Covalent immobilization of luminescent oxygen indicators reduces cytotoxicity

Luminescence-based oxygen sensing is a widely used tool in cell culture applications. In a typical configuration, the luminescent oxygen indicators are embedded in a solid, oxygen-permeable matrix in contact with the culture medium. However, in sensitive cell cultures even minimal leaching of the potentially cytotoxic indicators can become an issue. One way to prevent the leaching is to immobilize the indicators covalently into the supporting matrix. In this paper, we report on a method where platinum(II)-5,10,15,20-tetrakis-(2,3,4,5,6-pentafluorphenyl)-porphyrin (PtTFPP) oxygen indicators are covalently immobilized into a polymer matrix consisting of polystyrene and poly(pentafluorostyrene). We study how the covalent immobilization influences the sensing material’s cytotoxicity to human induced pluripotent stem cell-derived (hiPSC-derived) neurons and cardiomyocytes (CMs) through 7–13 days culturing experiments and various viability analyses. Furthermore, we study the effect of the covalent immobilization on the indicator leaching and the oxygen sensing properties of the material. In addition, we demonstrate the use of the covalently linked oxygen sensing material in real time oxygen tension monitoring in functional hypoxia studies of the hiPSC-derived CMs. The results show that the covalently immobilized indicators substantially reduce indicator leaching and the cytotoxicity of the oxygen sensing material, while the influence on the oxygen sensing properties remains small or nonexistent.

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Transparent microelectrode arrays fabricated by ion beam assisted deposition for neuronal cell in vitro recordings

Microelectrode array (MEA) is a tool used for recording bioelectric signals from electrically active cells in vitro. In this paper, ion beam assisted electron beam deposition (IBAD) has been used for depositing indium tin oxide (ITO) and titanium nitride (TiN) thin films which are applied as transparent track and electrode materials in MEAs. In the first version, both tracks and electrodes were made of ITO to guarantee full transparency and thus optimal imaging capability. In the second version, very thin (20 nm) ITO electrodes were coated with a thin (40 nm) TiN layer to decrease the impedance of O30 μm electrodes to one third (1200 kΩ → 320 kΩ) while maintaining (partial) transparency. The third version was also composed of transparent ITO tracks, but the measurement properties were optimized by using thick (200 nm) opaque TiN electrodes. In addition to the impedance, the optical transmission and electric noise levels of all three versions were characterized and the functionality of the MEAs was successfully demonstrated using human pluripotent stem cell-derived neuronal cells. To understand more thoroughly the factors contributing to the impedance, MEAs with higher IBAD ITO thickness as well as commercial sputter-deposited and highly conductive ITO were fabricated for comparison. Even if the sheet-resistance of our IBAD ITO thin films is very high compared to the sputtered one, the impedances of the MEAs of each ITO grade were found to be practically equal (e.g., 300-370 kΩ for O30 μm electrodes with 40 nm TiN coating). This implies that the increased resistance of the tracks, either caused by lower thickness or lower conductivity, has hardly any contribution to the impedance of the MEA electrodes. The impedance is almost completely defined by the double-layer interface between the electrode top layer and the medium including cells.

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A modular brain-on-a-chip for modelling epileptic seizures with functionally connected human neuronal networks

Epilepsies are a group of neurological disorders characterised by recurrent epileptic seizures. Seizures, defined as abnormal transient discharges of neuronal activity, can affect the entire brain circuitry or remain more focal in the specific brain regions and neuronal networks. Human pluripotent stem cell (hPSC)-derived neurons are a promising option for modelling epilepsies, but as such, they do not model groups of connected neuronal networks or focal seizures. Our solution is a Modular Platform for Epilepsy Modelling In Vitro (MEMO), a lab-on-chip device, in which three hPSC-derived networks are separated by a novel microfluidic cell culture device that allows controlled network-to-network axonal connections through microtunnels. In this study, we show that the neuronal networks formed a functional circuitry that was successfully cultured in MEMO for up to 98 days. The spontaneous neuronal network activities were monitored with an integrated custom-made microelectrode array (MEA). The networks developed spontaneous burst activity that was synchronous both within and between the axonally connected networks, i.e. mimicking both local and circuitry functionality of the brain. A convulsant, kainic acid, increased bursts only in the specifically treated networks. The activity reduction by an anticonvulsant, phenytoin, was also localised to treated networks. Therefore, modelling focal seizures in human neuronal networks is now possible with the developed chip.

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Applications of nanocellulose/nanocarbon composites: Focus on biotechnology and medicine

Nanocellulose/nanocarbon composites are newly emerging smart hybrid materials containing cellulose nanoparticles, such as nanofibrils and nanocrystals, and carbon nanoparticles, such as “classical” carbon allotropes (fullerenes, graphene, nanotubes and nanodiamonds), or other carbon nanostructures (carbon nanofibers, carbon quantum dots, activated carbon and carbon black). The nanocellulose component acts as a dispersing agent and homogeneously distributes the carbon nanoparticles in an aqueous environment. Nanocellulose/nanocarbon composites can be prepared with many advantageous properties, such as high mechanical strength, flexibility, stretchability, tunable thermal and electrical conductivity, tunable optical transparency, photodynamic and photothermal activity, nanoporous character and high adsorption capacity. They are therefore promising for a wide range of industrial applications, such as energy generation, storage and conversion, water purification, food packaging, construction of fire retardants and shape memory devices. They also hold great promise for biomedical applications, such as radical scavenging, photodynamic and photothermal therapy of tumors and microbial infections, drug delivery, biosensors, isolation of various biomolecules, electrical stimulation of damaged tissues (e.g., cardiac, neural), neural and bone tissue engineering, engineering of blood vessels and advanced wound dressing, e.g., with antimicrobial and antitumor activity. However, the potential cytotoxicity and immunogenicity of the composites and their components must also be taken into account.

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Cardiomyocytes: Analysis of Temperature Response and Signal Propagation between Dissociated Clusters Using Novel Video-Based Movement Analysis Software

Human-induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) provide a great resource for functional cell and tissue models that can be applied in heart research, pharmaceutical industry, and future regenerative medicine. During cell model experiments, precise control of environmental parameters is important. Temperature is a fundamental parameter, and the acute effect of temperature on hiPSC-CM functions has previously been studied. This paper reports on long-term, systematic temperature response studies of hiPSC-CM cultures. The studies were conducted outside an incubator in a modular cell culturing system along with a temperature sensor plate (TSP) and a new beating analysis software (CMaN -cardiomyocyte function analysis tool). Temperature sensing at the actual cell location is challenging with bulky external sensors; however, a TSP with resistive microsensors provides an effortless solution. Experimental results showed that temperature nonlinearly affects the hiPSC-CM beating frequency with a Q10 temperature coefficient of 2.2. Both the active (contraction) and passive (relaxation) movements were influenced by temperature, and changes in the relaxation times were larger than the contraction times. However, the contraction amplitudes exhibited a greater spread of variation. We also present novel results on the visualization of hiPSC-CM contractile networking and non-invasive image-based measurement of signal propagation between dissociated CM clusters. Compared with previously reported tools, CMaN is an advanced and easy-to-use robust software. It is faster, more sensitive, computationally less expensive, and
extracts six different signals of the contractile motion per process, providing at least one useful beating signal even in complex cases. The software also supports movement center detection and independent computation of the relaxation and contraction parameters.

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Co-culture of human induced pluripotent stem cell-derived retinal pigment epithelial cells and endothelial cells on double collagen-coated honeycomb films
In vitro cell culture models representing the physiological and pathological features of the outer retina are urgently needed. Artificial tissue replacements for patients suffering from degenerative retinal diseases are similarly in great demand. Here, we developed a co-culture system based solely on the use of human induced pluripotent stem cell (hiPSC)-derived cells. For the first time, hiPSC-derived retinal pigment epithelium (RPE) and endothelial cells (EC) were cultured on opposite sides of porous polylactide substrates prepared by breath figures (BF), where both surfaces had been collagen-coated by Langmuir–Schaefer (LS) technology. Small modifications of casting conditions during material preparation allowed the production of free-standing materials with distinct porosity, wettability and ion diffusion capacity. Complete pore coverage was achieved by the collagen coating procedure, resulting in a detectable nanoscale topography. Primary retinal endothelial cells (ACBRI181) and umbilical cord vein endothelial cells (hUVEC) were utilised as EC references. Monocultures of all ECs were prepared for comparison. All tested materials supported cell attachment and growth. In monoculture, properties of the materials had a major effect on the growth of all ECs. In co-culture, the presence of hiPSC-RPE affected the primary ECs more significantly than hiPSC-EC. In consistency, hiPSC-RPE were also less affected by hiPSC-EC than by the primary ECs. Finally, our results show that the modulation of the porosity of the materials can promote or prevent EC migration. In short, we showed that the behaviour of the cells is highly dependent on the three main variables of the study: the presence of a second cell type in co-culture, the source of endothelial cells and the biomaterial properties. The combination of BF and LS methodologies is a powerful strategy to develop thin but stable materials enabling cell growth and modulation of cell-cell contact. Statement of significance: Artificial blood-retinal barriers (BRB), mimicking the interface at the back of the eye, are urgently needed as physiological and disease models, and for tissue transplantation targeting patients suffering from degenerative retinal diseases. Here, we developed a new co-culture model based on thin, biodegradable porous films, coated on both sides with collagen, one of the main components of the natural BRB, and cultivated endothelial and retinal pigment epithelial cells on opposite sides of the films, forming a three-layer structure. Importantly, our hiPSC-EC and hiPSC-RPE co-culture model is the first to exclusively use human induced pluripotent stem cells as cell source, which have been widely regarded as an practical candidate for therapeutic applications in regenerative medicine.

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Microflow-Based Device for In Vitro and Ex Vivo Drug Permeability Studies

This paper presents a novel microflow-based concept for studying the permeability of in vitro cell models or ex vivo tissues. Using the proposed concept, we demonstrate how to maintain physiologically relevant test conditions and produce highly reproducible permeability values for a range (31) of drug compounds. The apparent permeability coefficients \( P_{\text{app}} \) showed excellent correlation (0.89) with the values from experiments performed with a conventional Ussing chamber. Additionally, the microflow-based concept produces notably more concentrated samples than the conventional Ussing chamber-based approach, despite the fact that more than 10 times smaller quantities of test compounds and biological membranes are needed in the microflow-based concept.
Transferring scents over a communication network

In our work on scent technology, we have come across technology that can be used, in a limited way, to achieve scent transfer. In this paper, we document the scent transfer demonstration that we constructed for a science fair in 2018. Scent transfer requires a means to measure, transmit, classify, and reproduce scents. First, an ion-mobility spectrometer was used to measure scents. This data was sent to a server on the Internet. From the server, the measurement data was downloaded, baseline-corrected, and classified with an algorithm based on weighted K nearest neighbors and time series measurements. The classification result was used to instruct an olfactory display prototype to reproduce the scent for humans to sense. Our demonstration included two scents. Many more could be included, but a general-purpose scent reproduction is beyond our, and as far as we know, beyond anybody's current capabilities. Image and audio transmission technology are mature, but in the chemical senses such as olfaction and taste, significant challenges remain before they can be routinely included in multimodal interfaces.

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Co-stimulation with IL-1β and TNF-α induces an inflammatory reactive astrocyte phenotype with neurosupportive characteristics in a human pluripotent stem cell model system

Astrocyte reactivation has been discovered to be an important contributor to several neurological diseases. In vitro models involving human astrocytes have the potential to reveal disease-specific mechanisms of these cells and to advance research on neuropathological conditions. Here, we induced a reactive phenotype in human induced pluripotent stem cell (hiPSC)-derived astrocytes and studied the inflammatory natures and effects of these cells on human neurons. Astrocytes responded to interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) treatment with a typical transition to polygonal morphology and a shift to an inflammatory phenotype characterized by altered gene and protein expression profiles. Astrocyte-secreted factors did not exert neurotoxic effects, whereas they transiently promoted the functional activity of neurons. Importantly, we engineered a novel microfluidic platform designed for investigating interactions between neuronal axons and reactive astrocytes that also enables the implementation of a controlled inflammatory environment. In this platform, selective stimulation of astrocytes resulted in an inflammatory niche that sustained axonal growth, further suggesting that treatment induces a reactive astrocyte phenotype with neurosupportive characteristics. Our findings show that hiPSC-derived astrocytes are suitable for modeling astrogliosis, and the developed in vitro platform provides promising novel tools for studying neuron-astrocyte crosstalk and human brain disease in a dish.

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**Controlled Physiologically Relevant Conditions in a Portable Hypoxic Cell Culture Incubator**

We have developed a portable cell incubator that maintain and control the cultured cells in physiologically more relevant conditions compared to normal culture inside the incubator. The battery powered device control the temperature and supply premixed oxygen contained gas from small refillable bottles to the culture chambers maintaining the supplied oxygen levels. This will mimics better the human cells as in in vivo condition. Furthermore, single platform can hold six individual cell culture chambers. Chambers are tightly sealed to avoid evaporation and thus reduce the concentration of the culture liquid, which is typical in incubators in busy laboratories. The device can be transported to another lab or another campus for further studies while maintaining the desired conditions. The main advantage is to enable live imaging for example on confocal microscope or on any microscope for extended time for time laps imaging. Another interesting application area is the radiation studies. WE have demonstrated that by maintaining the low oxygen during the radiation it minimize the destructive effect of additional oxygen for DNA double stand breaks [1]. Therefore, the device enhance the quality of cancer treatment studies providing more stable, controlled and physiologically relevant culture conditions for the cells during the experiments.

