Intrinsic Fiber Optic pH Sensor for Measurement of pH Values in the Range of 0.5–6

Thu Hien Nguyen, Thillainathan Venugopalan, Tong Sun, and Kenneth T. V. Grattan

***Abstract*— The development, design, and evaluation of an intrinsic optical fiber pH sensor for low pH values (in the range of 0.5–6) based on fluorescence from a novel coumarin dye, which is covalently immobilized onto the end surface of an optical fiber is described. The sensor provides a rapid response (of approximately 25 s) over this pH range of 0.5–6.0, showing with very good stability over a period of several months. The sensor has also demonstrated insensitivity to ionic strength and excellent photostability through a series of laboratory tests.**

***Index Terms*— Optical fiber sensor, fluorescent sensor, pH sensor, coumarin dye.**

I. Introduction

OPTICAL FIBER pH sensors have been actively investigated in recent years because of their importance for both *in situ* and *in vivo* pH measurements in various aspects of scientific research and in a range of practical applications, in particular those where available conventional glass electrodes are not suitable [1]–[4]. The key strength of the fiber optic approach lies in the advantages offered in terms of small size, immunity to electromagnetic interference, remote sensing capability, resistance to chemicals and biocompatibility [5], [6]. Several types of pH optrodes (the optical fiber analog of electrode) have been proposed and demonstrated over the years. A small number of them are based on refractive index changes in certain parts of the fiber caused by pH induced swelling/shrinking of a deposited nanostructured film, which lead to changes in the fiber transmission or reflection spectra [7]–[9]. This type of pH sensors can be highly accurate in principle. However, they can be influenced by temperature fluctuations, stress, vibrations and certain chemical interferences. The majority of pH optrodes therefore have been developed to function through monitoring the changes in the absorbance or fluorescence properties of certain pH sensitive indicators which are immobilized on/in proton-permeable solid substrates [10].

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Although there have been a number of reports on the development of fiber-optic pH sensors in the literature, most of them were constructed to operate, with certain limitations, in the physiological or near neutral pH region. Only a few optrodes have been reported for use in either the low or high pH region where the pH response of most glass pH electrodes is imperfect [11], [12]. The reasons for limited success with many previous designs are quite varied but the use of appropriate pH indicators and the effective immobilization of the indicators are probably the key factors in the development of an optimum optical pH sensor, as they govern the lifetime and signal stability of the sensor, and often have not be achieved in previous designs. Prior work has shown that poor immobilization results in dye leaching and consequently a drifting of the calibration of the probe, which leads to the gradual breakdown of its useful sensing ability [10], [13]. Among several widely used immobilization methods are included absorption or entrapment [6], [14], [15], layer-by-layer (LbL) electrostatic self-assembly [16], [17] and covalent binding [13], [18]–[22]. The covalent binding method can produce more reliable and durable sensors, as the indicators are virtually bonded to the substrate therefore they are unlikely to leach out under normal conditions, although the fabrication process is relatively complicated and time-consuming [23]. Under extreme conditions, however, the sensor reliability and durability are not just determined by the immobilization method used, but also by other factors, such as the stability of the pH indicators themselves, the stability of the substrates and the linking bonds between the fiber substrate and the sensor material. The commonly used ester linkage and acidamide linkage are not very stable in acidic or alkaline aqueous conditions [2], [10].

In this work, a new approach is taken for the development of an intrinsic pH sensing system to overcome the common disadvantages of optical fiber pH sensors mentioned above, thus creating more stable and therefore more useful devices. A novel polymerisable coumarin dye, bearing a carboxylic acid group was designed and synthesized. Coumarins have been chosen for this application as they are widely used as laser dyes for single-molecule fluorescence and so they are 'tried and tested' in terms of the key property of being photo-stable [24], [25]. The dissociation of the carboxylic acid group allows for the determination of pH in the acidic region of the pH scale which makes it suitable for gastric measurements [26], [27] and acidic soil measurements [28] as well as the measurement of pH in certain chemical reactors. The dye was covalently bound to the fiber surface by polymerization, in an approach similar to the method reported by Uttamlal *et al.* [13], [29] but allyltriethoxysilane (ATES)

was used to functionalize the fiber surface with polymerizable groups rather than 3-(trimethoxysilyl) propyl methacrylate to avoid the unstable ester linkage. The fluorescence detection method was employed rather than the simpler commonly used method based on colorimetric measurements as fluorescent sensors are usually more precise and offer higher sensitivity than their colorimetric counterparts [3], [30].

