Fiber-optic Mach–Zehnder interferometer as a high-precision temperature sensor: effects of temperature fluctuations on surface biosensing

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In this article, we report the use of a fiber-optic Mach–Zehnder interferometer as a high-precision temperature sensor, and we investigate the effects of small temperature fluctuations on the reliability of the device as a surface biosensor. We found that typical temperature fluctuations generally cause sensor responses large enough that they must be compensated for before reliable surface chemistry measurements can be undertaken. These findings are particularly relevant in light of the recent surge of interest in fiber-optic based biosensors of various designs. © 2010 Optical Society of America

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In recent years, fiber-optic sensors have increasingly been investigated as attractive alternatives to more conventional molecular biology assays. These sensors may offer considerable advantages over assay techniques currently in use, having the potential, in particular, to provide highly sensitive real-time detection of unlabeled biomolecular targets [1]. Some of these sensors, particularly long-period fiber grating (LPFG) sensors and fiber taper-based Mach–Zehnder interferometers, are also highly sensitive to temperature change, since both of these use as their sensing arms evanescent fields from fiber cladding modes [2,3]. Because of their high temperature sensitivities, applying these devices as reliable, routine biosensors may be challenging, as the sensor signal is often subject to noise caused by typical fluctuations in the ambient room temperature. In this paper, we investigate the effects of such fluctuations on a fiber-optic Mach–Zehnder interferometer that is used to monitor the real-time hybridization of 10-base pair DNA strands.

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The sensor used was a double-pass Mach–Zehnder interferometer built by tapering two successive regions of optical fiber. The fiber was tapered by an Ericsson FA995 fusion splicer using an automated tapering program, and each taper was approximately 2 mm in length. The two concatenated tapers were separated by a stretch of bare, uncoated fiber approximately 20 cm long, which made up the instrument's sensing region. The sensor was mounted onto an open plastic stage for DNA hybridization experiments (see Fig. 1) and was secured in place with epoxy glue. The chemicals required for the immobilization of DNA onto the cladding surface of the sensing region were then added and removed from the stage using a micropipette. In the experimental setup, broadband light (1300 –1600 nm) entered the interferometer, struck a gold-coated mirror, then passed a second time through the interferometer from the opposite direction before entering an optical spectrum analyzer via a circulator. This double-pass configuration has been shown to improve the contrast of the transmission spectrum [2] and is depicted schematically in Fig. 2.

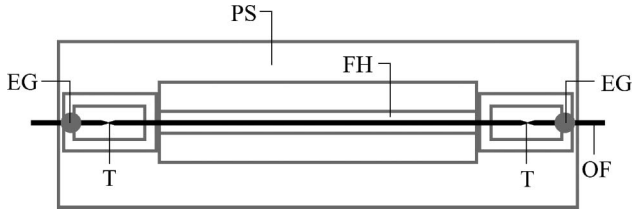

Fig. 1. Schematic diagram of the Mach–Zehnder apparatus as used in the experiment described in the text (not to scale). PS, plastic stage; OF, optical fiber; T, tapered regions of optical fiber; EG, epoxy glue used to secure the fiber to the stage; FH, fiber holder, into which reagents were added and removed over the course of the experiment. The sensing region of the interferometer comprises the stretch of optical fiber between the two tapers (T).

The fiber-optic Mach–Zehnder interferometer operates on the principle that a change in the refractive index of the medium surrounding the sensor causes a change in the effective refractive index of the fiber cladding, whereas the effective index of the core remains nearly unchanged [4]. This sensor configuration is advantageous because the fiber core acts as the reference arm of the interferometer, whereas the cladding functions as its sensing arm, thereby allowing the entire device to be contained within the short stretch of fiber between the two tapers. This configuration also minimizes the path length difference between the reference and sensing arms of the device.

