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# Dissolved ammonia sensing in complex mixtures using metalloporphyrin-based optoelectronic sensor and spectroscopic detection

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ABSTRACT

We demonstrate dissolved ammonia ($NH_3$) sensing in complex mixtures using an optoelectronic sensor comprising a composite sensing material based on a metalloporphyrin zinc tetraphenylporphyrin (ZnTPP) and spectroscopic detection. The metalloporphyrin dye is incorporated within ion-exchange polymeric microbeads arranged in a microfluidic array. Spectroscopic analysis at multiple wavelengths allows sensitive detection in complex backgrounds. The sensor shows preferential sensitivity to ppm levels of concentrations of $NH_3$ dissolved in water, as well as in human saliva, making it relevant for medical diagnostic applications (e.g. detection of stomach bacterial infections). The microfluidic platform and a miniaturized optical arrangement provide a potential for the development of a portable low-power sensor for detection of dissolved ammonia for a variety of applications.

## 1. Introduction

Detection of ammonia ($NH_3$) is of great importance in a variety of fields, including life sciences, medicine, biotechnology, environment and agriculture [1]. Conventionally, $NH_3$ detection was based on electrochemical measurement using potentiometric electrodes [2–4]. However, electrochemical $NH_3$ sensors are not accurate as their performance can be affected by surface potentials leading to a signal drift and suffer from long-term reliability. Another type of ammonia sensors is based on solid-state semiconductor devices [5]. However, these sensors are insufficiently selective, since they respond to other gases and even changes in humidity.

As an alternative, several types of optical sensors have been suggested for detection of $NH_3$ in gaseous and liquid environments. One possible configuration is a device consisting of an optical fiber covered with a solution of ninhydrin embedded in a polymeric matrix that changes its color on contact with gaseous $NH_3$ [6]. However, the ninhydrin reaction is chemically irreversible and also sensitive to amines. A reversible optical sensor based on an oxazine perchlorate dye was shown to be capable of sensing $NH_3$ vapors in 60–1000 ppm range using absorbance measurements [7]. The sensor consisted of a glass capillary tube fitted with a light-emitting diode and a phototransistor detector and coated with a thin solid film containing the dye.

Another configuration is sensors based on optical fibers, using pH indicator dyes embedded within polymeric matrix [8–15], sol–gel films [16–18] or gels [19,20] as a sensing material. Such sensors can be used for $NH_3$ detection in liquid environments [15,20], requiring, however, some kind of selectively permeable membrane. The main disadvantages of such sensors are lack of selectivity and a limited range of response, due to the unselective nature and narrow pH range of sensitivity of the pH indicator dye. Ion pair-based $NH_3$ sensors, with the pH indicator dye forming an ion pair with a lipophilic quaternary ammonium salt, have also been developed. The advantage is that such ion pairs can be homogeneously dissolved in various polymeric matrixes that can also serve as a separator [21].

A relatively recent approach applied for colorimetric detection of gases (including $NH_3$) [22,23] and organic compounds dissolved in water [24] is based on the use of metalloporphyrins. Metalloporphyrins are metal ion containing organic dyes that respond to analytes capable of Lewis acid/base interactions, in contrast to pH indicator dyes that respond to changes in the proton (Brønsted) acidity or basicity. Ammonia can act as a Lewis base, donating its free electron pair, which makes metalloporphyrins a favorable

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choice for detection of $NH_3$ dissolved in water. Of course, $NH_3$ detection in complex aqueous samples can be still very challenging, due to the possible interference with other compounds and leaching of the sensing material in contact with water.

In this contribution, we demonstrate a novel approach for aqueous phase ammonia sensing, which is based on a composite sensing material and microfluidic optoelectronic sensing platform with spectroscopic detection. The sensing material is composed of zinc tetraphenylporphyrin (ZnTPP) dye impregnated in ion-exchange polymer microbeads arranged in a microfluidic array. Such configuration allows for effective sensing in direct contact with aqueous environment, while preventing undesirable washout of the dye. As a sensing strategy, we employ spectroscopic analysis of optical transmission in a visible range of spectrum (instead of measurement at a single wavelength), using white light-emitting diodes as a source of irradiation, optical fiber as a light guide and a portable miniature spectrometer as a detector. The sensor is sensitive to ppm level concentrations of dissolved $NH_3$ and has enhanced sensitivity to $NH_3$ as compared to other strong and weak bases we tested. Moreover, detection of ppm concentrations of $NH_3$ dissolved in human saliva was possible, providing a potential for medical diagnostic applications, such as noninvasive detection of some stomach bacterial infections, e.g. *Helicobacter pylori* infection, which is a primary identified cause of stomach cancer. This bacterium survives in a highly acidic stomach environment by converting urea into $NH_3$ (decreasing the acidity) [1,25,26].

