Highly selective detection of methanol over ethanol by a handheld gas sensor

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Methanol poisoning causes blindness, organ failure or even death when recognized too late. Currently, there is no methanol detector for quick diagnosis by breath analysis or for screening of laced beverages. Typically, chemical sensors cannot distinguish methanol from the much higher ethanol background. Here, we present an inexpensive and handheld sensor for highly selective methanol detection. It consists of a separation column (Tenax) separating methanol from interferants like ethanol, acetone or hydrogen, as in gas chromatography, and a chemoresistive gas sensor (Pd-doped SnO₂ nanoparticles) to quantify the methanol concentration. This way, methanol is measured within 2 min from 1 to 1000 ppm without interference of much higher ethanol levels (up to 62,000 ppm). As a proof-of-concept, we reliably measure methanol concentrations in spiked breath samples and liquor. This could enable the realization of highly selective sensors in emerging applications such as breath analysis or air quality monitoring.
Ingestion, inhalation, or skin absorption of methanol leads to irreversible tissue damage, especially to eyes and nervous system, or even death. This is attributed to metabolism of methanol to toxic formic acid and formaldehyde, if not immediately treated. Especially in developing countries, methanol poisoning outbreaks occur frequently with hundreds of victims due to adulterated alcohol as shown recently in Iran (Oct. 2018, 959 cases), Cambodia (May 2018, 237 cases), and India (Feb. 2019, > 95 cases). Furthermore, methanol is often used as solvent or chemical feedstock in laboratories and chemical plants, posing a potential hazard of intoxication.

The gold standard for detection of methanol intoxication is blood analysis by gas–liquid chromatography, but more frequent in hospitals is the indirect diagnosis through blood gas analysis. However, both require trained personnel, are expensive and rarely available in developing countries where most outbreaks occur. Blood methanol levels can also be determined non-invasively in exhaled breath, analogous to ethanol as widely applied by law enforcement. The challenge is thereby the selective detection of methanol in the presence of much higher ethanol background typically present after consumption of tainted alcoholic beverages and during therapy where ethanol is used as an antidote. Even more interesting might be simple methods for screening of alcoholic beverages to prevent methanol poisoning. But here too, the same challenge is met. Thus, inexpensive and portable devices are needed for rapid screening of methanol poisoning in breath and liquid by paramedics or even laymen.

Chemical gas sensors are promising due to their low cost, high miniaturization potential, and simple use. In particular, metal-oxide sensors show high sensitivity when nanostructured, capable to detect analytes down to 5 ppb within seconds. But, such sensors are typically non-selective, especially for chemically similar molecules (like methanol and ethanol), representing a long-standing challenge in the field. Therefore, current chemoresistive and electrochemical methanol gas sensors show cross-interferences to ethanol and other alcohols, hindering them for the targeted applications.

Filters can drastically improve the selectivity of chemical sensors by exploiting additional molecular properties of the target analyte. For instance, highly selective formaldehyde detection was possible even with a non-specific SnO₂-based sensor by placing a microporous zeolite membrane to filter molecules by size. This way, formaldehyde was detected down to 30 ppb in 90% relative humidity (RH) without interference of 1 ppm ammonia, acetone, isopropene, and ethanol. Also a sorption packed bed separation column of polar, nanostructured alumina enabled separation of hydrophilic from hydrophobic compounds, analogous to a gas chromatographic (GC) column. This has led to highly selective (>100) sensing of isopropene down to 5 ppb at 90% RH despite the presence of much higher (4–8 times) methanol, ammonia, and acetone concentrations. Non-polar adsorbents, such as Tenax TA, on the other hand, can separate molecules by their molecular weight and chemical functional groups. They are widely used in air sampling, whereby heavy molecules are retained longer than lighter ones due to stronger adsorption by van-der-Waals forces. Thus, they are also promising to separate methanol from ethanol as done already in GC for the analysis of liquor (e.g., detected by olfactometry with humans) and human breath (e.g., by mass spectrometry).

Here, we present a handheld and inexpensive methanol detector (Fig. 1a) capable to quantify methanol selectively in the presence of ethanol and other analytes (e.g., acetone, H₂). It consists of a small packed bed of Tenax (Fig. 1b) to separate the analytes and a highly sensitive, but non-specific microsensor (Fig. 1d) consisting of flame-made Pd-doped SnO₂ nanoparticles on interdigitated sensing electrodes. In comparison to typical GC instruments, our device is much smaller and less expensive. It is benchmarked by detection of methanol in the relevant concentration range in the presence of much higher ethanol levels at high RH. Ultimately, the methanol detector is tested to sense toxic methanol levels in tainted rum and even in spiked human breath.

