POCDx 2022 – Posters

Titles

Abstracts

Poster 1: Direct, Label-free, and Multiplexed Biosensing by Scalable and Lithography-Free Metaplasmonic Surfaces for the Point-of-Care

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Plasmonic metasurfaces have been widely widespread in the last years, motivated by the recent advances in the nanofabrication field and the increasing demand for high throughput biosensing platforms at the Point-of-Care. The recent advances in electronics, microfluidics, and signal processing have enabled the complete development of highly integrated prototypes for Point-of-Care applications. However, the progress observed from a fabrication point of view has been remarkable, led by the potential benefits metamaterials can offer in plasmonic sensing: sensor miniaturization, multiplexing opportunities, and extreme sensitivity biodetection. Although conventional top-down approaches, i.e., electron-beam lithography, have been extensively employed to develop plasmonic metasurfaces for biosensing, lithography-free bottom-up nanofabrication strategies based on nanopatterned thin-films by Glancing Angle Deposition (GLAD) and Thermal Dewetting (TDW) are candidates to surpass the limitations of top-down lithographic techniques with large-scale and high-throughput fabrication processes for 2D and 3D plasmonic metasurfaces over a broad material set. We focus on the challenges and opportunities to achieve lithography-free plasmonic metasurfaces by combining GLAD and TDW in single fabrication processes to conduct scalable and high-throughput plasmonic metamaterials for direct, sensitive, and multiplexed metaplasmonic biosensors for Point-of-Care applications.

Poster 2: Implementation of rotational thromboelastometry in patients undergoing cardiac surgery

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Background: Perioperative coagulopathy and postoperative bleeding are the most common complications in patients undergoing cardiac surgery, especially when the cardiovascular surgery is associated with cardiopulmonary bypass (CPB). In this context, some studies suggest that implementation of viscoelastic point-of-care tests (POCT), such as rotational thromboelastometry (ROTEM , in conjunction with a specific algorithm for coagulation management, allow for better control of hemostatic pathology.

Methods: Retrospective cohort study including 675 patients who underwent cardiac surgery with cardiopulmonary bypass. The incidence of clinical postoperative complications were analyzed before and after ROTEM® implementation.

Results: Following viscoelastic testing and the implementation of a specific algorithm for coagulation management, the incidence of any allogeneic blood transfusion decreased (41.4% vs 31.9%, p=0.026) during the perioperative and postoperative period (26.5% vs 19.2%, p=0.061). In addition, significant reductions were detected in the incidence of heart disease (57.7% vs 55.8%, p=0.275; statistically significant reductions were detected in the incidenceof postoperative pericarditis (3.6% vs 1.2%, p=0.043), postoperative renal failure (1.6% vs 3.2%, p=0.435), postoperative sepsis (1.2% vs 0.9%), p=0.337) and postoperative hematologic complications (postoperative bleeding (9.5% vs 5.3%, p=0.037), surgical reexploration (6.0% vs 2.9%, p=0.035).and length of Intensive Care Unit (ICU) stay (6.0 days vs 5.3 days, p=0.026). Finally, we observed a statistically significant decrease in the lengths of Intensive Care Unit (ICU) stay (6.0 days vs 5.1 days, p=0.026), after implementation of the POCT system and the specific algorithm for coagulation management. There were no statistically significant group differences with respect to total hospital stay (16.7 days vs 13.5 days, p=0.076). In-hospital mortality associated with cardiac surgery also did not change (4.5% vs 2.4%, p=0.132).

Conclusion: The monitoring of hemostasis by ROTEM® in cardiac surgery, was associated with decreased incidence of allogeneic blood transfusion, clinical postoperative complications and lengths of hospital and ICU stay.