## 2. Experimental

### 2.1. Materials

The following materials were used for preparation of the sensing material: Zn(TPP) (5,10,15,20-Tetraphenyl-21*H*,23*H*-porphine zinc, Sigma–Aldrich) and cation exchange resin microbeads powder (Dowex® 50WX4 hydrogen form, ~40–80 μm, Sigma–Aldrich). Ammonium hydroxide solution 28–30% $NH_3$ basis (Sigma–Aldrich), sodium hydroxide 0.1 M (Sigma–Aldrich), sodium bicarbonate powder >99.5% (Sigma–Aldrich), pyridine >99% (Sigma–Aldrich) and deionized water were used for preparation of analyte solutions.

The saliva sample was collected and processed at our lab. After a 30 min period of food and liquid abstinence, the volunteer was instructed to expectorate every 30 s into a 50 ml glass beaker. A total of 10 ml of whole saliva was collected. The saliva was diluted 10-fold by adding deionized water under continuous stirring using a Teflon bar magnetic stirrer. The saliva sample was analyzed immediately after the collection [27–29].

### 2.2. Microfluidic device fabrication

The details of the microfluidic device fabrication procedure can be found in our previously published work [30]. Briefly, a mask with desired master features was first fabricated. A photoresist SU-8 2100 was spin-coated on a clean wafer, followed by soft bake. The wafer was then placed into the OAI Model 204 mask aligner and exposed to 365 nm light, followed by post exposure bake. The wafer was then developed in the SU-8 developer, rinsed with isopropanol and dried using nitrogen gun. The PDMS base/curing agent ratio was 10:1. The prepared PDMS mixtures were first placed in a vacuum desiccator for degassing and then poured on top of the master, followed by vacuum degassing again. The master was then placed inside an oven to cure the device layer. The PDMS mold was cut around the edge of the master wafer and peeled up. Fluid inlet and outlet holes of the PDMS device were punched using a 16 gauge needle before placing it into the Reactive Ion Etcher (RIE) chamber. The March CS-1701F RIE was used (50 mT). Immediately after removing from the RIE chamber, the PDMS molds were pressed gently, ensuring that a strong bond is formed.

### 2.3. Sensing material preparation and deposition

The dye solution was prepared by first dissolving 22.5 mg of Zn(TPP) dye in 1 ml of ethanol (>99.5%, Sigma–Aldrich) followed by adding of 4 ml of deionized water. Subsequently, 563 mg of cation exchange resin microbeads powder and 5 ml of deionized water were added to the dye solution and stirred for 5 h at room temperature, in order to create ionic bonding between the Zn(TPP) dye and the beads.

During the deposition, the (previously prepared) suspension of Zn(TPP)-doped microbeads was continuously stirred (using a magnetic stirrer). The microbeads were deposited into the wells (500 μm diameter and depth) of the microfluidic device by circulating the microbeads suspension through the device for 5 min using a peristaltic pump (Fig. 1a). Fig. 1b shows a microfluidic device and a close-up on an array of microwells with deposited Zn(TPP)-doped microbeads. A micrograph of the doped microbeads within the microwells is shown in Fig. 1c.

### 2.4. Experimental setup

Fig. 1a shows the experimental system composed of an optical setup and a flow system. White LED was used as a light source. The light transmitted through the sensing array was guided by an optical fiber (QP400-2-UV-VIS 400 μm premium fiber, UV/VIS, 2 m with 74-UV UV/VIS collimating lens, 200–2000 nm, Ocean Optics) connected to a portable spectrometer (USB650, Ocean Optics).

## 3. Results and discussion

### 3.1. Sensor response to dissolved $NH_3$, $NaHCO_3$, $C_5H_5N$ and NaOH

Fig. 2 shows continuous wavelength transmission spectra recorded under the sensor exposure to dissolved $NH_3$ (17 ppm), $NaHCO_3$ (830 ppm), $C_5H_5N$ (1000 ppm) and NaOH (40 ppm). All spectra (recorded with integration time of 100 ms) were first normalized to the maximal transmission intensity and the reference spectrum obtained with deionized water was subsequently subtracted, i.e. $\Delta T = 0$ means no response and higher $\Delta T$ (absolute) magnitude indicates higher response. For $NaHCO_3$ and $C_5H_5N$ (pyridine), significantly higher concentrations (as compared to $NH_3$ and NaOH) were required in order to obtain detectable responses.

