A measuring setup with a differential generator photoionization detector for determining biomarkers in exhaled gas

Natalya I Ivanova and Konstantin V Sidorov
Tver State Technical University, 22, Afanasy Nikitin Emb., Tver, 170026, Russia

E-mail: bmisidorov@mail.ru

Abstract. The paper presents the results of the development of a differential generator photoionization detector that is capable of determining the concentration of biomarkers in the exhaled gas of a person. There is a description of the differential generator photoionization detector design, its principle of operation. The authors consider the possibility of using a differential generator photoionization detector in a measuring setup designed to determine the concentration of biomarkers during respiration to detect gastrointestinal diseases. The paper presents a setup diagram and describes its operation and elements. The possibility of using the setup for determining the ammonia concentration in the range of 10–200 ppm and measuring the hexane concentration in the range of 0.5–1 ppb to a precision of ±10% has been experimentally confirmed.

1. Introduction

Nowadays, the direction of medical diagnostics based on measuring the concentration of molecules – biomarkers in the gas flow exhaled by a person is actively developing. This area is often called respiratory diagnosis. The advantages of such diagnosis are non-invasiveness, rapidity and relative simplicity of implementation.

It is known that the exhaled gas stream contains about 600 volatile compounds with 1 ppm concentration or less [1]. The molecules of these compounds appear due to various processes in the human body that contain information about biochemical reactions, changes in body structures and the occurrence of pathological processes.

Based on the analysis of modern publications, the paper [1] provides generalized information on the relationship between a number of diseases and the presence in the exhaled gas flow of characteristic molecules – biomarkers, such as: H₂, CO, NH₃, CH₄, H₂O₂, C₂H₄, C₂H₆, CH₃OH, C₄H₁₀, as well as a number of alkanes, aromatic hydrocarbons, alcohols, etc.

Nowadays, the most significant results are in the respiratory diagnosis of a gastrointestinal tract. For this purpose, the measurement of the ammonia concentration in the exhaled gas is used.

In the general case, the problem of determining biomarkers in an exhaled gas flow is connected with the need for highly sensitive selective measurement of its molecule concentration. For this purpose, now [1] are used: gas chromatography, mass spectroscopy combined with gas chromatography, electrochemical and chemiluminescent sensors, infrared, optoacoustic, Fourier and laser spectroscopy. Apart from electrochemical and chemiluminescent sensors, the listed analytical tools are quite complex measuring devices that are difficult to use in medical institutions.
As follows from the above, an indispensable condition for solving the problem of respiratory diagnostics is the ability to measure microconcentrations of molecules – biomarkers. In this regard, it should be noted that currently the most sensitive simple and universal gas detectors are photoionization detectors.

A number of designs of these detectors is known [2, 3]. Moreover, in all the above mentioned photoionization detectors, a separate stabilized power supply connected to its electrodes is used to collect gas ions formed in the detector chamber, which complicates a detector design.

The paper [4] proposes a fundamentally new photoionization detector that collects ions appearing in its chamber under the action of a contact potential difference arising between two electrodes made of different metals. The studies of this photoionization detector, which was called the generator photoionization detector (GPID), have proved [5] that it can be used as a highly sensitive and versatile detector in packed and capillary gas chromatography.

2. Methods

2.1. A description of the experimental setup

This paper discusses the possibility of using GPID to measure the concentration of biomarkers in exhaled gas. To increase GPID stability, as well as to obtain the ability to measure the concentration of biomarkers, a differential GPID (DGPID) was created [6]. This detector and a method known in analytical technology as a method for transforming an analyzed medium [7] have become the basis for creating a measuring installation for determining biomarkers in exhaled gas, its diagram is shown in figure 1.

![Figure 1. A setup diagram: 1 – UV lamp power supply; 2 – UV lamp; 3 and 9 – ring aluminum electrodes; 4 and 8 – fluoroplastic gaskets; 5 and 7 – ring nickel electrodes; 6 – a quartz disk-window; 10 – an electrometric amplifier; 11 – recorder; 12 – mouthpiece; 13 – a connecting pipe; 14 – a collector for collecting saliva and condensate; 15 – a filter – gas stream dryer; 16 and 17 – AC-chokes; 18 – a filter – an absorber of the analyzed flow determined component; 19 – 22 – a fittings group; 23 – a flow booster; 24 – a fluoroplastic insulator cup; 25 – a glass; 26 – fluoroplastic discs.]

The setup contains: DGPID – I; measuring and recording means for signals DGPID – II and auxiliary devices – III that provide the supply of the analyzed gas and its preparation for analysis.

DGPID consists of two photoionization generator cells identical in parameters and containing nickel and aluminum ring electrodes that are separated from each other by ring fluoroplastic insulators. These cells are separated from each other by a quartz disk-window, and are illuminated by a single radiation flux created by an ultraviolet glow-discharge lamp (UV lamp). The upper cell (in
figure 1), which is a measuring one, is directly illuminated by ultraviolet radiation, and the lower one (comparative) is illuminated through a quartz disk-window.

2.2. A description of the working experimental setup
The setup works as follows. The exhaled gas flows through the mouthpiece and connecting pipe to the saliva collector and condenser. A flow booster creates a small vacuum at the outlet chokes of DGPID cells. Therefore, gas flows through cell chambers; namely, a small part of the exhaled gas from the collector enters the stream dryer (a plastic tube 0.5 m long and 8 mm in inner diameter filled with CaCl₂) and then through AC-chokes used to set the values of gas flow rates into DGPID cells. Additionally, the stream enters the measuring cell directly, and into the comparative one – through an the determined component absorbing filter.

