Breath Acetone Biochip Diet Support

Technology Reports

Breath Acetone Analyzer to Achieve "Biochip Mobile Terminal"

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NTT DOCOMO continues to investigate ways to achieve a "biochip mobile terminal" that will enable health management and diagnosis through biochemical analysis of biological samples that can be collected easily. In recent years, lifestyle-related illnesses have become more pronounced as social problems, and with obesity as a root cause of a number of illnesses, there has been a growing demand for technologies that enable quick and easy checking of the state of fat burning in the body. Responding to this demand, we have prototyped a portable breath acetone analyzer that enables the user to "see" the state of body fat burning simply by blowing into the smartphone-connected analyzer. This analyzer makes it possible to offer diet support programs tailored to the individual user's metabolism, exercise tolerance and so forth.

1. Introduction

Accounting for the greater part of national medical expenditure, general medical costs have been steadily increasing in recent years. About one third of these costs are due to lifestyle-related illnesses [1]. Lifestyle-related illnesses are diseases such as cancer, heart disease and cerebrovascular disease whose pathogenesis has a close relationship with an individual's lifestyle including diet, exercise, smoking and drinking and so forth. Thus, altering an individual's lifestyle can act as "preventive care*1" to prevent the onset of disease, or retard its advance.

For preventive care to be successful, simple and easy-to-use devices that enable users to check and confirm the state of their health in detail on a daily basis, and advisory services tailored to the health conditions of individuals must be provided. Therefore, since a massive 84.6% of the Japanese population use a mobile terminal like a smartphone or feature phone [2], portable measuring devices that can easily connect to these types of mobile terminals promise to be an effective tool in developing preventive care services.

For these reasons, we are continuing research into achieving a "biochip mobile terminal" that can offer preventive care services including advanced individualized health management and diagnosis. Here, biological samples*2 that users can easily collect themselves, such as saliva, sweat and breath undergo biochemical analysis using a biochip*3 connectable with mobile terminals [3].

*1 **Preventive care**: Medical actions and services that serve to prevent illnesses before they happen, or detect an illness in its early stages to prevent it from advancing.

This article describes an analyzer we have successfully prototyped to measure the concentration of acetone[*4] in the breath - a marker of fat burning. This portable analyzer can be connected to a smartphone (reference exhibited at CEATEC JAPAN 2011[*5] [4]) (**Figure 1**).

The following describes issues with breath acetone measurement, an overview of the prototyping, experimental results, examples of diet support services using breath acetone measurement, and the outlook for the future.

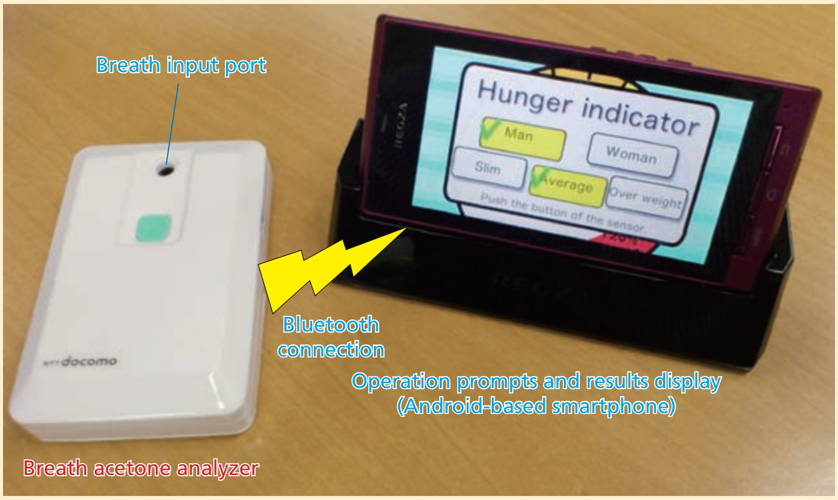

Figure 1 CEATEC JAPAN 2011 reference exhibit

2. Issues with Breath Acetone Measurement

Acetone is a gaseous metabolite produced in the blood during exercise or times of hunger when body fat is broken down, and is expelled through alveoli of the lungs when exhaling [5] [6]. Thus, there is a strong correlation between the concentration of breath acetone and the concentration of blood acetone [7], which means that it is easy to objectively measure the state of fat burning or the level of hunger by using the breath, instead of taking a blood sample. If the concentration of breath acetone is high, the concentration of blood acetone is also high, which indicates an elevated rate of fat burning in the body or low sugar levels resulting from hunger.