**Nanocellulose films as substrates for printed electronics**

Microfibrillated cellulose (MFC) was fabricated from cellulose pulp using in-house mechanical fibrillation equipment. Subsequently, freestanding MFC films were fabricated with in-house developed hot-plate drying technique. The MFC films were tested as substrate materials for printed electronics patterns. Conducting patterns were fabricated on the MFC films using screen printing and vacuum evaporation. Electrical conductivity of the fabricated patterns was measured using four-wire technique. It was shown that the MFC films are suitable substrate materials for printing of functional electronic ink patterns, and thermal annealing of the patterns.
Pneumatic unidirectional cell stretching device for mechanobiological studies of cardiomyocytes

In this paper, we present a transparent mechanical stimulation device capable of uniaxial stimulation, which is compatible with standard bioanalytical methods used in cellular mechanobiology. We validate the functionality of the uniaxial stimulation system using human-induced pluripotent stem cells-derived cardiomyocytes (hiPSC-CMs). The pneumatically controlled device is fabricated from polydimethylsiloxane (PDMS) and provides uniaxial strain and superior optical performance compatible with standard inverted microscopy techniques used for bioanalytics (e.g., fluorescence microscopy and calcium imaging). Therefore, it allows for a continuous investigation of the cell state during stretching experiments. The paper introduces design and fabrication of the device, characterizes the mechanical performance of the device and demonstrates the compatibility with standard bioanalytical analysis tools. Imaging modalities, such as high-resolution live cell phase contrast imaging and video recordings, fluorescent imaging and calcium imaging are possible to perform in the device. Utilizing the different imaging modalities and proposed stretching device, we demonstrate the capability of the device for extensive further studies of hiPSC-CMs. We also demonstrate that sarcomere structures of hiPSC-CMs organize and orient perpendicular to uniaxial strain axis and thus express more maturated nature of cardiomyocytes.

Online Scent Classification by Ion-Mobility Spectrometry Sequences

For ion-mobility spectrometry (IMS)-based electronic noses (eNose) samples of scents are markedly time-dependent, with a transient phase and a highly volatile stable phase in certain conditions. At the same time, the samples depend on various environmental factors, such as temperature and humidity. This makes fast classification of scents challenging. The present aim was to develop and test an algorithm for online scent classification that mitigates these dependencies by using both baseline measurements and sequences of samples for classification. A classifier based on the K nearest neighbors approach was derived. The classifier is able to use measurements from both transient and stable phase, yields a label for the analyzed scent, and information on the trustworthiness of the returned label. In order to avoid the classifier being fooled by irrelevant features and to reduce the dimensionality of the feature space, principal component analysis...
was applied to the data. The classifier was tested with four food scents, each presented in two different ways to the IMS. By using baseline measurements, the misclassification rate was reduced from 20.0 to 13.3%. A second experiment showed that the used IMS type experiences device heterogeneity.
A compartmentalized neuron-oligodendrocyte co-culture device for myelin research: design, fabrication and functionality testing

Microfluidics devices for co-culturing neurons and oligodendrocytes represent an important in vitro research tool to decipher myelination mechanisms in health and disease and in the identification of novel treatments for myelin diseases. In reported devices using primary rodent cells, the spontaneous formation of myelin sheaths has been challenging and random orientation of neurites impedes the analysis of myelination. Furthermore, fabrication methods for devices show limitations, highlighting the need for novel in vitro cell-based myelination models. In the present study, we describe a compartmentalized cell culture device targeted for neuron-oligodendrocyte co-culturing and myelination studies. In the device, neurites from primary rat dorsal root ganglion (DRG) neurons were capable of forming aligned dense networks in a specific compartment that was physically isolated from neuronal somas. Co-culture of rat DRG neurons and oligodendrocytes, a well-known model to study myelination in vitro, led to interactions between oligodendrocytes and neurites in the device, and the deposition of myelin segments in an aligned distribution was spontaneously formed. For the fabrication of the device, we present a new method that produces polydimethylsiloxane (PDMS)—based devices possessing an open compartment design. The proposed fabrication method takes advantage of an SU-8 photolithography process and 3D printing for mould fabrication. Both the microscale and macroscale features are replicated from the same mould, allowing devices to be produced with high precision and repeatability. The proposed device is applicable for long-term cell culturing, live-cell imaging, and by enhancing aligned myelin distribution, it is a promising tool for experimental setups that address diverse biological questions in the field of myelin research.

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Versatile Application of Nanocellulose: From Industry to Skin Tissue Engineering and Wound Healing

Nanocellulose is cellulose in the form of nanostructures, i.e., features not exceeding 100 nm at least in one dimension. These nanostructures include nanofibrils, found in bacterial cellulose; nanofibers, present particularly in electrospun mats; and nanowhiskers, nanocrystals, nanorods, and nanoballs. These structures can be further assembled into bigger two-dimensional (2D) and three-dimensional (3D) nano-, micro-, and macro-structures, such as nanoplatelets, membranes, films, microparticles, and porous macroscopic matrices. There are four main sources of nanocellulose: bacteria (Gluconacetobacter), plants (trees, shrubs, herbs), algae (Cladophora), and animals (Tunicata). Nanocellulose has emerged for a wide range of industrial, technology, and biomedical applications, namely for adsorption, ultrafiltration, packaging, conservation of historical artifacts, thermal insulation and fire retardation, energy extraction and storage, acoustics, sensors, controlled drug delivery, and particularly for tissue engineering. Nanocellulose is promising for use in scaffolds for engineering of blood vessels, neural tissue, bone, cartilage, liver, adipose tissue, urethra and dura mater, for repairing connective tissue and congenital heart defects, and for constructing contact lenses and protective barriers. This review is focused on applications of nanocellulose in skin tissue engineering and wound healing as a scaffold for cell growth, for delivering cells into wounds, and as a material for advanced wound dressings coupled with drug delivery, transparency and sensorics. Potential cytotoxicity and immunogenicity of nanocellulose are also discussed.

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Scent Classification by K Nearest Neighbors using Ion-Mobility Spectrometry Measurements

Various classifiers for scent classification based on measurements using an electronic nose (eNose) have been studied recently. In general, classifiers rely on a static database containing reference eNose measurements for known scents. However, most of these approaches require retraining of the classifier every time a new scent needs to be added to the training database. In this paper, the potential of a K nearest neighbors (KNN) classifier is investigated to avoid the time-consuming retraining when updating the database. To speed up classification, a k-dimensional tree search in the KNN classifier and principal component analysis (PCA) are studied. The tests with scents presented to an eNose based on ion-mobility spectrometry (IMS) show that the KNN method classifies scents with high accuracy. Using a k-dimensional tree search instead of an exhaustive search has no significant influence on the misclassification rate but reduces the classification time considerably. The use of PCA-transformed data results in a higher misclassification rate than the use of IMS data when only the first principal components explaining 95% of the total variance are used but in a similar misclassification rate when the first principal components explaining 99% of the total variance are used. In conclusion, the
proposed method can be recommended for classifying scents measured with IMS-based eNoses.

**A Portable Microscale Cell Culture System with Indirect Temperature Control**

A physiologically relevant environment is essential for successful long-term cell culturing in vitro. Precise control of temperature, one of the most crucial environmental parameters in cell cultures, increases the fidelity and repeatability of the experiments. Unfortunately, direct temperature measurement can interfere with the cultures or prevent imaging of the cells. Furthermore, the assessment of dynamic temperature variations in the cell culture area is challenging with the methods traditionally used for measuring temperature in cell culture systems. To overcome these challenges, we integrated a microscale cell culture environment together with live-cell imaging and a precise local temperature control that is based on an indirect measurement. The control method uses a remote temperature measurement and a mathematical model for estimating temperature at the desired area. The system maintained the temperature at 37±0.3 °C for more than 4 days. We also showed that the system precisely controls the culture temperature during temperature transients and compensates for the disturbance when changing the cell cultivation medium, and presented the portability of the heating system. Finally, we demonstrated a successful long-term culturing of human induced stem cell–derived beating cardiomyocytes, and analyzed their beating rates at different temperatures.
Transportable system enabling multiple irradiation studies under simultaneous hypoxia in vitro

Background
Cells in solid tumours are variably hypoxic and hence resistant to radiotherapy - the essential role of oxygen in the efficiency of irradiation has been acknowledged for decades. However, the currently available methods for performing hypoxic experiments in vitro have several limitations, such as a limited amount of parallel experiments, incapability of keeping stable growth conditions and dependence on CO2 incubator or a hypoxia workstation. The purpose of this study was to evaluate the usability of a novel portable system (Minihypoxy) in performing in vitro irradiation studies under hypoxia, and present supporting biological data.

Materials and methods
This study was conducted on cancer cell cultures in vitro. The cells were cultured in normoxic (~21% O2) or in hypoxic (1% O2) conditions either in conventional hypoxia workstation or in the Minihypoxy system and irradiated at dose rate 1.28 Gy/min±2.9%. The control samples were sham irradiated. To study the effects of hypoxia and irradiation on cell viability and DNA damage, western blotting, immunostainings and clonogenic assay were used. The oxygen level, pH, evaporation rate and osmolarity of the culturing media on cell cultures in different conditions were followed.

Results
The oxygen concentration in interest (5, 1 or 0% O2) was maintained inside the individual culturing chambers of the Minihypoxy system also during the irradiation. The radiosensitivity of the cells cultured in Minihypoxy chambers was declined measured as lower phosphorylation rate of H2A.X and increased clonogenic capacity compared to controls (OER~3).

Conclusions
The Minihypoxy system allows continuous control of hypoxic environment in multiple wells and is transportable. Furthermore, the system maintains the low oxygen environment inside the individual culturing chambers during the transportation and irradiation in experiments which are typically conducted in separate facilities.
Portable cell culture device for maintaining low oxygen environment: CASE STUDY - proliferation of fibroblasts under hypoxic conditions

Here we present a portable cell culture instrument that increase the biomimicry of traditional cell research applying and maintaining low oxygen or hypoxic environment around the custom made culture chambers. It is well known that most of the cells in vivo experience considerably less than 10% oxygen concentration and some cells/organs even less than 1% [1]. It is also well known that cells behave significantly differently when exposed to lower oxygen than normal incubator condition (~19% O2) [1]. Even though researchers are aware of the drastic effect of low oxygen and hypoxic condition for the cells these conditions are not widely applied in basic biological studies.

One reason for low number of hypoxia studies is lack of commercial tools and devices available to maintain the low oxygen conditions in a chip/dish. For example, to use a normal Petri dish and in a stationary hypoxia incubator or large hypoxia workstation might be difficult to perform high quality or long-term imaging studies. Taking the Petri dish out from the incubator/workstation expose the culture immediately to reoxygenation (oxygen level increase) and increasing temperature, which could affect remarkably to cell behavior. Furthermore, these stationary systems reserve large space from the lab, which might be a huge cost issue as well. In addition to these stationary systems, there are few commercial portable systems available. However, they typically lack of temperature and/or oxygen control and therefore are difficult to maintain for example under long-term microscopy.

In this study, we present the portable cell culture instrument that include battery to maintain the temperature control and preloaded gas containers to maintain the predefined oxygen level inside the six individual culture chambers (See Figure 1). The flow divider unit can be extended from the base unit while maintaining temperature and gas supply. This enables the use microscope for extensive study of live cell imaging without affecting to the cell culture environment. Furthermore, the cells in the chambers can be cultured and maintained in hypoxic conditions. The dynamics of oxygen conditions inside the chamber was studied with in house build non-invasive optical oxygen sensor [2] while maintaining temperature at 37 °C. We also demonstrated the effect of hypoxia on proliferation of mouse embryonic fibroblasts (MEFs) under different oxygen levels (1%, 5% and 19%); each containing 5% CO2; 19% O2 mimicking incubator conditions). MEFs were cultured in the instrument and image ones per day to determine the proliferation rate in hypoxic conditions. Zeiss Observer Z1 microscope was utilized to automatically image entire culture area (16mm in diameter) by tiling and stitching 96 single images to one large image. This allow us to analyze the entire culture area and thus avoiding poorly selected random shots around the well, which might finally be misleading. Images were processed using MATLAB to obtain relative proliferation growth rate data that is based on area cell are covering (See Figure 2). The results showed that the proliferation rate is enhanced in 5% oxygen compared to 1% and 19% oxygen conditions (See Figure 3). This also demonstrated that cell proliferation varied in gas concentrations and reach confluent after 3 days. Therefore, our portable culture instrument can be utilized in physiologically more relevant low oxygen studies in different cell- and organ-on-a-chip applications.

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Microelectrode array for noninvasive analysis of cardiomyocytes at the single-cell level

Microelectrode arrays (MEAs) are widely used to assess the electrophysiology of human pluripotent stem cell-derived cardiomyocytes (hPS-CMs). Traditionally, MEAs have been used to record data at the cell population level, but it would be beneficial to be able to analyze also at the single-cell level using MEAs. To realize this, we present a special MEA platform for recording field potential from single beating cardiomyocytes. The size and location of transparent indium tin oxide (ITO) electrodes have been optimized to make noninvasive studies of the electrophysiological activity of cardiomyocytes at the single-cell level possible and also to enable simultaneous video imaging through transparent electrodes and thus image-based analysis of the mechanical beating behavior of the same cardiomyocytes. Because of these characteristics, this novel platform provides a powerful tool for assessing the functionality of cardiomyocytes in basic cardiac research, disease modeling, as well as drug development and toxicology.

