Portable E-nose for Diagnostic of Inflammation and Diverse Variation in Health Status of Humans and Animals

Anastasiia Shuba
Physical and Analytical Chemistry Department
Voronezh State University of Engineering Technologies
Voronezh, Russia
e-mail: shuba1nastya@gmail.com

Ruslan Umarkhanov
Physical and Analytical Chemistry Department
Voronezh State University of Engineering Technologies
Voronezh, Russia
e-mail: rus_270487@mail.ru

Tatiana Kuchmenko
Physical and Analytical Chemistry Department
Voronezh State University of Engineering Technologies
Voronezh, Russia
e-mail: tak1907@mail.ru

Anton Chernitskiy
Research Center for Clinical Pharmacology and Therapy,
Quality and Safety of Raw Materials and Products
All-Russian Scientific Research Veterinary Institute of
Pathology, Pharmacology and Therapy
Voronezh, Russia
e-mail: cherae@mail.ru

***Abstract*—This paper discusses an application of a portable electronic nose based on an array consisting of 8 piezoelectric sensors with nanostructured solid-state coatings to detect volatile biomolecules secreted by nasal mucus and skin. A fundamentally new approach is proposed for a quick assessment of the status of the human body as a whole (normal, stress, inflammation) and the work of individual systems (reproductive, endocrine, digestive), based on the results of the assessment of the qualitative and quantitative composition of the gas mixture of biomolecules secreted by the skin in the Zakharyin-Ged zone. An algorithm is proposed for reading and visualizing signals from an array of sensors understandable to any user. Also, a portable electronic nose was applied in the veterinary field for assessment of the health status of calves' respiratory system. Unlike the traditional approach in diagnostics using sensor array, one sample of nasal mucus was monitored for 5-9 hours with an interval of 2-3 hours. The integral analytical signal of sensors, in that case, was connected to the microbiological contamination of the sample or its absence. The speed and simplicity of measurement using an electronic nose with nanostructured piezoelectric sensors allow painlessly scanning the body for metabolic disturbances and estimating the presence of certain pathologies as well as the effectiveness of treatment.**

Keywords- sensor; electronic nose; method; volatile compounds; skin; metabolism; respiratory disease; calf; non-invasive diagnostic; screening.

I. INTRODUCTION

Biosamples are complex objects to analyze. The problem of their study consists not only in the absence of a constant composition, but also in its almost instantaneous change when substances are excreted from the sample. Despite the emergence in recent years of new methods for the analysis and study of biostructures at the level of individual cells, the scheme still remains traditional: selection of biomaterial, sample preparation and detection of target components. The use of highly selective and effective methods of analysis (gas chromatography-mass spectrometry, high-pressure liquid chromatography, etc.) suggests a special sample preparation, which can change the natural profile of the biosamples. The method of sample preparation is determined by the purpose of the analysis, but the integrity of the biological object is lost. Also, the results obtained by advanced analysis methods do not reflect the complex structure and behavior of a biological object. Therefore, recently, in the analysis of complex living objects (food, environmental objects, human and animal biosamples), complex methods with a multivariate analytical signal have been used more often. Such methods, by their methodology, include systems of artificial tongues, noses, eyes [1]. The undoubted advantage of highly sensitive sensor systems with the rapid response is the ability to monitor the state of small volumes and masses of biological samples in a fairly short time (from 2 to 9 hours). Given the lack of their contact with the environment (in vitro), primarily with oxygen, small volumes of biosamples, which means fast processes of changing their properties, open up a unique opportunity to obtain information about the status of the studied object, even if the specific methods for determining individual substances or laboratory indicators (primarily microbiological) are unavailable.

A possible approach for assessing the status of the body in the absence of biomaterial selection is to analyze the chemical composition of the gas, sweat of the skin in the zones of Zakharyin-Ged. Earlier, the presence of redness, peeling, rash, temperature changes in these areas was widely used as an additional parameter to confirm the malfunction of organs corresponding to these zones. The detection limits of modern methods of analysis, the complexity of the instrumentation of the most sensitive methods do not allow non-invasive scanning and determining the chemical composition of the gas phase of secretions from the skin. Therefore, the creation of an integrated system for scanning a volatile metabolome [10] using a device with a sensitive detection from biomolecules of normal and disordered metabolism, inflammation, to microbial metabolites is actual for now.

There are some state-of-the-art approaches, including portable devices, for assessing the state of the body using electronic noses and various data processing methods: for exhaled breath air [2][4], for the analysis of biomaterials (blood, urine, secrets of the endocrine glands, etc.) [5][7]. Different approaches for assessment of health status by skin based on using electrochemical or optical methods are proposed in [8][9]. The authors did not find in the literature similar hardware solutions about the development of an electronic nose for diagnosing human health by volatile metabolites secreted by the skin.