Results
Detector design. Figure 1a shows the handheld methanol detector. It consists of a separation column upstream of a micromachined metal-oxide gas sensor housed inside a Teflon chamber. Breath or the headspace of a beverage can be drawn by a pump through the separation column to the sensor. The separation column is a miniaturized GC column with Tenax TA as the stationary phase (shown in Fig. 1b) featuring lower adsorption strength to methanol over ethanol. Figure 1c shows a scanning electron microscopy (SEM) image of a Tenax particle’s surface revealing its high speciﬁc surface area (35 m² g⁻¹) and porosity (average pore size 200 nm). Compared to typical GC columns, the separation column used here is much shorter (4.5 cm) and thicker (4 mm inner diameter). Together with the small amount of adsorbent used (150 mg) and its large particle size (~200 µm), this results in a sufﬁciently small pressure drop (<20 mbar) to provide the required flow rate (25 mL min⁻¹) to the sensor.

Figure 1d shows the sensor bonded on a chip carrier. It is micromachined, offering small size and minimal power requirement (76 mW at 350°C) readily suitable for integration into a handheld device. Figure 1e, f show top-view SEM images of the sensing film made of chemoresistive Pd-doped SnO₂ nanoparticles offering high porosity and speciﬁc surface area (~80 m² g⁻¹) for similarly prepared Pt-doped SnO₂. The open ﬁlm structure enables fast diffusion of analytes and interaction with the large surface area, important for rapid and highly sensitive methanol sensing. Such sensors have been used, for instance, for detection of only 3 ppb formaldehyde with fast response (140 s) and recovery (190 s) times, and good reproducibility (~10% response variation).

Fig. 1 Images of the handheld methanol detector. a it consists of a microsensor (in Teflon housing) connected to a separation column (Tenax TA particles in Teflon tube). b Close-up of the separation column with particles inside a glass tube for better visibility. c Magniﬁed images of a particle’s surface. d The sensor chip carrier with a mounted microsensor. e, f Top-view images of the sensing ﬁlms consisting of a ﬁne network of agglomerated and aggregated Pd-doped SnO₂ nanoparticles.
Selective methanol detection. Figure 2a shows responses of the Pd-doped SnO2 sensor without separation column to 10 s exposures of 5 ppm hydrogen (purple line), methanol (red line), acetone (green line), and ethanol (blue line) at 50% RH. The sensor quickly reacts to all these analytes with responses between 10 and 25. However, it cannot differentiate between them. This becomes even more evident when exposing the sensor to a mixture of these analytes (Fig. 2b). The sensor gives now a much higher response, slightly lower than the sum of the individual ones, as typically observed for chemoresistive sensors at such ppm concentrations. As a consequence, this sensor cannot measure methanol selectively in the presence of such interferents.

When combined with the separation column, the sensor responses are separated as in a chromatograph. The response to hydrogen (purple line) remains the same (Fig. 2c). This is expected as hydrogen features low molecular weight and is not retained by Tenax. For the other analytes, however, a different behavior is observed. In fact, methanol (red line) is now detected after >1 min with a maximum sensor response (i.e., retention time $t_R$, dashed lines) after 1.7 min. Note that the maximum methanol response is lower than without separation column, as the column dissipates it over a longer time period, in line with theory. Most importantly, ethanol (blue line, $t_R = 8.7$ min) and acetone (green line, $t_R = 33$ min) are retained for much longer, in agreement with literature ($t_R = 2.2$, 10.8, and 36 min for methanol, ethanol, and acetone, respectively, at 20 °C). As a result, the separation column enables selective methanol detection. Interestingly also, the ethanol and acetone responses decrease with increasing $t_R$. In fact, the response to 5 ppm acetone is barely picked up by the sensor (while it was twice that of methanol without separation column, compare Fig. 2a, c).

When exposing the sensor with separation column to a mixture of the same analytes and concentrations (Fig. 2d), the analytes can be detected individually at their specific retention time with very high selectivity, identical to the single analyte exposures (Fig. 2c). Most remarkably, for the targeted applications, methanol is detected without ethanol interference, superior to state-of-the-art methanol sensors where the highest selectivity to ethanol (>30) has been reported for imprinted Ag-doped LaFeO3 core-shell particles.