Microelectrode array for noninvasive analysis of cardiomyocytes at the single-cell level
Optimizing elastomeric mechanical cell stretching device

Olfactory display prototype for presenting and sensing authentic and synthetic odors

Olfactory display prototype for presenting and sensing authentic and synthetic odors

A compact olfactometer for IMS measurements and testing human perception

Production of easily controllable and measurable odor stimuli is needed when studying human olfaction, olfaction-related physiology and psychological reactions to odors. Controlled odor producing instruments are called olfactometers. For testing and calibrating new olfactometers or sensor arrays, a reliable input signal has to be produced to verify their accurate functionality. A common input signal in various olfactometers has been the use of volatile organic compounds (VOCs) in gaseous form. We present a compact olfactometer able to produce controlled continuous odor stimuli from three individual channels. For measuring the output gas flow, we used a ChemPro 100i (Environics, Finland) device that is based on aspiration ion mobility spectrometry (aIMS). IMS is a robust and sensitive method for measuring VOCs and is used especially in detecting toxic industrial chemicals and chemical warfare agents, but the technology is also suitable for other olfactory-related applications. The olfactometer was used to produce synthetic jasmine scent using three main odor components from jasmine oil and all the components were diluted using propylene glycol. The dilutions were supplied to the system using programmable syringe pumps, which guided the dilutions to individual evaporation units. We conducted experiments to verify the functionality of our olfactometer. Analysis of the ChemPro100i data showed that olfactometer can use different odor components to produce continuous, stable output flows with controlled concentrations.
Modeling and Control of Microscale Cell Culture Environments

Culturing cells in vitro is one of the core techniques used in a wide range of biomedical engineering areas. Special care is required to successfully grow cells in an artificial environment. It is essential to ensure that the culture environment is cell-friendly and sterile, supplies important products such as nutrients and growth factors, and provides a proper physiological microenvironment. To optimize long-term cell culturing, parameters such as pH, oxygen concentration, and temperature, should be precisely maintained at the desired levels. Furthermore, it is sometimes desirable to change environmental parameter(s) in a controlled way to study the cell response.

Bioreactors are typically used for cell culture in vitro. However, precise control of each cell culture’s microenvironment is difficult, leading to uneven culture conditions that can affect cell behavior. Furthermore, studying how certain environmental parameter affect the cultures is challenging, as it is difficult, or even impossible, to vary certain parameters in a controlled manner between each culture.

Microscale cell culture systems, known as microbioreactors, have recently been extensively studied to enhance control and improve long-term cell culturing by better mimicking cells’ microenvironments. Microbioreactors provide better environment control, thereby enhancing long-term cell cultivation. Unfortunately, integrating microbioreactors with the required sensors, actuators, electronics and other required devices can be challenging. Implementing sensors near the cell culture can also disturb them or prevent other measurements, such as optical microscopy. Certain measurements, such as direct long-term pH measurement, can be impossible, as there are no suitable microscale sensors available.

For these reasons, there is a huge demand for methods that can be used to study and develop proper microbioreactors. This thesis includes several studies in which modeling was used as design tools to improve and control culture environments. First, an analytical model to study gravity-driven flows in microfluidic devices is developed. Next, developed finite element method (FEM) computer models are used to study fluid flow profiles, drug distributions, shear stress levels on cells, and sensitivity of a calorimetric flow measurement system. A FEM model of carbon dioxide transport and liquid pH is also created. Additionally, the thesis proposes a novel method to indirectly control the cell culture temperature. Using system identification techniques, a developed estimation model can precisely control temperature with a sensor that does not disturb cells or other measurements. Although this thesis only demonstrates temperature control in the cell culture, the method can potentially be used to control other environment parameters as well. Lastly, this thesis considers the limitations of the presented models and control methods, and provides recommendations for future studies.
Mini-incubator for prolonged hypoxia studies on MEA: Effect of hypoxia for iPSC-derived cardiomyocytes

Motivation
Cells are normally cultured inside an incubator where 5% from atmospheric air is replaced by CO2. That leads to oxygen concentration around 20% (19.95%) which is not physiologically relevant environment for majority of the cells and tissues. To mimic physiological conditions in vitro, cells should be cultured in a biomimetic and controlled environment. For example, for a muscle, the physioxia (normal O2 partial pressure for this specific tissue) is from 3% to 5%, for brain tissue from 0.5% to 7%, and inside tumors it could be near 0%. It is also known that exposing cells to low oxygen atmosphere, near their natural environment in vivo (0-10% O2), the behavior of cells is drastically different. Moreover, it has been shown that low oxygen conditions can promote growth and influence differentiation of stem cells in vitro. Furthermore, constant culture conditions are difficult to maintain outside an incubator. For example, during the prolonged extracellular recordings with microelectrode arrays (MEA) altering gas concentrations, temperature variations, and evaporation are typical challenges. That leads to the variation of pH and molecular concentrations of media due to the evaporation. Therefore, to maintain the good culture conditions cells should be cultured in a biomimetic and controlled environment.

We have developed a cell culture platform that provides controlled environment for prolonged hypoxia, physioxia, and standard-like 5% CO2 “normoxia” studies during the MEA recordings on MEA amplifier. The chamber maintains the pH, temperature and constant gas concentration, for 5% CO2, physioxia and hypoxia conditions.

Material and Methods
A customized culture chamber is based on the earlier studies [1] and provides platform for studies in controlled truly hypoxic (low oxygen) conditions. This mini-incubator platform consist of (1) a culture substrate (e.g. MEA, Petri dish, or glass plate), (2) a 1-well cell culture chamber, (3) a lid to seal the chamber from contaminations, (4) a lid lock to seal the lid water tightly and (5) a cover to create environment around the chamber. A supply of very low flow rate (5 ml/min) of non-humidified (dry) gas is required to maintain the gas environment for the culture.

In this study we demonstrate the functionality of our mini-incubator platform. We measure the oxygen concentration in the cell culture chamber (without cells) utilizing in-house made a non-invasive optical sensing method for dissolved oxygen. We characterize the dynamics of the culture chamber for response of four different gas concentrations (0%, 1%, 5%, and 10%) of oxygen. We also characterize the evaporation and pH from the single mini-incubator chambers after three days. We also demonstrate the functionality of the mini-incubator platform for long term experiments and recordings on MEA using cardiomyocytes. We compare the beating rate of cardiomyocytes in hypoxic conditions (1% O2, 5% CO2, 94% N2) to “normoxic” conditions (19% O2, 5% CO2, 76% N2).

Results
We show that we can maintain the pH (~7.3) and evaporation (1 – 3 µl/h) inside the mini-incubator. Compared to standard incubator these parameters are much better maintained in our platform. pH could rise above 7.5 inside an incubator which might partly be due to the evaporation that could be also relatively high (5-7 µl/h). Especially in busy labs where incubator is frequently opened.

We also show that we can create truly hypoxic conditions in the cell culture chamber utilizing in-house made non-invasive optical sensing method. This demonstrates the efficiency of the platform. Target levels of gas concentration can be reached and rise time for step response from air saturation to different oxygen concentrations is ~1 hours.

We also demonstrate that we can maintain the cardiomyocytes on MEA amplifier for five days using 19% O2 + 5% CO2 gas supply and record stable beat rate during the period of experiment. We further show that exposing the cells to reduced oxygen concentration decrease the cardiac beating rate but recover back to normal when reoxygenated back to 19% O2. This will demonstrate that the mini-incubator platform is useful tool for prolonged experiments on MEA but also can be utilized in other heavily used lab tools like microscopy to maintain physiological environment.

Conclusions
Low oxygen concentration is a normal condition for most of the cells in vivo. Therefore, it is important to develop tools to study cells in these biomimetic conditions. Here we demonstrate the functionality of our mini-incubator for hypoxia and physioxia studies. Truly hypoxic conditions can be maintained on prolonged time on MEA.

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High throughput mechanical micro-scale characterization of composites and the utilization of the results in finite element analysis

This study presents preliminary results from the micro-scale behaviour of aged glass fibre composites. The examined composite systems consist of a simple epoxy matrix and glass fibres representing E and E6CR compositions. The micro-scale properties are analysed with single fibre tensile tests and microbond tests to study the properties of the glass fibres and the fibre/matrix interphase, respectively. The ageing environments examined in the study are deionized water and 1 g/dm3 sulphuric acid at elevated temperatures. The high-throughput testing equipment enables large series of samples: a total of 220 single-fibre tensile tests and 425 microbond tests were performed for this study. Selected samples were subjected to pyrolysis gas chromatography/mass spectrometry analysis for information about the chemical structures present in the systems. The data from the microbond test was utilised in finite element analysis to analyse the effects varying material properties have on the results. This procedure revealed crucial information of the effects of aqueous environment ageing and the viability of the microbond test as an experimental characterization method in glass fibre reinforced composites.
Hydrazone crosslinked hyaluronan-based hydrogels for therapeutic delivery of adipose stem cells to treat corneal defects

Corneal blindness is a worldwide problem, plagued by insufficient amount of high-quality donor tissue. Cell therapy using human adipose stem cells (hASCs) has risen as an alternative to regenerate damaged corneal stromal tissue, the main structural and refractive layer of the cornea. Herein we propose a method to deliver hASCs into corneal defects in hyaluronan (HA)-based hydrogels, which form rapidly in situ by hydrazone crosslinking. We fabricated two different HA-based hydrazone-crosslinked hydrogels (HALD1-HACDH and HALD2-HAADH), and characterized their swelling, degradation, mechanical, rheological and optical properties and their ability to support hASC survival. To promote hASC attachment and survival, we incorporated collagen I (col I) to the more stable HALD1-HACDH hydrogel, since the HALD2-HAADH hydrogel suffered swift degradation in culture conditions. We then used an organ culture model with excised porcine corneas to study the delivery of hASCs in these three hydrogels for stromal defect repair. Although all hydrogels showed good hASC survival directly after encapsulation, only the collagen-containing HALD1-HACDH-col I hydrogel showed cells with elongated morphology, and significantly higher cell metabolic activity than the HALD1-HACDH gel. The addition of col I also increased the stiffness and reduced the swelling ratio of the resulting hydrogel. Most importantly, the corneal organ culture model demonstrated these hydrogels as clinically feasible cell delivery vehicles to corneal defects, allowing efficient hASC integration to the corneal stroma and overgrowth of corneal epithelial cells.
A portable live-cell imaging system with an invert-upright-convertible architecture and a mini-bioreactor for long-term simultaneous cell imaging, chemical sensing and electrophysiological recording

Cell culture in-vitro is a well-known method to develop cell and disease models for studying physiologically relevant mechanisms and responses for various applications in life sciences. Conventional methods for instance, using static culture flasks or well plates, have limitations, as these cannot provide accurate tractable models for advanced studies. However, microscale systems can overcome this since they mimic the cells' natural microenvironment adequately. We have developed a portable live-cell imaging system with an invert-upright-convertible architecture and a mini-bioreactor for long-term simultaneous cell imaging and analysis, chemical sensing and electrophysiological recording. Our system integrates biocompatible cell-friendly materials with modular measurement schemes and precise environment control, and can be automated. High quality time-lapse cell imaging is hugely useful in cell/disease models. However, integration of advanced in-vitro systems into benchtop microscopes for in-situ imaging is tricky and challenging. This is especially true with device based biological systems such as lab/organ/body-on-chips, or mini-bioreactors/microfluidic systems. They face issues ranging from optical and physical geometry incompatibilities to difficulties in connectivity of flow and perfusion systems. However, our novel modular system either as an inverted or as an upright system can easily accommodate virtually any in-vitro devices. Furthermore, it can accept additional sensor or measurement devices quite freely. Cell characterization, differentiation, chemical sensing, drug screening, microelectrode-array-electrophysiological recordings and cell stimulation can be carried out with simultaneous in-situ imaging and analysis. Moreover, our system can be configured to capture images from regions that are otherwise inaccessible by conventional microscopes, for example, cells cultured on physical or biochemical sensor systems. We demonstrate the system for video-based beating analysis of cardiomyocytes, cell orientation analysis on nanocellulose, and simultaneous long-term in-situ microscopy with pH and temperature sensing. The compact microscope as such is comparable to standard phase-contrast-microscopes without any detectable aberrations and is useful practically for any in-situ microscopy demands.

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Screen-printed curvature sensors for soft robots
Castable elastomers have been used to fabricate soft robotic devices and it has been shown that the technique scales well from prototyping to mass manufacturing. However, similarly scalable techniques for integrating strain or curvature sensors into such devices are still lacking. In this paper, we show that screenprinted silver conductors serve well as curvature sensors for soft robotic devices. The sensors are produced onto elastomer substrates in a single printing step and integrated into soft pneumatic actuators. We characterized the resistance-curvature relationship of the sensors, which allows the curvature of the actuators to be estimated from the sensor measurements. Hysteresis was observed, which does limit the absolute accuracy of the sensors. However, temperature characterizations showed that the sensor measurements are not significantly affected by temperature fluctuations during normal operation. Dynamic experiments showed that the bandwidth of the sensors is larger than the bandwidth of the actuators. We experimentally validated that these sensors can be used to detect whether the motion of an actuator has been blocked, clearing the way towards simple-to-fabricate soft robots that react to their surroundings. Finally, we demonstrate a three-fingered soft robotic gripper with integrated sensors. We conclude that screen-printing is a promising way to integrate curvature sensors into soft
Robots.