The primary applications-focus of the work has been for the determination of pH changes in acidic conditions for a range of industrial applications, where the interest ranges from chemical processing to biomedical applications, in which precise and continuous pH monitoring is critical for both process control and medical diagnosis.

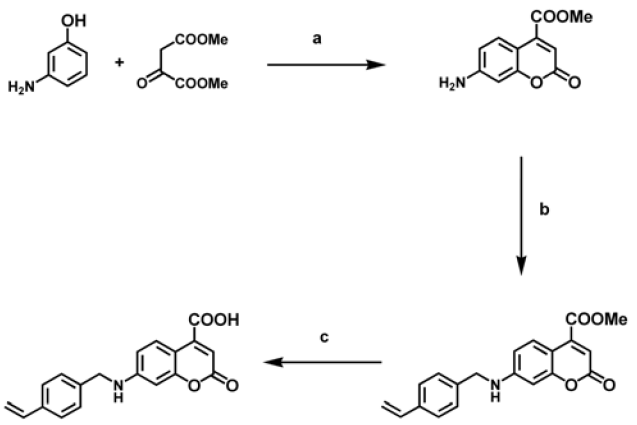
II. Experimental Approach

A. General

All chemicals were of analytical grade, purchased from Sigma-Aldrich and were used without further purification. All solvents used were of HPLC grade from Fisher Scientific. All aqueous solutions were prepared using distilled water. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 500 spectrometer. Mass spectra were run by negative ion Electrospray (ES) mode on a Water LCT Premier XE mass spectrometer. IR spectra were recorded on a FTIR 8700 Shimadzu Fourier Transform Infrared Spectrophotometer. Melting points were recorded on a Stuart SMP30 melting point apparatus and were uncorrected. Elemental analyses were carried out at the Microanalytical Laboratory, Department of Chemistry, University College London. Absorption and fluorescence measurements of aqueous solutions containing fluorophores were carried out on a PerkinElmer Lambda 35 spectrophotometer and a Horiba Jobin Yvon Fluoromax-4 spetrofluorometer system with FluorEssence^{TM} as driving software, respectively. Refractive indices were measured on an Abbe refractometer. Quantum yields of fluorescence were determined using quinine sulfate as the standard ($\Phi = 0.55$) [31], [32].

B. Synthesis of the Fluorescent Dye

7-Vinylbezylaminocoumarin-4-carboxylic acid (7-VBACC) was prepared by hydrolyzing methyl 7-vinylbenzylaminolcoumarin-4-carboxylate which was synthesized from methyl 7-aminocoumarin-4-carboxylate [33] and 4-vinyl benzyl chloride as shown in Scheme 1. Red solid, mp 222-224 °C; IR (KBr) ν_{max} (cm^{-1}) 3348, 2499, 1708 (C=O), 1625, 1552, 1497, 1469, 1382, 1261, 1222, 1149; ^{1}H-NMR (500 MHz, DMSO-d_6) δ(ppm): 7.78 (d, 1H, H_5, $J_{5,6}$ = 8.9 Hz), 7.46 (s, 1H, H_3), 7.43 (d, 2H, $H_{arom.}$ J = 7.3 Hz), 7.33 (d, 2H, $H_{arom.}$ J = 7.3 Hz), 6.70 (dd, 1H, C***H***=CH_2, J = 10.8 Hz, J = 18.0 Hz), 6.68 (d, 1H, H_6, $J_{6,5}$ = 8.9 Hz), 6.43 (t, 1H, NH), 6.28 (s, 1H, H_8), 5.79 (d, 1H, CH=C***H***$_a$H$_b$ J = 18.0 Hz), 5.22 (d, 1H, CH=CH$_a$***H***$_b$, J = 10.8 Hz), 4.37 (d, 2H, CH_2, J = 5.4 Hz). ^{13}C-NMR (DMSO-d_6) δ(ppm): 171.4 (COOH), 166.0 (C2), 160.5 (C9), 153.9 (C4), 152.5 (C7), 138.7 (***C***CH_2NH), 136.3 (***C***H=CH_2), 132.0 (CCH=CH_2), 127.5 (aromaticC), 127.4 (C5), 126.2 (aromaticC), 125.0 (C3), 124.7 (C6), 122.5 (C10), 114.0 (CH=***C***H_2), 109.2 (C8), 45.6 (CH_2NH); MS (ES$^-$): Calcd. m/z = 320.0923 ($C_{19}H_{14}NO_4$). Found m/z = 320.0932 (M-H$^-$); Elem. Anal. Calcd. for $C_{19}H_{15}NO_4$ (321.33): C 71.02, H 4.71, N 4.36. Found: C 70.53, H 4.65, N 4.26.



