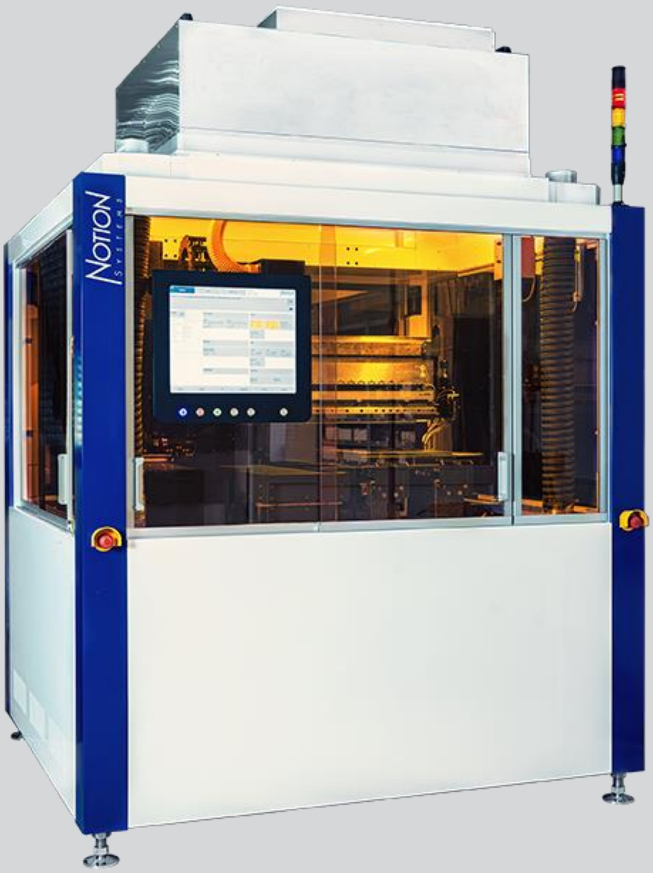
FRAUNHOFER-INSTITUT FÜR BIOMEDIZINISCHE TECHNIK IBMT

Thomas Velten (editor)

Nano-based portable electronics for the diagnosis of mental disorders and functional restoration, production technologies and devices



SPONSORED BY THE

Federal Ministry of Education and Research

רשות החדשנות
Israel Innovation Authority

Nano-based portable electronics for the diagnosis of mental disorders and functional restoration, production technologies and devices

Results of the German-Israeli collaborative project NanoEDGE

Dr. Thomas Velten (editor)

Fraunhofer-Institut für Biomedizinische Technik IBMT, Sulzbach

The German part of this research and development project was funded by the German Federal Ministry of Education and Research (BMBF) in the "Innovations for Production, Services and Work of Tomorrow" program with the funding numbers 02P17W000 and 02P17W001 and was managed by the Project Management Agency Karlsruhe (PTKA).

Part of the project work was undertaken in collaboration with Israeli partners under the "German-Israeli Bilateral R&D Cooperation in the Field of Applied Nanotechnology". Furthermore, this project is co-funded by Israeli Innovation Authority (IIA). The IIA is the Israeli's innovation agency. It works with people, companies and partner organisations to find and drive the science and technology innovations that will grow the Israeli economy.

The authors are responsible for the content of this publication.

SPONSORED BY THE

Federal Ministry of Education and Research

רשות החדשנות
Israel Innovation Authority

Preface

Electrodes are often used to examine patients' health, for example to record electrical muscle signals (EMG) or neuronal signals (EEG). Today's electrodes are made of metal and are provided with a gel layer for use. The gel dries during long-term examinations and prevents reliable measurements on the patient. With wafer-thin electrodes that adapt exactly to the skin surface, measurements without gel and over longer periods of time are now possible. Particularly good electrical contact with the skin can be achieved with printed electrodes made of carbon nanoparticles, such as graphene nanoparticles. The commercially available graphene inks required for this so far have not been suitable for industrial inkjet printing.

The aim of the NanoEDGE research project was therefore to develop an ink made of graphene nanoparticles for inkjet printing and a scalable printing process. In addition, a resource-efficient process chain for the production of electrodes for direct skin contact was developed.

For this purpose, commercial inks were examined for their suitability and then further developed for inkjet printing. Particle size, viscosity, surface energy, electrical conductivity and skin compatibility were decisive. The next step was the development of resource-efficient printing processes for the targeted application of, for example, graphene ink and other printable materials. These included printing large-scale, electrically insulating areas, plasma processes to increase the adhesion of printed electrodes, and post-treatment processes for crack-free drying of printed layers. Due to their flexibility, the developed methods are equally suitable for prototype production and series production.

After successful implementation, the user-specific printing processes will be able to be used both for medical technology and for other areas of application, such as photovoltaic modules, displays and for printed antennas. The Israeli project partners brought experience with very thin, gel-free electrodes for EMG and EEG measurements into the cooperation. In addition to the project, cooperation in the area of printed electrodes for therapeutic applications and biosensors for blood diagnosis are expected in the future.

The German partners in this joint project with Israeli partners were funded by the "Innovations for the Production, Services and Work of Tomorrow" program of the Federal Ministry of Education and Research (BMBF). We would like to take this opportunity to thank everyone who has contributed to this pioneering research and development work with their knowledge, commitment and experience.

Project Management Agency Karlsruhe (PTKA)
Production, Service and Work
Karlsruhe Institute of Technology (KIT)

Stefan Scherr
December 2021

MANAGED BY

PTKA
Project Management Agency Karlsruhe
Karlsruhe Institute of Technology

Duration:	1st January 2018 – 30st June 2021
Coordinator:	Fraunhofer Institut für Biomedizinische Technik Joseph-von-Fraunhofer-Weg 1, 66280 Sulzbach, Deutschland
Coordinator	**Dr.-Ing. Thomas Velten** Phone: +49 (0)6897-9071-450 E-Mail: thomas.velten@ibmt.fraunhofer.de

Project partners and authors

Fraunhofer Institut für Biomedizinische Technik (IBMT)
Joseph-von-Fraunhofer-Weg 1, 66280 Sulzbach, Deutschland
Dr. Thomas Velten, Herbert Schuck, Thorsten Knoll, Dr. Sylvia Wagner

Notion Systems GmbH
Carl-Benz-Str. 22a, 68723 Schwetzingen, Deutschland
Dr. David Volk

Tel Aviv University Ltd.
P.O. Box 39296, Tel Aviv 6139201, Israel
Prof. Yael Hanein, Prof. Talma Hendler

Sensomedical Labs LTD
Nazareth Industrial Parks, Mount precipice, Nazareth 1612102, Israel
Maroun Farah, Luai Asfour

Content

1 Objectives and consortium

1.1 Objectives of the research project

The NanoEDGE project aims at converging production techniques for functionalized electrodes with expertise in nanomaterial fabrication and characterization, state of the art engineering, and neuroscience to pave the way for the production of multi-level sensors that can rigorously enhance the performance of established monitoring methods like electroencephalography (EEG) and electromyography (EMG).

In brief, the project objectives are as follows:

Objectives to be achieved in Germany

- Resource-efficient production process for inkjet printing of electrically conductive structures based on nanoparticulate inks, including graphene inks or inks comprising carbon nanomaterials.
- Nanoparticulate graphene ink suited for inkjet printing. A modified composition of the ink shall be suited for printing of biodegradable structures.
- Scalable process chain suited and efficient for small scale and high throughput production.
- Processes for substrate pre-treatment in order to facilitate inkjet printing of structured layers and locally functional surfaces.
- In-line process for post-treatment of structures printed using nanoparticulate ink.
- Concept and design for the equipment of an industrial inkjet printing system with a roll-to-roll transport unit.

Objectives to be achieved in Israel

- Miniature EEG, EMG and neuromodulation wearables with the following specific goals:
    - Specialized low-power electronics for continuous 24 hours monitoring and disposable ultralow power sources based on light-weight miniature coin batteries; without the risk of detachment when wearing or influencing the skin electrodes.
    - Flexible antennae for close skin contact; interference of the body needs to be avoided and broad bandwidth transmission must be enabled.
    - MRI compatibility to allow for combined electrophysiology with imaging.
- EEG system with skin electrodes suited for application in neuro-modulation.
- EEG sensors based on nanomaterials having improved recording performance.

1.2 Consortium

The project consortium comprised four partners, two from Germany and two from Israel. The NanoEDGE consortium developed a nanoparticulate graphene ink suited for inkjet printing, designed a resource-efficient production process for inkjet printing and, based on that, established a scalable process chain suited for small scale and high throughput production. These results were implemented into the development and production of a miniature wearable EEG system with skin electrodes based on nanomaterials. This system was validated for improved recording performance and suitability for applications in neuro-modulation.

Project tasks include formulation of graphene-based inks optimized for inkjet printing, by firstly evaluating commercially available inks (Fraunhofer Institut für Biomedizinische Technik (IBMT), Tel Aviv University (TAU)) and secondly modifying the ink formulations (IBMT) in order to optimize printability. Resource-efficient inkjet printing processes for graphene-based inks were developed (Notion Systems) including plasma processes for pre-treatment (IBMT) as well as thermal or optical post-treatment (Notion Systems).

Based on the new processes two wearable systems, which report on muscle (EMG) and brain (EEG), were designed (TAU) and printed (IBMT, Notion Systems). Combining the printed components with a miniaturized, light-weight and ultra-low power state-of-the-art signal acquisition and modulation electronics (Sensomedical) led to a functional wearable system that provides an easy to use, wearable endogenic neuromodulation technique, which offers an EEG-based neurofeedback system. The system was evaluated by TAU and Sensomedical.

The work division of the partners is shown in the following diagram (Figure 1).

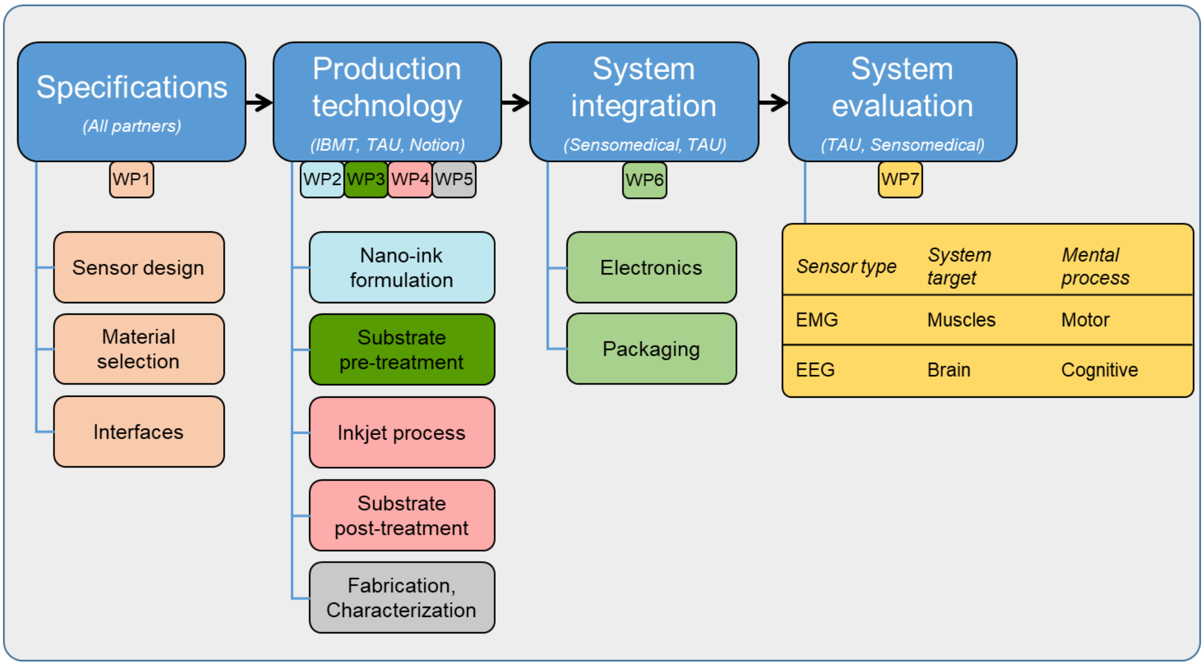


Figure 1: Overview of the work division of the partners and assignment between work packages and tasks.

2 Conditions under which the project was carried out

NanoEDGE is a joint R&D project comprising participants from Germany and Israel. NanoEDGE refers to the "German-Israeli Call for Bilateral R&D Cooperation in the Field of Applied Nanotechnology, 2017 – 2019" published at http://www.internationales-buero.de/en/4687.php. NanoEDGE also refers to the German "Bekanntmachung im Rahmen der Strategie der Bundesregierung zur Internationalisierung von Wissenschaft und Forschung Richtlinien zur Förderung der Intensivierung der Zusammenarbeit mit Israel: Deutsch-Israelische Kooperation in der Angewandten Nanotechnologie vom 7. Oktober 2016".

NanoEDGE especially addresses the following priority research fields:

- Solutions for new production modules that enhance resource-efficiency in the production of locally functional surfaces considerably.
- Bio-medical technologies: medical, biological, lab-on-a-chip, single cells, single molecules, low-quantity tests, high-throughput methods, cell sorting technologies, 3-D imaging and diagnostics based on microfluidics.

The problem to be solved within the NanoEDGE project involves two aspects, a) the aspect of production technology for electrode manufacturing with new nanomaterials and b) the application aspect, i.e. treatment of mental disorders.

a) Electrodes are the main element of many systems like e.g. electro-chemical sensors and biosensors, monitoring systems like EEG and EMG, and electro stimulators, either implanted or applied on the skin. One requirement for electrodes is that they must be electrically conductive. Further, their direct contact to skin, tissue or electrolyte solutions – depending on the specific application – means that further requirements have to be fulfilled like biocompatibility, high catalytic activity, high charge injection capacity, low contact resistance or good conformability to the contours of skin or tissue. Latest research of the NanoEDGE consortium and others had shown that printed electrodes made of carbon nanomaterials, especially of graphene nanoparticles fulfill many of the above requirements in an extraordinary way. The initial situation before the start of the NanoEDGE project was that hardly any graphene inks suited for inkjet printing were commercially available. Consequently, industrial scale printing processes or even process chains for printing products, like e.g. electrodes, made of these graphene inks were also lacking. There was a need for the transfer of the knowledge and techniques available in the NanoEDGE consortium into resource-efficient production technologies not wasting the precious nanoparticulate inks and suited for industrial-scale fabrication.
b) Neurological and psychiatric disorders become manifest in a combination of motor, cognitive and emotional abnormalities. To recover from these mental diseases, any efficient treatment and functional restoration requires the monitoring of the neurophysiological activities and interactions of the relevant brain areas. With regard to the complexity and the widespread distribution of these neurophysiological processes within the brain, the reliable, cost effective and representative depiction of the hardly accessible electro-chemical nerve signals still remains an exceptional challenge. Thus, novel tools are highly welcome, which can continuously monitor and also modulate the electro-chemical signals originating from our brain and body under various mental states. One NanoEDGE goal is

integrating a novel wearable EEG system with a new way of recording deeply located brain signals with functional MRI inspired EEG. The main hurdles in the attempt to develop this novel technology are theoretical and technological. Technological: 1) The EEG device must be comfortable, easy to wear and compact, without compromising the reliability of the brain signal. Reliability of the signal relies on the availability of reliable and reproducible production technologies for manufacture of electrodes interfacing with the skin. 2) Reliable algorithms depicting brain functions relevant for mental disorders must be derived from a small number of wearable EEG sensors. Theoretical: Neural element identification (regions or networks) for valid targeting of specific mental processes are known to be critical in neuropsychiatric disorders. This depends on robust non-invasive EEG recordings with high spatial and temporal resolution that can reliably depict mental process related brain activity and connectivity.