We can see clear changes in transmittance upon the exposure to dissolved $NH_3$ (Fig. 2a). There are opposite shifts in different ranges of the spectrum: for 430–460 nm and 630–680 nm the shift is positive, while for 510–530 nm it is negative, with essentially no response for 530–630 nm. The spectrum shifts correspond to the change in the Zn(TPP) dye color, from green to purple under exposure to dissolved $NH_3$, hence the transmission increases in the purple part of the spectrum (430–460 nm) and decreases in the green range (510–530 nm). This observation emphasizes the advantage of the sensing strategy that employs spectroscopic analysis of the entire visible spectrum rather than focusing at a specific wavelength or a narrow range. The same approach was also successfully employed in our prior work for detection of $CO_2$ [30].

In order to evaluate the sensor performance with respect to other bases, we selected two weak bases, which can act as Lewis bases donating a lone electron pair: sodium bicarbonate ($NaHCO_3$) and pyridine ($C_5H_5N$). In addition, we tested the sensor response to a strong base sodium hydroxide (NaOH). Obviously, the hydroxide anion resulting from the NaOH dissociation can also act as a Lewis base, since it has lone electron pairs, which can be donated to Lewis acids, such as metalloporphyrins. The spectra are shown in Fig. 2.

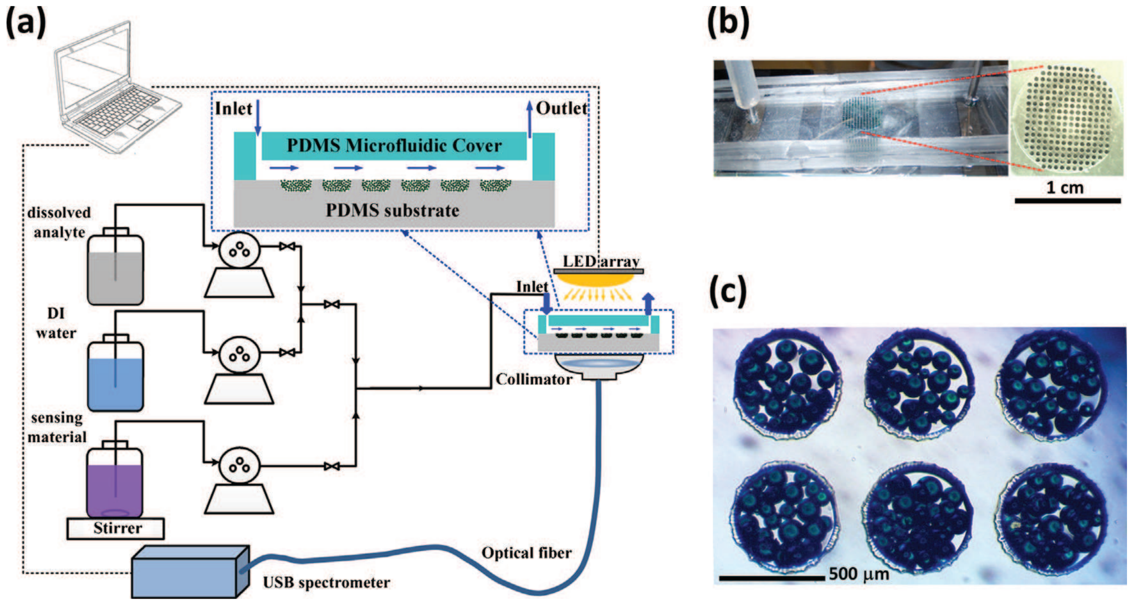

**Fig. 1.** (a) Schematic representation of the optical setup and flow system; (b) array of Zn(TPP)-doped microbeads embedded in the microfluidic device; and (c) a micrograph of Zn(TPP)-doped microbeads trapped inside microwells.