Scheme 1. Preparation of fluorescent monomer 7-VBACC. (a) 110 °C, 2 h, 42%; (b) $CH_2 = CHC_6H_4CH_2Cl$, K_2CO_3, KI, MeCN, 85 °C, 50 h, 44%: (c) 1 M NaOH, EtOH/THF (2:1), 50 °C, 12 h, 94%.

C. pH Probe Design and Fabrication

Building on the work done to create an appropriate indicator dye, the next step in the development of the sensor was the creation of an appropriate pH sensing probe incorporating the dye developed. This requires a multi-step process and the fabrication of the pH sensing probe used in the work is shown schematically in Fig. 1.

The distal end of a 1000 μm diameter UV multimode fiber (purchased from Thorlabs) was polished in succession with 5 μm, 3 μm and 1 μm polishing pads (Thorlabs) and washed with acetone to create a clean, polished surface. The distal end was then immersed in 10% KOH in isopropanol for 30 min with subsequent rinsing in copious amounts of distilled water and dried with compressed nitrogen. After that, it was treated in a 30:70 (v/v) mixture of H_2O_2 (30%) and H_2SO_4 (conc.) (Piranha Solution) for 60 min, rinsed in distilled water for 15 min and dried in an oven at 100°C for 30 min. This procedure leaves the surface with exposed hydroxyl groups which facilitate bonding of ATES.

The fiber surface was then modified by silanizing for 2 h in a 10% solution of ATES in ethanol. The fiber was washed with methanol and distilled water respectively in an ultrasonic bath. Subsequently, it was dried in an oven at 60°C for 2 h. This procedure functionalizes the fiber surface with polymerizable allyl groups.

Monomer stock solution was prepared by dissolving 7-VBACC (6.4 mg, 0.02 mmol), 1,4-bis(acryloyl)piperrazine cross linker (19.4 mg, 0.1 mmol), acrylamide co-monomer (2.8 mg, 0.04 mmol), AIBN initiator (4 mg) in 200 μL dimethylformamide (DMF). The stock solutions were purged thoroughly with argon for 10 min. A small volume of the solution was placed into a capillary tube *via* syringe and the distal end of the fiber was inserted. They were sealed quickly with PTFE tape and polymerized in an oven at 80°C for 18 h. This procedure forms a polymer layer of the dye which is covalently bound to both the cylindrical surface and the distal

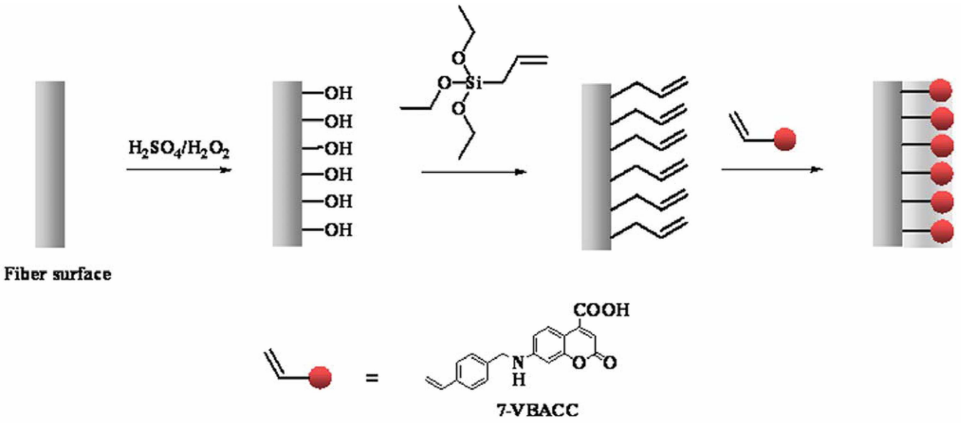


Fig. 1. Preparation of a pH sensor probe: schematic of the processes involved.