The own prior work and knowledge of the NanoEDGE project participants can be described as follows: Within recent research projects, IBMT has developed electrodes based on graphene platelets[1]. They were fabricated by roll-to-roll (gravure) printing, a process being well-suited for high throughput production and for combination with roll-to-roll hot embossing, also available at IBMT, but less-suited for downscaling. Interestingly, electrode characterization has revealed (unpublished results of IBMT) that the charge injection capacity is up to 20 times higher compared to electrodes made of platinum making carbon nanomaterials a good candidate for electrostimulation applications. Concerning applications in EMG or EEG monitoring, graphene electrodes show higher impedance compared to platinum. Quite recently, TAU has investigated screen-printed carbon-based skin electrode arrays. It was demonstrated that plasma polymerized 3,4-ethylenedioxythiophene can reduce the impedance of carbon material based electrodes by a factor 10. All the just mentioned processes for fabrication of carbon-based flexible electrodes are proven lab-scale techniques available at IBMT and TAU.

TAU core technology is skin electronics for EMG, EEG and sympathetic-state monitoring[2]. Wearable EEG devices in particular promise to revolutionize the field of brain-machine interfacing (BMI). Combined with a novel neural profile approach of high temporal and spatial resolution, such cutting-edge EEG sensing will allow on-line-monitoring of brain function, as well as reinforcing learning through neuro-feedback (NF), a procedure in which brain signals are used in a closed-loop training procedure. NF can be used to modulate brain activity and connectivity associated with specific mental processes, and as such has the potential to significantly improve contemporary mental disorder diagnosis, restore mental functioning and thus alleviate suffering in a wide spectrum of disturbed mental states.

---

[1] Knoll, T., et al. "High-resolution gravure printing of graphene biosensors" Proceedings of The Global Conference on Micro Manufacture, Incorporating the 11th International Conference on Multi-Material Micro Manufacture (4M) and the 10th International Workshop on Microfactories (IWMF) (4M/IWMF2016), 13-15 September 2016, Kgs. Lyngby, Denmark.

[2] Bareket, L., et al. "Temporary-tattoo for long-term high fidelity biopotential recordings" Scientific reports 6.1 (2016): 1-8.

3 State of the art at the beginning of the project

3.1 State of the art in electrodes for medical applications

Metals, e.g. platinum, are the standard materials for electrodes, both for monitoring and electrostimulation tasks. Rigid metal electrodes are usually shaped as wires or disks and may be quite expensive, especially when made from platinum. Furthermore, mechanical flexible electrodes are known, which, compared to rigid electrodes, adapt well to the contour of skin or tissue. They may be based on thin laser cut metal sheets bonded to a thin substrate. Even more flexible are thin-film electrodes produced by a sputtering process, which is not resource-efficient at all.

Recently, new attempts of fabricating flexible skin electrodes by conventional screen printing and inkjet printing have been reported. These new printed electrodes open entirely new opportunities in ambulatory sensing: While conventional electrodes are mainly restricted to laboratory or clinical setups and required highly trained professionals, flexible printed sensors can be conveniently integrated with local amplifiers and wireless electronics. Thus, the number of sensing elements can be significantly increased and the electrode array placement is a straightforward task that requires no training. So far, printed electrodes exhibited mild overall improvement compared with conventional electrodes, owing to limitation in existing production methods including relatively rigid substrates, and the fact that available inks are not optimized for wearable sensing applications.

Nano-based electrodes (e.g. graphene and carbon nanomaterials) can help to overcome many limitations exhibited by conventional metallic electrodes. These approaches include a) reduced electrode rigidity for improved attachment to the skin and b) improved surface area for enhanced electro-chemical coupling (critical for both recording and stimulation purposes), as well as for improving electrode surface modification and sensor stability[3,4]. These two factors have far-reaching implications for electrophysiological and electrochemical sensing. Soft electrodes capable of conforming to human skin do not require the use of gels to achieve EMG and EEG recordings. By rendering the gel superfluous, the complexity of the electrode production and especially its long-term stability improves markedly. Increased roughness can dramatically (up to 3 orders of magnitude) reduce electrode impedance and consequently can contribute to reduced noise and improved signals. It is important to note that improved flexibility and enhanced surface areas are two critical properties that impact many sensing and stimulation schemes including electrical and electro-chemical.

3.2 State of the art in nanoparticulate inks

Inks which are electrically conductive already existed at the start of the project and were developed specifically for printed polymer electronics applications. Organic conductive inks have been prepared but have low electrical conductivity due to low mobility of the charge carriers (e.g.

[3] Eleftheriou, Cyril G., et al. "Carbon nanotube electrodes for retinal implants: a study of structural and functional integration over time" Biomaterials. 112 (2017): 108-121.
[4] David-Pur, M., et al. "All-carbon-nanotube flexible neuronal electrodes" Biomed Microdevices 16 (2014): 43-53.

<0.5 $cm^2V^{-1}s^{-1}$)[5]. Electrically conductive nanoparticles such as polysilicon[6], zinc oxide nanoparticles[7], or carbon nanotubes[8] have also been used to improve the conductivity. However, metal nanoparticle based inks are not stable in typical solvents such as de-ionized water, acetone or isopropanol[9]. Therefore, they must be chemically modified by means of suitable stabilizers. However, these stabilizers are not long-term stable and the metal nanoparticles also begin to oxidize after printing[10].
Electrically conductive inks based on carbon nanotubes have achieved charge carrier mobilities of up to 50 $cm^2V^{-1}s^{-1}$ [11]. With graphene-based inks, even a mobility of 95 $cm^2V^{-1}s^{-1}$ was achieved[12]. However, the graphene ink was not developed for biomedical applications, but for the printing of electronic printed circuit boards.
First development work towards a graphene ink suitable for biomedical applications are described[13] and were conducted at the University of Maryland, USA.
Commercial graphene-based inks have been rarely found in the US and the Far East. Company VorbeckMaterials (USA) offers a graphene ink which has been developed for applications in the field of batteries and not for biomedical applications. In addition, the Thai company INNOPHENE offers a graphene ink. According to the company home page of INNOPHENE, graphene inks are available for screen printing, roll-to-roll printing and for inkjet printing.
In Europe, there are only a few commercial suppliers of graphene ink, like e.g. the British company Haydale Ltd. The graphene ink of Haydale Ltd. was developed for screen printing. For inkjet printing, Haydale Ltd.'s graphene ink is so far not suitable.
In Europe, therefore, there is a need for catching up on graphene inks which are suitable for inkjet printing processes and / or which have the biocompatibility required for biomedical applications.

3.3 State of the art in printing of electronically conductive structures

For many years, printing technologies are used to produce conductive structures. Especially screen printing is widely used. A prominent example is e.g. printing the conductive fingers for solar cells. The drawback of screen printing is its limitation in terms of throughput, minimal feature size and flexibility. The throughput can be increased by roll-to-roll printing technologies such as flexo-printing. This technology also allows to create very fine conductive features. But all printing technologies with a fixed print form to transfer the image have the drawback that changing between different patterns is very time consuming. Also, individualization of products during production is practically impossible. Therefore, inkjet printing has become very popular in order to produce conductive features. By stacking print heads, the throughput of the system can easily be increased. Fine conductive feature sizes down to 20 µm have been demonstrated. Its

[5] Singh, M., et al. "Inkjet Printing Process and Its Applications" Advanced materials 22.6 (2010): 673-685.
[6] Shimoda, T., et al. "Solution-Processed Silicon Films and Transistors" Nature 440.7085 (2006): 783-786.
[7] Noh, Y.Y., et al. "Ink-jet Printed ZnO Nanowire Field Effect Transistors" Appl. Phys. Lett. 91 (2007), 043109–3.
[8] Okimoto, H., et al. "Tunable Carbon Nanotube Thin- Film Transistors Produced Exclusively via Inkjet Printing" Advanced materials 22.36 (2010): 3981-3986.
[9] Singh, M., et al. "Inkjet Printing Process and Its Applications" Advanced materials 22.6 (2010): 673-685.
[10] Luechinger, N.A., et al. "Graphene-Stabilized Copper Nanoparticles as an Air-Stable Substitute for Silver and Gold in Low-Cost Ink-Jet Printable Electronics" Nanotechnology 19.44 (2008): 445201.
[11] Ha, M., et al. "Printed, Sub-3V Digital Circuits on Plastic from Aqueous Carbon Nanotube Inks" ACS nano 4.8 (2010): 4388-4395.
[12] Torrisi, F., et al., Inkjet-Printed Graphene Electronics, ACS nano 6.4 (2012): 2992-3006.
[13] Han, X., et al. "Scalable, printable, surfactant-free graphene ink directly from graphite" Nanotechnology 24.20 (2013): 205304.

digital and contact free working principle allows a quick change between assignments and a personalization during production. Inkjet printing was demonstrated to print all sorts of conductive materials such as inks comprising silver nanoparticles, copper nanoparticles inks, silver metal-organic-decomposition inks, carbon nanotubes or lately first attempts of graphene inks.

3.4 State of the art in sensors for detection of biological signals that are indicative for mental state

Mental state can be assessed using a wide range of sensing methodologies, including physiological, mechanical and chemical. EEG as a primary example is intensively studied in recent years as a tool for mental state diagnostics (for a review see Cohen Trends in NSC 2017[14]). Yet, although being accessible and cost effective, EEG suffers from several limitations for precise brain mapping especially in psychiatry. First, the most widely used systems are very bulky including the need to attach many electrodes to the scalp with a gel and lowering resistance by scratching each electrode site, resulting in discomfort and long testing. Today, efforts are directed towards miniaturization of the recording setup by reducing the number of recorded sites, while still keeping the meaningful information. Improved algorithms to extract meaningful data from a small number of recording electrodes will achieve better user experience. Another limiting issue with EEG is its poor spatial resolution due to the unresolved inverse problem of source estimations from scalp electrodes. This problem is especially critical when dealing with deep brain areas such as in the limbic system e.g. amygdala, nucleus accumbens and ventromedial prefrontal cortex. These areas are commonly indicted in mental health disorders such as depression and anxiety disorders. To improve spatial resolution of EEG the Hendler group at TAU developed an fMRI inspired EEG pattern that is based on simultaneous recording of EEG/fMRI in combination with learning algorithms. This resulted in EEG patterns (termed hereby Electrical Finger Print, EFP) that correspond to fMRI activity in designated deep brain regions such as the amygdala[15]. A further validation study demonstrated on a new group that the EFP indeed correspond to fMRI modulation in the region used for developing the combined model[16]. Having a signature of limbic areas with EEG only opens a wide horizon for applying continuous monitoring of specific functional brain patterns as well as serving as probe for home based treatment in psychiatry with neurofeedback (NF). NF is a kind of brain computer interface approach that relies on conscious effort to guide volitional neuromodulation in a desired brain region that is guided by rewarding feedbacks[17].

[14] Cohen, Michael X. "Where does EEG come from and what does it mean?" Trends in neurosciences 40.4 (2017): 208-218.
[15] Meir-Hasson, Y., et al. "An EEG Finger-Print of fMRI deep regional activation" Neuroimage 102 (2014): 128-141.
[16] Keynan, Jackob N., et al. "Limbic activity modulation guided by functional magnetic resonance imaging–inspired electroencephalography improves implicit emotion regulation" Biological Psychiatry 80.6 (2016): 490-496.
[17] Sulzer, J., et al. "Real-time fMRI neurofeedback: progress and challenges" Neuroimage 76 (2013): 386-399.

4 Planning and execution of the project

In order to achieve the objectives, the project is structured in 8 work packages (Table 1). Three project milestones are defined:

Milestone 1 (month 9): Detailed specifications are available.
Milestone 2 (month 15): Nanoparticulate ink formulations are available.
Milestone 3 (month 30): Skin electrode arrays produced with the new production processes are available.

In total, eight full consortium meetings (either face-to-face or virtual) and six technical meetings were held. These meetings have resulted in good synchronisation and coordination of the collaboration.

Table 1: Original timing of work packages and project-related resource planning.

Start Month/Year	**End** Month/Year	**WP-** Number	**Work package (WP)**
1/2018	12/2019	1	System and component specification
4/2018	3/2019	2	Nanoparticulate ink formulation
4/2018	12/2019	3	Process chain and pre-treatment processes
7/2018	3/2020	4	Inkjet process and post-treatment processes
10/2018	6/2020	5	Skin electrode array production and characterization
7/2018	6/2020	6	Electronics and electrical contacting
1/2020	12/2020	7	System evaluation
1/2018	12/2020	8	Management, dissemination, exploitation

Due to the COVID-19a pandemic, both the German and the Israeli partners had to temporarily stop their project work, which led to corresponding delays in the project work. In addition, unforeseen technical difficulties led to a further delay. Overall, the delay in the project work was 6 months and the project duration has been extended by 6 months.

5 Results

The project NanoEDGE is divided into seven technical work packages (see Table 1) and one work package for management, dissemination and exploitation. The results achieved during the project period in technical work packages 1 to 7 are presented in the following subchapters.

5.1 System and component specification (WP1)

5.1.1 User requirement specifications for sensors

The user requirements for the EEG sensor and the EMG sensor were defined in this task. They are the basis for defining the technical specifications.

The requirements includes specification that the system shall be applicable on the skin of humans. To accommodate this demand, biocompatibility tests of the foil substrates and inks were defined based on biocompatibility standards (ISO-10993). In the scope of the NanoEDGE project, no requirement was stated for self-use. The electrodes and system were design to be applied and operated by a trained person. Figure 2 shows two electrode layouts that were defined as a basis for the electrode development.

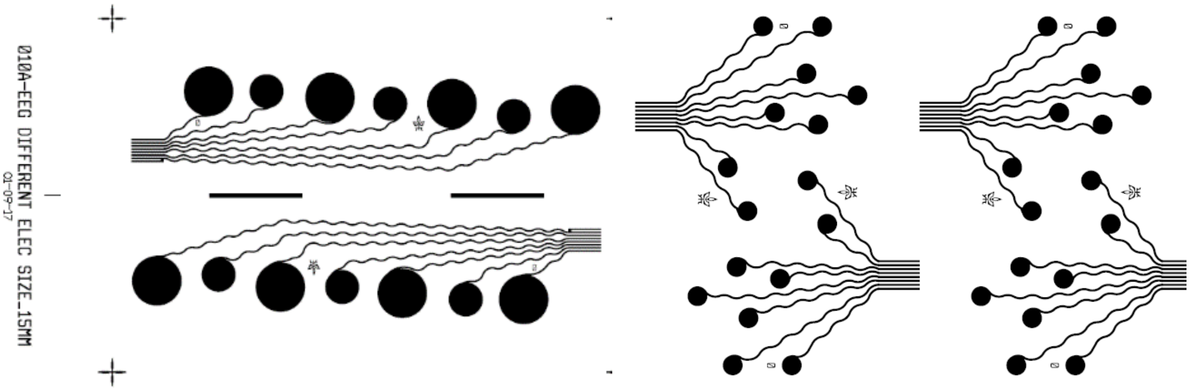


Figure 2: EEG (left) and EMG (right) layouts used to establish the adherence of the printed electrodes with the NanoEDGE specification document. Electrode diameters are 15 mm and 10 mm for the array on the left and 4 mm for the array on the right.

