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PII: S0039-9140(17)30239-4
DOI: http://dx.doi.org/10.1016/j.talanta.2017.02.025
Reference: TAL17301

To appear in: *Talanta*

Received date: 16 December 2016
Revised date: 7 February 2017
Accepted date: 10 February 2017

Cite this article as: N.T. Brannelly and A.J. Killard, An electrochemical sensor device for measuring blood ammonia at the point of care, *Talanta* http://dx.doi.org/10.1016/j.talanta.2017.02.025

An electrochemical sensor device for measuring blood ammonia at the point of care

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Abstract

The level of ammonia in blood is relevant in a number of medical conditions. While ammonia is a marker of dysfunction, elevated ammonia is itself a serious medical emergency and can lead to significant and permanent neurological impairment if not addressed quickly. Blood ammonia testing is typically performed in the central laboratory. While a number of point of care devices have been developed, these are based on classical enzymatic or colorimetric principles and have not been widely adopted. In this work, an electrochemical sensor device was developed for measuring blood ammonia. The device was based on the deposition of polyaniline nanoparticle films onto screen printed interdigitated electrodes using inkjet printing and their integration into a polymer microfabricated device with a polytetrafluoroethylene membrane. The device required a 52 µL serum sample and measured the change in impedance of the sensor with respect to air at 1 kHz, 5 mV rms. The device was capable of the measurement of ammonia in serum across the physiologically relevant range of 25 to 200 µM (r^2 = 0.9984) and had a limit of detection of 12 µM (n = 3). The device showed no significant issues with common electrochemical interferences in blood. The device was also validated against a commercial spectrophotometric assay which resulted in excellent correlation (r = 0.9699, p < 0.0001) between both methods (n = 3). When stored under desiccation, devices displayed minimal variation over time (0.64%) with respect to their impedance in air (n = 12) and could be stored in desiccant for at least five months.

Introduction

Ammonia is produced in the body during the metabolism of amino acids. In the liver, it is converted to urea via the urea cycle and excreted by the kidneys as urine. Normal levels are between 11 and 50 µM, whereas a blood ammonia level of approximately 100 µM indicates pathology [1]. Elevated blood ammonia is associated with a number of pathological conditions. Many of these can affect brain function, causing hyperammonaemic encephalopathy and can be fatal. This is particularly critical in many disorders such as hyperammonaemia of the new-born, inborn errors of metabolism including urea cycle defects, organic acidaemias, hyperinsulinism/hyperammonaemia and liver disease [2]. There has been an increase in research efforts around electrochemical sensors for healthcare use due to increases in population and lifespan along with the need to reduce ever-increasing healthcare costs [3]. Electrochemical sensors have demonstrated the capability of addressing point of care (POC) testing requirements by providing accurate and rapid measurement in complex matrices such as blood. Together with mass production and fabrication techniques they are used to deliver inexpensive, disposable, single use sensors [4]. Polyaniline has been employed as a sensing layer for a range of analytes. The most studied is its interaction with ammonia [5]. Polyaniline has an affinity for ammonia which operates on the deprotonation of the polyaniline backbone, leading to the formation of an ammonium ion. In this work, polyaniline nanoparticles were fabricated and inkjet-printed onto silver screen printed electrodes. The sensors were then incorporated into devices containing a gas-permeable membrane, which facilitated the measurement of gaseous ammonia from a liquid sample

(blood) using electrochemical impedance spectroscopy. The combination of impedance spectroscopy with a gas-permeable membrane allowed the measurement of gaseous ammonia from solution.

Materials and Methods

Materials

Acetaminophen (AC100) and L-ascorbic acid (BDH9242) were purchased from the British Drug House Ltd. (Poole, UK). Potassium chloride (P/4280/53), potassium dihydrogen orthophosphate (P/4800/53), 2-propanol (A461), sodium chloride (S/3160/60), sodium dodecyl sulphate (S/5200/53), sodium hydroxide (S/4920/60) and disodium hydrogen orthophosphate (S/4520/53) were purchased from Fisher Scientific UK Ltd. (Loughborough, UK). Ammonium chloride (326372), ammonium persulphate (A7460), aniline (132934; distilled and stored frozen under nitrogen before use), cellulose acetate dialysis tubing 22 mm width with a molecular weight cut off of 14 kDa (D9777), creatinine anhydrous (C4255), L-glutamic acid monosodium salt monohydrate (49621), uric acid (U2625) and Whatman® 0.2 µm polytetrafluoroethylene (PTFE) membrane filters (WHA10411411) were purchased from Sigma-Aldrich Company Ltd. (Dorset, UK).

