

Exploitation of a pH-sensitive hydrogel disk for CO₂ detection

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Abstract

In this paper is described how hydrogel is exploited as sensor material for the detection of carbon dioxide (CO₂). A pH-sensitive hydrogel disk, which swells and deswells in response to pH changes, was clamped between a pressure sensor membrane and a porous metal screen together with a bicarbonate solution. CO₂ reacts with the bicarbonate solution resulting in a pH change, which is converted into a pressure by the enclosed hydrogel. This pressure is a measure for the partial pressure of CO₂. The main advantage of this sensor principle is the fact that a reference electrode as required for potentiometric sensors is no longer needed.

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1. Introduction

Hydrogels are cross-linked hydrophilic polymers that can contain a large amount of water [1,2]. By incorporating functional groups, a hydrogel can be made stimulus-sensitive. Such stimulus-sensitive hydrogels can undergo volume changes in response to changes in stimuli [3–7]. These stimuli can be pH, temperature, light, ion concentration or electric field. Applications for stimulus-sensitive hydrogels have been mostly proposed in the biomedical field [3,4], e.g. for controlled drug delivery, but also for sensors and actuators [5]. Hydrogel-based sensors usually consist of a particular stimulus-sensitive hydrogel, which is used as sensing element, and a transducer to convert the swelling of the hydrogel to the optical or electrical domain. Conductometric, amperometric, optical and mechanical methods have been explored to measure the hydrogel swelling [5].

In this paper, a CO₂ sensor is presented which makes use of a pressure sensor as transducer and a pH-sensitive hydrogel as sensing material. Fig. 1 shows a schematic representation of the sensor. A pH-sensitive hydrogel is placed in a bicarbonate solution enclosed by a porous cover and a pressure sensor. CO₂ reacts with the bicarbonate solution, resulting in a pH decrease according to the Severinghaus principle [8]. In response to the pH decrease the pH-sensitive hydrogel starts to swell but since its volume is fixed by the

porous cover, a pressure will be generated (isometric conditions). This pressure is a measure for the partial pressure of carbon dioxide. The advantage of this sensor is that a reference electrode, showing typical problems like drift, leakage and fouling, is no longer needed. In future, a CO₂ permeable membrane must be added to complete the sensor.

The main application of the proposed sensor is to measure the partial pressure of carbon dioxide in the stomach. High P_{CO₂} levels can indicate that a person has gastrointestinal ischemia caused by occlusion of arteries or veins, or by general circulatory failure resulting in splanchnic hypoperfusion (insufficient blood circulation in stomach and/or intestines) [10]. Because the CO₂ measurements takes place in situ, miniaturization is required to be able to insert the sensor, applied on a catheter, in the stomach through the nose. Further possible applications are in the automobile industry, in horticulture and for environmental monitoring instruments.

2. Optimization

Recently, initial results of the proposed CO₂ sensor with pH-sensitive hydrogel microspheres have been presented [9]. The present paper reports the continuation of this research, where the microspheres are replaced by a thin layer of pH-sensitive hydrogel. Further miniaturization of the sensor is obtained by using a micro pressure sensor. The replacement of the microspheres by a thin layer was a done for several reasons. Hydrogel microspheres are difficult to handle, hard to dose and difficult to confine, all due to their

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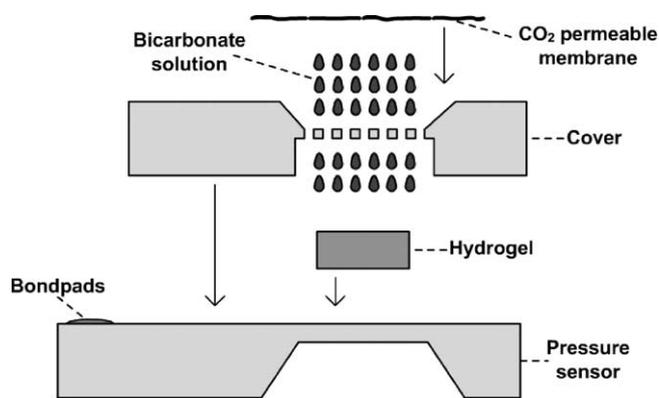


Fig. 1. Schematic representation of the hydrogel-based P_{CO_2} sensor.

small size of a few micrometers. Another disadvantage was that an additional membrane with small pores ($<2\ \mu\text{m}$) was required to enclose the microspheres. Diffusion of ions to the hydrogel was slowed down by this membrane which resulted in a relative longer response time of the sensor. Furthermore, the microspheres moved during swelling, resulting in noise and hysteresis in the measurement signal. Using a thin layer of hydrogel has many advantages—ease of handling, well-defined dimensions and it can be confined by a cover with large pores. Larger pores allow faster diffusion and consequently a decrease in the sensor response time.