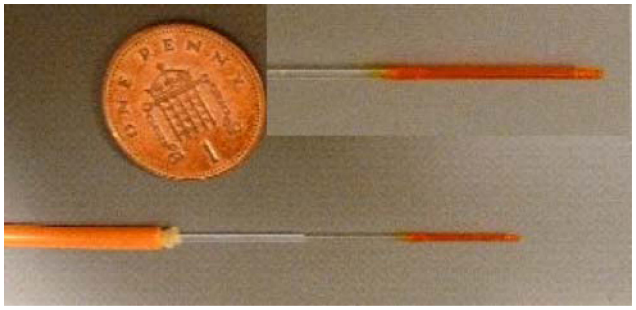


Fig. 2. Typical pH sensor tip prepared in this work showing the active distal end of the sensor.

end surface of the fiber. However, only the polymer on the distal end surface is responsible for the fluorescence signal which is produced by direct excitation from the light source. The polymer on the side plays no role in the sensing process since evanescent wave excitation is eliminated by keeping the cladding of the fiber intact. A typical pH probe prepared by this procedure is shown in Fig. 2 where it can be seen that the distal end of the probe shows a distinctive coloration due to the presence of the dye. The sensor tip was placed in pH 7 buffer for 24 h to remove all unreacted materials and the excess amount of polymer formed which was not directly bound to the fiber. The probe was then stored in a cool and dark place until use.

D. Experimental Set-Up

With the probe having been fabricated as described above, it was necessary to undertake a calibration of its performance prior to its use in the applications domain. The set-up used for the measurements undertaken to calibrate the probe is as presented in Fig. 3, where light from a LED (Roithner Lasertechnik), emitting at a center wavelength of 400 nm is coupled through a multimode UV/Visible fiber (with hard polymer cladding, 1000μm silica core and numerical aperture NA of 0.37, Thorlabs), using collimation and focusing lenses (Comar), into one branch of a 2×1 multimode fiber coupler (Ocean Optics). The other end of the fiber coupler is connected to the sensor probe with the active sensing region being located at the distal end of the fiber. Following pH interaction with the active region, a portion of the total light emitted from the sensing layer is collected and guided through the other branch of the fiber coupler to an Ocean Optics USB2000 spectrometer, with the output being displayed on a computer screen.

E. Principle of pH Measurement Based on Fluorescence Intensity and pK_a Calculation

The development of the present pH optrode is basically based on the fluorometric determination of pH. As stated above, it makes use of the coumarin dye as fluorescent indicator, HA, to induce pH sensitive changes in the measured fluorescence intensity. In aqueous solution, the following equilibrium can be reached:

$$HA \leftrightarrow H^+ + A^-$$

The relationship between the protonation state of the indicator and the pH is governed by the Henderson-Hasselbalch equation:

$$pH = pK_a + \log\frac{[A^-]}{[HA]} \tag{1}$$

where [A^-] and [HA] are the concentrations of the dissociated and undissociated forms of the indicator and pK_a is the acid-base constant. [A^-] and [HA] are related to fluorescence intensities by [A^-] $= F - F_{\max}$ and [HA] $= F_{\min} - F$ where F is a measured fluorescence intensity of the system, $F_{\max}$ is the fluorescence intensity of the fully protonated system and $F_{\min}$ is the fluorescence intensity of the deprotonated system. The expressions are then substituted into (1) to provide (2).

$$pH = pK_a + \log\frac{F - F_{\max}}{F_{\min} - F} \tag{2}$$

Equation (2) can be re-written in terms of F to give

$$F = \frac{F_{\max} + F_{\min} \times 10^{(pH-pK_a)}}{10^{(pH-pK_a)} + 1} \tag{3}$$

This results in an 'S-shaped' relation of the fluorescence intensity versus pH graph, centered on the pK_a value. Equation (3) is used as a model for a nonlinear fitting method to calculate the pK_a value, which is the pH where 50% of the dye population in solution is protonated.

