

Kislyakova L.P., Kislyakov Yu.Ya., Zaiceva A.Yu., Gulyaev V.I.

Multisensory educational system “electronic tongue” for the diagnosis of the functional state of the human body on the characteristics of exhaled breath condensate

The structure of a learning diagnostic system, produced on basis of a new concept of multi-parameter electrochemical analysis, simulating the organization and functioning of biological sensory systems, is developed. System features: 1) the use of an array of multi-selective sensors with cross-sensitivity to different chemical components in the investigated medium, 2) evaluation of the measurement results using the methods of processing large amounts of multi-dimensional information and pattern recognition. Such analysis systems are called “electronic tongue”. The purpose of this paper is to investigate the possibility of application of analytical trained multisensor system for non-invasive monitoring of individual functional state of the human body using exhaled breath condensate indicators. The diagnostic system consists of two units - the measuring and informational. They realize the basic functions of the system: learning and recognition of multi-dimensional “images” formed by the sensor module. Studies performed on the test subjects have shown that each of them has its own individual reproduced “image” of exhaled breath condensate and can be identified on this “image”. The results obtained indicate the possibility of developing on this basis a new non-invasive method of rapid diagnosis of the functional state of the person on indicators of exhaled breath condensate.

INTRODUCTION

Human activity is largely determined by the metabolic processes in the organs and tissues. Their products are distributed throughout the internal environment (cells, extracellular space, blood plasma, exhaled air, urine, etc.). They are indicators of the functional state of physiological systems and characterize the “image” of the functional state of the organism. Therefore the analysis of the chemical composition liquid and gaseous media of the body is the leading technology of diagnosis, prognosis and monitoring of the treatment process [6, 7]. This procedure requires the precise measurement of large quantities of chemical components. For example, in human exhaled air detected over 600 chemicals indicators its functional state.

A significant number of laboratory diagnostic tests, that determine the content of chemical substances (indicators of disease) in the body,

are made using electrochemical methods. These methods are used in most modern analytical devices to measure the content of organic and inorganic materials in different media of the body. Their sensors (in most cases) are sensitive not only to main test substance, but also a number of related (“interfering”) substances [1, 2, 5]. This increases the error of measurements. Meanwhile, biological sensory systems with high accuracy recognize complex “images” of the object being analyzed, precisely because their sensors have cross-sensitivity to a range of substances contained in it. These properties are determined their two features: a - their receptors are cross sensitivity, b - in the process of identification of the object involved “information system” - the brain, which carries out the processes of learning and pattern recognition. These principles of sensory analysis systems of humans and animals were

© Kislyakova L.P., Kislyakov Yu.Ya., Zaiceva A.Yu., Gulyaev V.I.

the basis of a new, intensely developed areas multiparametric electrochemical analysis of complex multicomponent biological media. Analytical systems created on this basis were called "electronic nose", "electronic tongue". They have been successfully used to control of the liquid and gaseous body media, environment and the food [3, 8, 4]. Their features are: 1) the measurement is made with the use of sensors with cross-sensitivity to different groups of important chemical components of the medium, 2) evaluation of the results of measurements carried out with the help of pattern recognition methods, processing of large arrays of multidimensional data and mathematical models of neural networks.

The purpose of this study is development multi-sensor analysis system using an array of sensors with cross-sensitivity to different groups of important chemical components of exhaled breath condensate, able to create an "image" of the functional state of the human body for later use it for diagnosis of various diseases.

DESCRIPTION OF THE DIAGNOSTIC SYSTEM

The diagnostic system consists of two units - the measuring and informational. The first unit includes of sample preparation module, sensors module, measurement module. The second unit includes modules: learning, pattern recognition and visualization of images.

Sample preparation module is designed to obtain condensate from exhaled air of test subject.

Sensor module consists of six electrochemical electrodes (sensors), each of which has a high sensitivity to the main determining ion (Na^+ , K^+ , Ca^{+2} , NO^{-3} , NH_4^+ , H^+) and the cross-sensitivity to biologically important components (other inorganic ions, proteins, fats, organic acids, products of lipid peroxidation, the white blood cells, foreign substances). Each of the sensors, placed in exhaled air condensate, generates its electrical potential. Their composition forms the "image" of the condensate of the diagnosed

person. The composition and number of sensors are selected based on their cross-sensitivity to diagnostically significant components of the object.

Measurement module (based on microprocessor) performs high-precision measurement of the electrical potentials of the electrodes (measuring range $+4.0$ V, permissible limit of error ± 0.005 mV) and the transfer of this information to the computer. This information is statistically processed and displayed graphically on the computer screen.

