

Anti-biofouling coatings for optical fiber sensors

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ABSTRACT

One of the most serious problems relevant to the use of optical fiber sensors in real-world environments is surface fouling, that is, the cumulative build-up of undesirable material on the working surface of a sensor. This paper presents the results of anti-biofouling tests on coated fiber optic probes for reflectance spectroscopy in blood-simulating 'foul' media, namely Bovine Serum Albumin (BSA) and Fibrinogen. The anti-biofouling coating, a proprietary invention of Biocompatibles Ltd., was a cross-linkable Phosphorylcholine (PC) polymer with Silane functionality, to improve adhesion to silica-containing substrates. All tests in BSA and Fibrinogen showed that PC-1036 coating was efficient in avoiding the build-up of biological material. In fact, optical signal variations of un-coated probes showed fluctuations in the 6-20% range, while coated probes exhibited a nearly-stable optical signal. These results were also confirmed by a microscopic check, which showed adhesions of biological material to un-coated probes.

1. INTRODUCTION

An accurate description of the functions of physiological systems and organs was performed *in vivo* by means of direct observations and measurements of a number of fundamental variables. Hence, this was done because sensors of physiological parameters represent one of the most important aspects of biomedical instruments, and their use can result in better diagnoses and a better quality of health care ^[1].

A major cause of loss or failure in sensor performance in medical applications is the growth of biological material which comes to live in contact with a wide variety of surface materials. The problem is particularly serious for optical systems designed to sense biological fluids: this is because these are well-suited to support organic growth, but most optical sensors require good and reproducible transmission into and out of the external solution. This means that the use is precluded of many otherwise-excellent sensors, in which fouling can occur.

For medical applications, a distinction must be made between invasive (e. g. in the blood-stream or in tissue) and non invasive (e. g. on the skin) measurements. Clearly, there is a preference for non-invasive measurements with a view to patient safety and comfort. However, the necessity for more accurate and reliable evaluations of the physiological parameters measured may require the use of invasive sensors. Hence, miniaturization is essential for invasive sensors, and the bio-compatibility of the materials is important ^[2]. Mechanisms that can give rise to problems include plaque aggregation and coagulation ^[1,3].

This paper discusses the anti-biofouling capacity of a polymer coating for optical sensors when the latter are exposed to blood-simulating fluids, such as Bovine Serum Albumin (BSA) and Fibrinogen, in a dynamic environment.

Optical tests on coated and un-coated probes performed during long-term exposure, together with comparisons of their results, provide a means not only for understanding the anti-biofouling capacity of polymer coating, but also for evaluating whether the fouling occurs and when it occurs in the case on both coated and un-coated probes.

2. POLYMER COATING

Many materials used in the medical device industry were not originally developed for these applications. In general, such materials elicit adverse biological responses when in contact with body fluids such as blood, and the sequence of events in which blood interacts with an artificial surface is well known. Protein adsorption, platelet adhesion, and activation of the coagulation pathway can subsequently lead to thrombus formation, with grave clinical consequences in the absence of anticoagulants. In recent years, various approaches have been advocated for overcoming these problems by improving the bio-compatibility of the materials. One approach is that of bio-membrane mimicry, whereby the surface of a material is coated with a derivative of Phosphorylcholine (PC). The PC anti-biofouling coating used by probes as presented in this paper is a proprietary invention of Biocompatibles Ltd.

PC is the major lipid head-group component found in the outer surface of biological cell membranes. The application of PC coatings to a range of materials has been studied, and the surfaces using in vitro bio-compatibility tests have been characterised^[4]. Studies of Fibrinogen adsorption, platelet binding, and bacterial adhesion have pointed out significant reductions in the adsorption of these components to various PC-coated materials relative to un-coated controls. Materials tested include PVC, polyethylene, polycarbonate, and nylon, among others.

