NATIONAL ACADEMY OF SCIENCES OF UKRAINE
INTERNATIONAL RESEARCH AND TRAINING CENTER FOR INFORMATION TECHNOLOGIES AND SYSTEMS OF THE NAS OF UKRAINE AND OF MES OF UKRAINE
V.M. GLUSHKOV INSTITUTE OF CYBERNETICS OF THE NAS OF UKRAINE

Cybernetics and Computer Engineering

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CONTENTS

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НАЦІОНАЛЬНА АКАДЕМІЯ НАУК УКРАЇНИ
МІЖНАРОДНИЙ НАУКОВО-НАВЧАЛЬНИЙ ЦЕНТР
ІНФОРМАЦІЙНИХ ТЕХНОЛОГІЙ ТА СИСТЕМ НАН УКРАЇНИ І МОН УКРАЇНИ
ІНСТИТУТ КІБЕРНЕТИКИ ІМ. В.М. ГЛУШКОВА НАН УКРАЇНИ

Кібернетика та обчислювальна техніка

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MATCHING BASED MULTISTYLE LICENSE PLATE RECOGNITION

Introduction. *A State-of-the-Art of license plate (LP) recognition from images is observed. Despite the fact that License Plate Recognition (LPR) is often regarded as a solved task, country-specific systems are mostly designed that limits their application. Pay attention to the increasing mobility, effective LPR systems must handle multistyle LP including multinational ones that have different fonts and syntax. Another bottleneck of LPR is that accuracy of recognition at varying environmental conditions as well as of low resolution or degraded LP usually is rather low.*

The purpose *of the article is to develop algorithms for multistyle single line LP learning and recognition from images as well as for comparatively low resolution LP processing.*

Methods. *Randomized Hough transform is used for detecting horizontal frame lines and subsequent LP localization in image. Structural feature matching approach is used for character recognition. Correction of recognition results is based on calculation of modified Levenstein distance (MGED) between LP description and templates.*

Results. *New algorithms for multinational license plate learning and recognition from images are proposed. Localization of LP in images is based on LP frame detection using a randomized Hough transform to detect horizontal contour frame line segments. Recognition of segmented characters inside LP is based on searching key points in skeletonized character images and matching these points with etalons. Correction of recognition LP output is carried out by matching and defining MGED between LP input description and templates. Online active learning for recognition of new LP symbols and templates is also proposed. Results of testing developed algorithms and software are described.*

Conclusions. *Algorithms for multistyle LP localization and recognition from images are proposed. Control and correction of recognition results is based on calculation of MGED between input LP description and templates which are more general in comparison conventional text lines. As future work, it is planned to increase accuracy by learning feature etalon weights, as well as to consider other LP types for recognition and to test developed means on more representative data samples.*

Keywords: *license plate localization and recognition, key points matching, Levenstein distance.*

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INTRODUCTION

The task of automatic search and recognition of license plates of cars (LP) in images (LPR — license plate recognition) is a special case of recognition of text information in the world around us. This task is considered more complicated in comparison with the recognition of texts on paper, since it must be solved in uncontrolled conditions and with limited possibilities for using reference data to correct recognition results. LPR systems [1–6] are actively used to automate payment for travel and parking, fix accidents, track vehicles and solve other important problems. The development of new, more effective LPR tools remains relevant for the following main reasons:

1. Reliability of LP recognition in uncontrolled conditions is relatively low (60 % – 80 % according to [4]) due to the influence of interfering factors (speed, weather conditions, changes in illumination, various angles of vision). Recognition accuracy also depends on the camera-to-car distance: the well-known LPR suggest that the size of the character in the image should be at least 25–30 pixels, and the size of the license plate should be 100–130 pixels [1–2].

2. The number of license plate styles (types) is constantly growing, but most of the well-known LPR systems are designed to recognize national LP of their countries and have limited options for online learning and recognition of new LP types or styles.

Most LPRs consist of three main parts: 1) LP localization in the image, 2) segmentation of the LP image into separate characters, 3) segmented character recognition using optical character recognition (OCR). The OCRs used are usually developed on the basis of learning (neural networks, SVM, AdaBoost) [1–6] using a large number of positive and negative examples of symbol images. As a result, learning requires a lot of time for the preparation of input data and subsequent implementation. So, e.g., in [6], for the deep learning of a neural network to recognition of two types Brazilian license plates was used about 4000 allocated and marked by operators LP images (40 % of the total number, recognition accuracy on the control part of the set — 85 %). To search for LP in images, another neural network was used, previously learned on another training set, and the authors consider the learning to recognize other types of characters and symbol fonts [6] as a rather complicated task that will need to be solved in the future.

When performing the work, two main goals were pursued: 1) the development of online learning tools for recognizing various types of single-line LPs and 2) the recognition of relatively small size noisy LPs. The work is going on of [7] — new algorithms are considered: 1) preprocessing and segmentation of LP into symbols; 2) character recognition based on matching of so-called "key points" on the skeletonized image representation [8]; 3) correction of recognition results based on the modified Levenshtein edit distance (ED) technique [9].

LP recognition accuracy can be significantly increased on the base of calculation the ED between the input text line and each of the reference LP lines that can be in view of the camera. This method can be used only in some especial cases — creating and maintaining a database of all cars is almost impossible, given the huge number of cars used. In this regard, another correction is considered, based on comparison of the input LP description with LP type templates.

In each country, a relatively small number of templates (types) of national license plates are used, which specify most of the license plates used and facilitate the task of recognizing them. The description of the template can be presented in the form of a list of minimal rectangles, such that each of them bounds LPs character and has an attribute defining one or more valid codes for this character. In the simplest case, this attribute takes two values — '0' if character is a digit, and '1' otherwise. If we neglect size and relative positions of the characters, we get a description in the form of a text string consisting of 0 and 1. The correction of the output text line can be performed based on the calculation of the modified ED (MGED) between the LP input description and the template descriptions taking into account the sizes and relative arrangement of the constituent characters. The weights of editing operations (deleting, replacing and inserting characters) when calculating MGED, in contrast to [9], are not constant values, but depend on characters, the reliability of their recognition and position in the line. The MGED features will be considered in more detail below in Section 3. The LP localization in image and recognition of the LP characters are performed uniformly for all recognized types of license plates, the structure of which is taken into account only at the stage of MGED calculation between the recognized string and license plate templates.

Learning to LP recognition from images can be performed in offline, online or online-offline modes. In the offline mode, the learning process is close to [1–3, 5–6] — the operator generates training samples and defines LPs templates followed by adjusting of etalons feature weights in the best way to classify training images. In the online mode, the formation of symbol etalons and LP templates is performed during the operation of the system. In the combined online-offline mode, feature weights of etalons are further adjusted.

The rest of the paper is organized as follows. Section 1 discusses the LP localization algorithm in images, and in Section 2 algorithms for preprocessing LP images, segmenting them into individual characters, and recognizing these characters are considered. Section 3 contains descriptions of LP templates and the MGED between LP descriptions. Section 4 describes LPR learning and Section 5 presents the results of preliminary testing of the developed tools. In conclusion, a discussion of results and directions for further research is given.

LP LOCALIZATION IN IMAGE

The main stages of the localization and recognition of license plates in images are presented in Fig. 1.

At the initial stage, LP localization in image is carried out using the randomized Hough transform for horizontal contour lines detection of the LP frame [10, 11]. To avoid detection of these lines in LP characters area, preliminary image erosion operation is performed in the horizontal direction (to erode areas with low brightness). The vertical lines of the frame are detected by tracing vertical edges in the image. The result of the LP localization is a certain number of quadrangles (FS), ordered by the conformity assessment estimates of the LP frame. The value of this estimate depends on the editing operations of the contour line segments during the formation of the FS, the difference in the angles of inclination of the opposite sides, as well as the ratio of the lengths of the horizontal and vertical sides.

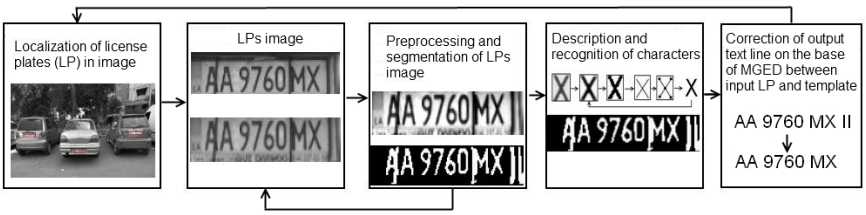

Fig. 1. Localization and recognition of license plates in images.

Hough transform is a relatively time-consuming operation. Therefore, in order to speed up the search, the contrasty image areas, which may include car numbers, are preliminarily found, and only then, within these areas, more accurate LP localization based on the Hough transform is performed. The main feature of such areas is a large number of vertical edges of the contour. The search for these areas is performed using the so-called "integral" image representation [12] — in each pixel of the integral image the total number of contour points located to the left and above this pixel is stored. The integral contour image lets to calculate the number of contour points in any rectangle using several operations.

PREPROCESSING AND RECOGNITION OF LP IMAGE

At subsequent stages, processing and recognition of the selected image parts with the highest values P is performed. First, the image is processed to transform quadrangle to a rectangle with the given dimensions. After that, normalization of the image by brightness, adaptive image binarization and character segmentation are performed [7]. Segmentation of LP image into separate areas is performed by selecting connected objects in a binary image and leaving as candidates for characters those ones whose sizes and additional parameters satisfy certain restrictions. If the size of the area significantly exceeds the average size of the characters, the operation of dividing this area into several parts is performed based on the use of horizontal projections of the binarized and brightness-normalized image of this area. An example of segmentation and binarization of characters in a license plate image is shown in Fig. 2, and examples of processing an image of a single character are shown in Fig. 3.

Character image recognition consists of the following basic operations:

1. Normalization by brightness, binarization and scaling of the input image within the symbol area (Fig. 3).

2. Skeletonization of the symbol image [8] and detection the so-called "key points (KP)" (Fig. 4) on symbol skeleton representation. The main KPs are the points of ends or intersections of the symbol lines, as well as the points of changing the bypass direction (clockwise or counterclockwise) of its skeleton (e.g., the point in the middle of the symbol 'S'). Additional KPs are the central points of the inner contours in symbol images such as '0', 'O', 'D' or 'P'. Generating description of each KP: normalized values of its coordinates, type and weight (from 0 to 1) KP , as well as the directions of the skeleton line segments emerging from the main KP. Symbol description includes its KPs descriptions, width and height of the minimum rectangle bounding the symbol, as well as features of fragments (a line or curve indicating its position relative to the KP pair), between some basic KPs.

3. Calculation of the distance between the input description and the set of reference descriptions of symbols used. If this distance is less than the threshold value, the name of the reference corresponding to this distance is assigned to the input symbol. Otherwise, the above operations (items 1–3) are performed once more, but with the other parameters of preprocessing and noise removing on the skeletonized representation of the symbol (feedback between the result of recognition of the symbol and its preprocessing in Fig. 1). In both cases, the recognition confidence (0–100) is calculated based on the obtained distance and the threshold used.

Fig. 2. Position adjustment (b) of the input LP image (a). Brightness normalization (c) and binarization (d) of the image (b).

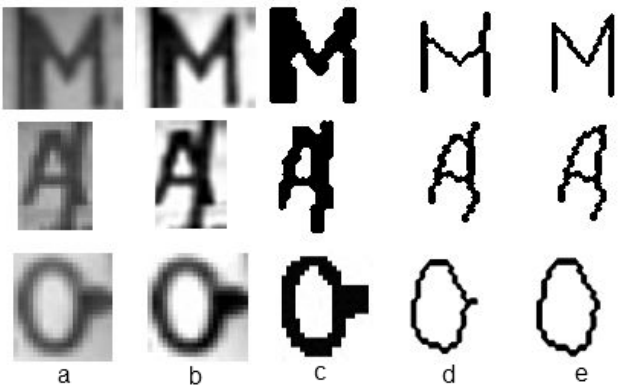

Fig. 3. Examples of brightness normalization (b), binarization (c), skeletonization (d) and noise removing (e) of character images (a).

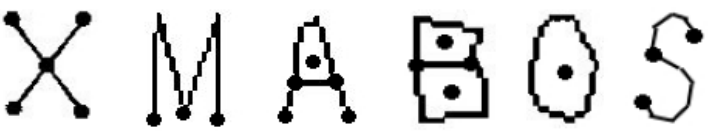

Fig. 4. Key points examples on skeletonized representations of symbols.

In the online learning mode weights of key points depend on their types and conditions used of detection in the symbol image. In two other modes, the point weights are adjusted during learning on a set of image examples. The distance between the two compared characters is defined on the base of matching of their KPs. Let $P_1 = \{p_i^1\}, i = 1,...n_1$ and $P_2 = \{p_j^2\}, j = 1,...n_2$ be sets of key points in two symbols; $R(p_i^1 \in P_1)$ — correspondence function: $R(p_i^1 \in P_1) = p_j^2 \in P_2$, if p_i^1 corresponds to p_j^2, и $R(p_i^1) = 0$ otherwise; matching — $M(P_1, P_2) = \{(p_i^1, p_j^2) \mid R(p_i^1) = p_j^2\}$.

Maximal matching $M_m(P_1, P_2)$ is the matching with size equaled to $n = |M_m(P_1, P_2)| = \min(n_1, n_2)$ value. Distance $D(P_1, P_2) = (D_{del} + D_{cor})/w$ between two symbols descriptions is defined on the base of finding optimal matching $M^*(P_1, P_2)$ of KPs:

$$M^{\bullet}(P_1, P_2) = \arg\min_{M_m(P_1,P_2)} D_M = \sum_{k=1}^{n} (w_i^1 + w_j^2) d((p_i^1, p_j^2)_k \in M_m(P_1, P_2)),$$

where $d(p_i^1, p_j^2)$ — distance between two KPs and $(w_i^1 + w_j^2)$ — sum of these points weights; $D_{del} = K_{del} w_{del}$ — cost of deletion $|n_2 - n_1|$ non matched points; w_{del} — sum of weights of deleted KPs; w — total sum of KPs weights; K_{del} — deletion cost of KP with weight, equaled to 1; D_{cor} — value D_M that corresponds to optimal matching $M^*(P_1, P_2)$.

The distance between two KPs depends on the differences in their coordinates and types, as well as in the directions of the corresponding line segments emanating from these points. To make decision about the input symbol it is necessary to define the distance of its description to the set of reference descriptions. Therewith, the input symbol belongs to a certain class if the distance of the description of the symbol to set of reference samples of this class is the smallest among other classes and less than the specified threshold value.

The distance D_{cor} (therefore, $D(P_1, P_2)$) can be calculated using optimal algorithms [13–15] or algorithm [7], which belongs to type of so-called "greedy" algorithms ($O(n_1 n_2)$). As a result, the correspondence (optimal matching) of the KPs of two compared symbols is defined, which is used to verify features of the traced skeleton segments between the pairs of corresponding main KPs of these symbols.

MODIFIED LEVENSTEIN DISTANCE AND LPs TEMPLATES

The Levenshtein distance (ED — edit distance) $lev_{a,b}$ between two lines of characters a, b is equal to the minimum total cost of deleting, inserting and replacing characters of the first line to convert to the second one [9]. Let C_{del}, C_{ins}, $C_{sub}(a_i \neq b_j)$ be the costs of deleting, inserting, and replacing (0, if $a_i = b_j$, and 1 otherwise) a single character. Then the distance $lev_{a,b}(i, j)$ between the first i characters of the text line a and the first j characters of the text line b can be calculated using the following formulas:

$lev_{a,b}(i, j) = \max(i, j)$, if $\min(i, j) = 0$, and

$lev_{a,b}(i, j) = \min(lev_{a,b}(i-1, j) + C_{del}, lev_{a,b}(i, j-1) + C_{ins}, lev_{a,b}(i-1, j-1) +$

$+ C_{sub}(a_i \neq b_j)$, if not.

The ED between two lines is equal to the minimum number of operations to delete, insert, and replace characters in one line to convert it to the second one and is a measure of the proximity of two lines. This measure is not always effective in solving problems of searching, comparing, and correcting texts;

therefore, in [13–15] more general types of ED were proposed for assessing the proximity of compared strings. In [13] the weight of operations depends on the names of symbols and operations (generalized edit distance — GED), in [14] in addition to [13] an extended list of editing operations is proposed. In [16] a more general case (Markov edit distance — MED) was considered to evaluate the likelihood of each sequence of editing operations and it was shown that ED and GED are particular cases of MED. The book [17] contains a detailed analysis of the most common issues related to the use of ED. In this paper we propose the modified Levenshtein distance (MGED) to evaluate the proximity of the description of the LP recognition result not only to the reference lines, but also, unlike [1, 4, 5, 9, 13–15] to the LP templates.

Let $R = \{r_i\}, i = 1,...n$ be the set of minimal rectangles bounding the images v_i of symbols s_i on a license plate; N_S — the number (size of the alphabet) of the characters used; $E_j = \{e_{j,k}\}, j = 1,...N_S; k = 1,...n_j$ — set of etalons (references) of symbol s_j; $d_{i,j}(v_i, E_j) = \min_k dist(v_i, e_{j,k} \in E_j)$ — distance between image v_i and symbol s_j; $dg(s_j)$ — a feature equal to 1 if s_j is a digit, and 0 otherwise.

Consider the following three types of LP descriptions. The first description is a list of rectangles, to each $r_i \in R$ of which correspond N_S distances between v_i and symbols. The second description is different in that to each $r_i \in R$ two pairs of values correspond: 1) the recognized character s_i and corresponding to it the smallest distance ($d_{i,j1}$); 2) $(s_i^{'}, d_{i,j2} = \min_{j \neq j1} d_{i,j} \mid dg(s_i) \neq dg(s_i^{'}))$. The third description differs from the first one in that it does not contain data on the size and coordinates of the recognized characters.

Consider also the corresponding LP reference descriptions. The first description defines the LP template as a set of rectangles, within each of which there can be one character from the valid lists. The second description differs from the first in that to each rectangle has not a symbol, but a feature (1 or 0) that this symbol should be a number or a letter. The third description represents a text string of characters. The MGED value represents the minimum cost of changing the input description to bring it into correspondence (matching) with the LP reference description. Similarly to GED [13], MGED uses the operations of replacing, inserting and deleting characters, the cost of which depends on the names of the characters being edited and the type of operation, but there are also differences from [9, 13–15].

Using the description of the first type, the cost of replacing the s_i character in the input description with the s_j character in the reference is equal to $C_{sub}(s_i, s_j) = \min_{k \in S_j} d_{i,k}(v_i, E_k) + ds(i, j)$, where S_j is the list of numbers of valid characters for replacement and $ds(i, j)$ is the penalty for differences in sizes and relative coordinates of the characters s_i and s_j. Using the description

of the second type, $C_{sub}(s_i, s_j) = d_{i,j1}(v_i, E_{j1}) + ds(i, j)$, if $dg(i) = dg(j)$, and $C_{sub}(s_i, s_j) = d_{i,j2}(v_i, E_{j2}) + ds(i, j)$ otherwise. The cost of replacing one character with another is lower, the closer these characters are in their drawing, size and position on the LP relatively to other characters. For example, the cost of replacing '5' with 'S' is much lower than replacing '5' with '8' or '4'. Data on the proximity of individual pairs of characters is either predefined or generated during the operation of the recognition system.

The cost of deleting a symbol depends on its similarity with the nearest reference (increases with increasing similarity), as well as on the position of the symbol in the line (decreases at the beginning and end of the line, since there is a greater chance of interference). The cost of inserting a character is small if there is a gap in the LP image at the place of insertion that is not covered by recognized characters. This symbol cannot be taken from the templates of the first two types — when using them, the missing symbol can be determined only by additional recognition of the license plate in defined part of the input image, and the correction of the results should be performed not outside the LPR, but in the process of recognition.

LP RECOGNITION LEARNING

LP learning can be performed in offline, online or online-offline modes. In the first case, the learning process is close to [1–3, 5, 6] — the operator generates a training set of images, and also defines LP templates. Therewith, due to the use of informative features and essential part of noise removing at the processing stage, smaller training set can be used in comparison with most other works. In subsequent learning weights of character feature weights are adjusted to minimize image recognition errors from the training set.

In the online mode, the formation of symbols references and LP templates is performed during the system operation. In this case, the weights of the symbols features depend on the conditions used of their detection in the image and are not formed on the base of learning. Before learning it is assumed that there is a rectangular frame on the LP image and no data on the characters and type format of recognized license plates. LP search, segmentation and recognition of characters is performed uniformly for all LP types, the structure of which is taken into account only at the stage of MGED calculation between the recognized string and LP templates. If the program cannot recognize the symbol, the image of this symbol is presented to the user for identification and creation of an additional reference in taking an appropriate decision. Each group of recognized characters is checked by the program for matching with previously added LP templates and, in the absence of close matching, is presented to the operator for taking a decision on adding a new LP template. The input LP image and its recognition result can also be presented to the user for verification and correction of these results. The indicated actions can be considered as the process of the so-called "active learning" of the program for recognizing new characters and license plate patterns in images. In the online-offline mode, automatic adjustment of the features weights of the references is performed after learning recognition in online mode. After completing the learning process, the

program switches to a mode in which insufficiently reliable results are stored in memory and can be viewed by the user at a convenient time for him.

EXPERIMENTAL TEST RESULTS

During the testing, LP were searched and recognized on the following two sets of images. The first set (B1) consists of 175 images in which cars are photographed at various distances and angles with respect to the camera. This set contains 19 types of license plates, including three types of Ukrainian numbers, seven — Polish, three — Belarusian, in two — Russian, Moldavian and Lithuanian. The second set contains 85 images of two types of Greek numbers from a database [2]. Of these 85 images, 65 are simpler to recognize (sample "day color" — B2) and 20 are most complex of this database (sample "difficult_color_more_than_one" — several cars, different shooting angles, lighting conditions, small size LP — B3). During the testing, the LP image was considered correctly recognized if all characters of the text line on this LP image were correctly recognized. Examples of images from samples B1, B2, B3 (by two images in the upper, middle and lower parts) and the results of their recognition are presented in Fig. 8.

Images from sample B2 in Fig. 8 (middle part) have interference in the form of touching the characters to the frame (left image) and varying lighting. Images from sample B3 in Fig. 8 (lower part) have a horizontal size of less than 65 cells. At the same time, five out of six LPs are recognized correctly, one of the LPs (left image) is detected, but not recognized. Main recognition results:

1. Recognition accuracy on sets B1–B2 is 97 % and on set B3 is 72 %, provided that the horizontal size of the LP in the image is not less than 65 pixels. Character references and descriptions of the LP templates were obtained during online learning.

2. For learning in online mode, it is enough to have a relatively small number of examples of LP types and the characters used. The number of character references after learning is from one to four for different characters.

3. The average processing time for an input image of 800x600 and 1600x1200 is respectively 0.14 sec. and 0.52 sec.

The database [2] was created in 2008 to provide the possibility of comparing different LPRs on the same data, since usually the developer provides recognition results on his data that are not available for testing other LPRs. However, we are not aware of publications containing comparative test results for recognizing systems on this database.

Fig. 8. Examples of localization and recognition of license plates in images from test samples B1, B2 and B3 (by two images in the upper, middle and lower parts).

The introduced restriction of 65 pixels on the minimal horizontal size of the LP in images is relatively weak. So, for example, the "Nomerok-4" system [18] provides 95 % of the correct recognition of state Ukrainian and Russian LP when the following conditions are met: 1) the speed of the car is not more than 120 km / h; 2) the horizontal size of LP in the frame is at least 130 cells; and 3) LP in frame can be recognized by the operator. The developers of the SecurOS Auto intelligent video analysis system [19] claim to recognize with reliability up to 96 % of state license plates of vehicles moving at speeds up to 180 km / h, without providing data on the fulfillment of conditions for recognition and used restrictions on the size of the number in the frame. With a decrease in the size of the license plate, the task of its localization and recognition in the image becomes more complicated. On the other hand, recognition of LP with small sizes provides the possibility of further video surveillance and control.

CONCLUSION

Algorithms for localizing, processing and recognizing LP in images are considered. Algorithms and software for online learning to recognition new characters and LP templates are developed. Recognition of each character is performed based on the detection of key points on the skeletonized representation of the character image and matching them with the key points on each of the compared reference images. The minimum allowable size of LP in the image is 65 pixels, which provides the possibility of more distant video surveillance compared to other systems.

The recognition results are controlled and corrected based on the calculation of the modified Levenshtein distance between the description of the input LP and the reference descriptions of LP templates. These descriptions are more general than usually used text strings on these LP, which are available only for some applications. In subsequent studies, it is planned recognition also of two-line types of LP and increasing reliability by additionally adjusting the weights of symbol reference features during learning. It is also necessary to implement LP recognition in the video stream and test the developed tools on more representative data samples.