5.1.2 Technical specifications for sensors, production equipment and production processes

The technical specifications for the two different sensor types as well as the inks, the production equipment and production processes were defined in this task and summarized in a specifications document. They were the basis for the work on the ink development and the inkjet printing process performed in work packages 2, 3 and 4. Furthermore, the technical specifications of the sensor electronics and the final sensor systems (work package 6) were defined.

The requirements include electrode trace conductivity and physical dimensions, number of electrodes and their size (depending on the application), electrode rigidity (defined relative to substrate rigidity), and substrate mechanical and physical properties. All these considerations are fully described in the NanoEDGE specification document compiled in June 2018.

With regard to the development of the ink formulations and the printing process with the available inkjet printers, Fraunhofer IBMT and Notion Systems defined a two-step approach: development of inks and establishing of printing parameters were performed with the lab inkjet printer DMP-2800 from FujiFilm Dimatix, which was available to both partners. The final production of sensor electrodes was then carried out on an industrial inkjet printer from Notion Systems.

5.2 Process chain and pre-treatment processes

Two different process chains for sensor fabrication were developed. To reach the aim of flexible electrodes with maximum skin contact, the process sequence illustrated in Figure 3 was defined. Structuring of a water-soluble film by a hot embossing process is the initial step to obtain 3D-shaped electrodes with a maximum surface. Conductive and insulating layers are then printed onto this pre-patterned substrate. Depending on the achievable electrical conductivity, the structures are printed with two different inks. One ink with high conductivity is used for the conductor tracks. The other ink can have lower conductivity, but must be biocompatible for contact with the skin. After printing, the water-soluble foil is removed after lamination of a thin adhesive tape to obtain the final sensor that will be used for application on the skin.

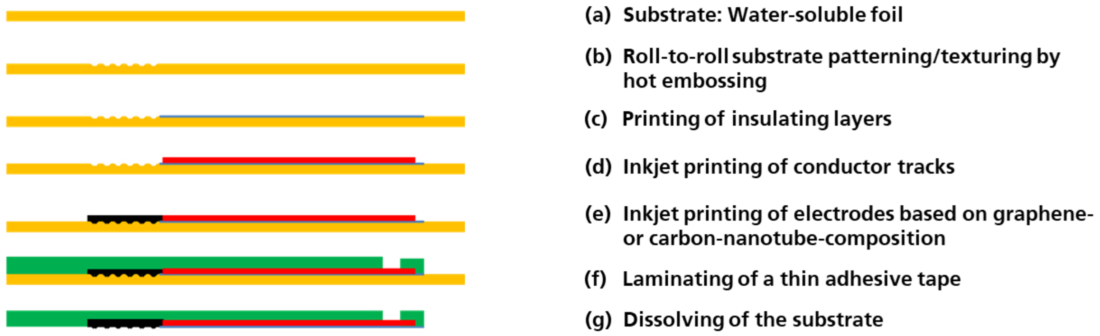


Figure 3: Production process with water-soluble foils and 3D-patterning of the skin electrodes.

Hot embossing, thermoforming and printing were used for the pretreatment of water-soluble PVAL films (Solublon type CS or PT) with different thicknesses (30 to 75 µm). It was investigated how a structure can be created in the film by molding, embossing (roll-to-roll hot embossing, thermoforming) or by printing with water or inks. Experiments were also carried out with carrier foils made of COC in order to achieve a higher dimensional accuracy, as this was required for the subsequent printing process. Patterning of the water-soluble PVAL substrate film was possible with all mentioned methods. However, the low dimensional stability of the film, e.g. due to deformation during treatment, made the necessary automation for the subsequent printing process with graphene or silver inks impossible.

An alternative process sequence was developed based on polyurethane (PU) foils, which had been previously used by the project partner TAU for fabricating screen-printed flexible electrodes. This material replaced the water-soluble film. Furthermore, the 3D pre-structuring of the foil substrate was not pursued further. According to the new process sequence (Figure 4), conductor tracks from highly conductive silver ink are printed on the PU foil. After drying and sintering, the actual active electrodes are printed with the biocompatible graphene/carbon ink. In the next step, a double-sided adhesive tape is pre-structured to give access to the electrodes and is laminated onto the PU film. This adhesive tape serves for the fixation of the sensor to the skin and at the same time for the electrical insulation between the electrode conductor paths and the skin.

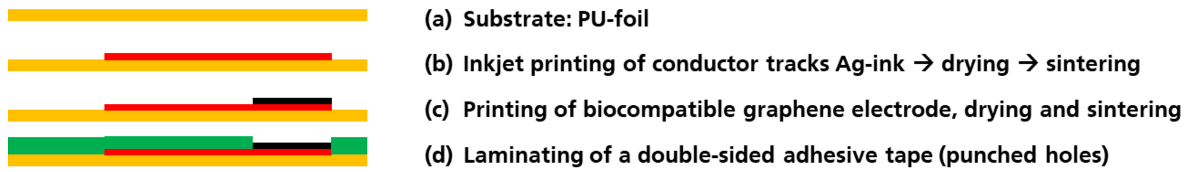


Figure 4: Production process with PU substrates.

The PU film EU94DS (manufacturer: SWM, UK) with a thickness of 80 µm was used as substrate for the flexible electrodes in combination with the medical grade transfer adhesive 3M 1524 for insulation and fixation.

5.3 Nanoparticulate ink formulation (WP2)

A nanoparticulate carbon ink for the use with the Dimatix Materials Printer DMP-2850 was developed. This ink was based on the commercial inkjet graphene ink GRA-9003 from Dycotec (UK). Other commercial and R&D carbon and silver inks were tested to identify the most suitable material combination for the final production of the sensors with the industrial printer from Notion Systems. Due to the high resistivity of the carbon-based inks, the use of silver ink was necessary with regard to the later sensor geometry with long conductor tracks. The carbon ink Metalon JR-700 HV and different silver inkjet inks (Metalon JS-A 101-A, Metalon JS-A 102-A, Metalon JS A191, Metalon JS A291) from Novacentrix (USA) were used, furthermore the silver ink AG-LT-20 from Fraunhofer IKTS (Dresden). Printing of all inks was established on PU films, as these substrates were selected with regard to the later sensor application. All selected inks (Table 2) adhered well to the PU substrate when the films were activated before printing. Details on this substrate pre-treatment are described in chapter 5.5. The adhesion of printed structures was checked in the form of a wipe test with a cloth soaked in water.

Table 2: Inkjet inks used in the project

Ink name	**Conductive material**	**Manufacturer**	**Components**
IBMT-graphene	Graphene + carbon black	Fraunhofer IBMT	Graphene ink GRA-9003 (2 wt.-%, Dycotec, UK), carbon black, dissolved in DMSO, ethanol, detergent Pluronic F-127
Metalon JR-700 HV	Carbon	Novacentrix	Carbon nanoparticles (5 wt.-%)
Ag-LT-20	Silver	Fraunhofer IKTS	Silver nanoparticles (21 wt.-%)
Metalon JS-A 101-A	Silver	Novacentrix	Silver nanoparticles (40 wt.-%)
Metalon JS-A 102-A	Silver	Novacentrix	Silver nanoparticles (40 wt.-%)

Carbon inks

The carbon ink developed at Fraunhofer IBMT consisted mainly of a commercial graphene ink (GRA-9003 from Dycotec, UK). Although specified as usable for inkjet printing, this graphene ink in its original composition was not usable with the Dimatix lab printer. Addition of a detergent (Pluronic F-127) and ethanol was necessary to modify the properties of the fluid for a successful and reproducible printing with the Dimatix lab printer. Carbon black was added to the ink to enhance the conductivity. Various configurations with different ratios of carbon black and Pluronic were evaluated to determine the optimum composition (Figure 5). The resistance of printed test structures with three layers having a length of 30 mm and a width of 1 mm was 53 kΩ (at a thickness of about 3 μm) corresponding to a sheet resistance of 1.77 Ω/□ for a 3 μm thick layer. This value is comparable with the sheet resistance of a graphene monolayer, which is 1.84 Ω/□[18]. The high resistance confirmed the need for a combination of the graphene-based ink with another ink with higher electrical conductivity, such as a silver ink. It turned out that DMSO, which was used as solvent for the carbon black, slightly dissolved the PU and thus further fostered the adhesion of the developed IBMT ink on the PU substrate.

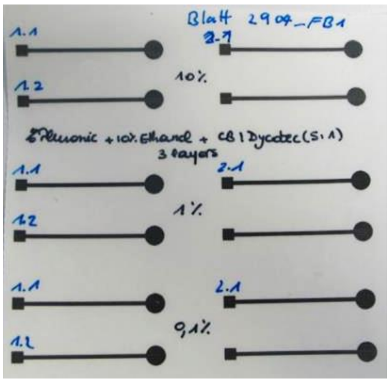


Figure 5: Electrodes printed with graphene-based inks using different detergent concentrations. Length of structures: 50 mm.

The preparation of the newly developed graphene-based ink required several complex process steps like degassing and ultrasound mixing that made it difficult to transfer the ink from the lab printer at Fraunhofer IBMT to the industrial printer at Notion Systems. Thus, the commercial carbon ink from Novacentrix was evaluated regarding its handling and printability. Sintering temperatures were in the same range as with the developed graphene-based ink. It turned out that it was not necessary to modify this ink for successful and repeatable printing results with the Dimatix lab printer. The transfer from the lab printer to the industrial printer was possible without the need for an elaborate handling procedure.

Silver inks

The silver inks from Fraunhofer IKTS and from Novacentrix performed well with the lab printer. Printing parameters for both inks were first established with the lab printer and then transferred

[18] Peng, S., et al. "The sheet resistance of graphene under contact and its effect on the derived specific contact resistivity." Carbon 82 (2015): 500-505.

to the industrial printer. Figure 6 shows electrodes printed with the lab printer using the silver ink from Fraunhofer IKTS. Next to the electrodes, additional rectangular structures can be seen. These leader bars have to be printed before the actual electrodes in order to obtain homogeneous ink transfer to the substrate.

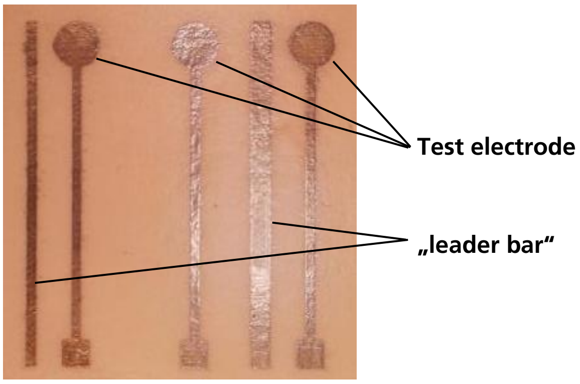


Figure 6: Electrodes printed with silver ink (Ag-LT-20), the two rectangles are leader bars that have to be printed to obtain homogeneous ink transfer. Length of structures: 50 mm.

After the coronavirus-related lockdown in spring 2020, it turned out that the long-term stability of the Metalon JS-A-102A Novacentrix silver ink was insufficient. Electrodes that were printed on PU film at the beginning of the year and that were electrically conductive showed severe cracking after a few weeks and months, which led to interruptions and a loss of electrical conductivity (Figure 7). Obviously, the storage conditions of the ink also had an impact on the performance. In a test print on PU film with a residual amount of the ink that had been stored at room temperature during the lockdown, electrically conductive structures could be produced. However, these also lost their conductivity after a few weeks due to increasing crack formation. Printing tests with ink that had been printed at room temperature and then stored for several months in a cold room at 4 – 8 °C and heated up to room temperature directly before performing the conductivity measurements, on the other hand, were unsuccessful. The structures were not conductive from the start.

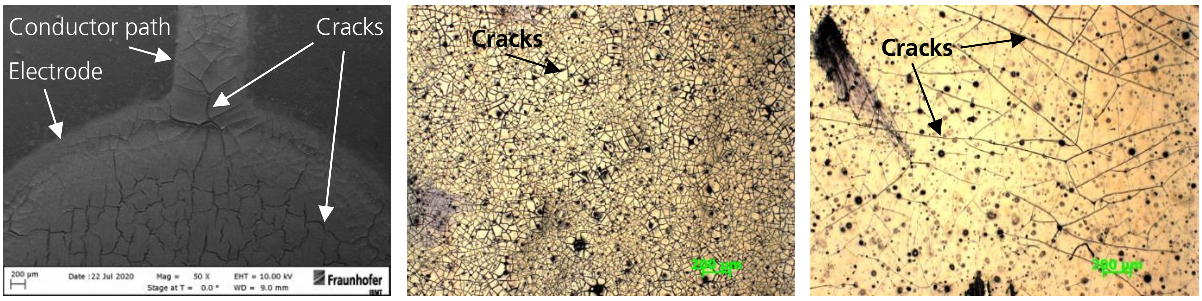


Figure 7: Cracks in silver structures (silver ink JS-A102A, Novacentrix) on 80 µm PU film (left and middle) and on 500 µm PU film (right) after 48 h storage at room temperature.

In order to examine the crack formation more closely, further test samples were printed on a 50 µm thin PET foil. Despite the cracks, which occurred on this less flexible substrate after sintering, the structures were electrically conductive even though the sintering temperature had to be reduced to 100 °C due to the thermally more sensitive substrate material. As a possible alternative to the Metalon JS-A-102-A silver ink, two other silver inks (Metalon JS A191 and Metalon JS A291) were tested after consulting the manufacturer. After printing on the PU substrates, these inks showed similar effects as the ink originally used and were no longer electrically conductive. In contrast, it could be shown that even single-layer prints were conductive on a smooth, rigid substrate such as polyimide film (UEB UPILEX 125 RN, thickness 125 µm). In these tests, it turned out that the combination of substrate material, substrate thickness and ink has a great influence on the generation and stability of conductive structures.

In contrast to the inks from Novacentrix, the silver ink from Fraunhofer IKTS did not show those negative long-term effects. This material had the best performance both with the Dimatix lab printer and with the industrial printer from Notion systems.

Biological tests of carbon and silver inks

With regard to the application as skin sensor, the biocompatibility of the selected inks was validated. This validation was done according to DIN ISO 10993 ("Biological evaluation of medical devices") by utilizing the WST-1-test, the BrdU-test and the live / dead staining of the cells. The first two procedures are extract tests according to ISO 10993-12. These quantitative techniques investigate the indirect influence of the material on cell viability, cell proliferation and metabolic activity: The WST-1-test determines the metabolic activity in form of an active respiratory chain, while the BrdU-test determines the rate of cell division. The samples (Figure 8) are incubated with the culture medium for 24 h to generate the extracts for the biocompatibility testing. Then these extracts are used for cultivation of the indicator cells. The live/dead staining is a qualitative direct contact test according to ISO 10993-5, where the indicator cells grow for 48 h directly on the samples with the printed patterns. The viable cells are stained using fluorescein diacetate (FDA) and appear as green fluorescent cells. The dead cells are stained with propidium iodide (PI) and appear as red fluorescent cells. As defined for biocompatibility tests, the human fibroblast cell line MRC5 was used as indicator cell line for the procedures described above.

