CARBON-BASED MATERIALS FOR HEALTHCARE MICRO-DEVICES

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ABSTRACT: Microtechnology is one of the key technologies supporting the behaviour for healthier life, including disease prevention and faster healing. An amazing demand for autonomous micro-devices in "healthcare" field is raising the need for miniaturized power sources. These micro-devices need to be made of durable, hard but flexible materials and also easy to use materials. For all these demands, a research on carbon-based materials was made. So, it was found that combinations of carbon-based materials can be made, because this need means more power, more strength and more rapid time of response. Graphene, Carbon Nanohorns (CNHs) and Carbon Nanotubes (CNTs) were the three carbon-based materials studied in this research and their properties of being adaptable to micro-devices for healthcare.
KEYWORDS: Carbon-based materials, micro devices, healthcare.

1. INTRODUCTION

The microtechnology field doesn't know any limitations, beeing constantly on the rise. An area of great social interest, which benefited and will continue to benefit from the developements of strikethrough is "medicine". Furthermore, the developments of „**Micro**" and „**Nano**" **technologies** are greatly supporting - together with the latest developments in Materials Science [1] - the reasearch and innovation work pursued by the medical world. The last twenty years have been marked by a substantial increase in the complexity of equipments and devices used in the medical field, during all the specific stages of the medical act: diagnosis, clinical investigations, invasive and non-invasive surgical procedures, monitoring, therapeutic procedures and, treatments, physical and neuromotor recovery [2]. Medical equipment and technologies that are designed for hospitals and clinics can be ill-suited for home use. Illness, injuries, and other adverse health consequences often result from poor interactions between care recipients and the health care delivery system [3]. So, new devices must be developed, and it is a double advantage if the devices are of small sizes, so they can be transported anywhere they are needed.

Microtechnology and **Nanotechnology** have a set of processes, techniques and tools used to create structures having at least one dimension of a functional feature in order of micrometer and nanometer. Their advantages are found in: taking up less space, using less construction material, and costing less money.

Micro devices have drastically decreased in size and their functionalities have remarkably increased in the last years [4]. We can see the statistics from Healthcare market in [5]. Any device on the micro scale has communication facilities and it is often part of the feed back system (measurements, analyzes, decisions). Data analysis and interpretation allows the development of "Personalized Services" [1].

In order to build these micro devices, we have to ask ourselves some important questions, that will be useful:

- What do these medical devices require?
- Is the device providing critical health information?
- Who needs these devices?
- How much time it takes to get results?
- In what environment is such a device used?
- How much does this device cost?

There are two large categories of people who specially need such medical devices:

- middle-aged and older persons;
- children with chronic health problems or disabilities [3].

The aim of this work is to show how the micro devices are personalized and how useful they are, but also their connection with the materials they are produced from. Integration of the results provided by micro- and nanotechnologies can have a major impact in solving critical medical challenges and, ultimately, deliver better patient care and life quality [6].

As we can find in literature [7], the first portable micro device, from which all the other devices were developed is the glucose sensor for diabetes, invented by L. Clark. It is used to quickly determine the amount of glucose from blood [8].

The materials used for micro devices are investigated widely in the literature using different approaches. In one of these studies, the correlation between the materials and the devices is reached in [9]. The importance of materials in the miniaturized technology is presented in the report [10]. Some of the properties that a material used in fabricating micro devices must have are: strenght, flexibility and resistance. Utilization of graphene is significant for our studies, so [11] was used for information. Similar to this, we can find information of the other materials in [12].

Diagnosis and prevention are usually aided by wearable / patchable devices. We have some well-known examples, like the glucose sensor or the revolutionary DxtER Tricorder Sensor Kit (that can diagnose up to 34 various health conditions) [13]. In case of treatment, we can talk about the injectable nanobots [14]. Information about their shape, size, the way they are introduced in the liquid and their interaction with the cells and tissues are presented in a great work research in [15]. As well as diagnosis, prevention and treatment, recovery is very important and it is the one that most requires customized devices. This fact is illustrated in [1]. In the technologies era, the monitoring can be made by using an application from the cell phone.