Other materials were obtained as follows: Ammonia Assay Kit – Modified Berthelot (ab102509) was purchased from Abcam® Plc. (Cambridge, UK). Compressed air was provided by BOC (British Oxygen Company Ltd., Manchester, UK). Dodecylbenzene sulphonic acid (DBSA) soft type (D0989) was purchased from TCI Europe N.V. (Zwijndrecht, Belgium). Pooled delipidated processed serum (S139) was purchased from Scipac Ltd. (Kent, UK). Rubber o-rings (BS013 Viton) were purchased from Polymax Ltd. (Hampshire, UK). Polyester pressure sensitive adhesive (PSA, ARcare 92712) of 48 µm thickness were supplied by Adhesives Research Inc. (Limerick, Ireland). Preshrunk polyethylene terephthalate (PET) substrates of 175 µm thickness were supplied by HiFi Industrial Film Ltd. (Hertfordshire, UK). Sericol (ZT639) was purchased from Fujifilm Dimatix Inc. (Santa Clara, CA). Electrodag PF-410 silver conductive ink was purchased from NorCote International, Ltd. (Hampshire, UK).

Instrumentation

Screen printing was performed with a semi-automated DEK-248 printing machine (DEK International, Dorset, UK). Inkjet printing was carried out using a Dimatix Materials Printer DMP-2831 with Dimatix Drop Manager DMP-2800 series software (Fujifilm Dimatix Inc., Santa Clara, CA). The MEMS-based Dimatix cartridge with 16 nozzles (20 µm diameter) spaced at 254 µm was used. Centrifugation of polyaniline nanoparticles was carried out using a Beckman Coulter Allergra X-22R Centrifuge with a Beckman C0650 conical rotor head. A Graphtec CE5000-40 Craft Robo Pro cutting plotter (Graphtec GB Ltd., Wrexham, UK) and Robo Master-Pro software were used to prepare the PSA patterns for encapsulation of the sensor. All electrochemical protocols were performed on a Metrohm Autolab PGSTAT 128N potentiostat (Metrohm UK Ltd., Cheshire, UK) with Nova 1.6 software equipped with a FRA2 electrochemical impedance analyser. Unless otherwise stated all measurements were performed at room temperature 25 ± 3°C. A Fluostar Optima spectrophotometer was used to analyse spectrophotometric results (BMG LabTech Ltd., Buckinghamshire, UK).

Electrode fabrication via screen printing

Silver screen printed interdigitated electrodes (IDEs) were fabricated using a DEK-248 screen printer with a polyester screen with a mesh thickness 77 T (filaments per cm) and mounted at 45° to the print stroke. Briefly, Electrodag PF-410 (Henkel, Netherlands) silver ink was deposited onto a 175 µm thick PET substrate and cured at 120°C for 5 min [6,7]. IDEs were designed in a two-electrode configuration with a working electrode and a common reference and auxiliary electrode. The electrodes were then modified with polyaniline nanoparticles.

Polyaniline nanoparticle synthesis and inkjet printing

Polyaniline nanoparticles were synthesised using the modified rapid mixing method [8]. Synthesis was as follows: dodecylbenzene sulphonic acid (DBSA; 3.6 g) was made up to 40 mL with deionised water, ammonium persulphate (APS; 0.36 g) dissolved in 20 mL of the DBSA solution. The remaining DBSA solution was stirred at 20°C and aniline (0.6 mL) was added, followed quickly by the DBSA-APS solution. The mixture was left stirring for 2.5 hr. A 0.05 M solution of sodium dodecyl sulphate (SDS) was prepared by dissolving 14.4 g of SDS in deionised water. After stirring, 20 mL of SDS was added to the dispersion which was centrifuged for 30 min at 3000 × g. The supernatant was finally dialyzed for 48 hr against 500 mL of SDS to remove excess material such as unwanted aniline. The final product was a dark green aqueous ink that was inkjet-printed onto the SPIDEs using a Dimatix Drop Manager Inkjet Printer [9].

Polyaniline nanoparticles were syringed into a Fujifilm Dimatix ink cartridge using a Thermo Syringe combined with an Acrodisc polyvinyl fluoride (PVDF) Syringe Filter (0.45 µm) and needle to inject 2 mL of the polyaniline nanoparticulate solution. The Fujifilm Dimatix inkjet printer cartridges contain 16 nozzles that eject 10 pL of ink. The cartridge was placed into the Dimatix inkjet printer at a head angle of 4.5° where 10 layers were printed onto the silver IDEs. The operating conditions were optimised with a voltage of 18 V and pitch density spacing set to 20 µm and the substrate temperature was set to room temperature. After printing the sheets of dry sensors were lightly rinsed with deionised water to remove residual SDS, the sensors were then placed in a dry-heat oven at 70°C for 30 min.

Ammonia sensor device fabrication

The printed ammonia sensors were further assembled into a device suitable for measuring ammonia in solution (Fig. 1). An o-ring with a thickness of 1.78 mm was bonded to the sensor using a 48 µm thick PSA to create a headspace of 247 mm^3 between the sensor and a gas-permeable PTFE membrane, with a 0.2 µm pore size and a diameter of 25 mm, which was also fixed above the o-ring using PSA. The distance between the sensor and membrane was 1.88 mm. A PSA lid layer was then attached to create a sample chamber with a capacity of 52 µL. Inlet and outlet ports were created using two hypodermic needles inserted into the o-ring at opposite sides of the device to allow the passage of compressed air over the sensor surface to remove matrix related interferences.