The stability of PC coatings has been studied by using radio-labelled derivatives. Results of the use of several materials show that physisorbed PC coatings are extremely stable, thus making the coatings suitable for use in a wide variety of medical applications. Extensive biological evaluations to assess the toxicological profile of PC polymers and coated devices have also been carried out. In all tests, the materials have been shown to be non-toxic, thus making them suitable for human use. PC polymers must adhere to specific optical substrates, i.e. glass and silica, and must produce a biocompatible interface. This PC biocompatible interface then has the potential to reduce the amount of biological fouling that can occur on these surfaces. The coating must have sufficient durability to remain on the surface and, for optical sensors, the coating must not interfere with the optical properties of the device.

In particular, among all PC coatings prepared, the best results have been obtained by using the PC-1036 polymer, which is designed with 23%wt PC, a hydrophobic film-forming monomer and a Silane functional cross-linker. Biocompatibility tests of it have shown a 76% reduction in Fibrinogen adsorption, relative to un-coated controls, and an 81% reduction in *E. Coli* adhesion, relative to un-coated controls.

PC-1036 has the added benefit that the Silane functionality has the potential to interact chemically with surface Si-OH groups on glass and silica, thus making possible even greater stability.

The optical properties of polymer are very encouraging. Polymer has very little absorption in the useful part of the UV/VIS spectrum (250nm upwards) and only specific IR absorptions. These IR absorptions occur between 500-4000 cm^{-1} , and are likely to be very similar for all PC polymers as they are mainly due to the residual methacrylate functionality that is common to all the PC polymers produced.

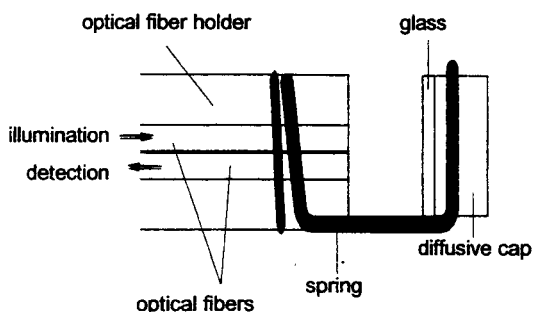


Figure 1. Optical fiber probe: basic design

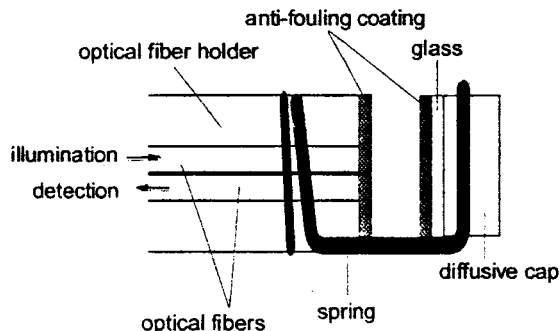


Figure 2. Optical fiber probe coated with anti-fouling PC coatings

Table I. Materials used for implementing the optical fiber probe	
<i>Component</i>	<i>Material</i>
Optical fibers	3M-TECS: FT-200-EMT, core diameter: 200 μm , clad diameter: 230 μm , jacket diameter: 500 μm
Optical fiber holder	Nylon
Cap	Moplen
Glass	Slide for microscopy, Cole-Palmer #E-48500-00
Glue	Norland adhesive #61, UV curing
Spring	Stainless steel

3. FIBER OPTIC PROBES

A special fiber optic probe is considered, which makes possible: a) interaction between optical signal and polymer coating to see any possible surface fouling, b) deposition of the polymer coating and c) contact between the blood-simulating fluids and the fiber optic ends.

The basic optical fiber probe is outlined in Figure 1. A pair of identical optical fibers are inserted and then glued together, inside a plastic holder. A light-diffusing plastic cap containing a glass disk is placed in front of the fiber ends by means of a spring. The optical fiber holder is threaded in order to optimize the cap positioning with respect to the fibers, by simply screwing or unscrewing the spring.

