Design of a noninvasive diabetes detector based on acetone recognition

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Abstract. This paper presents the design project of a new type of diabetes detector system, consisting the unique gas sensor, the container, the conditioning circuit as well as the computer GUI developed by CVI. Noninvasiveness and the basis on acetone recognition are the most apparent characteristics of the system. The gas sample of the patients are collected and led to the gas container before reacting with the sensor and finally put out data on the screen at regular intervals. A controlled experiment is conducted to verify the precision of the PID sensor compared with the existing GC-MS method in the process of determining acetone concentration. The experiment shows that the system is effective and convenient in detecting low concentrated acetone exhaled by the patients, and an innovative product inspired by this may be prospective to be put into use in certain areas.

1. Introduction

The daily monitoring of diabetes mainly relies on the household blood glucose meter, and its accuracy and sensitivity are not very satisfactory. There are four main diagnostic methods for diabetes mellitus [1]: glycosylated hemoglobin diagnosis, oral glucose tolerance test (OGTT), VOC comprehensive diagnosis and gene diagnosis. At present, the existing blood glucose detection technology in the market mainly includes the professional testing equipment based on blood testing in hospital, as well as household handheld blood glucose detector. Both are invasive testing equipment which need regular needle detection, the operation is complex, and cost is high.

In recent years, the development of exhaled breath volatile organic compounds (VOC) [2] analysis technology provides the possibility of routine monitoring and early screening of diabetes. Exhaled acetone concentration is considered to be a reliable indicator of diabetes [3][4]. Many people around the world have studied the role of acetone in the diagnosis and treatment of diabetes, which is based on the fact that acetone is released from the skin, and its concentration is related to the h-hydroxy butyric acid.

A group of control experiments with cold trap and gas chromatography were carried out by Norio Yamane and his research team [5], they found that the skin acetone concentration in diabetic patients was significantly higher than that of control group (non-diabetes patients), and patients under different treatments show similar skin acetone content. The concentration of acetone in the skin is related to h-hydroxy butyric acid, blood glucose and glycosylated hemoglobin. Acetone concentration in the skin was significantly higher in patients with diabetic ketoacidosis (990ppb), but decreased to 80ppb after insulin treatment. On the conditions that the analysis of methods and tools are simplified,
measurement of acetone concentration in the skin can be used as a screening test for ketoacidosis and can be used as the index of diabetes control and diabetic ketoacidosis and other ketogenic output.

Marco Righettoni et al developed a non-invasive respiratory monitoring detector [6] which is resisted to chemical corrosion, and in ideal conditions and real conditions are able to do rapid measurement of very low concentration of acetone. It also has high signal-to-noise ratio. The detector film is made of pure silicon and silicon hybrid WO3 nanoparticles in the gas phase, and placed directly on the cross electrode. The sensing characteristics, relative humidity and interference concentration. When the humidity was 90% and temperature was 400°C, there was a significant difference in acetone respiration between healthy people and patients with diabetes. There was a gap of 40% in the detector. So it shows that this new type of instrument that detects diabetes through breath analysis can provide a portable, cost-effective system to replace the cumbersome invasive diabetes detection system.

Acetone can be used as a promising biomarker for non-invasive diagnosis and detection of diabetes [7]. Researchers used the aluminum foil bag to collect the breath acetone of 25 patients with type 2 diabetes and 44 healthy people and analyzed through gas chromatography, discovering that acetone concentration found in T2D patients were significantly higher than those of healthy people and its characteristics curve indicates that the optimal cut-off value for diagnosis is 0.891 (the area under the curve is 0.999, sensitivity 100%, specificity 97.7%) when T2D patients were compared with healthy test-takers. It was also found that the ratio of acetone to total exhaled air and net exhaled air was 1:18 and 1:17. Therefore, breathing with high acetone percentage might be a useful indicator for accurate diagnosis and monitoring of diabetes.

In summary, acetone is closely related to diabetes [8], exhaled acetone concentration can be detected by gas chromatography, and a high probability exists to distinguish between diabetes and healthy people.

Compared with the traditional invasive and regular method of detecting blood sugar with expensive and big devices, the portable and convenient feature of the acetone recognition detector provides a better way to help diagnose, monitor and evaluate the treatment for diabetes [9]. Electronic nose instrument making more precise and accurate prediction of diabetes is also in continuous development, and the utilization of it is promising [10]. In this paper, acetone is used as the main indicating gas, assisted by other VOC together for diabetes monitoring and diagnosing. The ultimate aim is to design the different components of an effective recognition system.