The sensor should be able to measure CO_2 levels from 22.5 to 135.0 mmHg for the medical application. The relation between the $[\text{H}^+]$ and the partial pressure of CO_2 (mmHg) is given by the following equation [8,9]:

$$P_{\text{CO}_2} = \frac{[\text{H}^+]^2 + [\text{NaHCO}_3][\text{H}^+] - K_w}{SK_1K_h(1 + (2K_2/[\text{H}^+]))} \quad (1)$$

where S is the Henry's coefficient (M/mmHg; representing the solubility of CO_2 in water), K_h the Henry's law constant, K_w the water dissociation constant and K_1 and K_2 , the first and second dissociation constants of H_2CO_3 . When the clinical CO_2 values are substituted in Eq. (1) for a 100 mM bicarbonate solution, the pH range of the bicarbonate solution can be calculated and is between pH 7.48–8.25. Consequently, the hydrogel should swell in this range. It is known that hydrogels swell around the $\text{p}K_a$ of the titratable monomers that are used [7]. So, a hydrogel has to be used with a $\text{p}K_a$ in the basic region around 7.8. For our sensor we used a hydrogel consisting of dimethylaminoethyl methacrylate (DMAEMA), because the $\text{p}K_a$ of the protonable monomer is approximately 8. The sensitivity of the sensor can be defined as the change in generated pressure per change in CO_2 partial pressure:

$$S = \frac{\Delta P}{\Delta \log P_{\text{CO}_2}} = \frac{\Delta P}{\Delta \text{pH}} \frac{\Delta \text{pH}}{\Delta \log P_{\text{CO}_2}} \quad (2)$$

The pH response to a change in CO_2 ($\Delta \text{pH}/\Delta \log P_{\text{CO}_2}$) depends on the concentration of bicarbonate used and is theoretically optimal at 1 mM or higher (8). The pressure

response to a change in pH ($\Delta P/\Delta \text{pH}$) is optimal when the $\text{p}K_a$ is near the centre of the range where the pH varies.

3. Experimental

3.1. Materials

Hydroxyethyl methacrylate (HEMA) and DMAEMA were purchased from Acros. Tetraethyleneglycol dimethacrylate (TEGDMA) was obtained from Fluka and 2,2-dimethoxy-2-phenylacetophenone (DMPAP) from Aldrich. The HEMA and DMAEMA were purified by distillation. The other chemicals were used as received.

The pressure sensor was obtained from Honeywell (26PC series). The metal screen, used to enclose the hydrogel, was cut out of a fine-mesh gas filter.

3.2. pH-sensitive hydrogel disk preparation

A pH-sensitive hydrogel disk was prepared from HEMA and DMAEMA by UV-polymerization. A monomer mixture of HEMA and DMAEMA was made with a mole ratio of 95:5 and to the total mole amount, 1.5% cross-linker TEGDMA and 3% photoinitiator DMPAP was added. Silicon moulds were prepared in the cleanroom. With reactive ion etching a square cavity was created with 2000 μm sides and a depth of 50 μm . An amount of hydrogel monomer mixture was pipetted in the cavity and covered with transparent Mylar foil, which prevents oxygen to interfere with the polymerization, but allows UV light to pass. By pulling the foil over the mould, abundant solution is removed until the cavity is exactly filled with the monomer mixture. A mask was placed on top of the foil with a circular aperture (diameter 750 μm) through which UV can pass. The hydrogel was polymerized by 366 nm UV light for 90 s. The principle is shown in Fig. 2. By using this method a hydrogel disk with a diameter of 750 μm and a thickness of 50 μm was created. The disk was removed from the mould by placing the mould in a pH 6 buffer, which makes the hydrogel to swell, and carefully extracting the swollen disk with a scalpel.