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Cellulose Nanofiber Alignment Using Evaporation-Induced Droplet-Casting, and Cell Alignment on Aligned Nanocellulose Surfaces
This work investigates droplet-evaporated cellulose nanofiber (CNF) alignment and cell responses on CNF surfaces. Surfaces of unmodified (u-), anionic (a-), and cationic (c-) CNFs were fabricated using an evaporation-induced droplet-casting method and characterized in terms of degree of orientation. Circular variance (CV) values obtained using Cytospectre software to analyze the degree of orientation from AFM images showed a significantly higher degree of orientation on c- and u-CNF surfaces (average CV 0.27 and 0.24, respectively) compared to a-CNF surfaces (average CV 0.76). Quantitative analysis of surface roughness plots obtained from AFM images confirmed the difference between the direction of alignment versus the direction perpendicular to alignment. AFM images as well as observations during droplet evaporation indicated c-CNF alignment parallel to a dry-boundary line during droplet evaporation. Fibroblasts were cultured on the u-, a-, and c-CNF surfaces with or without a fibronectin (FN) coating for 48 h, and the cell response was evaluated in terms of cell viability, proliferation, morphology, and degree of orientation. Cell viability and proliferation were comparable to that on a control surface on the a-CNF and c-CNF surfaces. Although an FN coating slightly enhanced cell growth on the studied surfaces, uncoated a-CNF and c-CNF surfaces were able to support cell growth as well. The results showed cell orientation on aligned c-CNF surfaces, a finding that could be further utilized when guiding the growth of cells. We also showed that the alignment direction of c-CNFs and thus the cell orientation direction can be controlled with a contact-dispensing technique.

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Publication information
Optimised PDMS tunnel devices on MEAs increase the probability of detecting electrical activity from human stem cell-derived neuronal networks

Measurement of the activity of human pluripotent stem cell (hPSC)-derived neuronal networks with microelectrode arrays (MEAs) plays an important role in functional in vitro brain modelling and in neurotoxicological screening. The previously reported hPSC-derived neuronal networks do not, however, exhibit repeatable, stable functional network characteristics similar to rodent cortical cultures, making the interpretation of results difficult. In earlier studies, microtunnels have been used both to control and guide cell growth and amplify the axonal signals of rodent neurons. The aim of the current study was to develop tunnel devices that would facilitate signalling and/or signal detection in entire hPSC-derived neuronal networks containing not only axons, but also somata and dendrites. Therefore, MEA-compatible polydimethylsiloxane (PDMS) tunnel devices with 8 different dimensions were created. The hPSC-derived neurons were cultured in the tunnel devices on MEAs, and the spontaneous electrical activity of the networks was measured for 5 weeks. Although the tunnel devices improved the signal-to-noise ratio only by 1.3-fold at best, they significantly increased the percentage of electrodes detecting neuronal activity (52–100%) compared with the controls (27%). Significantly higher spike and burst counts were also obtained using the tunnel devices. Neuronal networks inside the tunnels were amenable to pharmacological manipulation. The results suggest that tunnel devices encompassing the entire neuronal network can increase the measured spontaneous activity in hPSC-derived neuronal networks on MEAs. Therefore, they can increase the efficiency of functional studies of hPSC-derived networks on MEAs.

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Fluorimetric oxygen sensor with an efficient optical read-out for in vitro cell models
This paper presents a phase fluorimetric sensor for the monitoring of the oxygen concentration in in vitro cell models. The sensing surface of the sensor consists of oxygen sensitive fluorescent dyes (platinum(II) octaethylporphyrinketone) embedded in a thin polystyrene film. In order to optimize the optical read-out scheme of the sensor, we carried out electromagnetic simulations of a fluorescently doped polystyrene film deposited on a glass-water interface. The simulation results showed highly anisotropic angular emission distribution with the maximum irradiance being at super critical angles, which attracts tailored optical designs to maximize the fluorescence collection efficiency. For this purpose, we applied an efficient optical read-out scheme based on an in-contact parabolic lens. The use of parabolic lens also facilitates confocal total internal reflection excitation from the substrate side. This makes the excitation effective and insensitive to biofouling or other optical changes in the sensing surface and, more importantly, greatly reduces the amount of excitation power radiated into the cell culture chamber. Experimental results show that when applied together with phase fluorimetric lifetime sensing, this optical scheme allows one to use thin films.

Pneumatically actuated elastomeric device for simultaneous mechanobiological studies & live-cell fluorescent microscopy
In this study, we demonstrate the functionality and usability of a compact, pneumatically actuated, elastomeric stimulation device for mechanobiological studies. The soft mechatronic device enables high-resolution live-cell confocal fluorescent imaging during equiaxial stretching. Several single cells can be tracked and imaged repeatedly after stretching periods. For demonstration, we provide image based analysis of dynamic change of the cell body and the nucleus area and actin fiber orientation during mechanical stimulation of mouse embryonic fibroblast (MEF) cells. Additionally, we present the characteristics of the device utilizing computational simulations and experimental validation using a particle tracking method for strain field analysis.
The effect of equiaxial stretching on the osteogenic differentiation and mechanical properties of human adipose stem cells

Although mechanical cues are known to affect stem cell fate and mechanobiology, the significance of such stimuli on the osteogenic differentiation of human adipose stem cells (hASCs) remains unclear. In this study, we investigated the effect of long-term mechanical stimulation on the attachment, osteogenic differentiation and mechanical properties of hASCs. Tailor-made, pneumatic cell stretching devices were used to expose hASCs to cyclic equiaxial stretching in osteogenic medium. Cell attachment and focal adhesions were visualised using immunocytochemical vinculin staining on days 3 and 6, and the proliferation and alkaline phosphatase activity, as a sign of early osteogenic differentiation, were analysed on days 0, 6 and 10. Furthermore, the mechanical properties of hASCs, in terms of apparent Young's modulus and normalised contractility, were obtained using a combination of atomic force microscopy based indentation and computational approaches. Our results indicated that cyclic equiaxial stretching delayed proliferation and promoted osteogenic differentiation of hASCs. Stretching also reduced cell size and intensified focal adhesions and actin cytoskeleton. Moreover, cell stiffening was observed during osteogenic differentiation and especially under mechanical stimulation. These results suggest that cyclic equiaxial stretching modifies cell morphology, focal adhesion formation and mechanical properties of hASCs. This could be exploited to enhance osteogenic differentiation.

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A durable and biocompatible ascorbic acid-based covalent coating method of polydimethylsiloxane for dynamic cell culture

Polydimethylsiloxane (PDMS) is widely used in dynamic biological microfluidic applications. As a highly hydrophobic material, native PDMS does not support cell attachment and culture, especially in dynamic conditions. Previous covalent coating methods use glutaraldehyde (GA) which, however, is cytotoxic. This paper introduces a novel and simple method for binding collagen type I covalently on PDMS using ascorbic acid (AA) as a cross-linker instead of GA. We compare the novel method against physisorption and GA cross-linker-based methods. The coatings are characterized by immunostaining, contact angle measurement, atomic force microscopy and infrared spectroscopy, and evaluated in static and stretched human adipose stem cell (hASC) cultures up to 13 days. We found that AA can replace GA as a cross-linker in the covalent coating method and that the coating is durable after sonication and after 6 days of stretching. Furthermore, we show that hASCs attach and proliferate better on AA cross-linked samples compared with physisorbed or GA-based methods. Thus, in this paper, we provide a new PDMS coating method for studying cells, such as hASCs, in static and dynamic conditions. The proposed method is an important step in the development of PDMS-based devices in cell and tissue engineering applications.

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Cell culture chamber with gas supply for prolonged recording of human neuronal cells on microelectrode array

Background Typically, live cell analyses are performed outside an incubator in an ambient air, where the lack of sufficient CO2 supply results in a fast change of pH and the high evaporation causes concentration drifts in the culture medium. That limits the experiment time for tens of minutes. In many applications, e.g. in neurotoxicity studies, a prolonged measurement of extracellular activity is, however, essential. New method We demonstrate a simple cell culture chamber that enables stable culture conditions during prolonged extracellular recordings on a microelectrode array (MEA) outside an incubator. The proposed chamber consists of a gas permeable silicone structure that enables gas transfer into the chamber. Results We show that the culture chamber supports the growth of the human embryonic stem cell (hESC)-derived neurons both inside and outside an incubator. The structure provides very low evaporation, stable pH and osmolarity, and maintains strong signaling of hESC-derived neuronal networks over three-day MEA experiments. Comparison with existing methods Existing systems are typically complex including continuous perfusion of medium or relatively large amount of gas to supply. The proposed chamber requires only a supply of very low flow rate (1.5 ml/min) of non-humidified 5% CO2 gas. Utilizing dry gas supply makes the proposed chamber simple to use. Conclusion Using the proposed culture structure on top of MEA, we can maintain hESC-derived neural networks over three days outside an incubator. Technically, the structure requires very low flow rate of dry gas supporting, however, low evaporation and maintaining the pH of the culture.

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Computer Vision Measurements for Automated Microrobotic Paper Fiber Studies

The mechanical characterization of paper fibers and paper fiber bonds determines the key parameters affecting the mechanical properties of paper. Although bulk measurements from test sheets can give average values, they do not yield any real fiber-level data. The current, state-of-the-art methods for fiber-level measurements are slow and laborious, requiring delicate manual handling of microscopic samples. There are commercial microrobotic actuators that allow automated or tele-operated manipulation of microscopic objects such as fibers, but it is challenging to acquire the data needed to guide such demanding manipulation. This thesis presents a solution to the illumination problem and computer vision algorithms for obtaining the required data. The solutions are designed for a microrobotic platform that comprises actuators for manipulating the fibers and one or two microscope cameras for visual feedback.

The algorithms have been developed both for wet fibers, which can be treated as 2D objects, and for dry fibers and fiber bonds, which are treated as 3D objects. The major innovations in the algorithms are the rules for the micromanipulation of the curly fiber strands and the automated 3D measurements of microscale objects with random geometries. The solutions are validated by imaging and manipulation experiments with wet and dry paper fibers and dry paper fiber bonds. In the imaging experiments, the results are compared with the reference data obtained either from an experienced human or another imaging device. The results show that these solutions provide morphological data about the fibers which is accurate and precise enough to enable automated fiber manipulation. Although this thesis is focused on the manipulation of paper fibers and paper fiber bonds, both the illumination solution and the computer vision algorithms are applicable to other types of fibrous materials.
Automated high-throughput microbond tester for interfacial shear strength studies

This study presents a new high-throughput instrument for characterizing the shear strength of fibre/matrix interface. The developed instrument is applied to mechanical characterization of glass fibre/epoxy interface. As an application example, the time-dependent degradation of the adhesion properties of glass fibre sizing is studied. For this purpose, 480 microbond tests on ECR-glass/epoxy samples were performed. The degradation of the interfacial shear strength of the studied glass fibre was shown to be notable over time.

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Covalently coated cell stretching devices for osteogenic differentiation of human adipose stem cells

Cells can sense and adapt to the prevailing mechanical environment in vivo. By mimicking such stimulus in vitro, the behaviour and differentiation of stem cells can be guided and modelled. Furthermore, new and more effective differentiation methods are needed for tissue engineering applications to make the process faster, more cost-efficient and to avoid the use of expensive and contradictory growth factors.

In the current study, we aimed to investigate the effect of equiaxial stretching on the attachment and osteogenic differentiation of human adipose stem cells (hASCs) using a polydimethylsiloxane (PDMS) based cell stretching device (Figure 1). As a highly hydrophobic material, pristine PDMS does not support cellular attachment, and physisorbed protein coating does not withstand dynamic loading. Therefore, we developed and characterized a durable covalent coating method for PDMS which supports the attachment and viability of hASCs during mechanical stimulation.

The hASCs were cultured under static and dynamic (cyclic equiaxial strain of 2 to 5 %) conditions on covalently coated PDMS substrate up to 10 days. Based on DNA amount and ALP activity analyses, our results indicated that stretching delayed proliferation and promoted osteogenic differentiation of hASCs. Immunocytochemical vinculin detection and actin staining with phalloidin revealed that stretching also reduced the size of the cells and intensified focal adhesions and actin cytoskeleton.

The developed stretching system can be utilized in the future for studying the effect of different stretching parameters on stem cell behaviour. Furthermore, our results suggest that equiaxial stretching could be used as an additional osteogenic differentiation method for hASCs in bone tissue engineering applications in the future.
Dispenser system for nanocellulose 3D printing

A 3D-printed stepper motor dispenser assembly for a 10ml plastic syringe was constructed. This dispenser assembly was used to run a set of calibration experiments to evaluate its suitability to dose nanocellulose mass. The control of the dosing was done with a Labview software along with an Arduino Uno board. A set of dosing trials was conducted with three different dosing speeds and two different dosing volumes to verify the accuracy and repeatability of the constructed system in the nanocellulose mass dosing. The average dosing accuracy of the system was estimated to be at acceptable level for the application.