The purpose of this paper is the development and application of a new mobile device based on piezoelectric sensors (portable electronic nose) for assessing the health status of organs and systems of humans and animals by analyzing the volatile metabolome.

We will demonstrate our approach in two ways: 1) analysis of nasal mucus samples of calves for the diagnosis of respiratory diseases and 2) characterizing of the health status of humans by skin odor in the Zakharyin-Ged zones.

In Section 2, the features of the experiment, description of biosamples and methods of analysis are presented. Section 3 contains technical characteristics of the proposed device, characteristics of the used sensors and their coatings, and a description of the procedure for obtaining and recording of output data of the sensor array. In Section 4, we show the results of the application of the proposed portable electronic nose (e-nose) for solving diagnostic problems according to the purpose of the work. Section 5 is devoted to conclusions and perspective of development.

II. Materials and Methods

A. Diagnosis of Respiratory Diseases in Calves

17 samples of nasal mucus from calves (10-20 days of life) both with signs of respiratory system damage and conditionally healthy were analyzed. A sampling of nasal mucus was carried out with sterile cotton swabs in individual sterile containers. The time from sampling to analyzing on e-nose was taken into account.

All calves were clinically studied in detail using a point system (WI score) developed at the University of Wisconsin-Madison (USA) [11] with mandatory laboratory control at the All-Russian Scientific Research Veterinary Institute of Pathology, Pharmacology and Therapy: bacteriological and molecular genetic (PCR) studies of nasal swabs for infectious rhinotracheitis, parainfluenza-3, viral diarrhea-disease cattle mucous membranes, rotavirus, adenovirus, chlamydia, pathogenic mycoplasmas (*M. bovis, M. bovirhinis*), hematological indicators of inflammation in the blood (leukogram, haptoglobin concentration) were determined.

For the isolation of cultures and typing of microorganisms, meat and peptone broth and agar, milk salt, enterococcal agar, Endo medium, blood agar, glucose-serum broth and agar produced by NICF (St. Petersburg, Russia) were used. The isolated Escherichia coli were typed in an agglutination reaction using O-serums.

B. Characterizing the Some Deviation from Normal Status by Human Skin Odor

The area of the forearm of human skin was chosen to analyze the volatile metabolome by a portable electronic nose. Over 100 conditionally healthy volunteers took part in the investigation duration for 2 years. The volunteers periodically were clinically (visits to physicians) and laboratory (general analysis of blood, urine, biochemical analysis of blood (glucose, cholesterol, some hormones)) tested to control health status. For conditionally healthy volunteers, the results of laboratory tests corresponded to the norm, and the symptoms did not match with clinically significant for illness. Clinically not diagnosed conditions, so-called descriptive states (tiredness, excitement, agitation, stress, lack of sleep, spasm, pain), were recorded from the words of the volunteers.

III. Description of Portable E-nose and Measurement Technique

A. Making of Piezoelectric Sensors

We used piezoelectric quartz resonators (PQR) with a natural frequency of 14 MHz with an established linear response with a film mass on its electrodes up to 20 μg/cm^2. The array contained 8 piezoelectric sensors with electrodes covered by films of carbon nanomaterial, biohydroxyapatite, zirconium salts of different mass (1-5 μg) (NANO-BIO array).

1) Characteristics of the Used Sorbents

Hydroxyapatite $Ca_5(PO_4)_3OH$ was obtained by the sol-gel method developed at Nizhny Novgorod State University named after N.I. Lobachevsky and optimized by us to obtain nanostructured coatings with good sorption properties.

The reaction was carried out according to the following equation:

$$5Ca(NO_3)_2 \cdot 4H_2O + 3H_3PO_4 + 10NaOH \rightarrow Ca_5(PO_4)_3OH + 10NaNO_3 + 29H_2O$$

To a solution of calcium nitrate (2 mol/dm^3) prepared from $Ca(NO_3)_2 \cdot 4H_2O$ in bidistilled water has added a solution of H_3PO_4 in the amount necessary to maintain the ratio Ca/P = 5/3. The resulting solution was thermostated for one hour at 37 °C, then its pH was adjusted to 7-8 using a NaOH solution with a concentration of 2 mol/dm^3. At pH = 4, a $Ca_5(PO_4)_3OH$ sol began to form. The reaction mixture was kept at this temperature for 1 hour. Then, the resulting gel was centrifuged and dried in air. The obtained sorbent can be stored for at least 0.5 years in airtight conditions. Multi-walled carbon nanotubes were obtained by gas-phase chemical deposition during ethanol pyrolysis. Nickel was used as a catalyst; the temperature of deposition was 450-500 °C. Then nanotubes were washed with HNO_3 concentrated (Institute for Extra Pure Materials of the Russian Academy of Sciences, Chernogolovka). The solvent for the suspension of hydroxyapatite and carbon nanotubes was chloroform. Zirconium nitrate ($ZrO(NO_3)_2 \cdot 2H_2O$), (chemically pure) was obtained from aqueous solutions containing zirconium and nitrate ions (Reachem, Russia). The solvent for the suspension of zirconium nitrate was acetone. These sorbents are selective and sensitive to volatile metabolites of bacteria and inflammation according to the results of a preliminary experiment [12].