3.3. Sensor fabrication

The Honeywell 26PC pressure sensor consists of a silicon pressure sensor chip and a plastic housing. The housing can easily be removed to obtain the sensor chip. A hole was drilled in a PCB stick and the pressure sensor chip was glued at all four sides in it in such a way that the bondpads and front and back side of the pressure sensor membrane were kept free. The bondpads on the chip were connected to the electrode tracks on the PCB by wirebonding. The wirebonds and electrode tracks were then isolated with two-component glue. The cavity of the pressure sensor chip was filled with silicone rubber. After hardening of the rubber, a thin layer of Teflon coating was applied to prevent sticking of the

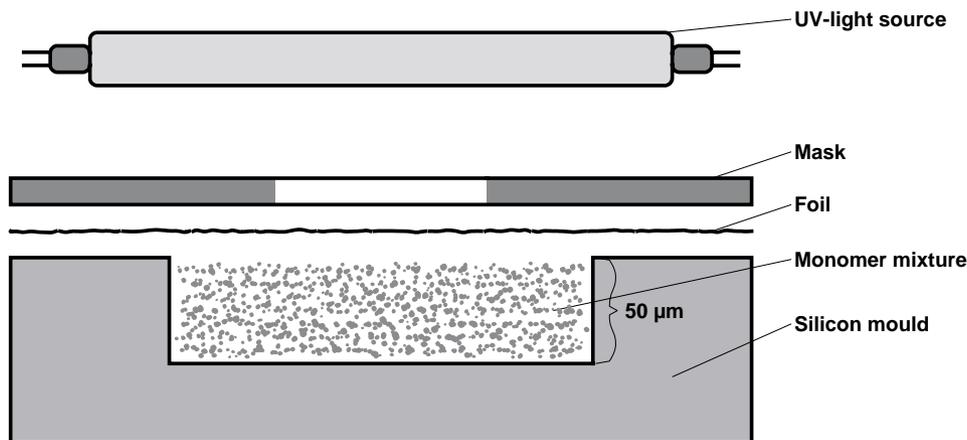


Fig. 2. Schematic representation of the setup that is used to obtain HEMA-co-DMAEMA hydrogel disks with a diameter of 750 μm and a thickness of 50 μm .

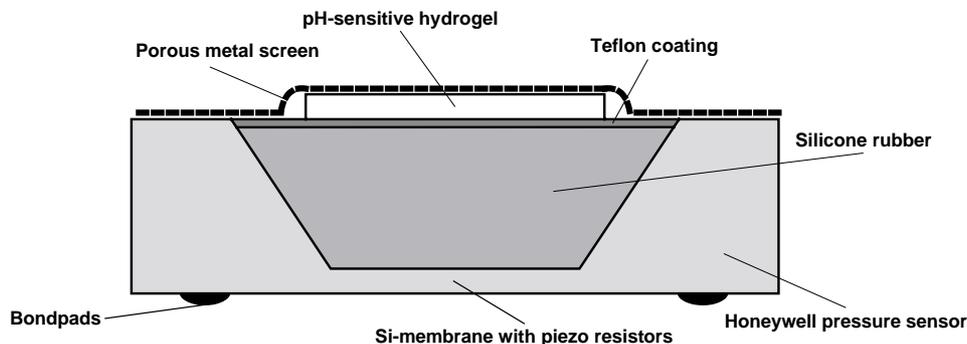


Fig. 3. Schematic representation of the fabricated hydrogel-based sensor.

hydrogel disk that is placed on it afterwards, see Fig. 3. This is because, otherwise, the disk will not generate pressure in an uniform way. The disk is then clamped by a porous metal screen which is kept on place by a thick-wall shrink tube. Fig. 4 shows a photo of the fabricated sensor.

3.4. Experimental setup

Both the hydrogel-based sensor and a pH electrode were connected to a National Instruments data acquisition card. LabView software was written to monitor the pH and pressure versus time. All experiments were performed at room temperature.

