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SOFTWARE FOR AUTOMATED COMPUTER-BASED DIAGNOSTIC SYSTEM

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Abstract: *The report presents new software for automated computer-based diagnostics system, designed to analyze heart rate variability (HRV) based on digital electrocardiographic and photoplethysmographic signals. Interest in HRV analysis is increasing worldwide, due to the possibility of early diagnosis of working-age cardiovascular diseases. In the past 2-3 years, in connection with increasing the computing power of modern smartphones and different personal mobile devices, the software for personal diagnosis and prognosis of heart disease has also been developed. Leading companies develop and produce personalized heart rate analyzers that are worn on a wrist, hand, or attached to the body. The analysis of HRV in this article is presented by applying time-domain, frequency domain and non-linear (Poncaré plot) methods. The advantage of the used mathematical methods is their ability to detect minor cardiovascular deviations. The analyzed deviations by applied methods are an effective way in assessing the overall functional capabilities of the body. The detection of early disease abnormalities through the developed software system can lead to the introduction of measures to prevent serious cardiovascular disease. The created software system is a contribution to the theory and practice of applying state-of-the-art scientific engineering methods for medical research and is supposed to be applied in modern clinical practice by offering an effective approach to long-term research and monitoring in the patients' health.*

Key words: *Electrocardiographic signal, Phothoplethysmographic signal, Heart Rate Variability, Time-domain analysis, Frequency-domain analysis, Poincaré analysis.*

1. INTRODUCTION

According to the World Health Organization, the main cause of mortality in the population is cardiovascular disease. Cardiovascular diseases take the lives of 17.7 million people each year, accounting for 31% of all deaths worldwide [15]. Heart rate is an indicator of emerging variations in the autonomic nervous system [5]. The change in heart rate is the earliest prognostic sign of many diseases such as cardiovascular, internal, nervous, mental, and other [8]. The HRV is a method measuring the time intervals between two adjacent heartbeats [5, 9, 10]. Heart rate changes continuously, even in a state of rest.

In 1996 HRV standardization was performed by a working group of the European Cardiological and North American Electrophysiological Society, which makes recommendations for its use in clinical practice [9]. As a result of the introduced new standard, HRV has become a rapidly evolving strand in cardiology, where the possibilities of using mathematical methods of analysis in the diagnosis of a number of diseases are fully realized. However, HRV methods are not designed to diagnose clinical pathologies, where traditional visual and measurement analysis tools work well. The advantage of this new direction is the ability to detect the most subtle variations in cardiac activity, so its methods are particularly useful for assessing the body's overall functional abilities in normal and early abnormalities that, in the absence of the necessary preventative procedures, can gradually to develop into a more serious illness.

It is known that the heart reacts to the smallest changes in human organs and systems, which is why the HRV can be used to diagnose and predict future illnesses.

Mathematical methods for analyzing HRV are two main classes: linear and non-linear [5]. The quantitative dimensions of the investigated parameters using linear mathematical methods of analysis have significant clinical use because the norm-pathology limits are known to be in line with the standard introduced in 1996 [9]. The analysis of HRV using non-linear mathematical methods can provide not only detailed information about the physiological state of the patient but also provide an opportunity to predict future illnesses. Modern principles of cardiovascular prophylaxis are based not only on combating the causes, but also on the development of effective methods and devices for the diagnosis, treatment and prophylaxis of these diseases. Traditionally, signals that are subject to HRV evaluation are captured by electrocardiographic devices. As result of the today's technology development, the signals for heart activity can be reliably detected and recorded using

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photoplethysmographic sensors, smartphones, and other mobile devices [2, 3, 6].

The objectives of the report are:

1. Presentation of a new software system for automated computer-based diagnostics of digital signals registered by portable photoplethysmographic sensor and devices, as well as by electrocardiographic or holter devices.
2. Mathematical analysis of (photoplethysmographic) PPG signals in 2 groups of subjects: healthy subjects and patients with arrhythmia.