As shown in Fig. 2c, d, the detector fully regenerates from each analyte or mixture exposure by flushing with air. The recovery time depends on the analyte and is about two to three times its retention time, in agreement with literature. The recovery time can be decreased considerably by simply increasing the flow rate or by slight heating of the separation column (e.g., acetone from ~60 min to 20 s when increasing column temperature and flow rate briefly to 80 °C and 100 mL min$^{-1}$).

Dynamic range. Methanol concentrations in the targeted applications may occur from several ppm in breath up to several hundred ppm in the headspace of beverages. Figure 3 shows the Pd-doped SnO2 sensor response with separation column when exposed for 10 s to 1–918 ppm of methanol at 50% RH. The median methanol concentration in healthy breath (green line), and the range of exogeneous (orange line) and toxic breath methanol concentrations (red area) are also indicated. The response curve is non-linear, in line with diffusion-reaction theory for such semiconductive metal-oxide films at high analyte concentrations. Nevertheless, as a result, this separation column–sensor system can discriminate clearly toxic from non-toxic levels and even detect low concentrations of 1 ppm with a signal-to-noise ratio >100. Lower concentrations are not relevant for the liquor headspace and breath analyses, but such Pd-doped SnO2 gas sensors can detect volatile organic compounds down to single ppb levels (e.g., 3 ppb formaldehyde). In contrast, other benchtop methanol detectors (e.g., PTR-TOF-MS) can detect such low concentrations as well, but they have a much smaller dynamic range and require dilution to measure the high ppm concentrations present in breath or the headspace of beverages.

Please note that the response curve in Fig. 3 is valid for a separation column temperature of 22 °C at 50% RH. With increasing column temperature, the sensor responses become higher as $t_R$ decreases (Supplementary Fig. 1a). Most importantly, however, methanol is clearly separated and detected individually.
High ethanol background. To analyze methanol in the head-space of alcoholic beverages or in intoxicated breath, the detector must remain accurate in the presence of very high ethanol concentrations. Figure 4a shows the response of the detector when exposed to 1 ppm methanol with interfering ethanol concentrations of 5 (green line), 650 (1% relative saturation, blue line), and 32,500 ppm (50% relative saturation, red line). Despite the significantly higher ethanol concentration, methanol is detected first ($t_R = 1.5–1.7$ min) giving comparable responses to the single gas calibration (Fig. 3). Ethanol is detected later with breakthrough times ($t_B$) that decrease with increasing concentration (5.7 min at 5 ppm to 2.2 min at 50% saturation) but are always higher than the $t_B$ of methanol. In GC, the same phenomenon is observed when overloading the column with analyte.

Interestingly, at 50% ethanol saturation concentration, methanol is detected slightly earlier with higher peak maximum and narrower peak width. Probably, this is due to competitive adsorption on Tenax where methanol is displaced by ethanol that adsorbs more strongly. Nevertheless, the resulting error of 17% is sufficiently small for the targeted applications as the difference between normal and toxic methanol concentrations in liquor and breath are much larger (e.g., human breath median 0.46 ppm vs. intoxicated 133 ppm). If higher accuracy is required, alternatively, the area below the methanol response could be evaluated, as commonly done in gas chromatography.

In fact, the peak areas below the methanol response are basically identical (within 2%), irrespective of the ethanol concentration (Supplementary Fig. 2). Most importantly, the methanol response is clearly separated from that of ethanol even at very high concentrations. This is shown in Fig. 4b where the $t_R$ of methanol (solid line) and $t_B$ of ethanol (dashed line) are plotted for ethanol concentrations in the range of 5–62,000 ppm (95% saturation). The $t_B$ decreases exponentially with increasing concentration, in line with literature at lower concentrations. Even at the most extreme conditions of 95% saturated ethanol atmosphere, methanol is detected independently of ethanol as its response is clearly separated from the breakthrough of ethanol. These results are astonishing considering the simplicity of this device and outperform other methanol detectors.