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РОЗПІЗНАВАННЯ НОМЕРНИХ ЗНАКІВ НА ЗОБРАЖЕННЯХ З КОРЕКЦІЄЮ РЕЗУЛЬТАТІВ

Вступ. Розглянуто сучасний стан розпізнавання номерних знаків (НЗ) автомобілів на зображеннях. Відомі системи розпізнавання номерних знаків (СРНЗ) зазвичай забезпечують порівняно високу надійність у сприятливих умовах тільки найпоширеніших (національних) типів НЗ у кожній країні. Можливості цих систем для оперативного налаштування на розпізнавання нових типів НЗ та символів є доволі обмеженими, що ускладнює їхнє застосування. Беручи до уваги швидке збільшення мобільності пересування транспортних засобів, у багатьох роботах зазначається, що найактуальнішими завданнями для розроблення сучасних СРНЗ є розпізнавання різних типів НЗ, особливо в складних та неконтрольованих умовах змінення зовнішнього освітлення та наявності різних завад як на самих НЗ, так і у навколишньому середовищі.

Метою роботи є розроблення алгоритмів пошуку і розпізнавання різного вигляду однорядкових НЗ автомобілів на зображеннях в умовах наявності завад та порівняно малих розмірів НЗ на зображеннях.

Методи. Рандомізоване трансформування Хафа використовують для пошуку горизонтальних контурних ліній рамки НЗ та наступної локалізації НЗ на зображеннях. Розпізнавання сегментованих символів на зображенні НЗ виконується шляхом пошуку та розмітки так званих «особливих точок» на скелетизованих поданнях цих символів. Корекція результатів розпізнавання реалізують шляхом обчислення модифікованої відстані Левенштейна (МВЛ) між вхідним описом та шаблонами НЗ.

Результати. Розглянуто нові алгоритми пошуку і розпізнавання різного вигляду однорядкових номерних знаків автомобілів на зображеннях. Локалізація НЗ виконується за допомоги пошуку горизонтальних контурних ліній рамки номера за методом Хафа. Розпізнавання сегментованих зображень символів на НЗ реалізовано шляхом виділення «особливих точок» на скелетизованих поданнях символів і пошуку відповідності цих точок еталонним описам. Контроль і корекція результатів розпізнавання НЗ виконують на основі обчислення МВЛ між вхідним описом НЗ і шаблонами типів НЗ. Запропоновано та реалізовано засоби активного навчання під контролем оператора розпізнаванню нових типів НЗ та символів у процесі роботи системи. Наведено результати тестування розроблених алгоритмів у разі розпізнавання НЗ різних країн.

Висновки. Запропоновано нові алгоритми локалізації та розпізнавання різних типів НЗ. Контроль та корекція отриманих результатів базується на обчисленні модифікованої відстані Левенштейна вхідного опису НЗ до множини шаблонів типів НЗ, які мають більш загальний вигляд порівняно з еталонними текстовими рядками. У подальшому виконанні роботи заплановано розгляд алгоритмів розпізнавання НЗ, які містять декілька текстових рядків, а також підвищення надійності розпізнавання шляхом оптимального налаштування за допомогою навчання вагів особливих точок символів.

Ключові слова: *пошук та розпізнавання номерних знаків на зображеннях, відповідність особливих точок, відстань Левенштейна.*

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РАСПОЗНАВАНИЕ НОМЕРНЫХ ЗНАКОВ НА ИЗОБРАЖЕНИЯХ
С КОРРЕКЦИЕЙ РЕЗУЛЬТАТОВ

Рассмотрены алгоритмы поиска и распознавания различного вида однострочных номерных знаков (НЗ) автомобилей на изображениях. Локализация НЗ выполняется с помощью поиска горизонтальных контурных линий рамки номера методом Хафа. Распознавание сегментированных изображений символов на НЗ реализовано путем выделения особых точек на скелетизированных представлениях символов и поиска соответствия этих точек с эталонными описаниями. Контроль и коррекция результатов распознавания НЗ выполняется на основе вычисления модифицированного расстояния Левенштейна между входным описанием НЗ и шаблонами типов НЗ. Приведены результаты тестирования разработанных алгоритмов при распознавании НЗ из различных стран.

Ключевые слова: *поиск и распознавание номерных знаков на изображениях, соответствие особых точек, расстояние Левенштейна.*

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THE USE OF COMPLEXITY AND VARIABILITY CHARACTERISTICS FOR THE ANALYSIS OF COMPLEX DYNAMIC SYSTEMS

Introduction. *The normal dynamics of a healthy organism is chaotic and the observed "chaos" is inherent in the very nature of the dynamic processes taking place in the organism and the degree of chaotic of these processes may vary in case of pathology in one direction or another. The electrical activity of the brain is also characterized by signs of deterministic chaos, and changes in parameters of its nonlinear dynamics testify to the characteristic changes in brain functioning. The problem of diagnostics and identification of the moment preceding an epileptic seizure or other periods of brain functioning in epileptic patients is not only a problem of choosing a classification method but also of determining quantitative estimates of dynamics reflecting the complexity and variability of the Electroencephalography (EEG) signal.*

The purpose of the *paper is to form an effective ensemble of features from the characteristics reflecting the complexity and variability of the EEG signal,to construct the prognostic models for the course of epilepsy and to develop the information technology to support diagnostic decision-making based on them.*

Methods. *The methods of mathematical statistics for the processing of diagnostic information, the methods of mathematical modeling (stepwise logistic regression) — for the construction of prognostic models for estimating the course of epilepsy were used; methodological bases for the creation of information technology for the diagnosis of epilepsy according to the EEG.*

Results. *Changes in indicators such as Hurst Index, fractal dimension, logistic mapping, and algorithmic signal complexity have been investigated. The mathematical models*

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include variables that are calculated from the EEG data and are available during patient observation. As a result of the application of step-by-step algorithms, the most informative features are included in the models. The selected features allow for the most accurate identification of individual periods of epilepsy flow from the EEG data. It has been established that the use of a decision support system increases the reliability of determining the periods of an epileptic seizure (conditional norm, before, during and after an attack) by an average of 6.6% for children and 8% for adults.

Conclusions. *The proposed prognostic models allow to obtain additional information about the periods of epileptic seizures and to predict their onset in time.*

Keywords: *information technology, EEG, epileptic seizures, epilepsy, complexity and variability indicators, predictive models, logistic regression.*

INTRODUCTION

The objects, the analysis of which is offered in the work, belong to the class of dynamic systems, classifying states of which is one of the most difficult task. It is impossible to apply directly the classical methods of object analysis, set by one multidimensional observation, to solve the problems of this class. The reason for the discrepancy of the developed methods is that the state of such systems can be described only by the type and character of the movement, and it can be both chaotic movement and steadfast trajectory. Consequently, the various types of integral characteristics of the system movement according to a class of dynamic systems were developed and they have become an instrumental bridge to the application of classical methods of classification of objects. Below it is suggested to consider the use of indicators of complexity and variability of the system motion to assess changes in functional states in patients with a focal form of epilepsy.

The prevalence of epilepsy in developed countries is 5–10 cases per 1000 population. According to the results of population studies conducted in developed countries, the incidence of epilepsy ranges from 0.28 to 0.53 cases per 1000 population. In Europe about 6 million people suffer from epilepsy, 40 % of them are not receiving proper treatment [1, 2]. In the diagnosis and treatment of epilepsy, photo stimulating and hyperventilation tests are used, which are performed under EEG control. They allow estimating readiness for epileptic seizures and reaction to treatment, i.e. efficiency of medication therapy. In this case, the doctor's knowledge of the functional state of the cortex for situational decision-making is essential for the effectiveness of the treatment process. Therefore, the development of mathematical means of recognition of brain functioning features before, during and after an epileptic seizure, as well as in the periods between seizures, is an actual task.

PROBLEM STATEMENT

It was found that the normal dynamics of a healthy organism is chaotic and the observed "chaos" is inherent in the very nature of the dynamic processes taking place in the organism [3–5], and the degree of chaotic of these processes may vary in case of pathology in one direction or another [6]. It has been proved that besides periodic processes, the electrical activity of the brain is also characterized by signs of deterministic chaos, and changes in parameters of its nonlinear dynamics testify to characteristic changes in brain functioning [7, 8].

Such apparent changes can also be observed in epileptic signals of electroencephalograms. The nature of epilepsy is such that corresponding pathological

changes in the brain cause certain differences in the signs of chaotic dynamics (i.e. "degree of chaoticity") of the signal. There are a number of works devoted to the analysis of chaotic dynamics, which use such indicators of complexity as Hurst index, logistic mapping, fractal dimensionality and algorithmic complexity of the signal. A number of studies of dynamic systems of the healthy human brain based on EEG methods of nonlinear analysis have been conducted [5, 9]. In the opinion of the authors of the work, the increase in complex dimensionality of the EEG superficial in the performance of tasks related to memory operation is shown and reflects the increase in degrees of freedom in competitive interactions between neural ensembles [7, 10]. However, to solve the problem of identification of periods of brain bioelectrical activity in epileptic seizures, it is necessary to investigate the suitability of the developed indicators for solving problems of the corresponding classification. Therefore, the problem of diagnostics and identification of the moment preceding an epileptic seizure or other periods of brain functioning in epileptic patients is not only a problem of choosing a classification method but also of determining quantitative estimates of dynamics reflecting the complexity and variability of the EEG signal.

The purpose of the article is to form an effective ensemble of features from the characteristics reflecting the complexity and variability of the EEG signal,to construct the prognostic models for the course of epilepsy and to develop the information technology to support diagnostic decision-making based on them.

THE FUNCTIONAL STATES CLASSIFICATION METHODS OF THE CEREBRAL CORTEX-EPILEPTIC AND BETWEEN EPILEPTIC PERIODS

The data of recorded signals are structured in such a way that for each patient the data structures characterizing the following functional cortical states are allocated [11, 12, 13, 14]:

- between seizures or periods of the conditional norm (interictal) — periods between the seizures in which there are no manifestations of the pathological activity;
- before the seizure (preictal) — periods characterized by the appearance of noticeable deviations from the normal state;
- seizure (ictal) — existing characteristic manifestations of the pathological activity of the brain.
- after the seizure (postictal) — attenuation of the pathological activity.

Based on existing nonlinear analysis methods studies of epileptic EEG signals in order to assess the suitability for classifying these periods, the following parameters of chaotic dynamics were selected: Hurst index, fractal dimension, Kolmogorov algorithmic complexity, logistic mapping and LZW archiving.

The Hurst Index is a measure of the smoothness of the fractal time series, based on the evaluation of the expression of its long-term dependence [15]. Due to its clear range boundaries, the Hurst Index is widely used in the analysis of time series of complex systems. It contains minimum assumptions about the system under study and allows us to determine the classification of time series depending on the nature of the signal [16, 17]. Studies [18] have shown that periods between seizures (conditional norm) correspond to smaller values of the Hurst index than for the seizure period. Values for the period after an seizure are close to 0.5. The pre-seizure and postseizure periods vary greatly, but a notice-

able difference can be seen. The pre-seizure and postseizure periods are characterized by lower values, which indicate antipersetic properties.

Fractal dimensional (FD) is a natural tool for detecting the level of complexity and compactness of chaotic processes. It can be used to measure the complexity of biological signals. The analysis of the fractal dimensionality of the Minkovsky EEG signal calculated by the Box Counting method shows that epileptic seizures are a state with a lower fractal dimensionality of the EEG signal compared to a conventionally normal state [6, 13]. Intermediate values of fractal dimensionality are characteristic for the periods between seizures (conventional norm) because this period is more complex. In the period before the seizure and during the seizure, an increase in fractal dimensionality is observed, which indicates a decrease in the signal complexity.

The Lempel Ziv archiving method (LZ or CrossTable) is an algorithm for lossless data compression, and is a convenient estimation of complexity, characterizing the degree of order or disordered space-time patterns [19]. The parameter LZ-complexity as a measure of regularity and complexity of time series is included in nonlinear parameters of estimation, and it is expedient to use it for the analysis of the non-stationary biomedical signals of small length.

The Lempel-Ziv-Welch (LZW) data compression method [20] is based on calculating the number of letter pair repetitions in an encoded sequence and replacing the most common pairs with a new value. The method can be used to determine the level of complexity of a sequence and is analyzed. When working with EEG signals, the efficiency of the method is higher, the more pronounced is the epileptic seizure. The results of the study of patients with focal epilepsy showed high values of complexity during the period of the conditional norm, progressively less before and during the seizure, and increased (even in comparison with the conditional norm) after the seizure.

One of the possible ways to determine the nature of the trajectories of nonlinear systems after signal sampling can be realized by means of logistic (square) map. Below is the map (1), for which the character of trajectory changes from the value of r:

$$x_{n+1} = r x_n \left(1 - x_n\right), \tag{1}$$

where n is a discrete-time step, r is a control parameter. According to the graph of dependence of x_n on r, it is possible to track changes in the state of such a system, including the transition from chaotic motion to stable trajectories. [21]. After substitution a number of neighboring points x_n, x_{n+1} of the EEG trajectories in (1) and determination of the value (moving average) of the r parameter, it is possible to obtain an estimate of the trajectory character by the logistic map.

According to the obtained values, the postseizure period coefficients are in the range of $2 < r < 3$ and indicate that the signal is going to a stationary value $(r-1)/r$, but will first oscillate around it. The preseizure and postseizure periods are characterized by values in the range of $3 < r < 1+\sqrt{6}$ which indicates that the system is moving chaotically.

The development of the classifiers models of brain activity periods with EEG can provide three possible strategies for comparing periods with each other [22]:

The strategy "one to three" or "one against all": the comparison of one period with respect to three other periods (Fig. 1). Scope: standard procedure for determining membership class.

1. The strategy "one to one": a pairwise comparison of periods with each other. Scope: solving the conflict of the classifiers, that can be obtained according to item 1.

2. Strategy "two to two": a comparison of any two periods combination with any two others; Scope: indirect definition of the class by the classifiers for "groups" of classes, when the allocated class is surrounded by other classes.

Further, we will focus on the strategy "one against all" only.

The selection of informative channels was also carried out. There is the own set of informative channels for each brain area in focal epilepsy [23–25]:

- the set for frontal area consists from Fp1, Fp2, F3, F4, F7 and F8;
- the set for frontal parietal area consists from Fp1, Fp2, F3, F4, F7, F8, P3 and P4;
- the set for the parietal area consists from P3 and P4;
- the set for the central area consists from C3 and C4;
- the set for the central area consists from C3 and C4;
- the set for the parietal-occipital area consists from P3, P4, O1 and O2;
- the set for temporoparietal central area consists from T3, T4, C3, C4, T5, T6, P3 and P4.

To obtain the classifiers, a standard procedure was used to select the best linear combination of activity periods features and a complicated procedure using functional transformations of primary features. For this purpose, the inverted indicators ($1/x_i$) and variables of the type ($x_i \cdot x_j$) and (x_i / x_j) were included in the models as the applicants besides the initial features. Further, we will call them generalized variables.

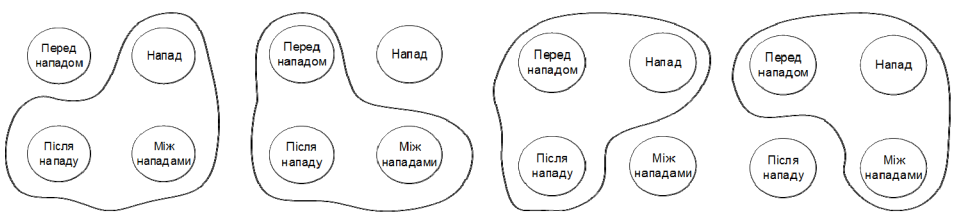

Fig. 1. Possible combinations of strategies "one against all" comparing the periods of epileptic seizures among themselves

Multivariate statistical methods were used to solve the following problems. The primary selection of features was carried out on a degree of statistical connection between the bioelectric indicators calculated by the methods of nonlinear dynamics and the indicators of patients' states. Next, the classifiers were found on the basis of statistical methods of modeling, and periods of an epileptic seizure were distinguished with high accuracy.

Methods of regression and discriminant analysis, logistic regression method were used to construct the classifiers. The best results were obtained by step algorithm of the logistic regression method, classifier models were built as a logistic regression model:

$$p(y) = \frac{1}{1+e^{-y}}, \tag{2}$$

where $y = y\,(x)$ was obtained in linear (3) or non-linear (4) form:

$$y = b_0 + \sum_{k=1}^{m} b_{i_k} x_{i_k} \tag{3}$$

$$y = b_0 + \sum_{k=1}^{m} b_{i_k} \varphi_{i_k}(\mathbf{x}), \tag{4}$$

where x_i, $i = 1, ..., M$ are the primary features, x_{i_k}, $k = 1, ..., m$ is the best linear ensemble of features, $\varphi_{i_k}(\mathbf{x})$, $k = 1, ..., m$ is the best nonlinear ensemble of generalized variables, b_0, b_{i_k}, $k = 1, ..., m$ is the regression coefficients.

DEVELOPMENT AND APPLICATION OF MODELS TO CLASSIFY PERIODS OF BRAIN ACTIVITY STATUS

Classification models for each pathological zone of the brain are given below in the form of linear (3) and nonlinear equations (4). The contenders for inclusion in the predictive models are the selected complexity indicators (Hurst index, fractal dimensionality, logistic mapping, Kolmogorov algorithmic complexity, LZW method archiving) and variability indicator (standard deviation). Informative channels of electroencephalograms in a certain pathological region of the brain in prognostic models are indicated by the indices of the corresponding indicator.

EEG studies were conducted at the Department of Functional Diagnostics and Ultrasound of the Cardiovascular System of the Consulting and Diagnostic Center of the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department. Two age groups of volunteers — children (under 18 years) and adults (over 18 years) — were formed from the Center's patients. All the participants gave their written consent to the anonymous use of the data and research based on it. Fifteen people with focal epilepsy were investigated. A diagnostic study and advisory opinion on the International Classification of Diseases (ICD-10) resulted in the diagnosis of G40 epilepsy (11, 12, 26). The models used the following designations of brain regions for focal epilepsy: frontal (F), frontal-parietal (FP), parieto-occipital (PO), parietal (P), central (C), temporal-parietal (PTC).

Models for groups of children and adults were developed separately.

Prognostic models to study focal epilepsy [22] in the frontal area (F) of the brain for children using linear functions were obtained in the form:

$$y_{(F)\,preictal} = 0{,}018 \cdot \sigma_{F7} + 0{,}058 \cdot \sigma_{F8} + 71{,}151 \cdot LZW_{Fp1} - 109{,}845 \cdot LZW_{F8} - \\ - 40{,}937 \cdot FD_{F3} + 52{,}680;$$

$$y_{(F)\,ictal} = 32{,}275 \cdot LZW_{F7} - 12{,}908 \cdot CrossTabe_{F4} - 27{,}527 \cdot FD_{F3} + \\ + 21{,}577 \cdot FD_{F7} - 0{,}715 \cdot LogRefl_{F7} + 5{,}563;$$

$$y_{postictal} = 15{,}819 \cdot Hurst_{F4} + 20{,}547 \cdot FD_{F3} - 25{,}528;$$

$$y_{(F)\,interictal} = -15{,}986 \cdot Hurst_{F4} + 15{,}210 \cdot LZW_{F8} + 3{,}773,$$

where σ_{F7} and σ_{F8} are standard deviations of channel signals F7 and F8 respectively, LZW_{Fp1} and LZW_{F8} — the method LZW archiving of channel signals Fp_1 and F8 respectively, FD_{F3} and FD_{F7} is the fractal dimension of channel signals F3 and F7 respectively, $CrossTabe_{F4}$ is the Kolmogorov algorithmic complexity of channel signals F4, $LogRefl_{F7}$ — logistic map of channel signals F7, $Hurst_{F4}$ — Hurst index of channel signals F4;

The found models using the non-linear functions:

$$y_{(F)\,preictal} = 19867{,}414 \cdot FD_{F8} + 116{,}577 \cdot \sigma_{F8} \cdot LZW_{Fp1} - 62190{,}942 \cdot LZW_{F8} \cdot FD_{F7} - \\ - 3116{,}873 \cdot \frac{\sigma_{F8}}{\sigma_{F7}} + 9792{,}292 \cdot \frac{LZW_{Fp1}}{Hurst_{F4}} - 1802{,}285 \cdot \frac{FD_{F3}}{Hurst_{F4}} - 18475{,}975 \cdot \frac{FD_{F3}}{FD_{F7}} + 15963{,}319;$$

$$y_{(F)\,ictal} = 0{,}106 \cdot \sigma_{Fp1} - 0{,}121 \cdot \sigma_{F4} - 85{,}626 \cdot FD_{F8} - 16{,}224 \cdot \frac{FD_{F3}}{LZW_{F8}} + 2098{,}599 \cdot \frac{FD_{F7}}{\sigma_{F7}} + \\ + 54{,}981 \cdot \frac{FD_{F7}}{LogRefl_{F7}} + 103{,}510;$$

$$y_{(F)\,postictal} = -0{,}014 \cdot \sigma_{Fp1} + 28{,}714 \cdot FD_{F8} + 15{,}856 \cdot \frac{1}{Hurst_{F4}} + 169{,}545 \cdot Hurst_{F4} \cdot FD_{F3} - \\ - 16{,}884 \cdot \frac{LZW_{Fp1}}{LZW_{F8}} + 32{,}035 \cdot \frac{LogRefl_{F7}}{\sigma_{F8}} + 0{,}468 \cdot \frac{LogRefl_{F7}}{LZW_{F3}} - 124{,}749;$$

$$y_{(F)interictal} = -723{,}256 \cdot CrossTable_{Fp1} + 13885{,}269 \cdot \frac{1}{\sigma_{F7}} - 65504{,}719 \cdot \frac{Hurst_{F4}}{\sigma_{F7}} - \\ - 497{,}085 \cdot \frac{LZW_{F3}}{LZW_{Fp1}} + 1071{,}683,$$

where, σ_{Fp1}, σ_{F4}, σ_{F7} and σ_{F8} — are standard deviations of channel signals Fp1, F4, F7 and F8 respectively, LZW_{Fp1}, LZW_{F3} and LZW_{F8} — the method LZW archiving of channel signals Fp1, F3 and F8 respectively, FD_{F3}, FD_{F7} and FD_{F8} — is the fractal dimension of channel signals F3, F7 and F8 respectively, $CrossTable_{Fp1}$ is the Kolmogorov algorithmic complexity of channel signals Fp1, $LogRefl_{F7}$ logistic map of channel signals F7, $Hurst_{F4}$ — Hurst index of channel signals F4.

The prognostic models to study focal epilepsy in the frontal- parietal (FP) region of the brain for children using the linear functions are obtained in the form:

$$y_{(FP)\ preictal} = -53,773 \cdot LZW_{F3} + 34,476 \cdot LZW_{P4} + 7,626;$$

$$y_{(FP)ictal} = -0,05 \cdot \sigma_{F8} - 0,018 \cdot \sigma_{P4} - 45,589 \cdot Hurst_{F7} + 88,175 \cdot LZW_{F3} - \\ -142,462 \cdot LZW_{F4} + 40,366 \cdot FD_{F7} - 3,998;$$

$$y_{(FP)postictal} = 17,682 \cdot FD_{F8} - 17,350;$$

$$y_{(FP)interictal} = -25,651 \cdot Hurst_{F8} + 10,644,$$

where σ_{F8} and σ_{P4} — standard deviations of channel signals F8 and P4 respectively, LZW_{F3}, LZW_{F4} and LZW_{P4} — the method LZW archiving of channel signals F3, F4 and F8 respectively, FD_{F7} and FD_{F8} is the fractal dimension of channel signals F7 and F8 respectively, $Hurst_{F7}$ and $Hurst_{F8}$ — Hurst index of channel signals F7 and F8 respectively.

The found models using the non-linear functions:

$$y_{(FP)preictal} = 39,411 \cdot LZW_{P4} - 57,386 \cdot LZW_{F3} \cdot FD_{F7} - 0,603 \cdot FD_{F8} \cdot LogRefl_{F7} + 10,530;$$

$$y_{(FP)ictal} = 41,336 \cdot \frac{1}{FD_{F7}} - 0,306 \cdot \sigma_{P4} \cdot Hurst_{F7} + 0,257 \cdot \frac{\sigma_{F4}}{LogRefl_{F7}} - \\ -4,359 \cdot \frac{\sigma_{F8}}{\sigma_{F4}} - 2159,452 \cdot \frac{LZW_{F4}}{\sigma_{F8}} + 90,158 \cdot \frac{FD_{F7}}{FD_{F4}} - 100,411;$$

$$y_{(FP)postictal} = 14,164 \cdot FD_{F4} \cdot FD_{F8} - 14,216;$$

$$y_{(FP)interictal} = 9,866 \cdot LogRefl_{F8} - 230,279 \cdot \frac{Hurst_{F8}}{FD_{F7}} - 13,741 \cdot \frac{FD_{F4}}{Hurst_{F7}} + 95,697,$$

where, σ_{F4}, σ_{F8} and σ_{P4} are standard deviations of channel signals F4, F8 and P4 respectively, LZW_{F3}, LZW_{F4} and LZW_{P4} the method LZW archiving of channel signals F3, F8 and P4 respectively, FD_{F4} and FD_{F7} is the fractal dimension of channel signals F4 and F7 respectively, $LogRefl_{F7}$ and $LogRefl_{F8}$ logistic map of channel signals F7 and F8 respectively, $Hurst_{F7}$ and $Hurst_{F8}$ — Hurst index of channel signals F7 and F8 respectively.