The following process takes place in each DGPID cell. The molecules of the gas mixture flowing through the measuring and reference cells are ionized by the ultraviolet radiation generated by the UV lamp. Due to different work functions of electrons from electrodes made of nickel and aluminum, a contact potential difference arises [8]; it affects the collection of ions in the measuring and reference cells, and ion current flows between their electrodes while determining the signals of these cells. Electrically, DGPID cells are back-to-back, therefore, the resulting signal, which is equal to the difference between the named cells signals, is measured by an electrometric amplifier and recorded by an automatic potentiometer or a computer with an analog-to-digital converter.

Auxiliary devices provide the transmission of a part of the exhaled gas through the mouthpiece, a collector for collecting saliva and condensate into a filter for drying the gas stream and then to AC-chokes. Moreover, before entering the comparative cell, the gas stream passes through the filter-absorber of the determined component, where this component is excluded from the gas stream. To transport gas streams through DGPID cells, we use a flow booster (membrane microcompressor).

3. Results
3.1. Mathematical description of the differential photoionization generator detector (DPGD) signal
According to the DPGD signal model [9], the signals of the DGPID measuring and comparative cells can be described by the following expressions:

\[ U_1 = k_1 \cdot \sigma_{cm1}, \]
\[ U_2 = k_2 \cdot \sigma_{cm2}, \]

where \( U_1 \) and \( U_2 \) are signals of the DGPID measuring and comparison cells; \( k_1 \) and \( k_2 \) are conversion coefficients of the DGPID measuring and comparative cells by physicochemical property; \( \sigma_{cm1} \) and \( \sigma_{cm2} \) are effective cross-sections for gas mixture photoionization flowing through the DGPID measuring and comparative cells.

It is known that the sum of the volume concentrations of the determined and undetectable components is described as follows:

\[ 1 = \alpha_0 + \alpha_n, \]

where \( \alpha_0 \) and \( \alpha_n \) are volume fractions of the determined and undetectable components in the analyzed gas.

Taking into account the expression (3), effective photoionization cross-sections \( \sigma_{cm1} \) and \( \sigma_{cm2} \) can be represented as follows:

\[ \sigma_{cm1} = \sigma_0 \cdot \alpha_0 + \sigma_n \cdot (1 - \alpha_0), \]
\[ \sigma_{cm2} = \sigma_0 \cdot \alpha_0 + \sigma_n \cdot (1 - \alpha_0). \]
If the conversion coefficients for the physicochemical property of the DGPIID measuring and comparative cells are the same \(k_1=k_2=k\), then the DGPIID signal is described as follows:

\[
U_1 - U_2 = k \cdot (\sigma_0 - \sigma_n) \cdot \alpha_0 .
\tag{6}
\]

When the composition of the undetectable components contained in the exhaled gas changes slightly, the expression (6) can be represented as follows:

\[
U_1 - U_2 = K \cdot \alpha_0 ,
\tag{7}
\]

where \(K = k \cdot (\sigma_0 - \sigma_n)\) is the DGPIID conversion coefficient by concentration.

The above expression describes the DGPIID signal when its DPGD cells are back-to-back (see figure 1).

When the composition of undetectable components in the exhaled gas can significantly change, it is necessary to separately measure the signals of the DGPIID measuring and comparative cells. In order to calculate the concentration of the determined component, it is necessary to use the following expression:

\[
\alpha_0 = \frac{U_1 - U_2}{k \cdot (\sigma_0 - \sigma_n)} .
\tag{8}
\]

The described measuring system with DGPIID for absorbing the determined components in the gas stream entering the comparative cell involves use of indicator tubes, which are currently commercially available in a wide range.

3.2. Experimental studies

The experiments used the measuring setup to measure the ammonia concentration to diagnose Helicobacter infection and the concentration of hexane, which is used to diagnose lung cancer [1]. When measuring the ammonia concentration, RYuAZh 415522.505 plastic indicator tubes were used as an absorbing filter; when measuring the hexane concentration – there were RYuAZh 415522.505-11 tubes [10].

In the experiments on the described setup, the gas flow rates in the DGPIID measuring and comparative cells were 2 l/h. We used ring nickel and aluminum electrodes with an outer diameter of 20 mm, a hole diameter of 6 mm and a thickness of 0.2 mm, fluoroelastic gaskets with an outer diameter of 20 mm, a hole diameter of 10 mm, and a thickness of 0.5 mm in the cells. The volume of the detector cell chambers was \(\approx 40 \mu\text{L}\). DGPIID signal was measured by the IMT-05 electrometric amplifier and the KSP-4 self-balanced potentiometer.

The results of measuring ammonia and hexane microconcentrations in air are shown below (see figures 2 and 3).

Figure 2. The dependence of the detector signal on the ammonia volume concentration.
Figure 3. The dependence of the detector signal on the hexane volume concentration.

The experiments have revealed that the setup provides measurement of the ammonia concentration in the range of 10–200 ppm and the hexane concentration in the range of 0.5–1 ppb to a precision of ±10%.

4. Conclusion
The experimental studies have resulted in creating a setup for the express measurement of the biomarkers concentration in exhaled gas. The setup is highly sensitive and allows determining the parameters (1-8) of various biomarkers during respiratory diagnostics by replacing indicator tubes.

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