Methanol-spiked liquor and breath. Drinking as little as 6 mL of methanol can be fatal. Thus, a methanol detector for screening of alcoholic beverages could help to prevent methanol poisoning outbreaks. The safety threshold for naturally occurring methanol in liquor (40 vol% ethanol) is 0.4 vol% (US$^{34}$ and EU$^{36}$), as such low levels are a byproduct of fermentation. The detector must therefore be able to distinguish “safe” alcoholic beverages from tainted ones with typically much higher methanol content. Figure 5a shows the responses to pure (green line) and laced Arrack (common liquor in Southeast Asia) with 0.3 (blue line), 0.4

Fig. 3 Dynamic range of the detector. Response of the detector (Tenax separation column + Pd-doped SnO$_2$ sensor) to 1–918 ppm methanol concentrations (black squares and dashed line). The median methanol concentration in healthy breath (green dashed line), exogeneous concentrations (black squares and dashed line), and toxic breath levels (red dashed line and shaded area) are indicated. Measurements were performed with 10 s exposure of all methanol concentrations at 50% RH and a flow rate of 25 mL min$^{-1}$ through the detector from ethanol even at 40 °C. Such temperature effects could be accounted for by a temperature sensor. At higher humidity, $t_R$ does not change, in line with literature, but the responses decrease (Supplementary Fig. 1b). This is typical for such doped SnO$_2$ sensors and can be addressed by using a sensor material less sensitive to humidity (e.g., Sb-doped SnO$_2$) or by correction with a humidity sensor as done with sensor arrays to monitor volatile emission from human breath and skin.

Fig. 4 Methanol detection with high ethanol interference. a Responses of the methanol detector upon exposure to 1 ppm methanol in the presence of 0.3 (blue line), 0.4 (green line), 0.5 ppm (1% relative saturation, blue line), and 32,500 ppm (50% relative saturation, red line) ethanol. Corresponding ethanol breakthrough times ($t_B$, dashed lines) are indicated. b The ethanol $t_B$ (squares and dashed line) and methanol retention time ($t_R$, circles and solid line) as a function of interfering ethanol concentration of 0.3 (blue), 0.4 (green), 0.5 ppm (50% relative saturation, red), and 32,500 ppm (95% relative saturation, purple).
Detection of methanol in laced liquor (Arrack). a Response of the detector to pure liquor (green line) containing 40 vol% ethanol and laced with methanol of 0.3 (blue line), 0.4 (orange line), 0.5 (purple line), and 1 vol% (red line). b Sensor responses as a function of methanol content (0–10 vol%) in the liquor (black circles). The red dashed line indicates the legally allowed (US34 and EU36) naturally occurring methanol content in liquor (40 vol% ethanol). Error bars indicate the standard deviation of at least three measurements (i.e., repeatability) with <15% variation.

Most importantly, the response increases with increasing methanol concentration and even small differences between 0.3, 0.4 and 0.5 vol% (i.e., close to the allowed limit) can be clearly resolved by the sensor with high signal-to-noise ratio >100. In all cases, the response steeply increases after 3 min, corresponding to the high concentrations of ethanol. Also at higher methanol contents of 5 and 10 vol% the sensor response continues to increase (Fig. 5b). As a result, the methanol detector can clearly distinguish pure Arrack from that laced with toxic levels of methanol at the expected $t_R = 1.7$ min, matching the retention time of methanol in laboratory gas mixtures (Figs. 2c and 4).

As a proof-of-concept for breath analysis, we evaluated the methanol detector on the original and methanol-spiked breath of an intoxicated volunteer (0.54‰ blood alcohol level) sampled from Tedlar bags. The blue dashed line shows the measurement from the normal breath sample and the red solid line from the spiked sample with 135 ppm methanol, indicating methanol intoxication. The PTR-TOF-MS measurements with separation column and dilution of the same samples for methanol and ethanol. The instrument shown in is a PTR-TOF-MS 1000 (ionicon, Austria) used for sensor validation. Hydrogen ($H_2$) is not retained by the separation column and does not interfere with the methanol detector.

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additional dilution (please see Methods). Methanol and ethanol were detected at \( R_g \) identical to the sensor, confirming the sensor results.

As a result, this detector can clearly differentiate between normal and methanol-spiked breath. Therefore, this is promising for fast and non-invasive sensing of methanol poisoning. Given the high signal-to-noise ratio at 135 ppm methanol, it also shows promise for monitoring methanol elimination during treatment\(^{11} \). Of course, the results are rather preliminary (only one subject tested) and further validation with extended cohorts is required as done recently with breath acetone and a similar sensor (Si-doped WO\(_3\)) for body fat burn monitoring during exercise\(^{15} \) and dieting\(^{49} \).

Photoluminescent Tb\(^{3+} \) are either liquid sensors that cannot be used for breath (e.g., ethanol in realistic samples of liquor and breath. Other sensors for the detection of relevant concentrations in the presence of tuning fork-based sensor\(^{51} \)) or were not tested in gas mixtures (synthetic air or ambient air in case of breath and liquor headspace analysis) and carbon-nanotube\(^{57} \)- or graphene-based\(^{58} \) technologies that often lack selectivity, such as optical sensors (e.g., photoluminescent Tb\(^{3+} \), fluorescent\(^{54} \), gas ionization detectors\(^{55} \), electrochemical cells\(^{56} \), and carbon-nanotube\(^{57} \), or graphene-based sensors\(^{58} \). Based on their small size and low price, such separation columns could enable highly selective, compact, and portable gas detectors for emerging applications including medical breath analysis, food spoilage, and air quality monitoring.