Impedimetric measurement of ammonia

Impedance measurements were carried out on the sensor devices. Devices were typically exposed to ammonia as ammonium chloride in 0.1 M PBS pH 7.4, unless otherwise stated. In order to change the pH of the solution to pH 11.0 a 1:25 5 M NaOH to ammonia in PBS was left to incubate at room temperature for 10 min. 52 µL sample volume was left to incubate on

the sensor surface for 15 min. Ammonia was measured at 10^3 Hz, 5 mV amplitude and a 1 s sampling rate for 161 s. To compensate for variation in baseline impedances of printed sensors (6.9%), a ratiometric impedance measurement method was employed [10]. This method was established based on initial sensor baseline in air (Z_{air}) and the response of the sensor to ammonia (Z). Each individual sensor response was normalised (Z/Z_{air}) with respect to its initial baseline (Z_{air}) and its response to ammonia (Z). It was found that the sensors maintained a constant sensitivity to ammonia when measured in this manner. This method was also adopted throughout this work to compensate for changes in initial sensor (baseline) impedance.

Preparation of serum calibration standards and test samples

Calibrator standards were prepared in serum using a 10 mM ammonium chloride calibrator provided in the Abcam® assay kit. Test serum samples were prepared in-house by spiking serum with known concentrations of ammonium chloride.

Spectrophotometric measurement of ammonia

The Abcam® ammonia assay kit was used for the spectrophotometric assays carried out to validate the aqueous ammonia device. This assay utilises the Berthelot reaction [11]. Unless otherwise stated, 100 µL of ammonia chloride standards (25 to 200 µM) were prepared using a provided calibrator stock of 1 mM ammonia. Standards were made up in 0.1 M PBS pH 7.4 and were analysed in triplicate in a 96 well plate. To the standards, 80 µL of Assay Reagent 1 (nitroferricyanide, 2-phenylphenol) and 40 µL of Assay Reagent 2 (sodium hypochlorite) were added and incubated for 30 min at room temperature and measured at 650 nm.

Results and Discussion

The blood ammonia measurement device was developed based on a combination of several principles. Previous work had demonstrated that thin, inkjet-printed films of polyaniline nanoparticles were capable of very sensitive detection of ammonia in air and also in highly humidified breath samples [12]. The present device was designed to allow measurement of ammonia from the gas phase from a liquid blood sample. Previously, it was shown that the use of this type of sensor in combination with a hydrophobic membrane facilitated impedimetric measurement of ammonia in refrigerant fluids using a two-electrode system [13]. The same principle was applied here in a miniaturised format. However, even though the membrane was hydrophobic, water vapour was still able to traverse the membrane. As a solution to this, a method to purge the sample gas from the headspace above the sensor was developed using two hypodermic needles attached to a compressed air line. In this way, ammonia which was tightly bound to the polymer could be detected as an increase in impedance, while the loosely bound water vapour could be easily removed [5,14].

Measurement of ammonia in PBS

Initial experiments to assess and optimise the performance of the device were performed in buffer. While samples were prepared at neutral pH, a sample pre-treatment step was introduced to increase the pH to 11, thereby altering the equilibrium in the sample from predominantly NH_4^+ to NH_3 [15]. At neutral pH, ammonia is predominantly in the soluble NH_4^+ form and so would reduce the molar mass of ammonia available to be detected by the sensor, which needs to be in the gaseous NH_3 form. Ammonia was measured in the range of 25 to 200 µM (n = 3) (Fig. 2). The relationship between ratiometric absolute impedance at 1

kHz (Z/Z_{air}) and ammonia concentration resulted in good linearity across the range with an r^2 of 0.9868, a slope of 0.0043, an intercept of 0.9562 and RSDs in the range of 0.8 to 4.2%.

Interference study

Electrochemical sensors for measuring blood-borne analytes are typically susceptible to interference from other species in blood, often as a result of unwanted redox process, where amperometric sensors are used. The present device is impedimetric and has the potential to be influenced by species which alter conductivity. However, as measurements are made in the gas phase, interfering species must also be volatilisable and be able to traverse the membrane. To compare the current device with other electrochemical sensors, its response to the presence of a number of common potential interferents was evaluated at typical concentrations [16-20]. Acetaminophen (600 µM) and ascorbic acid (100 µM) were assessed, along with related nitrogenous and ammoniacal compounds such as creatinine (45 µM), glutamic acid (100 µM) and uric acid (500 µM), and compared with impedimetric responses in PBS and 30 µM ammonia. Their absolute impedance spectra with respect to air are shown in Fig. 3 and their Z/Z_{air} values at 1 kHz summarised in Table 1. All interferences displayed a higher response than PBS (0.945). The Z/Z_{air} values for acetaminophen, glutamic acid and ascorbic acid were all negligible, being very close to 1. Creatinine and uric acid displayed increased Z/Z_{air} values corresponding to 18 and 33 parts per thousand, respectively, and still negligible with respect to 30 µM ammonia. The results from this study suggested that the ammonia device was suitable for the selective determination of ammonia in the presence of potential interferents commonly found in blood and serum.

Table 1. Summary of the impedance responses of the device to PBS containing a number of common blood-borne interferences. Z/Z_{air} taken at 1 kHz.

