UNIVERSITY „POLITEHNICA” FROM BUCHAREST

DOCTORAL SCHOOL ETTI-B

Nr. Decision *756* / 08.11.2021

THESIS

CONTRIBUTIONS TO INTELLIGENT MEDICAL SYSTEMS

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DOCTORAL COMMISSION

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BUCHAREST 2021

Content

Chapter 1 - Introduction

The introduction presents the field of the thesis, the purpose of the thesis and its content and make a short presentation of each chapter of thesis. It is described each chapter with theroy and research, test and results.

Smart medical systems differ from human specialists in many respects in that an Smart Medical System cannot come to conclusions intuitively. He also cannot examine a situation from various perspectives. They cannot use primordial principles to reason and cannot draw analogies. They usually cannot learn from experience. But with the evolution of technology, intelligent Medical Systems could be developed that can learn, and be able to improve their dynamic knowledge. This would be a close collaboration with Neural Networks, collaborations that could give exceptional results and that could be of real help. And in this sense we can talk about neural systems and their realization in the form of medical computer modules. In this sense we can speak of nonlinear adaptive systems, whose outputs and inputs can be modified by adjusting some parameters during a training process with exclusively bio-medical data.

At the moment the general trend is to replace the human expert with the artificial one because the human specialist is more difficult to approach, is very busy and cannot be in more places, or more experts and specialists are needed, but they do not they are used to confronting their points of view. Also, in the case of process management systems, it is possible to expand human expertise in a way that benefits from a shorter reaction time and increased memory and learning capacity

Chapter 2 – Achievements in the field

This chapter discusses artificial intelligence in medical smart systems, the contributions that have been made to these systems, how they work, and what achievements have been made so far. In this sense, human knowledge in the analysis of complex medical data can be organized and automated with the help of intelligent medical systems, whose main purpose is to analyze the relationship between prevention or treatment techniques and patient outcomes, based on the acquisition of non-invasive signals. Thus, the processing of digital bio-medical signals is an area that can help the rapid diagnosis and treatment as reliable as possible to patients.

The combination of medical signals, such as ECG combined with EMG or EEG, helps a lot in the careful observation of the diseases that patients suffer from. In this chapter we discussed the classic methods of measuring glucose, which use the oxidation of glucose in oxidized glucose-catalyzed glucolactone (GOX). A similar catalyzed reaction called glucose dehydrogenase (GDH) is also used, due to its higher sensitivity to oxidized glucose catalysis, and reactions with other substances. These methods tend to be replaced by modern methods of glucose detection, namely modern non-invasive spectroscopic methods, promising results appearing in the field of NIRS (near-infrared spectroscopic wave).

Chapter 3 – Intelligent medical systems

This chapter deals with intelligent medical systems, what they are, what they do and what solutions they propose for the medical field. Thus, an intelligent medical system is a program that aims to obtain results related to a medical activity or field in which this is difficult to achieve, in a manner similar to that used by human experts. The skeleton of an intelligent medical system is primarily related to a knowledge base and a search algorithm specific to the method used by reasoning. Thus, it can be said about an intelligent medical system, that it successfully treats problems where there is no clear solutionon.

Chapter 4 – Measurement and detection of blood glucose by noninvasive methods

The chapter discusses the detection and measurement of blood glucose by non-invasive methods, current or older methods of measuring blood sugar, current and future research. Noninvasive methods aim to measure blood sugar without taking blood samples. Blood sugar has always been a challenge for specialists. Detection of blood glucose plays an important role in a patient's health, as glucose must be maintained in a constant proportion of the body and carries large amounts of glucose from the body's blood and tissues. The new non-invasive methods are based on spectroscopic monitoring, through near infrared sensors with wavelengths between 900 ~ 2000 nm.

Chapter 5 – Absorbance and colorimetry algorithms for measuring blood glucose

This chapter discusses methods and algorithms for detecting and measuring blood glucose by non-invasive methods. The studied methods are: amperometric method, spectrophotometric method, reflectometric method, nuclear magnetic resonance, colorimetric method, spectroscopic photo-acoustic method and NIR spectroscopic. The problems are focused on the absorption of light in matter and the measurement of blood glucose based on chromatic calculus. In chromaticity the values depend only on the dominant wavelength and saturation. Complementary colors are those that can be mixed to produce white light, which would represent the presence of glucose.

