Biomedical optoelectronic sensor system for fluid analysis based on optical microring resonators

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Introduction

A precise measurement and analysis of liquids as a point-of-care solution in the field of biomedicine leads to high demands on the measurement technology to be developed. The aim of this project was the design of a measurement system based on optical microring resonators (MRRs) in combination with a tunable vertical-cavity surface-emitting laser (VCSEL) of 1550 nm wavelength and a sensitive optoelectronic signal processing chain of InGaAs photodiodes with transimpedance amplification as a promising solution to this problem.

Methods

In the laboratory sample designed for this purpose, MRRs based on silicon nitride (SiN_X) are used, which are selective for different fluidic solutions. To achieve this effect, their surfaces are functionalized, which leads to a very high measurement sensitivity. The application of an analyte to the functionalized MRRs causes a refractive index change in the single-mode optical waveguide. Consequently, an optoelectronically detectable resonance wavelength shift occurs in the resonators. The main component of the subsequent diode current-voltage conversion is the high-speed transimpedance amplifier OPA380. This integrated circuit is well suited for the measurement system due to its high precision and low-noise characteristics. To reduce aliasing effects, a low-pass filter with a cut-off frequency of 10 kHz was introduced. The integration of a proper fluidic system for the application of the liquid to be analyzed on the sensor array allows for a rapid detection of relevant substance compositions.

Results

Initial experimental measurements have shown a reproducibility of the resonance wavelengths of 10 pm and a selectivity of different sodium chloride water solutions in the range of 0.056 % to 0.9 % NaCl.

Conclusion

In the future, the biophotonic system developed could in some cases make complex laboratory tests unnecessary, thus creating considerable savings for users in terms of time and costs.

Approaches for Solution-Processed Encapsulation of Printed Medical Wearable Devices

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Introduction

Wearable medical devices offer a great potential for human healthcare by opening up the opportunity to comfortably monitor vital signs or body fluid compositions. The use of printing technologies is a promising approach to fabricate the wearables. A growing number of printed medical wearables is being setup successfully on surface-conformal substrates, like flexible plastic foils or papers. A pressing challenge hereby is to achieve long-term stability and reliability of those printed wearables.

Methods

In this paper, the encapsulation requirements of printed wearable medical devices are discussed. Materials and the encapsulation approaches such as barrier foil lamination, thin film encapsulation and solution-processed encapsulation are outlined based on various examples.

Results

Barrier foil lamination and thin film encapsulation can provide a good protective performance but they have their own drawbacks or limitations for the fabrication of printed wearables. For instance, by using barrier foil lamination, a 3D surface cannot be well encapsulated. For thin film encapsulation, additional equipment like atomic layer deposition reactors or vacuum chambers are needed. Thus, we highlight the solution-processed encapsulation approaches, which can be integrated into a printing process flow with compatible materials and printing technologies.

Conclusion

Generally, researches for printed wearable medical devices are primarily focused on their function and performance but with little focus on their stability and reliability or with additional cost to protect the devices. Thus, it is concluded that integrating the solution-processed encapsulation into the printing process flow can be a novel fabrication approach for printed wearable medical devices.

Modelling and prototyping of a microfluidic cartridge for extracting immune cells from small volume blood samples

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Introduction

Traceless Affinity Cell Selection Technology (TACS®) is a method for selective, unaffected isolation of various immune cell species with high purity. Up to now the technology is used within a syringe like cartridge in combination with an automated handling system (Fabian®) to process 60 mL of blood within one batch. Nevertheless for diagnostic applications the amount of blood is limited to several tens of microliters. Thus the aim of this work was to transfer the TACS® technology from an existing large volume cartridge into a miniaturized microfluidic prototype.

Methods

SimulationX® (ESI ITI) was used to create a multi domain physical systems model of the cartridge to support the miniaturisation process. The miniaturized cartridge was manufactured by multilayer lamination. The microfluidic control setup to soak the fluids through the miniaturized cartridge was created by using a syringe pump and integrated micro valves and their control system. Finally the quantification of cells within the samples was measured using a FACS Canto II flow cytometer.

Results

The cartridge model was specified by tribology measurements. Based on these findings the core features of the miniaturized cartridge were determined by simulating fluid forces and pressure. Subsequently serval prototypes of that cartridge were manufactured. Afterwards a combination of the prototype cartridge and the microfluidic control was used to isolate lymphocytes from a blood sample of 60 µL. The isolated cell sample had a purity of 93,2 % lymphocytes, what is comparable to the purity of the established TACS® technology.

Conclusion

Here we could show that the simulation based down scaling is a suitable method to transfer a laboratory cartridge for cell separation from milliliter to microliter range. The prototype of the microfluidic cartridge yields to similar purity in the isolation of lymphocytes compared to the established high volume technology.