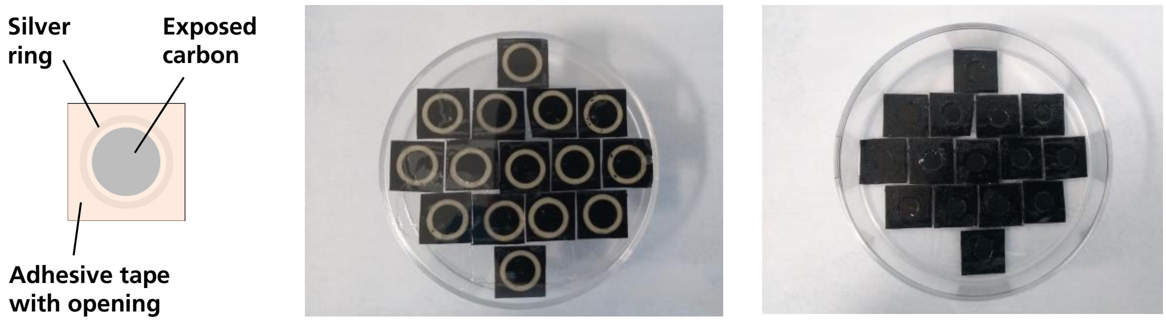


Figure 8: Samples for biocompatibility tests glued to the bottom of a 60 mm petri dish. Left: drawing of electrode layout with adhesive tape, sample size: 10 mm x 10 mm; middle: the view through the bottom of the petri dish shows the silver ring under the carbon; right: the view from top shows the full area of carbon over the silver ring and the adhesive tape on top.

We performed the direct and indirect tests according to ISO 10993 with the two carbon inks (the developed graphene-based IBMT ink and the commercial carbon ink from Novacentrix), with the silver ink from Fraunhofer IKTS and with a combination of the IKTS silver ink and the

Novacentrix carbon ink. All ink samples were printed on PU foil. The samples with silver and carbon had a silver ring covered by a full area of carbon and an adhesive tape with a round opening on top. This opening had a smaller diameter than the silver ring. This is to avoid that even if the carbon layer is defective and not completely closed, silver can diffuse through it and reach the cells or the culture medium. As expected, the pure silver samples had a cytotoxic effect on the indicator cell line. Both carbon inks as well as the combination of silver covered by carbon did not have any negative effect on the cells. The diagrams in Figure 9 show, that the samples with the carbon circle on the silver rings did not show any negative effect on the indicator cells. The measured metabolic activity and the cell proliferation were higher than the threshold of 70 %. The optical analysis of the cells after the direct contact test showed the intact cell morphology and their viability (indicated by the green fluorescence, see Figure 10).

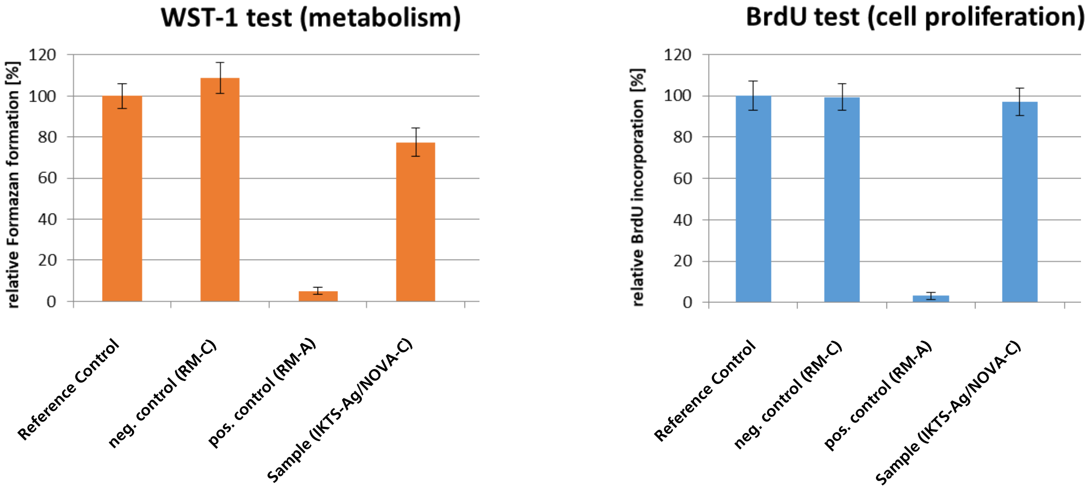


Figure 9: Extract test. Left: indicator cells show sufficient metabolic activity (> 70 %) after contact with extract, right: value for cell proliferation is at > 90 %.

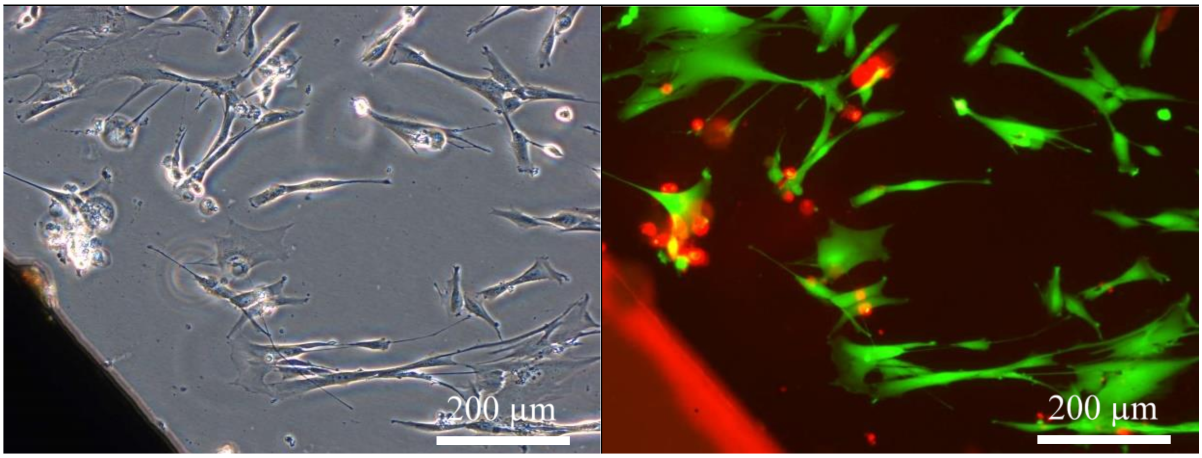


Figure 10: Direct contact test with MRC-5 cells on PU film with carbon on silver. Left: phase-contrast image, right: viable cells show green fluorescence.

In addition to the standard tests according to the ISO standard, we performed a HET-CAM assay. This test is normally used to investigate the mucosal compatibility of liquids and gels, but also solid samples can be tested. Chicken eggs are incubated and at day 8 the egg is opened so that the chorioallantoic membrane (CAM) is exposed. The samples are then placed on the CAM and the effect on the vascularization of the chicken embryo is optically examined.

The HET-CAM tests were performed with the Novacentrix carbon ink and with the combination of the carbon ink and the IKTS silver ink. The tests with the double layer (carbon on silver) should prove the ability of the carbon layer to cover the underlying silver completely. Figure 11 shows microscopic images of the samples on the CAM five minutes after exposition. Both images do not show any negative effects in the vascularization of the chicken embryo. Therefore both sample configurations passed this test.

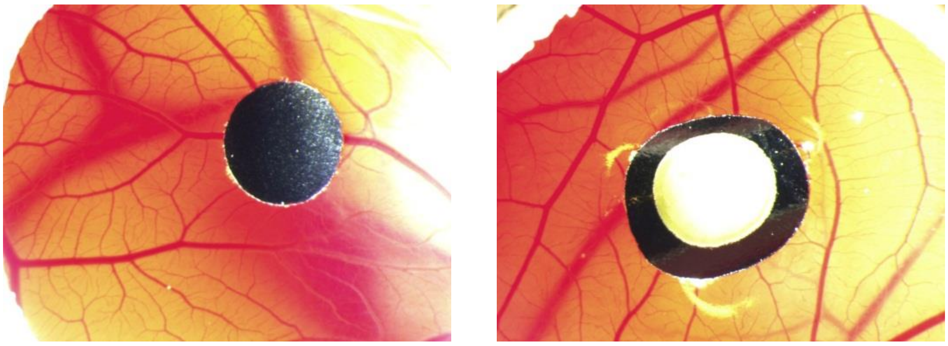


Figure 11: HET-CAM test with carbon layer (left) and silver layer covered with carbon (right). Both images show no alteration of the vascularization due to the exposition to the samples. Sample diameter was 5 mm.

Ink selection for sensor fabrication

Of the silver inks, the ink Ag-LT-20 from Fraunhofer IKTS showed the best long-term stability and the best performance with the industrial printer. For that reason, it was selected for the production of the sensors. Due to the complex handling procedure, the developed graphene-based ink proved to be unsuitable for use at Notion Systems. Instead, the commercial carbon ink (JR-700HV) from Novacentrix was selected for the production of the final sensors with the industrial printer. The printability of this carbon ink was further improved by changing the solvent combination. With the solvent combination of the Novacentrix silver ink the printing performance with the industrial printer was much better. Thus, Novacentrix provided a modified carbon ink with changed solvents for better printability.

5.3.1 Biodegradable ink formulations

Aside from the work with the nanoparticulate metal and carbon inks, we explored the feasibilty of a biodegradable ink. Those special formulations are seen as a promising approach for biomedical applications with printed sensors beyond the use of skin electrodes. In this context we developed Poly(lactide-co-glycolide) (PLGA) nanoparticles for the production of flexible and biodegradable electrodes. PLGA is a biodegradable and biocompatible material approved by the Food and Drug Administration (FDA) for use in medical devices. The synthesis was carried out using two different manufacturing methods, nanoprecipitation and the double emulsion solvent evaporation process. Nanoprecipitation was used to produce nanoparticles with a size of 121.8 ± 3.6 nm, a polydispersity index (PDI) of 0.05 ± 0.02 and a zeta potential (ZP) of

- 37.7 ± 1.5 mV. The synthesis of the nanoparticles by the double emulsion solvent evaporation process resulted in a particle size of 112.6 ± 7.2 nm, a PDI of 0.07 ± 0.02 and a ZP of - 37.7 ± 1.5 mV. With both processes, it was thus possible to produce nanoparticles with a monodisperse particle size distribution. In addition, various surface modifications were established which enable the surface properties of the nanoparticles to be changed, which among other things improves stability and enables controlled adhesion to surfaces. These biodegradable nanomaterials were then combined with electrically conductive nanomaterials in various compositions in order to obtain new biodegradable ink formulations. For this purpose, carbon black was added as conductive material. This process is known from the literature for the introduction of magnetic properties and was transferred to the ink development described above. In the double emulsion solvent evaporation process, carbon black was placed directly in the organic phase together with PLGA. Finally, after the particles were synthesized, they were coated with Poloxamer 407 in order to increase their stability. It was possible to produce particles in a size range of 375 – 465 nm, with a PDI of 0.4 – 0.6. Printing of this new ink with the Dimatix lab printer (Figure 12) resulted in electrodes with very high resistance values between 0.3 and 2.5 MΩ. The structures were not mechanically stable and were removed completely during the abrasion tests.

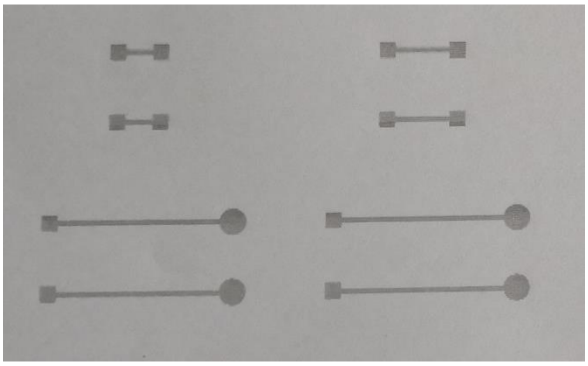


Figure 12: Sample electrodes printed with PLGA nanoparticles mixed with carbon black.

Most likely, the conductive carbon black was incorporated into the particle matrix in a way that the polymer base material shielded the conductive material. The ink produced in this way did not meet the technical requirements of the project and the approach was therefore not pursued further.

5.4 Process chain and pre-treatment processes (WP 3)

5.4.1 Pre-treatment process

The substrate pretreatment is very important in inkjet printing, since the inkjet inks have a very low viscosity in the range of 8-20 mPas. Due to this low viscosity, the dominant effect of the substrate wetting is the ratio of the surface energies of the substrate and the ink. Since the parameters of commercially available inks can no longer be adjusted, the wetting can only be controlled by changing the surface energy of the substrate.

The following pretreatments were investigated as part of the project:

- Oxygen plasma pretreatment (Tetra 30, Diener electronic, 100 W, 200 mTorr, 20 sccm gas flow, 50 s duration)

- Flaming (20 s)
- UV-ozone (Novascan PSD ProSeries Digital UV-ozone system, 30 °C, 10 min)

Very good results were achieved with plasma and UV-ozone. Flaming, a common technology for printing on glass, is unsuitable for heat-sensitive film substrates. Figure 13 shows an identically printed Ag structure on a pretreated and a non-pretreated PU substrate. Without treatment, the ink is spreading on the substrate and the structure does not have clear contours. In contrast, the structural fidelity on the pretreated substrate is very good.

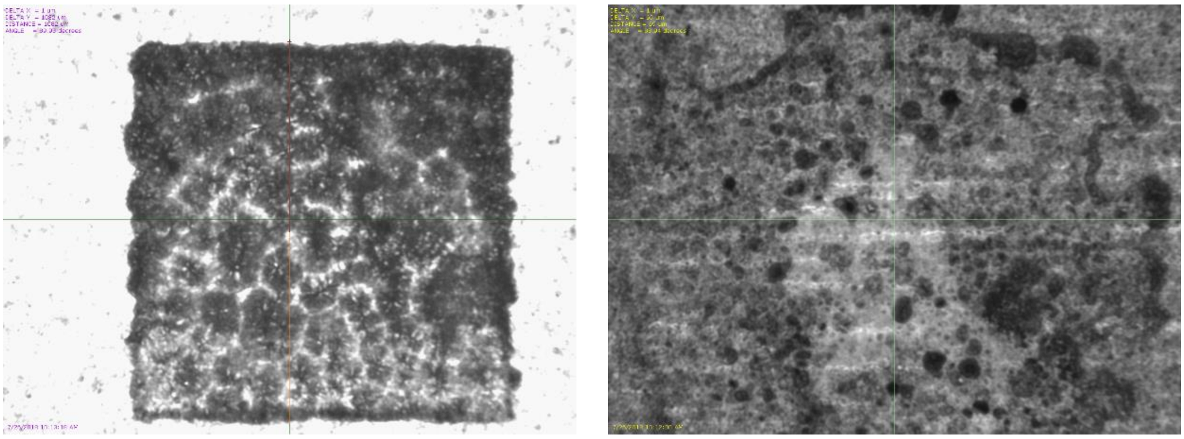


Figure 13 Printed Ag structure with (left) and without (right) UV-ozone treatment. Only with treatment (left picture), a clearly defined structure is obtained. The printed square in the left image has a size of 1 mm x 1 mm.

5.4.2 Conception and design study, facilitating the integration of inkjet printing with roll-to-roll based process chains

A concept for integrating a Notion inkjet printer into a roll-to-roll process chain was developed by taking the following points into account:

Print head and ink tank system

An inkjet print basket was developed that can accommodate up to nine industrial print heads. It is designed in such a way that different web widths can be flexibly printed. The arrangement is also chosen so that the substrate can be printed in one pass.

A recirculating tank system for inks was also designed for inks with a high particle density.

Flexible adjustment of the print width

The print basket was designed in such a way that the number of print heads allows flexible bandwidths from 60 to approximately 180 mm to be covered.

Alignment

A software solution was developed to align on registration marks in roll operation and to control the print heads accordingly. In the previous systems from Notion Systems with single substrate handling, this was not possible.