The prognostic models to study focal epilepsy in the frontal-parietal (FP) region of the brain for adults using the linear functions are obtained in the form:

$$y_{(FP)ictal} = -0,014 \cdot \sigma_{F4} + 2,296;$$

$$y_{(FP)\ postictal} = 2568,138 \cdot Hurst_{P3} - 28,909 \cdot LogRefl_{F7} - 594,780;$$

$$y_{(FP)\ interictal} = -56,141 \cdot Hurst_{P4} + 23,304,$$

where σ_{F4} is standard deviations of channel signal F4, $LogRefl_{F7}$ — the method LZW archiving of channel signal F7, $Hurst_{P3}$ and $Hurst_{P4}$ — Hurst index of channel signals P3 and P4 respectively.

The found models using the non-linear functions:

$$y_{(FP)preictal} = 29778,394 \cdot \frac{Hurst_{F7}}{\sigma_{F4}} - 10611,242 \cdot \frac{FD_{F8}}{\sigma_{F4}} + 43,472;$$

$$y_{(FP)ictal} = -0,016 \cdot \sigma_{F4} \cdot FD_{F7} + 2,463;$$

$$y_{(FP)posticta} = -287,725 \cdot \frac{1}{Hurst_{P3}} - 0,053 \cdot \sigma_{P4} \cdot LogRefl_{F7} + 1014,848;$$

$$y_{(FP)interictal} = -8290,740 \cdot Hurst_{F7} \cdot Hurst_{P4} + 1311,756,$$

where σ_{F4} and σ_{P4} are standard deviations of channel signals F4 and P4 respectively, FD_{F7} and FD_{F8} is the fractal dimension of channel signals F7 and F8 respectively, $LogRefl_{F7}$ — logistic map of channel signal F7, $Hurst_{F7}$, $Hurst_{P3}$ and $Hurst_{P4}$ — Hurst index of channel signals F7, P3 and P4 respectively.

The prognostic models to study focal epilepsy in the parietal (P) region of the brain for children using the linear functions are obtained in the form:

$$y_{(P)preictal} = -24,651 \cdot LZW_{P3} + 10,655 \cdot CrossTable_{P3} + 3,545;$$

$$y_{(P)ictal} = -0,002 \cdot \sigma_{P3} + 24,725 \cdot LZW_{P4} - 16,024 \cdot CrossTable_{P4} + 1,424;$$

$$y_{(P)posticta} = -6,280 \cdot FD_{P3} - 5,478;$$

$$y_{(P)interictal} = -10,782 \cdot Hurst_{P3} - 12,988 \cdot CrossTable_{P4} + 10,927,$$

where σ_{P3} is standard deviations of channel signal P3, LZW_{P3} and LZW_{P4} — the method LZW archiving of channel signals P3 and P4 respectively, FD_{P3} is the fractal dimension of channel signal P3, $CrossTable_{P3}$ and $CrossTable_{P4}$ are the Kolmogorov algorithmic complexity of channel signals P3 and P4, respectively, $Hurst_{P3}$ — Hurst index of channel signals P3.

The found models using the non-linear functions:

$$y_{(P)preictal} = -3,892 \cdot \frac{LZW_{P3}}{Hurst_{P3}} + 4,061;$$

$$y_{(P)ictal} = -0,009 \cdot \sigma_{P3} \cdot LZW_{P4} - 4,064 \cdot \frac{CrossTable_{P3}}{LZW_{P3}} + 7,700;$$

$$y_{(P)posticta} = -4,648 \cdot \frac{LZW_{P4}}{CrossTable_{P4}} + 4,410;$$

$$y_{(P)interictal} = -29,175 \cdot Hurst_{P3} \cdot CrossTable_{P4} + 6,045,$$

where σ_{P3} is standard deviations of channel signal P3, LZW_{P3} and LZW_{P4} — the method LZW archiving of channel signals P3 and P4 respectively, $CrossTable_{P3}$ and $CrossTable_{P4}$ are the Kolmogorov algorithmic complexity of channel signals P3 and P4 respectively, $Hurst_{P3}$ — Hurst index of channel signals P3.

The prognostic models for studying focal epilepsy in the parietal (P) region of the brain for adults using the linear functions are obtained in the form:

$$y_{(P)ictal} = -51,835 \cdot FD_{P4} - 54,674;$$

$$y_{(P)posticta l} = 26,498 \cdot CrossTable_{P4} - 9,427;$$

$$y_{(P)interictal} = -5895,187 \cdot Hurst_{P3} - 9107,335 \cdot FD_{P4} + 12515,278,$$

where FD_{P4} is the fractal dimension of channel signal P4, $CrossTable_{P4}$ is the Kolmogorov algorithmic complexity of channel signal P4, $Hurst_{P3}$ — Hurst index of channel signals P3.

The found models using the non-linear functions:

$$y_{(P)preictal} = -5,035 \cdot \frac{CrossTable_{P3}}{Hurst_{P3}} + 7,825;$$

$$y_{(P)ictal} = 0,049 \cdot \frac{\sigma_{P3}}{CrossTable_{P4}} + 1923,627 \cdot \frac{FD_{P4}}{\sigma_{P3}} - 36,725;$$

$$y_{(P)posticta l} = -4,553 \cdot \frac{FD_{P3}}{CrossTable_{P4}} + 13,637;$$

$$y_{(P)interictal} = -65,351 \cdot Hurst_{P3} \cdot CrossTable_{P3} + 12,834,$$

where σ_{P3} is standard deviations of channel signals P3, FD_{P3} and FD_{P4} are the fractal dimension of channel signals P3 and P4 respectively, $CrossTable_{P3}$ and $CrossTable_{P4}$ are the Kolmogorov algorithmic complexity of channel signals P3 and P4 respectively, $Hurst_{P3}$ — Hurst index of channel signals P3.

The prognostic models for studying focal epilepsy in the parieto-occipital (PO) region of the brain for adults using the linear functions are obtained in the form:

$$y_{(PO)preictal} = 0,005 \cdot \sigma_{P3} + 25,671 \cdot Hurst_{P4} + 27,684 \cdot CrossTable_{P4} -$$
$$-60,768 \cdot FD_{P3} + 44,055;$$

$$y_{(PO)ictal} = -34,620 \cdot CrossTable_{O1} + 12,894;$$

$$y_{(PO)posticta l} = 38,967 \cdot Hurst_{P3} - 49,711 \cdot Hurst_{O1} + 64,554 \cdot CrossTable_{O2} +$$
$$+25,089 \cdot FD_{P3} - 40,953;$$

$$y_{(PO)interictal} = 0,018 \cdot \sigma_{O1} - 278,473 \cdot Hurst_{P4} + 110,532,$$

where σ_{P3} and σ_{O1} are standard deviations of channel signals P3 and O1 respectively, FD_{P3} is the fractal dimension of channel signal P3, $CrossTable_{P4}$, $CrossTable_{O1}$ and $CrossTable_{O2}$ are the Kolmogorov algorithmic complexity of channel signals P4, O1 and O2 respectively, $Hurst_{P3}$, $Hurst_{P4}$ and $Hurst_{O1}$ — Hurst index of channel signals P3, P4 and O1 respectively.

The found models using the non-linear functions:

$$y_{(PO)preictal} = 245,764 \cdot FD_{P4} + 108,356 \cdot \frac{1}{CrossTable_{P4}} + 0,037 \cdot \sigma_{O1} \cdot Hurst_{O1} -$$

$$- 113,627 \cdot \frac{FD_{P3}}{CrossTable_{P4}} - 232,824;$$

$$y_{(PO)ictal} = -0,501 \cdot \sigma_{P3} \cdot CrossTable_{O1} - 3239,140 \cdot CrossTable_{O1} \cdot CrossTable_{O2} + 613,546;$$

$$y_{(PO)postictal} = 245,981 \cdot Hurst_{P3} \cdot CrossTable_{O2} - 20,143 \cdot \frac{Hurst_{O1}}{CrossTable_{O1}} +$$

$$+ 2,522 \cdot \frac{FD_{P3}}{CrossTable_{P4}} - 11,320;$$

$$y_{(PO)interictal} = -9814,647 \cdot \frac{Hurst_{O1}}{\sigma_{O1}} + 7,892.$$

where σ_{P3} and σ_{O1} are standard deviations of channel signals P3 and O1 respectively, FD_{P3} and FD_{P4} are the fractal dimension of channel signals P3 and P4 respectively, $CrossTable_{P4}$, $CrossTable_{O1}$ and $CrossTable_{O2}$ are the Kolmogorov algorithmic complexity of channel signals P4, O1 and O2 respectively, $Hurst_{P3}$ and $Hurst_{O1}$ — Hurst index of channel signals P3 and O1 respectively.

The prognostic models for studying focal epilepsy in the temporoparietal occipital (PTC) region of the brain for children using the linear functions are obtained in the form:

$$y_{(PTC)preictal} = 0,231 \cdot \sigma_{T5} - 21,572;$$

$$y_{(PTC)ictal} = -6,560 \cdot \sigma_{T5} - 80,380 \cdot LogRefl_{T3} + 1013,659;$$

$$y_{(PTC)interictal} = 904,653 \cdot LZW_{T3} - 277,853.$$

where σ_{T5} is standard deviations of channel signal T5, LZW_{T3} is the method LZW archiving of channel signal T3, $LogRefl_{T3}$ — logistic map of channel signal T3.

The found models using the non-linear functions:

$$y_{(PTC)preictal} = -3390,068 \cdot \frac{LZW_{T3}}{\sigma_{T5}} + 13,639;$$

$$y_{(PTC)ictal} = 483,953 \cdot \frac{1}{LogRefl_{T3}} - 8,054 \cdot \sigma_{T5} \cdot LZW_{T3} + 199,664;$$

$$y_{(PTC)interictal} = -86,406 \cdot \frac{1}{LZW_{T3}} + 282,378.$$

where σ_{T5} is standard deviations of channel signal T5, LZW_{T3} is the method LZW archiving of channel signal T3, $LogRefl_{T3}$ — logistic map of channel signal T3.

The prognostic models for studying focal epilepsy in the central (C) area of the brain for children using the linear functions are obtained in the form:

$$y_{(C)postictal} = 70{,}859 \cdot Hurst_{C3} - 61{,}025 \cdot Hurst_{C4} + 17{,}968 \cdot FD_{C3} - 20{,}258;$$

$$y_{(C)interictal} = -21{,}227 \cdot Hurst_{C3} + 10{,}020,$$

where FD_{C3} is the fractal dimension of channel signal C3, $Hurst_{C3}$ and $Hurst_{C4}$ — Hurst index of channel signals C3 and C4 respectively.

The found models using the non-linear functions:

$$y_{(C)preictal} = -13{,}350 \cdot \frac{Hurst_{C3}}{Hurst_{C4}} + 15{,}023;$$

$$y_{(C)postictal} = -18{,}864 \cdot \frac{1}{FD_{C3}} - 21{,}649 \cdot \frac{Hurst_{C4}}{Hurst_{C3}} + 41{,}673;$$

$$y_{(C)interictal} = -33{,}659 \cdot Hurst_{C3} \cdot Hurst_{C4} + 6{,}813.$$

where FD_{C3} is the fractal dimension of channel signal C3, $Hurst_{C3}$ and $Hurst_{C4}$ — Hurst index of channel signals C3 and C4 respectively.

The quality of the forecast of built models for children was tested on the test sample (Table 1).

The results of the comparison showed the advantage of applying a nonlinear basis, and the accuracy was obtained over 92 %. When applying the linear basis, the accuracy was about 81 %.

The quality of forecast of built models for adults was tested on a test sample (Table 2).

The results of the comparison showed the advantage of applying a nonlinear basis, while the accuracy was obtained over 95 %. When applying the linear basis, the accuracy was received on the average 83 %.

Studies of epileptic seizures periods for children using logistic regression yielded lower results in sensitivity, specificity and classification accuracy than those of adults, confirming that the children's nervous system is formed before the age of 18.

The algorithms for calculating complexity (Hurst, LZW, CrossTable, FD) and variability (σ), as well as the obtained classifier models to determine the probability of a certain period of epilepsy flow with EEG, were applied to support diagnostic decision making of automatic determination of the epileptic seizure periods.

A decision support system [22] has been developed to improve the information support for the doctor and to promote the objectification of the treatment process through automatic classification of EEG fragments in accordance with the calculated values of the functions of predictive models.

Table 1. **Comparison of learning and test sample results in a study of focal epilepsy for children**

Period	Function type	Sensitivity, %		Specificity, %		Accuracy, %	
		training	test	training	test	training	test
1	2	3	4	5	6	7	8
Focal epilepsy in the frontal area							
Preictal	Linear	87,5	83,1	96,5	100	93,8	91,7
	Non-linear	100	84,2	100	88,5	100	86,5
Ictal	Linear	69,2	86,3	87,3	89,7	81,5	88,2
	Non-linear	92,3	86,5	98,2	92,1	96,3	93,2
Postictal	Linear	53,3	92,7	93,3	75	87,7	87
	Non-linear	91,4	100	93,3	100	91,8	100
Interictal	Linear	50	88,5	95,8	82,7	87,7	85,3
	Non-linear	100	96,7	100	93,3	100	96,1
Focal epilepsy in the frontal parietal area							
Preictal	Linear	60	55,5	94,9	54,5	85,2	58,3
	Non-linear	96,7	91,9	94,9	90,9	95,6	90,9
Ictal	Linear	73,3	91,9	94,9	91,3	88,9	81,8
	Non-linear	93,3	89,7	97,4	91,7	96,3	91,3
Postictal	Linear	67,5	82,7	97,4	86,1	88,9	91,7
	Non-linear	83,3	100	94,7	100	96,3	100
Interictal	Linear	50	75	95,7	100	88,9	100
	Non-linear	100	100	97,8	100	98,1	100
Focal epilepsy in the parietal area							
Preictal	Linear	38,5	68,3	95,4	81,4	79,1	81
	Non-linear	78,5	76,4	92,3	85,7	86,9	86,4
Ictal	Linear	44,4	67,3	89,1	75,6	75,8	77,3
	Non-linear	96,1	86,4	92,6	85,4	98	86,4
Postictal	Linear	42,5	64,2	97	83,3	78,7	84,2
	Non-linear	85,5	78,9	95,5	76,7	92,6	78,9
Interictal	Linear	71,6	65,7	98,7	77,5	84,6	85,7
	Non-linear	87,1	85,7	97,4	85	93,5	85,7
Focal epilepsy in the parieto-occipital area							
Preictal	Linear	76,9	88,9	87	89,5	83,3	90
	Non-linear	92,3	100	95,7	100	94,4	100
Ictal	Linear	66,7	100	87,5	100	80,6	100
	Non-linear	100	100	100	100	100	100
Postictal	Linear	88,9	90	100	88,9	97,2	87
	Non-linear	93,1	90	100	88,9	97,2	87
Interictal	Linear	100	80	100	71,4	100	76,5
	Non-linear	90	80	100	71,4	97,2	76,5
Focal epilepsy in the temporo-parietal central area							
Preictal	Linear	75	85,7	100	85,7	93,3	77,5
	Non-linear	85	85,7	100	85,7	96,3	85
Ictal	Linear	100	85,7	100	81,8	100	84,4
	Non-linear	100	90,5	100	72,7	100	84,4
Interictal	Linear	100	81,8	100	72,7	100	78,8
	Non-linear	100	81,8	100	86,4	100	83,7
Focal epilepsy in the central area							
Preictal	Linear	-	-	-	-	-	-
	Non-linear	87,6	100	93,3	100	91,1	100
Ictal	Linear	78,6	75	93,3	100	86,1	87,5
	Non-linear	86,3	87,5	93,3	91,7	90,5	88,7
Interictal	Linear	53,3	65	100	100	88,5	92,3
	Non-linear	83,3	100	100	100	90,5	100

Table 2. **Comparison of learning and test sample results in a study of focal epilepsy for adults**

Period	Function type	Sensitivity, %		Specificity, %		Accuracy, %	
		training	test	training	test	training	test
		training	test	training	test	training	test
1	2	3	4	5	6	7	8
Focal epilepsy in the frontal parietal area							
Preictal	Linear	-	-	-	-	-	-
	Non-linear	100	100	100	100	100	100
Ictal	Linear	40	62,9	100	100	81,3	92,3
	Non-linear	80	90,9	100	100	91,5	94,1
Postictal	Linear	100	81,8	100	86,4	100	83,7
	Non-linear	100	80	100	77,8	100	75
Interictal	Linear	66,7	73,8	92,3	100	87,5	100
	Non-linear	100	100	100	100	100	100
Focal epilepsy in the parietal area							
Preictal	Linear	-	-	-	-	-	-
	Non-linear	75	100	93,8	100	90	100
Ictal	Linear	66,7	-	92,9	-	85	-
	Non-linear	83,3	75	92,9	80	90	77,8
Postictal	Linear	40	100	93,3	100	80	100
	Non-linear	91,3	-	93,3	-	92,1	-
Interictal	Linear	100	100	100	80	100	88,9
	Non-linear	80	85,7	93,3	84,2	95	85

Receiving information about the EEG period classes, the doctor makes an informed decision about the EEG as a whole.

To check the efficiency of the developed system, a comparative evaluation of the results of the classification of EEG fragments performed by functional diagnostics physicians during the EEG visual analysis and with the help of the developed decision support system on the examination sample (25 EEG — 10 children and 15 adults) was made.

The use of the developed information technology of EEG processing due to the classification of a certain period according to the EEG allows to orient the doctor in decision-making, to increase the accuracy of the classification of the conditional norm periods, before and after an seizure, on the average by 5.5 %, 4.4 %, 9, 9 % and 6.6 % respectively for children, and for adults by 9.2 %, 7.4 %, 8.5 %, and 6.9 % respectively. By reducing the time it takes for a physician to determine the period of epilepsy with the EEG, the use of developed information technology makes it possible to classify the conditional norm periods, before, during and after seizure more quickly for children by 19 %, 15.5 %, 15.4 %, 16 9 % respectively, and for adults by 23.9 %, 18 %, 23.3 %, 17.8 % respectively.

The application of the developed information technology is useful in evaluating the effectiveness of treatment at the stages of patient monitoring.

CONCLUSIONS

The described methods of nonlinear dynamics allow quantitatively to distinguish the periods of epilepsy flow according to the EEG data. Changes in indicators such as Hurst Index, fractal dimension, logistic mapping, and algorithmic signal complexity have been investigated. Significant differences between these indicators due to changes in the functional state of the brain, are well reflected in the EEG. The complex calculation of such indicators allows to quantitatively distinguish the periods of epileptic activity by EEG, and further is used to build classification and prediction models.

With the help of step-by-step logistic regression analysis, prognostic models were built to detect the risk of a certain period of EEG activity. The application of nonlinear models allowed to significantly increasing the sensitivity, the specificity, and the accuracy even test samples. The determining accuracy of the seizure period on a test sample was about 6–10 % higher than with the use of models with linear functions.

The mathematical models include variables that are calculated from the EEG data and are available during patient observation. As a result of the application of step-by-step algorithms, the most informative features are included in the models. The selected features allow for the most accurate identification of individual periods of epilepsy flow from the EEG data. The accuracy of classification by the test sample was in the range from 71 % to 99 %. Analysis of composition and structure of the features is also of interest for clinical analysis.

The results of the EEG classification were comparatively evaluated using the proposed technology and without it. It was found that the use of the decision support system increases the reliability of determining the periods of the conditional norm, before, during and after a seizure by an average of 6.6 % for children and 8 % for adults. It was also possible to reduce the doctor's determination of the conditional norm period based on the EEG before, during and after seizure by an average of 16.7 % for children and 20.8 % for adults.

A decision support system has been developed to be useful in the diagnostic departments of health facilities and in psychoneurological hospitals where EEG is registered and analyzed.

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ВИКОРИСТАННЯ ПОКАЗНИКІВ СКЛАДНОСТІ ТА ВАРІАБЕЛЬНОСТІ ДЛЯ АНАЛІЗУ СКЛАДНИХ ДИНАМІЧНИХ СИСТЕМ

Вступ. Нормальна динаміка здорового організму є хаотичною, оскільки спостережуваний «хаос» властивий самій природі динамічних процесів, що протікають в організмі. Окрім періодичних процесів, для електричної активності мозку також є характерними ознаки детермінованого хаосу і зміни параметрів її нелінійної динаміки свідчать про характерні зміни у функціонуванні мозку. Такі виражені зміни можна спостерігати і у епілептичних сигналах електроенцефалограм. Розроблення математичних засобів розпізнавання особливостей функціонування головного мозку до, під час та після епілептичного нападу, а також у періоди між нападами є актуальним завданням. Проблема діагностики та виявлення моменту, який передує епілептичному нападу, або інших періодів функціонування головного мозку у хворих на епілепсію є проблемою не тільки вибору методу класифікації, але і визначення кількісних оцінок динаміки, які відображують складність та варіабельність сигналу ЕЕГ.

Метою статті є формування ефективного ансамблю ознак з характеристик, що відображають складність та варіабельність сигналу ЕЕГ, побудова прогностичних моделей для перебігу епілепсії та розроблення на їх основі інформаційної технології підтримки прийняття діагностичних рішень.

Методи. Було використано методи математичної статистики для оброблення діагностичної інформації, методи математичного моделювання (покрокова логістична регресія) для побудови прогностичних моделей оцінювання перебігу епілепсії; методи створення інформаційних технологій діагностики епілепсії за даними ЕЕГ.

Результати. Було досліджено зміни таких показників, як показник Херста, фрактальна розмірність, логістичне відображення та алгоритмічна складність сигналу. За допомогою покрокового логістичного регресійного аналізу побудовано прогностичні моделі для виявлення ризику настання певного періоду за ЕЕГ. Застосування нелінійних моделей дало змогу суттєво підвищити чутливість, специфічність та точність навіть на тестових вибірках. Застосування розробленої інформаційної технології надало можливість підвищити достовірність визначення періодів епілептичного нападу (умовної норми, перед нападом, нападу та після нападу) в середньому на 6,6 % у дітей та на 8 % у дорослих.

Висновки. Запропоновані прогностичні моделі дають змогу отримати додаткову інформацію про періоди епілептичних припадків та вчасно передбачити їх настання.

Ключові слова: *інформаційна технологія, ЕЕГ, епілептичні напади, епілепсія, показники складності та варіабельності, прогностичні моделі, логістична регресія.*

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ИСПОЛЬЗОВАНИЕ ПОКАЗАТЕЛЕЙ СЛОЖНОСТИ И ВАРИАБЕЛЬНОСТИ ДЛЯ АНАЛИЗА СЛОЖНЫХ ДИНАМИЧЕСКИХ СИСТЕМ

Проблема диагностики и выявления момента, предшествующего эпилептическому припадку или других периодов функционирования головного мозга у больных эпилепсией является проблемой не только выбора метода классификации, но и определения количественных оценок динамики, отражающих сложность и вариабельность сигнала ЭЭГ.

Были исследованы изменения таких показателей, как показатель Херста, фрактальная размерность, логистическое отображение и алгоритмическая сложность сигнала. С помощью пошагового логистического регрессионного анализа построены прогностические модели для выявления риска наступления определенного периода по ЭЭГ. Применение нелинейных моделей позволило существенно повысить чувствительность, специфичность и точность даже на тестовых выборках. Применение разработанной информационной технологии позволило повысить достоверность определения периодов эпилептического припадка (условной нормы, перед нападением, нападения и после приступа) в среднем на 6,6 % у детей и на 8 % у взрослых.