For characterization of the hydrogel-based sensor, 100 mM pH buffers were prepared ranging from pH 4 to 10. The buffers were made with citric acid, mes, hepes, boric acid and glycine and all reagents were used as received. The sensor was placed in each of the buffers until the hydrogel was equilibrated with the pH. This way the relation between the pH and the generated pressure could be characterized.

For the CO_2 measurements a 100 mM sodium bicarbonate solution was prepared. The sensor was placed in the solution together with a Radiometer pH glass electrode. The solution was constantly stirred and CO_2 or N_2 were led trough the solution to change its pH.



Fig. 4. Photo of the hydrogel-based sensor.

4. Results and discussion

The pressure the hydrogel generated as a function of pH is shown in Fig. 5. The initial pressure was 0.7 bar at pH 10. This pressure is caused by two cumulative factors, namely the pressure generated by the neutral swelling of the hydrogel, due to its hydrophilicity, and the offset pressure, which is caused by the pressure that the metal screen exerts on the hydrogel disk. This last offset pressure was applied deliberately to be sure that the hydrogel disk is clamped sufficiently. As can be seen in the figure, the pressure increases with decreasing pH. At pH 4 the pressure increased to 1.34 bar. The pH range in which we are interested lies between pH 7.48 and 8.25. Expected was that the pressure response of the sensor would be optimal in this range. Unfortunately the response is poor above pH 8.

Fig. 5 shows that the hydrogel generates more pressure with decreasing pH. At decreasing pH more amine groups of the poly(HEMA-co-DMAEMA) hydrogel are protonated, resulting in an influx of counterions into the hydrogel. As a result, the osmotic pressure inside the hydrogel will be higher than the osmotic pressure of the solution, and consequently the hydrogel swells until the elastic forces inside the hydrogel are equal to the osmotic force. Note that when a hydrogel with functional acid groups would be used the pressure would increase with increasing pH.

The titration curve of DMAEMA is also given in Fig. 5. Expected was that the generated pressure curve would have a similar shape as the titration curve since DMAEMA is incorporated in the hydrogel. In our case the pK_a of the hydrogel can be defined as the pH at which half of the maximum pressure is generated. Fig. 5 shows that this pK_a is shifted down and that the pH response range is wider. This can

be explained as follows. Due to decreasing pH, the amine groups get protonated and thus, get a positive charge. Consequently, electrical fields are formed around the groups repelling H^+ ions. In the case of our pH-sensitive hydrogel the density of amine groups is high and the fields can overlap when protonated amine groups are within the electrical screening (Debye) length. The result is an equilibrium where the amount of H^+ ions around the hydrogel is higher than inside. Thus, the pH inside the hydrogel is higher than the pH of the surrounding solution, decreasing the number of protonated groups with respect to the monomer. Therefore an apparent pK_a of the hydrogel should be used [11,12]. The situation is schematically represented in Fig. 6a. Furthermore, the more amine groups get protonated, the more amount of work is needed to protonate the remaining groups due to the increasing presence of repellent electric fields. The result is the wide pH range in which the hydrogel responds. When the density of amine groups is lowered, the above effects are less prominent (Fig. 6b). This can be verified by adding solvent during synthesis as Sheppard et al. did [13,14]. The pK_a they found was closer to the pK_a of DMAEMA.

A CO_2 experiment was performed with the same device and the result is shown in Fig. 7. 100% N_2 gas was led through a 100 mM bicarbonate solution and at $t = 0$ s the N_2 was replaced by 100% CO_2 . The result is a decrease in pH from 8.9 to 6.7 by the acidification of the CO_2 causing an increase of the pressure generated by the hydrogel from 0.68 to 0.96 bar. At $t = 800$ s the CO_2 was replaced by the N_2 again. As expected, the pH increased and consequently the pressure decreased. The time the hydrogel-based sensor needed to reach equilibrium with the pH change caused by CO_2 was around 800 s, which is faster than in the former experiments with microspheres where it took more than 3000 s

