Adaptive Biofeedback with Signal Processing and Biosensors in Mobile Health

by

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ABSTRACT

Advances in miniaturized sensors and wireless technologies have enabled mobile health systems for efficient healthcare. A mobile health system assists the physician to monitor the patient’s progress remotely and provide quick feedbacks and suggestions in case of emergencies, which reduces the cost of healthcare without the expense of hospitalization. This work involves development of an innovative mobile health system with adaptive biofeedback mechanism and demonstrates the importance of biofeedback in accurate measurements of physiological parameters to facilitate the diagnosis in mobile health systems.

Resting Metabolic Rate (RMR) assessment, a key aspect in the treatment of diet related health problems is considered as a model to demonstrate the importance of adaptive biofeedback in mobile health. A breathing biofeedback mechanism has been implemented with digital signal processing techniques for real-time visual and musical guidance to accurately measure the RMR.

The effects of adaptive biofeedback with musical and visual guidance were assessed on 22 healthy subjects (12 men, 10 women). Eight RMR measurements were taken for each subject on different days under same conditions. It was observed the subjects unconsciously followed breathing biofeedback, yielding consistent and accurate measurements for the diagnosis. The coefficient of variation of the measured metabolic parameters decreased significantly (p < 0.05) for 20 subjects out of 22 subjects.
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Chapter 1

MOBILE HEALTH

One of the main problems in healthcare is the lack of availability of physicians/clinical infrastructures for frequent health monitoring. Mobile Health (m-health) is intended to offer less expensive solutions with more accurate and convenient diagnosis by providing remote monitoring systems for patients, and even in hospitals. Also, mobile health can provide effective healthcare solutions for people living in remote rural areas and for patients in need of continuous health monitoring. The introduction of communication technologies, wireless and mobile networks bring hopefulness for such patients with more accessible and affordable healthcare solutions [1, 2, 3].

1.1 Overview

Rapid advancements in smartphones/tablets and wireless networks continue to have a significant impact on the healthcare for the society. The main goal of m-health is to bring the patient and the doctor closer to provide an efficient quality of healthcare service by monitoring patient’s health conditions anytime and anywhere without restricting the patient’s movement. With the miniaturized sensors and use of wireless interface to transmit data recorded by the sensors, remote health monitoring is possible beyond hospital environments [4]. This enables the physician to monitor the patient’s progress remotely and provide quick feedbacks and suggestions in case of emergencies without any inconvenience and expense of hospitalization, reducing the cost of healthcare and financial burden to the society. There are also open issues and challenges
involved in providing reliable m-health that will be discussed in later part of this chapter.

The UN foundation has formed the m-health alliance specifically to explore and promote the importance of mobile computing technologies for improving healthcare in developing nations [5]. A m-health system consisting of personal mobile devices, portable sensors and wireless interface is targeted to serve various purposes: early diagnosis by detecting behavioral peculiarities, track conditions of patients at home for quick response in emergencies, athletes willing to monitor the progress of physical fitness, individuals seeking to change their fitness goal by losing or gaining weight, for patients with chronic medical conditions and many more.

Mobile health has been a potential research area from past few years that exploit the developments in the mobile and wireless communications technologies providing the approach for highly effective medical services that are not possible with standard telephony. Mobile health systems can commendably provide healthcare services in understaffed areas like remote rural health centers, ambulance vehicles, ships, trains, airplanes and patient’s homes [6,7]. Pervasive Healthcare can be defined as “healthcare to anyone, anytime, and anywhere by removing locational, time and other restraints while increasing both the coverage and the quality of healthcare” [8], which includes prevention, healthcare maintenance and checkups, short-term and long-term health monitoring, incidence detection, emergency intervention, monitoring on transportation. Mobile health fulfills the vision of pervasive and ubiquitous health monitoring. The role of
wireless infrastructure in mobile health systems is expected to become more prominent with increasing smartphone users and rapid deployment of mobile and wireless networks.

1.2 m-health System Architecture

An m-health system consists of an interface between hardware, software and wireless communication channel to connect distant geographical locations to exchange medical information between different locations. The hardware consists of the sensing device with a short-range wireless radio for transmitting the data to a smart mobile phone. The sensing devices are usually biomedical sensors detecting the parameters that directly or indirectly match with the health conditions of the user. Environmental sensors may also be considered in some m-health systems to compare the environmental effects on health conditions. The software in the mobile phone enables the acquisition of data from the sensing devices and performs signal-processing operations to compute the desired information. Typical m-health system architecture is shown in figure 1 below. Some systems store the data locally and transmit to the physician over the wireless interface. The wireless communications technologies include GSM, GPRS, Wireless LAN, 3G and 4G system standards, and these will be discussed in section 1.5. Recently m-health system architecture is moving towards adopting cloud computing due to various advantages like higher storage space, computational capability, data security and this will be discussed with more details in section 1.6.
In this case, the data from the phone is transmitted to remote servers over wireless interface and the doctors can access data from the servers anytime. The servers will have capability to store the health records of many patients and intelligent algorithms can be developed in future to predict the consequences based on the history data available for the patients. One more reason for using cloud computing in m-health systems is for load shedding from mobile phone to server for the algorithms that need higher computation power. Any m-health system architecture should be built in such a way keeping in mind that the phone should be connected to a valid Internet connection or cellular connection. The architecture should also consider the compromise between the power consumption by the devices and the computation load.
To summarize the system components in typical m-health architecture, the hardware components involve a patient’s medical device consisting of sensors, microcontroller chip, short-range wireless radio module like Bluetooth or Zigbee, and a mobile phone. The software components involve the application program in the patient’s mobile phone, web application modules and the database in the remote servers. Wireless interface exist between device and the phone, and between phone and remote data accessing device (either a phone, tablet or a desktop) with the physician.

1.3 Related Works in m-health field

There has been significant works in the field of m-health in recent years by many researchers due to the growth and importance of m-health to provide efficient and less expensive health care with the advancements in mobile and wireless technologies. Few of them include long-term health monitoring by wearable devices [8], wireless telemetry system for EEG epilepsy monitoring [9], ring sensor for blood oxygen saturation level monitoring [10], a battery-less and wireless wearable stethoscope [11], ECG telemetry with Bluetooth technology [12], real-time monitoring for patients in home environments is presented in [13], remote heart monitoring using cellular wireless networks is discussed in [14], health monitoring system with wireless body area network (BAN) of sensors for stress monitoring is proposed in [15], and a design approach for ECG data compression for a mobile tele-cardiology model involving a significant compression ratio and reduction in transmission time over GSM network is described in [16].
Health problems related to diet has motivated researchers to provide an m-health solution for diet plan and fitness. A prototype system that uses a mobile device with a built-in camera, wireless network connectivity and intelligent image analysis algorithms that estimates the calorie intake is proposed in [17]. A mobile personal trainer wearable system that supervises physical activity and fitness exercises in outdoor activity is described in [18]. A mobile phone based health game that motivates users to practice healthy eating habits by providing scores based on healthiness of the food is presented in [19]. These fitness m-health systems available are either based on estimating the calories in food intake or estimating the physical activities by body movements. Currently, there is no portable mobile-based metabolic analyzer exists that measures the actual metabolic rate. This inspired our team to develop a novel m-health solution for accurate metabolic rate assessment by indirect calorimetry technique.