Ключевые слова: *информационная технология, ЭЭГ, эпилептические приступы, эпилепсия, показатели сложности и вариабельности, прогностические модели, логистическая регрессия.*

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METHODS OF MODEL PREDICTIVE CONTROL FOR DISCRETE MULTI-VARIABLE SYSTEMS WITH INPUT

Introduction. *There are a lot of systems which can be conveniently modelled as a discrete linear multi-input multi-variable system. When a control problem for such systems arises, it is usually done with methods derived from the control theory. But these methods have several known drawback. For example, for non-deterministic systems, they are based on assumption about certain convenient statistical properties of noises.*

The purpose of the paper *is to develop synthesis algorithms based on ideas and approaches of the Model Predictive Control (MPC).*

Methods. *In contrast to the common approach, in this work we aim to synthesize the best control sequence in terms of some criterion. We use results derived from the Kuhn-Tucker theorem for control synthesis.*

Results. *A new class of methods capable of leading linear system's state to zero (or, in case of noisy environment, to its neighbourhood) and stabilization of cognitive map's functioning was developed. These new methods are capable of controlling not only stable systems, but also unstable and semi-stable ones, even in presence of random perturbations and with constrained control resource. These methods differ in efficiency of control resource utilization and required computational resources. More efficient methods require more computations. That's why it is necessary to choose an appropriate method in each particular case.*

Conclusions. *The developed methods can be used to control both technical and any other kinds of systems represented either as controllable linear multi-variable systems with input or as controllable cognitive maps.*

Keywords*: variational method, cognitive map, control synthesis, discrete controllable system, moving horizon, linear system, MPC.*

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INTRODUCTION

Growing profit and activity in model predictive control (MPC) in recent years are first of all connected with an attempt to use the powerful computer technology to improve the control of multi-variable complex processes containing uncertainties and constraints. If five years ago MPC occupied modest place among popular control methods then now according to report presented by Allgöwer on the International Scientific Conference "Dynamical Systems: Stability, Control, Optimization", Minsk, Belarus, September 2018, these methods enter into leading position. It is no wonder that there are many publications devoted to MPC where one can find not only theoretical aspects of this problems [1–6] but also successful applications especially in the process industries [6, 7].

Original methods of MPC problem solving for discrete linear multi-input multi-variable (MIMV) system are proposed and theoretically substantiated in the paper. The approach is based on a Cauchy formula which represents through the use of the controllability matrix the solution for discrete linear multivariable system with input. Such approach reduces optimal control problems to squared programming ones, which in turn allows us to use necessary conditions for optimality in analytical form to write its solution. Due to this it is enough simply to take into account constraints for control and to apply different stabilizing control strategies under bounded uncertainty.

The paper is organized as follows. Problem Definition section contains the problem setting and MPC Approach to MINV Systems' Control section develops its formulation using for this MPC approach on the base of Cauchy formula for discrete systems. Some attainability conditions are formulated in the form of convergence theorems. Main results are contained in Solving Methods section where variational and optimal aim solving methods are stated. Feedback Stabilization section different control strategies on top of the developed solving methods are proposed. Lastly, there is Conclusions section which summarizes particular qualities of the findings related to the application of obtained results

PROBLEM DEFINITION

Let there be a controlled discrete dynamic multi-input multi-variable system. It can be either deterministic or stochastic. The system is defined as

$$x_{k+1} = Ax_k + Bu_k + d_k, \tag{1}$$

where x_k and x_{k+1} are consecutive states of the system, u_k is a control, applied to it at k-th point of time, d_k is the random perturbation at the moment k, A and B are system matrices. We assume that A and B have full ranks. States are n-dimensional vectors, and controls are r-dimensional. In deterministic variant perturbation d_k is always equal to 0.

There is a known state x_k at the moment k. Our task is to lead the system's state into a predefined point x^* (or, in stochastic case, into its neighbourhood) in finite time and keep it there for indefinite amount of time with synthesized controls.

In practice, control resource is usually bounded. So, we define its constraints as

$$|u_{ki}| \le u_{\max i},\ k \in \mathbf{Z},\ i \in \overline{1,r}, \tag{2}$$

where $u_{\max}$ is a vector of some positive values.

We also assume that values of *d* are constrained in a way, that they do not exceed the control resource, described in (2).

MPC APPROACH TO MINV SYSTEMS' CONTROL

Consider MPC approach to MINV control problem as given in (1). Its main aim is to produce a linear equation which allows to calculate on each step a new control using previous controls and system's states (or their estimations), so that the combination of the original system and such controller were stable in different senses and converge asymptotically to the needed point.

In contradiction with this, our approach is to find the best (in terms of some criterions) sequence of controls among the set of all possible such sequences, satisfying constraints (2).

The common point in the discussed methods is that the controls are calculated for predefined number of steps *s* called finite horizon at once. Thus, the defining equation of the system (1) in the deterministic case ($d_k = 0$) is transformed into

$$\Omega_s u(k,\ s) = x_{k+s} - A^s x_k, \tag{3}$$

$$u(k,\ s) = \begin{pmatrix} u_k \\ \vdots \\ u_{k+s-1} \end{pmatrix},$$

$$\Omega_s = \begin{pmatrix} A^{s-1}B & A^{s-2}B & \dots & AB & B \end{pmatrix}.$$

In this case our goal is to synthesize such $u(k,\ s)$, that provides $x_{k+s} = x^*$ and constraints (2).

In the stochastic case instead of (3) we get

$$\Omega_s u(k,\ s) = x_{k+s} - A^s x_k - \sum_{i=k}^{k+s-1} A^{k+s-1-i} d_i. \tag{4}$$

There are two main approaches in control of systems with random perturbations: robust and probabilistic. In next two subsections we will show from this two standpoints, that in the stochastic case we also should use the control, which satisfies (3), where $x_{k+s} = x^*$.

Robust control. According to (4), if there are no constraints on values of *d*, the system is assumed to be uncontrollable, because for every predetermined control $u(k,\ s)$ the set of possible future states at the $k+s$ point of time is

unbounded. If at the stage of controller development there are known constraints on perturbations in form

$$|d_{ki}| \le d_{\max i},\ k \in \mathbf{Z},\ i \in \overline{1,n}, \tag{5}$$

where vector $d_{\max}$ consists of given positive numbers, then the value of the future state x_{k+s} at the point of time $k+s$ with MPC without feedback is constrained by a polyhedron with point of symmetry $\Omega_s u(k,s) + A^s x_k$, according to formula

$$x_{k+s} = \Omega_s u(k,\ s) + A^s x_k + \sum_{i=k}^{k+s-1} A^{k+s-1-i} d_i$$

using measured current state x_k or its estimation.

Thereby, it is natural to synthesize such a control, that the point of symmetry of this polyhedron coincides with the aim x^*. Controls with this property are described with the same equation (3). This statement of the problem can be called robust with respect to external perturbations. Then there is a bounded neighbourhood of the aimed state, where the system is guaranteed to reach with the appropriately synthesized feedback controls if the perturbations do not violate their constraints (5).

Probabilistic control. If it is known about the perturbations, that $\mathrm{E}[d] = 0$ and that they are mutually independant, then we can express $\mathrm{E}[x_{k+s}]$ as in

$$\mathrm{E}[x_{k+s}] = \mathrm{E}\left[\Omega_s u(k,\ s) + A^s x_k + \sum_{i=k}^{k+s-1} A^{k+s-1-i} d_i \right] = \Omega_s u(k,\ s) + A^s x_k .$$

Thus, we get equation

$$\Omega_s u(k,\ s) = \mathrm{E}[x_{k+s}] - A^s x_k .$$

With this statement of the problem it is natural to synthesize such a control, so that $\mathrm{E}[x_{k+s}] = x^*$. This again reduces the control synthesis problem to solving the equation (3), where we substitute x_{k+s} with x^* with linear constraints (2).

Control update. It is obvious, that if we can measure each current state of the system, it is wise to recalculate future controls taking into account measured system state which may be different due to acting unknown perturbation. It gives us some kind of feedback MPC, that allows us to take into account previous disturbances. In practice, this allows us to realize effective control in noisy environment in comparison with unchanged synthesized control sequence.

ATTAINABILITY CONDITION

If for the particular prediction horizon *s* the aim x^* is not reachable from the current state x_k, it is desirable at least to have some kind of rule, which helps us to hand-pick some another reachable aim, so that sequence of such intermediate aims will either end up in a state, from where the original aim is reachable, or at least will converge to the original aim. It is obvious, that if the aim x^* is reachable in s_2 steps, where $s_2 = ks$, $k \in \mathbf{N}$, $k \geq 2$, than such sequence exists, but in general case it is not obvious how to construct it without simply incrementing *s* until we find the desired control sequence. But in case when $x^* = 0$ (stabilization problem) we can formulate such a rule, which satisfies conditions of theorem 1, 2, 3 or 4.

In the following theorems we assume, that $\|A\| \geq 1$, because otherwise the system will converge to 0 even without any controls.

Theorem 1 (1st convergence condition)**.** *Let* $\tilde{x}_0 = x_k$ *and* $\tilde{x}_{i+1}$ *be the next intermediate aim chosen from state* $\tilde{x}_i$*. If* $\|\tilde{x}_{i+1}\| \leq \|\tilde{x}_i\| - \delta$, $\delta > 0$, *then the system's state will reach* δ*-neighbourhood of* 0 *in finite number of iterations. If this inequality remains right until* 0 *becomes reachable in s steps, then the system will reach such state in finite number of iterations.*

Proof.

$$\|\tilde{x}_i\| \leq \|\tilde{x}_0\| - i\delta. \tag{6}$$

As we can see from (6), there is such number *i*, so that $\|\tilde{x}_0\| - i\delta \leq \delta$. □

Theorem 2 (Consequence of the theorem 1)**.** *Let* $\tilde{x}_0 = x_k$ *and* $\tilde{x}_{i+1}$ *be the next intermediate aim chosen from state* $\tilde{x}_i$*. If* $\left\|A^s\tilde{x}_i\right\| - \|\tilde{x}_{i+1}\| \geq \left(\left\|A^s\right\| - 1\right)\|\tilde{x}_i\| + \delta$, $\delta > 0$, *then the system's state will reach* δ*-neighbourhood of* 0 *in finite number of iterations. If this inequality remains right until* 0 *becomes reachable in s steps, then the system will reach such state in finite number of iterations.*

Proof.

$$\|\tilde{x}_{i+1}\| \leq \left\|A^s\tilde{x}_i\right\| - \left(\left\|A^s\right\| - 1\right)\|\tilde{x}_i\| - \delta \leq \|\tilde{x}_i\| - \delta. \tag{7}$$

From (7) follows, that the requirements of the theorem 1 is fulfilled. □

Theorem 3 (2nd convergence condition)**.** *Let* $\tilde{x}_0 = x_k$ *and* $\tilde{x}_{i+1}$ *be next intermediate aim chosen from state* $\tilde{x}_i$*. If* $\left\|A^s\right\|\|\tilde{x}_i\| - \|\tilde{x}_{i+1}\| \geq \left(\left\|A^s\right\| - 1\right)\|\tilde{x}_0\| + \delta$, $\delta > 0$ *for every i for which* 0 *is not reachable from* $\tilde{x}_i$ *in s steps, then the system will reach such state in finite number of iterations.*

Proof.

$$\begin{aligned}
&\|\widetilde{x}_{i+1}\| \le \|A^s\| \|\widetilde{x}_i\| - \left(\|A^s\| - 1\right)\|\widetilde{x}_0\| - \delta = \|A^s\|\left(\|\widetilde{x}_i\| - \|\widetilde{x}_0\|\right) + \|\widetilde{x}_0\| - \delta \le \\
&\|A^s\|\left(\|A^s\| \|\widetilde{x}_{i-1}\| - \|A^s\| \|\widetilde{x}_0\| - \delta\right) + \|\widetilde{x}_0\| - \delta \le \\
&\|A^s\|^2 \left(\|\widetilde{x}_{i-1}\| - \|\widetilde{x}_0\|\right) + \|\widetilde{x}_0\| - \left(1 + \|A^s\|\right)\delta \le \ldots \\
&\ldots \le \|A^s\|^{i+1} \left(\|\widetilde{x}_0\| - \|\widetilde{x}_0\|\right) + \|\widetilde{x}_0\| - \delta \sum_{k=0}^{i} \|A^s\|^k = \|\widetilde{x}_0\| - \delta \sum_{k=0}^{i} \|A^s\|^k .
\end{aligned} \tag{8}$$

As we can see from (8), this process can continue only finite number of iterations. □

Theorem 4 (Consequence of the theorem 3)**.** *Let* $\widetilde{x}_0 = x_k$ *and* $\widetilde{x}_{i+1}$ *is next intermediate aim chosen from state* $\widetilde{x}_i$*. If* $\left\|A^s \widetilde{x}_i\right\| - \|\widetilde{x}_{i+1}\| \ge \left(\|A^s\| - 1\right)\|\widetilde{x}_0\| + \delta$, $\delta > 0$ *for every i for which* 0 *is not reachable from* $\widetilde{x}_i$ *in s steps, then the system will reach such state in finite number of iterations.*

Proof.

$$\left\|A^s \widetilde{x}_i\right\| - \|\widetilde{x}_{i+1}\| \le \|A^s\| \|\widetilde{x}_i\| - \|\widetilde{x}_{i+1}\| . \tag{9}$$

From (9) follows, that the requirements of the theorem 3 is fulfilled. □

SOLVING METHODS

Variational Method

The core idea of the variational method is to calculate the optimal control without taking into account any constraints, and only after they will be taken in account for analytical solution obtained.

The control is calculated in following scheme: firstly, we partition Ω_s columnwise into matrices $\Omega_s^{I_1}$ and $\Omega_s^{I_2}$, so that $\Omega_s^{I_1}$ is square and invertible, and $\Omega_s^{I_2}$ contains all remaining columns.

We can calculate parts of $u(k, s)$ ($u_{I_1}(k, s)$ and $u_{I_2}(k, s)$) as in

$$u_{I_1}(k, s) = \left[\Omega_s^{I_1} + \Omega_s^{I_2} (\Omega_s^{I_2})^{\mathrm{T}} (\Omega_s^{I_1})^{-1}\right]^{-1} (x^* - A^s x_k) \quad \text{and} \tag{10}$$

$$u_{I_2}(k, s) = (\Omega_s^{I_2})^{\mathrm{T}} (\Omega_s^{I_1})^{-1} u_{I_1}(k, s) . \tag{11}$$

For detailed proof see [8].

As a result, we get a straightforward formula to calculate a control sequence $u(k, s)$ for every given current state x_k and aim x^* in form of a linear equation

$$u(k, s) = K(x^* - A^s x_k) ,$$

where *K* is built according to the equations (10) and (11).

As it was already said, the result calculated in this way is not necessarily satisfies constraints (2). But if $x^* = 0$, then we can use some kind of convergence strategy, as it was described in the Attainability Condition section. In this section we propose two different convergence strategies: linear approach and projection approach.

Linear Approach Strategy. The main idea of the linear approach is to apply control $\widetilde{u}(k, s)$, calculated as in

$$\widetilde{u}(k, s) = \left(\min_{i \in \overline{1 \ldots sr}} \frac{u_{\max i}}{\left| u_i(k,s) \right|} \right) \cdot u(k, s) \tag{12}$$

if $u(k,s)$ does not satisfy constraints (2).

Theorem 5. *If* $\left\| \widetilde{x}_0 \right\| < \dfrac{1}{\left\| A^* \right\| - 1} \min_{j \in \overline{1 \ldots sr}} \dfrac{u_{\max j}}{\left\| K_j \right\|}$, *where* K_j *is the j-th row of K, then applying* $\widetilde{u}(k, s)$ *calculated as in* (12) *to the deterministic variant of the system will produce a sequence of* $\widetilde{x}_i$, *which satisfies the theorem 4.*

Proof. If $u(k + is, s)$ satisfies constraints (2), then 0 can be reached from state $\widetilde{x}_i$ with $u(k + is, s)$ control. In other case, we can deduce following.

Let us denote α_i as in

$$\alpha_i = \min_{j \in \overline{1 \ldots sr}} \frac{u_{\max j}}{\left| u_j(k + is, s) \right|}.$$

It is obvious, that $0 < \alpha_i < 1$.

$$\Omega_s u(k + is, s) = 0 - A^s \widetilde{x}_i,$$

$$\Omega_s \widetilde{u}(k + is, s) = \widetilde{x}_{i+1} - A^s \widetilde{x}_i,$$

$$\widetilde{x}_{i+1} - A^s \widetilde{x}_i = \Omega_s \left(\alpha_i u(k + is, s) \right) = \alpha_i \Omega_s u(k + is, s) = -\alpha_i A^s \widetilde{x}_i,$$

$$\widetilde{x}_{i+1} = (1 - \alpha_i) A^s \widetilde{x}_i.$$

Using the Cauchy-Bunyakovsky-Schwarz inequality, we can limit α_i as in

$$\alpha_i = \min_{j \in \overline{1 \ldots sr}} \frac{u_{\max j}}{\left| K_j A^s \widetilde{x}_i \right|} \geq \min_{j \in \overline{1 \ldots sr}} \frac{u_{\max j}}{\left\| K_j \right\|} \cdot \frac{1}{\left\| A^s \widetilde{x}_i \right\|},$$

$$\left\| A^s \widetilde{x}_i \right\| - \left\| \widetilde{x}_{i+1} \right\| = \left\| A^s \widetilde{x}_i \right\| - (1-\alpha_i) \left\| A^s \widetilde{x}_i \right\| = \alpha_i \left\| A^s \widetilde{x}_i \right\| \geq$$

$$\min_{j \in \overline{1 \ldots sr}} \frac{u_{\max j}}{\left\| K_j \right\|} \cdot \frac{1}{\left\| A^s \widetilde{x}_i \right\|} \left\| A^s \widetilde{x}_i \right\| = \min_{j \in \overline{1 \ldots sr}} \frac{u_{\max j}}{\left\| K_j \right\|} > \left(\left\| A^s \right\| - 1 \right) \left\| \widetilde{x}_0 \right\|.$$

Let us define δ as

$$\delta = \min_{j \in \overline{1 \ldots sr}} \frac{u_{\max j}}{\left\| K_j \right\|} - \left(\left\| A^s \right\| - 1 \right) \left\| \widetilde{x}_0 \right\|.$$

Thus, we can write inequality

$$\left\| A^s \widetilde{x}_i \right\| - \left\| \widetilde{x}_{i+1} \right\| \geq \left(\left\| A^s \right\| - 1 \right) \left\| \widetilde{x}_0 \right\| + \delta .$$

$\delta > 0$, so the conditions of the theorem 4 are satisfied. □

As a byproduct of the variational method of control, we get theorem 6.

Theorem 6. *For the linear MINV system for every s there is an* ε*-neighbourhood of* 0*, from which it is reachable in s iterations with controls satisfying constraints* (2)*. Also,* $\varepsilon \geq \min_{i \in \overline{1 \ldots sr}} \frac{u_{\max i}}{\left\| K_i \right\|}$*, where* K_i *is the i-th row of K.*

Proof. Let's try to generate an *s*-step control sequence $u(k, s)$ from some state x_k to 0 using the variational method.

$$u(k,s) = -KA^s x_k .$$

Using the Cauchy-Bunyakovsky-Schwarz inequality, we get inequality

$$\left| u_i(k,s) \right| \leq \left\| K_i \right\| \cdot \left\| x_k \right\|, \; i \in \overline{1 \ldots sr} . \tag{13}$$

So,

$$u_{\max i} \geq \left\| K_i \right\| \cdot \left\| x_k \right\|, \; i \in \overline{1 \ldots sr} \tag{14}$$

is sufficient for control (13) to be valid.

From (14) we get

$$\left\| x_k \right\| \leq \min_{i \in \overline{1 \ldots sr}} \frac{u_{\max i}}{\left\| K_i \right\|} .$$

□

In the variational method the control synthesis problem was considered as one without any constraints on controls at first. After obtaining a solution in analytic form the set of reachable states is artificially reduced to those, which are reachable by using the controls synthesized with this method.

Projection Approach Strategy. Another approach is to select a projection of 0 onto the set of states reachable from $\widetilde{x}_i$ in *s* iterations with controls generated

with the variational method. In other words, each $\widetilde{x}_{i+1}$ is a solution of quadratic programming problem

$$\min_{x^{\#}} \quad \langle x^{\#}, x^{\#} \rangle$$

$$\text{subject to} \quad -u_{\max i} \le K_i(x^{\#} - A^s \widetilde{x}_i) \le u_{\max i}, \; i \in \overline{1 \ldots sr}.$$

It is obvious, that the resulting next intermediate aim $\widetilde{x}_{i+1}$ is such that its norm is less or equal to norm of the intermediate aim computed from the same current state $\widetilde{x}_i$ with linear approach. So, the projection approach strategy also satisfies the theorem 4.

Optimal Aim Approach

The optimal aim method was proposed in [8, Sect. 5]. In this method we are repeatedly solving the problem

$$\min J\big(u(k,s)\big) = \frac{1}{2}\Big(\langle \Omega_s u(k,s) + A^s x_k - x^*, \; \Omega_s u(k,s) + A^s x_k - x^* \rangle + \alpha \langle u(k,s), u(k,s) \rangle\Big)$$

with constraints (2), while decreasing values of positive coefficient α.

We can describe reachable states' set X_{reach} as

$$X_{\text{reach}} = \{x : x = \Omega_s u + A^s x_k, \; -u_{\max i} \le u_i \le u_{\max i}, \; i \in \overline{1 \ldots sr}$$

and projection $x^{\#}$ of x^* onto it as

$$x^{\#} = \arg \min_{x \in X_{\text{reach}}} \left\| x - x^* \right\|.$$

Theoretically, we can say, that statements

$$\Omega_s u(k,s) + A^s x_k \underset{\alpha \to 0}{\to} x^{\#} \qquad \text{and}$$

$$u(k,s) \underset{\alpha \to 0}{\to} \arg \min_{\Omega_s u + A^s x_k = x^{\#}} \langle u, u \rangle$$

are true, so this way we can find with certain precision a control, which brings the deterministic variant of system at the point of time $k+s$ as close as possible to x^*. It is uncertain, if it will produce a sequence of intermediate aims, which converges to the original aim x^* in general case.

Luckily, if $x^* = 0$, then this way we find a control $u(k,s)$, which brings the system's state even closer to 0 (or at least not further), than the linear approach of the variational method, in case we can not reach 0 in s iterations yet. This way we can guaranty, that in this case the sequence of intermediate aims will converge to 0.

We would like also to emphasize, that X_{reach} is a set of states reachable from the current state x_k in general, without considering any particular con-

trol synthesis algorithm. So, it is a superset of the set of states, reachable with controls generated by the variational method. As a result, this method also gives us intermediate aims not further, than ones generated by the projection approach of the variational method. So, using $x^{\#}$ computed this way as the next intermediate aim also satisfies the theorem 4.

But in practice we can't calculate the solution of the problem (15), (2) for any small α because of limited precision of computations with floating-point numbers. So, the best we can do is to stop decreasing α when next resulting control $u(k,s)$ leads the system into a state further from 0 than the one from previous result. This way we synthesize new sequence of controls with reasonable precision.

As a tradeoff between computation precision and speed, we also can choose a reasonably small α beforehand and solve the problem (15), (2) only with this value. Under uncertainty when x_k is known with errors it is fully acceptable.

Indexes Partitioning Method

This approach was proposed and considered for the first time in [8].

The main idea of this approach is as follows. Firstly we try guess a right partition of index set $\overline{1\ldots sr}$ into three subsets I_0, $I_{\min}$ and $I_{\max}$. Then we are trying to calculate a control $u(k,s)$ according to formulas:

$$u_i(k,s) = -u_{\max i}, \quad i \in I_{\min},$$

$$u_i(k,s) = u_{\max i}, \quad i \in I_{\max},$$

$$w_{I_{\min}\cup I_{\max}} = \left((\Omega^{-1})^{I_{\min}\cup I_{\max}}_{I_{\min}\cup I_{\max}}\right)^{-1} \cdot \left(u_{I_{\min}\cup I_{\max}}(k,s) - (\Omega^{-1})_{I_{\min}\cup I_{\max}} \cdot x^{**}\right),$$

$$u_{I_0}(k,s) = (\Omega^{-1})_{I_0} \cdot x^{**} + (\Omega^{-1})^{I_{\min}\cup I_{\max}}_{I_0} \cdot w_{I_{\min}\cup I_{\max}},$$

where $\Omega = \Omega_s^T\Omega_s + \alpha E$ and $x^{**} = \Omega_s^T(x^* - A^s x_k)$.

If resulting control satisfies constraints (2) and $w_{I_{\min}} > 0$, $w_{I_{\max}} < 0$ (strictness of this inequalities is significant), then we have found a solution of the problem (15) with constraints (2). In other case we should try another index set partition.

It would be great to have some kind of rule to choose next index set partition based on previous tried ones, so that it will lead us to the right one faster, than just trying all variants in sequence or randomly choosing next variant.

*Sequential traversal rule***.** In [8, Sect. 6] was proposed such a rule, but with a caveat: for some particular problems it will lead the search of partition into loop. So, if we want to implement it in practice, we will need to also implement check for such loops. If a search loop was detected, we should choose next index set partition in some other way - for example, randomly.

We also need to decide on partition to check first. We suggest it to be $I_0 = \overline{1\ldots sr}$, $I_{\min} = \varnothing$, $I_{\max} = \varnothing$, because if $A^s x_k$ is in certain neighbour-

hood of x^*, then the solution will correspond to this partition.