Engineering and Characterization of Bacterial Nanocellulose Films as Low Cost and Flexible Sensor Material

Some bacterial strains such as Komagataeibacter xylinus are able to produce cellulose as an extracellular matrix. In comparison to wood-based cellulose, bacterial cellulose (BC) holds interesting properties such as biodegradability, high purity, water-holding capacity, and superior mechanical and structural properties. Aiming toward improvement in BC production titer and tailored alterations to the BC film, we engineered K. xylinus to overexpress partial and complete bacterial cellulose synthase operon that encodes activities for BC production. The changes in cell growth, end metabolite, and BC production titers from the engineered strains were compared with the wild-type K. xylinus. Although there were no significant differences between the growth of wild-type and engineered strains, the engineered K. xylinus strains demonstrated faster BC production, generating 2–4-fold higher production titer (the highest observed titer was obtained with K. xylinus-bcsABCD strain producing 4.3 ± 0.46 g/L BC in 4 days). The mechanical and structural characteristics of cellulose produced from the wild-type and engineered K. xylinus strains were analyzed with a stylus profilometer, in-house built tensile strength measurement system, a scanning electron microscope, and an X-ray diffractometer. Results from the profilometer indicated that the engineered K. xylinus strains produced thicker BC films (wild type, 5.1 μm, and engineered K. xylinus strains, 6.2–10.2 μm). Scanning electron microscope revealed no principal differences in the structure of the different type BC films. The crystallinity index of all films was high (from 88.6 to 97.5%). All BC films showed significant piezoelectric response (5.0–20 pC/N), indicating BC as a promising sensor material.
Mini-incubator For Prolonged Cell Culture, MEA, And Hypoxia Studies Outside An Incubator

To mimic normal human body conditions in vitro, cells should be cultured in a biomimetic and controlled environment. Typically, living cells are cultured inside an incubator with 5% CO2 and atmospheric O2 concentration (~20%). However, this concentration is not physiologically relevant for most of the human tissues in vivo. For example, for the brain tissue, the normoxia (normal O2 concentration for this specific tissue) is from 0.5% to 7%, for eye from 1 to 5%, and for cancer cells it is near 0%. Moreover, it has been shown that low oxygen conditions can promote growth and influence differentiation of stem cells in vitro. Furthermore, constant culture conditions are difficult to maintain outside an incubator. For example, during the prolonged extracellular recordings with microelectrode arrays (MEA) altering gas concentrations, temperature variations, and evaporation are typical issues. That leads to the variation of pH and molecular concentrations of media. Therefore, to maintain the good culture conditions cells should be cultured in a biomimetic and controlled environment.

We have developed a cell culture platform that provides controlled environment for prolonged hypoxia/normoxia studies outside a traditional incubator, e.g. during the MEA recordings on MEA amplifier or on a glass plate on hot plate. The platform maintains the pH, temperature and constant gas concentration, for both 5% CO2 and hypoxia conditions. Truly hypoxic conditions can be maintained similarly as inside a commercial hypoxia chamber which was shown with HIF-1α induction of HeLa cells.

Challenges and capabilities of conductive polymeric materials for electromechanical stimulation of stem cells: A case study

Cell cultivation devices that mimic the complex microenvironment of cells in the human body are of high importance for the future of stem cell research. This paper introduces a prototype of an electromechanical stimulation platform as a modular expansion of an earlier developed mechanical stimulation device for stem cell research. A solution processable ink from PEDOT:PSS and graphene is studied as a suitable material for fabrication of transparent stretchable electrodes. Challenges of electrode integration on a flexible membrane using this material are critically discussed.
Nanocellulose based piezoelectric sensors

Cellulose based nanomaterials, generally known as nanocellulose [1], are interesting renewable bio-based nanomaterials which have potential applications in material sciences, electronics and biomedical engineering and diagnostic. A strong ability to form light-weight, highly porous, entangled networks makes nanocellulose suitable substrate or membrane material for various applications, such as supercapacitors [2,3]. It was proposed already in 1950’s, that wood has piezoelectric properties initiating from the highly crystalline assemblies of cellulose chains [4]. Experimental evidence of the piezoelectricity of cellulose nanocrystals (CNC) was reported only very recently [5,6]. Cellulose nanofibrils (CNF), produced by a mechanical homogenizing process from cellulose fibers, contain both crystalline and amorphous regions. CNC can be obtained from CNF by removal of amorphous regions using hydrolysis e.g. in sulfuric acid.Here, we report the experimental results on piezoelectricity of nanocellulose films prepared using different methods. The piezoelectric sensitivity of prepared sensor elements is measured using in-house built measurement setup equipped with a mechanical shaker and charge amplifier [7]. A randomly oriented CNF film (prepared by pressure filtering from aqueous CNF dispersion) showed piezoelectric sensitivities of 2-7 pC/N [8,9], which is between the piezoelectric coefficients of quartz (2.3 pC/N) and polyvinylidenefluoride (PVDF, -30 pC/N). Initial results from the nanocellulose based composite films gives promises for biomedical applications of nanocellulose based piezoelectric sensors. Keywords: Nanocellulose, piezoelectric sensor, cellulose nanofibrils, polyvinylidenefluoride

Cell Stretching Device for Live-Cell Confocal Microscopy
In this paper, we demonstrate a device with a stretchable cell cultivation substrate that is suitable for high-resolution confocal fluorescent microscopy imaging during mechanical stretching of cells. This small and innovative cell stretching device enables equiaxial strain (>10%) for cells. We demonstrate the capabilities of the device for semiautomatic real-time imaging of fluorescent fusion proteins localizing to actin fibers and nucleus of living cells. Furthermore, the stretching device is suitable for incubator conditions as it is fabricated solely from silicone and glass. Device fits to standard Petri dish frames that help the installation to a microscope for imaging. The stretching system provides different stretching waveforms, frequencies, and strain amplitudes.

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Automated Estimation of Contact Angle on Hydrophobic Fibers using a Microrobotic Platform
This paper presents an automated computer vision algorithm for estimating contact angles that a droplet of probe liquid forms on hydrophobic fibers. A specially designed microrobotic platform is utilized in manipulating the microscopic fibers, shooting droplets in the scale of tens of nanoliters on the fibers and capturing images of the experiments. The images are then processed with the automated computer vision algorithm. The algorithm is proven to be reliable and repeatable with totally 29 experiments on five different bio-based fiber samples.

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Study of Adhesion Force between Cellulose Micro-sphere and Cellulose Membrane

Development of novel high added value cellulose products requires improved understanding of interaction forces, which includes also the adhesion force, between cellulose surfaces. However, the interaction forces between cellulose surfaces have not been adequately studied. In this paper, cellulose-cellulose adhesion force is studied by using a customized dual-probe atomic force microscope (AFM) with a cellulose colloidal probe. Two different types of cellulose membranes (CM) with cellulose concentration of 1.5% and 2% are used as test samples, and about ten thousand tests are repeated on each CM sample type. Adhesion force histograms are provided and they show a large difference between the two types of CM. The average adhesion force on CM 1.5% is approximately 10 times higher than that on CM 2%. On CM 1.5%, the adhesion forces concentrate on the range from 450nN to 650nN, whereas on CM 2% the force distribute from 50 to 75nN. The difference in the adhesion force on these two types of CM can be attributed to their difference in surface roughness and surface energy.

Nanocellulose based piezoelectric sensors

Cellulose based nanomaterials, generally known as nanocellulose [1], are interesting renewable bio-based nanomaterials which have potential applications in material sciences, electronics and biomedical engineering and diagnostic. A strong ability to form light-weight, highly porous, entangled networks makes nanocellulose suitable substrate or membrane material for various applications, such as supercapacitors [2, 3].

It was proposed already in 1950’s, that wood has piezoelectric properties initiating from the highly crystalline assemblies of cellulose chains [4]. Experimental evidence of the piezoelectricity of cellulose nanocrystals (CNC) was reported only very recently [5, 6]. Cellulose nanofibrils (CNF), produced by a mechanical homogenizing process from cellulose fibers, contain both crystalline and amorphous regions. CNC can be obtained from CNF by removal of amorphous regions using hydrolysis e.g. in sulfuric acid.

Here, we report the experimental results on piezoelectricity of nanocellulose films prepared using different methods. The piezoelectric sensitivity of prepared sensor elements is measured using in-house built measurement setup equipped with a mechanical shaker and charge amplifier [7]. A randomly oriented CNF film (prepared by pressure filtering from aqueous CNF dispersion) showed piezoelectric sensitivities of 2-7 pC/N [8, 9], which is between the piezoelectric coefficients of quartz (2.3 pC/N) and polyvinylidene-fluoride (PVDF, -30 pC/N). Initial results from the nanocellulose based composite films gives promises for biomedical applications of nanocellulose based piezoelectric sensors.

A novel micro-robotic approach to study the environmental degradation of matrix and fibre materials

Design and simulation of a thermal flow sensor for gravity-driven microfluidic applications
CytoSpectre: A tool for spectral analysis of oriented structures on cellular and subcellular levels

Background: Orientation and the degree of isotropy are important in many biological systems such as the sarcomeres of cardiomyocytes and other fibrillar structures of the cytoskeleton. Image based analysis of such structures is often limited to qualitative evaluation by human experts, hampering the throughput, repeatability and reliability of the analyses. Software tools are not readily available for this purpose and the existing methods typically rely at least partly on manual operation.

Results: We developed CytoSpectre, an automated tool based on spectral analysis, allowing the quantification of orientation and also size distributions of structures in microscopy images. CytoSpectre utilizes the Fourier transform to estimate the power spectrum of an image and based on the spectrum, computes parameter values describing, among others, the mean orientation, isotropy and size of target structures. The analysis can be further tuned to focus on targets of particular size at cellular or subcellular scales. The software can be operated via a graphical user interface without any programming expertise. We analyzed the performance of CytoSpectre by extensive simulations using artificial images, by benchmarking against FibrilTool and by comparisons with manual measurements performed for real images by a panel of human experts. The software was found to be tolerant against noise and blurring and superior to FibrilTool when analyzing realistic targets with degraded image quality. The analysis of real images indicated general good agreement between computational and manual results while also revealing notable expert-to-expert variation. Moreover, the experiment showed that CytoSpectre can handle images obtained of different cell types using different microscopy techniques. Finally, we studied the effect of mechanical stretching on cardiomyocytes to demonstrate the software in an actual experiment and observed changes in cellular orientation in response to stretching.

Conclusions: CytoSpectre, a versatile, easy-to-use software tool for spectral analysis of microscopy images was developed. The tool is compatible with most 2D images and can be used to analyze targets at different scales. We expect the tool to be useful in diverse applications dealing with structures whose orientation and size distributions are of interest. While designed for the biological field, the software could also be useful in non-biological applications.
Adhesive Behavior Study Between Cellulose and Borosilicate Glass Using Colloidal Probe Technique

Cellulose-glass fiber hybrid composites have been introduced to introduce weight and price benefits compared to glass composites. However, the interactions between glass and cellulose have not been extensively studied. Understanding the interactions between these two materials will help to improve the mechanical properties of the cellulose hybrid composites. In this paper, by employing the colloidal probe technique, we investigated the interaction forces between glass and cellulose material. A silicon probe with a borosilicate glass microsphere attached as the probe tip was implemented into an atomic force microscope (AFM) to complete the task. Cellulose membranes were used as experiment samples. By pressing and releasing the colloidal probe against the cellulose membrane, the adhesion force and the adhesion energy were directly obtained through the measurements. The interfacial energy was revealed by applying the Johnson-Kendall-Roberts (JKR) model, and a theoretical calculation of the material stiffness was conducted.

Automated Microrobotic Manipulation of Paper Fiber Bonds

This paper presents a novel method for automated manipulation of individual paper fiber bonds using a microrobotic platform, a computer vision algorithm and a robotic software framework. This is a challenging task due to the three-dimensional, heterogeneous and complex morphology of the fiber bonds. The goal is to automatically grasp the fiber bond, and break it by pulling apart the fibers it consists of. We present the components of the microrobotic platform, and the different rules utilized in detecting suitable grasp points from a 3D reconstruction of the bond generated from an image pair. We demonstrate the functionality of the approach with bond breaking experiments of seven fiber bonds. The time required for grasping and breaking of a bond is 10 – 15 seconds making the approach much faster than the current state-of-the-art testing, which is based on manual manipulation. The success rate of the tests is as high as 80 %.
Automatic image-based detection and inspection of paper fibres for grasping

An automatic computer vision algorithm that detects individual paper fibres from an image, assesses the possibility of grasping the detected fibres with microgrippers and detects the suitable grasping points is presented. The goal of the algorithm is to enable automatic fibre manipulation for mechanical characterisation, which has traditionally been slow manual work. The algorithm classifies the objects in images based on their morphology, and detects the proper grasp points from the individual fibres by applying given geometrical constraints. The authors test the ability of the algorithm to detect the individual fibres with 35 images containing more than 500 fibres in total, and also compare the graspability analysis and the calculated grasp points with the results of an experienced human operator with 15 images that contain a total of almost 200 fibres. The detection results are outstanding, with fewer than 1% of fibres missed. The graspability analysis gives sensitivity of 0.83 and specificity of 0.92, and the average distance between the grasp points of the human and the algorithm is 220 μm. Also, the choices made by the algorithm are much more consistent than the human choices.