It can be seen that the response magnitude and the shape of the obtain spectra differ significantly depending on the analyte. In principle, such "signatures" can be used to distinguish between various analytes in complex environments, even using just a single dye. The response spectrum of $NaHCO_3$ solution resembles that of $NH_3$, but differs significantly in magnitude, particularly given the difference in concentrations used (17 and 850 ppm for $NH_3$ and $NaHCO_3$ respectively). Exposure to the 1000 ppm $C_5H_5N$ solution resulted in a positive shift in transmittance over most of the recorded range, with varying amplitude of the response, which was weak in overall.

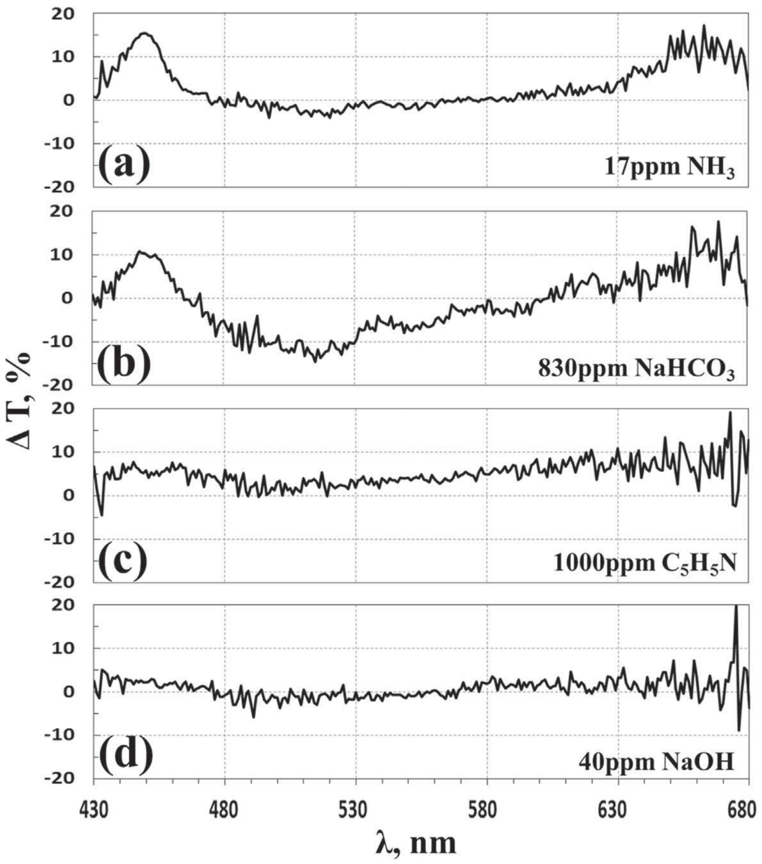

**Fig. 2.** Normalized transmittance spectra recorded under the sensor exposure to 17 ppm of $NH_3$ (a), 833 ppm of $NaHCO_3$ (b), 1000 ppm of $C_5H_5N$ (d), and 40 ppm of NaOH (e) dissolved in deionized water.