Learning and recognition module is presented in the form of a mathematical model. During training, the system creates a database ("images") in the form of a particular composition of electrical potentials of the electrodes that characterize the functional state of certain test subjects. In the recognition process, the composition of electrical potentials (registered by from the test subject) compared with the composition of known potential "images" in the database. Then, in accordance with a predetermined criterion (permissible deviations potentials recorded by the electrodes from their average values in the database), the decision is made about which the "image" of the database corresponds to the functional state of the test subject.

EXPERIMENTAL RESEARCH

Studies were carried out on three test subjects during five days. Following conditions are met: 1) the absence of signs of acute illness in the subjects, 2) lack of physical activity for 3 hours prior to the collection of condensate, 3) the experiment began not earlier than 3 hours after a meal, at one and the same time (12 hours). A sample of the condensate was collected for 10 minutes. The value of electrode potential in the obtained sample was measured for each of the sensors (Na^+ , K^+ , Ca^{+2} , NO^{-3} , NH_4^+ , H^+). The results of measurements were processed statistically. They are presented in Figure 1 as a visual "images" of the condensate - hexagons

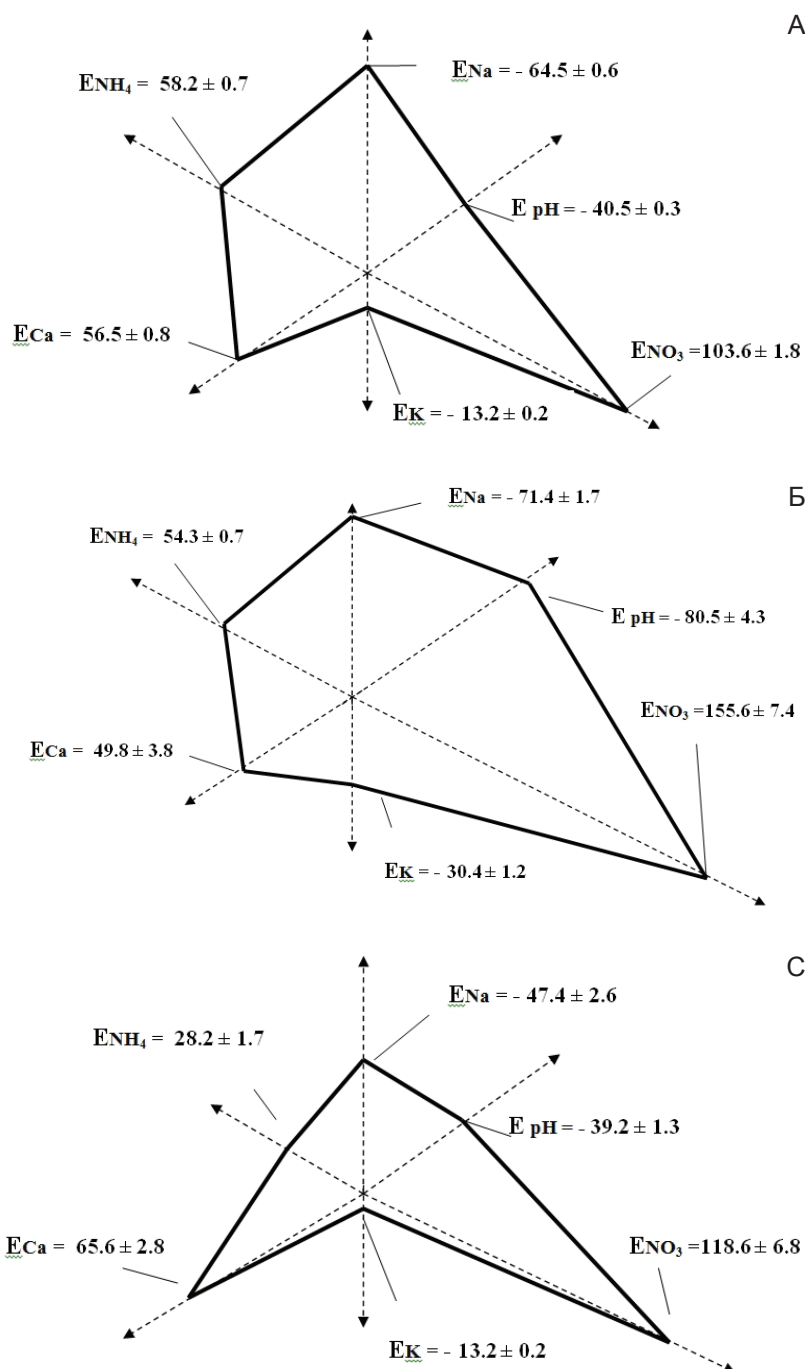


Figure 1. A visual representation of the “image” of condensate test subjects (A, B, C) in the form of diagrams - the hexagon. On the axes (dotted lines) are indicated average values ($n = 5$) electrical potentials of six electrodes. E_x - symbol represents recorded electrode potential (mV) with the basis of the ion (e.g., E_{Na} - is the total electric potential of the sodium electrode that includes potential generated ions Na, and additional potentials caused sensitivity of the electrode a number of chemical components in the sample). To the right of this symbol is shown the arithmetic mean value of the total electric potential of each electrode and the value of its mean square deviation

with rays (the coordinate axes), directed from the center to the point of intersection of the facets of the hexagon. The length of the rays at the points of intersection facets hexagon corresponds to the arithmetic mean of the measured electric potential (average of 5 samples) generated by each electrode.

