Metabolic Rate Monitoring and Weight Reduction/Management

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Abstract— **Engineering research may provide tools to the individual as well as to the public in general, to effectively monitor welness and health patterns, such as metabolic rate and weight control. Ketone bodies and acetone gas emissions in exhaled breath and skin, in particular, may be used as biomarkers of fatty acid metabolism and may be used in diet control. Two types of technologies, resistive chemosensors and chemomechanical actuators are outlined here as examples of such tools currently under development and of great promise.**

I. INTRODUCTION

Obesity is a lifestyle-related illness that has become a major social problem nationally and worldwide. According to recent data from the US center of disease control (CDC), more than one-third of US adults (approximately 97 millions) and 17% of children and adolescents were obese in 2009-2010 [1]. These statistics unfortunately are projected to grow, as the rate of increase in obesity prevalence in the US population at large has not exhibited slowing down or even leveling off trends [1]. The significant prevalence of obesity and overweight poses a major social and public health challenge; particularly as obesity is a root cause for increasing the risk of illnesses from hypertension, adverse lipid concentrations, type 2 diabetes, stroke, gallbladder disease, osteoarthritis, sleep apnea and respiratory problems, and various cancers (endometrial, breast, prostate, and colon) [2]. Moreover, morbidities associated with obesity have significantly driven the national medical expenditures upwards. For instance, according to the CDC website, the estimated annual medical cost of obesity in the U.S. was $147 billion in 2008, while the medical costs for obese people were $1,429 higher than those of normal weight.

To face the pressing national challenges (health, social and economic) associated with obesity and overweight, significant preventive care efforts and educative programs are continuously being proposed and executed to reverse the trends of obesity prevalence. These efforts are often led by non-profit organizations, school administrators, university researchers, state agencies as well as federal agencies (e.g., CDC, NIH, U.S. Department of Health and Human Services), to name a few. However, with all the exerted efforts, statistics (e.g. National Health and Nutrition Examination Survey, 2009-2010) show that the trajectory of obesity prevalence has not slowed much and, in fact, many of the set short term goals of U.S. Department of Health and Human Services (e.g. 2010 goal of limiting obese adults and children population to 15% and 5%, respectively) have not been met [1].

Most anti-obesity preventive care programs are designed around balanced nutrient consumption and exercising, and they target the individuals habits and call for life-style changes. Therefore, they are most effective when designed according to individuals needs and tailored based on feedback from individuals monitored progress. Accordingly, for the success of obesity preventive care programs, there is a need to provide users (patients) with the ability to quantitatively monitor their activities, metabolic rate and overall progress. For a long time, the monitoring tool available to the population at large has been the low cost weighing scale, and only recently, as wearable electronics are becoming more widespread, new tools such as step and calorie counters are becoming available.While these monitoring tools have been useful, scales provide feedback about the long-term progress and step/calorie counters provide approximations at best. In addition, they estimate the amount of total energy consumed during activities but cannot inform users about the source of this energy, whether it is from fat, glycogen or carbohydrate. Without knowing the energy source, individuals and obesity patients cannot ensure that their exercise routines and activities match their dietary habits and whether they are burning fat or have excess carbohydrate/glycogen. This is particularly relevant to individuals (often obese) who have fluctuating dietary habits and who get off-track and deviate, even occasionally, towards high calorie comfort foods.

To significantly increase the effectiveness of current obesity preventive care programs and to facilitate the development of the next generation preventive care programs that can be highly and accurately tailored to individuals day to day and instantaneous metabolic rates and body functions, there is a need for technological breakthroughs that would lead to personalized, easy-to-use, cheap, non-invasive and robust devices capable of giving users the ability to diagnose their metabolic and body fat burning rates continuously and in-situ during activities such as exercising.

II. PERSONALIZED METABOLIC RATE MONITORING

Knowing accurately the fat burning state and source of body energy (fat or carbohydrate) will provide quick, simple and accurate feedback information that can be used to monitor the effectiveness of anti-obesity preventive programs (e.g. ensuring that patients fat burning state hits the preventive care

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target); open horizons for creating very individualized interactive preventive care programs that change continuously based on the day to day fat loss and metabolic functions of individuals (e.g., a device can instruct users to reduce food intake or increase activities on a particular day based on their fat metabolic rate in the preceding hours); allow for optimizing exercise programs that encourage fat loss based on individuals body functions; provide added motivation to obese patients (e.g., they can get continuous affirmation that they are losing fat); alarm patients when they deviate from the preventive care program (e.g., consuming high carbohydrate foods).