Chapter 6 – Measurement of blood glucose by near-infrared skin spectroscopy

This chapter discusses various invasive and non-invasive methods available for measuring blood sugar. But for this we need to do a dermatological measurement first before it reaches the capillaries and the blood. There are several branches in the dermatological field that can make a timely measurement and diagnosis. Current diagnostic tools in dermatology include the analysis of a clinical history and the performance of a treatment based on visual examination, followed by a skin biopsy or by performing blood tests and cultures. These techniques have significant limitations and most are expensive and somewhat invasive. Skin cancer, inflammatory diseases and infectious skin diseases are all pathologies that would benefit from rapid, objective and non-invasive testing and diagnosis. In addition, we can measure blood glucose, because spectroscopic light passes through skin tissues. Thus, the measurement and determination of blood glucose require the measurement of collagen content, skin thickness, determination of the effectiveness of skin protection agents and the effects of irradiation of skin tissue. Diabetes is the most common condition in the world. Measurement of blood glucose by near infrared (NIR) is dependent in this respect on the measurements of light through the layers of the skin, before reaching the capillaries.

Chapter 7 – Glucometry and Pulse Oximetry - Comparative Noninvasive Methods for Determining Blood Glucose

The chapter aims to study non-invasive detection methods for determining blood glucose compared to pulse oximetry. Glucometry and pulse oximetry are two methods that are based on the absorption of light into tissues. Pulse oximetry measures the saturation of oxygen in the blood based on red light, using a wavelength of 600-750 nm, and infrared light, using a wavelength of 850-1000 nm. We will use the same method to detect blood glucose. Glucose has slight absorption points at wavelengths of 940 nm ~ 2326 nm. But at 940 nm, the attenuation of the wavelength by the optical signals of other blood constituents such as water, platelets, lymphocytes, etc. is the minimum wavelength where the actual blood glucose concentration can be determined. There are cases when during surgery or postoperatively, when these vital signs must be monitored continuously to ensure surgery on the patient. There are medical procedures that produce accurate results, but the only downside is that they are invasive, so they come with a pain factor. This non-invasive method is based on the principle of the pulse of the oximeter and combines the principle of the glucose meter called OGH monitor which calculates the oxygen saturation, glucose and heartbeat of an individual, without actually depending on parameters such as blood samples, urine samples. This monitoring is based on the principle of differential light absorption, which is considered the input parameter to produce three different parameters, such as the percentage of oxygen saturation, glucose and heart rate.

Chapter 8 – Blood analysis and measurement by infrared spectroscopy. Blood glucose - an element of study

Blood tests can help a doctor detect certain diseases that a patient is suffering from in time. A rapid analysis, done by modern means such as the NIRS method of spectroscopic analysis, can reduce the time of determination and analysis of the blood so that a patient can be prescribed the treatment as soon as possible. The blood is very complex and difficult to analyze, so several case studies have been taken. The element studied in this case was blood glucose, because too much leads to diabetes. Blood tests are one of the most important routine methods used by doctors to diagnose a patient's health or the evolution of a disease at a given time. These blood tests can help the doctor diagnose the functionality of certain internal organs such as the liver, heart, kidneys, etc., observe and prevent the occurrence of diseases such as anemia, diabetes, or check and evaluate certain prescribed treatments. This paper aims to analyze the blood by the method of absorption and reflection by near infrared (NIR), taking as a case study the analysis and monitoring of blood glucose, cholesterol or blood count.

Chapter 9 – Digital processing of biological signals: ECG, EMG

In this chapter, we will discuss methods and algorithms for processing biological signals and displaying their interpretation using development platforms, which allow digital acquisition and processing of biological signals. The digital signal processing is a bio-medical field that can help diagnose a faster and more reliable treatment of patients. The combination of digital medical signals, such as ECG or EEG with EMG, helps a lot in the careful observation of patients with the disease. Biological signals can come from different types of sources: audio, video, electrical, magnetic, etc. They have become electrical due to the methods of capturing and using transducers, such as sensors that measure physical and chemical values. The processing of the signal is based on the processing of the biological electrical properties of the material beings of the living body, which appear in the tissues.