2. Design of the acetone detector system
The design of the new system can be divided into three general modules: gas collection, reaction signal processing and data conversion. The second step are made up of three consecutive substeps while the other have two each. The gas gathered by the container is consumed by the sensor which generates signal into the computer for software output. The Figure 1 shows the detailed procedure of the system.

![Figure 1. Flow chart of the detection system.](image-url)
2.1 Type selection and curve correction of high precision gas sensor

The high demand for precision and efficiency requires the gas sensor to be sensitive and suitable enough for the normal testing environment. There are inevitable disturbing factors in the functioning process of the sensor that may greatly influence the testing results. So in order to solve the problem of cross sensitivity of sensors to non-target gases, the sensor array is used to increase the sensitivity to acetone.

According to the range of acetone content in the breath of diabetic patients and the convenience of the instrument, the electrochemical gas sensor of Baseline company is selected.

The main technical parameters are as follows:

- Accuracy: ±1%FS;
- Response time: ≤10s;
- Recovery time: ≤5s;
- Resolution: ±1ppm; ±1%LEL;
- Measurement range: 0-1500ppm;
- Humidity: ≤95%RH;
- Working temperature: -20 to 60℃; no frost.

After testing 100 sets of standard concentration acetone samples under different environment temperature, we measured the sensor output curve of voltage-actual concentration shown in Figure 2.

![Figure 2. Characteristic curve of the gas sensor.](image)

Conclusion can be made from the operation result that when the concentration is high, the output of PID is nonlinear, but repeatable, which can be corrected in software.

Because of the nonlinear of the curve, it is necessary to do the segmentation processing in the conversion process, after the test, the curve has high identification degree to the acetone gas of different concentration, with 200-1000 concentration of ppm resolution accuracy rate reaching 97%.

2.2 Design of autonomous container

In order to hold the gas exhaled by people, an autonomous container should be figure out and the gas channel should be carefully designed. The main purpose is to elevate the precision and convenience of the detection of samples.

The sealing device for experiment is designed as a cylindrical structure. The gas to be measured is led to the device bottom, so that it can fully react with the PID sensor and reduce the loss. The whole detection process is carried out in the device, so to improve the accuracy of the detection, the device needs to be a sealing one to prevent the impact of external environment, especially the air on detection.

Considering when the transparent plastics meet organic solvent like the acetone, organic solvent and the transparent plastic surface will produce a chemical reaction to generate other opaque material adhered on the surface of the transparent plastic, affecting the detection accuracy of the device, glass materials are used. Also, changing the gas channel from a silicone tube to fluorine hose can ensure measurement precision. At the mouth of the bottle, a matching frosted mouth is used to ensure the air...
tightly of the device.

The gas to be measured is made up by acetone and the corresponding VOC. The acetone gas is injected by glass syringe and then sampled by headspace sampling, and finally imported into the reaction device by glass syringe and fluoride hose. Nitrogen is used as carrier gas to clean the reaction device and transport acetone gas, which is led by fluoride hose and vacuum pump into the reaction device.

The PID sensor is connected to a special round conditioning circuit, and then the data is imported into the computer by wire. The glass tube at the top of the bottle mouth and the exposed wire are sealed by glass glue, so as to ensure the tightness of the device, as is shown in Figure 3.

![Figure 3. Cutaway view of the reaction bottle.](image)

Two glass tubes function as the gas intake and exhaust channel of the cylinder device. The gas is mixed by nitrogen and acetone in a certain proportion. PID sensor is placed at the bottom of the glass bottle and connected with the wire, following which is the conditioning circuit.

### 2.3 Millivolt level signal conditioning circuit design

Using the gas exhaled by diabetes as collect object, the sensor transforms the gas concentration into the electrical signal. Normally the output voltage signal of PID sensor changes with the concentration of acetone. The voltage signal goes through the signal conditioning circuit and finally into the NI6009 data acquisition card. In the PC the data (the exhaled acetone by healthy people is close to the normal level between 8.9 and 30.8nmol, while acetone concentration range for T2D patients exhaled gas is 73.9 to 152.6nmol. The range for the acetone concentration of T1D patients is between 86.2 and 690nmol) was compared with setting threshold of the acetone concentration in patients with diabetes, and display the concentration of acetone in the CVI interface, so as to provide a reliable basis for whether the test-taker needs further complete blood glucose monitoring.

As the acetone concentration in the exhaled air is very small, the sensor can only output mV level voltage, special circuit is designed to make the sensor output signal more accurate and stable, as is shown in Figure 4.
Figure 4. Design of signal conditioning circuit.

The core of the conditioning circuit is AD620 three stage amplifier chip, its magnification can reach 0-10000 times. We also designed the OP07 zeroing circuit to ensure that the reference voltage is 0, so that the true magnification of the circuit is more accurate.