Compound	**Concentration**	Z/Z_{air}
Ammonia	30 µM	1.197
Acetaminophen	600 µM	0.983
Ascorbic acid	100 µM	1.005
Creatinine	45 µM	1.018
Glutamic acid	100 µM	1.001
PBS	0.1 M	0.945
Uric acid	500 µM	1.033

3.3. Device performance in serum

The performance of the sensor device was tested in human serum and compared to a standard laboratory spectrophotometric assay (Abcam®). Calibration standards were prepared by spiking the Abcam® ammonia calibrator stock into human serum (25 to 200 µM) at $n = 3$. These standards were measured impedimetrically using the device and also spectroscopically with the Abcam® assay. The correlative relationship between the two methods using the calibration standards is shown in Fig. 4. A Pearson correlation coefficient (r) of 0.9699 ($p < 0.0001$) was achieved between the device and the Abcam® assay responses, demonstrating reliable agreement in the responses of both methods to ammonia levels in serum.

Calibration curves for both the device and the Abcam assay also demonstrated comparable performance (Fig. 5). Excellent linearity ($r^2 = 0.9984$) was obtained for the ratiometric impedance response of the calibration standards ($n = 3$). A slope of 0.0046 and an intercept of 1.15 were obtained, and RSD values ranged from 4.0 to 6.6%. The Abcam® calibration curve

for the same calibration standards also showed excellent linearity (r^2 = 0.9780) with a slope and intercept of 0.0031 and 0.42, respectively, and RSD values ranged from 1.8 to 10.3%.

The linear regressions obtained from the calibration standards were used to determine ammonia concentrations for a set of test serum samples prepared from ammonium chloride in serum at concentrations of 25, 50, 100 and 200 µM (n = 3). The calculated concentrations of ammonia for both methods along with their correlation with one another are shown in Fig. 6a. The resulting correlation between the two methods was good across the concentration range, with a Pearson coefficient of 0.9642 (p < 0.7312), with a slope and intercept of 1.1031 and -14.1310, respectively. The Bland-Altman analysis of the two methods is shown in Fig. 6b. Overall, there was very minimal mean bias between the two methods of 2.55 µM. In addition, all samples except one were within two standard deviations in terms of difference between methods. At lower concentrations, the positive bias was towards the device, while at higher concentrations, this was moderately positively biased towards the Abcam assay. However, in general, there was good agreement between the two assays for the measured test samples.

Comparisons between the actual ammonia concentrations in the test samples and the values determined following measurement using the two methods are shown in Table 2. While both tests were generally in good agreement with one another, they both consistently over-estimated the actual concentrations of ammonia in the test samples. In the case of the device, over-estimation was more significant at 100 and 200 µM, whereas the Abcam® assay showed greater over-estimates at 25 and 50 µM. The reason for the disparity between the calibration standards and the test samples is not clear. It cannot be due to differences in acid-base equilibria as the Berthelot reaction measures predominantly NH_3, while the sensor device effectively measures both NH_3 and NH_4^+ converted to NH_3 at pH 11. However, it may be due to proprietary methods of preparation and stabilisation if the calibrator standards which result in consistent systematic differences between them and samples prepared locally. In either case, there was no statistically significant difference between assays with regards to both calibration standards and test samples.

Table 2. Comparison of the precision and accuracy for the measurement of ammonia in serum using the Abcam® assay and the developed ammonia device (n = 3).

	Device			Abcam®		
Actual (µM)	Found µM	RSD (%)	Difference (%)	Found µM	RSD (%)	Difference (%)
200	277.80	6.89	38.90	256.68	13.88	28.33
100	153.90	6.82	53.90	151.52	14.56	51.52
50	75.43	17.82	50.87	92.81	10.56	85.61
25	41.00	38.34	64.00	54.63	11.83	118.53
Mean		**17.48**	**51.92**		**12.71**	**71.00**

Storage and lifetime of the blood ammonia device

To assess the lifetime of the device and investigate the effects of storage conditions, twelve devices were stored (a) under ambient conditions, (b) in a desiccator and (c) in a vacuum desiccator for a five month period. The impedimetric response of polyaniline films is known to be affected by humidity which may be absorbed from the atmosphere, or hydrolytic degradation processes which may be exacerbated in the presence of water vapour. Impedance baselines at 1 kHz in air were recorded every month and their ratiometric change over time

was recorded (Fig. 7). It can be seen for devices stored under ambient conditions (RSD = 6.8%, n = 12), impedances initially decreased at month 1, before increasing linearly through months 2 to 5. This pattern may relate to initial absorption of water vapour, followed by hydrolytic decomposition of the polymer, or as a result of absorption of atmospheric contaminants causing film deprotonation. Devices stored in the desiccator and under vacuum retained impedances similar to their initial values. The total RSD over the five month period for the desiccators and vacuum desiccators was 0.64 and 0.77%, respectively. While both desiccator and vacuum-stored devices showed little deviation in their impedances over the five months, the devices stored in the desiccator did exhibit a small, but still statistically significant decrease in impedance in months 4 and 5, while vacuum-stored devices showed no change in response. This may suggest that desiccation may reduce, but not eliminate changes to the behaviour of the film. Ideally, device should be stored under vacuum desiccation or in modified atmosphere to remove both water and oxygen. Under such conditions, devices exhibit excellent stability for at least five months.