The presented data shows that by using a selected set of potentiometric sensors with cross-sensitivity, may be obtain reproducible individual "images" of the condensate tested subjects (standard deviation of less than 5% of the arithmetic average of the electrode potential). These «images» in the process of «training» are stored in the computer's memory. The character of their changes, depending on the functional state of the tested subjects, will be the subject of follow-up studies.

The project was supported by grants of the Program of the Presidium Russian Academy of Sciences "Establishment and improvement of methods of chemical analysis and investigation of the structure of substances and materials."

Кислякова Л.П., Кисляков Ю.Я., Зайцева А.Ю., Гуляев В.И.

МУЛЬТИСЕНСОРНАЯ ОБУЧАЕМАЯ СИСТЕМА «ЭЛЕКТРОННЫЙ ЯЗЫК» ДЛЯ ДИАГНОСТИКИ ФУНКЦИОНАЛЬНОГО СОСТОЯНИЯ ЧЕЛОВЕКА ПО ХАРАКТЕРИСТИКАМ КОНДЕНСАТА ВЫДЫХАЕМОГО ВОЗДУХА

Разработана структура обучаемой диагностической системы, создаваемой на основе новой концепции многопараметрического электрохимического анализа, основанного на имитации способов организации и функционирования биологических сенсорных систем. Особенности системы: 1) использование массива полиселективных сенсоров с перекрестной чувствительностью к различным химическим компонентам исследуемой среды, 2) оценка результатов измерений с применением методов обработки больших объемов многомерной информации и распознавания образов. Подобные аналитические системы получили название «электронный язык». Целью настоящей работы является исследование возможности применения обучаемой мультисенсорной аналитической системы для не-

инвазивного индивидуального контроля функционального состояния организма человека по индикаторам конденсата выдыхаемого воздуха. Диагностическая система состоит из двух модулей: измерительного и информационного. Они реализуют основные функции системы: обучения и распознавания многомерных «образов», формируемых сенсорным модулем. Исследования, проведенные на испытуемых, показали, что каждый из них имеет свой индивидуальный, воспроизводимый «образ» конденсата выдыхаемого воздуха и может быть идентифицирован по этому «образу». Полученные результаты свидетельствуют о возможности разработки на их основе нового неинвазивного метода экспресс-диагностики функционального состояния человека по показателям конденсата выдыхаемого воздуха.

REFERENCES

1. Будников Г.К., Майстренко В.Н., Вяселев М.Р. Основы современного электрохимического анализа. М., Мир: Бином ЛЗ, 2003, 592 с.
2. Власов Ю.Г. Химические сенсоры: определение, классификация и история их создания. Проблемы аналитической химии. М., Наука, 2010, Т.14: Химические сенсоры. 2011, с. 9-30.
3. Власов Ю.Г., Легин А.В., Рудницкая А.М. Электронный язык – системы химических сенсоров для анализа водных сред. Российский химический журнал. 2008, т. LII, № 2, с.101-112.
4. Кисляков Ю.Я., Кислякова Л.П., Зайцева А.Ю. Обучаемая мультисенсорная электрохимическая система «Электронный язык» для контроля биологических сред. Ростов на Дону. Proceedings XVI International Conference on Neurocybernetics. p. 93-96, 2012.
5. Михельсон К.Н. Ионоселективные электроды с мембранами на основе ионофоров. Проблемы аналитической химии. М., Наука, 2010, Т.14: Химические сенсоры. 2011, с. 31-78.
6. Скрупский В.А. Эндогенные летучие соединения – биологические маркеры в физиологии и патологии человека и методы их определения. Научно-технический отчет. Институт океанологии РАН. 1994, 75 с.
7. Степанов Е.А. Методы высокочувствительного газового анализа молекул-био-маркеров в исследованиях выдыхаемого воздуха. Труды института общей физики им. А.М. Прохорова РАН. М., Наука, 1986, Т.61: Лазерный спектральный анализ молекул-биомаркеров для биомедицинской диагностики. М., Наука, 2005. с. 5-47.
8. Roberto Paolesse et.al. Development of electronic tongue system for wastewater treatment control. ISOEN 2007. International symposium on olfaction and Electronic Noses, Russia, St. Petersburg, 2007, p. 95- 96.

Institute for Analytical Instrumentation, Russian Academy of Sciences, St. Petersburg, Russia