2. SOFTWARE FOR AUTOMATED COMPUTER-BASED DIAGNOSTICS OF PPG SIGNALS

The traditional way to get heart rate information is through ECG-based devices. This way of monitoring and diagnosing of cardiovascular disease does not provide the necessary flexibility, portability and comfort for users. The use of PPG-based measuring devices is capable of solving these problems. PPG-based devices are easy to use, can be placed in different places on the human body and allow for the measurement of various parameters that take into account the health of the body such as: pulse, blood pressure, oxygen saturation, etc. [2]. Diagnosis of cardiac activity in medicine based on ECG signals was created earlier. Therefore, ECG devices are more widespread. They are stationary and mobile. The stationary ones are used in medical centers and they mostly register events that have already occurred - heart attacks, pre-infarction states. After creation of the mobile holter devices, it is possible to monitor and diagnose cardiac activity during the daily life of the patients over a longer period of time - 24, 48 hour periods.

The article describes a new software system for automatic computer diagnostics. There are similar software products that can process and analyze ECG data taken from electrocardiographic and holter devices [12, 13]. The novelty in the presented software is the ability to process and analyze in addition to ECG data obtained from electrocardiographic and holter devices and data taken from photoplethysmographic devices.

The signals in this article that are subject to processing and analysis are recorded using a portable photoplethysmographic device, which is the next stage in the technological development of cardiac monitoring and diagnostics. Normally such devices are connected to the computer via a USB cable or wireless connection. After recording the PPG signals, the preprocessor processing takes place, which involves the removal of artefacts, the determination of the P peaks and the PP intervals between the individual pulse waves. These intervals correspond to the RR intervals determined by an electrocardiogram signal. The specified RF intervals are automatically entered into the HRV software analysis program. The following data is displayed at the top of the title page (Fig. 1): the patient data file name, the number of pulse waves (QRS complexes in case the data is captured by ECG or holter devices), the duration of the test signal in format: e: hh: mm: sec. After this data, part of the RR (RR) intervals of the investigated patient are visualized, with the (←, →) buttons displaying the complete recordings. After selection of the analytical method (time-domain, frequency-domain, nonlinear analysis) at the bottom of the screen menu, the results of the selected type of analysis are displayed in the table and graphically, with the initial display of the patient data file (by default) the results of the time domain analysis. After the analysis, a test report is created, which is printed and archived for further patient tracking. When recording a deviation in the patient's results, short messages (SMS) can be sent to the attending physician, the patient and his or her relatives, a GP, or an emergency center as appropriate. The software was implemented using the C ++ and Matlab programming languages.

The article shows the results of the time-domain, frequency-domain analysis and non-linear (Poincaré plot) analysis of HRV in 2 patient groups: healthy subjects and patients with arrhythmia.

3. TIME-DOMAIN ANALYSIS OF PPG SIGNALS

Time domain analysis measures the changes in heart rate depending on the time parameter or measures the intervals between successive normal heart cycles. The analysis gives a quantitative estimation of the HRV in the time interval surveyed. The calculated time domain parameters are as follows:

- average PP (RR) intervals;
- SDNN - standard deviation of normal PP (RR) intervals;
- SDANN - calculate the mean values of normal RR (RR) intervals every 5 minutes of the study and calculate their standard deviation;
- RMSSD - the difference between each two adjacent normal NN intervals is squared and summed as the sum is divided by the number of intervals and the index is a square root of that number;
- pNN50 - the ratio of the number of adjacent NN intervals differing by more than 50ms (NN50) from the total number of NN intervals and multiplied by 100.

Fig. 2 shows the PP interval of a healthy subject and a patient with arrhythmia. The variability of the PP interval in the healthy subject is within the range of 1.1-1.7 seconds, whereas the patient with an arrhythmia is between 0.95-1.05 seconds, therefore the HRV of the healthy subject is higher than the patient with arrhythmia. In medical practice, the high HRV is considered an indicator of good health. Fig. 3 and Fig. 4 show the histograms of a healthy subject and of a patient with arrhythmia. It is clear from the graphs that there is a difference in the shape of the histograms in the patient with cardiovascular disease and the healthy subject. For robust controls, a central positioning of the poles in the PP ranges with the highest poles localization in the range of 0.6 - 0.8 seconds is typical. In the case of arrhythmias, a histogram shift of the PP interval is observed on the left. Similar is the behavior of histograms of HRV in various cardiovascular diseases, with displacement to the right, left, narrowing of the base and asymmetry [5].