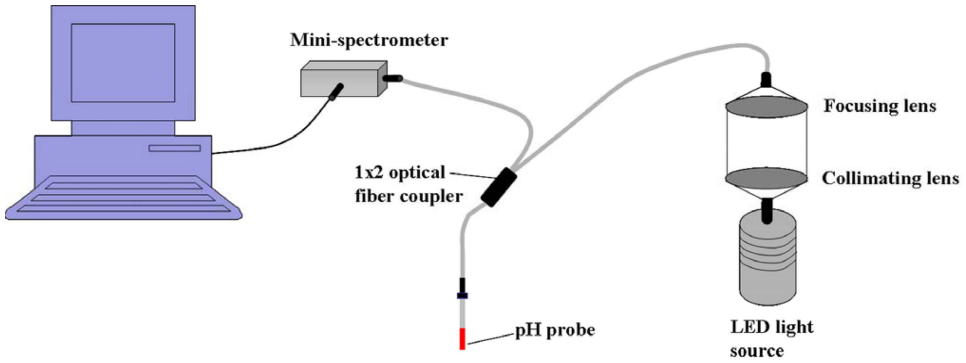


Fig. 3. Experimental set-up used in the evaluation of the performance of the probe designed.

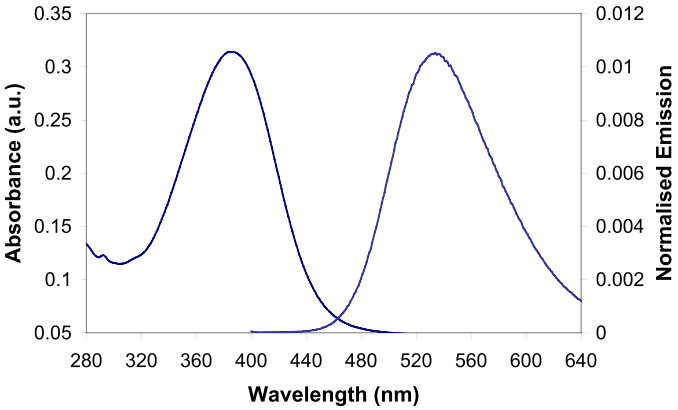


Fig. 4. Absorption (left) and emission (right) spectra of 7-VBACC (14 μM) in H_2O. Emission spectra recorded with $\lambda_{ex} = 380$ nm.

TABLE I
SPECTRAL DATA AND pK_a VALUE OF THE FLUORESCENT DYE

solvent	UV max (nm)	Emission max (nm)	Quantum yield	pK_a
EtOH	384	496	0.565	-
H_2O	387	534	0.146	2.40 ± 0.05

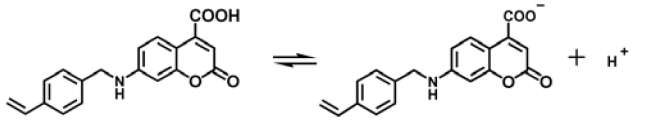
The pK_a value calculation for the polymer-bound dye was performed using the Boltzmann model – Equation (4) where dpH is the slope of the curve within its linear zone.

$$F = \frac{F_{\max} + F_{\min} \times e^{(pH-pK_a)/dpH}}{e^{(pH-pK_a)/dpH} + 1}. \quad (4)$$

III. RESULTS AND DISCUSSION

A. Properties of the Fluorescent Indicator 7-VBACC in Solution

The absorption spectrum of 7-VBACC shows only one main absorption band in the UV region (Fig. 4). The dye exhibits a large Stokes shift (the difference in wavelength between the absorption and the fluorescence spectral peaks) of 150 nm, which is very important for the sensor system design to minimize the interference of the excitation light with the fluorescence emission. The quantum yield of 7-VBACC is



Scheme 2. Equilibrium between the protomated and deprotonated forms of the dye in solution.