2. INTELLIGENT MICRO DEVICES

A medical device is "an instrument, apparatus, machine, implant, an in vitro reagent or other similar article that can be used in order to diagnose any disease or other conditions. It can also be used in treatment or prevention of disease" [3].

2.1 Making a micro device

A successful design and development of an (intelligent) micro device will be reflected in making a right balance between the Technological Factors (Measurement Sensors and Associated Electronics) and the Human Factors (Figure 1).

Technological factors are represented by the sensors that collect all the information about the physiological parameters.

Human factors are described as: "the discipline that takes into account human strengths and limitations in the design of interactive systems that involve people, tools and technology, and environments to ensure their safety, effectiveness, and ease of use".

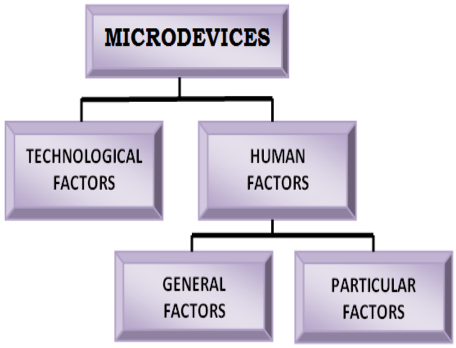


Figure 1. Factor categories

All the factors help determine: efficiency, efficacy, and safety [3]. Some of the *general human factors* (inputs) are: pulse; temperature; SpO_2 (Blood Oxygen Saturation); humidity; VOCs (Volatile Organic Compounds), etc. Must note that values associated with these parameters are highly dependent on particular factors, specific to each person and dependent on age, sex, living habits: sleep quality, diet, self-care, anxiety, stress, daily living routine, etc. A person's ability to use a health device depends on many factors, including:

- physical capabilities (size, strength, dexterity, flexibility, coordination);

- sensory capabilities (vision, hearing, touching);

- cognitive abilities (memory, literacy, language skills, knowledge, and experience base);

- general health;

- mental and emotional state;

- personal history and experience with home health care and medical care in general and

- ability to use a device.

Some micro devices for personal healthcare can be used in a nonclinical or transitory environment and they can be managed partly or wholly by the user safely and effectively [3]. Taking into acount both categories, we can make a medical personalized micro device that coresponds to the user.

2.2 Classification of micro devices

There are two types of health care micro devices that interact with the human body: patchable and implantable devices.

