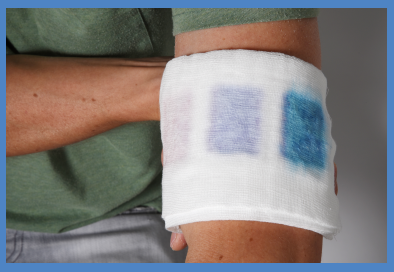
Prof. Bradley Nelson, ETHZ

FlusiTex

FABRICATION OF FLUORESCENCE SENSORS INTEGRATED INTO A TEXTILE DRESSING FOR NON-INVASIVE LIFETIME BASED WOUND MONITORING



Dr. Luciano Boesel, EMPA

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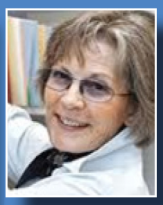

Prof. Brigitte von Rechenberg, UZH

What it's about…

Fabricating a sensing wound pad that can be used for non-invasive monitoring of the healing of chronic wounds, based on integrated fluorescence coupled (bio)sensors and fluorescence lifetime imaging using a TOF camera.

Context and project goals

FlusiTex will develop a wound dressing with an integrated sensing layer for non-invasive wound monitoring using fluorescence lifetime detection. The sensing strategy relies on a functionalized coating integrated onto commercially available wound dressings. Functionalization comprises fluorescence modified polymer hydrogels, enzymes embedded in fluorescence labeled polymer coatings, and functionalized nanoparticles that also serve as a component of the coating layer.

These sensing layers provide information on biochemically and physically relevant wound characteristics. A dedicated camera using a CMOS lock-in imager with fluorescence lifetime capability will be developed for periodically monitoring the response of the layers noninvasively, thus providing immediate feedback on the progression of wound healing at various points in time. Since the wound healing process is not yet fully understood, studies on factors relevant for the process will be conducted by a medical team in parallel with the development of the sensor-pad. The sensing elements will be integrated with a commercially available wound pad, and fabrication techniques will be developed to enable reliable large-scale production. The data from the embedded sensing elements will be collected by a specially developed fluorescence lifetime imager based on lock-in pixel technology and optimized to match the sensing needs, thus eliminating the for integrating expensive electronics with the wound pad. At the end of the project, a prototype of the system will be tested in vivo. A variety of companies have indicated strong interest in this project and will provide industrial expertise with the goal of joining the project at a later stage when technology transfer will follow, e.g. in the form of CTI projects.

The goal of the project is a (bio)sensing wound dressing suitable for read out using a fluorescence lifetime imager. While the wound pad to be developed is for use as a wearable wound-monitoring system, it can also be further extended to enable development of textile based environmental or food monitoring systems (a second application in the NanoTera research space). The technologies required to develop such a system are also congruent with the technology focus of Nano Tera projects; biotechnology, nanofabrication, biosensors and optical systems will be our main technology tools. The textile industry in Switzerland has suffered a dramatic decline in recent years due to the growing low-cost textile industry in Asia. This downturn can only be stopped and reversed by diversifying into high technology segments such as medical textiles, which have much higher margins than the conventional clothing segment. FlusiTex will enable the Swiss textile industry to enter untapped market segments by providing a state-of-the-art textile-based monitoring system.

How it differentiates from similar projects in the field

The approach to use multi-optical fiber sensing integrated into a wound pad for simultaneous monitoring of different parameters is novel. The data from the embedded sensing elements will be collected by a specially developed fluorescence lifetime imager based on lock-in pixel technology and optimized to match the sensing needs, thus eliminating the need for integrating expensive electronics with the wound pad.

For the first time, the response of the layers will be periodically monitored noninvasively and immediate feedback will be collected on the progression of wound healing at various points in time.

Quick summary of the project status

Hospital visits have been arranged to quantitatively study acute wounds on site. The metabolites playing a key role in wound healing have been identified. As the presence of proteases is crucial in wound healing, a fluorescent FRET-based biosensor specific for the serine-protease neutrophil elastase was engineered, produced, and immobilized. The team designed a strategy to integrate those markers into commercially available wound pads.

A compact optical setup for real-time wide-field fluorescence lifetime imaging (FLIM) in the nano- to microsecond range was developed. The setup was tested with rhodamine/dichlorofluorescein mixtures in solution, as well as in thin films. The system was also tested with Ruthenium-doped thin films used for oxygen sensing, yielding a lifetime of approximately 2 microseconds.

A standardized deep wound model in sheep is designed to reduce wound bed variability so that wound parameters are reliably and reproducibly recorded until closure (Oxygen, pH, metabolites).

Success stories

The meetings between UZH, ETHZ and EMPA led to the selection of key markers for detecting chronic wounds. To provide appropriate substrates with ideal optical and mechanical properties, several matrices have successfully been developed ranging from silicate over polymer nanoparticles to polymeric gels. Indicator dyes/chemical sensors could be coupled to these matrices. The first successful trials of lifetime measurements with these sensors have been conducted by CSEM.

The FLIM camera has been redesigned to optimize the sensitivity and accuracy of the measurements.

Main publications

Marín-Suárez M., Medina-Rodríguez S., Ergeneman O., Pané S., Fernández-Sánchez J., Nelson B.J., Fernández-Gutiérrez A., Electrophoretic deposition as a new approach to produce optical sensing films adaptable to microdevices, Nanoscale, 6:263-271 (2014).

Lindo A,, Pellicer E., Zeeshan M.A., Grisch R., Qiu F., Sort J., Sakar M.S., Nelson B.J., Pané S., The biocompatibility and anti-biofouling properties of magnetic core-multishell Fe@ C NWs/AAO nanocomposites, Physical Chemistry Chemical Physics 17:13274 (2015).

B. Özkale, N. Shamsudhin, G. Chatzipirpiridis, M. Hoop, F. Gramm, X. Chen, X. Marti, J. Sort, E. Pellicer, S. Pané, Multisegmented FeCo/Cu Nanowires: Electrosynthesis, Characterization, and Magnetic Control of Biomolecule Desorption, ACS Applied Materials and Interfaces, 7:7389 (2015).

"Fluorescence based wound monitoring pads with integrated biosensors may find broad application in strongly growing fields such as health care & medtech"