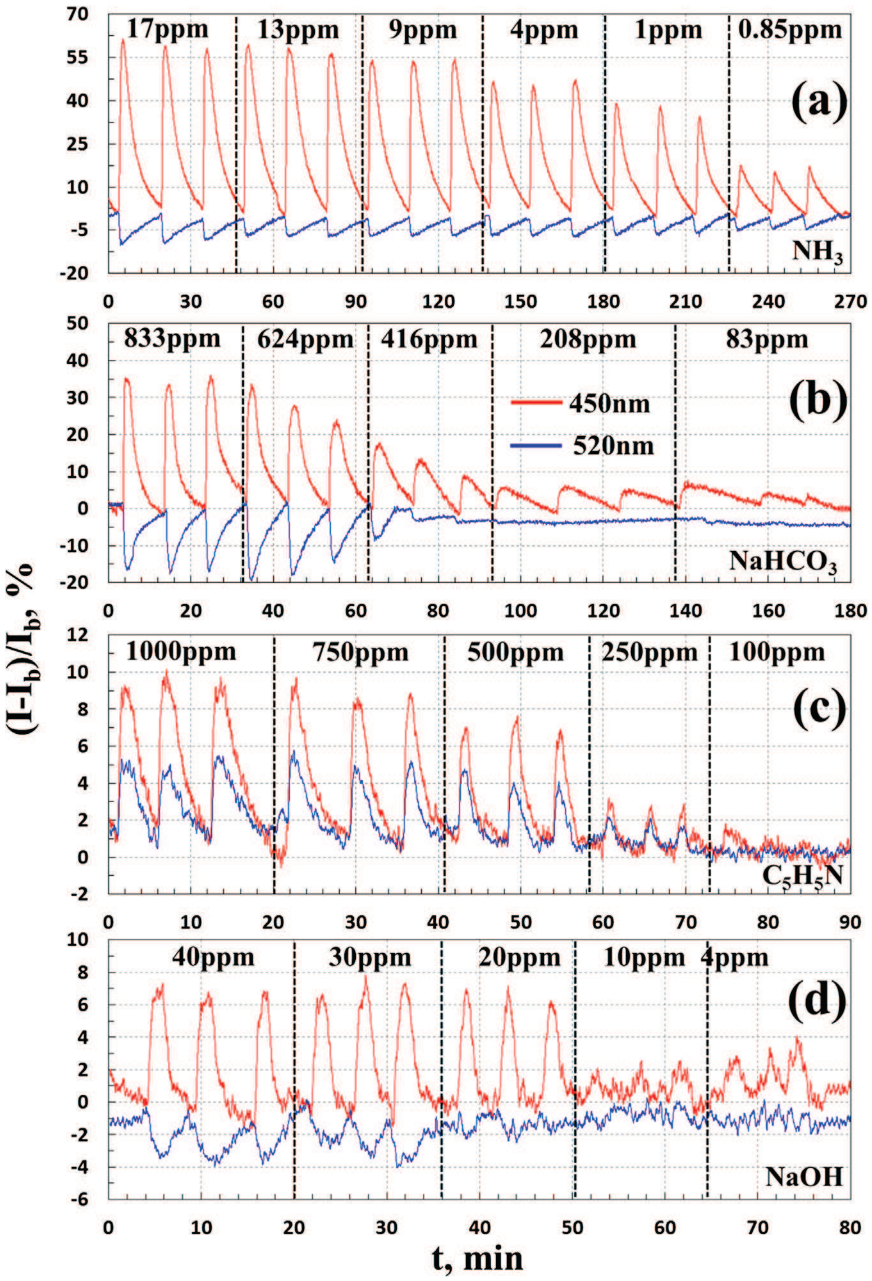

**Fig. 3.** Sensor response (transmittance normalized to baseline) to different concentrations of dissolved $NH_3$ (a), $NaHCO_3$ (b), $C_5H_5N$ (c), and NaOH (d) at 450 nm (red color) and 520 nm (blue color).

The spectrum obtained with the 40 ppm NaOH solution resembled the response to $C_5H_5N$ in both shape and magnitude. The observed changes in the Zn(TPP) dye color were from green (exposed to water) to different variations of purple, depending on the analyte.

### 3.2. Concentration dependent sensor response

Fig. 3 shows examples of the sensor response to decreasing concentrations of dissolved analytes, while using deionized water as a reference, at two wavelengths (450 and 520 nm). These wavelengths were selected because of relatively low noise level and the intensity was averaged over 10 measurements to further smooth the data (same procedure was applied for all data). The response is shown in terms of the measured intensity ($I$) normalized to the baseline intensity ($I_b$, recorded when the device is under constant flow of deionized water). The exposure time was 30 s of feeding the analyte solution through the device, followed by the recovery with a constant flow of deionized water (flow rate of 0.5 ml/min was used in all experiments). It should be noted here that, while the sensor response was fast, the recovery was relatively slow (Fig. 3).

For $NH_3$ (Fig. 3a), the range was 17 ppm–850 ppb of dissolved $NH_3$. The response sign was opposite for two wavelengths (450 and 520 nm) and the magnitude was different as well. It is important to note that the sensor showed high sensitivity toward dissolved $NH_3$, showing a clear response even to sub-ppm concentrations. The detection limit for dissolved $NH_3$ was 420 ppb (not shown in Fig. 3), while no response was obtained below 83 ppm for $NaHCO_3$, for any wavelength recorded. The dynamics of the response to dissolved $NaHCO_3$ was similar to that observed for $NH_3$ for relatively high $NaHCO_3$ concentration (>500 ppm, Fig. 3b). The sensor responses to dissolved $C_5H_5N$ (100–1000 ppm) and NaOH (4–40 ppm) were relatively weak.