When the probe is immersed in a liquid, the liquid flows between the fiber ends and the glass disk, coming in contact with both of them. Since the two fibers are coupled respectively to a source and to a detector, a transmission measurement is carried out and the signal detected gives an optical measurement of liquid-induced fouling of the fiber ends and the glass. The optical fiber probe treated with anti-fouling coating is similar to the basic one. In fact, as shown in Figure 2, only the fiber ends and the glass disk are treated with the polymer coating.

Table I summarizes the materials used for implementation of the optical fiber probe. The performance of coated and un-coated probes in environmental conditions can be controlled by immersing both probes in the same medium while optically exciting the illumination fibers and continuously detecting the back-transmitted signals. A comparison of the back-transmitted signals indicates the effectiveness of the anti-fouling coating.

4. EXPERIMENTAL SETUP AND RESULTS OF OPTICAL TESTS INVOLVING PC-1036 ANTI-FOULING COATED AND UN-COATED FIBER OPTIC PROBES

An outline of the experimental setup to control the performance of probes exposed to biological fluids is provided in Figure 3. Two identical fiber optic probes for reflectance spectroscopy described in the previous section were considered, one of which was coated with a PC-1036 layer. Coated and un-coated probes were immersed in a by-pass flow cell that was connected in series with both the reservoir containing the liquid being tested and a peristaltic pump. Both probes were optically excited, and the signals were continuously detected while the probes were immersed in the same 'clean' or 'foul' medium, with the by-pass-flow cell as dynamic test environment.

The probes were connected to a PC-interfaced electro-optic unit, which provided illumination, detection and data processing. A large-core optical fiber was connected to a LED and was split by a 1 x 3 coupler into three channels: one optical fiber was connected directly to a photodetector, providing a reference signal, while the other two fibers were connected to the illumination fibers of the probes under test. The detection fibers of the probes were directly connected to the remaining two photodetectors. Signals coming from the probes were referenced to the LED signal, in order to overcome possible LED fluctuations.

The electro-optic unit was driven by a Virtual Instrument for LabVIEW® which provided data logging and display. Optical signal variations in un-coated probes, but a nearly stable optical signal in coated ones, were expected.

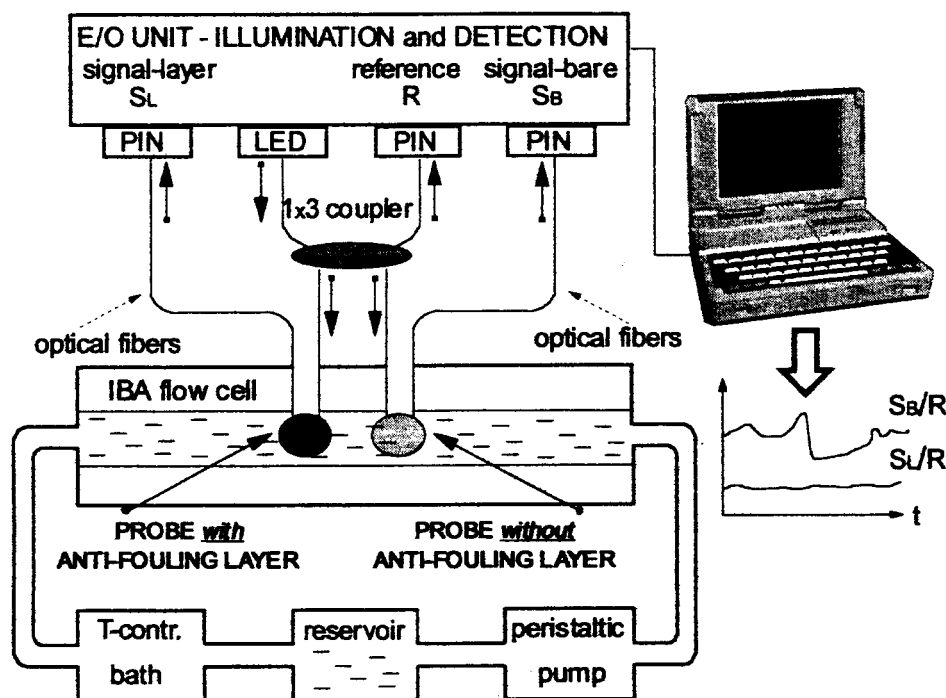


Figure 3. Experimental setup for fiber optic probe testings

Before any measurements were made, a photostability test over 24 hours was carried out in order to check the photostability of the anti-fouling coating. The optical signal variation within $\pm 1\%$, of the same order of electronic noise, was usually measured, and demonstrated excellent photostability of the coatings.