Fig. 1. Software for analysis of PPG signal

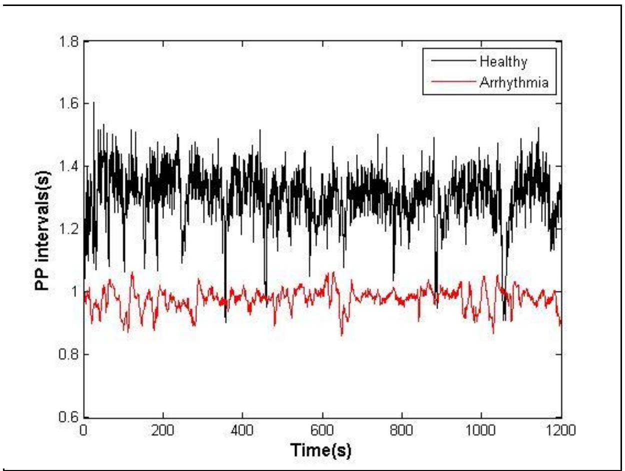

Fig. 2. PP interval series of a healthy subject and a patient with arrhythmia

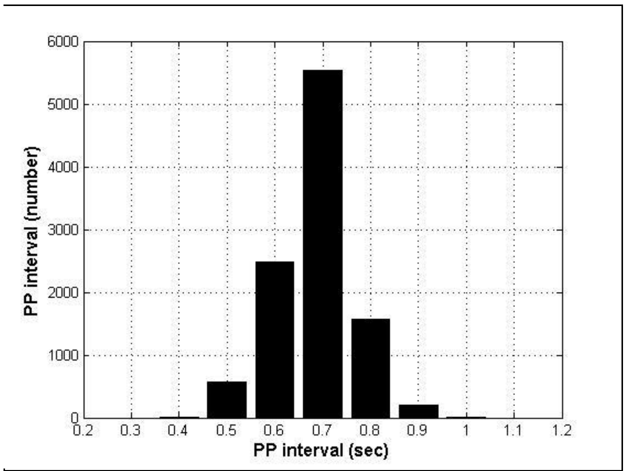

Fig. 3. Histogram of a healthy subject

The results of the time domain analysis of the study groups of patients: Group 1 - healthy controls, Group 2 - patients with arrhythmia are shown in Table 1. The results are presented as mean ± standard deviation (mean ±sd). The differences between the values of the parameters of the test groups were tested by the ANOVA test and were considered reliable at a level of significance p<0.05. From the parameters studied, the SDNN, SDANN, RMSSD and pNN50 parameters have statistical significance (p <0.05).

Table 1

Time-domain analysis of healthy subjects (Group 1) and patients with arrhythmia (Group 2)

Parametrs	**Group1** (n=15)	**Group2** (n=15)	**p-value**
	mean±std	mean±std	
Mean PP(ms)	870.2±66.2	829.1±73.0	0.12
SDNN	143.2±7.3	75.1±8.0	0.0001
SDANN(ms)	129.1±28.9	148.1±19.9	0.05
RMSSD	29.1±11.2	40.8±10.7	0.007
pNN50(%)	13.4±10.9	22.2±10.7	0.03