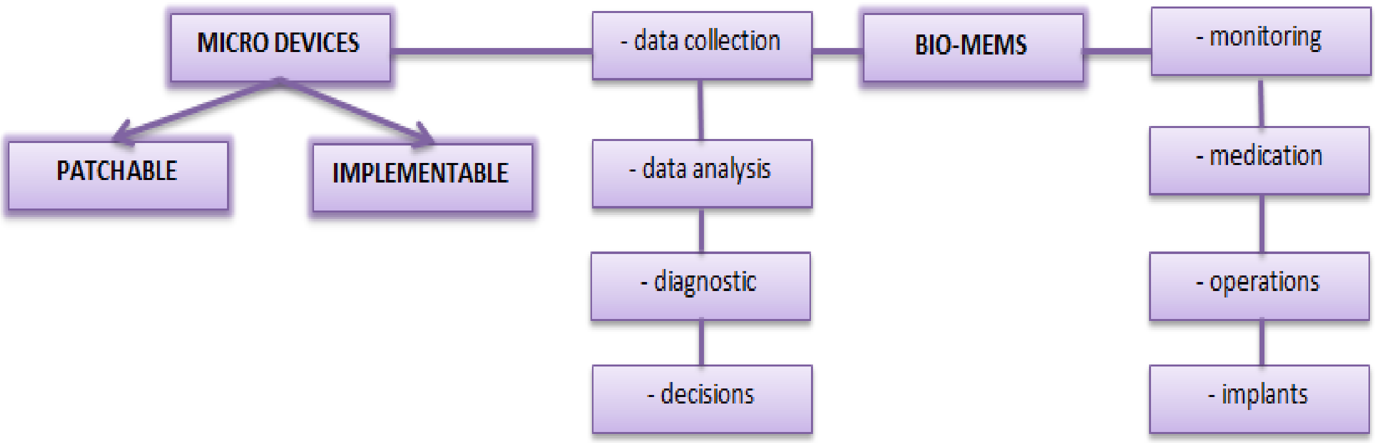


Figure 2. Micro devices and BioMEMS

In Figure 2 we have the classification of micro devices and for what they are used in medicine. "BioMEMS" is the term used for the science and technology of micro-devices manufactured for biological and medical applications. BioMEMS applications include biomedical, microfluidic, medical implants, microsurgical instruments and tissue engineering. Furthermore, the differences and the bonds between the „on skin" devices, the traditional portable devices and the implemented ones with the help of which we can gather all the informations needed with precision, continuity and convenience are presented.

2.2.1 Patchable/ Wearable (devices)

They are not surgically implanted, are easier to wear than other health trackers, making it possible to collect data for uninterrupted periods of time or they are with skin-touch / portable devices that you can easily care thanks to their reduced dimensions.

Patchable devices that interface with the skin across a wide range of size scales, from cellular level to molecular level, become increasingly attractive in biomedical research. These devices hold the potential for diagnositic and therapeutic functions with exceptional spatiotemporal precision, continuity, and convenience. Skin provides the outmost pathway for diagnosis and therapeutic options throughout the whole body [16]. Some exemples of popular patchable devices are: hearing devices, orto proheseses or even the blood glucose sensing.

2.2.2 Implantable devices

We can talk about nanorobots at this category. Interface across a wide range of size scales, from cellular level down to molecular level, become increasingly attractive in biomedical research. Mini-invasive techniques in surgery have led to a growing need for small, highly reliable components that can go through arteries or veins [4].

Nanorobots are injected into the patient to perform medical procedures at a cellular level. Mobile micro - and nanorobots show great potential for applications in various fields due to their small size and mobility. In biological and medical fields, they are promising tools for minimally invasive surgery, cell manipulation and analysis, and targeted therapy. In environmental fields, they have potential for use in decontamination and toxicity screening under conditions too dangerous or too small for humans to access. In microfluidics, they can be used for the manipulation and transportation of micro-objects and chemicals in lab-on-a-chip devices [14]. Another example of well-known implementable device is the pacemaker.

2.3 Carbon-based Nano materials for micro devices

Carbon is a very versatile material, with many allotropic structural representations, from 1D to 3D. There are various carbon-based nanomaterials (CBNs), such as: fullerenes, graphene, nano crystalline graphene (NCG), nanodiamonds, single wall nanohorns, carbon nanotubes, and carbon nanodots.

Carbon-based nanomaterials have found an increasingly wide utility in numerous and diverse fields such as: physics, electronics, optics, mechanics, biology and medicine. The carbon-based nanomaterials (CBNs) are of great promise for biomedical applications due to their unique characteristics, like: ultrahigh mechanical strength and conductivity [3], [4].

For building a micro device in general are used one or more materials. But there are a few cases when a whole micro device is bult from one material only [16]. The most relevant carbon-based nano materials used as sensitive layers for making humidity sensors in our experimets are: **Graphene** [18], **Carbon Nanohorns (CNHs)** and **Carbon Nanotubes (CNTs)**.