Biological signals can be correlated with mechanical, magnetic and used in the analysis of the biological signal. In terms of biological signal acquisition technique, it is currently working with the latest Biological Signal Import Module (BSIM) technology that supports the acquisition of analog biological signals (2.5 V) from sensors such as a pH electrode or a detector. UV. BSIM aims to act in several channels to acquire and interpret data based on the appropriate software on several acquisition channels. Thus, a module that receives signals from multiple electrodes may be able to generate data for ECG and EMG signal type analysis.

Chapter 10 – Blood analysis by near-infrared spectroscopically

This chapter aims to address the measurement of blood elements based on non-invasive spectroscopic methods, namely by close infrasound. The analysis of blood vessels and the blood itself are very important in medical research. Human blood provides information about the health and possible diseases or strokes that a patient may have at some point. In this chapter we will discuss the method of blood analysis by near infrared. For this we have developed a software that takes the data and analyzes the results at the same time as the heartbeat.

Chapter 11 – Near infrared mass spectrometry on tissues

Spectroscopic analysis of human tissue starts from the analysis of cell mass spectrometry. This technique interdisciplinary combines the laws of chemistry, physics and biology. The technique could in the near future recompose both biologically-physically and imagistically, a human tissue following a faithful spectroscopic investigation, or it could help to treat and prevent diseases. Mass spectrometry analyzes tissues and cell masses at the level of biomolecule, small organic molecules, as well as their atoms and isotopes. Mass spectroscopy, which we will refer to in this chapter, in connection with mass analysis of tissues and molecular cells, has applications at this time in all fields of science, from chemistry to physics, biology, medicine and pharmacology.

Chapter 12 – Hardware and software prototype

The hardware part of the prototype proposed in this thesis deals with data acquisition and uses development boards that can communicate serially, can collect signals directly from sensors or other modules can be attached to the basic prototype. All retrieved data is transmitted serially to a device with an operating system to be processed and interpreted. The software part is the one that collects the data from the hardware prototype. The data is collected by first communicating the development board (Arduino in our case) with the attached sensors or modules.

Chapter 13 - Conclusions

3.1 Conclusions on the thesis

This thesis deals with a study related to medical contributions through noninvasive spectroscopic analysis, which has recently become a very rapid diagnostic tool for many medical situations. In this sense, the measurement and monitoring of blood glucose, the rapid analysis of blood by non-invasive spectroscopic methods are currently challenges that will revolutionize the medical world and come to the aid of patients.

The research in this thesis is focused on improving and expanding knowledge on non-invasive spectroscopic methods. These proposed methods are included with their implementation theories and philosophies to evaluate their performance using different types of ultrasound images. Spectroscopic scanning and monitoring are beginning to play an increasing role in contemporary medical technologies due to the short time and easy results that can be obtained. Spectroscopic blood analysis is a challenge that can bring amazing results related to the monitoring and measurement of certain elements in the human body: blood, skin, glucose, or other tissues or organs in the human body. That is why in this thesis we focused more on studies related to noninvasive near-infrared (NIR) spectroscopy, because it works in an approximate band length that covers several tissues and elements in the human body.

Wavelength values are between 480 ~ 1800nm, enough wavelengths to analyze certain layers. In order to reach the capillaries, the spectroscopic wave must first pass through the layers of the skin. The absorption rate and the reflection rate are two parameters that help us calculate how much of the light passes through absorption, and how much of it is reflected back. This rate allows us to calculate layer by layer to capillaries, which is the area of interest. In modern medicine, the analysis of blood and its compositional structure is a great challenge, when classical invasive methods must be replaced by non-invasive ones. The absorption of light in matter is the solution by which we can separate ourselves from invasive methods and follow a new path, that of non-invasive spectroscopic methods. Because these methods have unimaginable advantages for the rapid monitoring, measurement and diagnosis of a patient suffering from certain diseases. Time and noninvasive measurement are the two gains of these non-invasive spectroscopic methods.