2) The Method of Forming Films on the Surface of the Piezoelectric Quartz Resonator

To change and control the sensitivity and selectivity of micro-weighing of vapors of organic substances, thin films were uniformly deposited to the electrodes of piezoelectric quartz resonators, fat-free with acetone or chloroform, by immersion in solutions of sorbents suspended by ultrasound.

The hydroxyapatite, as well as carbon nanotubes and zirconium nitrate, formed the sensors using the following procedure:

Step 1 – the measurement of the initial oscillation frequency of the piezoelectric resonator (10 or 14 MHz) *F*0, Hz with an accurate record, for example, 9999280 Hz;

Step 2 – suspension was prepared in the beaker as dissolution of sorbent (0.5 g) in 10 ml of solvent;

Step 3 – processing in an ultrasonic bath for 15 minutes at a power of 90 W;

Step 4 – exposure of the quartz piezoelectric resonator in suspension for 15 s;

Step 5 – drying the coating in an oven (40 minutes at a temperature from 50 ° C) in the holder vertically;

Step 6 – the measurement of the oscillation frequency of the sensor, calculation of the coating mass (Δm) according to the Sauerbrey equation [13]:

$$\Delta m = \frac{\Delta F \cdot 0.2}{2.27 \cdot 10^{-6} \cdot F_0^2} \tag{1}$$

where ΔF is the change in the oscillation frequency of the quartz plate of the resonator after film deposition and removal of an unbound solvent, MHz;

$2.27 \cdot 10^{-6}$ – calibration constant of piezoelectric quartz resonator at normal condition, cm^2/g;

F_0 — base oscillation frequency of the PQR, MHz;

0.2 – the area of electrodes of PQR, cm^2.

B. *Characteristic of Portable E-nose*

The portable device for diagnosing the status of humans and animals is a miniature case, consisting of two functional parts (Figure 1): head 1 and the protective part of the body 6, a microprocessor 2 with terminals for sensor mount sockets, a block for fixing and transmitting information 3 to the recording device of any type (laptop, tablet, PC); the sockets are located in the cover 4, into which removable sensors 5 are mounted on the outside, separated from the environment by the protective part of the body 6, which is tightly attached to the head 1. Optionally e-nose is supplemented by an internal gas-permeable gasket 7, which separates the sensor region and the free air region of the body 6.

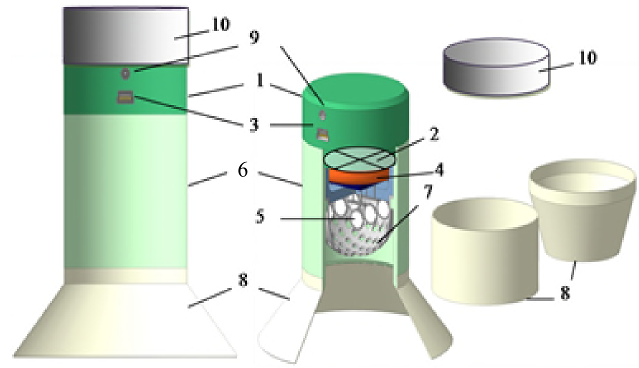

Figure 1. General view of the 3D model of the portable e-nose for diagnostics: 1 – head; 2 – microprocessor with terminals for sensor mount sockets; 3 – block recording and transmitting information to a recording device of any type; 4 – cover; 5 – removable sensors; 6 – protective part of the body; 7 – internal gas-permeable gasket; 8 – nozzles; 9 – power supply from the electricity; 10 – removable battery.

To reduce interfering factors (external fluctuation in airflow, temperature, air composition in the near-sensor space), protective nozzles of various types 8 from inert materials (fluoroplastic) are used in accordance with the nature of the analyzed sample. The e-nose is powered by either an electronic device, with which is combined via a USB cable, either from electricity 9 or a removable battery 10.

The developed portable device is an electronically counting frequency meter with 8 channels for measuring the oscillation frequency of BAW-type piezoelectric quartz resonators with a base oscillation frequency of 5 to 20 MHz with a resolution of 1 Hz and a time interval (step) of 1 second. The electronic counting frequency meter is switched on in the network (220 V); it warms up for 10-15 minutes. In this case, to reduce measurement errors, the sensors should be in the device. But their subsequent inclusion is also possible. It takes about 5-10 minutes to stabilize the baseline of the oscillation frequency of the quartz plate.