The idea of the sequential traversal rule is to decide next checked partition using calculations, which have been done for the previous partition. In particular, the next partition is generated as following:

- move from I_0 to $I_{\min}$ those $i \in I_0$, for which $u_i(k,s) < -u_{\max i}$ (this way it violates the constraint (2));
- move from I_0 to $I_{\max}$ those $i \in I_0$, for which $u_i(k,s) > u_{\max i}$ (this way it violates the constraint (2) as well);
- move from $I_{\min}$ to I_0 those $i \in I_{\min}$, for which $w_i \le 0$;
- move from $I_{\max}$ to I_0 those $i \in I_{\max}$, for which $w_i \ge 0$.

This algorithm has one important property: if we try to produce with it next partition from a partition which corresponds to solution, we will get the same partition.

As it was already said, this algorithm can produce loops. So, if we build a directed graph of partition traversal, it will consist of one or more connected components. One of them, obviously, will contain the solution, and we will reach the solution if we start from any of nodes from this component. Search started from any node from other component will lead into loop.

According to results of our test runs with randomly generated problems, the situation when the search process falls into a loop is relatively rare. But it is not too rare to ignore this possibility. The results of this test runs are shown in Table 1.

In this table columns contain following:

- n — dimensions of state;
- r — dimensions of control vector;
- s — number of produced control's iterations;
- Trivial — number of samples with solutions corresponding to partition $I_0 = \overline{1 \dots sr}$, $I_{\min} = \varnothing$, $I_{\max} = \varnothing$;
- Nontrivial — Number of samples, for which the solution was found without falling into a loop, excluding "Trivial" cases;
- First try — number of samples, for which the solution was found without falling into a loop ("Trivial" and "Nontrivial" cases);
- Loop — number of samples, for which search process have fallen into a loop;
- All — number of all problems with this n, r and s values tested.

We should empathise that distributions used in random sampling of problems are not chosen with some kind of reasonable methodology - it is only used here for illustrative purposes. The right way to do it is a topic for further discussion.

Table 1. **Distribution of search situations for randomly generated problems for sequential traversal algorithm**

n	r	s	Trivial	Nontrivial	First try	Loop	All
3	3	1	2117	7847	9964	36	10000
4	3	2	6519	3059	9578	422	10000
5	3	2	4646	4989	9635	365	10000
6	3	2	2676	7243	9919	81	10000
7	3	3	6125	3411	9536	464	10000

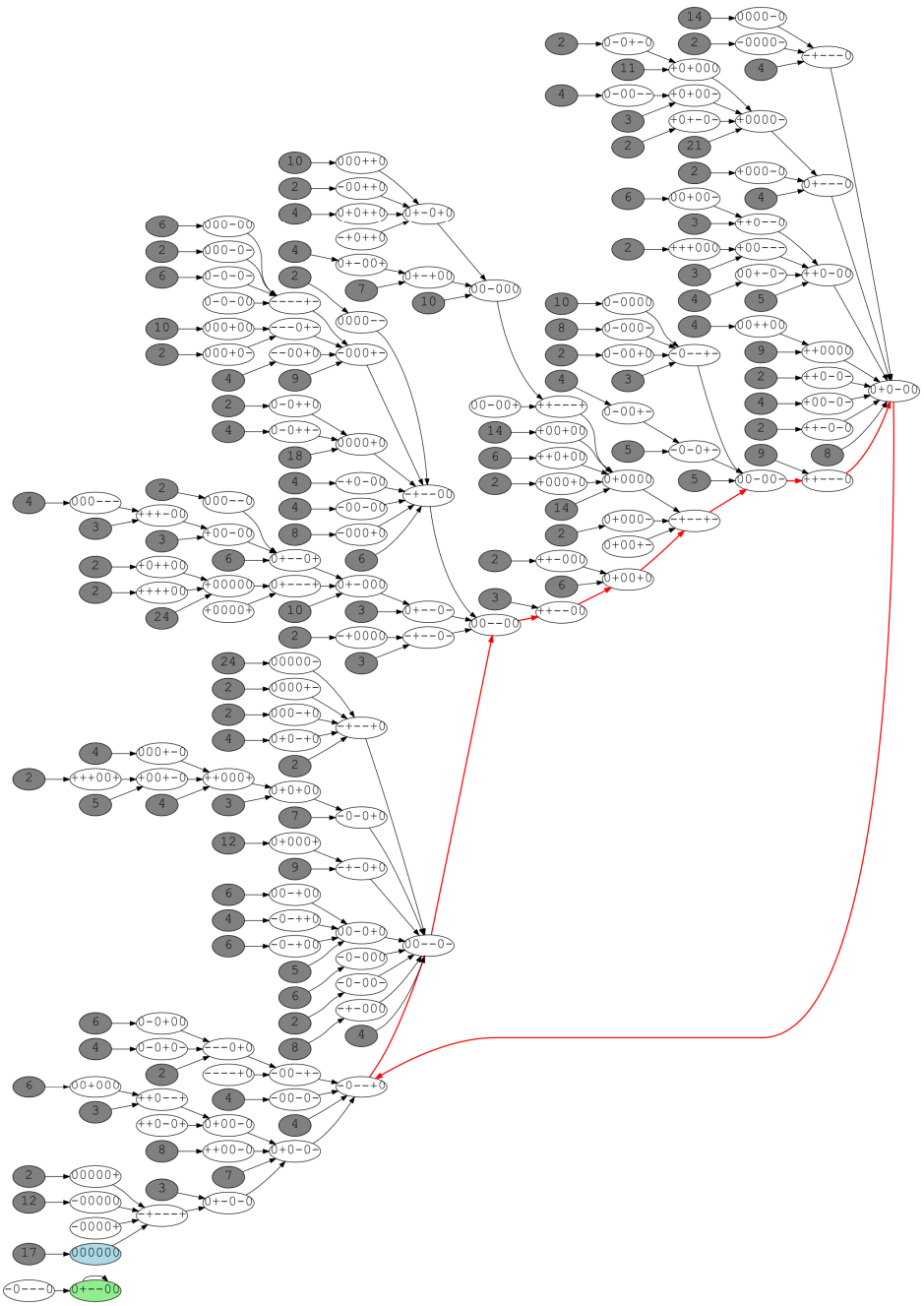

Fig. 1. A partition traversal graph with solution's component consisting of only two partitions

In those unfortunate cases, when the partition traversal graph consists of several components, the number of partitions we would check before finding the right one highly depends on size of the component containing the searched partition. It is due to the fact, that if we detected a loop, we need to choose next partition randomly, and probability of continuing search from within the right graph's component is equal to the size of this component divided by the size of a partition pool we are choosing from. An extreme example of a search graph with a solutions' component consisting of only two nodes is shown on Figure 1.

On this figure we represent partitions as a strings consisting of symbols 0, $-$ and $+$, where each next symbol indicates, that corresponding index belongs to I_0, $I_{\min}$ or $I_{\max}$ respectively. The solutions' partition is marked with light-green colour. It can be also identified by a self-loop on it. The trivial partition ($I_0 = \overline{1..sr}$, $I_{\min} = \varnothing$, $I_{\max} = \varnothing$) is marked with light blue. The traversal loop is marked with red colour. Multiple source nodes of traversal graph which leads into the same next node is grouped in gray-coloured vertices labeled with number of the grouped nodes.

Fortunately, in most cases the traversal graph consists of only one component. Obviously, in this case the problem solution's partition can be either trivial or nontrivial. On the other hand, we have also found some rare cases with three components.

Fortunately, in most cases the traversal graph consists of only one component. Obviously, in this case the problem solution's partition can be either trivial or nontrivial. We have also found cases with two or three components.

As an alternative to loop detection we can instead detect repeated visits of the same graph nodes. It will guaranty, that the solution will be found in finite time. It will also make the search faster. But it requires considerable amount of memory.

FEEDBACK STABILIZATION

If we have a controllable system, for which full state vector is either measurable (i.e. the system is measurable) or can be estimated, then we can construct a feedback loop to control its state. The approach of the control theory is to apply some kind of linear transformation to the measured (or estimated) system's state. Contrary to it, we propose to use one of the control synthesis algorithms described above in the feedback loop to transform the current measured (or estimated) state into the control vector. But here arises a contradiction: at each point of time we need to generate only one control vector, while this method generates a whole sequence of them. There can be different approaches how to cope with it.

Application schemes

As it was already said, to take noises' impact into account, we need to recalculate controls anew after each control iteration. Otherwise, at the point of time $k + s$ deviation from expected trajectory will accumulate. In case of unstable or metastable system ($\|A\| \geq 1$) the deviation can (and in most cases will) reach considerably large values.

Thus next questions arise: for what horizon synthesize controls next time and what aim state x^* to choose. The most evident application mode on fixed horizon is following:

1. at the point of time k calculate controls for points of time from k to $k+s-1$ inclusive and apply the first control from the calculated sequence. The expected state at the $k+s$ point of time denote as $x^{\#}$;

2. at each $k+i$ point of time, where $i \in \overline{1 \ldots s-1}$, calculate such control for horizon $k+i$ — $k+s-1$, so that deviation between new expected state at $k+s$ point of time and $x^{\#}$ is minimal. Apply the first control from the newly generated control sequence. If $i = s-1$, then $k := k+s$ and go to the first point.

This way we are striving to reach an intermediate aim $x^{\#}$ chosen at the point of time k. Let's call this scheme as a "strict with intermediate aim striving".

But it is not the most rational strategy. All theorems about attainability conditions proven here have one significant common point: the next intermediate aim's norm $\left\|x^{\#}\right\|$ must not be bigger than certain constraint. That's why we don't need to keep the same intermediate aim - it is enough to minimize the norm of the system's state at the $k+s$ point of time $\left\|x_{k+s}\right\|$. This approach is more rational, because in some cases noises may help us instead of interfering, and after their impact $x^{\#}$ may appear not to be the most close to 0 reachable state. Let's call this scheme as a "strict with striving for minimum".

There is also an experimental scheme, according to which we also recalculate the control sequence after each iteration, but we don't change the horizon length. Let's call this scheme as an "asymptotic". This scheme is not substantiated by the theorems proven in this article, but according to computational experiments it is also working.

If state measurement precision is proportionate to the trajectory deviation, it is appropriate to continue using previously generated control sequence.

Algorithm testing

Test were performed on a model cognitive map system, which can be described with equations

$$\Delta x_{k+1} = A\Delta x_k + Bu_k + d_k$$

$$\Delta x_k = x_k - x_{k-1},$$

where x_k is a state of the system, u_k is a control and, d_k is the random perturbation at the moment k; A and B are system matrices.

The particular values used for the model system are as follow:

$$A = \begin{pmatrix} 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ -0{,}025... & 0{,}083... & -0{,}449... & 0{,}706... & -1{,}305... & 0{,}636... & 0{,}59 \end{pmatrix}$$

$$B = \begin{pmatrix} -0{,}88 & 0{,}73 & -0{,}84 \\ -0{,}39 & 0{,}44 & -0{,}56 \\ 0{,}2 & 0{,}69 & -0{,}16 \\ -0{,}48 & 0{,}24 & -0{,}8 \\ -0{,}38 & 0{,}78 & 0{,}8 \\ 0 & -0{,}46 & 0{,}09 \\ 0{,}25 & -0{,}87 & 0{,}74 \end{pmatrix}$$

and uniformly distributed noise with interval [-0,01; 0,01]. Here matrix A is a transposed frobenius matrix with eigenvalues -1,27; 0,77 ± 0,53i; 0,08 ± 0,48i; 0,08 ± 0,3i. Thus A is an unstable matrix. The control synthesis were performed for horizons with length up to $s = 6$ iterations.

The results of modelling for control schemes described in subsection 6.1 with the optimal aim control synthesis algorithm are depicted on Figures 2, 3 and 4. The results of modelling with applying whole generated control sequence without changes (in other words, without feedback) are depicted on Figure 5.

On these figures real system's trajectory is shown as blue line and forecasted trajectories are shown with different shades from black to light-gray. Forecasts for 6 steps ahead are shown with black; the most pale shade of gray depicts one-step forecasts. For each scheme there are two representations: for x (actual system's state) and Δx (impulse values). Because figures for different vector's components are similar, here we show only one typical component for short.

On Figures 2 and 3 we can see that initial convergence for the strict schemes is faster than initial convergence for the asymptotic scheme, as shown on Figure 4. On the other hand, the asymptotic scheme gives us less drifting of the system's state x after initial stabilization phase in comparison with the strict schemes. And on Figure 5 we can see the consequences of applying whole generated control sequence to system without changes: the difference between forecasted and actual future state is rather big (except a few rather lucky occasions). The only reason why applying unchanged control sequence can still stabilize the system is because the noise's interval in this particular case is rather small.

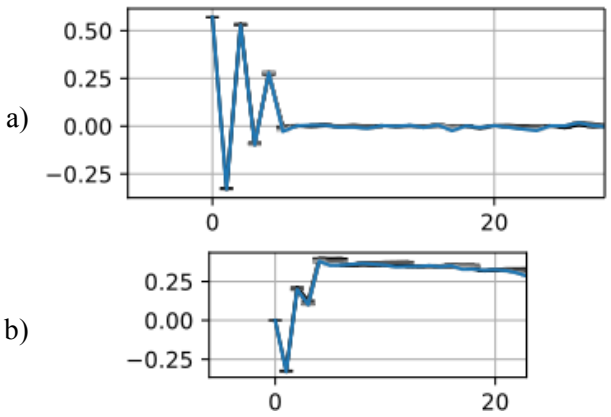

Fig. 2. Strict scheme with intermediate aim striving: a) for Δx , b) for x

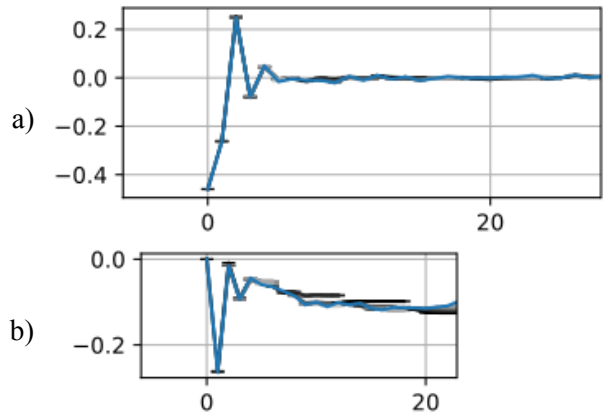

Fig. 3. Strict scheme with striving for minimum: a) for Δx , b) for x

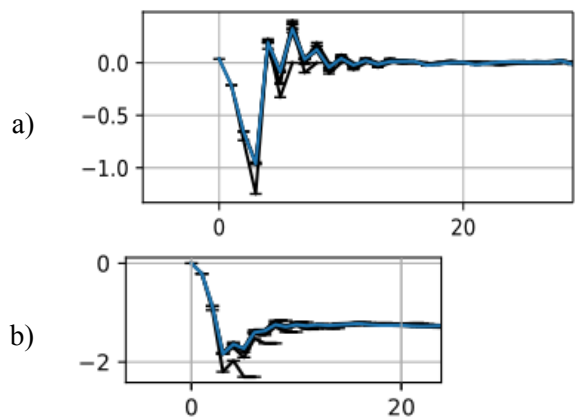

Fig. 4. Asymptotic scheme: a) for Δx , b) for x

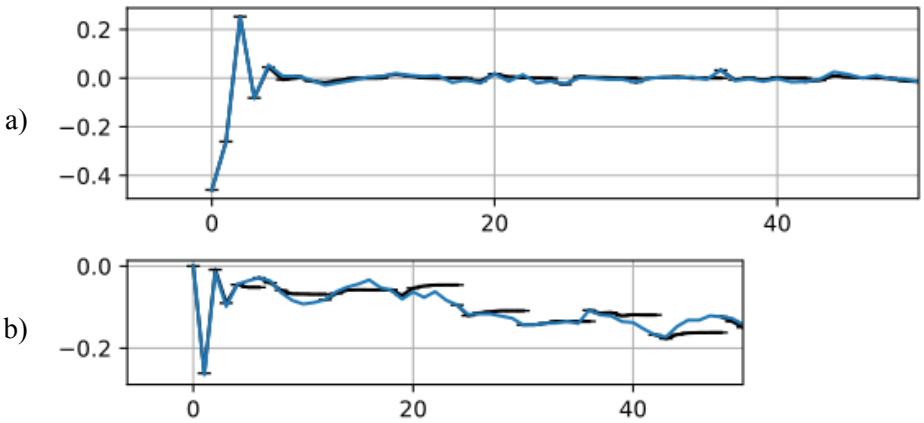

Fig. 5. *Control without feedback* a) for Δx , b) for x

Combining application schemes

The strict and asymptotic schemes have different qualities. The strict scheme is the most suitable for situations, when the last forecasted trajectory leads the system into 0, while the asymptotic scheme is good either when the system's initial state is already in certain neighborhood of 0 (which size is proportional to the noise's standard deviation) or as a fallback for situations, when we can't lead the system's deterministic model to zero during predefined horizon s.

As a result, we propose to dynamically change the applied scheme as following. Suppose we have a system with n-dimensional state vector x and m-dimensional control vector u, we have chosen maximum horizon s and we consider ε-neighborhood of 0. Let p be the smallest integer, for which $m \cdot p \geq n$. Then:

1. If the current system's state is out of the ε-neighborhood of 0, synthesize a control sequence for horizon s.

1.1. If this sequence leads the deterministic system's model to 0, then proceed with strict scheme by decreasing horizon length by one on each iteration. When the next horizon length according to the strict scheme should be less then p, decide again, what scheme to use. Also, if the system's state appear inside of the ε-neighborhood of 0, go to the second clause.

1.2. If this sequence does not lead the deterministic system's model to 0, then apply the first control of the generated sequence and decide again, what scheme to use. This way we will apply the asymptotic scheme until we can lead the deterministic system's model to 0 in s iterations.

2. If the current system's state is inside of the ε-neighborhood of 0, then synthesize a control sequence for horizon p. Apply the first control of the generated sequence and decide again, what scheme to use. This way we will apply the asymptotic scheme until the system's state will appear out of the ε-neighborhood of 0 for some unknown external reason.

CONCLUSIONS

Original theoretical results developed in the paper are first of all oriented on practical application of different control strategies based on MPC for discrete linear MIMV system and derived from the obtained methods. The concept of finite horizon enables coordination of predictive interval and bounded uncertainty in suitable way. Under uncertainty instead of prescribed terminal point system will reach its vicinity so-called invariant set. With proposed approach there is no need to use conventional concept of stability according to Lyapunov.

MPC may also be used in case when instead of a full state vector measurement we have an incomplete measurement that is a vector with dimension less than n. In that case control system should include a state observer.

For MPC in case of noisy measurements we can use a state estimator based on data on back moving interval like those described in [9].

One of perspective applications of proposed methods is control of processes in cognitive maps.

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МЕТОДИ КЕРУВАННЯ ЗА ПРОГНОЗНОЮ МОДЕЛЛЮ ДЛЯ ДИСКРЕТНИХ СИСТЕМ З БАГАТЬМА ЗМІННИМИ ТА ВХОДАМИ

Вступ. Значну кількість систем зручно моделювати як дискретну лінійну систему з багатьма входами та багатьма змінними. Коли постає задача керування такими системами, прийнято використовувати методи, розроблені на основі теорії керування. Проте ці методи мають низку відомих проблем. Наприклад, якщо розглядають недетерміновані системи, то виходять з припущення про певні статистичні властивості збурень.

Метою цієї статті було розроблення алгоритмів синтезу керування на основі ідей та підходів до керування за прогнозною моделлю.

Методи. На відміну від класичного підходу, у цій роботі за мету ставиться синтез найкращої за певним критерієм послідовності керування. Для синтезу застосовують результати, отримані за допомогою теореми Куна-Такера.

Результати. Отримано новий клас методів, здатних приводити стан лінійної системи до нуля (або у випадку наявності збурень — до його околу) та стабілізувати функціонування когнітивної карти за скінченний час. Отримані методи можуть керувати не тільки строго стійкими системами, а також і напівстійкими та нестійкими, зокрема і в умовах наявності випадкових збурень та з урахуванням обмеженості ресурсу керування.

Розроблені методи різняться за ефективністю використання ресурсу керування та необхідними обчислювальними ресурсами. Ефективніші методи потребують більше обчислень для отримання результату. Це призводить до необхідності вибирати оптимальний метод у кожному конкретному випадку окремо.

Висновки. Отримані методи можуть застосовуватися для керування як технічними, так і будь-якими іншими системами, які описуються як лінійні керовані системи з багатьма змінними та входами або як керовані когнітивні карти.

Розроблені методи залишають простір для подальших досліджень та покращень як самих обчислювальних алгоритмів, так і схем їхнього застосування.

Ключові слова: варіаційний метод, дискретна керована система, керування за прогнозною моделлю, когнітивна карта, лінійна система, синтез керування, ковзний інтервал.

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МЕТОДЫ УПРАВЛЕНИЯ ПО ПРОГНОЗИРУЮЩЕЙ МОДЕЛИ ДЛЯ ДИСКРЕТНЫХ СИСТЕМ СО МНОГИМИ ПЕРЕМЕННЫМИ И ВХОДОМ

Введение. Существенное количество систем удобно моделировать как дискретную линейную систему со многими переменными. Когда ставится задача управления такими системами, принято использовать методы, построенные на основе теории управления. Однако эти методы имеют перечень известных проблем. Например, в случае, если рассматривается недетерминированная система, то такие методы исходят из предположения о некоторых статистических свойствах, возникающих в системе возмущений.

Цель статьи — разработка алгоритмов синтеза управления на основе прогнозирующей модели.

Методы. В отличие от классического подхода, в данном труде за цель ставится синтез наилучшей по определенному критерию последовательности управлений. Для синтеза используются результаты, полученные с помощью теоремы Куна-Такера.

Результаты. Был получен новый класс методов, способных приводить состояние линейной системы к нулю (или, в случае присутствия возмущений, к его окрестности) и стабилизировать функционирование когнитивных карт за конечное время. Полученные методы способны управлять не только строго устойчивыми системами, но и системами на грани устойчивости и неустойчивости, в том числе и в условиях присутствия случайных возмущений и с учетом ограниченности ресурса управления.

Разработанные методы различаются эффективностью использования ресурса управления и необходимыми вычислительными ресурсами. Более эффективные методы требуют большего количества вычислений для получения результата. Это приводит к необходимости в каждом конкретном случае выбирать свой наиболее оптимальный метод.

Выводы. Полученные методы могут применяться в управлении как техническими, так и любыми другими системами, которые описываются как линейные управляемые системы со многими переменными и входами или как когнитивные карты.

Разработанные методы оставляют пространство для дальнейших исследований и улучшений как самих вычислительных алгоритмов, так и схем их применения.

***Ключевые слова**:* вариационный метод, дискретная управляемая система, управление по прогнозирующей модели, когнитивная карта, линейная система, синтез управления, скользящий интервал.

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CURRENT STATE AND PROSPECTS FOR THE DEVELOPMENT OF DIGITAL MEDICINE

Introduction. *According to the definition of the International Society of Digital Medicine, digital medicine is a field of science in which scientists strive to explain previously incomprehensible pathophysiological phenomena in the human body and to explore new medical procedures using modern digital technologies to improve the quality of human life.*

The purpose of the article *is to provide brief information about the current state and prospects for the development of digital medicine.*

Methods*. The analysis of the main directions of digital medicine is done. Basic definitions of the concepts "Intelligent IT signal processing" and "Effective computational procedure" are formulated. The role of intelligent IT in digital medicine is demonstrated on the example of fasegraphy method.*

Results. *Existing methods and means of digital medicine are used for diagnosis, treatment, rehabilitation, as well as to restore the lost functions of the patient (vision, hearing, movement). Such technologies make it possible not only to free medical workers from solving routine tasks, but also to increase the efficiency of performing surgical operations, radiation therapy and a number of other tasks of practical medicine.*

Unlike traditional IT, based on procedures for processing numerical data, intelligent IT operate with generalized concepts (images) that provide more complete information about the external environment, and the analysis of such images generates a holistic picture of the phenomena studied.

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Within the framework of the algorithmic approach, the construction of intelligent IT for solving the problems of digital medicine requires the active participation of a technology developer, who, using his natural intelligence, creates effective procedures for extracting diagnostic information from real data under disturbances.

***Conclusions**. Intelligent IT with the properties of natural intelligence (adaptation, generalization, learning, etc.) play an important role in expanding the functional capabilities and increasing the effectiveness of digital medicine.*

***Keywords**: digital medicine, intelligent IT, efficient computing procedures.*

INTRODUCTION

In the early 60^s of the last century, a new scientific direction was formed — biological and medical cybernetics, which has come a long way in the development of its own mathematical, instrumental and informational methods of gaining knowledge about living complex systems [1–3].

Subsequently, on the basis of the studies, mathematical models of both individual organs in normal and pathological conditions, and mathematical models focused on the diagnosis, prognosis and treatment of various diseases were created. Much attention was also paid to automation of organizational and managerial tasks in clinics and health authorities.