Novel dry electrode EEG headbands for home use: Comparing performance and comfort

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Introduction

In this paper, we investigate two concepts for dry electrode EEG headbands comprising commercially available dry electrode technologies. We compare the headbands in terms of electrode-skin impedance, EEG signal quality, application time and wearing comfort.

Methods

Two headbands were compared: a novel, highly flexible headband comprising multipin and multiwave electrodes, and a headband with spider-shaped and hydrogel electrodes. Both headbands were equipped with electrodes at positions AF3, AF4, PO3 and PO4 as well as a GND electrode at position Fpz.

The volunteers were asked for comfort evaluation immediately after application of the headband as well as 10 min, 30 min and 60 min later. Multiple EEG sequences were recorded, including 2 minutes of resting state EEG with eyes open as well as 2 minutes with eyes closed. Results were evaluated in terms of electrode-skin impedance, offset potentials and power spectral density (PSD) using the Welch estimation method.

Results

The comfort rating of the novel headband comprising multipin and multiwave electrodes was superior in comparison to the headband comprising hydrogel and spider-like electrodes. The electrodes spider and hydrogel electrodes exhibited higher electrode-skin impedances compared to the multipin and multiwave electrodes. In particular, the impedances at the frontal electrode positions were considerably increased for the hydrogel electrodes. The offset potentials for the hydrogel and spider electrode show a strong separation between the frontal (hydrogel) electrodes and the occipital (spider-shaped) electrodes. For the recordings of both EEG headbands and all four types of electrodes, no considerable difference was visible in terms of the average PSD.

Conclusion

In conclusion, the results of this study demonstrate the applicability of both headbands and electrode technologies for EEG acquisition. The performance and comfort of the multipin and multiwave electrodes contribute to an increased applicability for repeated and longterm at-home applications for e.g., neurofeedback and BCI.

In situ impedance measurements on postmortem porcine brain

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Introduction

Knowing the exact electrical properties of brain tissues is important for modeling non-invasive brain stimulation techniques. Previous studies were often based on inadequate and error-prone measurement procedures, conducted on a very small number of patients (N≈10) or only conducted for one particular frequency. In order to overcome these drawbacks, we plan to record broadband conductivity spectra of living human brain tissue. Here, we report a proof-of-principle study, testing the feasibility of our measurement technique in a postmortem porcine brain at its in situ position inside the head. Our goal was to prove the distinctness of grey and white matter by their impedances using equipment that is certified for neurosurgical application on humans.

Methods

The head was separated from the body and we exectured a craniotomy to get access to the brain. To replicate a measurement setup that would allow us to measure in vivo human brain tissue, we applied short current pulses recorded from a certified neurostimulator with a certified bipolar brain stimulation electrode. The electrode was direcly put on the tissue and the voltage response over the tissue and the electrode was recorded. The impedance was computed as the quiotient of voltage and current in the frequency domain.

Results

We could show the distinctness of grey and white matter with our measurement technique. Comparing different current strengths and pulse widths, we found out that current pulse of 100 μA with a pulse width of 200 μs meets the necessary requirements regarding signal-to-noise ratio.

Conclusion

It is noted that our results represent raw data, i.e. the total impedances, which are not yet corrected for the electrode impedance. Current investigations are devoted to correct the collected impedance data according to the individual electrode impedance. We expect the result to be even more significant with this correction.

Automatic Classification of the Movements of Directed and Undirected Subviral Particles

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Introduction

The development of a drug against the pathogens haemorrhagic fever, such as Ebolavirus, is a major challenge. A precise knowledge of the properties of the subviral particles in the host cell is required. Biosignal processing is based on fluorescence microscopically generated image sequences of cells infected with the Ebola virus. A particle tracking algorithm is used to detect the subviral particles. To classify the intracellular movement patterns, an algorithm for automation was developed. Active transport and brownian motion models are used for biological classification.

Methods

To arrange the subviral particles into classes, the mean square displacement (MSD) is calculated. The resulting curve usually follows the course of one of three functions. In order to speed up the classification and to achieve effective contrast formation, one of the functions has been omitted, as it is included by the other two under certain conditions. The curve is compared to two functions and the mean square error (MSE) is determined. By contrasting the MSE, the curve is assigned to a movement type such as directional or chaotic movement. A visualization of the motion characteristics is performed. The statistical distribution of the motion patterns is provided by a histogram.

Results

Application of the methods to simulated and real data yield fluorescence microscope images with superimposed colour-coded particle tracks. The histogram with a gaussian kernel function shows the distribution density of the classes. When viewing individual particles, the trace and graph are shown with the MSD curve. Combining particle tracks and MSD curve allows spatio-temporal analysis of particles' motion characteristics.

Conclusion

The algorithm allows the classification of movement patterns of subviral particles into biophysical models. The method was successfully tested on simulated and real data. The results show a good potential to automate parts of the evaluation process and thus support pharmaceutical researchers.