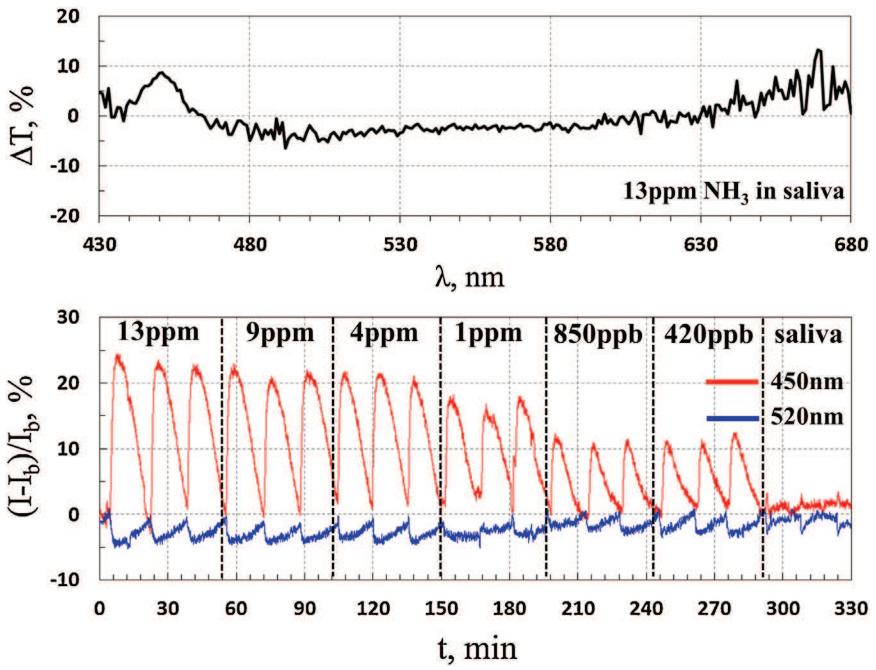

**Fig. 4.** Transmittance spectra recorded under the sensor exposure to 13 ppm $NH_3$ dissolved in diluted saliva (upper panel) and sensor response to different concentrations of $NH_3$ dissolved in diluted saliva at 450 nm (red color) and 520 nm (blue color).

### *3.3. Sensor response to dissolved $NH_3$ in human saliva background*

To evaluate the sensor potential for medical diagnostic applications we exposed the sensor to $NH_3$ dissolved in diluted samples of human saliva. Such sensing can be useful, for example, for non-invasive detection of stomach bacterial infection, e.g. *H. pylori* that survives in a highly acidic environment by converting urea into $NH_3$ [1,25,26]. Fig. 4 (upper panel) shows the transmission spectra (normalized and subtracted as explained in Section 3.1) recorded under the sensor exposure to diluted human saliva containing 13 ppm of $NH_3$ (the procedure of saliva samples preparation is described in Section 2.1). The bottom panel of Fig. 4 shows the sensor response to decreasing concentrations of $NH_3$, while using deionized water as a reference.

The spectrum shape resembles that obtained with $NH_3$ dissolved in deionized water, with a somewhat lower response magnitude. Given that the characteristic "signature" of dissolved $NH_3$ was obtained, it can be concluded that the sensor responded predominantly to $NH_3$. This conclusion is supported by the fact the sensor sensitivity to the reference sample (diluted saliva prepared as previously, but without any addition of $NH_3$) was very low (right side of the bottom panel in Fig. 4). Very low (but still detectable) responses to the diluted saliva sample may refer to salivary $NH_3$, as well as to other interfering molecules. In any case, there is very little interference with other compounds present in saliva, as compared