Inspection

Concepts were developed to integrate cameras to enable the alignment on registration marks and the control of the printed substrates.

Subsequent treatment of the substrate

Since Ag and graphene inks usually have to be cured thermally, a near-infrared (NIR) drying unit was integrated into the concept. This can be flexibly adjusted in length in order to provide sufficient performance even with future higher belt speeds or new inks.

Control

The software for controlling the Notion inkjet printer has been expanded. A decisive advance is that it is now possible to synchronize the data signals for controlling the drop ejection of the print heads with a tape movement. In the past, this was only possible with the systems from Notion Systems with encoders from linear motors.

5.5 Inkjet process and post-treatment processes (WP4)

Based on the developed process sequence defined in WP3, individual protocols for the inkjet printing of the sensors on PU films were developed for implementation with the lab printer at Fraunhofer IBMT and the industrial printer at Notion Systems. Figure 14 shows the sequence of the fabrication process.

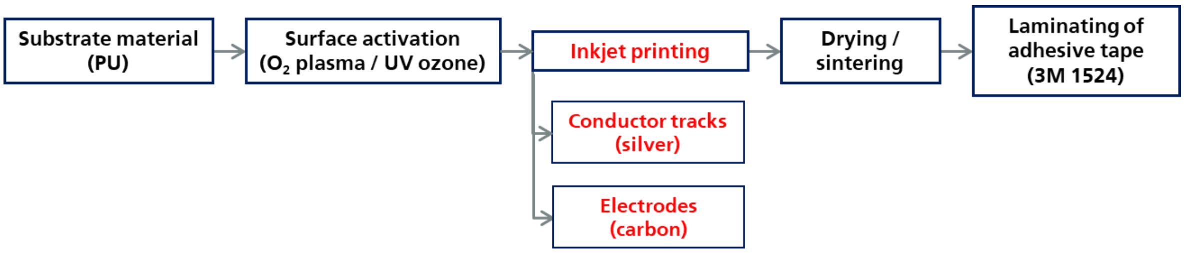


Figure 14: Production process for electrode fabrication.

Before printing, the PU film was activated in an oxygen plasma (100 W, 200 mTorr, 20 sccm gas flow, 50 s duration). This treatment enhanced the surface energy of the PU from 30 to 56 mN/m. As an alternative to the plasma activation, UV-ozone treatment (30 °C, 10 min) was also used before printing. The silver structures were printed with two or three layers of the Fraunhofer-IKTS ink at a resolution of 1260 dpi.

With the IKTS silver ink, we investigated the influence of the sintering process on the electrical conductivity. A low electrical resistance was achieved at maximum sintering temperatures of 120 to 150°C, a temperature range, which was still compatible with the PU foils. During the sintering process, clear changes in the coloration of the printed silver structures towards a shiny metallic surface were visible. Sintering times longer than 15 minutes at the maximum temperature and higher temperatures up to 200 °C resulted in corrugated and yellowish discolored PU films on which a second printing process could not be carried out.

A comparison with silver structures printed on polyimide films showed that the resistance of the printed test structures were comparable for the two materials (Figure 15). The slightly higher resistance measured on PU films is most likely due to the higher surface roughness of this film, leading to more inhomogeneous thicknesses of the printed silver structures.

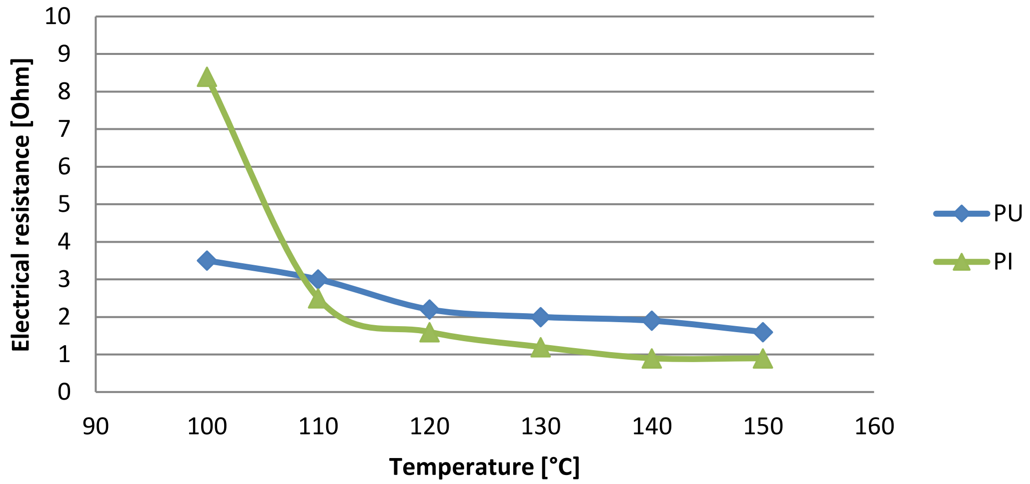


Figure 15: Electrical resistance of printed silver structures for different sintering temperatures (green: printed on polyimide film; blue: printed on polyurethane film). Sintering duration was 15 min after the target temperature was reached.

The sintering process must start at lower temperatures of 50 – 60 °C to minimize thermal impairment of the printed structures. A too fast temperature increase would lead to crack formation. Therefore, sintering of the silver was carried out in an oven starting at 50 °C. The temperature was increased to the maximum of 150 °C and after 15 minutes at this temperature, the substrates were taken out of the oven. The same drying procedure was also applied to the carbon structures, which were printed with the Novacentrix carbon ink in two layers onto the sintered silver.

After printing and sintering of the two materials, the PU substrates with the electrodes were covered by the medical grade adhesive to insulate the conductor paths and to build the interconnection layer to the skin. Round holes with a diameter of 4 mm were punched out at the positions of the active electrode area and the tape was then bonded to the PU substrate.

The number of layers, which had to be printed to obtain homogeneous and closed surfaces, differed between the lab printer and the industrial printer. Printing with the lab printer with its low number of nozzles (max. 16) required three layers of silver and six layers of graphene. Because of its several hundreds of active nozzles, the industrial printer only required two layers of each ink to create closed surfaces.

Layout considerations

Two different layouts for the active electrode area were designed, based on the results of the tests with the silver and carbon inks (Figure 16). The first option works with two full area circles of silver and carbon. Conductor tracks are printed with silver and the electrode area is a double layer of silver and carbon on top. The second option takes into account that there should be no silver directly under the carbon in the area of the electrode that will later be in contact with the skin. Electrical contacts, conductor tracks and a ring for circular interconnection with the carbon electrode were printed with silver. To define the actual electrode, a carbon circle, overlapping with the silver ring, was then printed onto the silver structure.

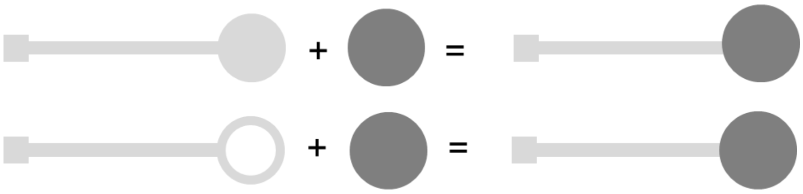


Figure 16: Schematic illustration of electrode layouts; top: full area circles of silver and carbon, bottom: silver ring and carbon circle.

The second design minimized both the risk of a possible diffusion of silver to the skin and the stiffness of the electrode. With the adhesive tape on top, the exposed area of the carbon circle is smaller than the inner diameter of the silver ring (illustrated in chapter 5.3, Figure 8). Thus, the active electrode area of the second design yielded the highest possible safety for the later application. This was also demonstrated and validated in the biological tests described before.

Test electrodes

Single test electrodes were printed with two different ink combinations, one with the graphene-based ink developed at Fraunhofer IBMT and one with the commercial carbon ink from Novacentrix (Figure 17). Both configurations showed a low resistance of < 10 Ohm, which was mainly caused by the resistance of the silver conductor track. As calculated, the graphene layer did not contribute significantly to the resistance.

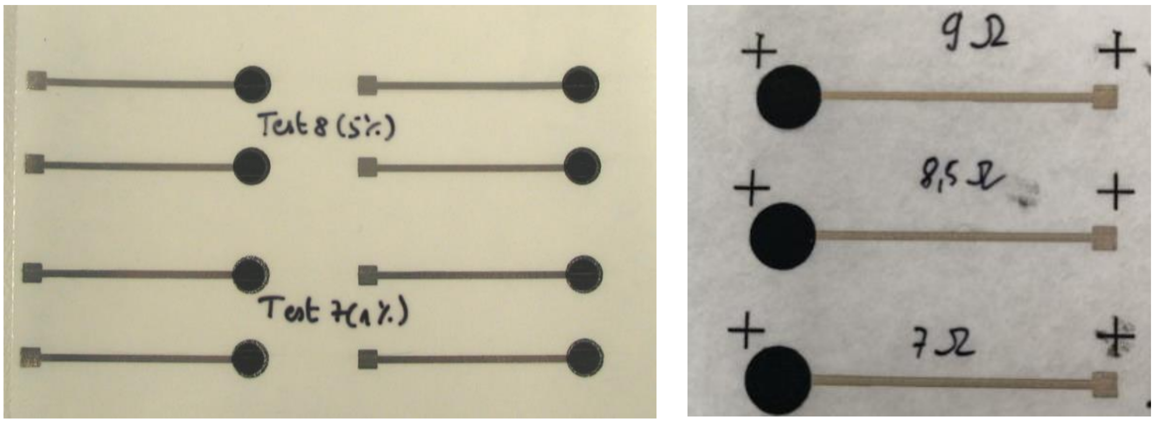


Figure 17: Test electrodes; left: electrodes printed with silver ink AG-LT-20 (Fraunhofer IKTS) and graphene-based ink with different detergent concentrations (Fraunhofer IBMT), right: electrodes printed with silver ink Ag-LT-20 and carbon ink JR700HV (Novacentrix, USA). Length of electrodes: 50 mm.

The high specific resistance of the carbon electrodes (0.0043 Ohm*m) does not have a significant effect on the conductivity of the electrode due to the very low layer thickness, which represents the actual length of the resistor for charge transfer between the skin and the sensor. Calculations showed that a circular electrode with 5 mm diameter and a supposed graphene thickness of 3 µm results in a resistance below 1 mOhm when only the thickness of the layers with < 5 µm is considered.

Two different multi-electrode configurations, designed by project partner TAU, were printed with the Dimatix lab printer using the combination of the IKTS silver ink and the developed graphene-based ink (Figure 18). The samples already had the required contact scheme for the later electrical connection with the electronics and showed the principal feasibility of this layout with the selected ink combination.

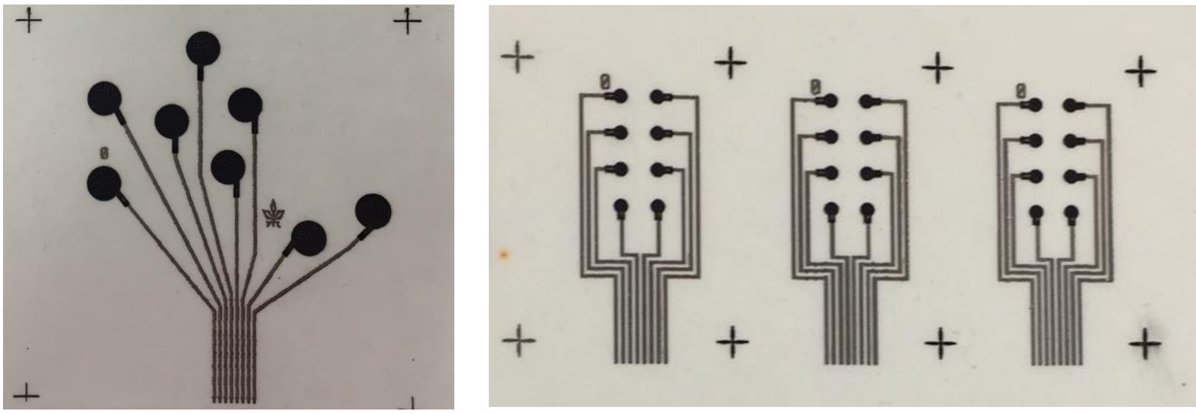


Figure 18: Multi-electrode sensors, printed with silver ink Ag-LT-20 and graphene-based ink (Fraunhofer IBMT). Left: sample size ~ 50 mm x 50 mm; right: sample size ~ 25 x 40 mm.

5.5.1 Inkjet Process

A wide variety of inks (graphene, carbon, Ag) were printed during the project period. The tests provided a comprehensive overview and the inks were sorted according to the following parameters, which were relevant for a successful printing with the industrial printer from Notion Systems:

- Waveform development
- Number of firing nozzles
- Maximum drop ejection frequency
- Temporal stability of the printing process
- Latency (how long a printhead cannot be used and when the process starts all nozzles fire)
- Sintering conditions to achieve electrical conductivity

The results of the inks used can be summarized as follows:

Carbon inks

The commercially available graphene inks used cannot be printed very reliably. Through research and the exchange of information with manufacturers of graphene products, it was found that individual graphene flakes are usually added to a liquid. There they can agglomerate and thus create a larger bond, which then clogs the inkjet nozzles. With this in mind, it is understandable that carbon inks with carbon nanoparticles should be preferred to graphene inks.

The commercial carbon inks show a better printing behavior both with the laboratory printer and the industrial printer from Notion Systems. However, the ink dries very quickly in the printhead, so that the preparation (cleaning of the printhead) before printing is more elaborate than with other functional inks.

Silver ink

The silver inks can be printed much better than the graphene and the carbon inks. In the course of the project, the printing results were transferred from the laboratory printer DMP 2850 (16 nozzles) to the Notion Systems njet lab platform with a KM1024i MHE print head (1024 nozzles). The printing time can be reduced from approximately 20 minutes to less than 10 seconds. Figure 19 shows two prints of sensor structures; one was printed with the laboratory printer from Fujifilm Dimatix and the other one with the industrial printer njet lab.

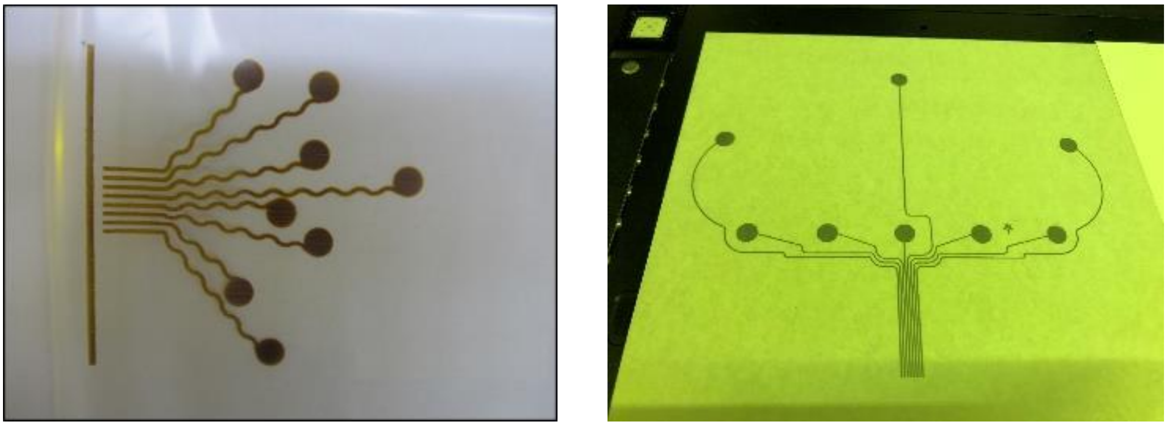
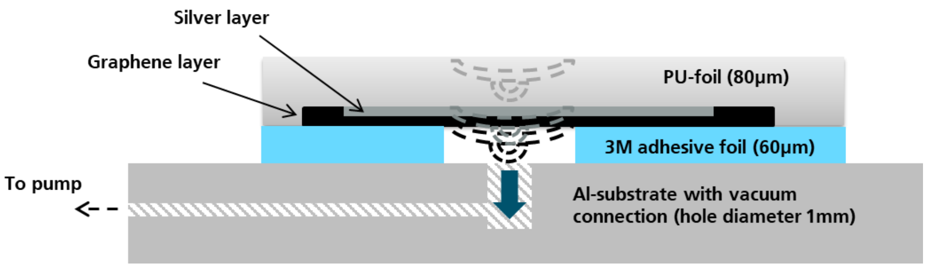


Figure 19: Inkjet-printed sensor structures. Left: sample size ~ 60 mm x 50 mm, printed with the DMP printer (printing time approximately 20 min); right: sample size ~ 90 mm x 160 mm, printed with the Notion Systems njet lab (printing time < 10 s).