To simultaneously record (read) the oscillation frequency of each sensor independently of each other every second for a certain time interval (from 1 s to a maximum of 6000 s), the device is connected to a computer via USB cable, and other connection options are possible (via Wi-Fi, Bluetooth).

Operating conditions and technical specifications of E-nose:

- Ambient temperature from +15 to +35 ° C.
- Increased humidity up to 98% at temperatures up to 308 K (+35 °C).
- The device is powered by an alternating current with a voltage of 220 ± 22 V and a frequency of 50 ± 0.5 Hz.
- Frequency range 4 MHz – 20 MHz.
- Reference frequency oscillator is 4 MHz.
- Overall dimensions – 38x120x170 mm.
- Weight with a cover – 0.40 kg.

C. *Specification of Software*

The responses are recorded in the instrument software, which not only saves the current measurement but also converts it into analytical information a change in the oscillation frequency of each resonator individually without load or with load at each measurement moment relative to the starting point of measurement (-Δ*F*, Hz). The full output curve is displayed in the form of a set of chronograms for all resonators installed in the e-nose (Figure 2). During the interaction of vapors with the surface of the piezoelectric sensors, sorption occurs on the films or electrodes, as a result of which the frequency changes. Individual colors reflect a change in time of the base oscillation frequency of each of the 8 piezoelectric sensors (Figure 2). In the developed software based on chronograms, the "visual print" is constructed using different algorithms depending on the purpose of analysis. The quantitative characteristic of "visual prints", therefore, the total amount of volatile substances excreted by samples and sorbed by piezoelectric sensors, is the area of "visual print" (*S*v.p., Hz´s). The area of "visual print" is calculated in software as a sum of definite integrals of time dependence the signals of sensors during measurement (chronograms).

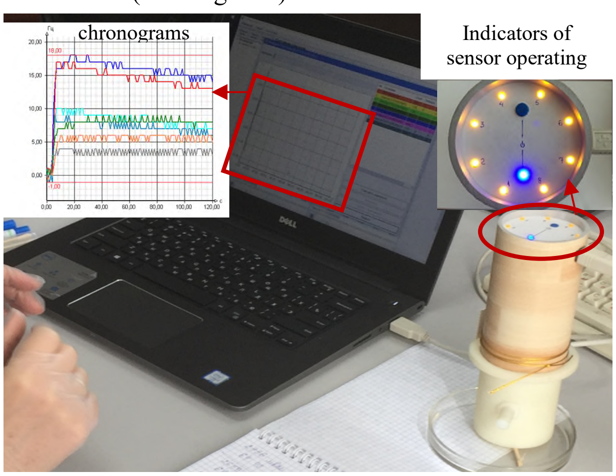

Figure 2. E-nose connected with the laptop when measuring the sample of nasal mucus.

Additionally, in software, the parameters of sorption (A(i/j)) are calculated, which can be used for the identification of volatile substances in the gas phase over samples [14] or to describe additional analytical information about sample characteristics.

D. *Technique of Measurement*

The gas phases over nasal mucus samples were studied with the front input method into the detection cell. For analyzing the volatile substances excreted by the skin on the forearm area (20 cm^2) the open detection cell of device contacted with this area. The registration time of the sorption of volatile substances excreted by the skin and nasal mucus was 80 s, the registration of desorption was 120 s. Thus, the full time of one measurement was 200 s.

IV. Results and Discussion

A. *Diagnosis of Respiratory Diseases in Calves*

Based on the results of clinical studies, the determination of hematological and biochemical markers of inflammation (leukocytosis, an increase in the concentration of haptoglobin in the blood serum), pathogens of viral and bacterial infections accompanied by damage to the respiratory system of calves, we selected three groups: "healthy respiratory system" (n=4), "with the subclinical course of respiratory diseases" (n=8), "early signs of respiratory disease" (n=5).

A natural change in the composition of the mucus taken at a weekly interval can reflect only significant changes in the condition - for example, a vivid manifestation of the inflammatory process. Unlike state-of-the-art approaches to the diagnosis of respiratory diseases by one measurement of biosamples [5-7], for the first time, it has been proposed monitoring one sample for 5-9 hours with an interval of 2-3 hours. It allows recording changes in the state at the micro-level associated with microbiological contamination of the sample or its absence. The areas of "visual prints" were calculated for all samples of nasal mucus. Early it was shown that the values of the area of "visual prints" correlate with biochemical indicators of inflammation characterizing the disease of respiratory organs in calves [15].

All results of one-day monitoring of nasal mucus biosamples can be divided into three groups (Figure 3).