Noting the undoubted importance of these results, it should be recognized, however, that at the initial stage of development biological and medical cybernetics did not provide an effective solution to a number of problems [4]. In particular, it was not possible to create conditions for mass preventive examinations, which provided the identification of dangerous diseases in the early stages, to reduce the cost of medical services, to ensure their accessibility to the general public, bringing diagnostic and treatment tools closer to patients.

It is clear that these problems could not be overcome only by minor modifications and simplification of clinical use devices. It turned out that the development of simple and reliable personalized medical devices requires the use of new approaches to information processing and specific methods for providing processing results to a user who does not have special medical knowledge [5].

The situation has changed dramatically with the advent of a new class of information technology (IT) — intelligent IT, which implements elements of natural intelligence. Unlike traditional ones, such technologies operate with generalized concepts — images, the analysis of which gives rise to a more complete and holistic picture of the phenomena studied, which allows to increase the reliability of decisions made.

The use of intelligent IT has led to a new healthcare paradigm — digital medicine.

The purpose of the article is to provide brief information about the current state and prospects for the development of digital medicine.

BASIC DIRECTIONS OF DIGITAL MEDICINE

The concept of "digital medicine" should not be equated with any medical device built on the elements of digital computer technology. For example, in medical practice digital electrocardiographs are widely used, which implement traditional diagnostic algorithms based on the many years of experience of cardiologists to visually evaluate an electrocardiogram (ECG).

Of course, the use of such electrocardiographs facilitates simplifies the work of medical personnel and reduces the time to obtain diagnostic results. However, in our opinion, digital electrocardiographs that implement only traditional approaches to ECG processing should not be classified as digital medicine products, since they did not lead to the achievement of the main goal — to increase the reliability of diagnostic results.

Let us give a general description of the tasks that digital medicine is oriented to.

According to the definition of the International Society of Digital Medicine [7], digital medicine is a field of science in which scientists seek to explain previously incomprehensible pathophysiological phenomena in the human body and to explore new medical procedures using modern digital technologies to improve the quality of human life.

The introduction of digital technologies in medicine opens up enormous prospects, allowing significantly improving the quality of medical care and fundamentally change the approach to early diagnosis and treatment of dangerous diseases, as well as innovative rehabilitation technologies to restore the functions lost as a result of diseases [8].

In recent decades, there has been a rapid development of new digital technologies for the rehabilitation of patients suffering from neurological disorders, which have several advantages over conventional approaches, allowing you to adjust the intensity and dose of the rehabilitation procedure depending on the individual characteristics of the body of a particular patient [9].

The original means of this area — the TRENAR® series devices were developed at the International Research and Training Center for Information Technologies and Systems of the NAS of Ukraine and MES of Ukraine (follow — IRTC ITS) [10]. The devices implement the technology of constructing an electronic image of movement, based on the registration of signals from a healthy organ (for example, a healthy hand) with the subsequent formation of electrostimulating impulses to a damaged limb (Fig. 1).

Fig. 1. TRENAR-01 device: the appearance of the device (left); rehabilitation technology (right)

An important place in digital medicine programs is given to the development of special tools for patients who, for one reason or another, cannot fully restore their natural physiological functions — vision, hearing, movement, etc. The use of “intellectual” prostheses (Fig. 2) allows such patients not only to return to a normal lifestyle, but also to work.

A special place in this direction is occupied by exoskeleton, which is an external wearable skeleton that allows people with paralysis of the lower extremities to walk (Fig. 3). Recent studies confirm the positive effect of the use of exoskeleton in patients with spinal cord injuries and brain stroke [11].

The rapid development of robotics and intelligent manipulators opens up new opportunities in many fields, including medicine [12]. According to the apt expression of D. Engelberger, who received the title of "father of robotics", the hospital is an ideal environment for using robots. Original scientific research aimed at creating an autonomous robot capable of navigating in the environment is being conducted at the IRTC ITS [13].

Fig. 2. Intelligent hand prosthesis

Fig. 3. Exoskeleton

Let us give brief information about medical robots that are already used in practice [14] and are able to take on the solution of routine tasks of practical medicine.

A drug delivery robot has been successfully used at Veterans Affairs Medical Center [15]. The robot is able to move around the clinic, performing the work of the average medical worker, thereby solving the acute problem of the shortage of nurses (Fig. 4).

Surgical manipulators, in particular the well-known da Vinci system [16], can significantly reduce the incision and blood loss during surgery, increase the accuracy of movements, reduce both the time of the operation itself and the period of postoperative rehabilitation (Fig. 5).

A special video camera allows you to project on the screen a three-dimensional picture of what is happening in the surgical field. It was the creation of the technology of three-dimensional vision that made it possible to implement the entire technology, since the usual two-dimensional image on the monitor screen does not allow the operator to accurately position the surgical instrument in space, especially in the "depth" of the image.

Fig. 4. The drug delivery robot

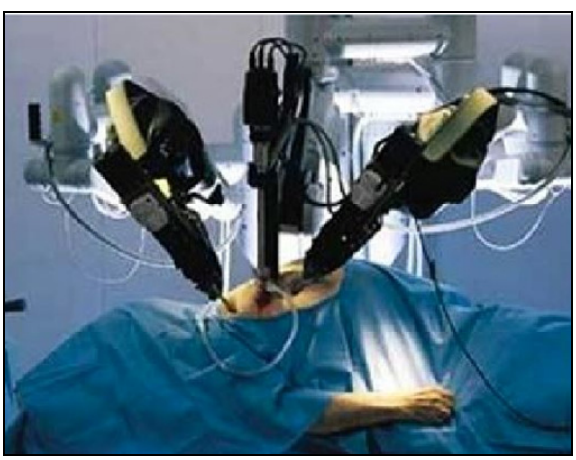

Fig. 5. Robot surgeon Da Vinci

The main advantage of the "robot surgeon" is the creation of the possibility for the human surgeon to remotely micromanipulate with any instrument without the risk of making an accidental awkward movement, which are automatically blocked by the system.

The technique of modern surgery is constantly complicated. Therefore, the risk of negative consequences for the patient increases both during the operation itself and in the postoperative period. One of the possible ways to reduce such risks is computer planning of surgical interventions, which allows you to prepare a surgeon for possible errors and provide ways to prevent them. Such studies are conducted in Ukraine, in particular at the Kharkov National University of Radio Electronics [17].

The New Zealand "robot therapist", who, according to the operator's commands, can measure the pressure and temperature of the patient, determine the presence of wheezing in the lungs and perform a number of other operations, has also gained fame [18] (Fig. 6).

Thanks to the advent of robotic manipulators, radiation therapy for cancer patients received a new impetus. The high accuracy of the positioning of the ionizing radiation beam and the ability to follow a moving target are critical when irradiating a tumor on organs such as the brain, heart, or lungs.

The Cyberknife radiosurgical robot knife allows similar procedures to be performed automatically [19] (Fig. 7).

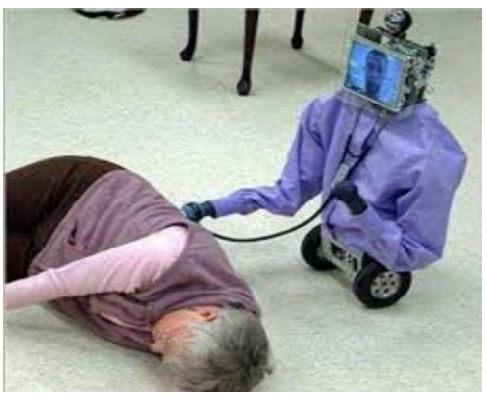

Fig. 6. New Zealand Therapist Robot

Fig. 7. Robot cyber knife

The built-in synchronization system monitors the movements of the patient and his organs with the help of an X-ray camera and optical markers from the patient's skin, and a precisely directed beam of particles from a small linear accelerator destroys cancer cells without touching healthy tissue even with significant displacements of the patient.

Intelligent medical simulators are another important area in the field of digital medicine. With the help of such systems, novice doctors can obtain the necessary knowledge and improve their skills without causing problems to real patients.

For example, the Japanese company Kokoro has created a robot simulator "Simroid", which can respond to pain and mimic the corresponding reactions [20]. If the dentist makes a mistake, the virtual patient, who has special sensors in his mouth, grimaces, demonstrating discomfort and, if necessary, produce the necessary voice messages (Fig. 8).

The Norwegian company Laerdal has developed an intelligent simulator "SimMan 3G" [21], which can simulate various human reactions in an accident: characteristic heart pulsations, pathological lung movements, bowel contractions, etc. (Fig. 9). Such a system can be invaluable in training novice specialists working in disaster medicine services.

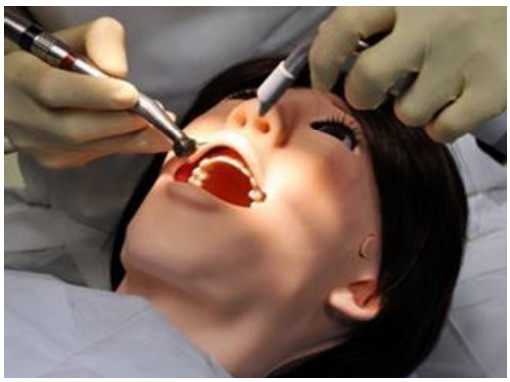

Fig. 8. Dental simulator

Fig. 9. Patient simulator SimMan 3G

For visual training of methods for restorative breathing and spinal restoration techniques 3-D models of virtual instructors were developed at the IRTC ITS (Fig. 10) [22]. Unlike traditional videos in which real training is demonstrated, virtual instructors adapt the recovery technique to the individual characteristics of a particular user, taking into account the recommendations of a rehabilitation doctor.

The modern capabilities of telecommunication technologies that provide almost instantaneous data transmission over long distances, Cloud Service, which allow you to remotely store huge amounts of biomedical data, and Grid-systems oriented to distributed computing, laid the foundation of telemedicine — a new promising area of healthcare [23].

According to the definition of the US National Medical Laboratory for Medical Terms [24], telemedicine provides interactive advisory and diagnostic services via remote communication (Fig. 11).

Distinguish between synchronous telemedicine systems that can provide real-time interactive services for emergency consultations, training large groups of students and medical consultations, and asynchronous telemedicine systems that exchange previously saved medical images and signals for consultations when interactive communication with the patient is not required.

Fig. 10. Virtual trainer for learning of the restorative methods

Fig. 11. Remote consultation

Consultations with a doctor via the Internet, obtaining a sick-list or prescription in electronic form, storing all medical documents of a patient in his personal office may soon become a common practice for most patients.

Global Market Insights predicts that by 2024, the global market for digital healthcare technologies, including IT solutions and wearable devices, will exceed $ 379 billion.

Telemedicine direction is developing intensively in Ukraine [25]. Suffice it to mention such developing telemedicine services as **LEKARIS.com**, which is a communication platform for doctors and patients. Its task is to translate the doctor's and patient's communication online, removing various barriers, thereby saving time on finding a doctor, consultations and personal receptions. Using the application, users can find the doctor of the desired specialization, urgently receive advice (messages, audio calls), schedule a consultation on a convenient day or make an appointment (Fig. 12).

The **LIKI24** Internet service provides round-the-clock drug delivery throughout Ukraine (Fig. 13). The system analyzes the prices of products in more than 1300 pharmacies every minute, finds the minimum, takes the order and delivers the medicine to the patient. Due to the mathematical model, which calculates the optimal route, one courier makes up to 60 deliveries per day.

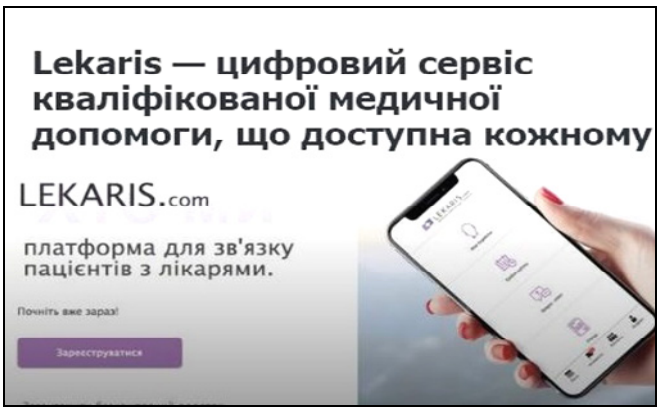

Fig. 12. LEKARIS.com service access window

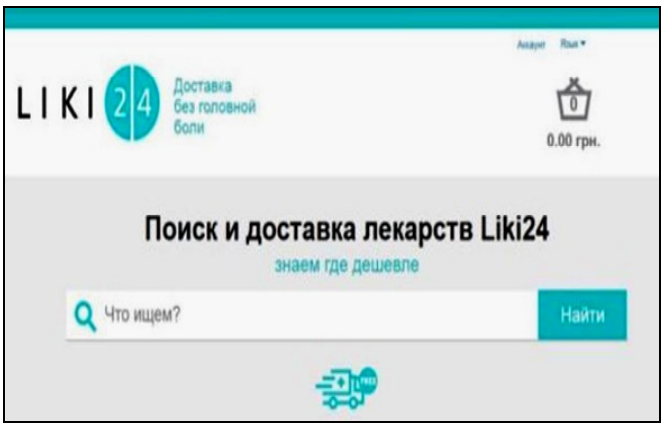

Fig. 13. LIKI24 service access window

MYLAB service of **Terra Lab Company** is to integrate laboratory research, clinics, and patients into a single ecosystem (Fig. 14). Using this service, the doctor can obtain the necessary information about the laboratory market, create electronic appointments, indicating the alleged diagnosis, receive "tips" about the studies and track the status of the study in your account.

The brief and far from complete overview shows that at the present stage of the development of society, the existing methods and means of digital medicine are already actively used to solve practically important problems.

A natural question arises: what are the main promising areas of digital medicine that can be expected in the near future.

Analysis of available publications allows us to distinguish two such areas (Fig. 15), which aim to further increase the effectiveness of diagnosis and treatment based on the principles of personalized medicine: "to treat a specific patient rather than a disease" [26].

Fig. 14. MYLAB service access window

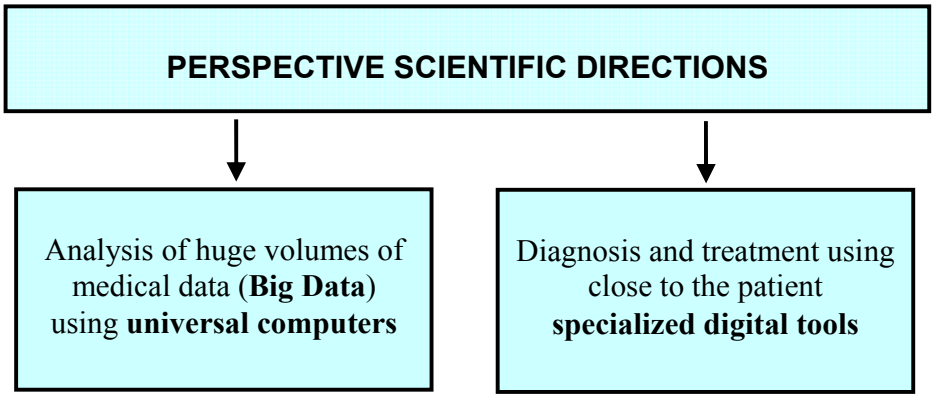

Fig. 15. The main directions of development of work in the field of digital medicine

Both directions are developing rapidly. Given the importance of these areas, we will dwell on them in more detail.

By 2018, IBM released software products for building machine learning models, which, according to [27], allow, at the request of a doctor, to read about 200 million pages of text from the Internet in just three seconds and structure the information received.

The doctor can use such information to support the adoption of diagnostic decisions and choose the optimal treatment tactics for a particular patient based on a comparison of physiological parameters, symptoms of the medical history, DNA and other individual characteristics of his body with similar cases in world medical practice.

The company focuses further development of this direction [28] on solving such problems:

- providing an individual approach for the treatment of cancer patients;
- studying of mutations of cancer cells, leading to the emergence of resistance to the effects of drugs;
- searching for new, more effective, medications based on the analysis of the genetic data of hundreds of thousands of patients and healthy people.

Important results were obtained in the field of the second direction of work. According to the results of analytical studies [29], recently the market for medical devices has significantly changed its direction from complex systems of clinical use where relative stagnation is observed, to portable digital devices that patients can use on their own.

The relevance of this area is obvious. Severe illnesses often require inpatient treatment. But few people feel comfortable in the hospital. Hospitalization causes especially significant psychological trauma to the elderly and children. In addition, inpatient care suffers significant economic losses for both the patient and the public health system.

Recently, a new term has appeared — “home hospital”. By this it is mean the program of constant supervision and rehabilitation at home of elderly people who have suffered serious illnesses — stroke, acute myocardial infarction, hip fracture, and the like. The patient is provided with medical care related to the constant monitoring of a family doctor, blood sampling, consultations of specialized specialists, medical injections, nurse services and more.

Let us show that the current level of development of inteligent IT already today can significantly increase the effectiveness of the "home hospital" by creating personalized means of processing physiological signals that the patient can independently use at home.

INTELLIGENT INFORMATION TECHNOLOGIES IN DIGITAL MEDICINE

Scientific research in the field of artificial intelligence (AI) began in the first half of the twentieth century, which laid the foundation for three areas (Fig. 16).

The founder of the algorithmic approach is rightfully considered the outstanding British mathematician Alan Mathison Turing. He set as goal to study the external side of human intelligence, in particular to analyze how a person performs calculations. These reflections in 1936 led to the creation of an abstract computer model, which was later called the Turing machine [30].

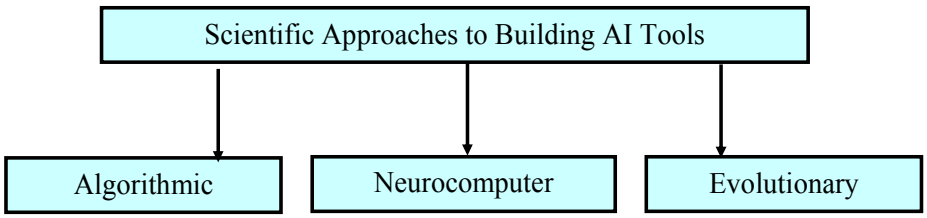

Fig. 16. The formed scientific directions of artificial intelligence

Despite the apparent simplicity, the Turing machine not only standardized the very concept of the algorithm, but also laid the foundation for the mathematical theory of complexity, the algorithmic theory of information, cryptography and many other scientific disciplines.

Discoverers of the neurocomputer approach were American physiologists Warren Sturgis McCulloch and Walter Pitts, who studied the internal organization of the human brain. Based on the study of brain cells, they first established that the process of thinking organizes by a complex combination of elementary logical operations such as AND, OR, NOT. As a result, in 1943, the simplest mathematical model of a neuron was proposed [31], which laid the foundation for neural network technologies.

And, finally, the formation of an evolutionary approach in the field of AI is associated with the name of the Italian mathematician Nils Barricelli, who set as goal to study the process of evolution of natural intelligence. By 1954, a model was proposed that served as the basis for a number of heuristic algorithms, in particular the so-called genetic algorithm [32], which actively uses the mechanisms of crossing, mutation, and inheritance, borrowed from Darwin's theory of the evolution of living nature.

For many years, these three areas developed in parallel and quite often unreasonably opposed to each other. However, the complexity of practical tasks requiring the use of AI tools led to a certain convergence of these approaches. Currently, scientific programs are actively being formed to create the so-called NBIC technologies based on the integration of nanotechnologies, biology, information technologies and cognitive sciences [33].

The priority direction of scientific and technological progress is the construction of intelligent IT, the concept of which was developed in Ukraine in the nineties of the last century [34]. Unlike traditional IT based on the procedures for processing numerical data, intelligent IT operate with generalized concepts (images) that provide more complete information about the external environment, and the analysis of such images generates a holistic picture of the phenomena studied.

The term intelligent IT is increasingly mentioned in the scientific and popular science literature. And this is no coincidence, since at the present stage of the development of society such technologies have a significant role in solving urgent applied problems, including in the field of digital medicine.

At the same time, the unreasonable application of these terms to application systems that are neither IT, nor even intelligent IT, can lead to the discrediting of these important scientific areas, as it has already been done more than once in the past, for example, to discrediting the term “Automated Control Systems".

Since science begins with definitions, let us give a more or less rigorous formulation of the concept of “intelligent IT signal processing”. To do this, we turn to the basic definition of the term "technology".

The word "technology" combines two terms: "Techno" (Greek "Téchnë" — art, skill, ability) and "Logic" (Greek “Logos” — science). Thus, in the general case, technology is the art of converting some raw material into a product (for example, iron ore into steel), and the science of technology is aimed at finding the most effective ways of such conversion.

This implies the following definition [35].

Definition 1. Intelligent IT for signal processing, including the physiological signal generated by a biological object is a set of computational procedures that have the properties of natural intelligence, which provide an effective transition from the observed signal (raw materials of the technology) to information about the current state of the object (technology product).

Formal and informal approaches to the construction of effective procedures that implement the individual stages of IT are possible. The first approach is based on the solution of the optimization problem: the computational procedure is constructed formally from the condition of minimum (maximum) of a certain criterion (super criterion) characterizing the effectiveness of a particular processing stage.

For example, the Bayesian classification is based on the minimum of the criterion, which represents the average risk of the decisions made, and the procedure for constructing the regression model is based on the minimum of the criterion, which is the standard error of the approximation of the experimental data by a function specified up to unknown parameters.

However, not all computational procedures can be built on the basis of a formal approach. It is far from always possible to express the effectiveness criterion for a particular stage of signal processing in the form of a convex function for which global optimization can be carried out. Other reasons for the limitations of the formal approach can be also pointed out.

In such situations, there is no choice but to build a computational procedure informally on the basis of intuition, and use the criterion only to assess its effectiveness.

Let $\mathfrak{I}_0$ be the a priori value of the criterion $\mathfrak{I}$ of an individual IT stage, which can be estimated (formally or by an expert) before using some computational procedure $\mathfrak{R}$, and let $\mathfrak{I}_1$ be the posterior value of the criterion $\mathfrak{I}$ estimated after using this procedure.

Then it is legitimate to introduce such definitions.

Definition 2. The procedure $\mathfrak{R}$ is effective if a strict inequality holds:

$$\mathfrak{I}_1 < \mathfrak{I}_0 . \tag{1}$$

Definition 3. The procedure $\mathfrak{R}^{(i)}$ is more effective than the procedure $\mathfrak{R}^{(j)}$ if for posterior values of the corresponding criteria the strict inequality holds

$$\mathfrak{I}_1^{(i)} < \mathfrak{I}_1^{(j)} . \tag{2}$$

Thus, when informally building an effective computational procedure, it is not necessary at all to solve the optimization problem of finding a global minimum.

Moreover, in accordance with the introduced definitions, the procedure remains effective even if it does not satisfy the local minimum of the criterion, but only allows to reduce the value of the criterion in comparison with its a priori value.

Of course, the formulated definitions can naturally be reformulated if the procedure $\Re$ is aimed at increasing the value of $\Im$.

Based on (1) and (2), the selection of a suitable procedure for the interactive synthesis of applied IT can be ensured by trial and error. For the practical implementation of this approach the tool system was developed at the IRTC ITS [36], which allows:

• conduct the necessary experiments to select and optimally configure computational procedures that implement individual stages of signal processing, including intelligent computational procedures;

• implement the technological chain of processing algorithms using ready-made computing components of the tool environment itself;

• expand, if necessary, the composition of the components of the instrumental system (Fig. 17).