**Methods**

**Sensor fabrication.** Palladium-doped SnO\(_2\) nanoparticles were produced by flame spray pyrolysis (FSP). So, Pd-acetylacetonate (Sigma Aldrich, >99.9%) was dissolved in tin-(II)-ethylhexanoate (Strem Chemicals, –90% in 2-ethylhexanoic acid) and xylene (Sigma-Aldrich, ≥98.5%) to obtain a total metal molarity (Pd and Sn) of 0.5 M and nominal Pd content of 1 mol%\(^{29} \). This precursor solution was fed through a capillary at 5 ml min\(^{-1}\), dispersed into a fine spray by 5.1 ml min\(^{-1}\) oxygen (pressure drop of 20 mbar) and ignited by a surrounding premixed mixture of methane and air (1.25/3.3 L min\(^{-1}\)). The FSP reactor design is described in more detail elsewhere\(^{26} \).

Nanoparticles were directly deposited\(^{26} \) for 4 min onto micromachined free-standing membrane-type sensor substrates (1.9 x 1.7 mm\(^2\), MSGS 5000i, Microsens SA, Switzerland) attached to a water-cooled holder at 20 cm height above the flame (1.25/3.3 L min\(^{-1}\)). The microsensor membranes feature an integrated heater layer underneath the interrogated sensing electrodes. Subsequent in-situ annealing with a particle-free flame for 30 s at a HAB of 14.5 cm improved adhesion and cohesion of the highly porous sensing film\(^{39} \). Interestingly, in liquor (Fig. 5) and human breath (Fig. 6), only methanol, ethanol and hydrogen (breath) are clearly detected by the sensor, although both liquor\(^{47} \) and breath\(^{48} \) are complex mixtures with more than 100 and 800 analytes, respectively. This is probably due to the higher molecular weight and different functional groups (e.g., diols or glycols) of most interferants, resulting in longer retention in the separation column than methanol (e.g., ethylene glycol 100 times longer than methanol\(^{30} \)). The most likely reason, however, is the much lower concentration of most confounders (e.g., 0.003 ppm trimethylamine in breath\(^{49} \), compared to >133 ppm of methanol in case of intoxication\(^1 \)).

To the best of our knowledge, this is the first methanol sensor for the detection of relevant concentrations in the presence of ethanol in realistic samples of liquor and breath. Other sensors are either liquid sensors that cannot be used for breath (e.g., photoluminescent Tb\(^{3+} \)-based metal-organic framework sensor\(^{50} \), do not offer the required detection limit (e.g., Quartz tuning fork-based sensor\(^{51} \)) or were not tested in gas mixtures (e.g., optical fiber sensor\(^{52} \)).

**Discussion**

We created an inexpensive, handheld and reliable methanol detector based on a separation column–sensor concept. The separation column is a small packed bed of polymer adsorbent (Tenax TA) that separates methanol from ethanol and other interferants including hydrogen and acetone analogous to a column in gas chromatography. So, methanol is detected within 2 min by a non-specific but highly sensitive nanostructured Pd-doped SnO\(_2\) gas sensor in a wide concentration range from 1 to 918 ppm without interference of much higher ethanol concentrations (up to 62,000 ppm). The detector successfully quantified methanol concentrations in laced rum (Arrack) down to 0.3 vol% by analyzing its headspace and distinguished it from pure liquor. As first proof-of-concept, the detector was also tested on breath of an intoxicated volunteer, where it could clearly identify the sample spiked with toxic methanol concentrations. Thus, it shows promise for quick and non-invasive screening of methanol poisoning from breath and laced alcoholic beverages and could be used by first responders in developing countries, where most outbreaks occur.