It is known that changes in the sizes of surface-bound molecules cause a change in the refractive index of the medium [5], as observed from the surface on which the molecules are attached. Therefore, any addition to or change in the surface-bound molecules should be expected to generate a change in the effective index of the cladding modes in the sensing region of the interferometer. The signal generated by the interaction of the core and cladding modes is a spectrum of peaks and troughs that correspond to the superposition of interferences between the various cladding modes and the reference core mode. As a surface reaction progresses and DNA molecules add onto the cladding surface, peak wavelengths shift in proportion to the change in effective cladding index caused by their attachment. This wavelength shift is often used as a measure of the effective index change, and, by extension, of the progress of the surface reaction. In the present experiment, however, the interference signal from the sensor was processed using the spectral differential integration (SDI) method [6], which uses the area bound by an unshifted reference spectrum and the new, shifted spectrum to quantify the effective index change. This essentially provides a composite measure of the shifts of all the spectral peaks in the interference pattern, eliminating the difficulties inherent in monitoring the wavelength shift of a single subjectively chosen peak [6]. In addition, the use of the SDI method in conjunction with the double-pass Mach–Zehnder interferometer improves the sensor's performance further, since the increase in contrast afforded by the double-pass configuration increases the area bound by the two spectra, thereby increasing the sensitivity of the device when the SDI method is applied [2,6].

The procedure used for the immobilization of probe DNA on the surface of the interferometer's sensing region was identical to that given in Ref. [7]. Briefly, the cladding surface was cleaned with 5 M hydrochloric acid (HCl), silanized with 10% 3-aminopropyltrimethoxysilane (3-APTS), and the cross-linker dimethyl suberimidate dihydrochloride (DMS, 25 mM) was applied to link the primary amino group of 3-APTS to the primary amino group on a molecule of 3′-aminated, 10-base pair single-stranded probe DNA. Once the probe DNA was immobilized on the cladding surface, a complementary 10-base pair target DNA was added, thereby initiating the hybridization reaction. The concentration of both the probe and target DNA solutions was 2 μM. Interference spectra were recorded at regular intervals over the 50 min following the immersion of the activated sensor into the target DNA solution. As a reference, the temperature of the solution was also measured regularly over the same time period, using a thermocouple accurate to within 0.1 °C. The SDI response of the sensor and the temperature of the solution are shown plotted against the reaction time in Figs. 3 and 4, respectively. The sensor response is plotted against the temperature in Fig. 5 in order to clearly illustrate the linear relationship between the two.

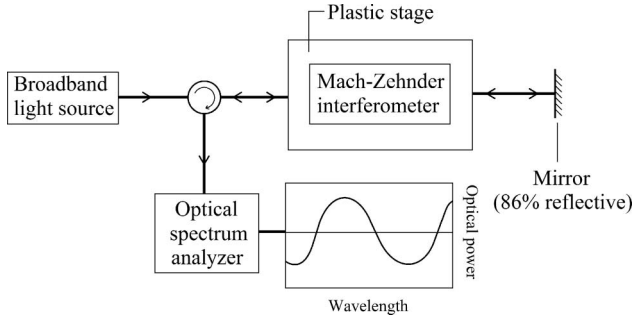

Fig. 2. Schematic diagram of the experimental apparatus. The chemical agents and DNA involved in the hybridization reaction were all pipetted into and out of the plastic stage surrounding the interferometer.

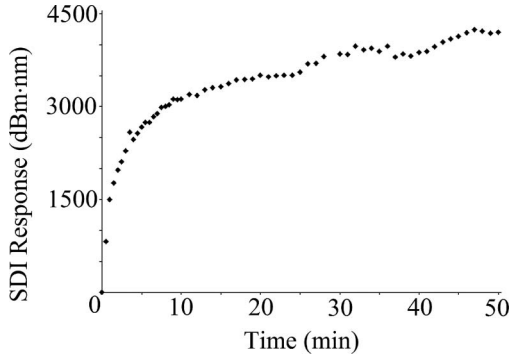

Fig. 3. Signal observed by the fiber-optic sensor during the first 50 min of the DNA hybridization reaction.