1) Positive (increasing) dynamics of changes in the value of the integral analytical signal of the sensor array (area of "visual print") - indicates the destruction of nasal mucus and production of a large number of volatile compounds including microorganisms metabolites.

2) The negative (decreasing) dynamics of the change in the value of the analytical signal of the sensor array indicates the decreasing of volatile substances excreted from nasal mucus due to increasing of its viscosity by the high level of proteins, mucin, which is observed in the acute phase of respiratory disease [16].

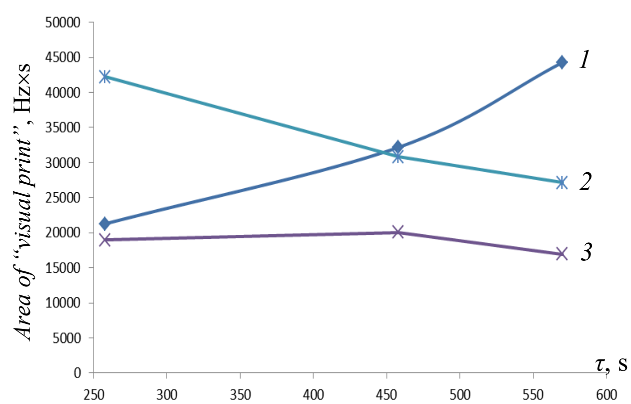

Figure 3. Total "visual prints" area of signals of the sensor array in vapors of nasal mucus of calves with different diagnoses: 1 –healthy respiratory system, 2- early signs of respiratory disease, 3 - with the subclinical course of respiratory disease.

3) The almost constant value of the integral signal from the array of sensors, which is observed at the first sign of respiratory disease (subclinical course), indicates that the excretion of substances at the destruction of nasal mucus and the production of metabolites by microorganisms are not so active. If one takes another sample of nasal mucus from an animal with the subclinical course of the respiratory disease within 5 minutes after the first selection, then the time dependence of area of "visual print" for this sample will be like for conditionally healthy (curve 1, Figure 3). It is in good agreement with the data on the formation of local protection of the respiratory tract of calves [16]. Thus, several measurements of one biosample during the day allow easy clarifying the diagnosis without multivariate analysis of sensor signals unlike modern approaches [3][5].

B. Characterizing the Some Deviation from Normal Health Status by Human Skin Odor

A forearm zone of skin was chosen for scanning the health status of the whole organism according to information about the diagnostic significance of the Zakharyin-Ged zone.

The primary database contained the responses of 8 sensors in 200 seconds of measurement (1590-1600 signals). Based on the analysis of the skin odor of 100 volunteers in various states according to their words and the results of laboratory tests, a primary algorithm of "visual print" construction has been developed for linking the features of the forms of "visual prints" with the human condition and possible causes of deviation (Table 1, Figure 4). The proposed algorithm is different from the traditional approach to visualize the sensor signals, used in the state-of-the-art methods [3]. Moreover, such visualization is simpler and clearer for the user.

TABLE I. ALGORITHM FOR CONSTRUCTING "VISUAL PRINTS" OF SIGNALS FROM AN ARRAY OF 8 SENSORS FOR ASSESSING THE HEALTH STATUS OF PEOPLE

Name of an algorithm of "visual print" construction (characteristic)	**Time of recording the sensor responses, s / number of sensors used to build a "visual print"**
"General state" (the most complete information about reproductive, digestive systems)	30, 45, 60, 80, 100, 120, 180 / 8
"Energy" (reflects the strength and intensity of the metabolome part, which shows the ability of the body to act)	110, 120, 130, 140, 150 / 3
"Endocrine system" (reflects malfunctions of the endocrine glands, primarily the pancreas)	10 20 30 60 / 4 Additionally, the parameter is calculated: $\gamma = \Delta F_4(60\ s)/\Delta F_4(20\ s)$. At $\gamma \leq 2$ pathology occurs
"Negative" (the severity of destructive processes in the body)	20, 30, 170, 180 / 8 Additionally, parameters are calculated: $\beta_1 = \Delta F_4(20\ s)/\Delta F_4(170\ s)$. $= \Delta F_4(30\ s)/\Delta F_4(180\ s)$. At β_1, $\beta_2 \leq 2.5$ pathology occurs