Poster 3: Measuring adalimumab and infliximab trough levels from finger prick blood with a rapid point-of-care assay

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Patients suffering from inflammatory bowel disease (IBD) can be treated with the biologics adalimumab (ADL) or infliximab (IFX). Previous studies demonstrated the usefulness of therapeutic drug monitoring (TDM) to adjust individually the patient's biologic concentration. A hindrance for TDM are long time to result and limited access to professional laboratory equipment near the patient. Patients and clinicians would benefit from a rapid point-of-care (POC) and easy to use assay, independent of laboratory equipment. ADL and IFX lateral flow serum kits (BÜHLMANN Laboratories AG) were extended in such way that capillary blood and (EDTA) whole blood can be used as analyte matrix. Disposable capillaries are used for blood collection from finger prick and for its transfer into dropper bottles that are prefilled with chase buffer. To measure ADL or IFX levels with a BÜHLMANN Quantum Blue® Reader the mixture is then applied on a Quantum Blue® Infliximab/Adalimumab lateral flow test cassette. In a matrix agreement study spiked EDTA whole blood, whole blood without anticoagulant and capillary blood samples showed good comparability to spiked serum samples used as reference. Both POC assays revealed a bias of less than 15% at the clinical decision points for ADL (5 – 12 µg/mL) and IFX (3 – 7 µg/mL). Linearity is given over a measuring range of 1.3 – 35 µg/mL and 0.4 – 20 µg/mL, respectively. Two POC assays for the determination of ADL or IFX in capillary or whole blood samples were successfully developed which can be used by non-laboratory professionals with time to result of only 15 minutes and without the need for additional laboratory equipment. The excellent agreement to serum levels shows that the BÜHLMANN Quantum Blue® Infliximab/Adalimumab Capillary Blood assays are ideal for IFX and ADL TDM analysis in a clinician's office or an infusion site

Poster 4: In vitro TBI: Release of brain injury biomarkers in a neurosphere model system

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Traumatic brain injury (TBI) is one of the most frequent neurological disorders. Among all the TBIs, mild traumatic brain injuries (mTBIs), also known as "concussions", constitute 70-90% of head injuries. [1] Since symptoms of mTBIs are often absent or not very specific, mTBIs are not always spotted with currently used diagnostic tools (CT scan or MRI). [2] As head injury might induce cellular damage in the brain leading to the release of TBI-related biomarkers in the bloodstream [2], biomarker quantification is a promising method for the detection of mTBI. To support the development of the next generation of mTBI tests, an in vitro platform was designed, to mimic and track brain injuries over time. This model is based on 3D brain cell culture derived from human induced pluripotent stem cells (iPSC), e.g. neurospheres [3], and a mechanical device allowing ejection of medium onto the neuronal tissue. Reproducing the trauma (pressure and velocity of ejection) is controlled by a microvalve. Electrochemiluminescence-based immunoassays were developed for four mTBI biomarkers to investigate the biomarker release kinetics. The assays were robust and sensitive enough, allowing the observation of significant biomarker increases 2 hours post-neurosphere injury. The analytical approach supports further studies into the exact injury kinetics and dynamics of brain cells having experienced a trauma. Ultimately, a better understanding of temporal biomarker injury profiles could enable the development of an integrated POC diagnostic device designed to detect a more comprehensive panel of mTBI biomarkers translating to a more sophisticated next generation TBI diagnosis.

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Poster 5: Drug Quantification in Whole Blood using a Paper-Analytical Device for Point-Of-Care Therapeutic Drug Monitoring

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Therapeutic Drug Monitoring (TDM) allows for personalized dosage during therapeutic treatments and is often mandatory for modern potent drugs against cancer, infections or in organ transplantation cases [1]. A prototypical example is the antibiotic tobramycin, which is often prescribed to neonates in case of bacterial infection and requires TDM to ensure efficacy while avoiding oto- and nephrotoxicity. Currently, the process of TDM is demanding for the patient as several milliliters of blood are required, is slow and costly due to the transfer of sample to a central laboratory, and suffers of limited efficacy owing to the difficulty to interpret the results for a non-specialist. To circumvent these problems, we aimed at developing a point-of-care device enabling the quantification of therapeutic drugs in blood [2]. Our strategy is based on the use of fluorescence-polarization immunoassay (FPIA), a simple and rapid assay that may however suffer from interferences caused by the micro-environment. Here, we show that FPIA can be downsized with reduced requirements in blood amounts (1 µL) and number of steps, without compromising reliability, and can be integrated within paper-like microstructures. For Tobramycin, the integrated assay enabled quantification in serum with satisfactory performance in terms of precision and recoveries. Furthermore, whole-blood measurements were made possible by using the same paper-like microchamber as a filtering device and a measurement chamber. The final TDM point-of-care test requires minute amounts of blood and minimal handling steps.