Performance comparison with other assays and devices

Table 3 lists the analytical performance characteristics of commercial point of care devices and assays. It can be seen that the developed device was comparable with all those listed. The LOD of the device was similar to those listed and suitable for measuring the bottom of the normal range of 11 to 30 µM [1]. Unlike most of the commercial kits, the developed device did not require operation at 37^{o}C and could be used under ambient conditions. Sample volume was in the range achieved by commercial kits and may be reduced by further miniaturisation of the device to make sampling less invasive and prone to pre-analytical errors. While the current device was developed using serum, further studies to investigate performance in whole blood, and the requirements for sample processing will be investigated. While the dynamic range of the device was only assessed up to 200 µM and some devices and assays extend beyond 500 and 1,000, key diagnostic thresholds indicating a dysfunction are typically between 100 to 200 µM. Precision and accuracy around these cut-offs is particularly important, while above these values, precision and accuracy are less relevant as values in excess of this require medical intervention to bring levels back below 100 µM. However, further studies may extend the dynamic range of the device. While analysis time was comparable to the Abcam® and Sigma Aldrich® kits, this could also be further optimised and reduced, for instance, by integration of the pH adjustment step into the device. These optimisations would offer a competitive edge for POC applications by providing a dry, single use test without the need for wet chemistry-based sample pre-treatment. The ability to measure blood ammonia electrochemically at the point of care may have potential advantages over current commercial bench-top instruments based on colorimetric techniques in that further integration, miniaturisation and cost reduction can be achieved.

Table 3. Analytical performance characteristics of a range of commercial kits and devices for the measurement of blood ammonia.

Product Name	**Technique**	**LOD (µM)**	**Range (µM)**	**Analysis Time (min)**	**Sample Volume (µL)**	**Operational Temperature (°C)**
Device	**Impedimetric**	**12**	**25-200**	**28**	**52**	**Ambient**
PocketChem™ BA and	Berthelot	Not specified	2-285	~6	20	10-35

ammonia test kit II						
Vitros® Chemistry Products AMON Slides	Berthelot	Not specified	8.7-500	5	10	37
Abcam® Ammonia Assay Kit - Modified Berthelot	Berthelot	>10	Not specified	30	100	37
Sekisui Ammonia L3K®	Enzymatic	4.1	8.8-1174	Not specified	Not specified	Not specified
Sigma Aldrich® Ammonia Assay Kit	Enzymatic	12	12-881	20	10-200	18-35

Conclusions

A device was developed for the measurement of ammonia in blood. The device employed inkjet-printed polyaniline films for the sensitive, impedimetric, gas-phase detection of ammonia. In combination with a water-impermeable membrane, a headspace and displacement of the headspace gas, the sensor was able to detect ammonia from liquid samples without interference from moisture. The device was validated in buffer and shown not to be susceptible to typical interferences from blood. It was further demonstrated in serum and was comparable in performance to a commercial assay for measuring blood ammonia. The device was able to measure ammonia in serum across the clinically relevant levels of 25 to 200 µM with a theoretical limit of detection (LOD) of 12 µM and a coefficient of determination of 0.9984. The device was statistically comparable with a commercially available assay kit. The device has potential application in the point of care determination of blood ammonia.

Acknowledgements

The research leading to this publication was funded by The University of the West of England.

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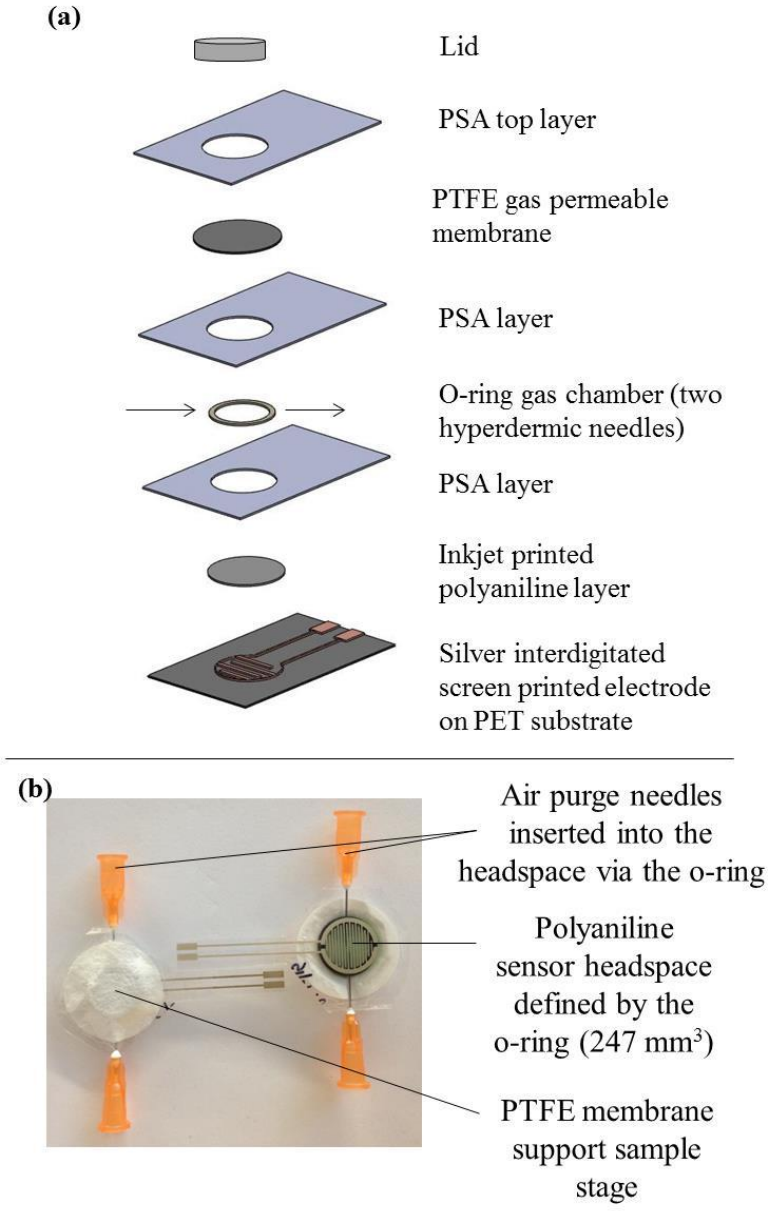