Since obesity increases the risk of lifestyle-related illnesses, enabling users to measure breath acetone concentration themselves and monitor the state of body fat burning could play a pivotal role in daily diet management [8]. The issue, however, is that the concentration of acetone in the breath is extremely low (typically between 0.1 and 2.0 ppm[*6]), and there are several hundred other types of gases in the breath, some of which have the potential to interfere with measurements (hereinafter referred to as "interference gases[*7]") [5] [6]. For this reason, large-size measurement apparatus such as a gas chromatography apparatus has been conventionally used to separate the gaseous constituents in the breath. However, because these devices are only available in specialized institutions such as hospitals, it has been hoped that portable devices can be developed for quick-and-easy use at home or when out and about.

To respond to this demand, we proposed a new gas detection mechanism using multiple semiconductor-based gas sensors[*8] with different sensitivity characteristics to gas constituents, and prototyped a portable device to detect the concentration of breath acetone that works without separating the various breath gases.

3. Overview of Prototyping

The main reason why conventional gas measuring apparatus is of a large size is because it is designed to separate sample gas constituents. Thus, we aimed to establish a new gas detection mechanism capable of detecting target gas constituents with a high degree of sensitivity, which does not include a gas constituent separation mechanism.

Specifically, we proposed a mechanism capable of calculating the breath acetone concentration from the signals

*2 **Biological sample**: A sample derived from a living organism for analytical purposes.
*3 **Biochip**: A chip which has a built-in mechanism to detect or analyze biological samples.
*4 **Acetone**: A highly volatile organic compound - chemical formula C_3H_6O.
*5 **CEATEC JAPAN 2011**: The largest international imaging, information and communications technology exhibition in Asia, held in October 2011 at Makuhari Messe in Chiba Prefecture, Japan.
*6 **ppm**: Unit used to indicate gas concentration. An abbreviation of "parts per million". 1 ppm = 0.0001%.
*7 **Interference gas**: Gas which has similar properties or structure to the gas targeted for detection, and thus can cause errors and adversely affect measurements.

output from multiple semiconductor-based gas sensors with different sensitivity characteristics. When compared with other gas sensing devices, semiconductor-based gas sensors are superior in that they are compact, highly sensitive, cheap, have a long service life and are maintenance free. These devices are often used in commercially available mouth odor and breath alcohol checkers. However, compared to mouth odor or alcohol sensing, the concentration of acetone is one or two orders of magnitude lower, which means the effects of interference from other types of gaseous constituents must be taken into account when detecting acetone gas in the breath. Human breath contains hydrogen, and depending on what has been eaten or drunk, it also may contain ethanol[*9]. These gases are also in comparatively large concentrations, and are the most significant causes of interference when detecting breath acetone.

In the device we have prototyped, we have included two types of semiconductor-based gas sensors to overcome the issues of interference gas constituents. For the first sensor (hereinafter referred to as "sensor 1"), we selected a sensor that uses tungsten oxide - a material that has a particularly high sensitivity to acetone, while for the second sensor (hereinafter referred to as "sensor 2"), we selected a sensor that uses tin oxide - a material which is almost equally sensitive to both acetone and ethanol. Then, we prepared mixtures of hydrogen and acetone gas, ethanol and hydrogen gas, and acetone, ethanol and hydrogen gas with known concentrations, and assessed the sensitivity characteristics of sensor 1 and sensor 2. We then used these results to find the calibration curve[*10], and recorded this in the device. Thus, when breath with unknown concentrations of acetone, ethanol or hydrogen is blown into the device, the changes in electrical resistance in sensors 1 and 2 enable the concentration of interference gas is to be estimated, which then enables the acetone concentration to be calculated more precisely by compensating for the effects of these gases.

Figure 2 shows a prototype of our proposed gas detection mechanism using multiple semiconductor-based gas sensors. Compared to conventional instruments that are designed to separate the gases for rigorous analysis, the portable device we have successfully prototyped is 1/100th of the size and 1/50th of the weight. Furthermore, this prototype can be configured to measure acetone and ethanol at the same time, the results of which can be sent to a smartphone via a wireless Bluetooth®[*11] connection. We have also prototyped an application that runs on an Android™[*12] operating system, which receives the data sent from the device and displays the current levels of fat burning and hunger visually using GUI[*13]. **Figure 3** shows example screen shots of our prototyped indicator application displaying the current levels of hunger and fat burning as a result of breath analysis.

4. Experimental Results

To verify the principle of the gas detection mechanism, we conducted feasibility tests on the prototype.