Equipping both patients and medical institutions (hospitals, laboratories, clinics, pharmacies) with such devices that do not require complex handling. Therefore, for example, to analyze an element in the blood, such as glucose, we need to consider all the phases that light absorption goes through. Before reaching glucose, light must pass through several environments in the human body to reach its destination. This involves the absorption and reflection of light through the environments it passes through. That is why we need to calculate the amount of light absorbed and reflected from each level passed by the light. The research in this thesis focused on near infrared light, due to the wavelengths that can be worked with, from 480 nm ~ 1800 nm, wavelengths that allow us to analyze the different tissue media on which light it crosses them. Light to reach the capillaries must pass through the first tissue medium of the human body: the skin. It has three solid layers, which contain different elements that strongly reflect light, thus making the absorption of light much more difficult.

The three layers of the skin, epidermis, dermis and hypodermis, have in their composition various elements that are in a lower or higher concentration depending on age, color and weight of tissue. All these details make it difficult to calculate absorption and reflection through matter. When it reaches the capillaries, the first element it hits is hemoglobin, the only element after which we can realize that we have reached the blood vessels from where we can make measurements on the blood and its elements formed. Each element in the blood has a wavelength in which it has a great absorption of light. A multi-channel sensor for different tissue media that light sneezes can help us realize how much light is absorbed by various media in biological tissue.

The role that contemporary noninvasive methods can have is revolutionary, due to the mode of action and the time gained in monitoring, measuring and diagnosing patients quickly.

In addition to the proposed hardware prototype for non-invasive spectroscopic measurement and monitoring, we also proposed software with a friendly interface to process and display the data to be purchased. Therefore, we can talk about an expert medical system that combines hardware and software. The applications of this intelligent medical system can be expanded and improved with each new version.

From glucometry to hemoleukogram and imaging or radiology. It all depends on the new modules that can be attached to this smart medical system. This smart medical system is cross-platform, it can be run on desktop systems, tablets or smartphones. In this sense, a serial communication interface has been developed that takes the data from the hardware and transmits it serially to a software application that can run on both smartphones and desktops. Portability is one of the attributes of this intelligent medical system that wants to cover as wide a range of medical solutions as possible in hospitals. In this thesis the focus was on measuring and monitoring blood glucose, but also on extending these analyzes to the skin and blood, as well as on the processing and interpretation of biological signals such as ECG and EMG, with the possibility of extension to EEG signals.

An intelligent medical system is useful given that it has a widespread use in as many fields as possible, from neurological problems to imaging and radiology problems. Non-invasive spectroscopic methods, along with imaging, electromagnetic, nuclear magnetic resonance, provide fast and accurate results. Unlike the other methods mentioned above, near infrared spectroscopic methods have the advantage of portability, discretion and speed. The accuracy of the results and the data processing algorithms are two indeterminate ones that will be improved over time to outline in the future an intelligent medical system that can measure, monitor and diagnose a patient in any location and at any time when the situation requires.

In conclusion, a smart medical system, in order to have success, needs to implement at the moment the following attributes: portability, speed, accessibility and accuracy.

3.2 Original contributions

- The original contributions in this thesis are related to the following aspects:
- Monitoring and measurement of noninvasive glucose by near infrared spectroscopy;
- Blood processing and analysis by spectroscopic methods: plasma and formed elements (erythrocytes, leukocytes, platelets, etc.);

- Processing and interpretation of biological signals: ECK and EEG;
- Development of a hardware prototype that implements the noninvasive method in near infrared (NIR);
- Development of software to acquire and process biological data;
- Development of an intelligent medical system, which incorporates the hardware and software component;

3.3 Original list of publications

The content of this thesis has been published in several nationally and internationally recognized conferences and journals:

- **Marius Ionescu** – "*Measuring and detecting blood glucose by methods non-invasive*", pp 1-6, ECAI 2018 - International Conference – 10th Edition Electronics, Computers and Artificial Intelligence, June 28 - 30, 2018, Iasi, ROMÂNIA, ISBN:978-1-5386-4900-8, **WOS: 000467734100014**
- **Marius Ionescu**, Pașca Sever – "Algorithms of Absorbance and Colorimeter for Measuring Blood Glucose", pp 1-6, ATEE 2019 - THE 11th INTERNATIONAL SYMPOSIUM ON ADVANCED TOPICS IN ELECTRICAL ENGINEERING, March 28-30, 2019, Bucharest, ROMÂNIA, ISSN: 2068-7966, **WOS: 000475904500043**
- **Marius Ionescu**, Pașca Sever – "Measuring blood with spectroscopy skin in near infrared", pp 1-6, ECAI 2019 - International Conference – 11th Edition Electronics, Computers and Artificial Intelligence, June 27 - 29, 2019, Pitesti, ROMÂNIA, ISBN:978-1-7281-1623-5, **WOS: 000569985400068**
- **Marius Ionescu** – "Glucometry and Pulse Oximetry - Comparative Noninvasive Methods for Determining Blood Glucose", pp 1-4, EHB 2019 - The 7th IEEE International Conference on E-Health and Bioengineering, November 21-23, 2019, Iasi, ROMÂNIA, ISSN: 2575-5137, **WOS: 000558648300132**
- **Marius Ionescu** – "Biological Digital Signal Processing Interpretation and Combination", pp 1-6, The Twelfth International Conference on Bioinformatics, Biocomputational Systems and Biotechnologies BIOTECHNO 2020, September 27, 2020 to October 01, 2020 - Lisbon, Portugal, ISSN: 2308-4383
- **Marius Ionescu** – "Analysis of blood by Spectroscopy Near Infrared", pp 1-6, ECAI 2020 - International Conference – 12th Edition Electronics, Computers

and Artificial Intelligence, June 25 - 27, 2020, Bucuresti, ROMÂNIA, ISBN:978-1-7281-6844-9, **WOS: 000627393500055**

- **Marius Ionescu** – "Measuring and analysis of blood glucose using near infrared spectroscopy", pp 1-4, 28th Telecommunications Forum TELFOR 2020, 24-25 November 2020, Belgrade, Serbia, ISBN:978-1-6654-0500-3, **WOS: 000666945500040**
- **Marius Ionescu** – "Spectroscopy mass of Near Infrared in medicine", pp 1-6, ATEE 2021 - THE 12th INTERNATIONAL SYMPOSIUM ON ADVANCED TOPICS IN ELECTRICAL ENGINEERING, March 25-27, 2021, Bucharest, ROMÂNIA, ISSN: 2068-7966, **WOS:000676164800023**

3.4 Area of future research

Future research will seek to expand the range of noninvasive spectroscopic applications in other medical fields, refining current ones. In this sense, the research will expand in the field of spectroscopic imaging trying to measure and monitor the functionality of several tissues and organs in the human body. But all this based on the results obtained and recognized in the current field of application of this thesis: the analysis of glucose and blood.

Spectroscopic techniques have found increasing applications in the field of biomedicine, especially in the field of disease diagnosis and monitoring, despite the rapid emergence of several techniques based on molecular biology. Spectroscopy can analyze areas of human tissue based on near-infrared light (NIR) very quickly and without physical intervention at the level of biological tissue.

That is why in the future we will focus on the following research:

• More accurate determination of glucose depending on age, skin color, stress;

• Detailed blood analysis: precise quantity by broken down quantity: plasma and formed elements (water, nutrients and formed elements erythrocytes, leukocytes and thrombocytes);

• In-depth analysis of skin layers and the amount of light reflected and absorbed;

• Extending spectroscopic measurements to other organs in the body: heart, liver, stomach, kidneys or brain;

• Continuing to develop and expand the functionality of the software application with the possibility of saving and journaling the data purchased on the patient;

• Creating a modular hardware device in the form of a smart device, which supports gsm, gps and other functions useful for data transmission. Possibility to add plug in modules on this device;

Future research will extend the results obtained in this thesis to other biomedical fields, hoping to bring improvements from one version to another.

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