In a broader sense, the present detector demonstrates how to possibily address a long-standing challenge of chemical sensors: the discrimination between analytes from the same chemical family. Giving comparable performance to a gas chromatographic column, such separation columns are much simpler in design, modular, and can be combined flexibly with other sensor technologies that often lack selectivity, such as optical sensors (e.g., plasmonic\(^{33} \), fluorescent\(^{54} \), gas ionization detectors\(^{55} \), electrochemical cells\(^{56} \), and carbon-nanotube\(^{57} \), or graphene-based sensors\(^{58} \). Based on their small size and low price, such separation columns could enable highly selective, compact, and portable
Fig. 7 Schematic of the synthetic gas mixing setup and the methanol detector. The methanol detector (orange box) consisting of the packed bed separation column of polymer (Tenax TA, red) particles, followed by the chemoresistive (Pd-doped SnO₂, green) sensor and the vane pump that draws 25 mL min⁻¹ of gas sample. For characterization with synthetic gas mixtures, the detector is connected to a gas delivery system. It supplies the detector with a constant flow of humidified air by mixing dry and humidified synthetic air (syn. air). Analyte exposures are generated by admixing analytes from calibrated gas standards or by bubbling syn. air through analyte/water mixtures to the humidified syn. air stream with a capillary through a septum. Flows are accurately controlled by calibrated mass flow controllers (MFCs) by measuring the counts per second at a mass-to-charge ratio by measuring the counts per second at a mass-to-charge ratio of 33.0335 of methanol (m/z) of 33.0335 units.

Evaluation of the headspace of drinks and human breath. For testing of methanol-spiked drinks and breath, sensors were stabilized in ambient air with analyte background concentrations of methanol <0.3 vol% are not relevant for the liquor screening as the legal limit is 0.4 vol%. Higher ethanol concentrations (250–300 mL min⁻¹) were generated similarly by bubbling air through pure ethanol (absolute, >99.8%, Fisher Chemical) and dilution with synthetic air. Generated concentrations were calculated from the weight loss of the bubbler after bubbling with air for 0, 2, 4, 6, and 8 h, while room temperature was kept constant at 22 °C.