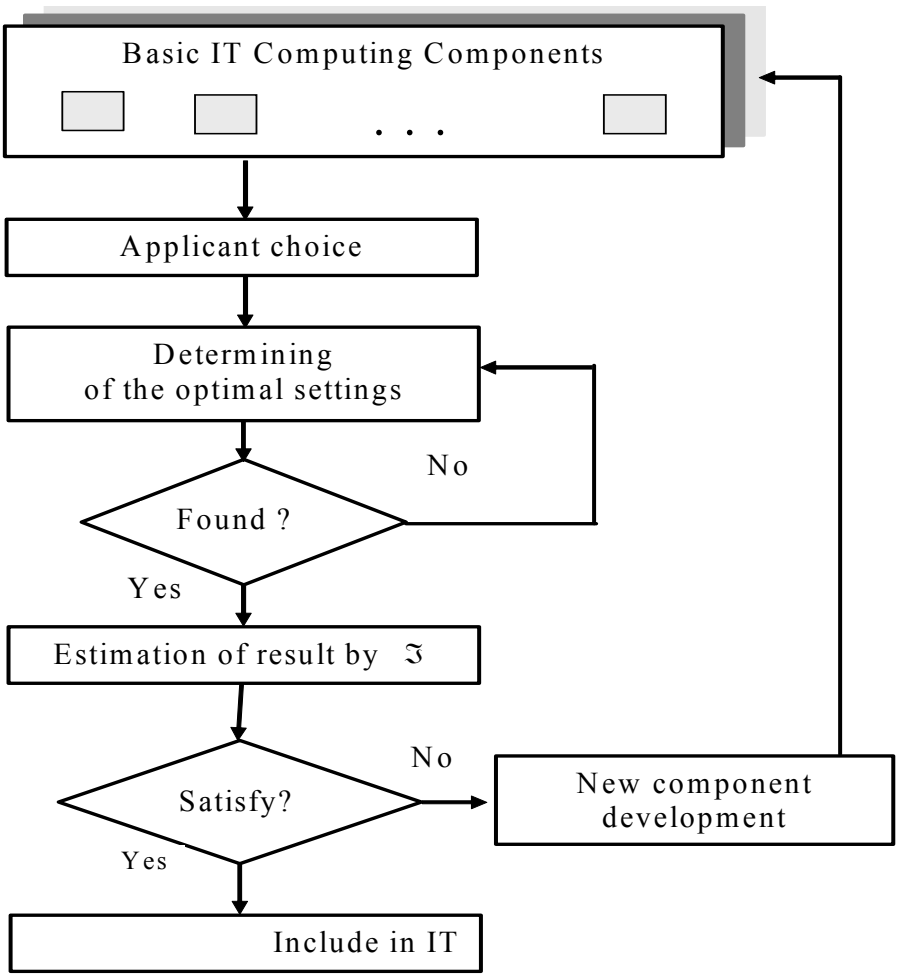

Fig. 17. The conceptual idea of interactive synthesis of IT

The instrumental system made it possible to solve successfully a number of urgent applied problems, in particular, to create an original technology for processing electrocardiograms (ECG), which was called fasegraphy and is a vivid example of the successful use of intelligent IT in digital medicine [37, 38].

The technology is implemented in the FASEGRAPH® complex, which received a certificate of state registration of medical devices with unlimited validity and is mass-produced. FASEGRAPH® consists of a microprocessor sensor that provides the convenience of registering the first standard lead ECG using finger electrodes, and a computer program that implements all stages of signal processing (Fig. 18).

Despite the fact that such single-channel ECG recorders (Home ECG monitors) are already quite widespread in the markets of medical equipment, FASEGRAPH® still has undoubted advantages compared to well-known counterparts such as Health Frontier (Canada), Win Health (Great Britain), Vitaphone (Germany), Cardiovit MT100 / 200/3 Schiller (Switzerland), Monebo (USA), J1 Portable ECG Monitor (China), CardioQVARK (Russia) and others, which allow you to control only the heart rate.

The main advantage of FASEGRAPH® is not the sensor itself, but high-tech information technology that implements the original method of processing ECG on the phase plane. Such an approach to ECG processing made it possible to expand the system of diagnostic features based on an assessment of the speed characteristics of the process, in particular, to implement for the first time a procedure for reliable determination of the indicator characterizing the symmetry of a repolarization fragment of an averaged phase trajectory.

Large-scale clinical trials have confirmed that this indicator increases the sensitivity and specificity of ECG diagnostics, even in cases where ECG analysis in 12 traditional leads is not informative. FASEGRAPH® is recommended by the Ministry of Health of Ukraine for coronary artery disease screening [39].

Fasegraphy is based on original computational procedures [40], which have the properties of natural intelligence, including properties:

- adaptations for the effective suppression of internal and external disturbances with incomplete a priori information about the characteristics of the interference;
- invariance of the shape of the reconstructed useful signal based on averaging of the distorted phase trajectories of the cardiac cycles of the observed ECG with possible time shifts (occurrence non-synchronism) of the same type of fragments;
- generalizations in the classification of typical and atypical ECG cycles in the absence of an analytical description of recognizable classes and the inability to determine generalizing features by machine learning methods;
- learning ability in the automatic assessment and constant correction of the personal norm of a particular patient to expand the functionality of the complex through the implementation of the idea of a personalized diagnosis of cardiac activity;
- sociability, which ensured the provision of test results in a convenient and accessible manner, taking into account the user's qualifications, in particular, the provision of information to a patient who does not have a medical education.

The experience in the development of fasegraphy has shown that, within the framework of the algorithmic approach, the construction of intelligent IT involves the active participation of a technology developer who, using his intelligence, creates effective computational procedures for extracting diagnostic information from real signals under disturbances (Fig. 19).

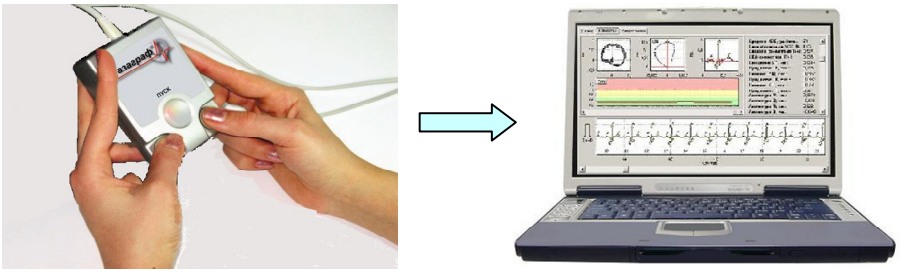

Fig. 18. FASEGRAPH® complex

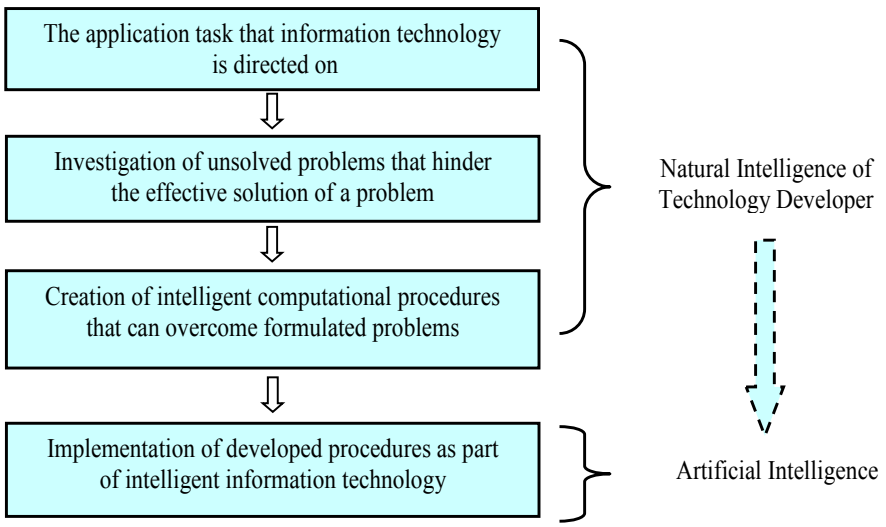

Fig. 19. Stages of building intelligent IT

FASEGRAPH® has proven its effectiveness in various fields of application, including screening for coronary heart disease [41], in pediatric cardiology to assess cardiometabolic risk in adolescents, the functional state of children with diabetic cardiopathy, cardiorespiratory desynchronism, and the effect of motor activity in schoolchildren [42–46], in sports medicine for the rapid assessment of overtraining and the general functional level of highly qualified athletes [47], in the clinical setting for evaluating the effects of drugs during the drip of drugs to cardiological patients and the effectiveness of surgical interventions [48], when performing scientific research, including studying the effects of external fields on a person during solar activity, the harmful effects of smoking on the human body and the search for objective chrono-predictors carrying information about the level of threat to the patient [49].

FASEGRAPH® occupies a special place in the market of medical equipment (Fig. 20). Before it appearance, the cardiological patient had only two possibilities: either use the home ECG monitors (smartphone gadgets), which in the best case allow diagnosing life-threatening cardiac arrhythmias, or conduct a complete traditional ECG examination in a medical facility using an expensive and not always affordable professional electrocardiograph.

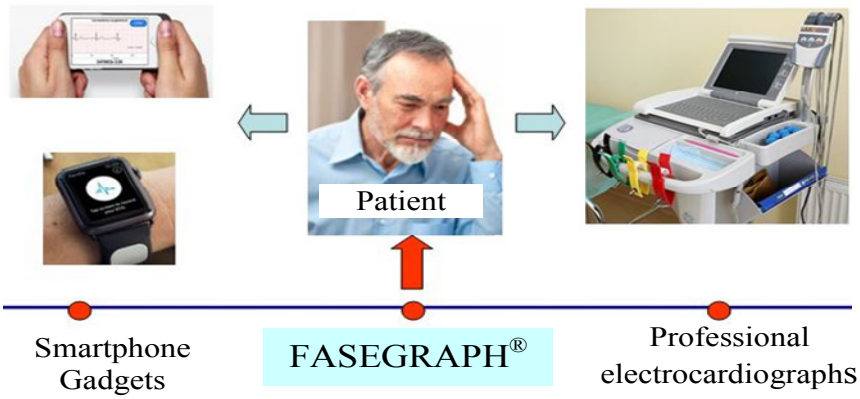

Fig. 20. The situation in the medical equipment market

The permanent use of FASEGRAPH® at home allows the patient:

- to optimize a way of life, reasonably distributing a mode of loadings and rest;
- to determine the need for additional intake of medications prescribed by a doctor;
- to evaluate possible dangerous deviations in the work of the heart from the personified norm;
- independently accumulate data over a long period of time for subsequent consultations with a doctor, which provides a more complete and reasonable assessment of the patient's functional state than episodic contact with a doctor using traditional clinical tools.

The mobile fasegraphy platform currently being developed, which provides for the implementation of technology elements on a smartphone, provides the opportunity not only to conduct operational testing in any conditions, but also to organize a virtual connection between a patient and a family doctor using Internet technologies [50–52].

Fasegraphy has opened the way to the construction of new methods for biometric identification of individuals based on the unique properties of ECG phase portraits [53–54].

The intelligent capabilities of phase printing are constantly being developed due to the inclusion of new program modules in FASEGRAPH®, including modules for evaluating the randomness of the processed signal shape parameters [55], a phase portrait of permutation entropy, which confirmed the high sensitivity when evaluating subtle ECG changes under the influence of various factors, in particular , to detect the effect of electrical heart alternation, which is used by doctors as a predictor of sudden cardiac death [56], as well as to assess the tolerance to physical stress based on the regulatory patterns and their display in the form of cognitive graphic images [57].

Further development of fasegraphy involves the implementation of new promising approaches to the processing of cyclic signals, in particular, the method of displaying a signal in a multidimensional parameter space, which, using unified methodological principles, makes it possible to evaluate the randomness of the waveform, detect atypical cycles, interpret the signal, personify diagnostic solutions and economical coding of the signal when it transmission and storage [58, 59], and

the linguistic method of signal analysis and interpretation based on the calculation of the Levenshtein distance between codograms of real signals [60].

Preliminary studies have shown that intelligent computational of fasegraphy procedures allow you to create a new class of competitive medical devices, in particular, finger photoplethysmograph, which records the patient's pulse wave using the built-in smartphone camera without additional external signal sources [61], as well as an intelligent home blood pressure monitor with advanced functional opportunities.

CONCLUSION

An analysis of the available literature showed that at the present stage of the development of society, the existing means of digital medicine are used to solve many urgent problems of practical medicine, including in the diagnosis, treatment and restoration of lost functions. Such technologies make it possible not only to free medical workers from solving routine tasks, but also to increase the efficiency of performing surgical operations, radiation therapy and a number of other complex tasks.

Intelligent IT with the properties of natural intelligence (adaptation, generalization, learning, etc.) play an important role in expanding the functionality and increasing the effectiveness of digital medicine. Unlike traditional IT based on the procedures for processing numerical data, intelligent IT operate with generalized concepts (images) that provide more complete information about the external environment, and the analysis of such images generates a holistic picture of the phenomena studied.

Using the example of successful development of the fasegraphy method, it is shown that, within the framework of the algorithmic approach, the construction of intelligent IT for solving digital medicine problems involves the active participation of a technology developer who, using this natural intelligence, creates effective procedures for extracting diagnostic information from real data distorted by disturbances.

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СУЧАСНИЙ СТАН І ПЕРСПЕКТИВИ РОЗВИТКУ ЦИФРОВОЇ МЕДИЦИНИ

Вступ. Згідно з означенням Міжнародної асоціації цифрової медицини, цифровою медициною є галузь науки, в якій вчені прагнуть пояснити раніше незрозумілі патофізіологічні явища в організмі людини і досліджувати нові медичні процедури з використанням сучасних цифрових технологій для поліпшення якості життя людини.

Мета статті – надати коротку інформацію про сучасний стан і перспективи розвитку засобів цифрової медицини.

Методи. Проведено аналіз основних напрямів цифрової медицини. Сформульовано базові означення понять «Інтелектуальна ІТ оброблення сигналів» та «Ефективна обчислювальна процедура». На прикладі методу фазаграфії продемонстровано роль інтелектуальних ІТ в цифровій медицині.

Результати. Наявні методи і засоби цифрової медицини застосовують для діагностики, лікування, реабілітації, а також для відновлення втрачених функцій пацієнта (зір, слух, рух). Такі технології дають змогу не тільки звільнити медичних працівників від виконання рутинних завдань, а й підвищити ефективність виконання хірургічних операцій, променевої терапії та ряду інших складних завдань практичної медицини.

На відміну від традиційних ІТ, основаних на процедурах оброблення числових даних, інтелектуальні ІТ оперують узагальненими поняттями (образами), що дають повнішу інформацію про зовнішнє середовище, а аналіз таких образів породжує цілісну картину досліджуваних явищ.

В рамках алгоритмічного підходу побудова інтелектуальних ІТ для вирішення завдань цифрової медицини передбачає активну участь розробника технології, який, застосовуючи свій природний інтелект, створює ефективні процедури для одержання діагностичної інформації з реальних даних, спотворених збуреннями.

Висновки. Інтелектуальні ІТ, які мають властивості природного інтелекту (адаптація, узагальнення, здатність до навчання та ін.), відіграють важливу роль у розширенні функціональних можливостей і підвищення ефективності засобів цифрової медицини**.**

Ключові слова: цифрова медицина, інтелектуальні ІТ, ефективні обчислювальні процедури.

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СОВРЕМЕННОЕ СОСТОЯНИЕ И ПЕРСПЕКТИВЫ РАЗВИТИЯ ЦИФРОВОЙ МЕДИЦИНЫ

Введение. Согласно определению Международной ассоциации цифровой медицины, цифровой медициной называют область науки, в которой ученые стремятся объяснить ранее непонятные патофизиологические явления в организме человека и исследовать новые медицинские процедуры с использованием современных цифровых технологий для улучшения качества жизни человека.

Цель статьи — дать краткую информацию о современном состоянии и перспективах развития средств цифровой медицины.

Методы. Проводится анализ основных направлений цифровой медицины. Формулируются базовые определения понятий «Интеллектуальная ИТ обработки сигналов» и «Эффективная вычислительная процедура». На примере метода фазаграфии демонстрируется роль интеллектуальных ИТ в цифровой медицине.

Результаты. Существующие методы и средства цифровой медицины применяют для диагностики, лечения, реабилитации, а также для восстановления утраченных функций пациента (зрение, слух, движение). Такие технологии позволяют не только освободить медицинских работников от решения рутинных задач, но и повысить эффективность выполнения хирургических операций, лучевой терапии и ряда других задач практической медицины.

В отличие от традиционных ИТ, основанных на процедурах обработки числовых данных, интеллектуальные ИТ оперируют обобщенными понятиями (образами), дающими более полную информацию о внешней среде, а анализ таких образов порождает целостную картину изучаемых явлений.

В рамках алгоритмического подхода построение интеллектуальных ИТ для решения задач цифровой медицины предполагает *активное* участие разработчика технологии, который, применяя свой естественный интеллект, создает эффективные процедуры для извлечения диагностической информации из реальных данных, искаженных возмущениями.

Выводы. Интеллектуальные ИТ, обладающие свойствами естественного интеллекта (адаптация, обобщение, обучаемость и др.), играют важную роль в расширении функциональных возможностей и повышении эффективности средств цифровой медицины.

Ключевые слова: цифровая медицина, интеллектуальные ИТ, эффективные вычислительные процедуры.

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ЗАСТОСУВАННЯ ІНФОРМАЦІЙНОЇ ТЕХНОЛОГІЇ ВИЗНАЧЕННЯ ЦИРКУЛЮЮЧИХ ПУХЛИННИХ КЛІТИН ДЛЯ ДІАГНОСТУВАННЯ ЗЛОЯКІСНИХ ПУХЛИННИХ ЗАХВОРЮВАНЬ

Вступ. *Дослідження можливості використання визначення циркулюючих пухлинних клітин в крові хворих за різної локалізації злоякісних новоутворень як діагностичного критерію та критерію ефективності конкретної тактики лікування є одним з актуальних питань сучасної онкології.*

Метою *статті є аналіз результатів використання розробленої інформаційної технології визначення циркулюючих пухлинних клітин для дослідження зразків крові пацієнтів з метою підтвердження чи відхилення первинного діагнозу з онкологічного захворювання різної локалізації.*

Результати. *Запропоновано інформаційну технологію,щобазується на використанні удосконаленого методу виділення цілісних і неушкоджених циркулюючих клітин, відмінність якого полягає в доповненні структури базового методу ISET новими режимами: режимом 100 % герметизації камери з гемолізатом і забезпечення в ній необхідного і постійного тиску протягом всього процесу фільтрації шляхом введення манометра негативного тиску, а також режимом трирівневої фільтрації ЦПК на послідовно розміщених полікарбонатних мембранах з діаметрами мікропор 8 мкм, 5 мкм і 3 мкм.*

Для оцінювання злоякісності виділених клітин у інформаційній технології використано метод визначення ЦПК за сформованим комплексом критеріїв, накопичено бази даних створених шаблон-масок ЦПК та контрольних шаблонів нормальних клітин у автоматизованому режимі. Проведено дослідження зразків крові пацієнтів з викори-

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станням розробленої ІТ. Аналіз результатів дослідження з урахуванням кожного кроку методики (з використанням різних фільтрів) показав, що з сумарна частка зразків, у яких додатково виявлено ЦПК із застосуванням не тільки фільтру 8 мкм, а й фільтрів 5 мкм та 3 мкм, склала 20,66 %.

***Висновки**. Використання розробленої інформаційної технології визначення циркулюючих пухлинних клітин підвищує ефективність визначення циркулюючих пухлинних клітин за рахунок скорочення часу тестування та розширення діапазону дослідження завдяки можливості виявлення клітин малих розмірів. Удосконалення ІТ за рахунок доповнення базою знань (комплекс шаблон-масок та відповідних експертних висновків) уможливлює застосування її у скринінговому дослідженні крові пацієнтів, в тому числі на доклінічному етапі обстеження.*

***Ключові слова**: інформаційна технологія, циркулюючі пухлинні клітини, метод ізоляції циркулюючих пухлинних клітин, автоматизована система, скринінгове дослідження крові пацієнтів.*

ВСТУП

Сучасна цифрова медицина потребує розвитку інформаційних технологій для використання у діагностичних та лікувальних процесах, особливо для онкозахворювань. У всьому світі високу смертність пацієнтів, хворих на рак, зумовлено тяжкістю захворювання та пізньою діагностикою, а саме пізніми термінами виявлення первинних пухлин, відсутністю високоточних методів контролю ефективності лікування на різних етапах лікування.

Сучасну діагностику раку здебільшого спрямовано на виявлення пухлин та їхніх ускладнень, тобто у періоди захворювання, коли пухлину можна побачити звичними способами візуалізації. Водночас, за результатами багатьох досліджень вважають доведеним, що у 20–70 % онкохворих в периферичній крові виявляють циркулюючі пухлинні клітини (ЦПК) [1–3], кількість яких в крові у хворих на ранній рак молочної залози виділяють у 30–52,6 % випадків, у хворих на місцевопоширений рак — у 36–52 %, у хворих на метастатичний рак — до 70 % випадків [4–6].

Дослідження можливості використання визначення циркулюючих пухлинних клітин в крові хворих за різної локалізації злоякісних новоутворень як діагностичного критерію та критерію ефективності конкретної тактики лікування є одним з актуальних питань сучасної онкології. Але відсутність чітких кількісних критеріїв оцінювання злоякісності виділених циркулюючих клітин, доступних інформаційних технологій виявлення ЦПК у крові пацієнтів з високою чутливістю та точністю аналізу та тлумачення зумовлює необхідність поглибленого дослідження та удосконалення методів виділення та оцінювання ЦПК [4, 7].

ПОСТАНОВКА ПРОБЛЕМИ

У 1869 р. австралійський патолог T. Ashworth вперше висунув гіпотезу про те, що циркулюючі пухлинні клітини (ЦПК) є основною передумовою метастазування [8]. Використання розроблених у 21-му столітті методів виявлення пухлинних клітин, які циркулюють у крові хворих на рак, дало змогу клініцистам дослідити їхню роль в канцерогенезі і поставити завдання їхнього використання як оцінювальних і прогностичних показників у клінічній практиці [7, 9–11]. Виявлені біологічні характеристики ЦПК, на відміну

від злоякісних клітин первинної пухлини, свідчать про набуття пухлиною нових якостей — інвазивності і здатності до метастазування та можуть бути новим прогностичним маркером, який відображає, зокрема, ефективність протипухлинного лікування.

На основі методів імунофлуоресценції, імуномагнітного поділу, проточної цитометрії та інших імуномагнітних методів створено низку інформаційних технологій та автоматизованих систем, які дають змогу виділити пухлинні клітини за допомогою магнітного поля, використовуючи властивість цих клітин взаємодіяти з антитілами проти маркерів ЦПК з кон'юктивними магнітними частинками [12–15]. Але досі немає методів та технологій аналізу ЦПК з метою раннього неінвазивного виявлення раку.

Багато дослідників для визначення ЦПК в крові пацієнтів з раком молочної залози використовували систему CellSearch компанії Veridex [12]. Цю технологію схвалено Управлінням з контролю за продуктами харчування та медичними виробами США (Food and Drug Administration, FDA, USA) для виявлення рівнів ЦПК у пацієнтів з метастазами. Система є напівавтоматичною і в її основі лежать методи імунофлуоресценції, імуномагнітного поділу і проточної цитометрії [13], однак без ухвалення можливості клінічного використання цієї системи. CellSearch дає змогу підрахувати ракові епітеліальні клітини, відокремлюючи лейкоцити, з точністю виявлення п'яти і більше ЦПК на 7,5 мл крові [12, 16]. Подібний до CellSearch принцип роботи реалізовано у системах Ariol. Перспективною є технологія CTC-chip [17], яка базується на мікропроточній системі з використанням розробленого чипу. Через цей чіп пропускають потік крові в умовах ламінарної течії. Чутливість методу висока (99 %), ця технологія дає змогу аналізувати невеликі об'єми крові (2–3 мл). У дослідженнях використовують поліуретановий фільтр Imugard III RC («Terumo», Японія) з діаметром пор до 30 мкм [4], що обмежує можливості виділення ЦПК меншого розміру.

На сьогодні розроблено більше 40-ка методів і засобів, орієнтованих на розв'язання завдання визначення ЦПК, однак більшість з них є ще далекою до клінічної реалізації [18]. Серед цих методів та технологій найточнішими та допущеними FDA (Food and Drug Administration) до клінічного використання в США є CellSearch та ISET (Isolation by Size of Tumor cells). Беручи до уваги результати клінічних досліджень та технічної реалізації методів ізоляції ЦПК на ранніх стадіях інвазії пухлини, актуальним є розвиток таких методів для їхнього практичного впровадження [19]. Необхідність розширення можливостей технології виявлення ЦПК та забезпечення автоматизованого режиму дослідження зумовило розроблення інформаційної технології з удосконаленням базового методу ізоляції ЦК, формуванням комплексу критеріїв оцінювання злоякісності виділених ЦК і залученням методів одержання та аналізу мікроскопічних зображень цих клітин [20].

Метою статті є аналіз результатів використання розробленої інформаційної технології визначення циркулюючих пухлинних клітин для дослідження зразків крові пацієнтів з метою підтвердження чи відхилення первинного діагнозу з онкологічного захворювання різної локалізації.

ІНФОРМАЦІЙНА ТЕХНОЛОГІЯ ВИЗНАЧЕННЯ ЦИРКУЛЮЮЧИХ ПУХЛИННИХ КЛІТИН

Запропоновано нами інформаційну технологію, що базується на використанні удосконаленого методу виділення клітин, які циркулюють у крові людини (ЦК), на основі методу ISET [21–23]. Метод ISET, який дає змогу ізолювати неушкоджені ЦК, є єдиним клінічно перевіреним методом для цитопатологічної діагностики ЦПК за звичайними цитопатологічними критеріями, які застосовують лікарі-цитологи у оцінюванні мазка за Папаніколау або тонкоголкової біопсії. ISET має набагато більшу чутливість, ніж інші методи ізоляції пухлинних мікроемболів (ЦПМ) або кластерів, що складаються з декількох ЦПК. Вважають, що наявність ЦПМ корелює з поганим прогнозом. Саме спроможність методу ISET виділяти і кількісно оцінювати ЦПК і ЦПМ крові дала можливість ввести в практику термін «Циркулюючі пухлинні мікроемболи».