1.4 Mobile Health Strategy

It is important to have a strategic framework or road map for sustainable m-health, as m-health has a crucial and inevitable role in future healthcare [20]. The benefit of mobile technologies with their comparatively low unit cost to the user is one of the reasons for their pervasiveness. This ubiquity makes them more preferable than desktop computers for telemedicine. The m-health strategy is on how to produce long-term benefits, sustainable beyond the short-term attraction with innovation. A strategic planning is required in a cross-sector perspective since m-health benefactors can be classified into different target groups as healthy
people, hospital patients and chronically ill patients. User-centric applications, integration, efficiency, and accountability are very important issues in chronic disease management. Mobile healthcare can play in wellness promotion and health management according to four categories: prevention (public health and lifestyle awareness), monitoring (pre-disease screening and assessment), treatment (providing efficient and effective care) and support (for patients and their caretakers) [20]. Further strategies have to be worked out in a way to succeed in the acceptability of technologies to both patients and healthcare practitioners by developing user-friendly, simple and effective m-health systems.

The major phases in m-health strategic framework can be classified into three categories: Identifying suitable applications, Continuous development activity, and Continued support for innovation even with successful existing applications.

Some of the m-health strategies for successful acceptance and sustainability are given below [20]:

- Easy to use and convenient
- Require less additional technical skills or time
- Fit easily with existing lifestyles
- Cost-effective for provider and consumer
- Make efficient use of resources
- Promote wellness and healthy lifestyles
- Emphasize integrated care
- Link well with existing processes/services by adding value to existing services
- Guarantee reliable services
- Maintain data quality during transmission
• Maintain provider and consumer acceptability
• Re-engineer processes to encourage holistic and seamless care
• Retain flexibility and openness to m-health innovation
• Data security: Ensure the privacy and confidentiality of information
• Explore and utilize the technical improvements
• Focus on portability and interoperability

1.5 Emerging Wireless Technologies for Health

In recent years, there has been increased research in wireless telemedicine using the current mobile communication technologies. The wider use of these systems in healthcare has been limited due to the restriction of limited bandwidth of current generation of cellular telecommunication systems. High-speed data, higher bandwidth, low power management and multimedia services are the major focuses of future wireless communication technologies for significant benefits in mobile healthcare.

Some of the existing and emerging wireless technologies like Wireless PAN including Bluetooth and Zigbee, Wireless LAN, Wireless BAN for medical sensors, 2G, 2.5G, 3G and 4G system standards are discussed in this section with the knowledge gained from [6,7].

(i) Wireless Personal Area Network (WPAN)

IEEE standard 802.15 defines the wireless personal area networks. Commonly used technologies in m-health are Bluetooth and Zigbee. Bluetooth operates in globally unlicensed ISM 2.4 GHz frequency band and supports mobile phones, PDAs and computers to communicate and send data wirelessly within the range of 10 to 100 meters at a data rate of up to 1 Mbps. It is low-cost, small size and low
power radio technology suitable for short-range personal area networks. Bluetooth supports different profiles, but either Serial Port Profile (SPP) or Health Device profile (HDP) is used in m-health applications. SPP is based on RFCOMM protocol and acts as a replacement for RS-232 serial communication. HDP is designed to facilitate transmission and reception of medical device data. Zigbee is designed as a low data rate, low complexity and longer battery life solution. It operates in the ISM radio bands with supporting data rates from 20 to 900 kbps. Currently, Bluetooth is widely used in m-health applications due to its wide popularity and default presence in almost any mobile phone. Recently few other technologies like ANT+ are emerging to provide better m-health solutions [21]. ANT+ is primarily designed for collection and transfer sensor data in the field of sport, wellness and home health. But ideally, the best technology for m-health will depend on wide acceptance and successful integration of these modules in mobile devices.

(ii) Wireless LAN (WLAN)

Most modern WLANs are based on IEEE 802.11 standards, marketed under Wi-Fi brand name. Wireless LAN is effectively Ethernet without wires and it allows users to access data networks like the Internet at high speed of up to 11 Mbps as long as users are located within a relative short range of a WLAN base station. WLAN connectivity is very important to connect and facilitate diagnostic data exchange between patients and doctors. WLAN feature is helpful for mobility in home and hospital environments.
(iii) Wireless Body Area Network (WBAN)

WBAN is an emerging technology in m-health and have great potential for continuous monitoring, early detection of abnormal conditions and supervised rehabilitation [22]. A typical WBAN consists of a number of inexpensive, lightweight and miniature sensor platforms each featuring one or more physiological sensors like motion sensing, ECGs, EMGs and EEGs [7]. These sensors could be located on the body integrated into clothing, where the sensors perform data acquisition and pre-processing. All the data are then collected by a network controller and processed on the mobile phone and then the results are transmitted to the physician for diagnosis.

(iv) 2G, 2.5G, 3G and 4G system standards

GSM and GPRS technologies that are under 2G system standards are the wireless technologies that were used initially in m-health systems a few years ago. GPRS technology is a packet-based and designed to work in parallel with the 2G TDMA systems such as GSM that are used for voice communications. EDGE technology is a standard that was been specified to enhance the throughput. But 2G wireless technologies failed to make a strong impact in m-health due to its low data rate which made them incapable of transmitting bio signals and medical images. The evolution of mobile telecommunication systems from 2G to 2.5G and 3G(W-CDMA, CDMA-2000, TD-CDMA) provided much higher data transfer enabling design and development of more effective m-health systems. 4G system standards (LTE and WiMAX 802.16m) tend to integrate existing wireless technologies and
newly developed technologies into a seamless system with higher transmission data rates. 4G networks are all IP-based and support higher data rates at lower transmission cost and has a higher system capacity. 4G systems will drive the effective m-health systems into the 21st century [7].

1.6 Cloud Computing for Mobile Health

Mobile devices are considered as service platforms for m-health information delivery, access and communication. But mobile devices face challenges to run heavy multimedia and security algorithms due to their limitations in computational capacity and power supply. Cloud computing is focused on relieving mobile devices from executing heavier algorithms in m-health systems. Cloud computing refers to both the applications delivered as services over the Internet and the hardware and systems software in the data centers that provide those services. The data-center hardware and software is termed as Cloud [23]. Figure 1 depicts the framework of cloud computing in m-health systems. The basic need is that the medical diagnosis that require multimedia signal processing with increased power consumption and computation capacity to execute in a mobile device. To prevent power drainage, the data is uploaded to the cloud to execute complex computation algorithms and the final results are downloaded back to the mobile phone. Also, one more need would be centralized data storage of all the patients to be accessed by the physicians anytime and anywhere. This is very critical when there is large number of users within a single m-health system and would require bigger memory space for data storage, and also useful for the
patient to access his data from any mobile device by logging into the user’s account. Cloud computing technology can be used to overcome the limitations of mobile devices for use as service platforms in m-health applications needing complex algorithms and centralized data storage space.

### 1.7 Issues and Challenges in m-health

Though m-health is growing at a fast pace in providing effective healthcare, it has a number of open issues including lack of comprehensive coverage of wireless and mobile networks, reliability of wireless infrastructure, general limitations of mobile devices, privacy and security. Deployment of next generation m-health systems with advanced wireless communication technologies will face some challenges including user acceptance issues such as light weight implementation, long battery life or battery-less sensors, maintainability, usability and reliability, seamless and secure connection, smart medical sensor design, efficient signal processing algorithms, computing and networking, and protocols for medical sensor networks.