References

1. The American Academy of Clinical Toxicology Ad Hoc Committee on the Treatment Guidelines for Methanol Poisoning. et al. American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. J. Toxicol. Clin. Toxicol. 40, 415–446 (2002).
2. Kruse, J. A. Methanol poisoning. Intensive Care Med. 18, 391–397 (1992).
3. Hovda, K. E. et al. Methanol outbreak in Norway 2002–2004: epidemiology, clinical features and prognostic signs. Intern. Med. 45, 181–190 (2005).
4. Agence France-Presse. Voice of America News: death toll in Iran alcohol poisoning jumps to 84. https://www.voanews.com/a/death-toll-in-iran-alcohol-poisoning-jumps-to-84/4633648.html (2018).
5. David, S. Köhler Times: More than 100 villagers return home after methanol poisoning. https://www.khohtimeskhem.com/50486781/more-than-100-villagers-return-home-after-methanol-poisoning/ (2018).
6. Schultz, K. & Kumar, H. The New York Times: Over 90 killed in India by toxic homemade liquor. https://www.nytimes.com/2019/02/23/world/asia/india-poison-alcohol.html (2019).
7. Lin, L. et al. Low-temperature hydrogen production from water and methanol using Pt/a-MoC catalysts. Nature 544, 89–83 (2017).
8. Krawt, J. A. Diagnosis of toxic alcoholic limitations of present methods. Clin. Toxicol. 53, 589–595 (2015).
9. D’Silva, J. India’s problem with toxic alcohol. BMJ 351, h3536 (2015).
10. Laakso, O. et al. FT-IR breath test in the diagnosis and control of treatment of methanol intoxications. J. Anal. Toxicol. 25, 26–30 (2001).
11. Reifkeinstein, R. F. & Smith, H. The breathalyzer and its applications. Med. Sci. Law 2, 13–22 (1961).
12. Krawt, J. A. Approach to the treatment of methanol intoxication. Am. J. Kidney Dis. 68, 161–167 (2016).
13. Günntner, A. T. et al. Breath sensors for health monitoring. ACS Sens. 4, 268–280 (2019).
14. Shulaker, M. et al. Three-dimensional integration of nanotechnologies for computing and data storage on a single chip. Nature 547, 74–78 (2017).
15. Gao, W. et al. Fully integrated wearable sensor arrays for multiplexed in situ perspiration analysis. Nature 529, 509–514 (2016).
16. Günntner, A. T., Pineau, N. J., Chie, D., Krumeich, F. & Pratsinis, S. E. Selective sensing of isopropanol by Ti-doped ZrO₂ for breath diagnostics. J. Mater. Chem. B 4, 5358–5366 (2016).
17. Lim, S. H., Feng, L., Kemling, J. W., Musto, C. J. & Suslick, K. S. An optoelectronic nose for the detection of toxic gases. Nat. Chem. 1, 562–567 (2009).
18. Han, D. et al. Enhanced methanol gas-sensing performance of Ce-doped In₂O₃ porous nanospheres prepared by hydrothermal method. Sens. Actuators B 216, 488–496 (2015).
19. Caravati, E. M. & Anderson, K. T. Breath alcohol analyzer mistakes methanol poisoning for alcohol intoxication. Ann. Emerg. Med. 55, 198–200 (2010).
20. Günntner, A. T., Abbeg, S., Wegner, K. & Pratsinis, S. E. Zeolite membranes for highly selective formaldehyde sensors. Sens. Actuators B 257, 916–923 (2018).
21. Van den Broek, J., Günntner, A. T. & Pratsinis, S. E. Highly selective and rapid breath isoprene sensing enabled by activated alumina filter. ACS Sens. 3, 677–683 (2018).
22. McNair, H. M. & Miller, J. M. Basic Gas Chromatography (John Wiley & Sons, 2011).
23. Maier, I. & Fischer, M. Retention characteristics of volatile compounds on Tenax TA. J. High. Resolut. Chromatogr. 170, 267 (1983).
24. Franitza, L., Granvogl, M. & Schieberle, P. In Food Chem. 9053 (2016).
25. Jones, A. W., Mårdh, G. & Änggård, E. Determination of endogenous ethanol in blood and breath by gas chromatography-mass spectrometry. Pharmaco. Biochem. Behav. 18, 267–272 (1983).
26. Mäder, L. et al. Direct formation of highly porous gas-sensing films by in situ thermophoretic deposition of flame-made Pt/SnO₂ nanoparticles. Sens. Actuators B 114, 283–295 (2006).
27. Mäder, L. et al. Sensing low concentrations of CO using flame-spray-made Pt/SnO₂ nanoparticles. J. Nanopart. Res. 8, 783–796 (2006).
28. Günntner, A. T., Koren, V., Chikkadi, K., Righettioni, M. & Pratsinis, S. E. E. nose sensing of low-ppb formaldehyde in gas mixtures at high relative humidity for breath screening of lung cancer? ACS Sens. 1, 528–535 (2016).
29. Gardner, J. W. A non-linear diffusion-reaction model of electrical conduction in semiconductor gas sensors. Sens. Actuators B 1, 166–170 (1990).
30. Scientific Instrument Services (SIS). Tenax* TA breakthrough volume data. https://www.sisweb.com/index/referen/tenaxta.htm. Accessed 20 Aug 2019.
31. Harper, M. Evaluation of solid sorbent sampling methods by breakthrough volume studies. Ann. Occup. Hyg. 37, 65–88 (1993).
32. Qian, R. et al. Highly selective and sensitive methanol gas sensor based on molecular imprinted silver-doped LaFeO₃ core–shell and cage structures. Nanotechnology 29, 14503 (2018).
33. Manura, J. J. Application note: calculation and use of breakthrough volume data. https://www.sisweb.com/index/indexes/resin10.htm. Accessed: 20 Aug 2019.
34. Levy, P. et al. Methanol contamination of romanian home-distilled alcohol. J. Toxicol. Clin. Toxicol. 41, 23–28 (2003).
