(P)	QRS	A(Q)	A(R)	A(S)	LGK	PGK	L(T)	A(T)	L(P)	A(P)	QRS	A(Q)	A(R)	A(S)	LGK	PGK	L(T)	A(T)
24	0,14	0,058	0,05	0	0,635	-0,81	0,02	0,03	0,26	0,577	0,11	0,057	0,1	-0,03	0,633	-0,81	0,04	0,06	0,23	0,338
	0,14	0,138	0,07	0	1,388	-1,29	0,03	0,04	0,26	0,533	0,12	0,06	0,1	-0,1	1,283	-1,35	0,05	0,05	0,25	0,411
	0,13	0,075	0,09	-0,14	1,008	-1,01	0,06	0,03	0,27	0,247	0,13	0,075	0,1	-0,14	1,008	-1,07	0,06	0,04	0,26	0,151
	0,15	0,132	0,05	0	0	-1,32	0	0,05	0,27	-0,38	0,15	0,132	0,06	0	0	-1,32	0	0,06	0,26	-0,49
	0,17	0,318	0,05	0	0	-1,06	0	0,05	0,31	-0,07	0,15	-0,1	0,08	0	0,337	-1,06	0,03	0,05	0,31	-0,07
	0,13	0,076	0,09	-0,13	1,175	-1,2	0,05	0,04	0,26	0,354	0,13	0,076	0,1	-0,13	1,175	-1,25	0,05	0,05	0,25	0,267
	0,11	-0,05	0,09	0	0,604	-0,64	0,04	0,05	0,23	0,229	0,11	0,055	0,11	-0,03	0,715	-0,87	0,05	0,06	0,22	0,142
34	0,12	0,074	0,11	-0,15	1,323	-1,45	0,05	0,06	0,27	0,44	0,12	0,074	0,11	-0,15	1,323	-1,45	0,05	0,06	0,29	0,44
	0,16	0,109	0,09	0	0,567	-0,78	0,02	0,07	0,29	0,338	0,16	0,109	0,09	0	0,567	-0,78	0,02	0,07	0,29	0,338
	0,09	0,039	0,09	0	0,328	-1,48	0,02	0,07	0,3	-0,26	0,1	-0,1	0,09	0	0,328	-1,48	0,02	0,07	0,32	-0,26
	0,12	0,03	0,07	-0,1	0,857	-0,67	0,04	0,03	0,31	0,121	0,13	0,054	0,08	-0,1	0,857	-0,83	0,04	0,04	0,3	0,213
	0,14	-0,06	0,05	0	1,341	-1,35	0,02	0,03	0,32	0,465	0,14	-0,06	0,05	0	1,341	-1,35	0,02	0,03	0,34	0,465

Rejections according to types:

Отклонения									
L(P)	A(P)	QRS	A(Q)	A(R)	A(S)	LGK	PGK	L(T)	A(T)
0,03	0,001	0,05	0,033	0,002	0,001	0,02	0,03	0,03	0,239
0,02	0,078	0,03	0,104	0,105	0,051	0,02	0,01	0,01	0,122
0	0	0,01	0	0	0,063	0	0,01	0,01	0,096
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0,008	0,032	0,012	0,017	0,025	0,124	0,004	0,008	0,094	0,228

Mean WT deviation from the manual measuring due to:

- amplitude values: SA=0,085 MB
- intervals values: ST=0,032C

Middle deviation the offered combined method from manual measuring due to:

- amplitude values: SA=0,086MB
- intervals values: ST=0,027C

Rapidness experiments had shown that comparison of ECG (using DTW) is N/E slower than proposed technique based on elastic comparison of SSR of ECG, where N – number of measurings in a cardiac cycle of the initial signal and E – number of points in SSR (~7 for ECG). Using m-estimations and binary simplifications during SSR construction speeds up the process up to log(N) times.

6 The relevance and the problem of optimal selection of drugs

To date a vast clinical experience of joint appointments of several drugs are accumulated. However, the understanding of the main interaction of drugs is not enables to predict the common effect on the body.

Thus, at cardiopatologies with different etiologies if the drug has low bioavailability as a result of high presystem metabolism then the concomitant appointment of drugs or other substances that are its inhibitors, may significantly shift its bioavailability, as well as its effect, and leads to undesirable effects. Conversely, a drug with high bioavailability can be with smaller risk of such interactions because its concentration in the blood under normal conditions closes to maximum. In modern literature described many cases of serious unwanted medical interactions between digidroperidins and immune blockers with low bioavailability.

There are some approaches for finding the optimal set of drugs based on concept decision-making procedures. Decision-making procedures consist on general steps: defining goals; the allocation of many possible ways to achieve it (the set of possible solutions); formation evaluation to determine order's level on the set of solutions (objective estimation); choosing the best solution (optimization problem).

These approaches provide to receive optimal recipe by three-way ranging system of effectiveness evaluating of drug action on the human body due to diagnoses according to respective functions of Gibson-Miller and Clark [Piotrovsky, 1987, Wanger, 2004]. The disadvantage of these approaches is losing of registration of pharmacological interaction between drugs.

There is simplex method for searching of optimal set of drugs [Borzenkov, 1987, Porvan, 2003] which does not take into account the diversity of pharmacological actions of drugs and constructing an isomorphism of graphs. In additional this method use non-linear logarithmic function of extremum search [Vysotskaya, 2004] which does not guarantee the completeness of the intersection of multiple pharmacological actions in finite set of drugs.