Firstly, we confirmed the sensitivity characteristics of both types of semi-

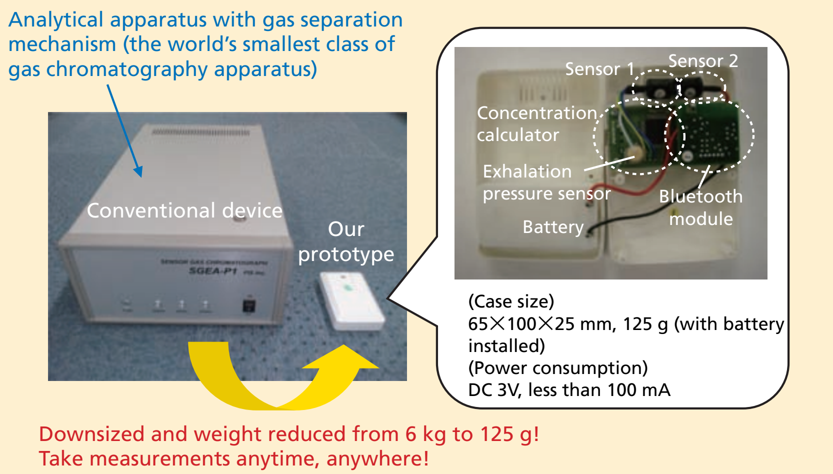

Figure 2 Example prototype of our breath acetone analyzer

*8 **Semiconductor-based gas sensor**: Using metallic oxide semiconductors as sensor elements, these sensors enable gas concentrations to be measured from the changes in electrical resistance in the sensor element that occur due to oxidation-reduction reactions with gas constituents in gaseous mixtures.

*9 **Ethanol**: A type of alcohol. The major ingredient in alcoholic beverages. Chemical formula C_2H_6O.

*10 **Calibration curve**: A curve that shows the relationship between measured data and standardized substances whose amounts and concentrations are known. In this case these are used to graph the relationship between the changes in gas sensors' electrical resistance for a gas mixture with known concentrations.

conductor-based gas sensors for various kinds of gases at concentrations of 100 ppm. **Figure 4** shows the results. Generally, that ratio of "Rair" - the resistance of the gas sensor in the air, and "R" - the resistance of the sensor in the target gas, is expressed as "R/Rair", a value that indicates sensitivity to gas. When this ratio is less than 0.8, gas detection is possible. From Figure 4, it can be seen that sensor 1 has a particularly high sensitivity to acetone, while sensor 2 has relatively broad sensitivity to other gases. Furthermore, we confirmed that sensor 2 has a relatively high sensitivity to interference gases such as hydrogen and ethanol, and that the changes in resistance in sensors 1 and 2 could be used to estimate and compensate for the effects of interference gases when calculating acetone concentration.

Next, to determine the lowest value of acetone concentration detectable with sensor 1, we assessed the sensitivity by blowing different concentrations of pure acetone into the prototype. **Figure 5** shows the detection limit. Here, we have indicated the distribution of "R/Rair" as standard deviation and its range has been denoted by error bars. From the graph, it can be seen that the gas sensitivity distribution of this sensor is extremely low, and the good reproducibility exhibited means the sensor can be used for repeated gas detection. Also, as mentioned, because gas detection is possible when the sensitivity is below 0.8, it can be seen that highly sensitive acetone measurement is possible down to approximately 0.2 ppm and since typical acetone concentration in breath ranges from 0.1 to 2.0 ppm, this is a level which is measurable by this