Besides assisting in increasing the effectiveness of obesity preventive care, diagnostic tools capable of providing users with information about their fat burning state can have another dimension and assist three different groups: (i) epileptic children on ketogenic diet, (ii) anorexics (in ketosis), and (iii) diabetic patients (susceptible to ketoacidosis). These three groups are routinely tested (blood or urine) to evaluate the rate at which their bodies are breaking fatty acids. For intractable childhood epilepsy, since 1921 an effective nonpharmacological treatment has been the ketogenic diet (KD) [3]. In this diet, children are put on a high fat, low carbohydrate diet to encourage their bodies to utilize fat as a source of energy. To ensure that the administered ketogenic diet is effective in encouraging bodies to burn fat, blood and urine tests are usually performed to confirm that fatty acids are consumed. Anorexia is often associated with ketosis where bodies are using fat as the primary source. For anorexia, blood and urine tests are often used to determine the extent of the state of ketosis (hyperketonemia) by monitoring the elevation in intermediate products (Ketone bodies) generated by fatty acids breakage. Moreover, for diabetics (type I), a state of ketoacidosis occurs when the body excessively breaks fatty acids. This state should be avoided and only with monitoring fat metabolism it can be detected. Accordingly, for the three groups, monitoring the fat metabolism state is essential and part of the treatment protocol. Therefore, they would benefit from non-invasive, easy-to-use and cheap devices that allow for continuous monitoring of their fat metabolism patterns.

III. State-of-the art in the diagnosis and monitoring of fatty acids

Methods designed for monitoring fatty acids metabolism are founded on one principle: they aim to detect Ketone bodies (β-hydroxybutyrate, acetoacetate and acetone) which are produced by the oxidation of fatty acids (metabolism) in the liver when glucose is not readily available [4]. Acetoacetate accumulates during fatty acid metabolism under low carbohydrate conditions. β-hydroxybutyrate is formed from the reduction of acetoacetate in the mitochondria. Acetone is generated by spontaneous decarboxylation of acetoacetate [4]. Upon generation in the liver Ketone bodies are carried by blood and exported to peripheral tissues (e.g., brain, heart, kidney and skeletal muscle) for use as energy fuels [5]. Accordingly, the concentration of Ketone bodies in human systems (and animals) can directly indicate the metabolism rate of fatty acids [6]. Well-established methods to test for Ketone bodies include invasive blood testing and urine testing (via a chemically coated color changing dipstick). Blood sampling and testing can reveal the concentration of β-hydroxybutyrate, acetoacetate and acetone in blood; however, blood sampling is invasive and can be associated with loss of blood, pain, discomfort and emotional stress [5]. Testing for ketones in urine samples is a very common practice. When ketones are detectable in urine (i.e., state of ketonuria) they can be detected using dipsticks. These dipsticks are sold in pharmacies under various brands (e.g., Ketostix from Bayer). The aforementioned methods are widely acceptable and used in the medical field.

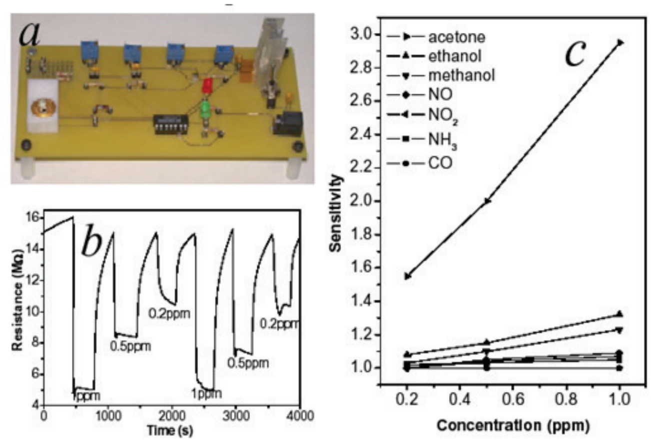

Fig. 1. Acetone breathalyzer for diet control [10].

