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Investigation of infectious diseases using a novel in vitro diagnostic microfluidic chip

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Malaria is an infectious disease in which parasites enter the human body through the bite of the Anopheles mosquito. When the pathogens are released into the bloodstream, at first nonspecific disease symptoms occur. To start the essential medical treatment, a fast and sensitive diagnosis is necessary. The gold standard method of malaria diagnostics is the microscopic examination of blood smears. However, this requires laboratory equipment and medical specialists, which is usually not present in the affected malaria centers. For this purpose, a novel microfluidic chip system has been developed. It is based on the optical detection of the specific coupling of the pathogens to the bottom of a microfluidic channel. While the laminar flow in a microfluidic channel causes the pathogens to remain in the center of the channel, we developed herringbone structures on the top surface of the channel to generate turbulences, which deflect the pathogens downwards resulting in an increase of the coupling. Mathematical simulations show that in the areas with herringbone structures, elevated velocities and turbulent flow could be observed. To verify these results, we developed channel systems with different herringbone structures, where the flow behavior was examined microscopically by using polymer beads. The experiments demonstrated clearly the formation of desired turbulences. For the final microfluidic system a reliable passive filling system is necessary. For that purpose we have combined the fluidic capillary forces inside narrow channels with the additional suction force of a nonwoven material. The experiments have shown that the flow behavior inside the system can be controlled by means of additional ventilation holes.

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Controlled infiltration of cells into electrospun scaffolds fabricated for applications in small diameter vascular grafts

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Owing to the paradoxical nature of electrospinning, it is difficult to produce a nanofibrous structure with large pores, the ideal environment for cell infiltration. The literature shows many attempts to achieve this with varied results. This project proposes a novel twist (alginate cell printing) to sacrificial electrospinning to increase cell infiltration. The aim is to fabricate a multilayered hybrid polymeric scaffold by electrospinning, characterise it, seed it with appropriate cells using a cell printer, and measure the cell infiltration of the resultant structure.
PCL-gelatin fiber mats with different concentration ratios were electrospun. Fiber diameter and pore size before and after gelatin leaching were measured and the mats were tested for tensile strength and wettability. 3T3 fibroblasts are printed on an optimised fiber mat with alginate in defined patterns as opposed to direct manual cell seeding (lacking in homogeneity). Multiple layers are stacked, incubated and allowed to attach to each other. Cell infiltration depth is then studied by z-axis fluorescence microscopy.
PCL-gelatin produces a wide range of nano-and microfibres (3.5±2.5µm) as compared to monodisperse fibres in PCL scaffolds (1.8±0.3µm). It is even possible to fabricate PCL-gelatin mats of thicknesses as low as 10µm, a clear advantage. Fiber diameters are reduced greatly after 8hrs of gelatin leaching in acidic water (2.3±1.5µm) indicating an increase in pore size. Contact angle measurements indicate a drastic increase in hydrophilicity on addition of gelatin.
The addition of alginate cell printing onto PCL-gelatin scaffolds is important to protect the cells from shear and mechanical stresses during printing and stacking. As both gelatin and alginate dissolve away during cell culture, the cells will be able to infiltrate the multilayered structure to a larger extent and with more ease than before.

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Rapid prototyping of implantable high accuracy platinum thin film tracks via laser evaporation

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Implantable printed circuit boards are often fabricated using a screen printing process (e.g. Pt/Au paste) in combination with alumina substrates. Due to inaccurate edges a minimal track distance of 0.125 mm occurs. Additionally, the need of screen printing masks limits the flexibility in design changes. As an alternative the sputter deposition of a platinum thin-film metallization followed by laser structuring was examined. Platinum was used because of its inert properties, which allows assembling (e.g. soldering) without chemical or mechanical postprocessing. We evaluated laser parameters to structure the sputtered metallization with different thicknesses (100 nm, 200 nm and 300 nm). The resulting metallization was characterized with respect to the quality of the edges and the adhesive strength to the substrate using a pull testing setup with a cartridge applying forces up to 100 N (Dage Series 4000 Bondtester). Therefore, copper wires were soldered onto 2x2 mm² Pt-pads. The edges of the metallization were sharply defined with a lateral deviation smaller than 2 µm whereby the minimal track distance was limited by the laser focus spot (≈60 µm). The 200 nm thick platinum layer featured the lowest median adhesive strength with a value of 5.83 MPa, followed by the 100 nm layer with 9.59 MPa and the 300 nm layer with 13.07 MPa. In all cases cohesive failure occurred. Taking into account the recommended threshold of reliable pad adhesion (=17 MPa) for screen printed metallizations, these values are comparatively small. Regarding the quality of the edges and the flexibility of the design the present process is encouraging. To handle the adhesive strength it is highly recommended to introduce an adhesion promoter (e.g. titanium), which develops a mixed oxide at the Pt-Al_2O_3 interface. Implementing this layer leads to a plurality of parameter combinations whereby an optimization with a Design of Experiment is proposed.

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Polarimeter compensation methods for drift and scattering effects by using information comprising signal frequency components

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Introduction: Glucose measurements play an important role in clinical medicine. Drawbacks of commonly used encymatic-amperometric reactions for determination could be overcome by polarimetry. This method is very sensitive to temperature-dependent drift and scattering effects occurring during measurements in tissue, blood or moving interstitial fluid. For accurate glucose determination there is a demand for a real-time compensation method of sample absorbance, drift and scattering effects with no additional hardware effort.
Methods: We built a polarimeter including two crossed Glan-Thompson polarizers, a flow-through cuvette and a Faraday rotator. A frequency analysis of the detector signal was performed to extract intensities at information-comprising frequency components and individual drift and scattering influences were investigated. We generated various flow profiles for glucose solutions by a syringe pump to determine their influence on the polarimeter signal. Ambient temperature was varied to investigate the influence on each intensity. Correlations between flow profiles, temperature fluctuations and signal intensities were calculated to evaluate possible compensation methods.
Results: Measurements show that sample scattering, drift and absorption effects could limit glucose prediction accuracy and that they have a unique influence on each frequency components. This unique influence enables sample absorption and light source drift compensation as well as the detection of scattering effects to prevent failure in measurements. A compensation of scattering effects is partially possible, but suffers from complex depolarization procedures. Moreover, strong scattering results in a detector saturation which leads to frequency shares and impedes every compensation approach.
Conclusion: By extracting information comprising polarimeter signal frequency shares we created a real-time compensation method for sample absorbance, and drift effects of light source or detector with no additional hardware effort. For non-saturated detectors this enables reliable glucose measurement and detection of occurring scattering to prevent failure measurements.