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[2] Fluorescence-polarization immunoassays within glass fiber micro-chambers enable tobramycin quantification in whole blood for therapeutic drug monitoring at the point of care, E.-D. Bojescu, D. Prim, M. E. Pfeifer, J.-M. Segura, Analytica Chimica Acta 1225 (2022) 340240

Poster 6: Innovative point-of-care platform applied to rapid and syndromic screening of human immunodeficiency virus and hepatitis B and C viruses

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So far, nearly 1.8 million people die every year from human immunodeficiency virus (HIV) and Viral Hepatitis B and C (HBV, HCV). To contain the growing epidemics, testing is crucial to improve the linkage to care. As those diseases have the same infection pathways (blood exposure, sexual and perinatal transmissions), these 3 diseases are recommended to be tested at the same time. It is recommended to systematically test pregnant women, blood donors and high-risk populations. While blood donors and pregnant women are well screened through conventional healthcare laboratories, high risk populations testing need to be further enhanced through outreach campaigns and multiplexed Point of care testing.
We present a technology that exploits magnetic nanoparticles (MNP), micro-magnets and fluorescence to provide rapid immunoassays at the point of care. Downscaling the size of magnetic particles is particularly interesting as it enables fast diffusion-based reactions. Besides, micro-magnets generate high local gradients required to capture MNP coated with antigens (Ag) or antibodies (Ab). After 10 minutes incubation with a fluorescent Ab, magnetic immunocomplexes are locally captured on micro-magnets. A differential measurement of the fluorescence localized on and besides micro-magnets allows specific detection of a molecule without any washing step. Based on this technology, we developed a portable and autonomous analyzer with a multiplexed cartridge dedicated to the simultaneous detection of anti-HIV, anti-HCV and hepatitis B surface Ag (HBsAg).
102 human plasmas were analyzed diluted 10 times. This first batch of sample shows promising performances: the correlation with the reference method (Abbott CE marked chemiluminescent immunoassays) is excellent with respectively 99%; 97% and 100% for HBsAg, anti-HCV and anti-HIV detection.
The next steps will be to validate the platform with capillary blood in medical environment.
These results pave the way to a new point of care platform to screen infectious disease with a syndromic approach.

Poster 7: Enhancing the sensitivity in the C-reactive pro

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In the Nano-Argovia project Printed Electrochemical Protein Sensor (PEPS), we are developing an electrochemical sensor for the analysis of protein biomarkers at the point-of-care (POC). Such a digital device could increase the convenience and effectiveness of the monitoring and diagnosis of various diseases on par with today's monitoring of diabetes with glucose meters. However, the industrialization of such sensors is hampered by problems related to unspecific surface fouling, low POC compatibility of the device, and expensive sensor fabrication. To address these limitations, we developed a laser-perforated sensor functionalized by a polymer with strong antifouling properties, that can be prepared using cost-effective and highly scalable printing processes. A hybrid vertical flow system has been designed for a user-friendly evaluation of the assay procedure. We present our progress regarding the sensor performances, including the results on the C-reactive protein (CRP) detection in buffer, obtained by coupling the sensor with a vertical flow platform. tein electrochemical detection as model system.

Poster 8: Point-of-Care Tests for Preeclampsia

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Preeclampsia is a syndrome which affects 2-8 % of all pregnancies worldwide and is a leading cause of maternal death. Fast and accurate detection is crucial to identifying women at risk and adjusting their care swiftly. Close monitoring of preeclamptic pregnancies allows doctors to optimize the methods and timing of interventions.
MOMM Diagnostics and its research partners the FHNW and CSEM are developing a fast and precise point-of-care test for the diagnosis and monitoring of preeclampsia. Our test will assist doctors on-site to save the lives of mothers and babies.
Our novel rapid diagnostic test technology allows the simultaneous quantification of two low-abundant biomarkers from a single drop of the mother's blood. It is based on enzyme-linked lateral flow immunoassays (ELLFIA) for signal amplification, in combination with a quantitative electrochemical readout, by integration of low-cost ion-sensitive electrodes in single-use test cartridges. This approach enables rapid biomarker quantification down to sub-picomolar concentrations and opens up previously laboratory-based diagnostic tests to point-of-need and self-testing.