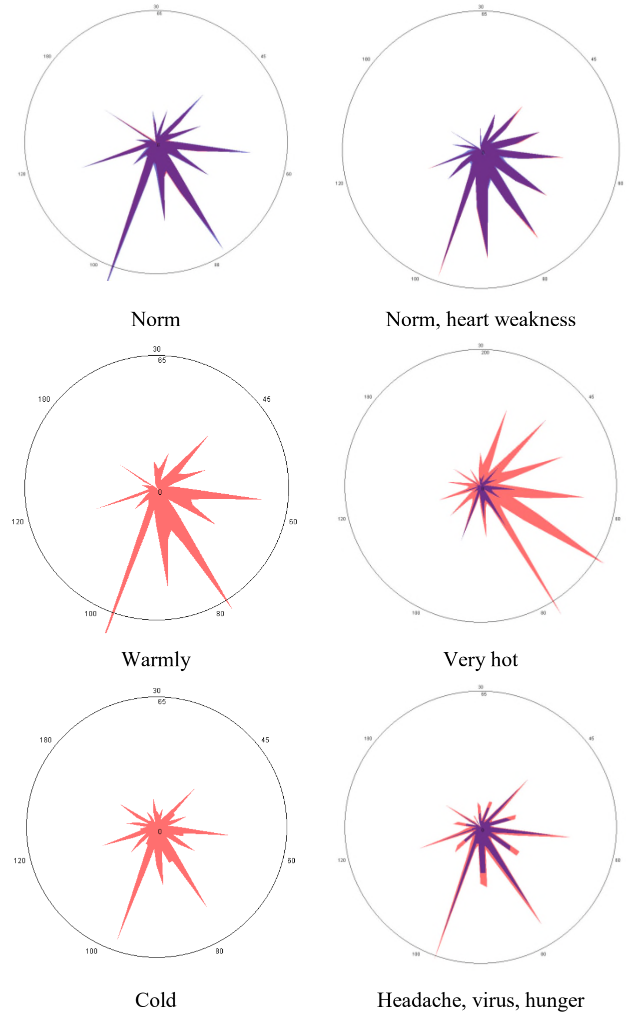

Figure 4. Statistically significant typical changes in the shape of the integral signals of the sensor array of the portable e-nose for different conditions of one person (for left forearm – the blue color and for right – red color).

Figure 4 shows the comparison of "visual prints" forms for left and right hands, which used for visual assessment of descriptive states. As a result, statistically reliable responses and smell trace forms were determined, what correspond to the physically normal functioning of the body (norm), stress, tiredness, inflammation, headache, and weakness, in total no less than 17 states (some of them are shown in Figure 4). This is more than in other research [4][5]. Besides, reference limits for the degree of its severity have been established for each state, for example, the low level of tiredness, the middle level of tiredness, the high level of tiredness and the critical level of tiredness. It is established that the geometric shape of the "visual print" is strictly individual for each person and the calculated parameters (A(i/j)) – for health status (Figure 4, Table 2). The shape of "visual print" is influenced to a greater extent by the health of the body, by the psycho-emotional state during measurement, by gender, and to a lesser extent by age. If we normalize for one person the average quantitative parameter of the smell trace (area of

 ISBN: 978-1-61208-766-5

"visual print") according to the results of not less than 500 measurements in different periods for 2 years, then the general nature of the displacement of this indicator will obey the laws presented in Table 3.

TABLE II. THE VALUE OF SOME PARAMETERS OF SORPTION A(I/J) IN VARIOUS STATES

Parameter A(i/j)	The numerical range of parameter values			
	Norm	*Description of the deviation state*		
Sector color	green	yellow	red	burgundy
A(1/5)	< 0.75	0.75-0.94 Stress, body weakness	> 0.90 Hormone imbalance	> 0.81 Stress, weakness, severe inflammation
A(1/7)	≤ 1.90	> 1.9	> 2.3 Adrenaline, severe stress	-
A(1/2)	> 1.15	0.90 – 1.14 Inflammation, very hot	< 0.9 Alcohol, Ketones	-
A(2/4)	≤ 0.1	-	0.25-0.30 Ketones, sugar is above normal, hormones are very unbalanced	0.16-0.24 Weakness, exhaustion

TABLE III. THE MOST TYPICAL EXAMPLES OF CHANGES IN THE AREA OF THE "VISUAL PRINTS" WITH SOME CHANGES IN HEALTH STATUS

Person's state	The trend of changing and the relative difference in the parameter $S_{v.p.}$,%
Norm	Differences between the left and right hands - 5-10%, for the left more than for the right
Norm, after eat	11-30% more for the right hand than for the left one
Norm, easy hunger	For the right hand less than for the left one by 11-25%
Norm, severe hunger	If the gallbladder is malfunctioning, a response increase of 15-20% for the right hand is observed due to the excreted of propandial
Cold, temperature for a long time 15-20°C	20% (before meals) – 10% (after meals), the shape of "visual prints" changes
Headache, toothache, other pain, spasm	10-35%, the shape of "visual prints" changes
Increase the air temperature up to 26-30°C	10-30%, at perspiration till 500%
Virus, malaise without fever	Decrease on the right hand to 38-40%
Menstruation	An increase in the side of the working ovary by 15-25%.
Fatigue, heart failure	The left side is smaller than the right in normal to 12-20%, the shape of "visual prints" changes
Bronchitis, inflammation	The difference between left and right Zakharyin-Ged zone of bronchi for acute bronchitis - 40 %, recovery – up to 15 %, healthy lung and bronchi – up to 5 %