With suitable user-friendly compact medical devices, the major challenge exists in providing a seamless wireless connectivity between the sensors and the mobile phone, and also the reliability in sending the result data to the physician for diagnosis through wireless networks. The data originating from the mobile devices and sent to the healthcare provider database must be secure, reliable and encrypted. Also, considerable challenges are there in mobile application development due to the limitation of the handheld mobile devices including small
screen size (limits text-based data entry), limited storage space, and slow processing that needs efficient programming skills. Overcoming these challenges, m-health will fundamentally change the present structure of healthcare systems.

1.8 Objectives and Scope of this Research

The objective is to develop a biosensor based mobile health system with adaptive biofeedback. The focus is on observing the effectiveness of biofeedback in mobile health system for metabolic rate assessment. The challenge is to accurately determine and track the metabolic rate with miniaturized sensors and mobile technologies. It is known that there are large variations in the metabolic rate measurements at different times under same conditions of the person, due to several factors [24]. One of the major factors was found to be the breathing pattern. The objective is to develop an algorithm that determines the breathing frequency with very high accuracy and provides adaptive biofeedback with musical and visual guidance correlating to the breathing rate of the individual. Also, the objective is to develop various adaptive biofeedback algorithms and compare them to conclude the best one for practically determining accurate and consistent metabolic rate. In the course of this research, I have concentrated mostly on the adaptive biofeedback algorithms for musical and visual guidance and their effects in determining accurate measurements of metabolic rate with the biosensor based metabolic analyzer, developing a user-friendly mobile health system.
1.9 Organization of the Report

This chapter was emphasized on the growth and importance of mobile health (m-health) in providing remote and low-cost healthcare solutions and the challenges involved in them. We spend chapter 2 on discussing the biofeedback, biosensors, fundamentals of metabolic rate and the motivation for this research work. Chapter 3 introduces the importance of biofeedback in determining the metabolic rate and emphasized on the breathing rate detection algorithm and the adaptive biofeedback algorithms. Chapter 4 presents the discussion of the results including validation of algorithms and impact of the adaptive biofeedback in metabolic rate assessment followed by the conclusion and the vision for future research directions in this domain.
Biofeedback is a technique of measuring certain physiological parameters such as blood pressure, heart rate, respiration rate, skin temperature, muscle tension, brain waves etc., and conveying the physiological information to the person in real-time to improve their health and performance. The use of biofeedback provides the user with immediate information from the biological processes usually beyond their awareness facilitating the regulation of body functions accordingly. It provides perceptible information that the user can utilize to gain voluntary control over various biological processes. Biofeedback method has been a significant tool in treatment of many disorders like asthma, anxiety, hypertension, depression, seizures and migraines [25]. Most of the stress related health disorders could be cured with biofeedback techniques of relaxation. Typically, a sensing device picks up electrical signals corresponding to body functions and translates into a feedback of visual, vibration, audio forms that people can interpret and react. Advanced biofeedback methods focus on providing virtual reality of feedback signals through audiovisual animations. The goal is to make the user feel the presence in virtual environment, while continuously confronted with the information about the physiological signals during the therapeutic training in an easy and intuitive way [26]. The connection between the body functions and the mind is the key for biofeedback. Biofeedback helps in providing a non-invasive methodology for the user to control the body functions, which is being used both in medical and psychological fields.
Different types of biofeedback methods are used in the treatment and rehabilitation of various disorders as mentioned below [27]:

- Bronchial asthma, hyperventilation syndrome: by means of capnographic biofeedback (based on CO$_2$ concentration in exhaled air)
- Anxiety and hypertension syndromes: by means of breathing biofeedback
- Addictions (drugs addiction, alcoholism, toxicomania): by means of neurofeedback therapy.
- Psychosomatic disorders (hypertension and depressions): by means of temperature-myographic training
- Spinal syndromes, paralysis after brain injuries

Biofeedback guides the users to correct strategies for bringing their biology into a proper range of functioning. The success of the methodology is also dependent upon the user’s desire to follow the guidance and apply them in daily life. Since visual and audio effects has a strong impact to mind, they are used as biofeedback tools to unconsciously make the user to follow the guidance. Biofeedback therapy is known to have no side effects. The mechanism by which reading and altering the brain waves is termed as neurofeedback. Thermal biofeedback involves measurement of body temperature and breathing biofeedback involves measurement and correction of respiratory rate.

The focus of this research work is to integrate biofeedback in the mobile health system. Resting metabolic rate assessment is considered as a model to study the effects of adaptive biofeedback with signal processing and biosensors in
mobile health. Hence the following sections provide the fundamentals of metabolic rate measurement, biosensors and the motivation for this research work.

2.1 Resting Metabolic Rate

Measurement and tracking of Resting Energy Expenditure (REE) or Resting Metabolic Rate (RMR) is a critical aspect in the research of healthcare and nutrition in analyzing obesity, malnutrition, metabolic syndrome and various other fields. The metabolic processes in body results in the production of heat. The rate of energy metabolism is assessed by the rate of heat production by cells, tissues, or the whole body. Calorimetry is the term used to define the measurement of energy expenditure as shown in Figure 2 below.

![Figure 2: Calorimetry of metabolic process [28]](image)
Energy expenditure can be determined by two methods, direct calorimetry and indirect calorimetry. Direct calorimetry is based on monitoring the temperature change in the chamber in which the subject could live. Some methods are airflow calorimeter and water flow calorimeter, which are based on determining the heat production with temperature change in air/water (respectively) that flows through an insulated space, multiplied by mass of air and specific heat within the chamber [28]. Indirect calorimetry is more widely used due to its simplicity and practicability, which is based on estimating REE by determining the rate of oxygen consumed and rate of carbon dioxide produced, explained with more details in section 2.4. There has been a lot of research performed from many decades in the domain of estimating the calorie intake for health and fitness management. The approach is the art of reverse engineering, by which the metabolic rate is measured to provide an accurate reference for calorie intake to achieve the desired health and fitness goal.

2.2 Motivation

Diet related health problems including obesity, malnutrition and cancer are major concerns in the human society. Obesity is one of the predominant chronic diseases across the globe, especially in United States. According to Centers for Disease Control and Prevention (CDC) as per the latest U.S National Health and Nutrition Examination Survey (NHANES), one-third of the American adults are currently obese and another one-third is overweight. Obesity is a major risk factor for cardiovascular diseases, type 2 diabetes, osteoporosis, some cancers and
depression [30]. More than hundreds of billion dollars were spent just in the United States for medical costs related to obesity in 2008, which increases the financial burden to the society [29,30]. This motivated to create an innovative, user-friendly and an effective solution to measure and track accurate Metabolic rate with cutting edge engineering principles and technologies.

Smart mobile phones with improved technical capabilities including high speed processing units, advanced digital signal processors, enriched memory, built in cameras of higher resolutions, short range wireless communications and wireless networking capabilities have enabled them to be used for real-time mobile health applications. The miniaturized biosensor technologies have been growing at a fast pace from past few years creating a strong impact in providing solutions for the society in health and environmental sectors. This motivated our team to develop a color-based sensor with non-invasive sensing technology to detect the metabolic parameters and utilize the technology advancements in smart phones by integrating wireless communication and digital signal processing techniques to provide a user-friendly mobile health application.