Fig. 1. (a) Design layout of the sensor device assembly. A silver interdigitated electrode screen-printed onto polyethylene terephthalate substrate was modified with ten layers of inkjet-printed polyaniline. A headspace of 247 mm^3 was created above the sensor using a 1.78 mm thick o-ring and PTFE membrane, bonded using layers of 48 µm thick PSA. The sensor and headspace along with the PTFE membrane were encapsulated using PSA and a lid was attached to create a sample chamber with a capacity of 52 µL. (b) Photograph of the sensor device. Left: Top view showing sample chamber and membrane. Right: Bottom view showing ammonia sensor. Also shown are two needles inserted into the 247 mm^3 headspace via the o-ring.

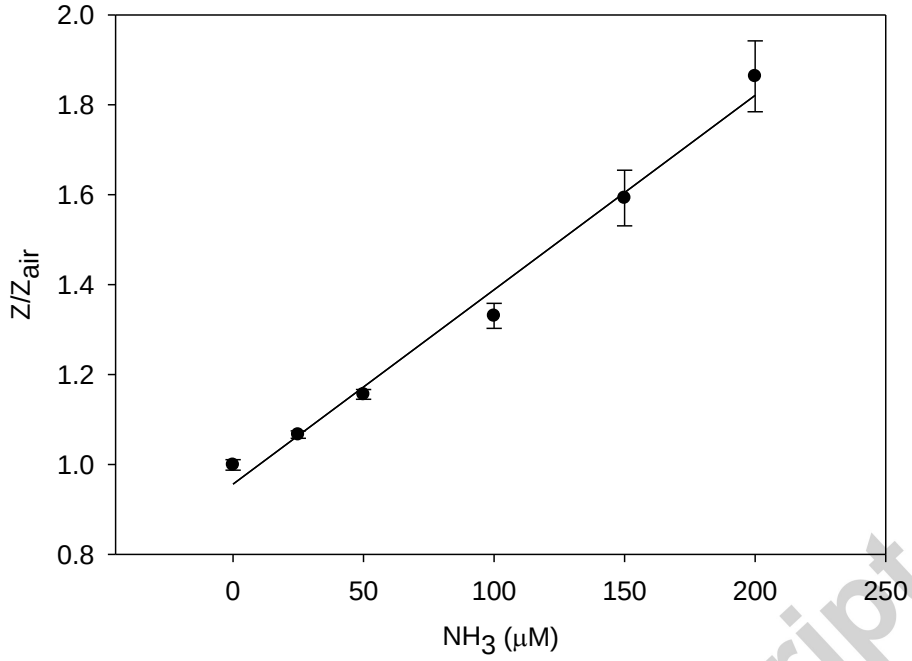

Fig 2. Impedimetric measurement (ratio of the absolute impedance in the sample with respect to air, Z/Z_{air}) of ammonia in PBS from 25 to 200 µM (slope = 0.0043, r^2 = 0.9868, *n* = 3) at 10^3 Hz, 5 mV rms.