5.5.2 Electrode rigidity characterization

A set-up for rigidity characterization of the flexible electrodes was developed in order to assess the mechanical properties of various electrode configurations and material combinations. The test samples were placed on a metal block that comprised two small holes with 1 mm diameter and was connected with a pump (Figure 20). Negative pressure sucked the foil samples (one without and one with printed layers) into the small hole. Pressure differences of 250, 500 and 750 mbar were applied and the resulting deformation of the samples was directly measured by a mechanical profilometer (DektakXT Stylus). The test samples comprised carbon electrodes, silver electrodes and combinations of carbon and silver, each produced on a 80 µm thin PU film by screen-printing, performed by partner TAU and inkjet-printing, performed by partner Fraunhofer IBMT. All samples showed the expected linear deformation behaviour and the measurements demonstrated the dependency of the extent of deformation on the layer thickness (Figure 21). The thickest screen-printed electrode (C200) had the lowest flexibility, whereas the thinner screen-printed electrodes (silver and carbon) and the inkjet-printed electrodes from one single material (carbon or silver) were most deformed. The thin inkjet-printed structures with thicknesses below 10 µm have a similar influence on the deformation as the thicker screen-printed structures.



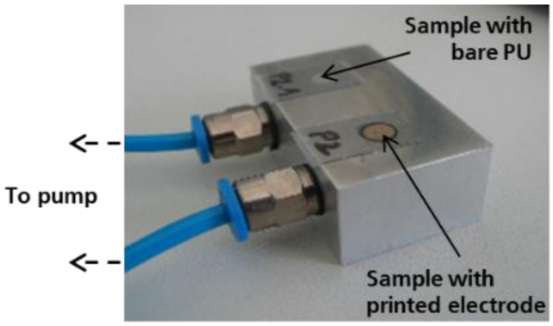


Figure 20: Set-up for rigidity measurements. Top: schematic drawing of metal block and foil stack, bottom: metal block with connection to the vacuum pump and sample foils.

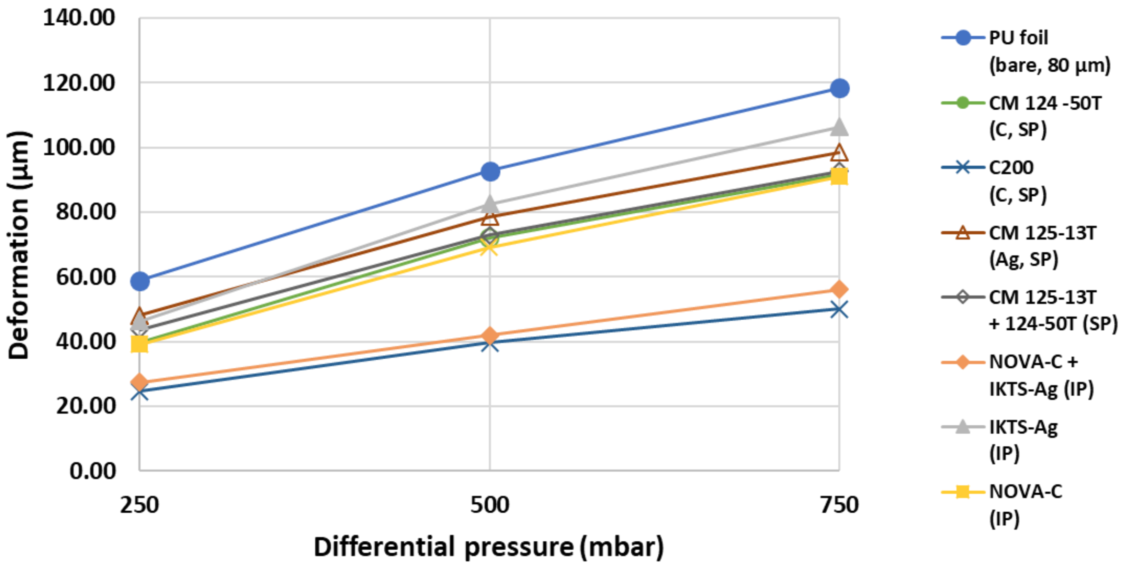


Figure 21: Deformation of printed samples at differential pressures of 250, 500 and 750 mbar.

The developed measurement set-up enables to correlate the mechanical properties of individual sensor electrodes with the electrical parameters obtained during EEG or EMG measurements. The mechanical stiffness of the electrodes was found to correlate with the level of noise in EEG recordings. This result supports the hypothesis underlying the project that mechanically easily deformable skin electrodes are better suited for the recording of EEG signals than mechanically stiff electrodes.

5.6 Skin electrode array production (WP5)

Production of foil-based basic sensor structures

A system with industrial Konica Minolta KM1024i print heads was set up at the njet lab in the technical center of Notion Systems. It turned out that, different from the first printing attempts on the DMP printer, no conductive structures could be created with the selected silver ink "Metalon A102A" from Novaventrix on PU foils. In contrast to that, conductive structures were obtained on PE foils. The microscope images in Figure 22 show the defects in the silver layer depending on the substrate material.

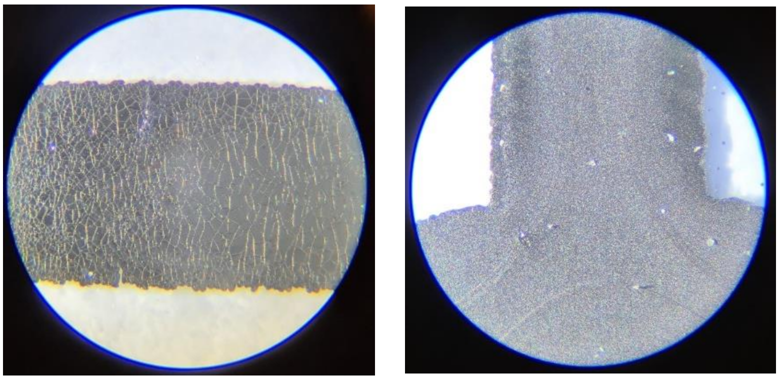


Figure 22 Microscope image of the dried silver layer of the Metalon A102A ink on PU film (left) and PE film (right). While cracks can be seen on the left, the layer on the right is without defects.

As this result confirmed the findings of the printing experiments with the different inks on the lab printer, the laboratory facility njet lab in the technical center of the company Notion Systems was finally set up with a system that contained the silver ink Ag-LT-20 from Fraunhofer IKTS and the carbon ink JR-700HV from Novacentrix.

With this material combination, the final electrode layout from partner TAU was printed by Notion Systems using the njet lab with the industrial Konica Minolta KM1024i print head. After UV-ozone activation of the PU substrate first the silver structures (contact pads and conductor paths) were printed in two layers at a resolution of 720 DPI. The silver was sintered in an oven at 150 °C and then the carbon structures (electrodes) were printed in two layers at a resolution of 720 DPI. The diameter of the carbon electrodes was larger than the diameter of the underlying silver. This overlap guaranteed the covering of the entire silver in the electrode area. Figure 23 shows a photograph of one printed electrode. In preparation for the measurements, the PU substrates with the electrodes were covered with the medical grade double-sided adhesive 3M 1524. This tape acts both as insulation layer and as interface to the skin. At first, the tape was mechanically structured to define openings at the positions of the electrodes. Then the tape was laminated on the PU foil with the electrodes.

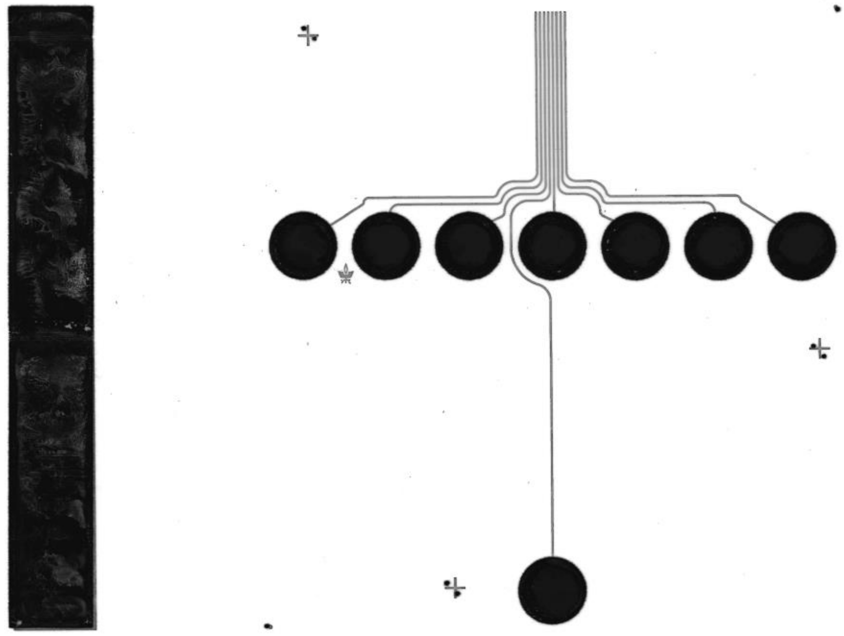


Figure 23 Inkjet-printed sensors for EEG and EMG measurements. The leader bar on the left has a length of 15 cm.

5.7 Electronics and electrical contacting (WP6)

In this work package, Sensomedical developed a miniature wireless ultra-low power system that can record electrophysiological signals from the brain, muscles or other sources.

On the basis of the BIOPOT 16-bit platform, an extremely low noise 24-bit version was developed. In addition, event-related potentials (ERP) were intensively studied and explored. The project was concluded with the submission of a patent application based on the ERP methods developed by Sensomedical as part of the project.

Another objective was the introduction of a platform that can support electrochemical sensing (bioimpedance at this stage). This platform was successfully developed and bench tested. The system was further designed to be MRI compatible.

The BIOPOT3 was updated to now have a 24-bit front end instead of 16 bits and upgraded from 8 channels to 24 channels. The system passed full electrical safety testing and can now be submitted to regulatory clearance. The noise level of the 24-bit electronics was reduced compared to the 18-bit electronics (see Figure 24).

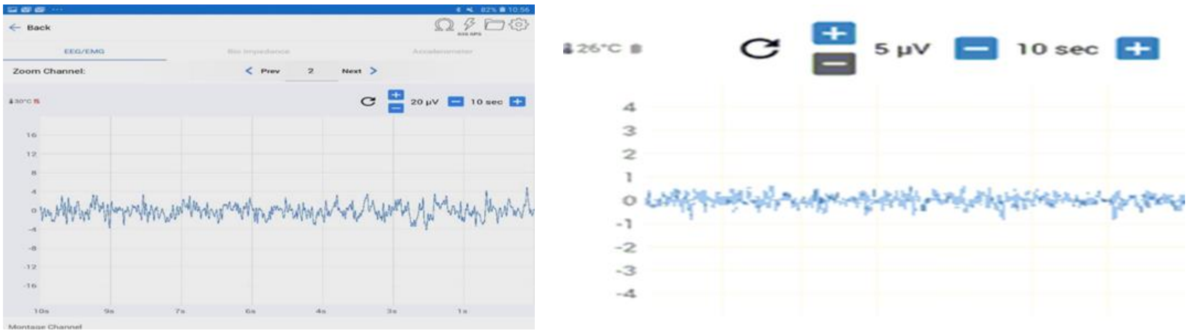


Figure 24: Left: noise of the 16-bit electronics (± 3 µV); right: noise of the 24-bit electronics (± 0.8 µV); grid scale is 1 µV.

A software development kit for device development with the BIOPOT was developed having the following features:

1. Allows device development on top of the BIOPOT platform
2. Signal acquisition and logging
3. 24 bits / 16 bits; up to 64 channels including bioimpedance and electrochemistry channels measurement
4. Standard European Data File (EDF +) / 24-bit file format
5. ERP recordings
6. Cybersecurity and vulnerabilities according to FDA guidance
7. Portability among operating systems (Windows, Android)

A robust connectivity between patch like printed electrodes and front end was achieved by integration of a customized ZIF connector (see Figure 25).

Figure 25: Special light-weight and low-profile connector that attaches to printed substrate patch and connects to the BIOPOT.

Extensive functional testing of the new device was performed with Sensomedical EEG stickers and off-the-shelf EEG caps (Figure 26). The volunteer was asked to relax, close his eyes for a few seconds and then open them: When eyes are closed, alpha waves are clearly visible on the lower two electrodes that are attached behind the ears (Figure 27).

Figure 26: Comparison of recording between off-the-shelf EEG headset (Muse) with BIOPOT3 24 bits (left); other electrode systems tested with BIOPOT system, e.g. electrode caps (middle); and BIOPOT sub-hairline stickers (right).

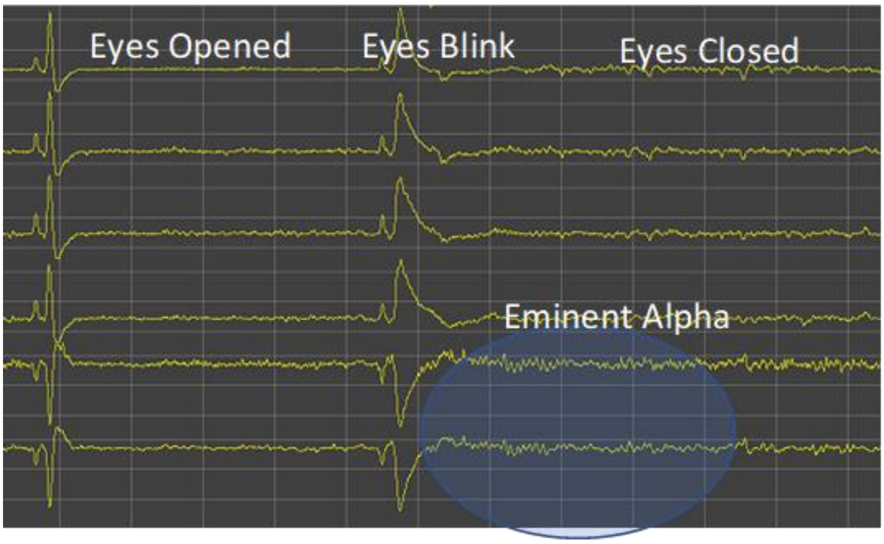


Figure 27: Recording traces of EEG recordings with eyes closed and open. The volunteer was asked to relax, close his eyes for a few seconds and then open them: When eyes are closed, alpha waves are clearly visible on the lower two electrodes that are attached behind the ears; y-axis scale is 20 microvolts per grid and 1 sec per grid for the x-axis.