Measurement of accurate REE is a challenging problem, since it not only depends on the metabolic parameters detected by the biosensor including rate of O\textsubscript{2} and CO\textsubscript{2} in the exhaled breath, but also depends on other parameters like breathing rate (BR) or breathing frequency (BF) and exhaled volume (V\textsubscript{E}). Also, since these parameters are determined by monitoring the breath for few minutes and extrapolated to 24 hour frame to calculate daily energy expenditure losses, very accurate measurements of metabolic parameters during the test time is of
prime importance. This motivated to develop an adaptive biofeedback solution to breathe with musical and visual guidance using digital signal processing techniques to accurately determine REE and reduce the variations across the different measurements. The ultimate goal is to introduce the adaptive biofeedback mechanism with signal processing and biosensors in the mobile health system with an example of resting metabolic rate assessment.

2.3 Biosensors

A biosensor is a sensing device comprised of a combination of a specific biological element and a transducer. They can essentially serve as low-cost and highly effective devices to detect the bio-agents. As the name suggests, they consist of a bio-element and a sensor-element. The bio-element may be an enzyme, antibody, living cells, or gases from exhaled breath and sensing element may be current/voltage, light intensity/absorbance and so on [31].

Biosensors are creating a great impact on our lives as they are being used in clinical applications for early detection of health problems and diseases. Based on different sensing technologies, the categories of biosensors that have been widely used from past few years include electrochemical biosensors, optical-detection biosensors, microcantilever biosensors and dielectric spectroscopic biosensors [31,32]. Each type of biosensor has its own significance based on the field of application. Electrochemical biosensors are based on monitoring current/voltage with an array of electrodes and work on the principle that the current/voltage between electrodes change when chemical reaction between materials attached on
the electrodes and biological samples surrounding the electrodes occur [31].

Electrochemical sensors directly output electronic signals and hence can be easily integrated with readout circuits. Light is the output-transduced signal for optical-detection biosensors. Microcantilever sensors are based on the principle of resonance, that there is a change in resonant frequency of the beam on addition of certain biosamples. Dielectric spectroscopic biosensors are based on the principle of impedance change. It can detect the change in humidity, temperature and concentrations of aqueous solutions by measuring the changes of impedance [32].

Prior arts for indirect calorimetry and resting energy expenditure monitoring are based on electrochemical and infrared detection. While the electrochemical technology faces lifetime issues, the infrared detection method falls short in selectivity. In addition, the cost of the analyzer combining both methods is expensive. The high cost inherent to these technologies prohibits them from reaching a larger consumer market. For acetone detection, enzymatic methods using electrochemical and electrical (metal-oxide) measurements have been developed [33]. These systems represent the state-of-the-art in this area, the use of enzymes in the electrochemical detection faces stability challenges, and the metal-oxide based electrical sensors require high temperature to operate, which leads to high power consumption. To overcome these difficulties and challenges, our team developed a novel low-cost color-based sensor that determines the rate of oxygen and rate of carbon dioxide from the exhaled breath based on the change of absorbance in the chemical sensor using photodiodes.
2.4 Indirect Calorimetry

Indirect calorimetry method is based on oxygen and carbon dioxide measurements in the exhaled breath to estimate the resting energy expenditure or metabolic rate. This indirect form of REE measurement through characterization of inhalation and exhalation gases is performed on humans due to its simplicity and accuracy. Indirect calorimetry yields results comparable to direct measurement in human calorimeter [28].

The relationship between energy expenditure and the rate of oxygen and carbon dioxide was first proposed by Weir in 1949 with the equation (1) below [34].

\[
\text{REE} = \left( 3.9 \times \text{VO}_2 \right) + \left( 1.1 \times \text{VCO}_2 \right) \times 1.44
\]  

(1)

Where; REE is resting energy expenditure in kCal/day

\( \text{VO}_2 \) is oxygen consumption in ml/min

\( \text{VCO}_2 \) is carbon dioxide production in ml/min

Oxygen consumption and carbon dioxide production are measured by different techniques in order to compute RMR/REE, using the indirect calorimetry technique [35,36]. Commonly followed indirect calorimetry procedures that measure oxygen consumption are: portable spirometry, bag technique and computerized instrumentation. With portable spirometry, the subject carries a box-shaped apparatus on the back and inspires ambient air through a two-sided breathing valve, while the expired air exits through a gas meter. The meter measures the expired air volume and simultaneously collects a small gas sample for later analysis of oxygen and carbon dioxide content. In bag technique, the subject breathes the ambient air through one side of the valve and
expels it through the other side. The expired air passes into a plastic or canvas Douglas bags to measure the expired air volume. Subsequent analysis is performed on the air inside the bag to determine oxygen and carbon dioxide composition. With advances in microprocessors and digital signal processors in computers and smartphones, computerized instrumentation method is being widely used and it basically requires a system to continuously sample the subject’s expired air, a flow-measuring device to record volume of air breathed, and oxygen and carbon dioxide analyzers to measure the exhaled gas mixture composition. The computer or the smartphone will perform signal-processing operations to perform metabolic rate calculations based on the electrical signals received from the instruments [28].

In this work, computerized instrumentation procedure of indirect calorimetry is followed to determine the resting energy expenditure with a color-based sensor device consisting of chemical sensor, photodiodes, LED’s, pressure sensor, microcontroller and a Bluetooth module with signal processing operations performed in the Android smartphone.

2.5 Respiratory Quotient (RQ)

Respiratory Quotient (RQ) determines diet composition. Due to inherent chemical differences in carbohydrate, fat and protein compositions, they require different amounts of oxygen for complete oxidation of each molecule’s carbon and hydrogen atoms to the carbon dioxide and water end products [28]. The carbon dioxide produced per unit of oxygen consumed varies with the type of
substrate (i.e. carbohydrate, fat, protein) catabolized. RQ is described with equation (2) below and categorizes the energy source / diet composition as given by Table 1 [37].

$$RQ = \frac{CO_2 \text{ produced}}{O_2 \text{ consumed}}$$

(2)

Table 1 Diet Composition

<table>
<thead>
<tr>
<th>Energy Source/ Diet Composition</th>
<th>RQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged Ketosis</td>
<td>&lt;0.70</td>
</tr>
<tr>
<td>Fat</td>
<td>0.7 to 0.8</td>
</tr>
<tr>
<td>Protein</td>
<td>0.8 to 0.85</td>
</tr>
<tr>
<td>Mixed Diet</td>
<td>0.85 to 0.95</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>&gt; 0.95</td>
</tr>
</tbody>
</table>
Chapter 3

BREATHING BIOFEEDBACK

Breathing biofeedback is based on providing guidance to the user by monitoring respiratory cycle and measuring the breathing rate. Biofeedback is getting popular in medical fields for various treatments since it is a natural therapy without the use of medications. I have implemented the breathing biofeedback mechanism in the system for accurate resting metabolic rate assessment.

3.1 Need for Adaptive Biofeedback in REE Assessment

The measurement of resting energy expenditure is based on the rate of oxygen and rate of carbon dioxide in the breath as described in the equations below:

\[ \text{VO}_2 = (20.9 - \text{Conc}_O_2) \times \left( \frac{V_E}{100} \right) \text{ ml/min} \]  (3)

\[ \text{VCO}_2 = (\text{Conc}_C O_2 - 0.06) \times \left( \frac{V_E}{100} \right) \text{ ml/min} \]  (4)

\[ V_E = \left( \frac{V_T}{60} \right) \times 0.872 \text{ ml/min} \]  (5)

\[ \text{REE} = \left( 3.9 \times \text{VO}_2 \right) + \left( 1.1 \times \text{VCO}_2 \right) \times 1.44 \text{ kCal/day} \]

Where; \( V_E \) is the exhaled volume in ml/min and \( V_T \) is the tidal volume in ml displaced in time ‘T’ seconds.