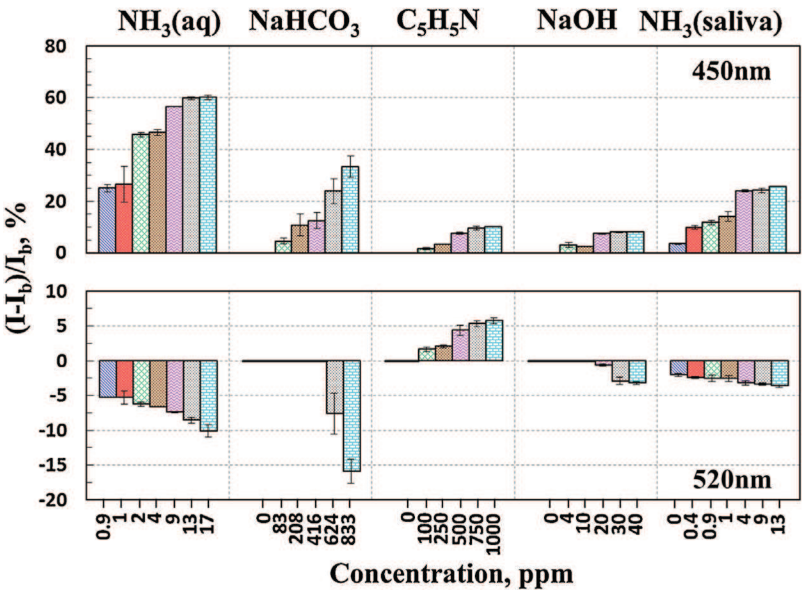

**Fig. 5.** Sensor response magnitude at 450 and 520 nm for different concentrations of $NH_3$, $NaHCO_3$, $C_5H_5N$, and NaOH dissolved in deionized water and of $NH_3$ dissolved in diluted human saliva. Error bars show standard deviation between three measurements.

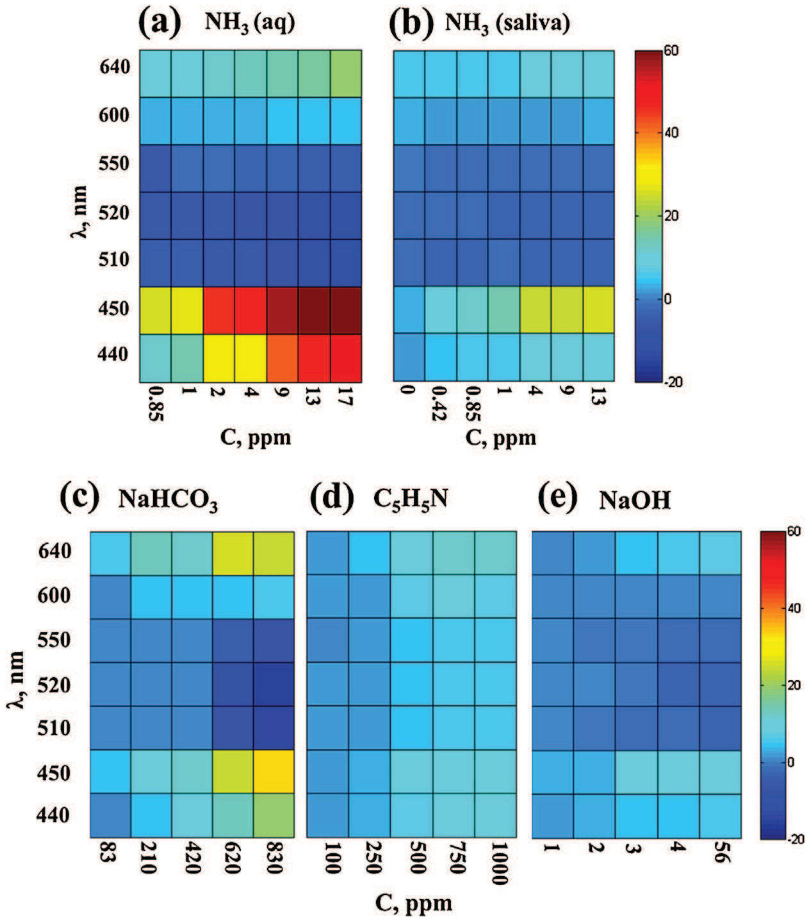

**Fig. 6.** Sensor response magnitude at a range of wavelengths for different concentrations of $NH_3$ dissolved in deionized water (a) and diluted human saliva (b). Sensor responses to $NaHCO_3$ (c), $C_5H_5N$ (d) and NaOH (e) dissolved in deionized water are also shown.

to sub-ppm levels of $NH_3$. As in case of $NH_3$ dissolve in deionized water, the sensor was sensitive even to sub-ppm $NH_3$ concentrations (bottom panel of Fig. 4).

### 3.4. Sensitivity and selectivity

Fig. 5 summarizes peak responses obtained at 450 and 520 nm (error bars show standard deviation between three responses). At 450 nm, the responses to all analytes are positive, but differ significantly in magnitude. At 520 nm, the response magnitude is significantly lower, but sensitivity to ppm levels of dissolved $NH_3$ is still good. Keeping in mind that different scales of concentrations were used, it can be concluded that the sensor is preferably sensitive to dissolved $NH_3$. A substantially high sensitivity is still obtained for $NH_3$ dissolved in diluted saliva.