Технологія ISET на основі методу вакуумної фільтрації забезпечує фільтрацію крові пацієнтів через полікарбонатну мембрану порами 8 мкм, після оброблення лікар отримує зразок клітинного препарату. Виявлені ЦПК переважно більші за розміром, ніж звичайні клітини крові і експресують на своїй поверхні епітеліальні молекули клітинної адгезії (EpCAM), які є специфічними маркерами для ракових клітин, що найчастіше використовують для виявлення ЦПК. Необхідність модернізації етапу ізоляції ЦПК для одержання неушкоджених клітин меншого розміру, а також автоматизація всього процесу дослідження — від виділення клітин до оцінювання їхньої злоякісності та надання відповідного висновку слугувала мотиваційним чинником проведеного нами дослідження та розроблення інформаційної технології визначення ЦПК у крові людини [20].

Структурна схема запропонованої інформаційної технології об'єднує три етапи (Рис. 1). На *першому етапі — отримання клітинного препарату для виявлення ЦПК* із зразка венозної крові пацієнта використано удосконалений нами метод ізоляції (виділення) за розміром пухлинних клітин. Відмінність запропонованого методу виділення цілісних і неушкоджених ЦПК полягає в доповненні структури базового методу ISET новими етапами (режимами), а саме: режимом 100 % герметизації камери з гемолізатом і забезпечення в ній необхідного і постійного тиску протягом всього процесу фільтрації шляхом введення манометра негативного тиску, а також режимом трирівневої фільтрації ЦПК на послідовно розміщених полікарбонатних мембранах з діаметрами мікропор 8 мкм, 5 мкм і 3 мкм. Отже, внаслідок виконання першого етапу буде затримано і виділено клітини, розмір яких більший за 3 мкм (а не 8 мкм як у стандартному методі ISET).

На *другому етапі* здійснюється *формування мікроскопічних зображень* з виділеними клітинами. Для автоматизації запропонованого методу використано підходи до оброблення мікроскопічних біозображень [24, 25]. Методику удосконалено внесенням додаткових кроків, а саме: на першому кроці передбачено вибір розміру вікна сканування мікроскопа таким, що не перевищує діаметр його світлового поля, процес оброблення зображень ЦК набуває поступово-послідовного характеру завдяки автоматизації переміщення предметного столика мікроскопа — програмуванню переміщень предметного столика мікроскопа з розміщеними на його поверхні полікар-

бонатними мембранами трьох видів за розмірами фільтрувальних пор. На цьому етапі отримане мікроскопічне зображення клітинного препарату проходить систему алгоритмів попереднього оброблення (фільтрів), що дає змогу підготувати зображення для аналізу і виключити артефакти (Рис. 2). Зазначимо, що до подальшого критеріального оцінювання виділених клітин на кожній із зазначених мембран не допускались зображення, які не містять великих неушкоджених клітин.

Третій етап спрямовано на *аналіз зображень ЦПК*, визначення злоякісності виділених клітин з використанням сформованого комплексу критеріїв за запропонованим методом визначення циркулюючих пухлинних клітин та надання відповідного висновку.

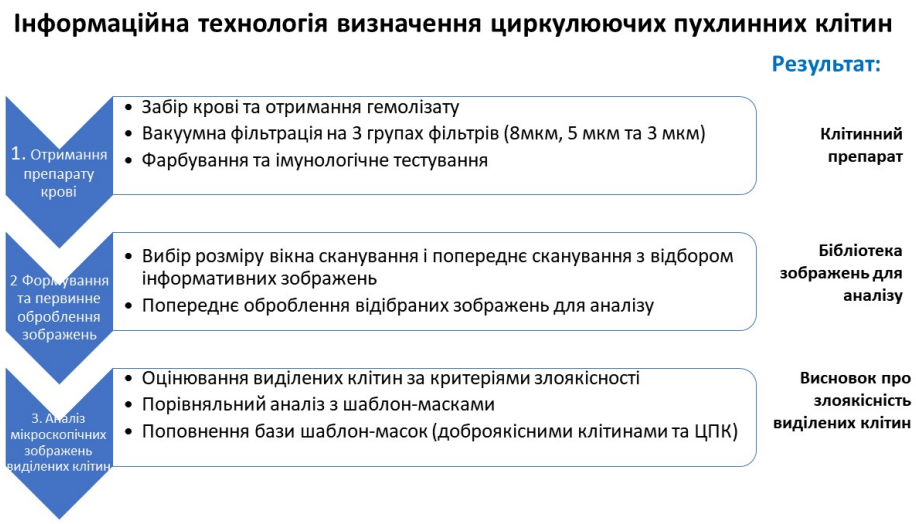

Рис. 1. Структура інформаційної технології визначення ЦПК у крові людини

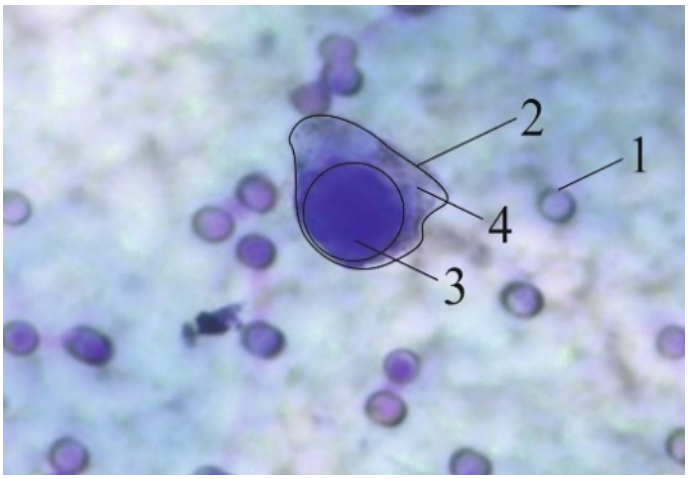

Рис 2. Збільшений виділений об'єкт мікроскопічного зображення: 1 — пора мембрани; 2 — клітина ЦПК (меланома); 3 — ядро ЦПК; 4 — цитоплазма

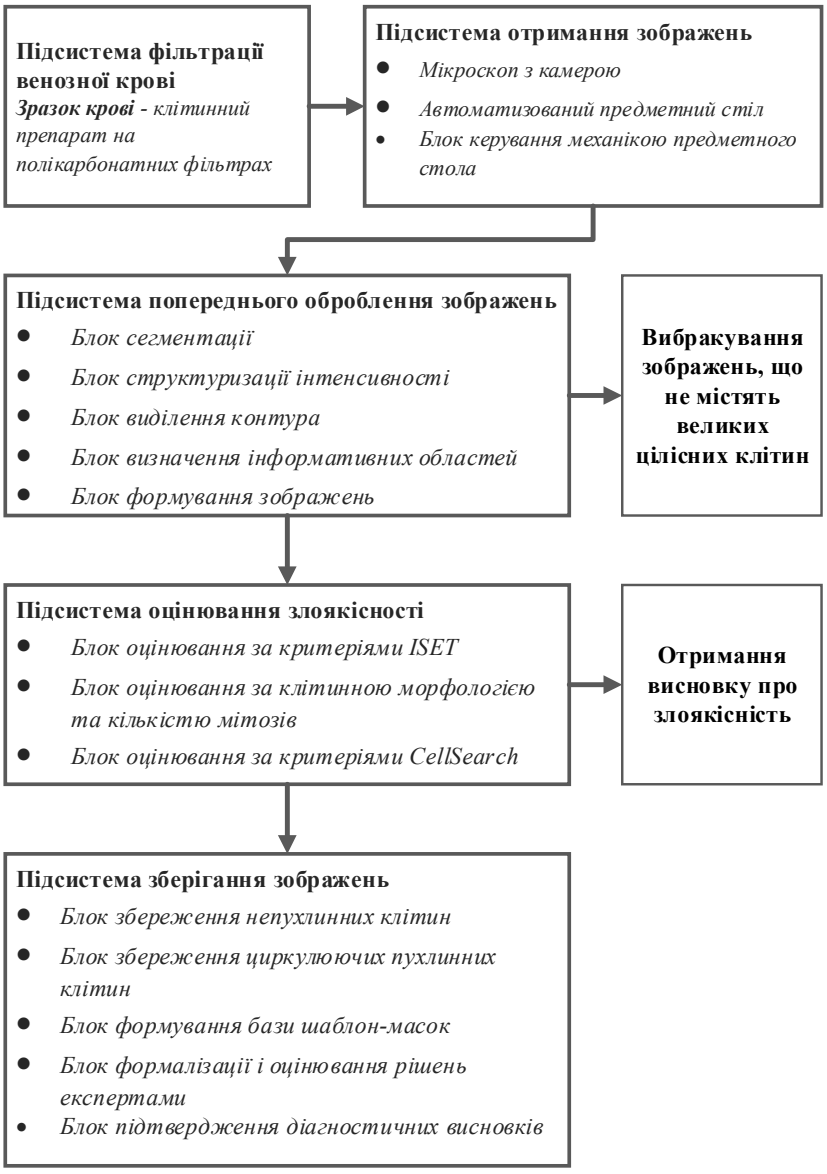

Рис. 3. Блок–схема автоматизованої системи для отримання та аналізу мікроскопічних зображень ЦПК

Для оцінювання злоякісності виділених клітин нами сформовано комплекс критеріїв [26], який об'єднує три групи критеріїв, перша з яких визначається за методом ISET, де клітина вважається злоякісною, якщо відповідає чотирьом із п'яти критеріїв з розширенням діапазону оцінювання на клітини розмірами від 9 мкм, а не 24 мкм, як в ISET (потрійний розмір пори найменшого фільтра). З метою уникнення гіпердіагностики за рахунок хибнопозитивних результатів ми вважали за потрібне доповнити цю групу критеріїв двома іншими, а саме: за модифікованою схемою P. Scarft, H. Bloom, W. Richardson та за прогностичним тестом медичного комплексу ім. Хаіма Шеба (Ізраїль).

На цьому етапі створюються шаблон-маски та формуються бази даних шаблон-масок ЦПК та контрольних шаблонів нормальних клітин.

Розроблену інформаційну технологію реалізовано з використанням автоматизованої системи для отримання та аналізу мікроскопічних зображень ЦПК, яка складається з чотирьох підсистем: фільтрації венозної крові; отримання і попереднього оброблення зображень ЦПК; формування зображень ЦПК та оброблення зображень ЦПК (Рис.3). Цю систему покладено в основу пристрою для виявлення циркулюючих пухлинних клітин в крові, розробленого разом з науковцями Вінницького технічного університету [27]. Накопичення бази шаблон-масок дозволить підключити аналіз з виділенням локалізації досліджуваних пухлин, розробити тканиноспецифічну класифікацію ЦПК та діагностування конкретних видів раку.

ОЦІНЮВАННЯ ЗЛОЯКІСНОСТІ ЦИРКУЛЮЮЧИХ КЛІТИН З ВИКОРИСТАННЯМ ІНФОРМАЦІЙНОЇ ТЕХНОЛОГІЇ

Для проведення апробації розробленого методу визначення ЦПК та його реалізації — інформаційної технології та автоматизованої системи, використано зразки крові, одержані з онкологічних центрів і клінічних установ м. Маріуполя та м. Вінниці. Метадані про надані зразки включали кодові позначення міста розташування клініки та порядковий номер. Зазначено також первинний чи верифікований раніше вид раку за кожним зразком.

Всі зразки відповідали стандартним вимогам: забір крові здійснено з периферичної вени — 10 мл в пробірки з антикоагулянтом EDTA; дотримання ліміту часу зберігання до початку аналізу — не більше 90 хвилин, та температури зберігання — 4 ˚C; розведення крові здійснено у співвідношенні 1:10 (до 100 мл) патентованим буферним розчином (санолін, параформальдегід, EDTA, бичачий альбумін), або дистильованою водою, який використовували для лізису еритроцитів.

Для оцінювання статистичної вірогідності результатів дослідження використано критерії чутливості, специфічності, точності, а також коефіцієнт асоціації Юла (r_Q):

$$r_Q = \frac{(TP + TN) - (FP + FN)}{(TP + TN) + (FP + FN)},$$

де *TP* — істинно позитивні результати обстеження; *TN* — істинно негативні результати обстеження; *FP* — хибнопозитивні результати обстеження; *FN* — хибнонегативні результати обстеження.

Використання розробленої ІТ уможливлює використання трьох різних фільтрів з мікропорами 8 мкм, 5 мкм та 3 мкм для виявлення та оцінювання можливого джерела походження пухлини. Розглянемо детально послідовні кроки здійснення дослідження за запропонованим методом.

На першому кроці здійснено виявлення ЦПК із застосуванням фільтру з мікропорами 8 мкм. З таблиці 1 видно, що із використанням фільтру 8 мкм середнє значення частки виявлених ЦПК за досліджуваними даними становить 76,037 %. Водночас, найбільша частка ЦПК виявлена у зразках з раком товстої кишки (81,82 %), найменша — у разі дрібноклітинного раку легенів. Це свідчить про наявність значної частки недіагностованих випадків за умови використання тільки фільтру 8 мкм.

Таблиця 1. **Розподіл кількості виявлених ЦПК за використання фільтру з мікропорами 8 мкм**

Локалізація злоякісних пухлин	Всього досліджених зразків	Виявлено ЦПК		Кількість зразків з різною часткою ЦПК			
		Кількість зразків	%	до 5	від 6 до 10	від 11 до 20	> 20
Товста кишка	33	27	81,82	4	10	8	5
Молочна залоза	24	19	79,17	1	6	7	5
Дрібноклітинний рак (рак легенів)	19	11	57,89	1	5	3	2
Простата	19	15	78,95	2	6	4	3
Шкіра	26	20	76,92	3	7	6	4
Всього, осіб	121	92	76,03	11	34	28	19

Таблиця 2. **Розподіл кількості виявлених ЦПК за використання фільтр з мікропорами 5 мкм**

Локалізація злоякісних пухлин	Всього досліджених зразків	Виявлено ЦПК		Кількість зразків з різною часткою ЦПК			
		Кількість зразків	%	до 5	від 6 до 10	від 11 до 20	> 20
Товста кишка	33	4	12,12	0	2	1	1
Молочна залоза	24	4	16,67	1	1	1	1
Дрібноклітинний рак (рак легенів)	19	4	21,05	1	2	1	0
Простата	19	2	10,53	0	1	1	0
Шкіра	26	3	11,54	1	1	0	1
Всього, осіб	121	17	14,05	3	7	4	3

Наступним кроком було виявлення ЦПК із застосуванням додаткового фільтру 5 мкм. Аналіз табл. 2 показав, що за використання цього фільтру найбільшу частку досліджених зразків з виявленими додатково ЦПК визначено у зразках у разі дрібноклітинного раку легенів (21,05 %), тоді як для раку простати (10,53 %) та шкіри (11,54 %) додано значно менші частки.

На завершальному кроці використано додатково фільтри 3 мкм (Табл. 3). Результати аналізу показали, що використання цього фільтру дало змогу виявити додатково ЦПК в середньому у 6,61 % досліджуваних зразків. Найбільшу частку зразків, у яких додатково виявлено ЦПК за допомогою фільтру 3 мкм, визначено, також, для дрібноклітинного раку легенів (15,79 %).

Таблиця 3. **Розподіл кількості виявлених ЦПК за використання фільтру з мікропорами 3 мкм**

Локалізація злоякісних пухлин	Всього зразків	Виявлено ЦПК		Кількість зразків з різною часткою ЦПК			
		Кількість зразків	%	до 5	від 6 до 10	від 11 до 20	> 20
Товста кишка	33	1	3,03	0	1	0	0
Молочна залоза	24	1	4,17	0	0	0	1
Дрібноклітинний рак (рак легенів)	19	3	15,79	1	1	0	1
Простата	19	1	5,26	0	0	1	0
Шкіра	26	2	7,69	1	0	0	1
Всього, зразків	121	8	6,61	2	2	1	3

Таблиця 4. **Кількість зразків, у яких виявлено ЦПК за використання різних фільтрів**

Досліджувані показники	Загальна кількість зразків	Розмір використаних фільтрів		
		8 мкм	5 мкм	3 мкм
Кількість зразків з виявленими ЦПК за використання різних фільтрів	117	92	17	8
Частка зразків з ЦПК (%)	96,69	76,03	14,05	6,61

Аналіз результатів дослідження з урахуванням кожного кроку методики (з використанням різних фільтрів) показав (Табл. 4), що з використанням фільтру 8 мкм виявлено ЦПК тільки у 76,03 % зразків, тоді як додаткове застосування фільтру 5 мкм дало змогу виявити ЦПК ще 14,05 % досліджуваних випадків, а додаткове застосування фільтру 3 мкм — 6,61 %. Сумарна частка зразків, у яких додатково виявлено ЦПК із застосуванням не тільки фільтру 8 мкм, а й фільтрів 5 мкм та 3 мкм, склала 20,66 %.

Отже, можна зробити висновок, що розроблений метод визначення ЦПК у крові людини, реалізований у запропонованій ІТ, дає змогу виявити додатково наявність злоякісних пухлин у 20,66 % випадків (коефіцієнт асоціації Юла $r_Q = 0{,}98$, $p < 0{,}001$). Тому вже під час початкових досліджень є можливість діагностувати наявність злоякісних пухлин і забезпечити своєчасне лікування кожному п'ятому пацієнту.

Отримані результати визначення ЦПК за допомогою інформаційної технології було передано в онкоцентри і клініки під тими ж кодами, під якими і отримано.

В процесі лікування для визначення ефективності операції, променевої та хіміотерапії, а також для визначення рецидиву пухлини і початку метастатичного процесу рекомендовано визначати наявність циркулюючих пухлинних клітин в крові пацієнта (з урахуванням виділених клітин малого діаметру). Використання третьої групи критеріїв у запропонованій технології рекомендовано для визначення можливого прогнозу перебігу захворювання.

ВИСНОВКИ

Застосування розроблених методу та інформаційної технології виявлення та оцінювання злоякісності виділених клітин малого розміру у зразках крові людини під час виконання досліджень у цитогістологічних лабораторіях, оснащених приладами світлової мікроскопії з відеозахопленням зображення, надає можливість одержати важливу та своєчасну додаткову діагностичну інформацію.

Накопичення бази даних продіагностованих зображень, які отримали експертні висновки щодо виду ЦПК, та подальше створення бази знань (шаблон-масок) забезпечить доповнення функціоналу запропонованої інформаційної технології визначення типу пухлинних клітин.

Використання розробленої інформаційної технології визначення циркулюючих пухлинних клітин підвищує ефективність визначення циркулюючих пухлинних клітин за рахунок скорочення часу тестування та розширення діапазону дослідження завдяки можливості виявлення клітин малих розмірів. Удосконалення ІТ за рахунок доповнення базою знань (комплекс шаблон-масок та відповідних експертних висновків) уможливлює застосовання її у скринінговому дослідженні крові пацієнтів, в тому числі на доклінічному етапі обстеження.

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APPLICATION OF INFORMATION TECHNOLOGY FOR DETERMINATION OF CIRCULATING TUMOR CELLS TO DIAGNOSTICS OF MALIGNANT TUMOR DISEASES

Introduction. The study of the possibility of using the circulating tumor cells (CTC) definition in the patients` blood with different localization of malignant tumors as a diagnostic criterion and the criterion of the effectiveness of specific treatment tactics is one of the topical issues in modern oncology.

The purpose of the paper is to analyze the results of using the developed information technology for identification of circulating tumor cells for the study of blood samples of patients in order to confirm or reject the initial diagnosis of cancer of different localization.

Results. Our information technology is based on the use of an advanced method of isolation of intact circulating cells, the difference of which is to supplement the structure of the basic ISET method with new modes: 100% sealing chamber with hemolysate and providing it with the necessary and constant pressure during the filtration process by introducing a negative pressure gauge, as well as the mode of three-level filtering of the CTC on consecutive polycarbonate membranes with micropore diameters of 8 μm, 5 μm and 3 μm.

To assess the malignancy of selected cells, the information technology used the method of determining the CTC according to the set of criteria, formed databases with created template CTC masks and control templates in the automated mode. Blood samples from patients were tested using IT. Taking into account each step of the technique (using different filters), analysis of the results showed that of the total proportion of samples, which additionally detected the CTC using not only an 8 μm filter, but also filters 5 μm and 3 μm, was 20.66 %.

Conclusions. The use of information technology to identify circulating tumor cells improves the efficiency of detecting these cells by reducing the testing time and expanding the range of research due to the ability to detect cells of small size. Improvement of IT by supplementing the knowledge base (complex of template mask masks and relevant expert findings) makes it possible to apply it in screening of patients' blood, including at the preclinical stage of the examination.

Keywords: *information technology, circulating tumor cells, method of isolation of circulating tumor cells, automated system, screening of patients' blood.*

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ПРИМЕНЕНИЕ ИНФОРМАЦИОННОЙ ТЕХНОЛОГИИ ОПРЕДЕЛЕНИЯ ЦИРКУЛИРУЮЩИХ ОПУХОЛЕВЫХ КЛЕТОК ДЛЯ ДИАГНОСТИКИ ЗЛОКАЧЕСТВЕННЫХ ОПУХОЛЕВЫХ ЗАБОЛЕВАНИЙ

Рассмотрены результаты использования разработанной информационной технологии определения циркулирующих опухолевых клеток (ЦОК) для исследования образцов крови пациентов с целью подтверждения или отклонения первичного диагноза онкологического заболевания различной локализации.

Для оценки злокачественности выделенных клеток в информационной технологии использованы: усовершенствованный метод выделения неповрежденных ЦОК, сформированный комплекс критериев, базы данных созданных шаблон масок ЦОК и контрольных шаблонов доброкачественных клеток в автоматизированном режиме. Проведено исследование образцов крови пациентов с использованием разработанной ИТ. Анализ результатов исследования с учетом каждого шага метода (с использованием различных фильтров) показал, что суммарная доля образцов, в которых дополнительно обнаружено ЦОК с применением не только фильтра 8 мкм, но и фильтров 5 мкм и 3 мкм, составила 20,66 %.

Ключевые слова: *информационная технология, циркулирующие опухолевые клетки, метод изоляции циркулирующих опухолевых клеток, автоматизированная система, скрининговое исследование крови пациентов.*

ДО УВАГИ АВТОРІВ!

У журналі надано результати досліджень в галузі теорії і практики інтелектуального керування, інформатики та інформаційних технологій, а також біологічної і медичної кібернетики.

Цільова аудиторія- науковці, інженери, аспіранти і студенти вищих навчальних закладів відповідного фаху.

Вимоги до рукописів статей

1. Рукопис надають на папері у двох примірниках (мова – англійська, українська, російська, 17-22 с.) та електронна версія. До рукопису додають:

• анотації – українською та англійською мовами (прізвище, ініціали автора/ів, місце роботи, місто, країна, назва статті, текст 250 -300 слів, з виділенням рубрик: вступ, мета, результати, висновки, ключові слова), російською мовою (УДК, прізвище, ініціали автора/ів, назва статті, 7-9 рядків тексту, ключові слова (5-8 слів);

• список літератури на мові оригіналу - в порядку згадування в тексті, за стандартом ДСТУ 8302:2015;

• список літератури - переклад джерел англійською мовою, прізвища та ініціали авторів - транслітерація:

• ліцензійний договір;

• відомості про автора/ів українською, англійською та російською мовами повинні містити: ПІБ, вчений ступінь, наукове звання, посада, відділ, місце роботи, поштова адреса організації, телефон (для зв’язку редактора), E-mail, авторські ідентифікатори ORCID або ResearcherID.

2. Текст статті подається з обов'язковими рубриками: вступ, постановка завдання/проблеми, мета, результати, чітко сформульовані висновки.

Вимоги до текстового файлу

Формат файлу * .doc, * .rtf. Файл повинен бути підготовлений за допомоги текстового редактора Microsoft Word.

Використовувані стилі: шрифт Times New Roman, 12 пт, міжрядковий інтервал – 1,5. Формат паперу А4, всі береги - 2 см.

Формули набирають у редакторі формул Microsoft Equation Editor 3.0. Опції редактора формул - (10,5; 8,5; 7,5; 14; 10). **Ширина формул -до 12 см**.

Рисунки повинні бути якісними, створені вбудованим редактором рисунків Word Picture або іншими Windows-додатками (рисунки надають окремими файлами відповідних форматів). **Ширина рисунків - до 12 см**.

Таблиці виконують стандартним вбудованим у Word інструментарієм «Таблиця». **Ширина таблиці - до 12 см**.

Передплату на журнал (друкована версія) в Україні здійснюють:

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