P 90

Development of micro electromechanical biosensor for fast detection of respiratory syncytial virus infections in newborns

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Infectious diseases are one of the world's leading causes of morbidity and death. In the case of newborns, infections with the Respiratory Syncytial Virus (RSV) are of particular significance. The guarantor of a successful treatment is an early disease diagnosis enabling the accurate patient stratification and prognosis of disease outcome. Conventional diagnostics for the identification of unknown pathogens require large sample volumes and are rather laborious and time-consuming. Therefore, rapid and ultra-sensitive point-of-care diagnostics, which enable faster and more personalized patient treatment for much lower costs, are gaining higher attention. The most critical component of these point-of-care devices is a bio-sensor that detects, with a high degree of precision, specific molecules.

In this work, a novel flexural plate wave (FPW) bio-MEMS sensor for the detection of RSV infections in newborns has been successfully designed, fabricated and tested. The sensor targets the detection of chemokines and an RSV protein in swab-samples, thus providing clinicians with reliable information on type and severity of the infection, and consequently enabling the adequate decision on the patient's treatment. The operating principle of the sensor, using the piezoelectric effect, is based on the frequency shift of a resonating membrane due to attachment of an additional mass.

The sensor's performance has been experimentally verified. The sensor's surface was functionalized with a layer of capture molecules (the layer is immobilized via click-chemistry) that specifically bind the target molecule. Clear resonant frequency shifts have been observed after the functionalized sensor was brought into contact with aqueous solutions (tris-buffer) of the chemokine, whereas bringing the sensor into contact with a non-target molecule led to hardly any frequency shift. This proves the selectivity of the fabricated device. The detection procedure using the developed sensor takes ca. 15 minutes, whereas with currently employed conventional methods several hours.

P 91

Registration and evaluation of alternative non-invasive parameters for orthostatic hypotension in geriatric patients

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Estimation of orthostatic hypotension by arm cuff blood pressure- and heart rate registration (Schellong test) is difficult to perform in cases of restricted mobility in geriatric patients. Therefore, alternative, non invasive parameters for the registration of orthostatic hypotension are requested in the elderly population.
In 60 patients of the Geriatrische Rehabilitationsklinik Dresden Löbtau (mean 82 years, 80% female) blood pressure, impedance- and electrocardiogram were recorded by VasoScreen 3000 (medis, Ilmenau, Germany) for 5 minutes in a lying and 5 minutes in a standing position. Additional arm cuff blood pressure reference measurements were performed 1x in a lying- and after 1, 2 and 3 minutes in a standing position. A subset of derived parameters was correlated to the blood pressure and heart rate course during the 10 min registration. 11 patients were excluded due to contraindications (absence of sinus rhythm, deficient data quality, inability for standing during investigation). Statistics were performed by Wilcoxon signed-rank test and U-tests (MATLAB 9.2.).
In 19 patients (39%) orthostatic hypotension could be demonstrated by the criteria of Schellong. Promising alternative parameters showed complete or partly significant correlation to the course of blood pressure- and heart rate regulation: pre-ejection period (time between electrocardiographic Q-beginning and B point of the impedance cardiogram), velocity index, acceleration index and cardiac index. Additional measurements of a larger population are needed for the validation of our results.

P 93

Investigation of the viscosity of human middle ear effusions by endoscopic optical coherence tomography

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A middle ear effusion is the result of an infection, a dysfunction or constriction of the Eustachian tube and is often associated with an inflammation of the ear (otitis media). More than 75 % of children at the age of 3 years have already suffered from otitis media. With the standard diagnostic methods, e.g. otoscopy, audiometry or tympanometry, it is not possible to characterize the effusion. At the moment, the effusion can be classified as serous or mucous by the physician only after paracentesis. The aim of our study is to support the physician in the decision whether the incision of the tympanic membrane is necessary.
In this study, we investigate model fluids, which simulate the viscosity and scattering properties of middle ear effusions ex vivo by endoscopic optical coherence tomography (EOCT). EOCT is a multifunctional diagnostic tool (combined otoscopy, laser doppler vibrometry) based on low coherence interferometry and has a penetration depth of 1 - 2 mm in scattering tissue. Using M-scans, the time dependent fluctuation of the intensity can be measured, which is the result of diffusion of particles in the effusion. By determination of the intensity-autocorrelation for each depth, a mean diffusion coefficient is calculated. By Stokes-Einstein equation, viscosity and diffusion coefficient are connected. In addition, all samples have been analyzed using a rheometer, which measures directly the viscosity of the effusion.

