Optical Fibre Functionalization for Measurement of pH and Matrix Metalloproteinases (MMPs) in Wound Dressing

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Plastic optical fibres were functionalized to be sensitive to biomarkers of the wound healing process. In vitro measurement of pH and protease activity was demonstrated in model wound exudate. Integration of plastic optical fibres in wound dressing with a wearable electronics will be the basis of a smart wound care management system.

In order to reduce health cost, the trend is to have more and more ambulatory patients, therefore remote monitoring system become essential. Following this trend, monitoring wound healing at home with a wound dressing integrating sensors was developed. Wound carers are interested in monitoring biological parameters in the wound to reduce their interventions leading to faster wound healing and patient comfort. The system consists of special optical fibres in contact with the wound exudate and connected to electronics that performs signal processing, data logging and communication [1]. The plastic optical fibres are particularly interesting for their flexibility that facilitates their integration in wound dressing and adaptation to the shape of the body. In the frame of the Nano-Tera project TecInTex [2], a system for monitoring several biomarkers in wounds was developed. The goal of the project was to develop smart textiles. New sensitized and functional fibers, which will allow in situ measurements of body functions and biological species in body proximity for application in healthcare, were one of the major demonstrators.

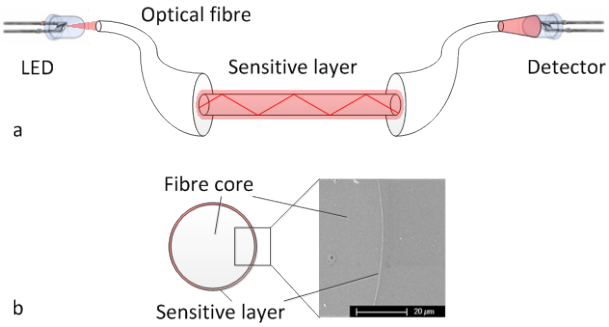

Figure 1: a) Optical fiber sensing principle, and b) scanning electron micrograph of a modified fiber cross-section with a pH sensing layer

Chronic wounds take several weeks even months to heal. The wound healing process follows successive main phases: inflammation, proliferation and remodeling. During these different phases, different biological processes occur and can be monitored by measuring the concentration of relevant biomarkers. Among these biomarkers, CSEM have focused on pH for inflammation status and Matrix metalloproteinase (MMP) for the proliferation status. The principle of the plastic optical fibre sensor is to replace the optical cladding of the fibre with a layer that is affected either by pH or by MMPs. The pH level will modify the absorption spectrum of the layer: the absorbance measurement of the light that is transmitted through the fibre at different wavelengths enables the accurate determination of the pH (Figure 1a). Similarly, the MMPs activity modifies the absorbance of the transmitted light at a layer specific wavelength: kinetics of the absorbance decrease informs on the MMPs activity. A light source and light detector placed at both fibre extremities enable the monitoring of the optical changes in a sensing layer previously deposited around the fibre core.

The pH sensing layer relies on the encapsulation of pH dyes into a sol-gel matrix. A mixture of different pH indicators was used to extend the pH detection range. pH variation results in color changes of the pH sensing layer, which will be measured by optical absorbance at 590 nm, corresponding to the wavelength of maximum absorbance variation for the dye mixture. The sensing layers were prepared by first mixing dyes with sol-gel precursors (tetraethyl orthosilicate and methyltriethoxysilane). After stirring the solution was deposited onto the core of the optical fiber by dip-coating, which resulted in layer thicknesses of 800 to 900 nm (Figure 1b).

For the monitoring of the protease activity, an innovative method has been developed, based on the degradation of a colored protein layer deposited on an optical fibre. The layer was designed for detecting matrix metalloproteinases 2 and 9, which belong to the gelatinase family. A sensing layer based on gelatin was deposited onto the activated optical fibre core. Optical fibres were dip-coated in 10 wt% cold water fish gelatin in saline buffer. The thickness of the layer can be tuned between 600 to 900 nm. The glutaraldehyde linker was used to ensure thermal and mechanical stability of the layer. Staining of the gelatin layer with a biocompatible chlorophyllin-copper complex enabled visualizing the speed of the layer degradation when in contact with MMPs by measuring the absorbance changes at 630 nm.

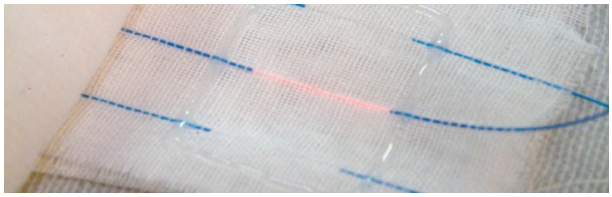

Figure 2: Biosensing optical fibres for smart wound dressing

The integration in an electronic system processes the signals of six different fibres [1], the door is now open to realize smart dressing (Figure 2) able to monitor remotely biological parameters in the wound bed. This will offer physicians a new way to perform wound care management and bring more comfort to the patients.

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[1] G. Voirin, *et al.*, "Wound healing monitoring system integrating plastic optical fibre sensors", CSEM Scientific and Technical Report (2012), page 80

[2] http://www.nano-tera.ch/projects/69.ph