The rate of oxygen and rate of carbon dioxide in the breath are dependent on two factors: the concentration of \( O_2 \) and \( CO_2 \) respectively and the exhaled volume. Our experiments and results (presented in chapter 4) showed that the \( O2 \) and \( CO2 \) concentrations determined by the chemical sensor were accurate and consistent,
but even then there were large variations in REE across the different measurements under same resting conditions.

It was due to the variation in exhaled volume, which was observed to be because of abnormal and different breathing patterns by the subjects at different times. Hence it is very important that the subject follows his/her natural breathing pattern consistently for accurate measurements and effective tracking of REE.

The bottom line is to come out with a solution that will reduce the variation in the breathing frequency at different times under similar resting state for an individual.

There is evidence for characteristic individuality of breathing pattern in conscious humans and there is high degree of reproducibility of breathing pattern within a subject [38]. An individual’s natural breathing pattern determination is the key point before proving the biofeedback. Adaptive biofeedback will provide freedom to the person to breathe at natural pace without an external biased control. Next, the challenges are to develop precise breathing pattern detection and adaptive biofeedback algorithms to provide effective biofeedback and also a successful method of reaching it to the user without any inconvenience. Literature reviews on music therapy demonstrates evidences that there are significant effects in controlling the respiratory pattern unconsciously with music [39, 40]. Hence we use an innovative approach of providing biofeedback with both musical and visual guidance. The motive is to guide the user to breathe at his/her individual resting breathing pattern unconsciously by following the music and visual effects that are correlated with the breathing pattern. Also, since the measurements of the metabolic parameters are based on short duration test and later extrapolated to 24-
hour time frame to estimate the energy expenditure in kCal/day. This requires a steady state measurement and adaptive biofeedback helps in maintaining steady state. Hence adaptive biofeedback is very crucial for accurate and consistent resting metabolic rate assessment.

3.2 Breathing Biofeedback in Wireless Energy Expenditure Analyzer

The breathing biofeedback in our system is based on using the pressure sensor in the device to acquire the breathing trace and transmit wirelessly to the Android smartphone via Bluetooth to determine the breathing frequency by digital signal processing techniques and provide musical and visual guidance to the user for breathing. I have developed a computationally efficient algorithm to determine the accurate breathing frequency from the breathing signal and call it “Dynamic Min-Max Algorithm” (DMMA). The schematic diagram of breathing biofeedback in the system is depicted in figure 3. The experiments and results (presented in chapter 4) shows that biofeedback with musical and visual guidance is capable of guiding the user to breathe conveniently at the user’s natural breathing rate and eventually make beneficial effects in measuring accurate resting metabolic rate by reducing variations between different measurements.
3.2.1. Musical Guidance

The algorithm as described in section 3.3.2 determines breathing frequency. Musical feedback through the smartphone speaker or earphone is provided to guide the user to inhale and exhale maintaining the natural breathing pace of the user. Three different musical options are provided to be selected based on the user’s choice. These music files have two rhythms to guide the user to breathe in and out at appropriate time. The tempo of the music is modified to correlate the rhythm with the breathing rate of the user. The tempo of the music is adjusted between 10 breaths per minute (bpm) and 20 bpm that are declared to be the normal breathing frequencies in humans at resting state [41]. Breath by breath real-time adaptive biofeedback was implemented, but later test-to-test adaptive biofeedback was implemented in the system in which Nth test is provided with the musical guidance correlating to the user’s breathing rate determined in (N-1)th test.
3.2.2. Visual Guidance

The system also provides visual feedback for breathing by showing the guidance on smartphone display. A pattern of feathers moving up and down freely in wave mode is shown to visually guide the users to adjust and reproduce their breathing patterns as shown in figure 4 below.

Figure 4: Visual Guidance

The wave pattern of the feathers indicates the user to breathe out when they flow upwards and to breathe in when they flow downwards. The moving pace of the feathers is determined by the breathing rate of the user similar to as described in musical guidance section with adaptive biofeedback. The visual guidance is delivered with the animation of 31 frames in the display layout. The visual guidance display consists of 3 breathing cycles as shown in figure. The time duration of each frame is determined by the breathing frequency to correlate the visual feedback with the breathing frequency of the user, given by equation (6) below.

\[
\text{Frame duration, } t = \frac{60 \cdot C \cdot 1000}{BF \cdot N} \text{ ms} \quad (6)
\]

Where; BF is breathing frequency in bpm

N=31, the number of frames

C=3, the number of breathing cycles in display layout
3.3 Breathing Signal Processing

The data from the pressure sensor is used as breathing signal for tracing the breathing pattern as shown in Fig 5 below.

![Breathing Signal]

Fig 5: Breathing Signal

A typical breathing signal consists of two phases: inspiration and expiration. An efficient algorithm has to be developed and implemented in smartphone to estimate the respiration phase and determine the breathing frequency to provide the biofeedback with musical and visual guidance for accurate resting metabolic rate assessment. The signal from the pressure sensor and the photodiodes are sampled by the microcontroller and transmitted through Bluetooth. Selecting the appropriate sampling rate is described below:

Nyquist-Shannon sampling theorem states that – “If a signal x(t) contains no frequencies higher than ‘B’ Hz, it is completely determined by giving its ordinates at a series of points spaced \( \frac{1}{2B} \) seconds apart” i.e., \( f_s >= 2*f_{max} \). [42].

Normal breathing rate for adults in resting state is stated to be between 10 bpm and 20 bpm. Considering a higher threshold with 24 bpm (0.4 Hz) to be the higher frequency content in the breathing signal, \( f_{max} = 24 \text{ bpm} = 0.4 \text{ Hz} \)
Sampling frequency, \( f_s \geq 2(0.4) \) i.e.; \( f_s \geq 0.8 \) Hz

Sampling Time, \( T_s \leq (1/0.8) \) i.e.; \( T_s \leq 1.25 \) s

Sampling frequency is chosen to be 4Hz, which is much higher than the Nyquist rate. Hence the breathing frequency can be accurately determined from the breathing signal that is sampled at the rate of 4Hz by the microcontroller and transmits the data wirelessly through Bluetooth to the smartphone via socket communication every 250ms.

Initially, the breathing frequency was determined by implementing Cooley-Tukey FFT algorithm in the smartphone. But this had several issues including the frequency resolution and computational complexity and hence had to develop an efficient algorithm to determine the accurate breathing frequency as described in following sections.

### 3.3.1 Problem in Breathing Frequency with FFT

Cooley-Tukey FFT (Fast Fourier Transform) algorithm was implemented to determine the breathing frequency. Let the sampled breathing signal be represented by \( p[n] \).

\[
\text{FFT}\{ p[n] \} = P[f]
\]

\[
\text{FFT size, } N \geq \text{number of samples in } p[n] = 2^n ; n = 1,2,3 \ldots \ldots
\]

\[
\text{Frequency, } f = \frac{f_s}{N}
\]

\[
\text{Frequency Resolution, } f_R = \frac{f_s}{N}
\]

\[
\text{Computation complexity} = N\log_2 N
\]
Where; I is the index corresponding to maximum amplitude in P[f]
f_s is the sampling frequency (4Hz in this application)
N is the FFT size

The problem faced is that the frequency resolution is bad with the low FFT size. To provide an effective biofeedback, the breathing frequency must be determined with accuracy close to 1 bpm (0.01666Hz). Better frequency resolution needs higher FFT size and it is known that the computational complexity is directly proportional to the FFT size given by N*\log_2 N for Cooley-Tukey algorithm. The comparison of frequency resolution in breathing signal with the required FFT size is shown in Table 2(a) and 2(b) below.