Electroplated nickel microspring and low-friction precision linear slider: A novel micro-force sensing tool

This paper introduces a novel micro-force sensing approach utilizing an electroplated nickel microspring and a precision linear slider (PLS) for micro-tensile testing applications. After investigating the effects of friction forces in a PLS, an electroplated nickel microspring is designed, fabricated and integrated into the PLS, and the proposed micro-force sensor concept is validated through experimental results. The microspring fabricated in this paper is limited to forces up to 6 mN.
with the average sensitivity of 36.63 μN/μm. It is shown that the friction forces introduce uncertainties only to the forces less than 500 μN. The proposed approach allows the fabrication of micro-force sensors for the force ranges of up to tens of Millinewtons for different applications.

**Microrobotic system for multi-rate measurement of bio-based fibres Z-directional bond strength**

The core content of this study is micro-testing of microscale objects - an emerging application area for microrobotics - where microrobotics has been used in paper industry for measuring properties at the single fibre level. Pulp and paper scientists are interested to have experimental data of single fibre-fibre bond strength distribution of paper/board products in different loading modes and rates. Meeting this demand is quite challenging since the system should be able to measure the bond strength i) in the individual fibre level, ii) in different loading modes, and iii) in different loading rates. The current methods of measurement do not satisfy all these three requirements. Among the four different loading modes, the Z-directional behaviour of paper/board products is a matter of high significance for papermaking and paper converting companies. The Z-directional properties influence compressive properties, and accordingly the performance of structural paper/board products. According to the literature, there is not any reported method to facilitate the measurement of Z-directional strength at the single fibre level in different loading rates. This paper reports an in-depth study of a measurement method for experimental evaluation of Z-directional individual fibre-fibre bond strength in multiple loading rates using microrobotics and a Polyvinylidene fluoride (PVDF) film microforce sensor. The results from the measurement system are promising. In summary, the first concept for multi-rate measurement of Z-directional bond strength at the individual fibre level is developed during this work which has a high practical impact on the fibre characterization research field.
Modeling and Experimental Characterization of Pressure Drop in Gravity-Driven Microfluidic Systems

Passive pumping using gravity-driven flow is a fascinating approach for microfluidic systems. When designing a passive pumping system, generated flow rates should be known precisely. While reported models used to estimate the flow rates do not usually consider capillary forces, this paper shows that their exclusion is unrealistic in typical gravity-driven systems. Therefore, we propose a new analytical model to estimate the generated flow rates. An extensive set of measurements is used to verify that the proposed model provides a remarkably more precise approximation of the real flow rates compared to the previous models. It is suggested that the developed model should be used when designing a gravity-driven pumping system.

PVDF Microforce Sensor for the Measurement of Z-directional Strength in Paper Fiber Bonds

The Z-directional strength of paper fiber bonds is an important parameter for the paper and board industry. The current methods of studying Z-directional paper fiber bond strength rely on handsheet measurements. This paper presents a novel tool for measuring the Z-directional strength of individual paper fiber bonds. A polyvinylidene fluoride (PVDF) film microforce sensor, with a special specimen holder, was designed, fabricated and calibrated to perform the measurements. The microforce sensor operates in a cantilever-like bending mode and is capable of measuring forces up to 10 mN. It is demonstrated that the output of our microforce sensor is linear, in addition to which it can measure forces higher than 3 mN with a coefficient of variation of less than 2%. This new microforce sensor was integrated into a microrobotic platform and is shown to be able to accurately measure the Z-directional bond strength of paper fibers.
In situ hybridization of pulp fibres using Mg-Al layered double hydroxides

Inorganic Mg2+ and Al3+ containing layered double hydroxide (LDH) particles were synthesised in situ from aqueous solution onto chemical pulp fibers of pine (Pinus sylvestris). High super saturated (hss) solution with sodium carbonate produced LDH particles with an average diameter of 100–200 nm. Nano-size (70 nm) LDH particles were found from fibers external surface and, to a lesser degree, from the S2 cell wall after synthesis via low super saturated (lss) route. The synthesis via slow urea hydrolysis (Uhyd) yielded micron and clay sized LDH (2–5 µm) and enabled efficient fiber densification via mineralization of S2 fiber wall layer as indicated by TEM and compliance analysis.

The Uhyd method decreased fiber compliance up to 50%. Reduction in the polymerization degree of cellulose was observed with capillary viscometry. Thermogravimetric analysis showed that the hybridization with LDH reduced the exothermic heat, indicating, that this material can be incorporated in flame retardant applications. Fiber charge was assessed by adsorption experiments with methylene blue (MB) and metanil yellow (MY). Synthesis via lss route retained most of the fibres original charge and provided the highest capacity (10 µmol/g) for anionic MY, indicating cationic character of hybrid fibers. Our results suggested that mineralized fibers can be potentially used in advanced applications such as biocomposites and adsorbent materials.
chips using oxygen plasma. (4) Oxygen plasma treatment also enabled the attachment of polyvinylpyrroldione (PVP) to the sample channel surfaces to synthesize hydrophilic polymer coating. A contact angle for the PVP treated PDMS was 21 after 17 days, indicating the formation of a long-term hydrophilic PDMS surface. Finally, the example SiNW sensor is modified to allow direct real-time detection of thyroid-stimulating hormone (TSH). The sensor was able to detect as low TSH concentration values as 0.5 mIU/l, which indicates a successfully integrated sample delivery system.
Image-based Measurements of Paper Fibers for Automatic Manipulation

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Integrated microfluidic culture environments for in vitro cell studies

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Integration of Robotic Software Frameworks for Convenient Software Component Exchange in Micro- and Nanoscale Applications

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Photocontrol of Mechanical Properties of Pulp Fibers and Fiber-to-Fiber Bonds via Self-Assembled Polysaccharide Derivatives

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Pneumatic cell stretching system for cardiac differentiation and culture

This paper introduces a compact mechanical stimulation device suitable for applications to study cellular mechanobiology. The pneumatically controlled device provides equiaxial strain for cells on a coated polydimethylsiloxane (PDMS) membrane and enables real-time observation of cells with an inverted microscope. This study presents the implementation and operation principles of the device and characterizes membrane stretching. Different coating materials are also analyzed on an unstretched membrane to optimize the cell attachment on PDMS. As a result, gelatin coating was selected for further experiments to demonstrate the function of the device and evaluate the effect of long-term cyclic equiaxial stretching on human pluripotent stem cells (hPSCs). Cardiac differentiation was induced with mouse visceral endoderm-like (END-2) cells, either on an unstretched membrane or with mechanical stretching. In conclusion, hPSCs grew well on the stretching platform and cardiac differentiation was induced. Thus, the platform provides a new possibility to study the effect of stretching on cellular properties including differentiation and stress-induced cardiac diseases.

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Releasing tool-adhered natural fibrous microscale objects with vacuum system

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Robotic software frameworks and software component models in the development of automated handling of individual natural fibers

General information
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MoE publication type: A1 Journal article-refereed
Organisations: Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering Research (ITTE)
Contributors: Von Essen, M., Hirvonen, J., Kuikka, S., Kallio, P.
Number of pages: 17
Pages: 29-45
Publication date: 2014
Peer-reviewed: Yes

Publication information
Journal: Journal of Micro-Bio Robotics
Volume: 9
Issue number: 1-2
ISSN (Print): 2194-6418
Ratings:
Scopus rating (2014): CiteScore 0.7 SJR 0.178 SNIP 0.074
Original language: English
DOIs:
10.1007/s12213-014-0078-8

Bibliographical note
Contribution: organisation=ase,FACT1=1<br/>
Portfolio EDEND: 2014-12-02<br/>
Publisher name: Springer
Source: researchoutputwizard
Source ID: 1762
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Semi-automatic Measurement of Microfibril Angle on a Microrobotic Platform

General information
Publication status: Published
The Effect of Refining on Z-directional Strength of Bleached Softwood Kraft Pulp Fibre Bonds using Microrobotics

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering
Contributors: Latifi, S. K., Saketi, P., Bozic, M., Kallio, P.
Number of pages: 3
Pages: 1-3
Publication date: 2014

Host publication information
Title of host publication: Progress in Paper Physics, (PPPS-2014), September 8-11, 2014, Raleigh, North Carolina, USA
URLs:

Bibliographical note
Contribution: organisation=ase,FACT1=1<br/>Portfolio EDEND: 2015-01-15
Source: researchoutputwizard
Source ID: 892
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Integration of Microfluidic System with Silicon Nanowires Biosensor for Multiplexed Detection

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering Research (ITTE)
Contributors: Gao, A., Dai, P., Lu, N., Li, T., Wang, Y., Hemmilä, S., Kallio, P.
Number of pages: 4
Pages: 348-351
Publication date: 2013

Host publication information
Title of host publication: Proceedings of the Third International Conference on Manipulation, Manufacturing and Measurement on the Nanoscale, 3M-NANO, Suzhou, China, 26-30 August, 2013

Publication series
Name: International Conference on Manipulation, Manufacturing and Measurement on the Nanoscale
ISSN (Print): 1932-4510

Bibliographical note
Contribution: organisation=ase,FACT1=1<br/>Portfolio EDEND: 2013-10-29
Source: researchoutputwizard
Kohti automaattista yksittäisten paperikuitujen manipulointia

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering
Contributors: Hirvonen, J., Kallio, P.
Number of pages: 6
Pages: 1-6
Publication date: 2013

Host publication information
Title of host publication: Proceedings of Automaatio XX-seminaari, Automation and systems without borders - beyond future, 21.-22.5.2013, Helsinki
Publisher: Suomen Automaatioseura ry
ISBN (Print): 978-952-5183-44-3

Publication series
Name: SAS julkaisusarja
No.: 42
ISSN (Print): 1455-6502

Bibliographical note
Contribution: organisation=ase,FACT1=1<br/>Portfolio EDEND: 2013-09-29<br/>Publisher name: Suomen Automaatioseura ry
Source: researchoutputwizard
Source ID: 2309
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Method for Investigations of Aged Fibre-Fibre Bonds with Micro and Nanorobotic Tools

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering
Contributors: Saketi, P., Mikczinski, M., Fatikow, S., Kallio, P.
Number of pages: 18
Pages: 125-142
Publication date: 2013

Host publication information
Title of host publication: Advances in Pulp and Paper Research, Cambridge 2013: Transactions of the 15th Fundamental Research Symposium, Cambridge, September 2013
Place of publication: Bury
Publisher: Pulp & Paper Fundamental Research Society
Editor: I’Anson, S.
ISBN (Print): 978-0992616304

Publication series
Name: Pulp and Paper Fundamental Research Symposium
Volume: 1

Bibliographical note
Contribution: organisation=ase,FACT1=1<br/>Portfolio EDEND: 2013-10-29<br/>Publisher name: Pulp & Paper Fundamental Research Society
Source: researchoutputwizard
Source ID: 3334
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Scale and Rotation Invariant Two View Microgripper Detection that Uses a Planar Pattern

In automated grasping of microparts or objects with unknown dimensions and orientations, at least two cameras have to be used to acquire the depth information. In addition to recognition and reconstruction of the real-world coordinates of the
target objects, the system has to be able to detect also the real-world coordinates of the microgrippers from the images. This paper presents a scale and rotation invariant microgripper detection method that uses a planar pattern. The method is suitable especially for prototyping systems, whose composition might vary between the experiments. The gripper detection is shown to be accurate enough for challenging micromanipulation tasks of small electronic components and individual paper fibers.

**General information**
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering Research (ITTE)
Contributors: Hirvonen, J., Kallio, P.
Number of pages: 9
Pages: 414-422
Publication date: 2013

**Host publication information**
Title of host publication: 6th IFAC Symposium on Mechatronic Systems, April 10-12, 2013, Hangzhou, China
Publisher: International Federation of Automatic Control
Editor: Ju, B.
ISBN (Print): 978-3-902823-31-1

**Publication series**
Name: Elsevier IFAC Publications / IFAC Proceedings series
ISSN (Print): 1474-6670
Electronic versions:
hirvonen_kallio_scale_and_rotation_invariant.pdf
DOIs:
10.3182/20130410-3-CN-2034.00056
URLs:
http://urn.fi/URN:NBN:fi:tty-201410101506

**Bibliographical note**
Contribution: organisation=ase,FACT1=1<br/>Portfolio EDEND: 2013-09-29<br/>Publisher name: International Federation of Automatic Control
Source: researchoutputwizard
Source ID: 2310
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

**Three-dimensional calibration of micromanipulators using stereo vision**
Calibration is of great significance in the development of automatic micromanipulation systems. This paper presents a novel vision based procedure for three-dimensional (3D) calibration of micromanipulators. Two major issues in the proposed calibration approach - vision system calibration and manipulator kinematic calibration - are discussed in detail in this paper. Verification and evaluation experiments are conducted using a 3D micromanipulator in a microrobotic fiber characterization platform. Experimental results demonstrate that the proposed calibration approach is able to achieve prediction errors below 5 μm. The proposed approach also demonstrates the feasibility of calibrating the decoupled motions, by reducing the undesired movement from 28 μm to 8 μm (for 4800 μm desired movement).

**General information**
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering Research (ITTE)
Contributors: Xiong, Y., Hirvonen, J., Kallio, P.
Number of pages: 12
Pages: 13-24
Publication date: 2013
Peer-reviewed: Yes

**Publication information**
Journal: Journal of Micro-Bio Robotics
Volume: 8
Issue number: 1
ISSN (Print): 2194-6418
Original language: English
Towards Fully Automated Pick and Place Operations of Individual Natural Fibers
This paper reports automated image-based pick and place procedures for manipulation of individual natural fibers. The developed procedures are part of an effort to develop a fully automated microrobotic-based platform for fiber characterization. The presented procedures are divided into unit operations, which can reused in multiple tasks that the platform must perform. Two different demonstrations: pick and place, and coordinated fiber lifting are presented. In addition, a component-based software that promotes reusability of the developed unit operations is presented.