2.4 GUI design
The output of data and its conversion into useful statistics should be accomplished by the computer and the commensurate software. The LABWINDOWS/CVI is chosen to do human-machine interaction.

Firstly, C language is used to edit the background code of the interface, then data is collected and analyzed by LABWINDOWS/CVI and PID sensor, which combines the advantage of professional detection tools with the virtual computer program. CVI software greatly integrated development environment, an interactive programming method, function panel and rich library function together to enhance the function of language, which provides an ideal software development environment for skilled developers to establish a data acquisition system.

On the other hand, NIDAQMIX software has powerful functions, and its effective cooperation with CVI can enable the data collected by the acquisition card to be accurately input the computer, thus providing help for the later processing and detection conclusions.

At the same time, one advantage is that the data of the gas concentration detected can be displayed on the interface. If necessary, excel can be imported for data analysis, and get the diagnosis results.

The user interface is composed of different buttons, text boxes and graphs to realize the function. The basic information of the patients, the channel chosen and the sampling frequency are all portrayed as system information. The two graphs indicate the output voltage signal as well as the concentration calculated from the detection result, as is shown in Figure 5.
3. Experiment simulation

To test the reliability of the PID gas sensor for exhaled acetone testing, we invited seven diabetics and a healthy breath of people to carry out clinical trials. No. 1 volunteer in the table 1 is healthy people. No. 2-8 are type 2 and type 1 diabetic patients in hospital, OHBA of the eight volunteers are measured in the hospital. Exhaled breath samples of the eight patients were collected using a 1.0-liter Tedlar bag and each volunteer generated two bags of exhaled breaths, one of which was analyzed by gas chromatography-mass spectrometry (GC-MS) to detect acetone content breath sample [11], another gas sample used PID sensing for detection. GC-MS test results are given in Table 1.

| Number | State of illness | Age | Gender | Acetone content of Exhaled gas(GC-MS)/ppm |
|--------|------------------|-----|--------|---------------------------------------|
| 1      | healthy          | 26  | Female | 0.486                                 |
| 2      | Type 2 diabetes  | 61  | Male   | 0.254                                 |
| 3      | Type 2 diabetes  | 62  | Female | 0.490                                 |
| 4      | Type 2 diabetes  | 57  | Male   | 0.640                                 |
| 5      | Type 2 diabetes  | 45  | Male   | 1.292                                 |
| 6      | Type 2 diabetes  | 30  | Male   | 1.840                                 |
| 7      | Type 2 diabetes  | 59  | Male   | 2.940                                 |
| 8      | Type 1 diabetes  | 43  | Female | 5.000                                 |

In the preliminary gas experiments, we recognized humidity, temperature, CO₂ and other influencing factors. Figure 6 gives the relationship between the concentration of acetone and the response measured by PID gas sensor, in which the condition that 35% RH pure acetone, 80% RH pure acetone, 35% RH humidity mixed gas (40000ppm CO₂ and acetone), 80% RH humidity mixed gas are given in it.

The relationship between the acetone concentration (GC-MS test results) and the response of the PID gas sensor in eight exhaled breath samples is indicated by the red pentagram. It can be seen that the corresponding points of the eight gas samples are well matched with the gas mixtures under the humidity of 35% RH. On the contrary, the stripline can be used to determine the actual acetone content.
in a sample of exhaled breath, thus achieving the purpose of eliminating CO$_2$ and interference gas. In fact, the gas cylinder design has taken into account the interference of other gas and ambient humidity on the PID sensor response.

![Figure 6. PID sensor response for acetone concentration. It indicates the relationship between acetone concentration test results by GC-MS and gas sensor of eight exhaled breath samples in Table 1.](image)

**4. Conclusion**

This paper presents the design and experiment verification of a brand new type of diabetes detection system based on the acetone recognition. A PID sensor type is chosen, a cylinder container for mixed gas is designed and made, a conditioning circuit is established and a graphic user interface is edited by C programming and supported by CVI and NIDAQMX. The most obvious characteristic of the system is its noninvasiveness and high sensitivity. Then a controlled experiment is conducted to demonstrate that the PID sensor in the collecting device and the software work well together to generate the desired results, although precise in a finite range.

The test results indicate that the detection is merely precise under 35%RH, which means the adoption of the system should meet the relatively narrow scope compared with invasive detection. However, the advantage is obvious that the product based on the innovative system, if manufactured, can greatly reduce the infection probability and increase the chance of diagnosis of diabetes before it is too late.

More research is required both to support the feasibility of this type of system and to integrate these parts into a single entity. It is promising that the product will be useful not only in medical apparatus and instruments field, but also in daily monitoring of human health.

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