Therefore, the sensor has no significant interference with salivary compounds and has a potential for use in medical diagnostic applications, with an important advantage of non-invasiveness, as compared to endoscopy. Typical $NH_3$ concentrations in gastric juice can vary from ~50 ppm for healthy individuals to ~200 ppm for those infected with *H. pylori* [31]. Breath analysis is an alternative, but ammonia presents in the breath at much lower concentrations of 100 ppb–2 ppm as a part of a complex mixture of other volatiles, making $NH_3$ detection quite challenging [25]. Salivary $NH_3$ concentrations are just slightly lower than those in the gastric juice starting from ~20 ppm [32]. The sensor we demonstrate here is sensitive to even much lower $NH_3$ concentrations (Fig. 5).

Fig. 6 summarizes the results obtained in the entire range of (visible) spectrum, in terms of the response magnitude in the two-dimensional plane of wavelength vs. concentration. Evidently, the sensor is predominantly sensitive to dissolved $NH_3$ (including in saliva). Moreover, though there are some similarities between these "fingerprints", they differ sufficiently in order to discriminate between dissolved $NH_3$ and other weak and strong bases tested. The similarity in response reflects the nature of the specific dye molecule electronic structure change as a result of the Lewis acid–base interaction with the analyte. This actually emphasizes the advantage of the spectroscopic sensing strategy (analyzing the entire spectrum) we have employed that allows for detection of rather subtle differences between analytes that interact with the dye molecule by a qualitatively identical mechanism. Though the "fingerprint" obtained with $NaHCO_3$ qualitatively resembles that of $NH_3$, it is very different quantitatively (compare the range of concentrations). These results indicate that the sensor can be used for detection of ppm and sub-ppm levels of dissolved $NH_3$ in complex aqueous environments, in the presence of other compounds that can act as Lewis bases.

### 3.5. Sensing mechanism

Generally speaking, metalloporphyrins are expected to be sensitive to Lewis bases that can donate their lone electron pairs to the metalloporphyrin metal ions that behave as Lewis acids. Since metalloporphyrins are always intensely colored and typically exhibit large spectral shifts upon analyte binding, they are expected to be suitable for sensing based on optical techniques. In addition to that, our findings indicate that a single metalloporphyrin dye (Zn(TPP)) incorporated into cation exchange polymeric microbeads can be used for discrimination between various compounds with Lewis basicity in aqueous environments and, importantly, without the use of any $NH_3$ permeable membrane or another kind of separation.

Due to the spectroscopic detection approach we have employed, shifts in different regions of the visible spectrum upon exposure to analytes are simultaneously recorded, providing characteristic signatures which can be used for sensing in complex environments. Specifically, the metalloporphyrin dye Zn(TPP) changes its color from green to purple under exposure to Lewis bases dissolved in aqueous medium, hence the transmission decreases in the green range (510–530 nm) and increases in the purple part of the spectrum (430–460 nm). Depending on the strength of the analyte–dye interaction, the color can change from bright purple to dark purple, resulting in corresponding differences in the spectrum shift magnitude (change in the transmittance intensity).

The enhanced sensitivity of the sensor to dissolved $NH_3$ could be attributed to the specific interactions between $NH_3$ (which is a good Lewis base) and Zn(TPP), but also to additional effects related to ionic interactions between the metalloporphyrin metal ion and the cation exchange resin (microbeads). Regardless, the use of the cation exchange micro-structured material provides important advantages of preventing washout and, simultaneously, high surface-to-volume ratio, which is essential for sensitivity.

## 4. Conclusions

A novel optoelectronic sensor for detection of dissolved $NH_3$ based on the metalloporphyrin dye Zn(TPP) incorporated into cation-exchange polymer microbeads incorporated inside a microfluidic channel is demonstrated. The use of the composite sensing material and spectroscopic detection offers sensitive detection of dissolved $NH_3$ in complex environment directly in liquid samples, without the use of any $NH_3$ separating membrane. The simple and flexible optical setup the microfluidic platform provides a potential for a variety of applications, where portable detection of dissolved ammonia in small liquid samples is required. The sensor has much more pronounced sensitivity to ppm and sub-ppm levels of dissolved $NH_3$, as compared to other strong and weak bases. In addition, we demonstrate that the sensor is suitable for sub-ppm level detection of $NH_3$ dissolved in human saliva which provides a potential for medical diagnostic applications.

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