<table>
<thead>
<tr>
<th>( f_R ) (bpm)</th>
<th>( f_R ) (Hz)</th>
<th>( N = \frac{f_s}{f_R} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25</td>
<td>0.004166</td>
<td>960.15</td>
</tr>
<tr>
<td>0.5</td>
<td>0.00833</td>
<td>480.01</td>
</tr>
<tr>
<td>1</td>
<td>0.01666</td>
<td>240.09</td>
</tr>
<tr>
<td>2</td>
<td>0.03333</td>
<td>120.01</td>
</tr>
<tr>
<td>4</td>
<td>0.06666</td>
<td>60.06</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FFT Size ( N )</th>
<th>( f_R ) (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1024</td>
<td>0.23</td>
</tr>
<tr>
<td>512</td>
<td>0.46</td>
</tr>
<tr>
<td>256</td>
<td>0.93</td>
</tr>
<tr>
<td>128</td>
<td>1.8</td>
</tr>
<tr>
<td>64</td>
<td>3.75</td>
</tr>
</tbody>
</table>

\( N = 2^n \rightarrow \)

Table 2(a) and 2(b): Comparison of Frequency Resolution (\( f_R \)) with FFT Size (\( N \))

Table 2(b) indicates that a minimum FFT size of 256 is required to determine the breathing frequency at resolution close to 1 bpm. But with the sampling rate of 4 samples per second, it is not possible to determine the breathing frequency breath-by-breath with FFT at normal breathing pattern. Also the volume reached target that has been set to 3L in the device will be achieved in less than 1 minute of time (corresponds to 240 samples of data) for humans breathing at normal breathing rate in resting state i.e. 12 bpm to 20 bpm. Hence it is impossible to determine breath-by-breath breathing frequency with a frequency resolution of
less than 1 bpm with FFT for this application. On the other hand, it will be possible to determine the frequency with lesser number of samples but with a bad frequency resolution. Also, the computational complexity grows exponentially with the frequency resolution as shown in Fig 6 below. Since breathing at resting state is very low frequency signal, computationally expensive FFT is not an appropriate solution in the required application according to the justifications mentioned above.

![Graph: Computational Complexity Vs Frequency Resolution](image)

Fig 6: Computational Complexity Vs Frequency Resolution

### 3.3.2 Dynamic Min-Max Algorithm (DMMA)

An effective and simple algorithm is developed to determine the breath-by-breath breathing frequency very accurately and call it as DMMA (Dynamic Min-Max Algorithm) since the algorithm keeps updating the minimum and maximum values of the breathing signal dynamically every breathing cycle.
The algorithm is described below and figure 7 depicts the same for first two cycles:

- Maintain four flags and a counter:
  - Flag 1 → To detect start of breathing and to initiate the musical and visual guidance
  - Flag 2 → To detect the inspiration phase i.e. falling profile in the breathing signal
  - Flag 3 → Reference for breathing cycle completion
  - Flag 4 → To detect the expiration phase i.e. raising profile in the breathing signal
  - Counter → To keep track of the breathing cycles

Flag 1 is used only once and all the other three flags are SET and RESET accordingly every cycle while processing the signal

- Initialize all the four flags to FALSE (RESET state) and count = 1
• Minimum (Min) and Maximum (Max) values are updated every breathing cycle.

• If \((p[i] - p[i-1]) > \text{Threshold}\), SET Flag1 and start musical and visual guidance.

• Detect for signal falling profile i.e. \(p[i] < p[i-1] \) and \(p[i-1] < p[i-2]\) SET Flag2 and RESET Flag4.

• If Flag2 is SET, check for \(p[i] \leq \frac{\text{Min} + \text{Max}}{2}\). SET Flag3 and increment count and capture the time index along with count number i.e. \(t_n\).

• If Flag3 is SET, check for signal raising profile. SET Flag4, RESET Flag2 and Flag3.

• Repeat the same for every breathing cycle and maintain a key-value pair of count and time-index in a Hash Map \(<N,t_n>\).

• Frequency is determined by: \(f = \frac{4(N-1)}{t_n - t_1} \text{ Hz} \) \(\text{(10)}\)

Breathing Frequency, \(BF = f \times 60 \text{ bpm} \) \(\text{(11)}\)

Where; \(N\) is the count value i.e. \((N-1)\) corresponds to number of cycles

For breath-by-breath, \(N=2\)

\(t_n\) is the time-index at \(N^{th}\) count

\(t_1\) is the time-index at \(1^{st}\) count

For breath-by-breath frequency measurement: \(BF = \frac{4 \times 60}{t_2 - t_1} \text{ bpm} \) \(\text{(12)}\)

• On computing the frequency at \(N^{th}\) count, assign \(t_1 = t_n\) and reset \(\text{count} = 1\) and repeat the algorithm till the volume target is reached (i.e. Status = 1).
The algorithm is robust and takes care of noise. Figure 8 shows the breath-by-breath breathing frequency determined from the breathing signal.

![Breathing Frequency Detection](image)

Figure 8: Breathing Frequency Detection breath-by-breath

### 3.4 Adaptive Biofeedback Algorithms

After determining the breathing frequency on breath-by-breath basis, the focus is on establishing an algorithm to evaluate accurate natural breathing rate of a person. Evaluation of precise breathing rate of a person is important in providing the biofeedback. If the biofeedback provided during REE measurement test does not match the person’s actual breathing pattern, then the algorithm determines the current breathing rate to adapt the musical and visual feedback to achieve suitable breathing pattern. The breathing biofeedback provided with musical and visual guidance must be adaptive to the previously determined breathing frequency to comfort the user to breathe naturally i.e.; the $N^{th}$ test is provided with biofeedback based on the breathing rate determined in the $(N-1)^{th}$ test. Three algorithms are proposed to evaluate the breathing signal and select the precise breathing rate of
the person to provide biofeedback, they are: Average Breathing Rate Selection (ABRS), Consecutive Occurrence Breathing Rate Selection (CBRS) and Maximal Breathing Rate Selection (MBRS). These algorithms are explained below with an example of a typical breathing signal as shown in figure 9 below.

(i) Average Breathing Rate Selection (ABRS)

The breathing rate selected for the biofeedback with musical and visual guidance is based on the average of the breath-by-breath breathing frequency detected by the DMMA algorithm.

\[ BF = \frac{\sum_{i=1}^{N} f_i}{N} \]  \hspace{1cm} (13)

Where; \( N \) is the number of breathing cycles in the signal
\( f_i \) is the breathing frequency of \( i^{th} \) cycle

In the case of breathing signal shown above with 9 cycles, the breathing frequency will be obtained as: \[ BF = \frac{11+13+13+9+13+15+11+13}{9} = 12.3 \text{ bpm} \]

(ii) Consecutive Occurrence Breathing Rate Selection (CBRS)

The musical and visual guidance are adapted to user’s breathing rate that occurs consecutively for at least three cycles. If more than one value occurs consecutively, then the average of them is taken.