Ketone bodies can also be detected in exhaled breath and skin released gas [6]. However, this is only applicable to the Ketone body (acetone). Few devices have been proposed to measure acetone in breath to monitor Ketone build up and fatty acids metabolism (e.g., [7]). While most of these devices depend on sampling exhaled breath and then utilizing complex gas chromatography to measure the acetone content in samples [4], [7], which is not practical, a novel single exhale acetone breathalyzer concept of high promise has been prototyped recently [8]. The detector operates on resistive chemosensors that work on the principle of ferroelectric poling [8], [9] and acetone monitoring is performed with high specificity. The detector is hand-held, portable, single exhale unit and it is equipped with a digital display for ease of use [8]. This is an inexpensive technology and once feasibility studies are complete it will be accessible to the individuals with no risk of use and thus it may revolutionize diet control.

IV. Chemomechanical nanosensors/actuators for weight control

Acetone is also released through skin, which is accessible (e.g. from hands, arms and fingers) [6]. This particular acetone source can be easily, continuously and non-invasively sampled. Moreover, the literature has shown that skin-released acetone has a linear relation to acetone content

Application:

- **Handheld breath-acetone monitor for diet control**
- Consumer product for diet control, daily repeated use, gives consumer direct measure of fat metabolism, indicates whether fat is burned instead of muscle

Biomarkers:	**Validation:**

• key biomarker**: acetone in breath**
• lipid degradation product
• Breath acetone of 500nmol/L indicates a weight reduction of about one-half pound per week*
  • The minimum acetone concentration that needs to be detected is 200ppb
  • Acetone content increases fivefold by day 3-4 so the maximum concentration to be detected should be few ppm
	• Demonstrated to-date: the sensitivity and step discrimination for acetone has been confirmed in the lab using controlled gas mixtures in a gas flow bench
	• The key validation necessary for feasibility is to run an experiment at a nutritionist's facilities with 25-50 healthy individuals on diet. Thus, we will be able to calibrate and validate the use of the breathalyzer for this application within weeks

Fig. 2. Summarizes the key features of the acetone breathalyzer developed by Gouma's group (see Figure 1) for metabolic rate monitoring.

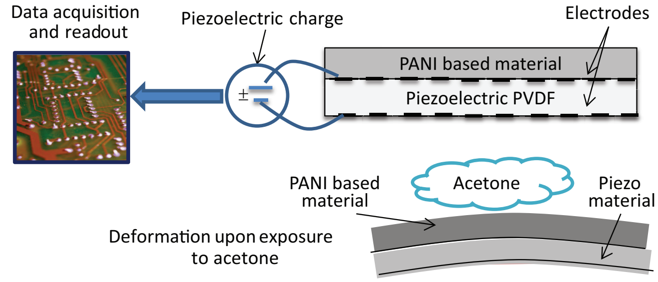

Fig. 3. Actuation mechanism (chemo to charge conversion).

in blood and fat loss rate. Monitoring of skin released acetone has closely followed methods for monitoring acetone in breath; skin released acetone is sampled by a plastic bag and gas chromatography or ion flow tube spectroscopy were used to measure its concentration [6], [7]. Reported skin released acetone levels ranged from 0.2 ppm to 1.2 ppm (here values changed with exercise) [11]. These values correlate linearly to exhaled acetone which ranged from (0.5 to 4 ppm) [11]. Clearly, both sources skin and exhale provide the same order of magnitude levels, which emphasized the detectability of skin released acetone.

A novel concept based on chemomechanical sensors that detect acetone gas (e.g. as emitted from the skin) instantly and with high selectivity [9] is being currently explored by the authors and its design is shown in Figure 3. The skin band metabolic monitor with wireless connectivity is expected to revolutionize non-invasive and personalized control of one's fitness.