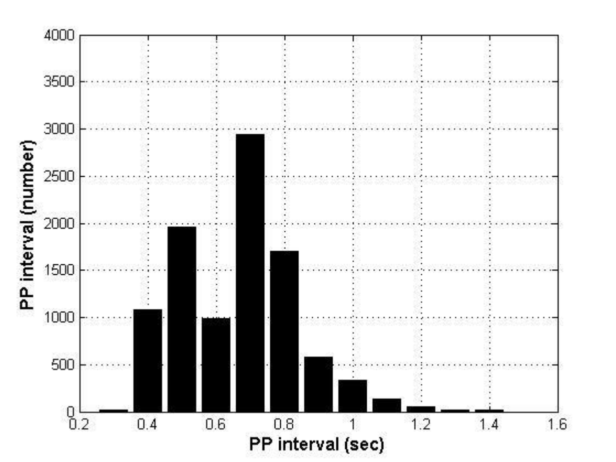

Fig. 4. Histogram of a patient with arrhythmia

4. FREQUENCY-DOMAIN ANALYSIS OF PPG SIGNALS

Frequency domain parameters are based on a spectral analysis that gives the distribution of each of the multiple frequencies present in the PP (RR) intervals. Studies have shown that there are three discrete components (VLF, LF, HF) in the frequency domain, each related to certain physiological causes [9]. Many researchers connect measurements in the frequency domain with various diseases [5, 7]. Low frequency fluctuations in heart rate (less than 1 Hz) are associated with the sympathetic and parasympathetic nervous system in general, whereas high frequency fluctuations result only from the parasympathetic system [1, 4]. The absence of these frequencies can give an assessment of the level of vagal efferent activity. Spectral analysis provides information on the energy distribution of the signal in function of the frequency. PSD-Power Spectral Density methods are combined into two classes: nonparametric and parametric.

4.1. Fast Fourier Transform

A typical representative of nonparametric methods is Fast Fourier Transform (FFT). In this method, the spectrum is calculated using the Welch periodogram. PP (RR) data is divided into overlapping segments, the overlap being fixed at 50%. Analyzing non-periodic signals, such as PP intervals, is a "spectrum blur" error. The blurring is expressed in misleading information regarding the spectral amplitudes and frequencies in frequency data analysis. To reduce the effect of blur, window functions are applied. In this case Henning's window function is used. The FFT spectrum is calculated for each window segment, and the segment is finally averaged.

The advantages of the FFT method are as follows:

- Simplicity of the algorithm used;
- High processing speed of the signal.

4. 2. AutoRegressive method

The AutoRegressive Method (AR-AutoRegressive) is a representative of parametric methods. The AR method is based on the assumption that each value of the test signal depends on the weighted sum of the previous signal values plus the noise. The AR model of row p is defined by the following equation [14]:

$$X_t = \sum_{i=1}^{p} a_i X_{t-i} + \varepsilon_t \qquad (1)$$

where:

- ε - noise;
- a - AR parameters.

When analyze digital ECG data and PPG signal data, the value of the parameter p is in the range (16-20) [14].

The advantages of the parametric AR method are:

- Smooth spectral components that can be distinguished from pre-selected frequency bands;
- Easy processing of the spectrum by automatic calculation of the signal components at low and high frequencies;
- Easy identification the base frequency of each component.

Spectral components of PPG (ECG) signals are calculated differently for short and long records. The short entries are 2 to 5 minutes long. The main spectral components that are recorded are three: Very Low Frequency (VLF), Low Frequency (LF) and High Frequency (HF).

These components are usually taken into absolute signal energy values (ms^2) but can also be measured in normalized values (n.u.) that represent the relative value of each energy component to the total sum minus the VLF component value. Long tapes are usually 24-hour records. These include the above three components and Ultra Low Frequency (ULF). The VLF components of the HRV correspond to sympathetic and parasympathetic nervous systems, whereas HF components only correspond to parasympathetic activity. Therefore, with the LF/HF ratio of the HRV signal, the level of sympathetic activity of the heart can be estimated, i. e. with the increase of this ratio increasing the sympathetic activity and, conversely, by reducing the ratio decreases the sympathetic activity [1, 5].

This article analyzes 20-minute PPG records, following the recommendations of the standard [9].

4. 3. Frequency analysis results

Table 2 shows the results of the spectral analysis of 2 groups studied: healthy controls and patients with arrhythmia. Signal energy at very low frequencies (VLF), low (LF) and high (HF) frequencies measured in ms^2 is within normal range and is often greater than patients with arrhythmia. According to recommendations [9], the LF/HF ratio should be within the range (1.5 - 2) in healthy subjects. As a result of the spectral analysis, this relationship is outside the acceptable range in patients with arrhythmia and is within normal range in healthy subjects.