Washing Durability of Embroidered Polymer Coated RFID Tags
This paper investigates the washing durability of embroidered polymer-coated RFID tags. The tags are tested under various wash conditions to evaluate their performance. The results show that the tags are durable and can withstand multiple wash cycles without significant degradation.

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering Research (ITTE)
Contributors: Von Essen, M., Hirvonen, J., Kuikka, S., Kallio, P.
Number of pages: 6
Pages: 21-26
Publication date: 2013

Host publication information
Title of host publication: Proceedings of the Third International Conference on Manipulation, Manufacturing and Measurement on the Nanoscale, 3M-NANO, Suzhou, China, 26-30 August, 2013
ISBN (Print): 978-1-4799-1213-1

Publication series
Name: International Conference on Manipulation, Manufacturing and Measurement on the Nanoscale

Bibliographical note
Contribution: organisation=ase,FACT1=1<br/>Portfolio EDEND: 2013-10-29<br/>Publisher name: Springer
Source: researchoutputwizard
Source ID: 3759
Research output: Contribution to journal › Article › Scientific › peer-review

Washing Durability of Embroidered Polymer Coated RFID Tags
This paper investigates the washing durability of embroidered polymer-coated RFID tags. The tags are tested under various wash conditions to evaluate their performance. The results show that the tags are durable and can withstand multiple wash cycles without significant degradation.

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Electronics and Communications Engineering, Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering Research (ITTE), Sensing Systems for Wireless Medicine (MediSense)
Number of pages: 2
Pages: 1490-1491
Publication date: 2013

Host publication information
A flexible microrobotic platform for handling microscale specimens of fibrous materials for microscopic studies

One of the most challenging issues faced in handling specimens for microscopy, is avoiding artefacts and structural changes in the samples caused by human errors. In addition, specimen handling is a laborious and time-consuming task and requires skillful and experienced personnel. This paper introduces a flexible microrobotic platform for the handling of microscale specimens of fibrous materials for various microscopic studies such as scanning electron microscopy and nanotomography. The platform is capable of handling various fibres with diameters ranging from 10 to 1000 μm and lengths of 100 μm-15 mm, and mounting them on different types of specimen holders without damaging them. This tele-operated microrobotic platform minimizes human interaction with the samples, which is one of the main sources contributory to introducing artefacts into the specimens. The platform also grants a higher throughput and an improved success rate of specimen handling, when compared to the manual processes. The operator does not need extensive experience of microscale manipulation and only a short training period is sufficient to operate the platform. The requirement of easy configurability for various samples and sample holders is typical in the research and development of materials in this field. Therefore, one of the main criteria for the design of the microrobotic platform was the ability to adapt the platform to different specimen handling methods required for microscopic studies. To demonstrate this, three experiments are carried out using the microrobotic platform. In the first experiment, individual paper fibres are mounted successfully on scanning electron microscopy specimen holders for the in situ scanning electron microscopy diagonal compression test of paper fibres. The performance of the microrobotic platform is compared with a skilled laboratory worker performing the same experiment. In the second experiment, a strand of human hair and an individual paper fibre bond are mounted on a specimen holder for nanotomography studies. In the third experiment, individual paper fibre bonds with controlled crossing and vertical angles are made using the microrobotic platform. If an industrial application requires less flexibility but a higher speed when handling one type of sample to a specific holder, then the platform can be automated in the future.
Characterizing leakage current in silicon nanowire-based field-effect transistors by applying pseudo-random sequences

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering
Research (ITTE), Smart Energy Systems (SES)
Number of pages: 5
Pages: 1-5
Publication date: 2012

Host publication information
Title of host publication: Proceedings of Second International Conference on Manipulation, Manufacturing and Measurement on the Nanoscale, 29 Aug. - 1 Sept. 2012, Xi’an, China
Publisher: Changchun University of Science and Technology
ISBN (Print): 978-1-4673-4588-0
ISBN (Electronic): 978-1-4673-4589-7

Bibliographical note
Contribution: organisation=ase aci,FACT1=1
Publisher name: Changchun University of Science and Technology
Source: researchoutputwizard
Source ID: 5193
Research output: Chapter in Book/Report/Conference proceeding » Conference contribution » Scientific » peer-review

Digital Imaging and Piezo-dispenser Actuator in Automatic Flocculation Control

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Contributors: Tomperi, J., Honkanen, M., Kallio, P., Leiviskä, K., Saarenrinne, P., Joensuu, I., Piironen, M.
Pages: 83-95
Publication date: 2012
Peer-reviewed: Yes

Publication information
Journal: Sensors and Transducers
Volume: 136
Issue number: 1
ISSN (Print): 1726-5479
Ratings:
Scopus rating (2012): SJR 0.145 SNIP 0.407
Original language: English
URLs:
http://www.sensorsportal.com

Bibliographical note
Poistettu tupla r=1369. ei ut-numeroa 30.8.2013
Contribution: organisation=epr,FACT1=0.5
Contribution: organisation=ase aci,FACT2=0.5
Publisher name: International Frequency Sensor Association IFSA
Source: researchoutputwizard
Source ID: 5438
Research output: Contribution to journal » Article » Scientific » peer-review

Integration of microfluidic sample delivery system on silicon nanowire-based biosensor
Pseudo-random sequences in analysis of polyvinylidene fluoride piezoelectric sensors

This paper describes rapid, simple, and cost-effective treatments for producing biocompatible and long-term hydrophilic polydimethylsiloxane (PDMS) surfaces identified in an experimental study investigating 39 treatments in all. The wetting of the surfaces was monitored during six months. Changes in surface morphology and chemical composition were also analyzed. Some of the treatments are presented here for the first time, while for earlier presented treatments the selection of investigated 2 parameters was wider and the observation period for the surface wetting longer. The PDMS surfaces were modified by surface activation, physisorption, and synthesis of both “grafting to” and “grafting from” polymer brushes. In surface activation, the PDMS sample was exposed to oxygen plasma, with several combinations of exposure time and RF power. In the physisorption and synthesis of polymer brushes, three commercially available and biocompatible chemicals were used: 2-hydroxyethyl methacrylate (HEMA), polyethylene glycol (PEG), and polyvinylpyrrolidone (PVP). Thirty-three of the 39 treatments rendered the PDMS hydrophilic, and in 12 cases the hydrophilicity lasted at least six months. Seven of these long-term hydrophilic coatings supported a contact angle of 30° or less. Three of the long-lasting
Hydrophilic coatings required only minutes to prepare.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering Research (ITTE)
Contributors: Hemmilä, S., Cauich-Rodriguez, J. V., Kreutzer, J., Kallio, P.
Pages: 9864-9875
Publication date: 2012
Peer-reviewed: Yes

Publication information
Journal: Applied Surface Science
Volume: 258
Issue number: 24
ISSN (Print): 0169-4332
Ratings:
Scopus rating (2012): CiteScore 3.5 SJR 0.913 SNIP 1.347
Original language: English
Electronic versions:
hemmila_rapid_simple_and_cost_effective_treatments.pdf
DOIs:
10.1016/j.apsusc.2012.06.044
URLs:
http://urn.fi/URN:NBN:fi:tty-201409261454

Bibliographical note
Contribution: organisation=ase mit,FACT1=1<br/>Publisher name: Elsevier
Source: researchoutputwizard
Source ID: 4212
Research output: Contribution to journal › Article › Scientific › peer-review

Small and Flexible Metal Mountable Passive UHF RFID Tag on High-Dielectric Polymer-Ceramic Composite Substrate

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Automation Science and Engineering, Department of Electronics, Integrated Technologies for Tissue Engineering Research (ITTE), Sensing Systems for Wireless Medicine (MediSense)
Contributors: Babar, A. A., Björninen, T., Bhagavati, V., Sydänheimo, L., Kallio, P., Ukkonen, L.
Pages: 1319-1322
Publication date: 2012
Peer-reviewed: Yes

Publication information
Journal: IEEE Antennas and Wireless Propagation Letters
Volume: 11
ISSN (Print): 1536-1225
Ratings:
Scopus rating (2012): CiteScore 3.9 SJR 0.877 SNIP 1.567
Original language: English
DOIs:
10.1109/LAWP.2012.2227291

Bibliographical note
ei UT:ta tarkastushetkellä 29.12.2012<br/>Contribution: organisation=ele rr,FACT1=0.5<br/>Contribution: organisation=ase,FACT2=0.5<br/>Publisher name: Institute of Electrical and Electronics Engineers IEEE
Source: researchoutputwizard
Source ID: 3878
Research output: Contribution to journal › Article › Scientific › peer-review

Structured PDMS chambers for enhanced human neuronal cell activity on MEA platforms
Structured poly(dimethylsiloxane) (PDMS) chambers were designed and fabricated to enhance the signaling of human embryonic stem cell (hESC) - derived neuronal networks on microelectrode array (MEA) platforms. The structured PDMS
chambers enable cell seeding on restricted areas and thus, reduce the amount of needed coating materials and cells. In addition, the neuronal cells formed spontaneously active networks faster in the structured PDMS chambers than in control chambers. In the PDMS chambers, the neuronal networks were more active and able to develop their signaling into organized signal trains faster than control cultures. The PDMS chamber design enables much more repeatable analysis and rapid growth of functional neuronal network in vitro. Moreover, due to its easy and cheap fabrication process, new configurations can be easily fabricated based on investigator requirements.

**General information**
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering Research (ITTE)
Contributors: Kreutzer, J., Ylä-Outinen, L., Kärmä, P., Kaarela, T., Mikkonen, J., Skottman, H., Narkilahti, S., Kallio, P.
Number of pages: 10
Pages: 1-10
Publication date: 2012
Peer-reviewed: Yes

**Publication Information**
Journal: Journal of Bionic Engineering
Volume: 9
Issue number: 1
ISSN (Print): 1672-6529
Ratings:
Scopus rating (2012): CiteScore 2.8 SJR 0.458 SNIP 1.332
Original language: English
Electronic versions:
kreutzer_structured_pdms_chambers_for_enhanced.pdf
DOIs: 10.1016/S1672-6529(11)60091-7
URLs: http://www.elsevier.com/wps/find/journaldescription.cws_home
http://urn.fi/URN:NBN:fi:tty-201409261455

**Bibliographical note**
Contribution: organisation=ase aci,FACT1=1<br/>Publisher name: Elsevier
Source: researchoutputwizard
Source ID: 4557
Research output: Contribution to journal › Article › Scientific › peer-review

**Vision based 3D calibration of micromanipulator in microrobotic fiber characterization platform**

**General information**
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering Research (ITTE)
Contributors: Xiong, Y., Von Essen, M., Hirvonen, J., Kallio, P.
Publication date: 2012

**Host publication information**
Title of host publication: Proceedings of the Second International Conference on Manipulation, Manufacturing and Measurement on the Nanoscale, 29 Aug. - 1 Sept. 2012, Xi'an, China
Publisher: Changchun University of Science and Technology
ISBN (Print): 978-1-4673-4588-0
ISBN (Electronic): 978-1-4673-4589-7

**Publication series**
Name: International Conference on Manipulation, Manufacturing and Measurement on the Nanoscale

**Bibliographical note**
Contribution: organisation=ase aci,FACT1=1<br/>Publisher name: Changchun University of Science and Technology
Source: researchoutputwizard
Source ID: 5603
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review
Automated Grasping in Manipulation of Individual Paper Fibers

General information
Publication status: Published
MoE publication type: B3 Non-refereed article in conference proceedings
Organisations: Department of Automation Science and Engineering
Contributors: von Essen, M., Hirvonen, J., Saketi, P., Kallio, P.
Publication date: 2011

Host publication information
Title of host publication: Proceedings of the First International Conference on Manipulation, Manufacturing and Measurement on the Nanoscale 3M-NANO, Changchun, China, August 2011
Place of publication: Changchun
Publisher: 3M-Nano

Publication series
Name: International Conference on Manipulation, Manufacturing and Measurement on the Nanoscale 3M-NANO
Publisher: 3M-Nano

Bibliographical note
Contribution: organisation=ase aci,FACT1=1
Source: researchoutputwizard
Source ID: 7535
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific

Automatic image-based detection of paper fiber ends
Understanding the properties of paper fibers and paper fiber bonds can be really significant in improving the quality of paper. The problem in gathering measurement data from individual paper fibers is the lack of reliable and efficient research instruments. Also, without automation the yield of experiments will be low and the results will depend on the skills of the operator. This paper presents an image-based method to automatically detect the endpoints of paper fibers. The method will be utilized in automatic control of a novel and tailor-made paper fiber manipulation and measurement platform. Performance of the method is extremely promising with adequate speed and very accurate results.