It is known the approach of finding the components of medicinal collection from plants with different mechanisms of achieving uniaxial pharmacological effect [Yoneyama, 2000], in which the quantitative ratio of the components of final recipe is defined by minimizing the function $F(X)$ by the formula:

$$F(X) = \sum_{I=1}^{m} [y_I^N (1 - \Delta y_I(x)) - y_I^{\circ}(x)]^2 \to \min_X \qquad (6.1)$$

where $x = (x_1 \ldots x_n)$ – drugs composed assumed plant's collection;

$y_I^{\circ}(x)$ – initial value of index I;

$y_I^N(x)$ – physiological value of index I;

$\Delta y(x)$ – relative value of pharmacological effect;

m – number of analyzing parameters;

n – number of components in medical collection.

However this approach does not allow carrying out choice of plants because here there is no registration of individual features of the restoration of human body balance and in contrary assume using up the medicines one axial pharmacological action. Implicit indication of analyzed parameters in minimized function can lead to errors of calculation, and thus to inefficient treatment.

Since the human body is an open system, which is influenced by various external factors, and processes in the body are partly probabilistic nature, it can be assumed that the change in the organism homeostasis will also be probabilistic in nature. In connection with this application of all the above described methods and models to adequately describe the evolution of homeostasis as a result of a comprehensive treatment of heart disease drugs is not possible.

7 Simulation of the optimal selection of drugs

Suppose there is a finite set of drugs that constitute the union T_U and set of pharmacological actions of drugs (DS). Let IT_U and IDE_U are sets of their indexes, respectively. And let the patient after surveys receive number of diagnoses from list of diagnosis and symptoms D_U due to international classificatory of diseases (ICD). Let set of indexes ID_U indices D_U.

Assume that the patient have set diagnoses $D = \{d_k\}$, $k \in ID$; $ID \subset ID_U$, where d_k - k-th diagnosis/symptom of the patient. In the treatment of the k-th diagnosis/symptom is recommended using set of DS $T_k = \{t^k_j\}$, $j \in IT_k$; $IT_k \subset IT_U$, where t^k_j – j-th DS useful in the treatment of the k-th diagnosis/symptom. Thus, we can determine set of DS that are recommended for this patient's symptoms, such as:

$$T_X = \bigcup_{k \in ID} T_k \tag{7.1}$$

At selection of treatment the age, immune status and degree of overall state of the patient must take into account. Therefore expanded base of diagnoses will have view:

$$D' = \{D, G_B, V, A\} = \left\{\{d_k\}, d_{M[D_U]+1}, d_{M[D_U]+2}, d_{M[D_U]+3}\right\},$$

where $d_{M[D_U]+1} = G_B$ – degree of overall state of the patient;

$d_{M[D_U]+2} = V$ – index of patient age: «0» for age 14 – 60 years old, «1» for 14 years old and after 60 years old patients;

$d_{M[D_U]+3}$ =*A* – allergies to certain drugs value of which can be «0» if the patient have not allergies, «1» – if patient have allergies.

Thus, assume that G_B, V and A can be attributed to the discharge diagnoses, set *k transform in next view*:

$$k' \in ID', ID' = ID \bigcup \{ M[D_U]+1, M[D_U]+2, M[D_U]+3 \},$$

where $M[D_U]$ - the number of diagnoses and symptoms in ICD.

As known, every diagnosis from D' has according set of contraindicated drugs $TP_{k'}$.

$$TP_{k'} = \{t_j^{k'}\}, j \in ITP_{k'}; ITP_{k'} \subset IT_U ,$$

where $ITP_{k'}$ - the set of indexes of contraindicated drugs at k'-th diagnosis/symptoms.
The total value of contraindicated drugs is equal:

$$TP = \bigcup_{k' \in ID} TP_{k'} \tag{7.2}$$

Then the set of drugs selected for treatment of the patient using (9) and (10) will defined as:

$$\Omega = T_X \setminus TP \tag{7.3}$$

with its set of indexes – IT_Ω..
Denote power of set of recommended drugs as $M_T = M[\Omega]$, then set of incompatible to j-th drug is:

$$TN_j = \{tn_g^j\}; j, g \in IT_U ,$$

where - g-th incompatible drugs with j-m drug.

Conclusion

Thus, application of scale-space representation of signal and its derivatives for clarification of positions of boundary points on results of wavelet detector provides authenticity of ECG elements recognition at the level of method of wavelet transformations and increase of determination accuracy of positions of bondary points in the automatic mode on 18%.

In addition, offered method for selection of informative cardiac cycle and also selection of cardiac cycles at the calculation of average signal on the basis of scale-space representation, allows to remove possibility of choice of cycles with distortions while averaging the signal, and also enables to recognize pathological rejections arising up in single cardiac cycles. Thus, the method works in N/E times faster than correlation method due to binary simplification (where N is an amount of measurings in a second, E – number of points in SSR).

Proposed method of optimal drug selection reduces recipe space more than doubled taking into account required for treatment of patient symptoms pharmacological actions of drugs. Analyzing the type of function of goal it is possible to get conclusion that in order to find extremum standard mathematical optimization methods can be used, such as method of variation of weight coefficients at private criteria and method of steepest descent. Using the obtained function as function of goal for deterministic parametric model of optimal selection of multi-direction activity drugs allows adequately and systematically complete process of selecting of effective treatment of all symptoms of patient.

The result of using the proposed method is optimally selected list of drugs most effective for treatment of patient. This method enables the physician to improve quality of the treatment of heart diseases and reduce time for optimal solutions, and also reduce impact of side effects of used drugs.

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