Poster 9: Hybrid paper-PDMS analytical microfluidic device for blood processing

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Preface: In order to check infection levels, physicians want to know the white blood cell (WBC) count as well as the concentration of h-CRP protein (human C-reactive protein) in the blood. These parameters vary with type of infection and incubation times. A capillary microfluidic device with consists of a PDMS chip component and a lateral flow paper component, that can give both parameters has been developed.
Methodology: A commercially available CRP LFA strip was used to develop this biosensor. The concentration of CRP protein in a sample is correlated to the colour intensity of the test line. The anatomy of the chip is as follows – 1. PDMS part – as blood is flowing through the microchannel, WBCs are imaged under microscope and count is extracted; 2. Axisymmetric blood plasma separation membrane, that separates plasma from whole/diluted blood; 3. Lateral flow assay strip, in which the test line is imaged under the microscope. With 3 uL of blood dropped on the chip, both parameters can be known.
Results: A double layer PDMS microfluidic chip was developed to account for the insertion of 370 µm thick blood separation membrane. The rest of the microfluidic channel thickness is 28 µm, inside which blood flows, while stained WBCs are imaged under a microscope. The blood drains into the blood separation membrane, plasma is separated, and with some buffer, the Lateral flow assay runs. The test lines were imaged under the microscope. Test line intensities were obtained for concentrations between 11ug/ml and 31 ug/ml of CRP. At low levels of concentration (1-5 µg/ml), cardiovascular risk can be assessed, and at greater levels of concentration (>10µg/ml), quick point-of-care information about infection and type of infection (usually bacterial >20 µg/ml or viral <20 µg/ml) can be assessed.

Poster 10: An AI-enabled diagnostic system for early thrombosis risk diagnosis and anti-thrombosis management

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About one out of three deaths are related to thrombosis, such as heart attacks and strokes, and this is a huge healthcare and social issues, exacerbated by the lack of a diagnostic tool to assess and predict the risk of thrombosis individually. Majority of these deaths and debilitation are preventable. Additionally, a diagnostic tool that enables the monitoring of the anti-thrombosis treatment in order to prevent drug adverse effects is lacking. Our mission is to close this gap of the urgent need for early diagnosis so that preventative measures can be initiated much earlier. Moreover, our solution will fill the urgent need of safe and effective drug treatment for patients taking antithrombotics.
Our solution is a point-of-care diagnostic device measuring a set of unique biomarkers and deriving diagnostic algorithm which reveal the activity of coagulation system, and using an IT-enabling system which connect the cloud solution to AI-enabled analytics so that effective antithrombosis program can be executed. The result will be a significant reduction in premature deaths and organ damage caused by thrombosis, and reduction in economical and social burdens. Additionally, value-based healthcare in the form of digital health and remote healthcare will become reality.
Significant feasibility and evidential data has been collected via oversized prototypes, the miniaturization of the device is not without risk. Due to the novelty of science, the adoption of such tool in antithrombosis management will be slow, initially. The regulatory path may be an unconventional one, as the product is novel, and has different elements, e.g. soft- and hard-ware, that are regulated separately by different rules. In order to be able to make early introduction of such solution to patients, the process of market approval and acceptance should be optimized through collaborative efforts from many stakeholders such as regulatory approval bodies and KOLs.

Poster 11: A new robust biosensor – focal Molography – and its applications in diagnostics, bioprocessing and drug discovery

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Focal molography is a new label-free detection method, which allows the real-time investigation of complex molecular interactions in the presence of a complex biological environment without any stabilization or equilibration. Thereby, opening up new perspectives and possibilities in drug discovery, bioprocessing or diagnostics and related disciplines. In particular, we have shown an interesting approach to diagnostics based on real-time immunosignaturing. This approach utilizes an array of molographic sensors to discriminate between different health conditions in a real-time direct binding assay format. We demonstrated the proof of principle with plasma profiling of different hemagglutinin-like peptides to discriminate different blood donors. In addition, we demonstrate other non-diagnostic applications of focal molography including the determination of binding parameters in complex samples, the characterization of membrane proteins in living cells5 as well as the real-time observation of cytosolic proteins in living cells.