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering (ITTE)
Contributors: Hirvonen, J., Saketi, P., Kallio, P.
Number of pages: 5
Pages: 1-5
Publication date: 2011

Host publication information
Title of host publication: Third International Conference on Digital Image Processing ICDIP 2011, Chengdu, China, April 15-17, 2011. Proceedings of SPIE
Place of publication: Bellingham, WA
Publisher: SPIE
Editor: Zhang, T.
Article number: 80092N

Publication series
Name: International Conference on Digital Image Processing ICDIP
Publisher: SPIE
Volume: 8009
Electronic versions:

DOI:
10.1117/12.896172
URLs:

Bibliographical note
Displacement control of piezoelectric actuators using current and voltage

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Automation Science and Engineering, Integrated Technologies for Tissue Engineering Research (ITTE), Smart Energy Systems (SES)
Contributors: Ronkanen, P., Kallio, P., Vilkko, M., Koivo, H. N.
Pages: 160-166
Publication date: 2011
Peer-reviewed: Yes

Publication information
Journal: IEEE - ASME Transactions on Mechatronics
Volume: 16
Issue number: 1
ISSN (Print): 1083-4435
Ratings:
Scopus rating (2011): CiteScore 5.8 SJR 1.373 SNIP 2.594
Original language: English
DOIs:
10.1109/TMECH.2009.2037914

Bibliographical note
Contribution: organisation=ase aci,FACT1=1
Source: researchoutputwizard
Source ID: 7139
Research output: Contribution to journal › Article › Scientific › peer-review

Fine Structure of Papermaking Fibres: The Final Report of COST Action E54 "Characterization of the fine structure and properties of papermaking fibres using new technologies"

General information
Publication status: Published
MoE publication type: C2 Edited books
Organisations: Department of Automation Science and Engineering
Publication date: 2011

Publication information
Place of publication: Brussels
Publisher: COST Office
ISBN (Print): 978-91-576-9007-4
Original language: English

Bibliographical note
Contribution: organisation=ase aci,FACT1=1
Source: researchoutputwizard
Source ID: 5687
Research output: Book/Report › Anthology › Scientific › peer-review

Konenäköalgoritmien käyttö mikrosysteemiteknikan tutkimuksessa

General information
Publication status: Published
MoE publication type: B3 Non-refereed article in conference proceedings
Organisations: Department of Automation Science and Engineering
Contributors: Hirvonen, J., Kallio, P.
Number of pages: 6
Measuring bond strengths of individual paper fibers using microrobotics

This paper introduces a microrobotic platform to make, manipulate and break individual paper fiber bonds. An individual paper fiber bond is the construction unit of a paper sheet and its properties affect the strength of the entire network of a paper sheet. In one hand, conventional laboratory tests on paper fiber bonds are mainly performed in a hand-sheet level. On the other hand, reported methods for paper fiber bond strength tests in individual bond level are either direct which are manual, laborious and have a low throughput or indirect which require data interpretation. The microrobotic platform presented in this paper performs direct and individual tests on paper fiber bonds. Making, manipulating and breaking individual paper fiber bonds are accomplished successfully demonstrating the first steps towards individual bond strength measurement.
Microrobotic platform for manipulation and mechanical characterization of individual paper fibres

General information
Publication status: Published
MoE publication type: B2 Part of a book or another research book
Organisations: Department of Automation Science and Engineering
Contributors: Saketi, P., Kallio, P.
Pages: 133-146
Publication date: 2011

Host publication information
Title of host publication: Fine Structure of Papermaking Fibres: The Final Report of COST Action E54 "Characterization of the fine structure and properties of papermaking fibres using new technologies"
Editors: Ander, P., Bauer, W., Heinemann, S., Kallio, P., Passas, R., Treimanis, A.
ISBN (Print): 978-91-576-9007-4

Bibliographical note
ei ut-numeroa 10.5.2014<br/>Contribution: organisation=ase aci,FACT1=1
Source: researchoutputwizard
Source ID: 7178
Research output: Chapter in Book/Report/Conference proceeding › Chapter › Scientific

The Effects of Laser Welding on the Heterogeneous Immunoassay Performance in a Microfluidic Cartridge

Sealing of a microfluidic cartridge is a challenge, because the cartridge commonly contains heat-sensitive biomolecules that must also be protected from contamination. In addition, the objective is usually to obtain a sealing method suitable for mass production. Laser welding is a rapid technique that can be accomplished with low unit costs. Even though the technique has been widely adopted in industry, the literature on its use in microfluidic applications is not large. This paper is the first to report the effects of laser welding on the performance of the heterogeneous immunoassay in a polystyrene microfluidic cartridge in which biomolecules are immobilized into the reaction surface of the cartridge before sealing. The paper compares the immunoassay performance of microfluidic cartridges that are sealed either with an adhesive tape or by use of laser transmission welding. The model analyte used is thyroid stimulating hormone (TSH). The results show that the concentration curves in the laser-welded cartridges are very close to the curves in the taped cartridges. This indicates, firstly, that laser welding does not cause any significant reduction in immunoassay performance, and secondly, that the polystyrene cover does not have significant effect on the signal levels. Interestingly, the coefficients of variance between
parallel samples were lower in the laser-welded cartridges than in the taped cartridges.

Towards automated manipulation and characterization of paper-making fibres and its components

Automated handling of bio-nanowires for nanopackaging
Compensation of detent torque in microstepping of linear permanent magnet stepping motors

**General information**
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering
Contributors: Vilkko, M., Kaivosoja, J., Mäki, A., Kallio, P.
Publication date: 2010

**Host publication information**
Title of host publication: The IEEE/RSJ 2010 International Conference on Intelligent Robots and Systems IROS 2010, Taipei, Taiwan, October 18-22, 2010
ISBN (Print): 978-1-4244-6676-4
DOI: 10.1109/IROS.2010.5649313

**Bibliographical note**
Contribution: organisation=ase aci,FACT1=1
Source: researchoutputwizard
Source ID: 7905
Research output: Chapter in Book/Report/Conference proceeding > Conference contribution > Scientific > peer-review

Control software for automated microrobotic paper fiber characterization

**General information**
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering
Contributors: von Essen, M., Kuikka, S., Kallio, P.
Publication date: 2010

**Host publication information**
Title of host publication: 12th International Conference on New Actuators, Actuator 2010, Bremen, Germany, June 2010

**Bibliographical note**
Contribution: organisation=ase aci,FACT1=1
Source: researchoutputwizard
Source ID: 9566
Research output: Chapter in Book/Report/Conference proceeding > Conference contribution > Scientific > peer-review

Dried nanoparticle label reagents for microfluidic Immunoassays

In this paper, we demonstrate and analyze the solubility and distribution of dried europium(III)-chelate dyed nanoparticles in mini channels of milled polystyrene (PS) cartridges. The particular objective for the study is to measure quantitatively the efficiency of the resuspension of dried nanoparticles from the surface of PS channels and to determine the homogeneity of the solute particles in a reaction chamber considering also the incubation time.

**General information**
Publication status: Published
Microrobotic platform for manipulation and flexibility measurement of individual paper fibres

This paper introduces a microrobotic platform to manipulate and characterize individual paper fibers. Mechanical characterization of individual paper fibers determines the key parameters which affect the quality of paper sheets. Current laboratory tests are based on bulk paper fiber measurements. This paper presents a microrobotic platform which is able to characterize the flexibility of individual paper fibers directly, not in bulk amount and using indirect estimations. The flexibility of three different pulp samples is measured and the experimental results are reported.

General information
Publication status: Published
MOE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering
Contributors: Saketi, P., Treimanis, A., Fardim, P., Ronkanen, P., Kallio, P.
Pages: 5762-5767
Publication date: 2010

Host publication information
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ISBN (Print): 978-1-4244-6676-4
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saketi_microrobotic_platform_for_manipulation_and_flexibility_measurement.pdf
DOIs:
10.1109/IROS.2010.5649723
Modeling continuous optoelectrowetting device

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering
Contributors: Mäki, A., Ronkanen, P., Zhou, Q., Kallio, P.
Number of pages: 10
Pages: 1-10
Publication date: 2010

Host publication information
Title of host publication: Proceedings of the 2nd European Conference on Microfluidics - Microfluidics 2010, Toulouse, December 8-10, 2010
ISBN (Print): 978-2-906831-85-8

New pneumatically actuated PDMS system for liquid handling in SPR devices

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering
Contributors: Hemmilä, S., Kreutzer, J., Kallio, P.
Publication date: 2010

Host publication information
Title of host publication: Proceedings of the 2nd European Conference on Microfluidics - Microfluidics 2010, Toulouse, December 8-10, 2010
ISBN (Print): 978-2-906831-85-8

Perfusion characterization using flow simulations and μPIV measurements

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering, Department of Energy and Process Engineering
Contributors: Kreutzer, J., Honkanen, M., Laaksonen, J., Kallio, P.
Number of pages: 9
Pages: 1-9
Publication date: 2010

Host publication information
Title of host publication: Proceedings of the 2nd European Conference on Microfluidics - Microfluidics 2010, Toulouse, December 8-10, 2010
Sample volume metering in a disposable microfluidic cartridge

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering
Contributors: Vanhanen, S., Järvelä, P., Kallio, P.
Pages: 1796-1798
Publication date: 2010

Host publication information
Title of host publication: Proceedings of the 14th International Conference on Miniaturized Systems for Chemistry and Life Sciences µTAS2010, Groeningen, the Netherlands, October 2010
Editor: Verpoorte, S.
ISBN (Print): 978-0-9798064-3-8

Bibliographical note
Contribution: organisation=ase aci,FACT1=1
Source: researchoutputwizard
Source ID: 9515
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Solubility of dried nanoparticles and their nonspecific binding in microfluidic polystyrene channels

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering
Contributors: Mäntymaa, A., Välimaa, L., Kallio, P.
Number of pages: 12
Pages: 1-12
Publication date: 2010

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Bibliographical note
Poistettu tupla r=3078<br/>Contribution: organisation=ase aci,FACT1=1
Source: researchoutputwizard
Source ID: 8745
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Tekesin rahoituksella kehitetään analytiikkaa myrkyllisten sinilevien tunnistamiseen

General information
Publication status: Published
MoE publication type: D1 Article in a trade journal
Organisations: Department of Automation Science and Engineering
Pages: 72-74
Publication date: 2010
Peer-reviewed: Unknown

Publication information
The effects of laser welding on the heterogeneous immunoassay performance in a microfluidic cartridge

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering, Department of Production Engineering
Contributors: Mäntymaa, A., Halme, J., Välimaa, L., Kallio, P.
Number of pages: 7
Pages: 1-7
Publication date: 2010

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Bibliographical note
Contribution: organisation=ase aci,FACT1=1
Source: researchoutputwizard
Source ID: 8779
Research output: Contribution to journal › Article › Professional

Volume estimation of a liquid plug in a microchannel using a machine vision system

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Automation Science and Engineering
Contributors: Heiskanen, V., Vanhanen, S., Kallio, P.
Number of pages: 10
Pages: 1-10
Publication date: 2010

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Bibliographical note
Contribution: organisation=ase aci,FACT1=0.75<br/>Contribution: organisation=tte,FACT2=0.25
Source: researchoutputwizard
Source ID: 8744
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Microrobotics platform for characterization and treatment of single paper fibres

General information
Publication status: Published
MoE publication type: B3 Non-refereed article in conference proceedings
Organisations: Department of Automation Science and Engineering
Contributors: Saketi, P., Kallio, P.
Pages: 41-52
Development of a Parallel Composite-Joint Piezohydraulic Micromanipulator

This thesis discusses the development of a novel parallel composite-joint piezohydraulic micromanipulator. The micromanipulator is composed of three prismatic actuators connected in parallel. The actuators are new piezohydraulic actuators, where the deformation of a piezoelectric disk is transformed into a linear displacement using hydraulic oil and a bellows. Three bellows, which are able to elongate along their longitudinal axis and bend about the other two axes, form the kinematic chains of the micromanipulator. Since the bellows is a monolithic element and possesses both translational and rotational degrees of freedom, that micromanipulator is composed of composite joints. The constructed piezohydraulic micromanipulator is the first parallel structure which is composed of composite joints and thus, does not need separate revolute, universal, spherical or prismatic joints. This is a beneficial feature in the fabrication and assembly of miniaturised micromanipulators. The micromanipulation system consists of five subsystems: the micromanipulator, a control system, a vision system, a signal processing system and accessories. The emphasis of this thesis is on the structure and experimental evaluation of the micromanipulator and the piezohydraulic actuator and on the development of position feedforward and position feedback control schemes. The position feedforward control is based on the inverse position kinematic equations. The thesis presents two inverse position kinematic models: a first generation model and a second generation model, the latter providing slightly better results in the feedforward control scheme. Two inverse Jacobian matrices are derived from the inverse position kinematic models. The second generation model is used in a vision-based control scheme and the first generation model in a Hall-sensor-based control scheme. Both control schemes are decentralised task space control schemes, which are composed of the position measurement system, independent single-input / single-output controllers for each joint and a static nonlinear decoupling element the inverse Jacobian. The micromanipulator controlled using the vision-based position feedback control scheme possesses the following performance: steady-state accuracy of ± 1 pixel in the xy plane. With the 100x magnification: 1,7 micrometres and 3,3 micrometres along the x and y axis, respectively; repeatability of 1 and 2,5 micrometres along the x and y axis, respectively with the 100x magnification; resolution of nanometres; an ellipsoid workspace, the length of the semi-axes of which are 250 µm x 250 µm x 100 µm; sampling frequency of 18 Hz. The Hall-sensor-based control scheme provides the same resolution and workspace. It possesses a limited accuracy of 20 micrometres but it can be employed at significantly higher speeds than the vision system. Therefore, the future implementation can be a system, where the Hall sensor measurement is used for high-speed course positioning and the vision system for precise positioning to move the end-effector close to the target.