1. Graphene is considered the basic building block of all graphitic forms. It possesses a single layer of carbon atoms in a closely packed honeycomb two-dimensional lattice [19]. It is known as the thinnest material in the universe. Also, it is the strongest material ever measured [11]. It has high crystal and electronic quality [20]. Graphene is a pH sensitive material and its interaction with the human body is very good [21]. Patchable devices tend to have sufficient bendability and stretchability to attach to the skin conformally and accommodate mechanical stretching by external forces or body motion. A straightforward way to modify the flexibility of a specific material is to prepare them in ultrathin layers, since the flexural rigidity or mechanical resistance of a material is proportional to the thickness of the material to the third power [16]. Graphene is the most used material in developing new devices used for healthcare. An important example is found in [22], presenting pressure sensors for fingertip based on a graphene film.

2. Carbon Nanohorns (CNHs) belong to the carbon allotrope family, being related to carbon nanotubes. They are materials that have a tubular structure with 2–5 nm in diameter and 40–50 nm in length [23], [24]. CNHs can be oxidized to air [25] by treatment with acids [26] or oxygenated water [27], yielding carbon nanowires with carboxylic groups These materials are hydrophilic in nature and are easily dispersible in water and organic solvents such as ethanol, isopropyl alcohol, etc. Due to this fact, their chemical functionalization is imperative.

3. Carbon Nanotubes (CNTs) are part of the fullerene family. They are cylindrical molecules that consist of rolled-up sheets of single-layer carbon atoms (graphene). They are ultra-high strength, low-weight materials that possess unique highly conductive electrical and thermal properties [28]. CNTs are highly stable, nontoxic on oral route, nonimmunogenic and also relatively inert [29].

3. EXPERIMENTAL

Intelligent sensors are the most important part of any device from which we need to receive information. They are presented as "extensions" of human senses (seeing, hearing, smelling, tasteing and sensing) [1]. Getting information is done in real time by mechanical, thermal, magnetic, chemical or electromagnetic measurements. The information is processed and transmitted [9]. For microsensors, a mechanically measured signal is usually converted into an electrical signal. In this paper we present a mixture of carbonic materials used in developing new and modern sensors. We focus on developing humidity sensors that can be used for patchable devices. These sensors can be used to measure the sweat from the human body. The sensing layer should be homogenous and the thickness of the sensing layer should be carefully optimized in order to get the best output in terms of response time and stability in time. Thus the preparation of the solution for the sensing layer must consider a step of ultrasonification in order to achieve a homogenous solution and to uniformly disperse sensing material. Sonochemistry involves high energies and pressures on a short time scale. The maximum power it can reach is 200W.

Figure 3. Ultrasonic homogenization step

After sonochemistry is done, we start depositing the layers on the surface of the electrode. In general, there are used IDTs from the silicon industry or IDTs from the flexible industry. The electrode that we used for the experiments is an Interdigitated Gold Electrode over plastic substrate, from the patchable industry, as we can see in Figure 4. It is composed of two interdigitated electrodes with two connection tracks made of gold, on a plastic and flexible substrate. We used this electrode because it permits us to work with low volumes of sample. The interdigitated configuration typically enhances sensitivity and detection limits. The dimensions for bands/gaps are 100 μm and the plastic substrate dimensions are: 22.8x7x0.175 mm (LxWxH).

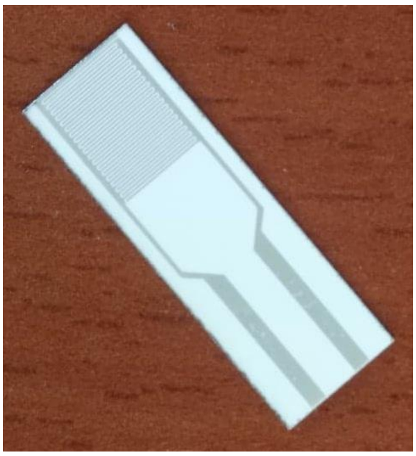
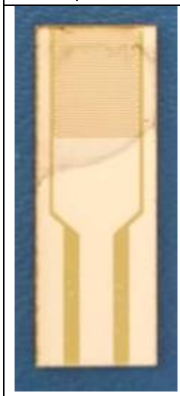
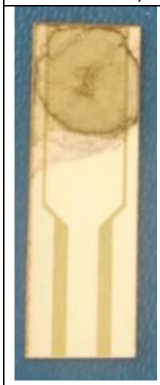