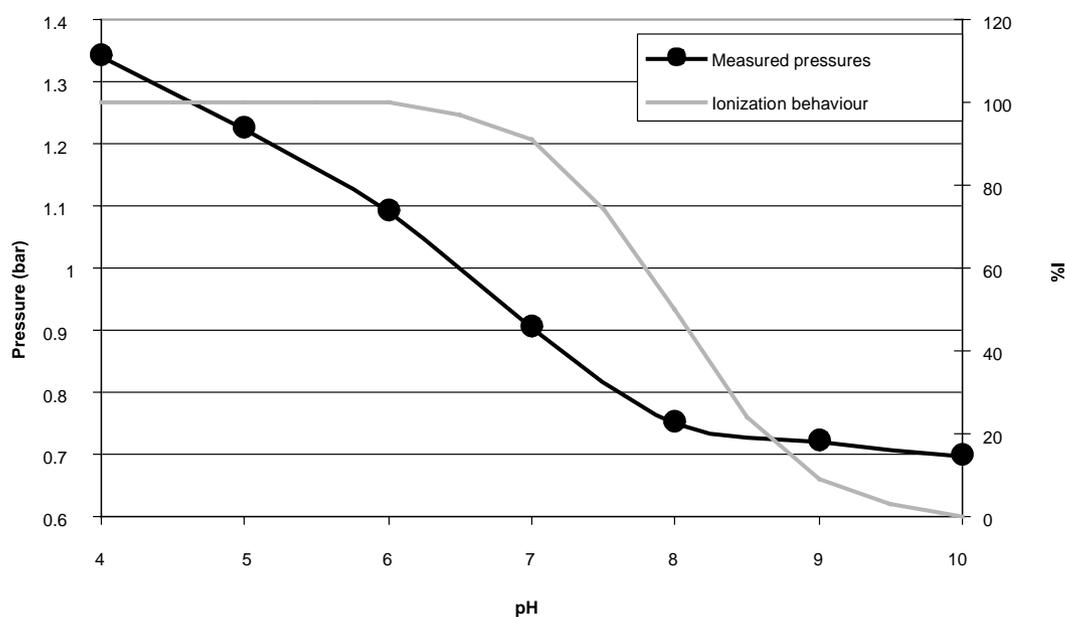


Fig. 5. The pressure the HEMA-co-DMAEMA hydrogel generates as a function of pH (black line, left y-axis) and the theoretical degree of protonation vs. pH for the monomer DMAEMA (grey line, right y-axis).