Figure 9: Breath-by-Breath breathing frequency
In the breathing signal above, only the cycles with breathing frequency equal to 13 occurs thrice consecutively. Hence 13 bpm will be selected for biofeedback in this case.

(iii) Maximal Breathing Rate Selection (CBRS)

The biofeedback with musical and visual guidance are provided such that they correlate with the breathing rate that occurs maximum number of times in ‘N’ cycles within a breathing test. If there is multiple frequencies occur with the maximum number of times, then the average of them is taken. In the breathing signal example shown in Fig 9 above, there are 9 cycles out of which 9 bpm occurs once, 11 bpm occurs twice, 13 bpm occurs five times and 15 bpm occurs once. Since 13 bpm occurs the maximum number of times, 13 bpm will be selected for biofeedback in this case.

Evaluation of ABRS, CBRS and MBRS algorithms for choosing the best one among these is presented in the next chapter.
RESULTS AND DISCUSSIONS

Reducing the coefficient of variation \( \frac{\sigma}{\mu} \) in the metabolic parameters between different measurements is of prime importance in accurate resting metabolic rate assessment. The metabolic parameters include breathing rate, \( V_E \), \( VO_2 \), \( VCO_2 \) and REE/RMR. The impact of adaptive biofeedback in achieving steady state during the REE measurement is assessed. The focus is not only on reducing the variations of metabolic parameters within a single measurement, but also on reducing the variations between different measurements and obtaining accurate resting metabolic rate for long term tracking of metabolism syndromes. The emphasis is to validate the breathing frequency detection algorithm to provide precise biofeedback with musical and visual guidance customized to an individual. Evaluation of the adaptive biofeedback algorithms described in section 3.4 is also important in selecting the best algorithm that determines the precise natural breathing rate of a person. With these pre-requisites for adaptive biofeedback, the study involved assessing the effect of musical guidance on breathing pattern, \( V_E \), \( VO_2 \), \( VCO_2 \) and REE with 22 healthy subjects. A comparison in the coefficient of variation of metabolic parameters with and without adaptive biofeedback was made for each subject. Oxycon\textsuperscript{TM} [43] instrument is used in the study, which is validated and approved by FDA (K023120). The subjects were ensured to be in resting state with four hours of fasting prior to each measurement and also the purpose of music played was not informed to check if they unconsciously followed their breathing pattern with the
musical guidance. More details on the experiments and test protocols are discussed in following sections along with the results and statistical analysis.

4.1 Validation of DMMA with Oxycon

The breathing frequency determined by the Dynamic Min-Max Algorithm (DMMA) is compared with the results obtained with commercial device Oxycon™ that has been well known for breath-by-breath measurements. The setup for the validation is as shown in figure 10 below, where the breath from the mouthpiece flows through the Oxycon™ device and our wireless energy expenditure analyzer simultaneously. The DMMA algorithm in the smartphone determines the breath-by-breath breathing frequency with signal processing techniques.

Figure 10: Setup for DMMA Validation
• Testing Protocol:

The tests were performed in such a way by following the musical guidance corresponding to breathing frequency in the range of 12bpm to 20bpm. Each test was performed for 1-minute duration and the final breathing frequency in Table 3 represents the average of breath-by-breath values obtained in the test.

Table 3: Comparison of DMMA with Oxycon™

<table>
<thead>
<tr>
<th>Breathing Frequency DMMA (in bpm)</th>
<th>Breathing Frequency Oxycon™ (in bpm)</th>
<th>% Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.02</td>
<td>12</td>
<td>0.16 %</td>
</tr>
<tr>
<td>13.06</td>
<td>13</td>
<td>0.46 %</td>
</tr>
<tr>
<td>13.90</td>
<td>14</td>
<td>0.71 %</td>
</tr>
<tr>
<td>15.04</td>
<td>15</td>
<td>0.26 %</td>
</tr>
<tr>
<td>16.02</td>
<td>16.15</td>
<td>0.80 %</td>
</tr>
<tr>
<td>17.01</td>
<td>16.83</td>
<td>1.06 %</td>
</tr>
<tr>
<td>18.04</td>
<td>18.14</td>
<td>0.55 %</td>
</tr>
<tr>
<td>18.98</td>
<td>18.85</td>
<td>0.68 %</td>
</tr>
<tr>
<td>20.01</td>
<td>20</td>
<td>0.05 %</td>
</tr>
</tbody>
</table>

• Statistical Analysis:

The validation results show that the breathing frequency determined by DMMA is very accurate and the error rate is less than 1%. The mean values of breathing frequency measured by DMMA and Oxycon™ are compared using paired t-test indicating the results obtained by two devices are not statistically different (p < 0.001). The correlation between the results obtained with DMMA
algorithm in the phone and Oxycon™ are assessed using linear regression analysis. Fig.11 below shows the regression analysis between the breathing frequency obtained by DMMA and Oxycon™ with correlation coefficient of R=0.99997. These results indicate that algorithm determines very accurate breathing frequency.

Fig. 11: Regression Analysis between DMMA and Oxycon™ for breathing frequency

4.2 Evaluation of Adaptive Biofeedback Algorithms

The hypothesis is to compare the Average Breathing Rate Selection (ABRS), Consecutive Occurrence Breathing Rate Selection (CBRS) and Maximal Breathing Rate Selection (MBRS) algorithms that determines the precise breathing rate of the person to provide the adaptive biofeedback focused on accurate metabolic rate assessment.
• Testing Protocol:

The tests were performed on 11 healthy subjects (4 males, 7 females) with Oxycon instrument. The measurements were taken for 10 minutes for each subject to determine the natural breathing rate in resting condition. The subjects were asked to relax and breathe normally with the mask at a comfortable seating position. Oxycon provides reading every 10 seconds, so there were totally 600 data points accumulated for every subject. This data was processed using the ABRS, CBRS and MBRS algorithms to determine the overall breathing rate for each subject.

The table below shows the comparison of breathing rate obtained with ABRS, CBRS and MBRS algorithms.

Table 4: Comparison of Adaptive Biofeedback Algorithms

<table>
<thead>
<tr>
<th>Subject</th>
<th>ABRS (bpm)</th>
<th>CBRS (bpm)</th>
<th>MBRS (bpm)</th>
<th>Coefficient of variation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13.5</td>
<td>13.35</td>
<td>13.5</td>
<td>0.64 %</td>
</tr>
<tr>
<td>2</td>
<td>19</td>
<td>19.5</td>
<td>19.75</td>
<td>1.95 %</td>
</tr>
<tr>
<td>3</td>
<td>18</td>
<td>---</td>
<td>19</td>
<td>---</td>
</tr>
<tr>
<td>4</td>
<td>11.67</td>
<td>11.7</td>
<td>12</td>
<td>1.52 %</td>
</tr>
<tr>
<td>5</td>
<td>19.6</td>
<td>19.3</td>
<td>19.5</td>
<td>0.56 %</td>
</tr>
<tr>
<td>6</td>
<td>14</td>
<td>14.75</td>
<td>14</td>
<td>0.3 %</td>
</tr>
<tr>
<td>7</td>
<td>22</td>
<td>---</td>
<td>19</td>
<td>---</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
<td>17.5</td>
<td>17</td>
<td>4.5 %</td>
</tr>
<tr>
<td>9</td>
<td>12.5</td>
<td>12.25</td>
<td>12</td>
<td>2.04 %</td>
</tr>
<tr>
<td>10</td>
<td>16</td>
<td>16.59</td>
<td>16</td>
<td>2.1 %</td>
</tr>
<tr>
<td>11</td>
<td>12</td>
<td>12.3</td>
<td>12</td>
<td>1.4 %</td>
</tr>
</tbody>
</table>
The results show that all the three algorithms provide almost similar overall breathing rates with the coefficient of variation being less than 5%. Also, overall breathing rate was not able to be determined with CBRS for two subjects since three consecutive equal breathing patterns were not observed (as shown in “---“ in the table). So clearly CBRS is ruled out. Among ABRS and MBRS, I chose ABRS algorithm for the study in experimenting the impact of adaptive biofeedback in REE assessment due to its simplicity in computing the overall breathing rate by averaging the breath-by-breath values and also provides similar results in par with the MBRS.