The electronic nose was trained by 45 individual substances of normal and pathogenic metabolism: C1-C5 alcohols, ketones, C5-C7 cyclic ketones, aldehydes, N-, S-containing aldehydes, C1-C5 carboxylic acids; primary, tertiary, cyclic amines, O-containing amines. Therefore, it is possible to evaluate the appearance of these substances in the descriptive states (Table 2). Thereby, using portable e-nose for scanning volatilome secreted by the skin allows determining the diverse variation in health status, including the descriptive states, the presence of 45 individual volatile substances at ppm-ppb level [14] in comparison with state-of-the-art methods [4][5][8][9].

For the convenience of deciding the health status of the organism, the state sphere is constructed using parameters A(i/j) (Figure 5), while the color of the sector corresponding to a certain parameter, which is determined by its numerical value in Table 2.

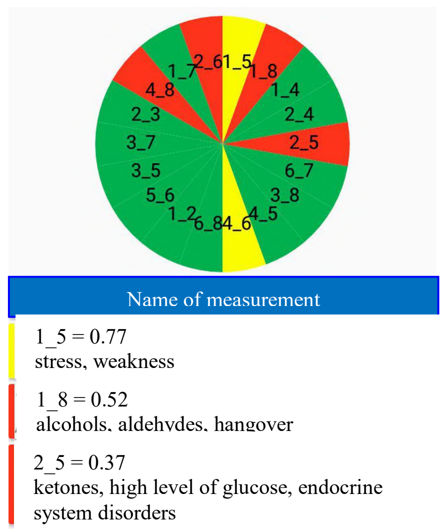

Figure 5. Example of the sphere for human health status on parameter A(i/j) in the dialogue window of the software.

The greener the sectors in the health status sphere, the closer it is to normal. For instance, in Figure 5 the value of parameter A(2/6) is in the red zone accordingly to the results of clinical and laboratory tests which are confirmed as an inflammatory process in the digestive and respiratory tracts. Thus, according to the parameters of sensor signals, one can easily and quickly obtain extended information about the work of both individual organs and the deviation of the health status from the average norm.

V. CONCLUSION AND FUTURE WORK

According to the responses of the electronic nose, when monitoring biosamples of nasal mucus from 17 calves during 5-9 hours, with an interval of 2-3 hours, it is possible to assess changes in the qualitative composition of biosamples gas phase in an atraumatic way, in place.

For the first time, a fundamentally new approach is proposed for a quick assessment of the health status of the human body as a whole (normal, stress, inflammation) and the work of individual systems (reproductive, endocrine, digestive), based on the results of an integrated assessment of the qualitative and quantitative composition of the gas mixture of biomolecules secreted by the skin in the Zakharyin-Ged zone.

The correct interpretation and prediction of the status of biosamples and a person's state have been proved by traditional diagnostic and analysis methods (leukogram, biochemical, microbiological, molecular genetic analysis). An algorithm is proposed for reading and visualizing signals from an array of sensors understandable to any user. More information about data processing for e-nose implementation will be in this paper [17].

The time of one analysis of volatile substances excreted by the biosamples or skin using portable e-nose, including visualization and processing, is up to 5 min, which is faster than that described in works [2][5] and without any sample preparation unlike other modern research works [2][7][8].

We believe that the approach proposed in this work for the analysis by sensor array is appropriate for other biosamples, such as blood, cervical mucus, exhaled breath condensate, and urine.

ACKNOWLEDGMENT

This work was financially supported by Russian Scientific Found (grant number 18-76-10015).

REFERENCES

[1] A. D. Wilson and M. Baietto, "Advances in Electronic-Nose Technologies Developed for Biomedical Applications", Sensors, vol. 11, pp. 1105-1176, Jan. 2011, doi: 10.3390/s110101105.

[2] A. T. Güntner, S. Abegg, K. Königstein, P. A. Gerber, A. Schmidt-Trucksäss and S. E. Pratsinis, "Breath Sensors for Health Monitoring", ACS Sens., pp. 268-280, Jan. 2019, doi: 10.1021/acssensors.8b00937.

[3] M. Yakob, D. Mustika, R. I. Nila and R. A. Putra, "Design of E-nose as an Instrument Identification of Diseases Through the Respiratory Tract", Journal of Physics: Conference Series (The 4th International Conf. on Applied Physics and Materials Application), IOP Publ., Feb. 2020, vol. 1428, 012062, doi:10.1088/1742-6596/1428/1/012062.