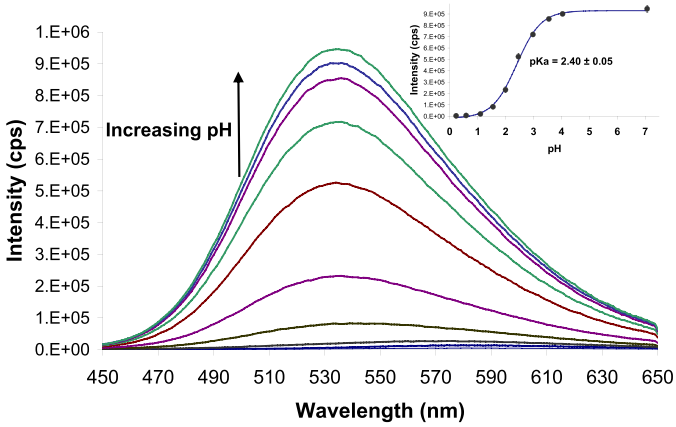


Fig. 5. Emission spectra of 7-VBACC at pH from 0.2 to 7.0. The inset shows the titration plots at 535 nm (λex = 380 nm). Error bars represent standard deviations in the calculated values.

reasonably good in ethanol and much higher in H_2O (details are shown in Table I).

In aqueous solution, there is equilibrium between the protonated and deprotonated forms of the dye as shown in Scheme 2. The deprotonated form is fluorescent and the protonated form is much less so. Therefore, the fluorescence intensity of the dye is higher at higher pH values. To determine the pK_a value for the free dye, a series of pH titration experiments was carried out using 50 mM citrate buffer solutions with different pH. In the titration, 50 μL of 0.8 mM dye stock solution in MeOH was added to 3 mL of buffer in a cuvette, followed by measurement of emission spectra. All samples were prepared in duplicate or triplicate and the data presented were average values. The calculation of the pK_a value was performed based on the fluorescence intensities at a fixed maximum emission wavelength (535 nm) using a nonlinear fitting method according to Equation (3). The emission spectra of 7-VBACC at different pHs and the titration curve are shown in Fig. 5. The data obtained for the dye are summarized in Table I.

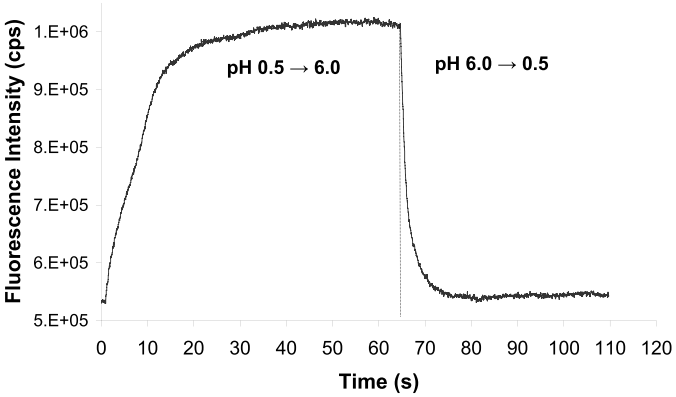


Fig. 6. Forward and reverse dynamic response of the sensor in the pH 0.5-6.0 range (λex = 380 nm, λem = 540 nm).

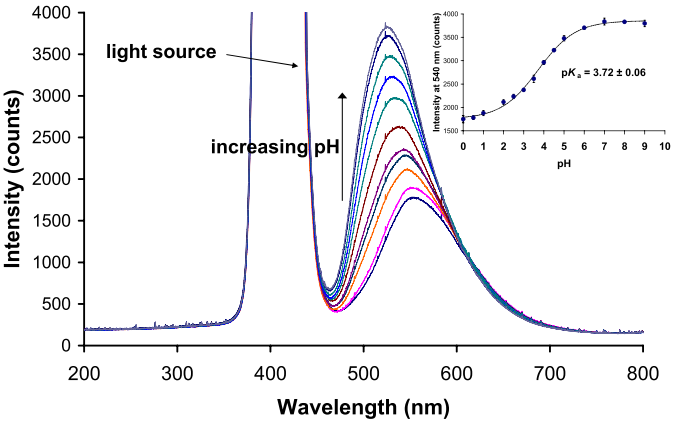


Fig. 7. The evolution of fluorescence spectra of the sensor probe with pH in the range from 0.5 to 7.0. Inset shows the titration plots at 540 nm. Error bars represent standard deviations in the calculated values.

