Nanoporous impedimetric fibre sensor for the detection of acute inflammation in wounds

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It is common clinical practice to change wound dressings in a certain time interval of 24 to 48 hours to control possible infections of the wound. This induces stress to the micro environment of the wound. Therefore, effort is made to monitor wound healing by non invasive sensor designs. A multi-parametric sensor integrated in the wound dressing was suggested, that detects an infection and, consequently, avoids stress factors given by frequent and unnecessary changes of bandages [1].

Neutrophils are among the first immune cells to arrive at the site of inflammation and released neutrophil proteases are involved in bacterial killing, tissue degradation and regulation of the inflammatory response [2]. Changes in neutrophil proteases and especially neutrophil elastase activity could be a potent signal for an ongoing wound inflammation in combination with parameters like change of pH value [3], temperature [4] or concentration of reactive oxygen species [5]. The authors have used AC impedance spectroscopy to detect protease activity based on thin film degradation of modified natural enzyme substrates deposited on the surface of interdigitated gold electrodes [6]. These measurements have been used for a redesign to improve the sensor responsivity and selectivity for neutrophil elastase.

A nanoporous fiber sensor was designed that would be integrable in wound dressings by automated stitching or weaving processes (Figure 1). The sensor is build up by thin fibrous electrodes embedded in a surrounding nanoporous membrane that will be constructed by a nanoparticle leaching process [7]. The detection principle is based on the change of ionic conductance through the nanopores after binding of neutrophil elastase to its immobilized inhibitor elafin by the mechanism of “volume exclusion” [8]. In a wound with ongoing inflammation neutrophile granulocytes release high amounts of neutrophil elastase. The present elastase binds to elafin immobilized in the nanopores of the sensor surface thereby blocking the ionic flow of wound exudate to the electrode.

As a proof of concept impedance measurements were performed with elafin immobilized in aluminum oxide nanomembranes. Gold was directly deposited on commercial anodized aluminum oxide (AAO) filter membranes and placed on a bare gold electrode to function as working electrode. The membrane was placed into the spectrometer flow chamber (Inphaze Impedance Spectrometer, Australia) and the gold wire counter electrode of the flow cell was used for a two electrode system.
The AAO membrane has two different pore diameters 20 nm diameter on the top side (1 µm thickness) and 200 nm on the bottom side (60 µm thickness) therefore the orientation of the membrane is of great relevance to the expected blocking of ionic flow to the electrode [9]. Measurements were performed with the 20 nm side of the membrane in close contact to the working electrode to ensure that the exclusion of ions by elastase will be measured. Figure 2 shows the effect of all performed modification steps on the AAO membrane.

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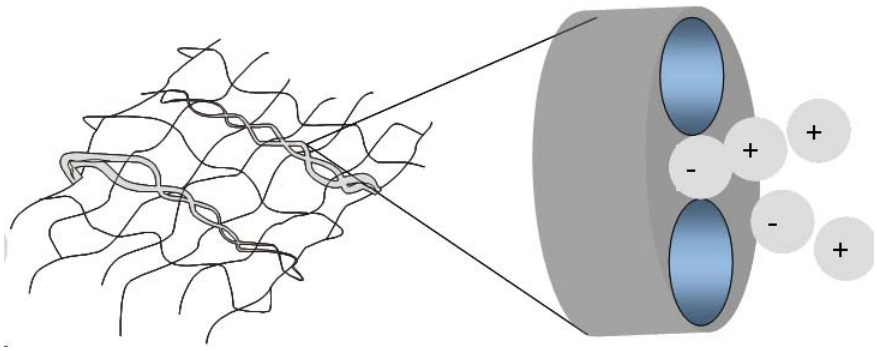

Figure1. Schematic illustration of the fibrous inflammation sensor. (a) Fiber electrodes integrated in a wound dressing. (b) Neutrophile elastase bound to the immobilized inhibitor elafin blocks the ionic flow of the wound exudate.

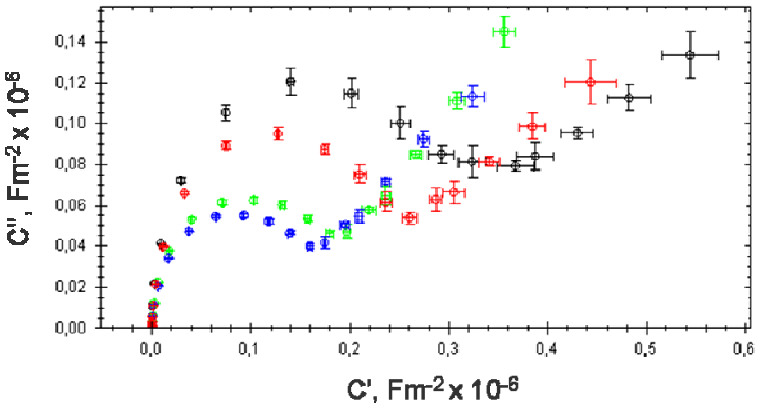

Figure 2. Cole-Cole (or Nyquist) plot of the capacitance per surface area of AAO membrane with Au film deposited on the 20 nm side measured in PBS buffer at 5 mV. Median of three measurement circles. Black measuring points, bare membrane; green dots, carboxysilane modified membrane; blue dots, membrane with immobilized elafin; red dots, elastase treated elafin-membrane.

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