[4] E. Kabir, N. Raza, V. Kumar, J. Singh, Y. F. Tsang, D. K. Lim, J. E. Szulejko and Ki-H. Kim, "Recent Advances in Nanomaterial-Based Human Breath Analytical Technology for Clinical Diagnosis and the Way Forward", Chem, vol. 12, pp. 3020-3057, Dec. 2019, doi:10.1016/j.chempr.2019.08.004

[5] Y. Y. Broza, Xi Zhou, M. Yuan, D. Qu, Y. Zheng, R. Vishinkin, M. Khatib, W. Wu and H. Haick, "Disease Detection with Molecular Biomarkers: From Chemistry of Body Fluids to Nature-Inspired Chemical Sensors", Chem. Rev., vol. 119, pp. 11761-11817, Nov. 2019, doi:10.1021/acs.chemrev.9b00437.

[6] T. A. Kuchmenko, A. A. Shuba, V. V. Bityukova and N. A. Matveeva, "Application of a Chemical Sensor Array to Assessing the Presence of Neoplasms by Blood Smell", Journal of Analytical Chemistry, vol. 73, pp. 91-101, Jan. 2018, doi: 10.1134/S1061934817110053.

[7] Q. Gao and W.-Y. Lee, "Urinary Metabolites for Urological Cancer Detection: a Review on the Application of Volatile Organic Compounds for Cancers", Am J Clin Exp Urol, vol. 7, pp. 232–248, Aug. 2019; ISSN:2330-1910/AJCEU0101247.

[8] G. E. Bergdahl, T. Andersson, M. Allhorn, S. Yngman, R. Timm and R. Lood, "In Vivo Detection and Absolute Quantification of a Secreted Bacterial Factor from Skin Using Molecularly Imprinted Polymers in a Surface Plasmon Resonance Biosensor for Improved Diagnostic Abilities", ACS Sens., vol. 4, pp. 717-725, Mar. 2019, doi:10.1021/acssensors.8b01642.

[9] S. Zhang, S. Li, Z. Xia and K. Cai, "A Review of Electronic Skin: Soft Electronics and Sensors for Human Health", J. Mater. Chem. B, vol. 8, pp. 852-862, Dec. 2019, doi:10.1039/C9TB02531F.

[10] A. Amann and D. Smith "Volatile Biomarkers. Non-invasive Diagnosis in Physiology and Medicine", Amsterdam: Elsevier, 2013. p. 568.

[11] S. M. McGuirk "Disease Management of Dairy Calves and Heifers", Veterinary Clinics of North America: Food Animal Practice, vol. 24, pp. 139-153, April 2008, doi: 10.1016/j.cvfa.2007.10.003.

[12] T. A. Kuchmenko and L. B. Lvova "A Perspective on Recent Advances in Piezoelectric Chemical Sensors for Environmental Monitoring and Foodstuffs Analysis", Chemosensors, vol. 7, pp. 39-45, Aug. 2019, doi: 10.3390/chemosensors7030039.

[13] G. Sayerbrey "Messung Von Plattenschwingungen Sehr Kleiner Amplitude Durch Lichtstrommodulation", Zeitschrift Fuer Physik, vol. 178, pp. 457-471, 1964.

[14] T. A. Kuchmenko and A. A. Shuba, "Informative Nature of the Electronic Nose Output Signals Based on the Piezoelectric Sensors", Analitika i kontrol' [Analytics and Control], vol. 21, pp. 72-84, June 2017, doi: 10.15826/analitika.2017.21.2.001 (in Russian).

[15] T. A. Kuchmenko, A. A. Shuba, R. U. Umarkhanov and A. E. Chernitskii "Electronic Nose Signals Correlation Evaluation for Nasal Mucus and Exhaled Breath Condensate of Calves with the Clinical and Laboratory Indicators", Analitika i kontrol' [Analytics and Control], vol. 23, pp. 557-562, Dec. 2019, doi: 10.15826/analitika.2019.23.4.014 (in Russian).

[16] Yu. Alekhin, M. Zhukov, V. Morgunova, G. Chusova and I. Klement'eva "Formation of Local Protection of the Respiratory Tract in Holstein Calves", Turk. J. Vet. Anim. Sci., pp. 656-661, Oct. 2019, doi:10.3906/vet-1903-73.

[17] T. Kuchmenko, I. Murakhovskiy, R. Umarkhanov and D. Kuchmenko, "Development of a Program for Analytical Systems of Personal Diagnostics of People and Animals on the Basis of Array of Piezosensors", Proc. of Conf. "The Twelfth International Conference on eHealth, Telemedicine, and Social Medicine", IARIA Publ., Mar. 2020, in press.