Poster 12: Matlab GUI enabling EEG signal processing in real-time and offline

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In human anaesthesia, several target-controlled infusion (TCI) pumps have been created to personalize intravenous injection of propofol based on pharmacokinetic (PK) models. Besides PK models, anaesthesia individualization can be performed based on objective measures of Depth of Anaesthesia (DoA) like electroencephalogram (EEG)-based bispectral index (BIS) and Patient State Index (PSI), which can then be used as automatic indicator of DoA or even serve as a feedback parameter for closed-loop technology. However, the algorithms computing these DoA indices are proprietary and developed for humans, and thus, cannot be applied or adapted to veterinary practice. Therefore, one must start from scratch and develop his/her own signal processing code for EEG analysis, which takes time. Moreover, often, signal processing algorithms are well known only to engineers, and are hard to be understood by medical or veterinary staff, who must be the main people to define “signature of DoA” – signal features the most relevant to DoA.
To simplify interdisciplinary communication, we have developed a Matlab based Graphical User Interface (GUI) that allow to analyse any EEG signal using classical signal processing algorithms, e.g., spectrogram, burst-suppression ratio’s (BSR), spectral edge (or median) frequency (SEF or SMF), spectral power ratio (SPR) by simply loading a file from an EEG device and then just pressing buttons to visualise the chosen EEG features. Recently, a real-time interface has been added to the GUI, thus allowing researched to capture signal and visualise it’s features within the experiment.

Poster 13: Miniaturized Fluorescence Biosensing Technology for Multiplexed Allergy Screening

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The incidence of immune-mediated diseases such as asthma and allergies is steadily increasing.[1] However, little is known yet about how genetics, environmental factors, and epigenetics can influence the onset and progression of these diseases.
Within the Human Exposomic Determinants of Immune-Mediated Diseases (HEDIMED) project, we are developing a portable multi-array system for immune-signature testing. Such a platform could help to quickly screen various biomarkers, such as antibodies, related to immune-mediated diseases.[2] In the present project, a multiarray for antibody detection has been developed for allergy profiling. Based on microfluidic chips of the size of a standardized microscopy slide, the multiarray is embedded in a microfluidic channel with microstructures functionalized with allergen extract or recombinant proteins. The use of a microfluidic chip enables the multiplexed screening of up to 88 different allergens from the patient (blood serum) with low sample volumes (80-150 uL). An automated sample-on-chip processing system has been developed to ensure the reproducible detection of allergy-specific IgEs using fluorescence-labelled antibodies. In addition, a compact, low-cost, and fast fluorescence reader has also been developed for simple measurements of the fluorescence signals and automated quantification of the allergic response.
We present our progress regarding the multiarray assay, the optical reader, and preliminary results on fluorescence signal detection in human serum. By testing the microfluidic system with a focus on pregnant women and newborn samples, this technology could help to find new correlations between multiple environmental factors and the onset and progress of immuno-mediated diseases at early ages, improving the prevention of such diseases in the future.
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Poster 14: Towards point of care DNA sequencing

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DNA sequencing is quickly becoming portable, holding great promises for point of care molecular diagnostics. Oxford nanopore technologies has developed nanopore sequencing, a technology that allows for real time and cheap DNA sequencing. Together with related developments in automated DNA preparation and bioinformatics, sequencing is becoming accessible to non-specialists outside of the laboratory. Here, we review the current state-of-the art in nanopore sequencing, specifically with regards to point of care diagnostics. Among other examples, nanopore sequencing allows for rapid identification of pathogens and characterization of antimicrobial resistance genes, which has the potential to bring significant improvements in clinical care. Finally, we review our own work with nanopore sequencing. In particular, we developed a diagnostic test to simultaneously identify specific pathogens at sub-species resolution and establish full bacterial profile in veterinary samples.