All solutions were sterile, and were handled inside the laminar flow hood so as to guarantee satisfactory sterility. Flow cell, glasses, and flow tubes were sterilized before each test while the fiber optic probes were not sterilized.

After 24-hour testing, a visual check of both probes was carried out by disassembling the probe and by checking the image of the fiber optic pair under the microscope.

Tests in 'clean' media were performed at first, in order to check the photo- and mechanical stability of the coating. The following 'clean media' were considered:

- Normal saline;
- Glucose solution;
- Ringer Acetate;
- Solution of electrolytes and glucose;
- Emulsion of micronized lipids and phospholipids;
- Solution of aminoacids and electrolytes;
- Normal saline and vister-based anticoagulant solution, for verifying the effects of an anticoagulant additive;
- Solution of aminoacids and electrolytes and purified human albumin.

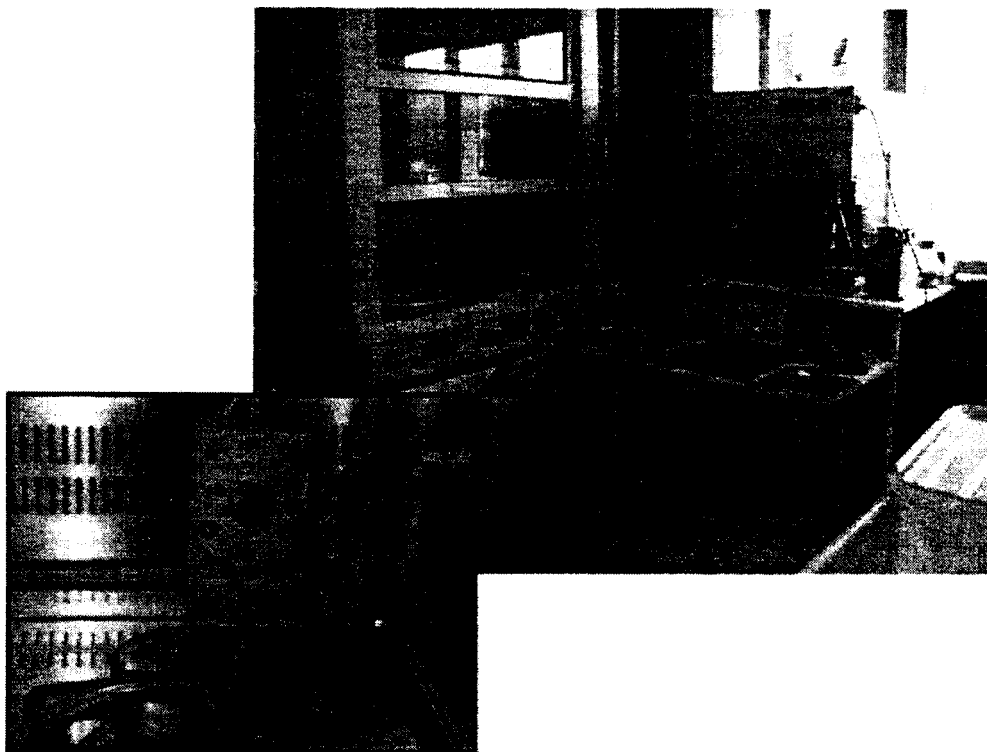


Figure 4. Experimental setup for optical tests of PC1036 anti-fouling coated and un-coated fiber optic probes

These tests showed good mechanical stability for the PC-1036 coating and a negligible fouling. Only, the last test, in which human albumin was added to a 'clean' solution, showed little fouling of the un-coated probe. The fouling was confirmed by means of a microscopic check.