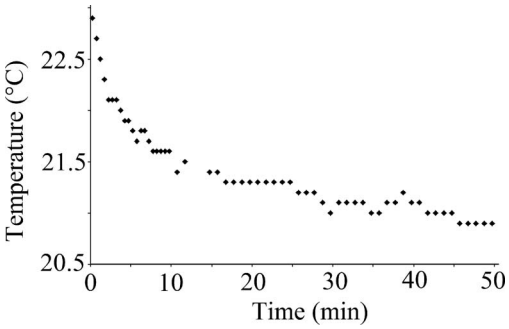

Fig. 4. Temperature of the solution of target DNA during the first 50 min of the DNA hybridization.

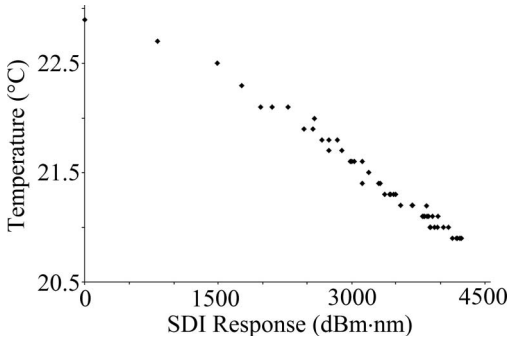

Fig. 5. Solution temperature plotted against the recorded signal.

An abrupt decrease in the temperature of the target DNA solution (Fig. 4) was observed immediately upon immersion, despite the solution and the sensor having both been kept at room temperature for several hours prior to the beginning of the reaction. This temperature drop occurred because the target DNA solution was kept in a sealed test tube so that the liquid and gaseous phases were allowed to come to thermal equilibrium inside the tube over time. Because the tube was sealed, at equilibrium there were as many molecules returning to the liquid phase as there were escaping from it, so no net evaporation of the liquid phase could occur after this time. When the solution was then transferred to the sensor holder, which was an open container, the water in the solution began to evaporate because the molecules escaping from the liquid phase could no longer return. Since the molecules that were traveling fast enough to escape the liquid phase were also those with the highest kinetic energies, the solution as a whole began to cool following its transfer from the closed to the open container. Evaporative cooling continued until the system reached a new thermal equilibrium state at a lower temperature. This new equilibrium point was reached once the rate of heat transfer to the liquid from the surroundings was equal to the rate of heat loss from the liquid through evaporation. In our experiment, the solution achieved rough thermal equilibrium after 15 min, having cooled by approximately 2 °C compared to its initial temperature (Fig. 4). It is clear from this and other work [2] that the Mach–Zehnder sensor that was used in these experiments is highly sensitive to temperature change, and in this case it appears that the sensor's temperature response overwhelmed any signal that may have originated directly from the DNA hybridization process.

However, it is also notable that, while the temperature of the solution tracks almost exactly linearly with the interferometer's response, for a brief period at the beginning of the experiment the sensor response is observed to change more quickly than would be expected, based on the later linear trend (Fig. 5). This unexpected increase may, in fact, be the result of the actual DNA hybridization signal that was to be recorded.

Clearly, the temperature response of the sensor is of critical importance in the design and eventual implementation of fiber-optic sensors as tools for biological or chemical assays. A sensing device that does not account for the effects of temperature is likely to suffer from reduced accuracy and reliability due to random fluctuations. For example, one recent study has reported the real-time detection of 15-base pair DNA hybridization using an LPFG sensor [7]. The results of the study were qualitatively very similar to those presented in Fig. 3, though no mention was made of temperature-dependence effects. It is, therefore, possible that this study may have inadvertently measured temperature change, rather than the progress of the DNA hybridization reaction, as was intended.

In summary, we have shown that a sensor response qualitatively identical to that expected by DNA hybridization was generated by the temperature change that occurs naturally by evaporation when a liquid is transferred from a sealed to an open container. We have also observed that, while the greater portion of the signal is due to the temperature change alone, the small anomalous signal occurring at the start of the experiment (Fig. 5) may reflect the DNA hybridization process, suggesting the possibility that the effects of temperature could be corrected for in biosensors like the one described here. It is clear from these results that fiber-optic devices relying on the modulation of evanescent waves by surface-immobilized molecules cannot function as effective biochemical sensors unless due corrections are made for the devices' temperature sensitivities.

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