The acetone-sensitive material in this design is based on polyaniline(PANI) films and is inspired by recent advances in the field of active and smart materials that mimic artificial muscles. In the last decades electroactive polymer materials that produce high-actuation displacement are finding uses in medical applications and as potential artificial organs. In particular, electroactive polymers that exhibit natural bidirectional actuation depending on the polarity are gaining interest as materials to be used to mimic artificial muscles (e.g., [12], [13]). Within the field of electroactive polymers there has been a growing interest accompanied by a shift towards the development of conducting polymer actuators, particularly as conductive polymers exhibit a low operating potential (typically $<$2V), and a high mechanical strength. Consequently, conductive polymers are becoming very attractive to applications that include advanced robotics, microactuators, and artificial muscles. In addition, conductive polymer actuators can be chemically and reversible triggered. This allows them to actually mimic biological organs with chemically triggered actuation. For instance, polymer actuators that are chemically stimulated can mimic biological muscles.

So far most of the proposed and applied smart materials tend to be electro-active rather than chemo-active. However, potential for chemical actuation has been demonstrated in porous asymmetric polyaniline membranes [9], [12]. Polyaniline is formed from the oxidation polymerization of the aniline monomer. The actuation of PANI films is primarily due to dimensional changes occurring upon a reversible redox reaction. As the polymer becomes protonated (addition of extra H+ ions), it increases in size and in an alkaline solution de-protonation occurs and the mat should decrease its size; this is a pH dependent redox reaction thus PANI may be used as an actuator in the presence of different pH media [14] (e.g., in the presence of hydrocarbons such as acetone) [9].

In the wearable acetone monitor concept (hand band device) of Figure 3, in addition to the PANI-based actuator, a piezoelectric component converts the chemomechanical action into an electric signal captured by a specially designed circuit. The acetone concentration is continuously monitored as the strain is converted first to charge and then to voltage through a charge amplifier. The signal processing module converts the acetone level changes into the metabolic and fat burning rates.

V. Experimental Method and Results

There are three steps used to synthesize a polyaniline/cellulose acetate(PANI/CA) actuator: solution preparation, casting and strip cutting [15]. The first step involved acid doping of leucoemeraldine(LEB) PANI by immersing it in HCl, followed by 6 cycles of centrifugation and acid removal. The air-dried product was mixed with acetone and following sonication, cellulose acetate was further added to it (PANI/CA ratio equals 1/5; total polymer concentration in acetone was 5% vol. The final mixture was poured on a clean flat glass side and a blade was used to even it out. When the films dried, they were removed from the glass slide, were cut into strips 40 mm long and 3 mm wide and were tested as actuators, as shown in Figure 4.

The PANI/CA thin film is porous. The pore size is 1-2μm. Fourier Transform Infra Red Spectrospopy(FTIR) data (not shown here) confirms that the polymers are interconnected. When exposed to the headspace of acetone the strips showed a maximum bending angle of 30 degrees, and a total response and recovery time of 7 seconds. The relative chemical sensitivity was determined also exposing the polymer actuator to

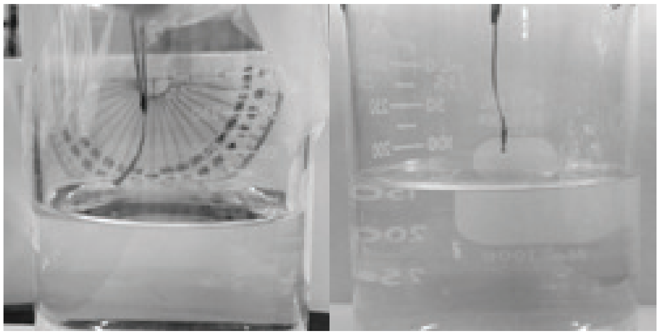

Fig. 4. *Left:* PANI/CA strip responds to acetone; *Right:* The same PANI/CA strip shows no observable response to 2-propanol under the same conditions.

the headspace of vials filled with ethanol, 1-butanol and 2-propanol respectively. The bending movement only appeared when exposed to the acetone vapor, which means PANI/CA actuator shows chemoselectivity to this gas.

VI. Conclusion

The breath and skin emitted acetone monitoring non-invasive tools that are currently under development aim to provide engineering solutions to the problem of personalized, efficient, and economic weight management. Unlike national health surveys, the new technologies outlined above can produce a database that will be instantaneous, continuously changing and will reflect social trends and show how the exercise and health habits of the public are affected by year-round events or factors (e.g. holidays, seasons, temperature fluctuations, national events). Engineering research can play a key role in metabolic rate monitoring and control and soon nanomedicine solutions are expected to hit the market.

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