P 94

Design of a switched-capacitor array for high-power applications with dense coverage of medium frequency-range

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Magnetic Hyperthermia has been studied for a number of years because of its suggested importance in therapeutic applications like cancer treatment. In addition to the magnetic field-generator which heats the magnetic nanoparticles with an alternating magnetic field, the behaviour of the used magnetic nanoparticles is of significant importance. It is well-known that the behaviour of the particles related to magnetic hyperthermia is dependent on several parameters like the amplitude of the magnetic field, the viscosity of the surrounding medium and the particles intrinsic properties. As it is relatively easy to arbitrarily change the amplitude of a magnetic field lots of studies have been carried out which examine the heating behaviour of magnetic particles depending on the amplitude of the magnetic field. However a change of frequency is technically more demanding, especially considering the typical frequency range of magnetic hyperthermia which is around $100\,\mathrm{kHz}$ to $1\,\mathrm{MHz}$ with corresponding amplitudes of around $3\,\mathrm{mT}/\mu_0$ to $30\,\mathrm{mT}/\mu_0$. Due to the technical difficulties it was only possible to select discrete frequencies to measure the magnetic heating behaviour of magnetic nanoparticle samples. As typical broadband matching techniques, like ladder-networks or transformer-based approaches fail due to either huge mismatch or limited bandwidth, only capacitive impedance matching provides the necessary quality of the impedance matching and equally tolerates the required amount of power to produce magnetic fields of a certain strength. This contribution presents a method to design a switched-capacitor array to provide a dense matching in the forementioned frequency-range while withstanding the high amounts of power that drive the field-generator. Besides the presentation of an design algorithm, a closer look will be taken on an exemplary result of this algorithm to show the feasibility of this approach to provide a measurement-system with arbitrarily selectable frequencies in the range of $100\,\mathrm{kHz}$ to $1\,\mathrm{MHz}$.

P 95

MEMS-FTIR-based reference system for glucose and lactate determination in the NIR wavelength range

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Introduction: Glucose and lactate represent an important indicator for human metabolism performance. The determination is important for sports and clinical medicine. Due to several disadvantages of commonly used encymatic-amperometric methods, an optical measurement is desirable. Main challenges for optical determination are spectral overlap of different blood components and low absorbance of physiological glucose and lactate levels.
Methods: We built a measurement setup using novel MEMS-based Fourier spectrometers to exploit absorbance of glucose, lactate and albumin in the NIR wavelength range of 1300-2500 nm. A multivariate regression model was created to investigate predictability. Therefore, we compared different wavelength ranges and their combinations to obtain best accuracy for mixtures of glucose, lactate and albumin. Additionally the influence of data preprocessing methods was investigated. We took continuous reference spectra for compensation purposes because drift effects of light source emission or temperature-depending sample absorbance have huge influence on prediction accuracy. Sample contamination by previous measurements as a possible source of error was reduced by improving cuvette flushing procedure and evaluation of various cuvette geometries.
Results: Best results were achieved for 2050-2400 nm where the strongest NIR absorbance was found. Our measurements show that the optical distinction between glucose, lactate and albumin is possible. Especially glucose shows a high correlation with diluted water which improves prediction without impurities, but makes the system sensitive to similar resulting drift effects of sample temperature. Therefore continuous reference measurements are essential to ensure reliable concentration prediction.
Conclusion: We showed that spectral detection of glucose, lactate and albumin with MEMS-based Fourier-spectrometers is possible. By systematic investigation of interferences we were able to improve stability. This new spectrometer generation enables new opportunities regarding cheap glucose and lactate determination by obtaining spectral resolved data from samples.