4.3 Impact of Adaptive Biofeedback in REE Assessment

REE is dependent on the rate of oxygen (VO$_2$) and rate of carbon dioxide (VO$_2$) in the breath, which are in turn dependent on exhaled volume (V$_E$) and the concentrations of O2 and CO2. The hypothesis is to measure accurate and consistent exhaled volume without user bias by unconsciously guiding the user to follow his/her natural breathing pattern in resting with musical rhythm that correlates with the breathing pattern. The music played for guidance is unique to a user and adapted to different pace correlating to the their regular breathing pattern in resting state.

- Testing protocol:

Twenty-two healthy subjects (12 men, 10 women) were tested with Oxycon$^{TM}$ Mobile instrument for the study of variations in metabolic parameters (BF,V$_E$,VO$_2$,VCO$_2$,REE) with and without adaptive biofeedback musical
guidance. Eight tests of 1-minute duration were taken for every subject among which, four tests were without biofeedback and four tests with adaptive biofeedback musical guidance. The tests were taken on different days and it was ensured that the subjects were in complete resting state with no heavy physical activities or exercises in four hours prior to the test. Also, the subjects were on four hours fasting before each test to avoid the thermogenic effects in energy expenditure measurement. The subjects were seated in a comfortable position during the test. The initial test was without any musical guidance to determine the natural breathing rate and subsequent tests with adaptive biofeedback were provided with the musical guidance correlating to the breathing rate determined in the previous test. The subjects were provided with three different music options and requested to select based on their preference. Each of the music had two rhythms to guide the user to breathe in and out at appropriate time. The tempo of the music was modified to correlate the rhythm with the breathing rate of the user. The users were not informed about the actual purpose of the music being played and were told that the music was to relax them. This was to avoid the user bias of conscious control on breathing and check whether they unconsciously followed their breathing pattern with the musical guidance.

The breathing signal plot in figure 12 below shows the variation of breathing frequency within a test in the absence of musical guidance and improved consistency with guidance. Also the bar graph depicts that the coefficient of variation of breathing frequency between different tests is reduced with adaptive biofeedback.
Figure 12: Impact on breathing with Adaptive Biofeedback musical guidance

The bar graph in the above figure shows the comparison of variations in breathing frequency with and without biofeedback for seven subjects. However, similar results are also obtained for the other subjects as shown in the summary table 6. The results obtained from the study for one of the subject are shown below. The mean and standard deviation are from the measurements obtained from four different tests i.e. four tests without any biofeedback and four tests with adaptive biofeedback.
Table 5: Comparison of metabolic parameters with and without biofeedback

<table>
<thead>
<tr>
<th>Metabolic parameters</th>
<th>Without Biofeedback</th>
<th>With Adaptive Biofeedback</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Coefficient of variation</td>
</tr>
<tr>
<td>BF</td>
<td>17.81 ± 1.21</td>
<td>6.79 %</td>
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<tr>
<td>VE</td>
<td>6506 ± 1755</td>
<td>26.97 %</td>
</tr>
<tr>
<td>VO₂</td>
<td>182.04 ± 39.79</td>
<td>21.85 %</td>
</tr>
<tr>
<td>VCO₂</td>
<td>149.16 ± 39.01</td>
<td>26.15 %</td>
</tr>
<tr>
<td>REE</td>
<td>1238 ± 287</td>
<td>23.18 %</td>
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</tbody>
</table>

Where; BF is the breathing frequency in bpm
VE is exhaled volume in ml/min
VO₂ is rate of oxygen in ml/min
VCO₂ is rate of carbon dioxide in ml/min
REE is resting energy expenditure in kCal/day

The results clearly indicate that the variations in the metabolic parameters are reduced by a significant amount with adaptive biofeedback. Also, it can be observed that the subjects unconsciously followed their breathing pattern with the musical guidance yielding consistent and accurate results for the REE assessment.

The comparison of coefficient of variation in the metabolic parameters with and without biofeedback is shown in Fig.13 below.

- **Statistical Analysis and summary:**

The variations in the metabolic parameters obtained with adaptive biofeedback and without biofeedback are compared using statistical f-test to determine whether an observed difference between standard deviations of two sets of data is statistically significant.
Fig. 13: Comparison of variations in metabolic parameters without and with biofeedback

The obtained f-statistic indicated that the variations in the metabolic parameters reduced significantly ($p < 0.05$) with adaptive biofeedback musical guidance. Table 6 provides the summary of improvement in the variations of metabolic parameters for 22 subjects indicating that the variations in breathing rate improved in 20 subjects (90.9%), exhaled volume improved in 19 subjects (86.36%), rate of oxygen and rate of carbon dioxide improved in 16 subjects (72.72%) and resting energy expenditure improved in 17 subjects (77.27%).
Table 6: Summary of improvements in results with adaptive biofeedback

<table>
<thead>
<tr>
<th>Subject</th>
<th>BF</th>
<th>VE</th>
<th>VO₂</th>
<th>VCO₂</th>
<th>REE</th>
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</table>

✔: Coefficient of variation reduced with adaptive biofeedback musical guidance
✘: Coefficient of variation not reduced with adaptive biofeedback musical guidance
CONCLUSION

An effective and user-friendly mobile health system with adaptive biofeedback technology was developed. Adaptive biofeedback can be used in mobile health systems for number of applications needing accurate physiological information in remote health monitoring and diagnosis. Resting metabolic rate measurement and tracking is one of the examples shown in this work. Mobile health systems developed with innovative engineering principles like adaptive biofeedback mechanisms with advanced wireless and mobile technologies may be used to benefit the society in achieving efficient healthcare.

This work has provided a comprehensive study and demonstrated the importance of adaptive biofeedback musical and visual guidance for accurate resting metabolic rate assessment along with the statistical evidence. The results obtained reveal that the subjects followed their breathing pattern with musical guidance unconsciously. This study also involved thorough evaluation of breathing rate detection algorithm and adaptive biofeedback algorithms for effective breathing guidance.
VISION FOR FUTURE RESEARCH

The future of mobile health systems relies on motivating the people to use these systems regularly with convenience. Disease preventing games with biofeedback mechanisms can be developed creating competitive spirit in the users by motivating them to be emotionally involved in the game. With the advancements in the multimedia technologies in the smartphones, enhanced games with visual and audio influence can be developed to control and regulate the physiological parameters like respiratory rate, blood pressure, heart rate etc. with adaptive biofeedback.

Cloud computing play a crucial role in the future of mobile health systems. A context aware framework with intelligent algorithms can be developed that automatically determines the abnormality in the health information of the patient and any health threat in advanced based on the patient’s historical health data available in the database of the cloud.
REFERENCES


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