5. NONLINEAR ANALYSIS OF PPG SIGNALS

The reason for the development and application of the nonlinear analysis of PPG signals is due to the need to study the dynamics of the complex interactions of a number of factors of the human health, such as: cardiovascular health, psychological stress, fatigue, sleeps quality and rest, as well as central and autonomic nervous system. HRV analysis based on non-linear mathematical methods can provide important information

Table 2

Spectral analysis of healthy subjects (Group 1) and patients with arrhythmia (Group 2)

Frequency band	**Power(ms^2) mean±std**			**Power(n.u.) mean±std**			**LF/HF ratio mean±std**		
FFT spectrum	**Group1 (n=15)**	**Group2 (n=15)**	**p-value**	**Group1 (n=15)**	**Group2 (n=15)**	**p-value**	**Group1 (n=15)**	**Group2 (n=15)**	**p-value**
VLF	1527±321	702±123	0.0001	-	-	-			
LF	1195±191	101±36	0.0001	66.1±8	1.52±1.0	0.0001	1.99±0.1	0.191±0.2	0.0001
HF	598±179	531±145	0.008	35.4±7	2.41±1.5	0.0001			
Total	3319±781	1360±201	0.0001	-	-	-			
AR spectrum	**Group1 (n=15)**	**Group2 (n=15)**	**p-value**	**Group1 (n=15)**	**Group2 (n=15)**	**p-value**	**Group1 (n=15)**	**Group2 (n=15)**	**p-value**
VLF	693.3±531	189±121	0.001	-	-	-			
LF	400.1±120	30.5±16.7	0.0003	69.2±12	0.201±0.19	0.0001	2.05±0.1	0.33±0.1	0.0001
HF	198.9±109	92.7±19.3	0.0001	34.4±8	0.799±0.23	0.0001			
Total	1471.3±1100	323.3±102	0.0004	-	-	-			

about the physiological status of patients as well as the risk of sudden death. [1, 9] The results of the non-linear analysis of PPG signals are presented by using the Poincare plot analytical method.

5.1. Poincaré plot

This mathematical method is a relatively new technique for analyzing non-linear dynamics of HRV. It is a geometrical model in which each of the RR (RR) intervals is represented as a function of the previous interval and is applied to the coordinate system [5, 7, 11]. Each pair of PP (RR) intervals (past and subsequent) has coordinates (x, y), where x is the value of the PPn (RRn) interval and y is the value of PP_{n+1} (RR_{n+1}). When the chart is formed, a "cloud" is created from points whose center is located on the line of identity. The line of identity is the graph of the function x = y ($PP_n = PP_{n+1}$). If the point is above the identity line, it means that x <y ($PP_n < PP_{n+1}$). Accordingly, if the dot is located below the line of identity, this indicates that the interval PP_{n+1} is shorter than the PP_n interval. Therefore, the form of the "cloud" of points (PP_n; PP_{n+1}) on the Poincaré graph reflects the change in the duration of the PP intervals, i.e. the dispersion. If an ellipse with a longitudinal and transverse axis is placed on the graph constructed using the Poincaré method, the following indicators can be derived:

- Ellipse length (SD2 [ms] parameter) - this indicator corresponds to the long-term variability of PP intervals and reflects the total CMS;
- Ellipse width (SD1 [ms] Parameter) - This metric represents the scattering of the points along the straight line of the line of identity and is associated with rapid variations between individual heart attacks;
- SD1 / SD2 ratio - this parameter reflects the relationship between short-term and long-term HRV;
- Area of the ellipse - the area of the ellipse is defined by the formula: S = (SD1 * SD2 * pi) / 4.

The feature used for HRV visual analysis using the Poincaré method is the shape of the main "cloud" of points. The form of the "cloud" is categorized for the different functional statuses of a person [5, 7]:

- The chart of the healthy subject has one main "cloud" of points to which even more points can be evenly scattered. The main "cloud" has the shape of a comet with a narrow lower part and gradually expanding towards the top.
- The subject's chart is in the form of a torpedo, fan or complex form (consisting of several "cloud") depending on the type of disease.

5.2. Results from the nonlinear analysis by Poincaré plot

Based on the values of the investigated PP intervals of the 20-minute PPGs records, Fig. 5 and Fig. 6 shows the graphs constructed by the Poincaré method for a healthy subject and a patient with arrhythmia. The healthy subject's graphic has the shape of a comet with a sharpened lower part and gradually expanding to the top. The graph of the patient with arrhythmia has the shape of a fan. The quantitative characteristics of the Poincaré method are significantly altered in patients with cardiovascular disease compared to healthy subjects.