The BIOPOT3 front end was changed to accommodate a 24-bit recording front end, getting to below 1 µV peak to peak of recorded noise when inputs are shorted to ground. In addition, power consumption fluctuations (a major source for noise) were balanced by software and other hardware filters to make the system quiet (Figure 28).

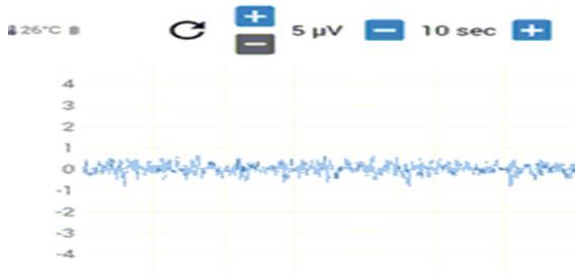


Figure 28: Recording background noise when channels are shorted to ground, with less than 1 µV peak to peak recording.

Bioimpedance recording was added to the BIOPOT front end. A signal is generated from the front end (frequencies between 100 Hz to 250 kHz) with amplitudes between 10 mV to 600 mV. Returned voltage amplitude and phase are measured and then resistance and reactance are extracted and displayed in real time along with EEG traces (Figure 29). The bioimpedance measurement tools can be used to predict mental states.

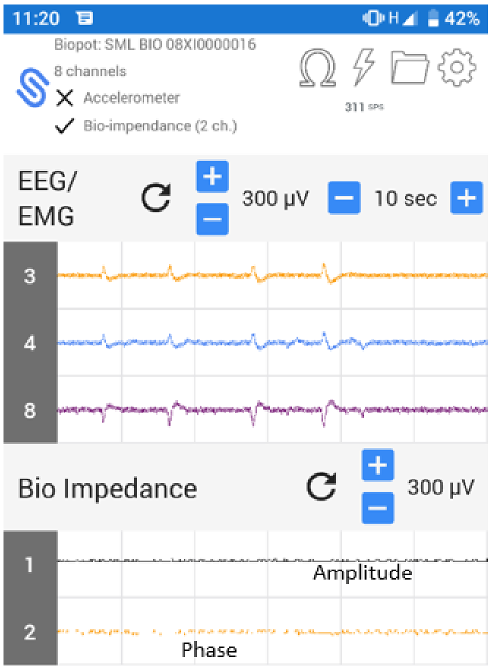


Figure 29: Real time acquisition of EMG and bioimpedance signals. Channels 3, 4 and 8 show the EMG signal traces; channels 1 and 2 include the bioimpedance real time measurement of amplitude in ohms and phase in degrees.

For data transmission, Bluetooth 5.0 was used to achieve extended range and throughput. We added and tested various synchronization methods with visual and sensory stimulation – for ERP experiments especially the connectivity to a smart phone. With regard to this development, a provisional patent was filed.

The BIOPOT3 was designed to be MR conditional to record EEG simultaneously with fMRI. An initial test was conducted to check whether an fMRI sequence would lead to device failure. Additional testing to fully qualify BIOPOT3 for compatibility with MRI should be conducted before use in clinical setup.

5.8 System evaluation (WP7)

The system with the printed electrodes was evaluated at two different levels. First, the base-line noise of the system was evaluated using base-line noise measurements. From these tests (40 Hz high-pass, $t \approx 15 - 20$ min) a median signal RMS of 19 was derived. This number was contrasted against values obtained under similar recording conditions using dry electrodes realized with various non-graphene inks.

For EMG applications, the system was used in a laboratory setup to measure muscle activity of the muscle of the forearm (Figure 30). Application of force validated high-fidelity recordings of EMG signal, equivalent to the state of the art in surface EMG (sEMG) recordings. For EEG validation, alpha waves were recorded (relaxed state with eyes closed) demonstrating the ability to perform EEG recordings (Figure 31). EEG responses were also tested using a python based setup, which was built for this project with electrode arrays that were designed and realized in the project. The recordings reveal initial demonstration of evoked response potential (ERP). We used a game paradigm in which a subject can either win or lose while his or her brain activity is monitored[19]. Each event is recorded and at the end of the session all win and lose events are grouped together to reveal a unique signature (Figure 32).

[19] Dvash, J., et al. "The envious brain: the neural basis of social comparison." Human brain mapping 31.11 (2010): 1741-1750.

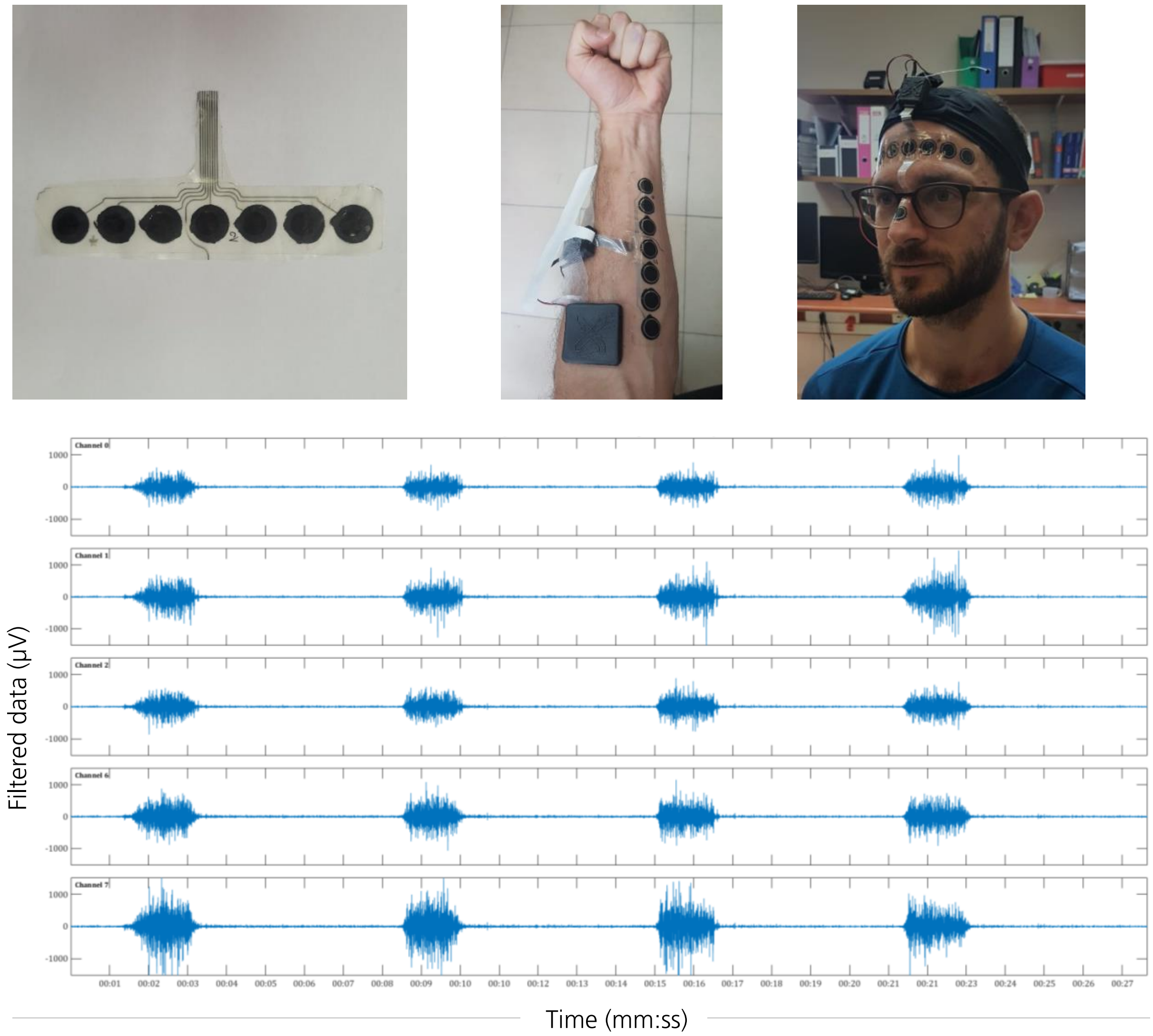


Figure 30: Printed electrode arrays (top left) with a wireless data acquisition unit positioned for surface EMG recordings (top middle) and EEG (top right). Bottom: EMG recordings with NanoEDGE electrode arrays. The data was collected with a wireless data acquisition system and was filtered with a 35-350 Hz bandpass filter and a 50 Hz notch filter. Data reveal high quality sEMG recordings.

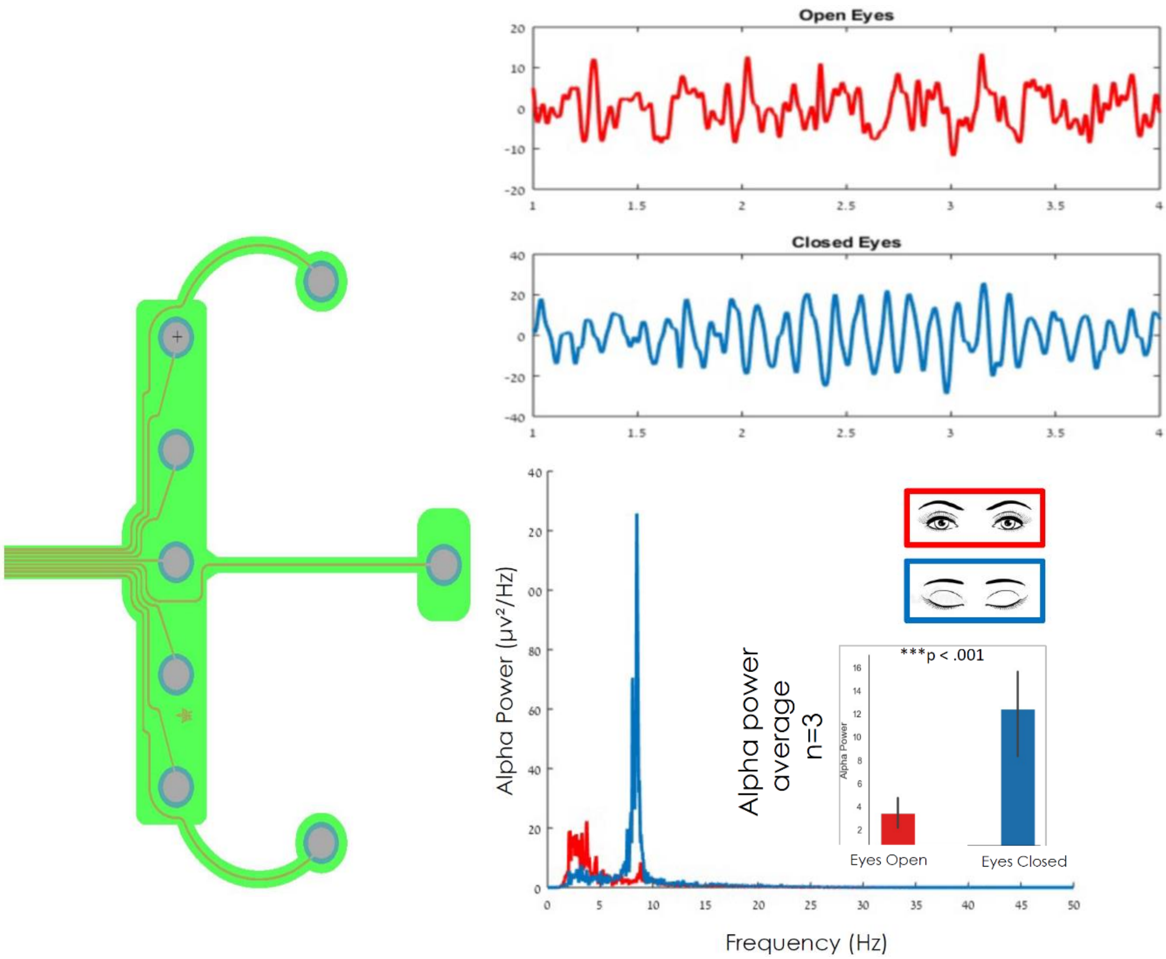


Figure 31: Layout of printed EEG electrode array (left) and alpha wave recordings (right). A strong alpha signal (10 Hz) shows when the eyes are closed indicating a relaxed state.

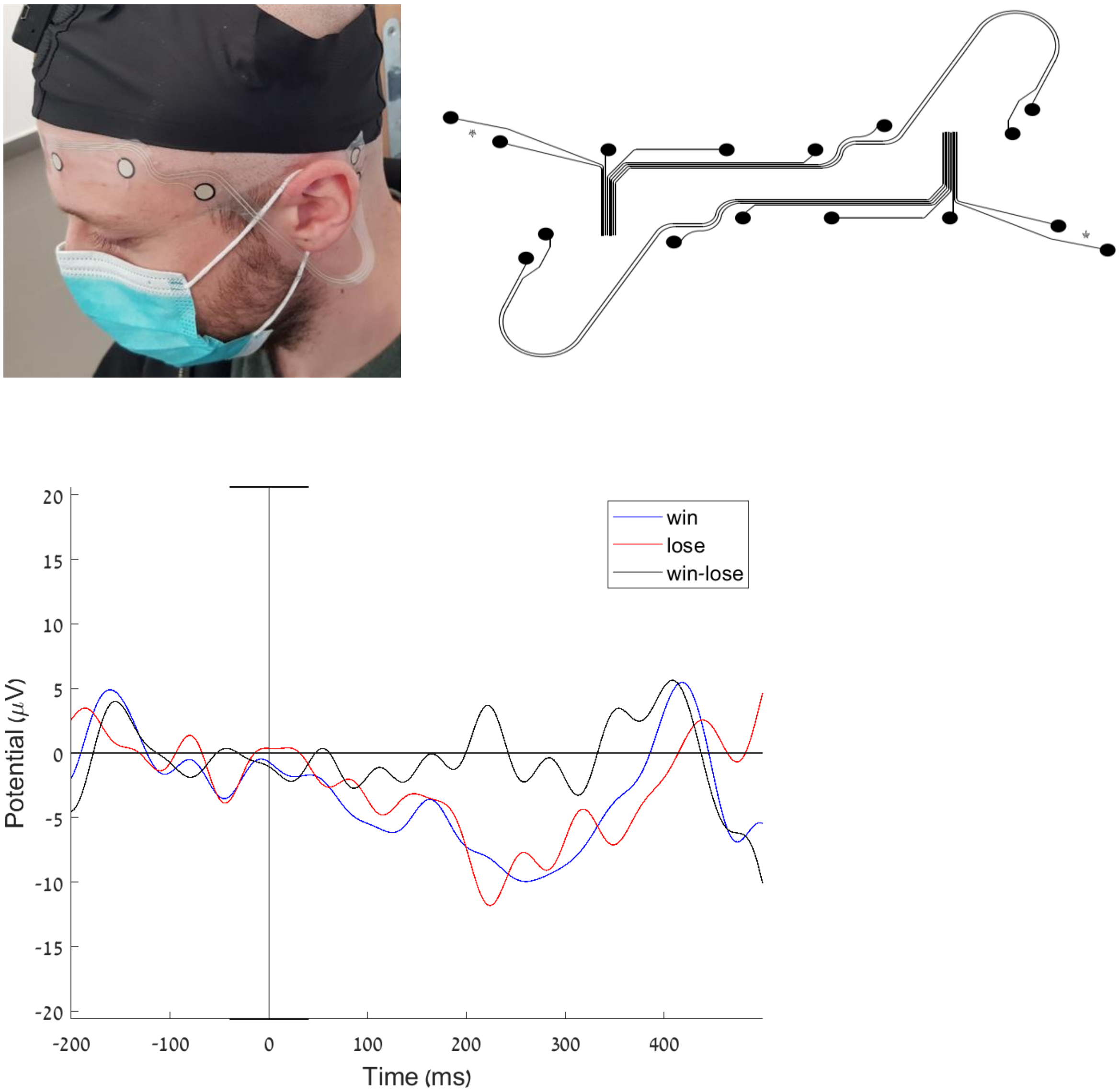


Figure 32: EEG setup (top left) with a dedicated layout (top right). EEG results (bottom) show average recorded potential for “win” events, “lose” events and the “win”-“lose” signal.