Hunger indicator | Fat burning indicator

Figure 3 Example of breath acetone measurement results displayed on smartphone

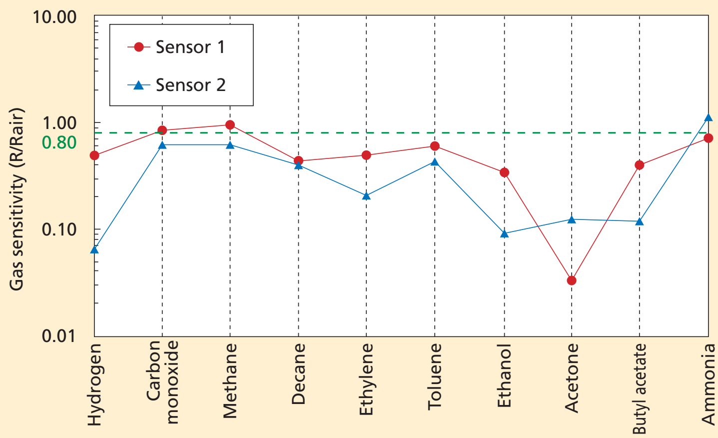

Figure 4 Sensor 1 and sensor 2 sensitivities to various gases

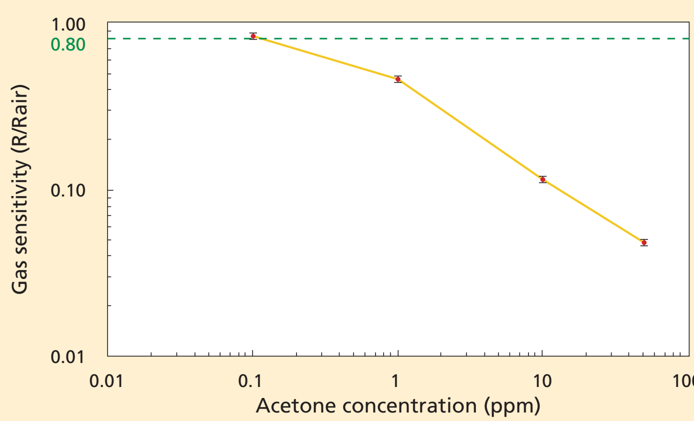

Figure 5 Acetone detection performance of sensor 1

*11 **Bluetooth®**: A standardized short-range wireless communication (IEEE 802.15.1) that operates in the 2.4 GHz band, and does not require registration or licensing for use. Bluetooth and the Bluetooth logo are registered trademarks of Bluetooth SIG, Inc. in the United States.

*12 **Android™**: A software platform consisting of operating system, middleware and main applications designed for smartphones and tablet computers. A trademark and registered trademark of Google, Inc. in the United States.

*13 **GUI**: A superior type of interface that offers visibility and intuitive operability by expressing operations and objects visually on a screen.

sensor.

Continuing, we compared the concentrations of breath acetone calculated by blowing into the prototype with a conventional large-size gas analyzer with gas separation mechanism (a commercial gas chromatography apparatus). **Figure 6** shows the results. From this, we were able to recognize a positive correlation between the results obtained from our prototype and the results obtained from conventional apparatus in which gases are separated for rigorous gas analysis (correlation coefficient[*14] R = 0.75). This level of accuracy is sufficient for applications in which the device will be used to provide a quick and easy-to-grasp general indication of the user's fat burning trends.

Furthermore, we confirmed that using both types of sensors in conjunction yielded an approximately 30% average improvement in detection accuracy, by comparing breath acetone concentration calculation using sensor 1 alone with the same calculation using both sensors. In other words, while the performance of this prototype remains close to conventional gas analysis apparatus, we have succeeded in drastically reducing size and weight.

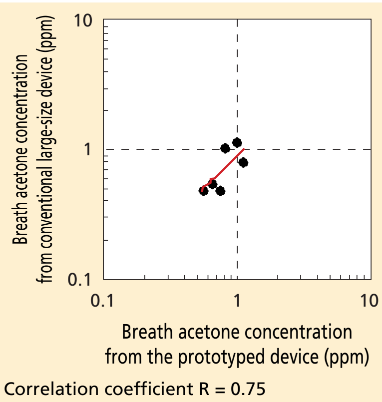

Figure 6 Comparison of breath acetone measurements

5. Service Development Example

Figure 7 shows an example of a service using the breath acetone analyzer. In this example, it is assumed that the user will blow into the analyzer several times during the day with arbitrary timing. The results of breath acetone concentration measured from the individual user are sent to a network server via the user's smartphone for storage and analysis. When a certain amount of data has been accumulated, daily fluctuation[*15] of the user's unique breath acetone concentration levels can be clarified, which will enable individualized lifestyle instruction that encourage fat burning, in terms of both diet and exercise. Specifically, this means understanding the characteristics of the user's metabolism, and offering dietary support programs that include information about optimized timing for meals and exercise, and the appropriate amount and load of exercise.