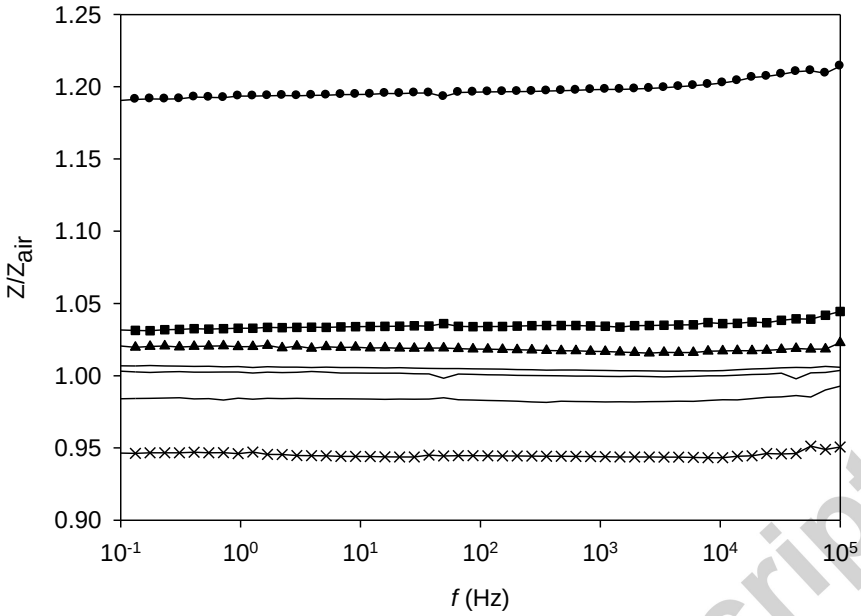

Fig. 3. Selectivity of the device to PBS (x), 30 µM ammonia (●), 600 µM acetaminophen (◊), 100 µM ascorbic acid (▽), 45 µM creatinine (▲), 100 µM glutamic acid (○) and 500 µM uric acid (■) across a frequency range of 10^{-1} to 10^{5} kHz.

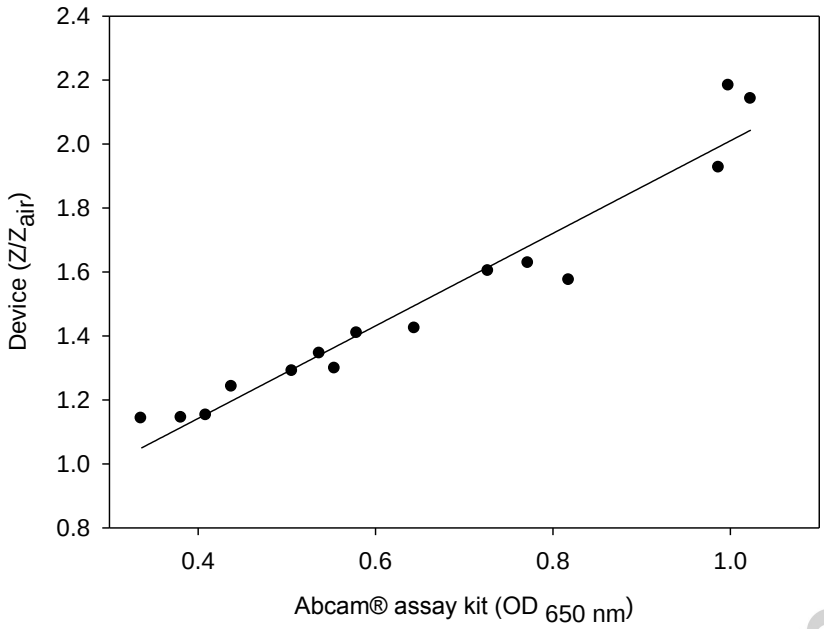

Fig. 4. Correlation of the spectroscopic and impedimetric responses of ammonia calibration standards. R = 0.9699, intercept = 0.5631 and slope = 1.4472, $p < 0.0001$.

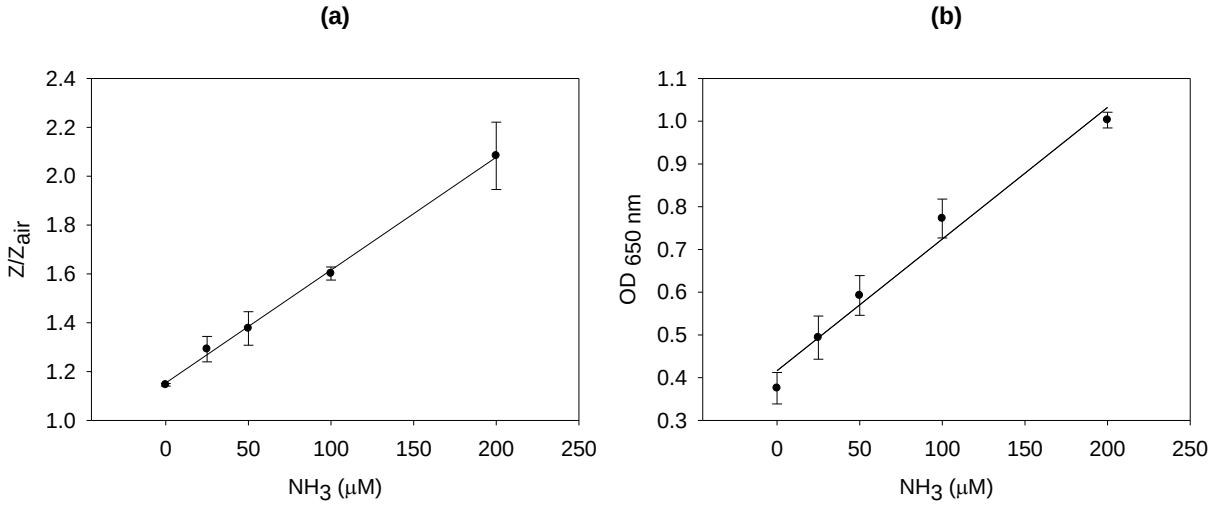

Fig. 5. (a) Impedimetric and (b) spectrophotometric results of ammonia standards (25 to 200 μM) in serum (*n* = 3). Equation of lines for the calibrations were as follows (a) $r^2 = 0.9984$, slope = 0.0046, intercept = 1.15 and (b) $r^2 = 0.9780$, slope = 0.0031, intercept = 0.42.