Figure 4. Interdigitated Gold Electrode

Initial measurements were made in order to correlate the electrical resistance with the thickness of the layer. Experimentally we did investigate how many layers are needed until the measured resistance reaches the 1-10 KΩ level where the optimum value for sensors is situated. In one of our experiments, we deposited 8 layers by the dripping method (2µL of solution were used for each layer) in order to reach the resistance needed, i.e., 6,1 KΩ**.** The depositions were made at normal room temperature: 26^0C, with a humidity of 30%. The resistance was measured after each deposition. The obtained measurements are presented in Table 1.

Table 1. The sequential formation of the layers

Layer 1 R=4,45 MΩ	Layer 2 R=1,44 MΩ	Layer 3 R=330 KΩ	Layer 4 R= 93 KΩ
			
Layer 5 R=48 KΩ;	Layer 6 R=23,5 KΩ	Layer 7 R=15,14 KΩ	Layer 8 R=6,3 KΩ
			

At 25^0C and a relative humidity of 50%, the average sweat rate in adults is about 500—700 mL/day with a maximum of 1.4 L/h or 20 nL/min per gland [30].

After we obtained the resistance we needed: 6,1 KΩ, we investigated the transfer function of the sensor to environments where the humidity level was changed, in a controlled manner, from 10% to 100%. (Figure 5) The sensor response due to changing humidity is tracked in real time, while an industrial grade, commercial sensor is used to provide the benchmark values.

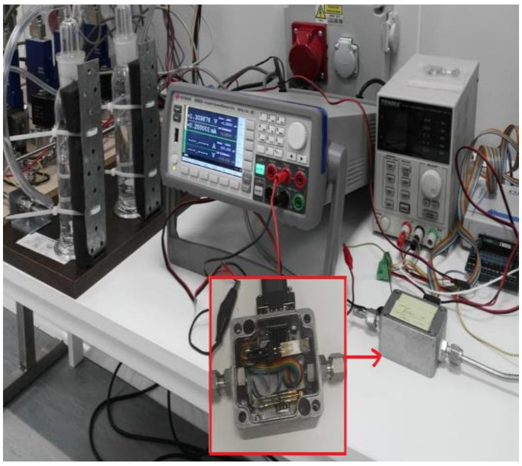


Figure 5. Humidity testing

4. RESULTS

Based on these researches, we developed a series of humidity sensors, resulted in the following patent applications:

- Moisture-resistant humidity sensor based on Fe_2O_3 nanocomposites / oxidized carbon nanohornes; OSIM A / 00153 / 06.03.2019 (in Romanian).

-New sensitive layer for relative humidity sensor and its manufacturing method; OSIM A-00156 / 11.03.2019 (in Romanian).

- Humidity sensor; OSIM A-00161 / 12.03.2019 (in Romanian).

- New chemirezistive sensor for humidity detection; OSIM A-00164 / 13.03.201 (in Romanian).

- Sensitive layer for humidity sensor with surface acoustic waves; A-00170 / 18.3.2019 (in Romanian).

5. CONCLUSIONS

The use of films made of new sensitive layers gives the sensor some significant advantages, of which we mention: superior mechanical properties given by the material and the rapid response of the sensor to variations in the relative humidity value. These sensors have high sensitivity, stability over time, good reproducibility, small size, very good reliability and reasonable production cost.

6. ACKNOWLEDGEMENT

This work was funded by a grant of the Romanian Ministry of Research and Innovation, CCDI-UEFISCDI project number PN-III-P1-1.2-PCCDI-2017-0619/Nano-Carbon Plus. within PNCDI III.

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