Human beings feel hunger in their brains due to the action of a number of factors such as hormones, so these feelings do not necessarily accurately reflect the level of sugar remaining in the body. Normally, human beings use body sugar as their main source of energy, but if the level of sugar in the body falls, fat is broken down and converted

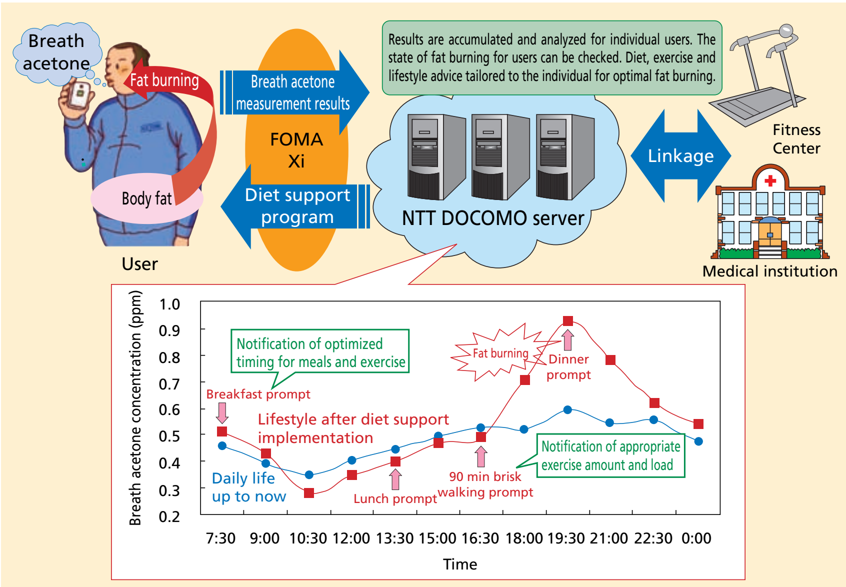

Figure 7 Example of service using breath acetone measurements

*14 **Correlation coefficient**: An index used in statistics to indicate the degree of similarity between 2 variables. The closer to 1 this value is, the more similar the variables, while the closer to 0, the more dissimilar.

*15 **Daily fluctuation**: Changes in measurement results that occur throughout the day.

into energy to compensate for the energy shortfall. Thus, it follows that if a healthy person has relatively high concentrations of breath acetone, and the person is not exercising, then the sugar level in the body has fallen and they are closer to being hungry. This could be the optimum time to take in energy from food. In contrast, even if hunger is felt in the brain, but the concentration of acetone in the breath is relatively low, it follows that there is still plenty of sugar left in the body, and there is no urgent need to eat for the purpose of taking energy. This fact can be exploited as a warning to prevent overeating. Furthermore, since it is assumed that when the concentrations of breath acetone are relatively high and body sugar levels are low, it is much easier for the body to use fat as a source of energy. Therefore, this could be the time to proactively exercise in order to burn fat most efficiently. In contrast, when breath acetone concentration is relatively low, exercising will probably only consume body sugar. The body cannot easily burn fat in this situation, and thus exercising at these times will be comparatively less effective.

Additionally, by comparing the concentrations of breath acetone before and after exercise, the user can determine whether the performed exercise has contributed to fat burning. If there is no change to the breath acetone concentration before and after exercise, the exercise load was probably too low or the length of exercise was too short. In this case, advice can be offered to the user to increase exercise load or length of time in steps.

In developing services linking up specialists in fitness centers and medical institutions, even more comprehensive diet support and health management services can be enabled by combining a range of smartphone functions such as the camera used to record the content of meals and acceleration sensors[*16] such as pedometers with the breath acetone detection to measure the amount of fat burning.

6. Conclusion

In this article, we have described a prototype that achieves a working example of a "biochip mobile terminal," - a portable breath acetone analyzer that enables users to visualize the state of body fat burning anytime and anywhere, just by blowing into the analyzer. The prototype is capable of high precision acetone measurement, even though the acetone exists in a mixture containing much higher concentrations of interference gases such as ethanol and hydrogen. While this prototype exhibits performance characteristics close to conventional high-precision gas analysis apparatus, it could be a world first in that it is dramatically smaller.

This prototype makes it possible to offer diet support programs tailored to an individual user's metabolism that include advice about the optimal timing, and appropriate amount and load of exercise for fat burning. Considering that the breath analysis requires a dynamic action of blowing for its use, it is vital that attractive services are developed, and their clinical effectiveness are verified in order to increase the number of users that continue to use the system.

We plan to continue researching and developing "biochip mobile terminals" into the future, and develop measuring devices that enable comprehensive analysis of constituents of sweat and saliva, and gases other than acetone or ethanol, and we aim to contribute to creating new value in the medical and health care fields through comprehensive services centered on the mobile terminal. Through these activities, we aim to find ways to alleviate the problems that society faces due to the high cost of nationalized medical care.

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*16 **Acceleration sensor**: A sensor that measures changes in speed. Equipping a mobile terminal with an accelerometer allows it to sense orientation and movements.

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