6 Exploitability of the results

6.1 Exploitability of results by Fraunhofer IBMT

The project results can be exploited in two ways:

a) The inks and production processes for production of biocompatible electrodes based on carbon nanomaterial can be used by users from different areas of sensors and devices for monitoring of signals from muscle cells or neuronal cells to produce competitive products. In these sensor and monitoring fields SMEs and start-ups are mainly active, whose innovative power and competitiveness are improved by the NanoEDGE results. In bilateral projects, IBMT would like to adapt the developed technologies to the specific needs of these companies. Specifically, this can mean that IBMT optimizes processes for the realization of electrodes of specific geometry and electrical characteristics with the existing experimental printing equipment and transfers the process parameters to these companies. The graphene and carbon inks suited for inkjet printing play an important role in the exploitation process. It enables using the scalable NanoEDGE production process which is based on inkjet printing. Scalability is important with regard to transfer of results of the R&D phase to production.
b) In addition to the NanoEDGE monitoring systems, application areas in the field of electrostimulation will be addressed. Based on the project results, Fraunhofer IBMT would like to develop and characterize printed stimulation electrodes based on graphene ink in bilateral research projects with medical technology companies.

6.2 Exploitability of results by Notion Systems

Notion Systems will benefit in several ways after the funding period.

a) First of all the project is a door opener to the market of wearable electronic devices and life sciences.
b) The process of inkjet printing graphene or other conductive inks on flexible and rigid substrates is suitable to be applied for many other applications, such as electrodes for photovoltaics or displays, electromagnetic shielding, or as a recyclable and biocompatible material for novel antennas of radio-frequency identification devices. Notion Systems estimates to sell up to 60 inkjet printers per year for these applications after a successful process development.
c) Third, up to now Notion Systems does not offer roll-to-roll equipment although such equipment is required for higher throughput when flexible substrates are used. With the design study of a highly accurate roll-to-roll printer Notion Systems can position itself in the area of flexible electronics, e.g. flexible displays or the use of printed electronics for packaging. After the design study, Notion Systems can build a prototype for a beta customer. Following that, up to 20 roll-to-roll inkjet printers per year can be placed in the market.

6.3 Exploitability of results by Tel Aviv University

Sensing electrode arrays developed in the NanoEDGE project will be designed according to specifications of Prof. Hendler's team and will be implemented in their work with patients.

Prof. Hendler's lab will focus on translating the newly developed imaging technique for monitoring deep brain activity via a single electrode in scalp EEG into the wearable system. Specifically, in recent simultaneous EEG/functional MRI (fMRI) studies, Hendler's group has derived EEG features predictive of the amygdala and the right inferior frontal gyrus (herby termed Electrical Fingerprint, EFP). They further showed that these features can be modified via NF procedure on healthy individuals and patients with chronic pain, attention deficits or post trauma disorders, modulating amygdala activity accordingly.

In the NanoEDGE project we further developed this EFP approach by transforming it into a wearable device as well as by expanding its localized and specific targeting. This was done by both, computational modeling of simultaneous EEG/fMRI data, as well as performing experiments to test and validate our combined developments in specific NF settings.

Combined, these two technologies will provide a first ever easy to use, wearable endogenic neuromodulation technique offering the EEG-based neurofeedback system. By monitoring brain activity over extended periods of time from many individuals, it will allow the generation of big data database on brain states under natural conditions, or with neurofeedback intervention. This new system will ultimately enable better training and more robust brain targeting, which in turn will lead to an increase in the brain-guided intervention effectiveness, and long-term therapeutic adherence.

6.4 Exploitability of results by Sensomedical Labs Ltd.

With the new developed sensors and hardware for EMG and EEG recording, Sensomedical was able to start expanding its R&D and OEM services in the field of neuroscience technology to its clients to include wearable OEMs that combine electrodes with electronics. The successful development of the new sensors and the production technology within the NanoEDGE project will shorten the time to market of these new wearable medical OEM products and contribute to the enablement of their successful realization. In addition, the successful exploitation of the project results will constitute a major contribution to revenues and company growth.

7 Cooperation with other agencies outside the collaborative project

On the part of IBMT there was no collaboration with other agencies outside the collaboration project.

Motivated by the project, Notion Systems initiated activities with the company Sixonia Tech GmbH for the development of a graphene ink. The company is a member of the "Graphene Flagship", an initiative of the European Union with the aim of bringing graphene beyond academic application to industry and the European community. The exchange is very valuable, as Notion Systems could learn a lot about the production, the limitations and the possibilities of graphene.

TAU collaborated with X-trodes, a spin-off company of TAU, which supported the data collection effort.

For Sensomedical there was no collaboration with other agencies outside the project. However, many entities have evaluated the BIOPOT technology or are in the process of using it as clients of Sensomedical. And some have already started using the technology in various applications.

Furthermore, the two academic partners TAU and IBMT see options for joint collaboration beyond the NanoEDGE project. In particular, besides the applications addressed within NanoEDGE, also biosensors and implantable stimulation and monitoring devices offer good opportunities for exploiting the project results and for future collaboration. Continued cooperation between the involved project partners will facilitate the development and implementation of those devices.

8 Progress made by others during the project duration

During the implementation of the project, no results or progress became known from other research groups that were directly related to skin electrodes made from carbon nanomaterials.

In March 2020, Ferrari et al.[20] published results related to inkjet-printed tattoo electrodes for application in clinical EEG recording. The electrodes sensing area and interconnections are made of PEDOT:PSS, a conducting polymer.

With respect to graphene/carbon and silver inks, we have identified new products on the market. Their suitability for the tasks of the NanoEDGE project was investigated and some of these inks were used for printing the final NanoEDGE electrodes with an industrial inkjet printer.

Notion System is not aware of progress in the field of inkjet-printed skin sensors by other R&D groups.

[20] Ferrari, Laura M., et al. "Conducting polymer tattoo electrodes in clinical electro-and magneto-encephalography." npj Flexible Electronics 4.1 (2020): 1-9.

9 Summary and conclusions

The NanoEDGE project had several important scientific results. Silver and carbon inks suited for inkjet printing with the Fujifilm Dimatix printer were identified and corresponding processes for pre-treatment, printing and post-treatment have been successfully developed and transferred to an industrial printer. Skin electrodes for EMG and EEG recording were successfully produced and tested. One important outcome of the project is the ability which IBMT and TAU developed to quantify the stiffness of electrode arrays produced using different inks. Some inks we tested for the production of the electrodes have inferior recording qualities which we can now directly associate with their poor bending properties.

We further demonstrated in the project the ability to perform ERP experiments with dry printed electrodes. These experiments have far reaching applications in cognitive neuroscience.

An extremely low noise 24-bit version of the BIOPOT system of Sensomedical was developed for recording electrophysiological signals from the brain, muscles or other sources. Combining Bluetooth low energy with wireless recording, 24-bit EEG recordings can be recorded with highest fidelity and quality. A novel method for synchronising signal recording with visual stimulation in ERP experiments - particularly the connectivity to smartphones - was developed and a provisional patent was filed.

One project finding was that finding suitable combinations of substrate materials and inks is essential concerning the occurrence of cracks on soft substrates. Further research is needed to investigate these complex interdependencies in detail. Another remaining challenge concerns the transfer of inks and printing processes from a laboratory printer to an industrial printer. Although this transfer has been carried out successfully, there is still a need to investigate the factors influencing repeatability and reproducibility of the transferred processes.

Further research is also needed on powering of wearable electronics. Also, additional research should be conducted in order to determine why dry skin electrodes are superior to wet electrodes. Other aspects that need further research are the cost benefit and patient benefit of nanotechnology-based medical devices, i.e. the question of the cost-benefit ratio. Additional research efforts and extensive testing are required prior to the market introduction to demonstrate that the benefits to patients outweigh the risks associated with the use of nanomaterials. Safety issues could for example become very important due to their nano size and possible interactions with DNA. Because of their novelty and not yet fully known biocompatibility, nanomaterials must show a significant increase in performance compared to conventional electrode materials in order to be considered for clinical applications.

Future research on the use of wearable EEG electrodes should focus on mechanical stability of the system to allow stable recordings despite mechanical movements. Further, there is a need to explore the best electrode positions that will allow for both improved electrophysiological data collection and increased user comfort during electrode array placement and extended use. For extended EEG use a full system should also take into account precise synchronization between the triggers and the recording system.

10 Publications, lectures, presentations, etc.

Doctoral, Master or Bachelor theses

Adeline Lefèvre (2019): Inkjet printing process for wearable electrodes on PU films. Master Thesis, Université de Mons (Belgium) / Fraunhofer IBMT

Neomi Singer, a joint post-doc with Profs. Talma Hendler and Yael Hanein performed her training as part of the NanoEDGE project.

Presentations

Maayan Doron, Netta Dunsky, Shiran Shustak, Lilah Inzelberg, Talma Hendler, Yael Hanein, Neomi Singer, Functional Feasibility of Recording High-resolution EEG via Dry Wearable/tattoo Electrodes, poster presentation at the Israel society for neuroscience (ISFN) annual meeting 2019, Eilat, Israel.

Oral presentation of the NanoEDGE project during the "Mid-term meeting German-Israeli cooperation in the field of Applied Nanotechnology", February 26, 2019, Bonn, Germany.

Press release "NanoEDGE: Wearable electronics and printed electrodes for EEG and EMG recordings" by Fraunhofer IBMT on November 25, 2019.

Flyer "NanoEDGE" available on the project website www.nanoedge.eu.

Brochure "NanoEDGE" distributed at the booth of project partner Fraunhofer during MEDICA 2019 exhibition, Düsseldorf, Germany.

Presentation of printed electrodes at Fraunhofer booth at MEDICA 2019 exhibition, Düsseldorf, Germany.

Oral presentation of the NanoEDGE project during a scientific session at the Fraunhofer booth during MEDICA 2019 exhibition, Düsseldorf, Germany.

Thomas Velten, Thorsten Knoll, Sylvia Wagner, Axel Brenner, Sascha Wien,Yael Hanein, Moshe David-Pur, Aaron Gerston, David Volk, Maroun Farah, Luai Asfour, Micha Plaksin, Evaluation of functional inks for printing of electrodes with direct skin contact, oral presentation at LOPEC 2021 Conference, March 24, 2021, Munich, Germany.

Oral presentation of the NanoEDGE project during the "Final Workshop of the Israeli-German Cooperation in Applied Nanotechnologies", virtual meeting on November 4, 2021.

11 Acknowledgement

The German part of this research and development project was funded by the German Federal Ministry of Education and Research (BMBF) in the "Innovations for Production, Services and Work of Tomorrow" program with the funding numbers 02P17W000 and 02P17E001 and was managed by the Project Management Agency Karlsruhe (PTKA).

The project partners thank the BMBF for the support of the project and the project supervisor.

Part of the project work was undertaken in collaboration with Israeli partners under the "German-Israeli Bilateral R&D Cooperation in the Field of Applied Nanotechnology". Furthermore, this project is co-funded by Israeli innovation authority. IIA is Israel's innovation agency. It works with people, companies and partner organisations to find and drive the science and technology innovations that will grow the Israeli economy.

The project partners would like to thank for the support.

12 List of references

[1] Knoll, T., et al. “High-resolution gravure printing of graphene biosensors” Proceedings of The Global Conference on Micro Manufacture, Incorporating the 11th International Conference on Multi-Material Micro Manufacture (4M) and the 10th International Workshop on Microfactories (IWMF) (4M/IWMF2016), 13-15 September 2016, Kgs. Lyngby, Denmark.

[2] Bareket, L., et al. “Temporary-tattoo for long-term high fidelity biopotential recordings” Scientific reports 6.1 (2016): 1-8.

[3] Eleftheriou, Cyril G., et al. “Carbon nanotube electrodes for retinal implants: a study of structural and functional integration over time” Biomaterials. 112 (2017): 108-121.

[4] David-Pur, M., et al. “All-carbon-nanotube flexible neuronal electrodes” Biomed Microdevices 16 (2014): 43-53.

[5] Singh, M., et al. “Inkjet Printing Process and Its Applications” Advanced materials 22.6 (2010): 673-685.

[6] Shimoda, T., et al. “Solution-Processed Silicon Films and Transistors” Nature 440.7085 (2006): 783-786.

[7] Noh, Y.Y., et al. “Ink-jet Printed ZnO Nanowire Field Effect Transistors” Appl. Phys. Lett. 91 (2007), 043109–3.

[8] Okimoto, H., et al. “Tunable Carbon Nanotube Thin- Film Transistors Produced Exclusively via Inkjet Printing” Advanced materials 22.36 (2010): 3981-3986.

[9] Singh, M., et al. “Inkjet Printing Process and Its Applications” Advanced materials 22.6 (2010): 673-685.

[10] Luechinger, N.A., et al. “Graphene-Stabilized Copper Nanoparticles as an Air-Stable Substitute for Silver and Gold in Low-Cost Ink-Jet Printable Electronics” Nanotechnology 19.44 (2008): 445201.

[11] Ha, M., et al. “Printed, Sub-3V Digital Circuits on Plastic from Aqueous Carbon Nanotube Inks” ACS nano 4.8 (2010): 4388-4395.

[12] Torrisi, F., et al., Inkjet-Printed Graphene Electronics, ACS nano 6.4 (2012): 2992-3006.

[13] Han, X., et al. “Scalable, printable, surfactant-free graphene ink directly from graphite” Nanotechnology 24.20 (2013): 205304.

[14] Cohen, Michael X. "Where does EEG come from and what does it mean?" Trends in neurosciences 40.4 (2017): 208-218.

[15] Meir-Hasson, Y., et al. "An EEG Finger-Print of fMRI deep regional activation" Neuroimage 102 (2014): 128-141.

[16] Keynan, Jackob N., et al. "Limbic activity modulation guided by functional magnetic resonance imaging–inspired electroencephalography improves implicit emotion regulation" Biological Psychiatry 80.6 (2016): 490-496.

[17] Sulzer, J., et al. "Real-time fMRI neurofeedback: progress and challenges" Neuroimage 76 (2013): 386-399.

[18] Peng, S., et al. "The sheet resistance of graphene under contact and its effect on the derived specific contact resistivity." Carbon 82 (2015): 500-505.

[19] Dvash, J., et al. "The envious brain: the neural basis of social comparison." Human brain mapping 31.11 (2010): 1741-1750.

[20] Ferrari, Laura M., et al. "Conducting polymer tattoo electrodes in clinical electro-and magneto-encephalography." npj Flexible Electronics 4.1 (2020): 1-9.

Link to the dataset in the database „Fraunhofer-Publica“
http://publica.fraunhofer.de/dokumente/N-6440648.html
urn:nbn:de:0011-n-6440648