Tests in 'foul' media' were performed by using:

1. BSA: 1 g/l in Normal Saline (0.9% NaCl solution)
2. Fibrinogen: 0.1 g/l in Normal Saline (0.9% NaCl solution).

5. RESULTS OF MEASUREMENTS

Tables II and III show the results of experimental tests, together with the images of the microscopic checks. These results were obtained by means of tests performed over a minimum period of 24 hours.

Tests in BSA showed excellent results as far as both optical signal behaviour and microscopic checks are concerned. The signal variations of un-coated probes were in the ± 10 -30% range, while coated probes exhibited a nearly stable optical signal. This excellent result was confirmed by microscopic checks, in which adhesions to un-coated fibers appeared.

Tests in Fibrinogen were also satisfactory. The signal variations of un-coated probes were in the ± 20 -35% range, while coated probes exhibited a nearly stable optical signal.

Table II: PC-1036 coated and un-coated optical fibers tested in a by-pass flow cell in BSA-Bovine Serum Albumin 1g/l in Normal Saline (0.9% NaCl Solution)

% variation of detected signals from optical fiber probes as a function of time	images of fibers before (§) and after (§§) immersion in BSA	
	coated	un-coated
<p>BOSS-layered (L) and bare (B) fiber optic probes in Bovine Serum Albumin - 0.9% NaCl solution, BSA 1g/l layer batch delivery #003358-PC1036</p> <p>— SL/R — SB/R — Temp</p>		
<p>BOSS-layered (L) and bare (B) fiber optic probes in Bovine Serum Albumin - 0.9% NaCl solution, BSA 1g/l layer batch delivery #003358-PC1036</p> <p>— SL/R — SB/R — Temp</p>		

Table III: PC-1036 coated and un-coated optical fibers tested in a by-pass flow cell in Fibrinogen 0.1g/l in Normal Saline (0.9% NaCl Solution)

% variation of detected signals from optical fiber probes as a function of time	images of fibers before (§) and after (§§) immersion in Fibrinogen	
	coated	un-coated
<p>BOSS-layered (L) and bare (B) fiber optics probes in Fibrinogen - 0.9% NaCl solution, Fibrinogen 0.1 g/l layer batch delivery #003640-PC1036</p> <p>— SLR — SBR Temp</p>	<p>§</p>	<p>§</p>
	<p>§§</p>	<p>§§</p>
<p>BOSS-layered (L) and bare (B) fiber optics probes in Fibrinogen - 0.9% NaCl solution, Fibrinogen 0.1 g/l layer batch delivery #003640-PC1036</p> <p>— SLR — SBR Temp</p>	<p>§</p>	<p>§</p>
	<p>§§</p>	<p>§§</p>

6. CONCLUSIONS

Optical fiber probes for reflectance spectroscopy were tested in blood-simulating media in order to demonstrate the effectiveness of anti-biofouling coatings. Blood is made of plasma plus cellular elements^[5]. Plasma is the liquid part of the blood: it is composed by many proteins, but the most representative ones are Albumin (55-69% min-max value), Globulin (26-50% min-max value) and Fibrinogen. Tests presented in this paper showed that the anti-biofouling coatings limited the build-up of biological material when BSA and Fibrinogen were considered. The results obtained were encouraging, because they were obtained with the most representative blood proteins, i. e. BSA and Fibrinogen.

These probes for reflectance spectroscopy have potentials for medical applications, especially for arterial blood oxygen saturation (SaO_2) continuous monitoring. In fact, SaO_2 is usually measured by multi-wavelength reflectance spectroscopy by means of an optical fiber bundle inserted in a pulmonary- or umbilical-artery catheter. To avoid clotting, all surfaces of the catheter in contact with blood are usually heparin-coated, and it is also recommended that a constant low-rate infusion of heparinized solution be maintained. However the use of heparin-based components is sometimes contra-indicated in patients with a sensitivity to heparin. The anti-biofouling coated fiber optic probes here presented can minimize or avoid the use of heparin.

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