Table 3 shows the values of parameters SD1 and SD2, the relationship between them and the areas of the ellipses of the groups surveyed. The value of SD1 decreases in patients with arrhythmia compared to healthy controls. This decrease was statistically significant ($p < 0.05$). The SD2 value is almost double in patients compared to healthy controls, and this decrease is also statistically significant ($p < 0.0001$). The lower values of SD1 and SD2 parameters in patients have reduced HRV. The ratio of SD2 / SD1 is at least in healthy subjects and also has statistical significance ($p < 0.005$). The reduction of the SD1 and SD2 parameters leads to a reduction in the ellipse faces of the patients.

The Poincaré method is a special tool that allows physicians to view the entire study at a glance (in this case 20 minutes, but it could be 24 hours). This method allows rapid detection of cardiovascular disorders that cannot be detected using traditional linear methods of HRV analysis.

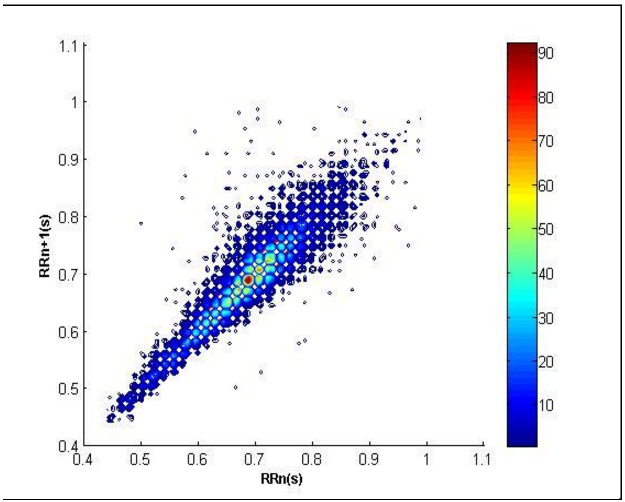

Fig. 6. Poincaré plot for healthy subject

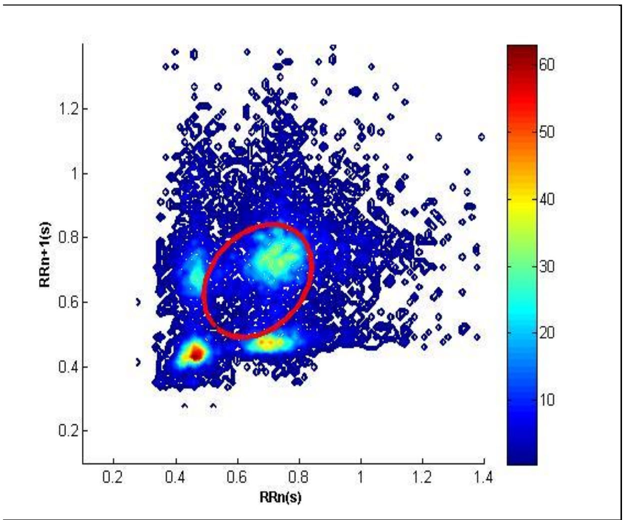

Fig. 7. Poincaré plot for patient with arrhythmia

Table 3

Nonlinear analysis of healthy subjects (Group 1) and patients with arrhythmia (Group 2)

Parametrs	**Group1** (n=15)	**Group2** (n=15)	**p-value**
	mean±std	mean±std	
SD1(ms)	45.14±15.5	62.2±11.2	0.002
SD2(ms)	115.2±21.6	265.1±27.8	0.0001
SD1/SD2	0.40±0.29	0.25±0.08	0.06
S(ms^2)	3 600±45	13 062±52	0.0001

6. CONCLUSIONS

The subject of this article is the presentation of the essence and principles of a software system for automated computer-based diagnostics of registered cardiac signals. What's new in the software system is that it can process and analyze signals taken away, apart from electrocardiographic and holter devices as well as photoplethysmographic devices. The analysis of signals is done by applying conventional (linear) and nonlinear mathematical methods. The article shows the results of the analyzed 20-minute PPG records, following the recommendations of the standard [9]. The quantitative dimensions of the investigated parameters in linear analysis have significant clinical use because the norm-pathology limits are known. The non-linear Poincaré method enables physicians to see the entire record of the patient under study and to quickly detect cardiovascular disorders, if any. This is due to the fact that the shape of the "cloud" of points is categorized for different functional states of a person. The importance of the established software system for automatic computer-based diagnostics consists in the formation of a parametric and graphical assessment of the patients' health status.

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