P 96

Impedance matching of small laser fabricated double-sided intrafascicular electrode arrays

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During the recent years we introduced a novel laser fabrication process for thin parylene C based electrode arrays. Utilizing a LUMERA LASER Rapid10 picosecond (ps) laser system the thickness of these electrode arrays can be driven below 40 µm. By only using materials classified for chronic implantation by the United States Pharmacopoeia (USP class VI) biocompatibility of the arrays was directly taken into consideration. This allowed for their application as an intrafascicular devices in long-term in vivo implantations. Whereas the inexpensive, maskless and flexible design are a clear advantage over lithographically structured thin film electrodes, the disparity in electrochemical behaviour between front –and backside electrodes might have unfavourable consequences.
Due to different approaches in opening the electrodes on the front -and backside, the active area of the opening varies, even though the geometrical area is the same. Sample electrode arrays were investigated optically and electrochemically to gain insight in the actual surface texture. Scanning electron microscope (SEM) imagining in combination with a focused ion beam (FIB) gave further insight in the porosity of metal surfaces treated by ultrashort laser pulses. Next to adjusting the geometrical area of the rougher electrode surfaces to achieve impedance matching, coating the electrodes with PEDOT and nanorough platinum was investigated.
It could be observed that the impedances of geometrically identical electrodes at 1 kHz differ about 30 % between the front and the back. This disparity overlaps with the rippled surface following laser hatching. While coating the electrodes only minimally changes the proportion, a drop of about one order of magnitude in impedance occurs. This drives the disparity towards the standard deviation of untreated electrodes, thus offering a second approach for impedance matching.
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P 97

Autonomous powered R wave detector

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Energy harvesting has the potential to substitute batteries for powering devices. Some industrial solutions are already available, but they use continuous energy sources, like temperature gradients or vibrations. For wearables, it is not possible to predict the time for energy input, so a smarter technology is needed to handle the energy input. The aim of the project is to monitor the instantaneous heart rate without the use of batteries powered only by discontinuous and stochastic power chunks.
The developed power management system collects electrical energy until the storage capacitor is fully charged. When it reaches a certain threshold, an ECG measurement is started for the next 3.5 seconds. The measured signal gets analyzed in real time with R wave detection and the result gets transmitted to a computer or mobile device via Bluetooth low energy.
The result is an ultra-low power circuit with a discrete signal processing unit. An analog Pan Tompkins Detector is implemented with low power optimized OPAs. A microcontroller detects the R wave peaks and measures the intervals which are transmitted via a separately powered Bluetooth low energy interface to a mobile device or PC.
The system is a functional prototype of a self-powered R wave detector for short time heart rate monitoring. The analog Pan Tompkins Detector of the developed prototype is optimized to spend minor energy. At a minor energy consumption, the device can measure only the ECG at rest. For a comfortable use of the device (for example as a sport wearable) the analog Pan Tompkins Detector must be optimized against motion artefacts. The future goal is to implement textile energy harvesters to power the circuit. Patches that use the triboelectrical effect can be integrated into normal clothes and gather energy during normal motion. The wireless communication will be powered by energy harvesting, too.

P 99

Health and sensors – sweat sensing

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We have to face a demographic change in many countries: People are getting older and older and suffer from a whole variety of age-related diseases. The rates of hospitalisation increase. Clinical and home surveillance has to include age-specific morbidity and mortality.
Now we have to answer the question, if it is possible to keep the aged people as long as possible at home to reduce costs but not the quality of services in medicine , care and general support.
Here interdisciplinary engineering and the digital transformation can help and represent excellent opportunities to solve the above mentioned problems. New ecosystems can be formed and new disruptive models are necessary. Sensors, electronics, software merge in combination with business models.
The presentation refers to digitally transformed processes and shows different applications on the field of body area networks and vital parameter measurement in the context of telemedical and clinical applications.
The sensing of biomarkers out of sweat becomes more and more important because sweat contains a huge variety of different molecules such as glucose, lactate or even cytokines.
These systems are of importance for the daily monitoring of patients as well as for the surveillance of risk patients in a intensive care unit.
We will present a demonstrator of such a small and effective sweat sensor and the combination with the vital parameter monitoring as described above.