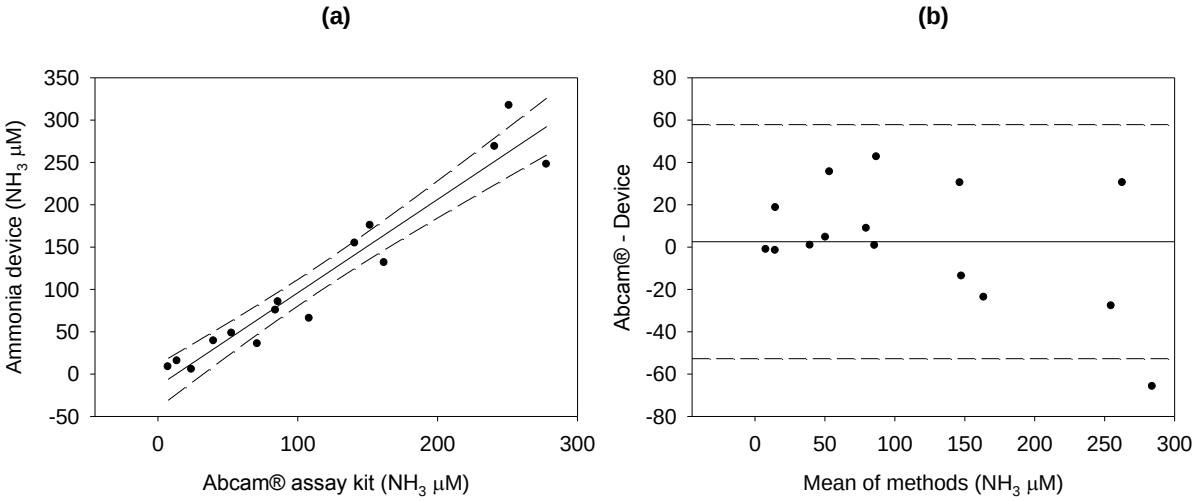

Fig. 6. (a) Correlative analysis of ammonia measurement in the device and Abcam® assay (n=15). R=0.9642, a slope of 1.1031, an intercept of -14.1310 ($p < 0.7312$) (95% confidence intervals) and (b) Bland-Altman plot of the two methods (2σ).

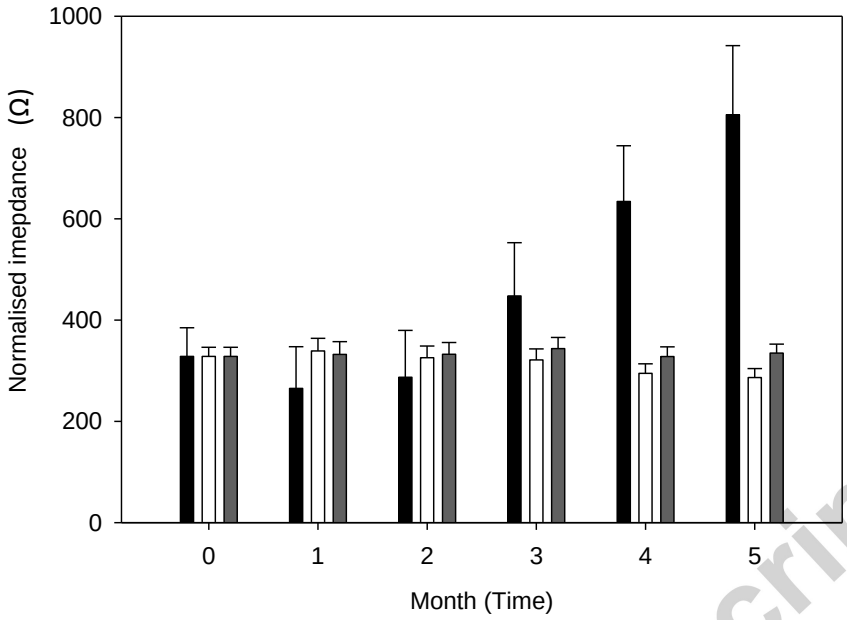

Fig. 7. Storage and lifetime study of the ammonia devices stored under ambient conditions (black), in a desiccator (white) and in a vacuum desiccator (grey), each at n = 12. Graph shows the normalised impedance following storage.

Highlights

A device for measuring ammonia in blood at the point of care has been developed.

A polyaniline nanoparticle ammonia sensor was integrated into a polymer microdevice.

Measurement was using electrochemical impedance of ammonia in the vapour phase.

Ammonia in serum could be measured in the range of 25 to 200 µM with an LOD of 12 µM.

The device has potential as a rapid screening tool for elevated ammonia levels.