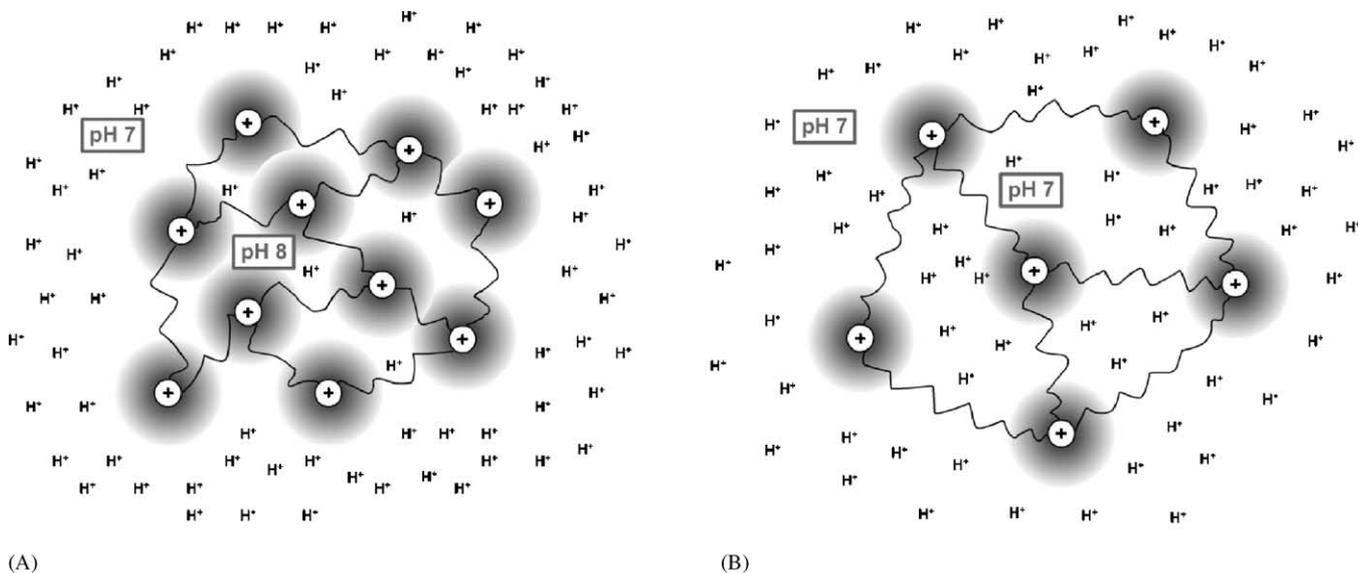


Fig. 6. (A) Schematic representation of a protonated high-density hydrogel with repellent electrical fields that prevent H^+ ions to enter the hydrogel. (B) Schematic representation of a protonated low-density hydrogel with repellent electrical fields. The H^+ ions can easily enter the hydrogel resulting in an equal pH inside and outside.

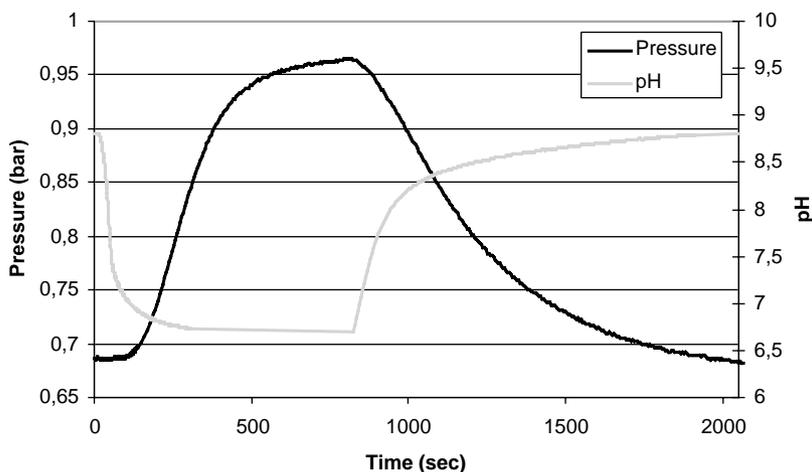


Fig. 7. Plot of the pH change of a 100 mM sodium bicarbonate solution and the pressure change of the hydrogel-based sensor as result of a gas flow change from 100% N_2 to 100% CO_2 (at $t = 0$) and back to 100% N_2 (at $t = 800$).

[9]. The experiment agrees well with the previous one. The acidification by 100% CO_2 gives the bicarbonate solution a pH of 6.7. Interpolation of this value in Fig. 5 yields a pressure of 0.95 bar which is almost equal to the 0.97 bar measured during the CO_2 experiment.

5. Conclusions and recommendations

A hydrogel-based P_{CO_2} sensor is demonstrated where a thin hydrogel disk is enclosed between a pressure sensor and a porous screen. Experiments showed that the sensor responded to CO_2 . The pressure generated by the pH-sensitive hydrogel due to the acidification by CO_2 agrees reasonably well with the pressure found by interpolation of the char-

acterization plot pressure versus pH. The redesigned sensor responded almost four times faster than the previous design. The faster response was obtained by using a thin hydrogel disk, instead of microspheres.

In future the use of thin layers hydrogel will be continued because they are easy to handle, simple to make, their dimensions are well-defined by photolithography and they generate a stable pressure signal. The apparent pK_a of the hydrogel should be increased to obtain a larger pressure response around pH 8 and thus, higher sensor sensitivity. This can be done by adding solvent to the hydrogel to decrease the density of titratable groups. This will also make the hydrogel faster because less protons need to diffuse into the polymer. Miniaturization will reduce the sensor response time even more. Decreasing the thickness of the hydrogel

layer results in a faster swell/deswell equilibrium but also in a decrease of generated pressure and thus, accuracy. A compromise should be found where both the response time and accuracy are acceptable. Miniaturization also involves the fabrication of a silicon porous cover since enclosing thinner hydrogels is hard to achieve by applying a metal screen by hand. Furthermore the sensor has to be completed with a CO₂ permeable membrane.

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