B. Response Time of the Sensor

Before performing calibration measurements with the sensor, its response time was investigated. Fig. 6 shows the dynamic response obtained from the spectrofluorometer of the sensing probe to a step change from pH 0.5 to pH 6 and back again. It can be seem from the figure that the response time depended on the direction in which the pH of the solution was varied. In this work, the response time is considered to be the time required for 95% of the total signal change and the measurement of the response time of the optrode for the low to high pH variation was found to be 25 s whereas the same amount of change for the reverse variation required less than half the amount of time. In comparison to other pH sensors such as the sensor reported by Wallace *et al.* [22] which showed a response time of around 500 s or the device reported by Netto *et al.* [26] which showed a response time of few minutes, this pH sensor responds much more rapidly. This is likely due to its key design features: both the relatively low thickness of the polymer film as well as its hydrophilicity. All this has obvious advantages where a rapid change of pH is to be monitored and a real-time measurement to be achieved.

C. Response of the Sensor to Different pH

The calibration measurements of the sensor characteristics were performed in 50 mM citrate buffer at different pH (note: citrate does not act as a good buffer at pH higher than 6 and lower than 3, however citrate was used for all pH to avoid any differences in fluorescence caused by the difference in buffer composition). They were carried out in duplicate and the data presented were average values. The titration curve is shown in Fig. 7. The sensor probe exhibited an increase in fluorescence intensity with increasing pH in the range from 0.5 to 6.0, which conveniently is wider than the dynamic response range of the free dye. The pK_a value calculated using Eq.(4) for the probe is 3.72 ± 0.06. This value for the immobilized form of the dye is slightly higher than that for its free form in solution and this arises probably because of the decrease in the polarity of the microenvironment [3].

TABLE II

pH MEASUREMENTS OF pH 4 AND pH7 BUFFER SOLUTIONS WITH DIFFERENT IS

IS (mM)	pH 4.00 buffer solution	difference	pH 7.00 buffer solution	difference
0	4.05	0.05	7.02	0.02
10	4.06	0.06	7.11	0.11
50	4.01	0.01	7.09	0.09
100	4.11	0.11	7.04	0.04
200	4.02	0.02	7.04	0.04
500	4.05	0.05	7.07	0.07
1000	4.07	0.07	7.10	0.10
2000	4.10	0.10	7.07	0.07

D. Effect of Ionic Strength (IS)

Sensitivity to IS can be a serious problem in the cases of optical fiber sensors as it affects pK_a values, thus resulting in errors in pH determination. The effect of IS was investigated with the prepared pH 4 and pH 7 buffer solutions adjusted with NaCl to different ionic strengths ranging from 10 mM to 2000 mM. The fluorescence intensity obtained for each solution was converted to a pH value using the calibration curve and this is presented in Table II. As can be seen from the table, there appears to be no sensitivity to IS for the sensor, even at very high concentrations of NaCl. The insignificant errors caused are probably due to the system error rather than the change in IS.

E. Reproducibility and Photostability

The stability of the probe both in terms of storage, its susceptibility to error due to intense irradiation of the sample and its reproducibility in use are all very critical to the successful application of the system. An evaluation of these parameters was made in order to understand better the performance of the sensor and establish its suitability for industrial applications. The stability of the sensor was tested by calibrating it with buffer solutions at different pH values ranging from 0.5 to 7.0 and recalibrating it after 24 h and then after five months. After each calibration, the probe was washed thoroughly with a pH 7.0 buffer, followed by the same procedure with distilled water and then it was stored in the dark until next use.

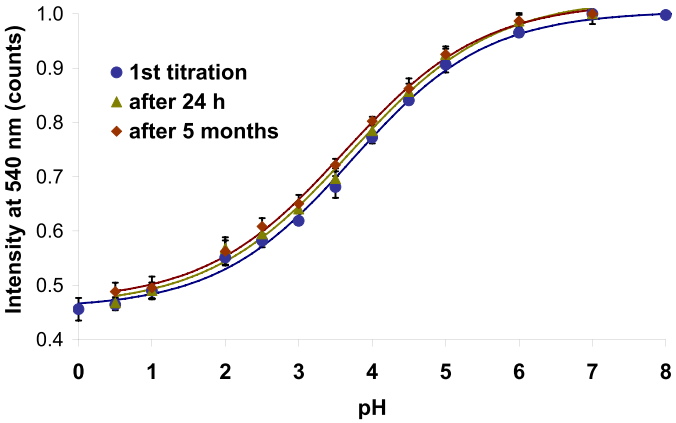


Fig. 8. Titration curves for the sensor probe obtained between 24 h interval and after 5 months. Fluorescence intensities are normalised to the maximum emission at 540 nm of the probe at pH 7.0 for each data set. The model fits are shown in continuous lines. Error bars represent standard deviations in the calculated values.

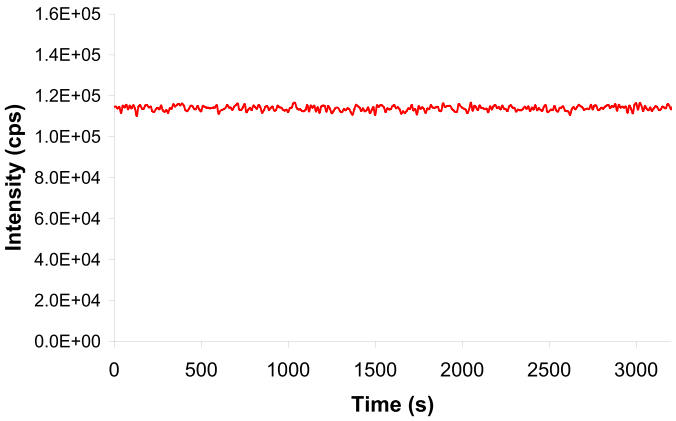


Fig. 9. Fluorescence intensity of the probe at the emission wavelength as function of time during 60 min of continuous illumination by light from a high power Xe lamp.

No significant difference was observed between the measurements and the pK_a values calculated, which were found to be 3.72 ± 0.06 (initial calibration), 3.70 ± 0.10 (after 24 hours) and 3.62 ± 0.05 (after five months). Is very pleasing to note that there was a very tiny drifting even after several months, illustrating the high stability of the sensor scheme produced (Fig. 8).

Photostability is one of the critical properties of fluorescent indicators and thus of the dye used in this sensor application. In order to test the photostability of the dye, the probe was coupled into the fluorimeter through a dichroic mirror using a fiber bundle. The excitation light (at a wavelength of 400 nm) was launched to the distal end of the probe illuminating the sensing material with light from the intense, high power Xe lamp of the fluorimeter continuously for 1 h. The fluorescence intensity data from the probe were collected over that period and displayed. As can be seen from Fig. 9, no photobleaching was observed over the time investigated and with the high flux of photons onto the probe. When compared to the results of other materials, this offers excellent performance: the decrease observed in the fluorescence intensity was 65% for carboxyfluorescein and 10-13% for iminocoumarin derivatives, again after 60 min of continuous illumination using a mercury lamp [3]. Thus an important conclusion is that the material prepared using the coumarin fluorophore and synthesized specifically for this application in this work possesses superior photostability, a feature that is critically important with excitation of sensor probes by high intensity solid state sources.

IV. Conclusion

In this paper, a novel and highly effective approach to the development of a pH sensor for measurement of low pH values, showing superior performance and fast response has been reported. The robust, compact and portable sensor probe system thus developed has been evaluated and preliminary results reported. The sensor design reported has shown an increase in fluorescence intensity in response to pH in the range from 0.5 to 6.0 with very good stability over a period of several months.

A further important feature of this type of sensor is that it is potentially inexpensive to produce in quantity and the large Stokes shift shown allows for more accurate measurements due to the minimum level of interference between light source and fluorescence signals generated. For industrial applications, the sensor would require further work to design a suitable 'packaging' to withstand use by inexperienced operators: however prior work with optical fiber relative humidity sensors by some of the authors and others has shown an effective design that could be employed to protect the sensitive fiber tip [34]. In addition, the intrinsic sensor design discussed in this paper has enabled direct light coupling between the fiber and the sensor material: therefore there is a minimum loss caused by the excitation or the fluorescence signal collection. Referencing schemes to allow for corrections due to fluctuations in the source light or environmental perturbation to the sensor system have been discussed elsewhere by the authors and others [5] and can be considered for incorporation into a sensor system of this type, either through using dynamic calibration or a built-in software correction algorithm. In addition, sensors of this design can readily be used together: multiplexed along a single optical fiber or along a parallel optical network, using various techniques to identify each individual sensor probe. Thus there is considerable flexibility in the approach and as various applications are considered, the sensor scheme can be tailored for different uses, thus emphasizing the versatility of the design discussed here.

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