35. Turner, C., Spanel, P. & Smith, D. A longitudinal study of methanol in the exhaled breath of 30 healthy volunteers using selected ion flow tube mass spectrometry, SIFT-MS. Physiol. Meas. 27, 637–648 (2006).
36. Paine, A. J. & Dayan, A. D. Determination of methanol in alcoholic drinks. Hum. Exp. Toxicol. 20, 563–568 (2001).
37. Suematsu, K., Sasaki, M., Ma, N., Yuasa, M. & Shimanoe, K. Antimony-doped tin dioxide gas sensors exhibiting high stability in the sensitivity to humidity changes. ACS Sens. 1, 913–920 (2016).
38. Güntner, A. T. et al. Snif for breath sampling in medical diagnostic research. Physiol. Meas. 28, 73–84 (2006).
39. Bennett, I. L., Cary, F. H., Mitchell, G. L. & Cooper, M. N. Acute methyl alcohol poisoning: a review based on experiences in an outreach of 323 cases. Medicine 32, 431–463 (1953).
40. Comes, P., Gonzalez-Flesca, N., Menard, T. & Grimalt, J. O. Langmuir-derived changes.
41. Güntner, A. T. et al. Noninvasive tool to diagnose nonalcoholic fatty liver disease in children. Toxicol. Clin. Toxicol. 56, 201–205 (2018).
42. Zhang, C.-Y., Lin, N.-B., Chai, X.-S., Zhong, L. & Barnes, D. G. A rapid method for simultaneously determining ethanol and methanol content in wines by full evaporation headspace gas chromatography. Food Chem. 183, 169–172 (2015).
43. Artursson, T. et al. Drift correction for gas sensors using multivariate methods. J. Chemom. 14, 711–723 (2000).
44. Bader, M. A systematic approach to standard addition methods in instrumental analysis. J. Chem. Educ. 70, 703–706 (1980).
45. Güntner, A. T. et al. Noninvasive body fat burn monitoring from exhaled acetone with Si-doped WO3-sensing nanoparticles. Anal. Chem. 89, 10578–10584 (2017).
46. Güntner, A. T. et al. Guiding ketogenic diet with breath acetone sensors. Sensors 18, E3655 (2018).
47. Maae, H. & Ten Hoen van der Brauw, M. C. The analysis of volatile components of Jamaican rum. J. Food Sci. 31, 951–955 (1966).
48. de Lacy Costello, B. et al. A review of the volatiles from the healthy human body. J. Breath. Res. 8, 014001 (2014).
49. Alkhouri, N. et al. Analysis of breath volatile organic compounds as a noninvasive tool to diagnose nonalcoholic fatty liver disease in children. Eur. J. Gastroenterol. Hepatol. 26, 82–87 (2014).
50. Fonseca, R. R. F., Gaspar, R. D. L., Raimundo, I. M. & Luz, P. P. Photoluminescent Tb3+-based metal-organic framework as a sensor for detection of methanol in ethanol fuel. J. Rare Earths 37, 225–231 (2019).
51. Sampson, S. A., Panchal, S. V., Mishra, A., Banerjee, S. & Datar, S. S. Quartz tuning fork based portable sensor for vapor phase detection of methanol adulteration of ethanol by using aniline-doped polystyrene microwires. Microchim. Acta 184, 1659–1667 (2017).
52. Liu, D. et al. High sensitivity optical fiber sensors for simultaneous measurement of methanol and ethanol. Sens. Actuators B 271, 1–8 (2018).
53. Hoen, B. S. et al. Plasmonic sensing and control of single-nanoparticle electrochemistry. Chem 4, 1560–1585 (2018).
54. Hu, Y. et al. Fingerstrip design and detection of gas-phase amines using a fluorescent sensor array assembled from asymmetric pyrene diimides. Sci. Rep. 8, 10277 (2018).
55. Modi, A., Koratkar, N., Lass, E., Wei, B. & Ajayan, P. M. Miniaturized gas ionization sensors using carbon nanotubes. Nature 424, 171–174 (2003).
56. Gebicki, J. Application of electrochemical sensors and sensor matrices for measurement of odorous chemical compounds. Trends Anal. Chim. 77, 1–13 (2016).
57. Kim, J.-H. et al. The rational design of nitric oxide selectivity in single-walled carbon nanotube near-infrared fluorescence sensors for biological detection. Nat. Chem. 1, 473–481 (2009).
58. Yun, J. et al. Stretchable patterned graphene gas sensor driven by integrated micro-supercapacitor array. Nano Energy 19, 401–414 (2016).
59. Tricoli, A. et al. Micro patterning layers by flame aerosol deposition-annealing. Adv. Mater. 20, 3005–3010 (2008).
60. Geanakoplis, C. J. Transport Processes and Separation Process Principles 4th edn. (Prentice Hall, 2003).
61. Spanel, P. & Smith, D. SIFT studies of the reactions of H2O, NO + and O2 + with a series of alcohols. Int. J. Mass Spectrom. Ion. Process. 167/168, 375–388 (1997).
62. Tippler, A. An Introduction to Headspace Sampling in Gas Chromatography Fundamentals and Theory (Perkin Elmer Inc., 2013.)
63. Steeghs, M. M., Cristescu, S. M. & Harren, F. J. The suitability of Tedlar bags for breath sampling in medical diagnostic research. Sensors 28, 19–36 (2018).

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Author contributions

J.v.d.B. and A.T.G. conceived the concept and experiments. J.v.d.B. performed the experiments and the data evaluation. S.A. designed and provided the microsensors and contributed to the experimental design. S.E.P and A.T.G were in charge and advised on all parts of the project. J.v.d.B., S.A., S.E.P., and A.T.G co-wrote the paper. All authors gave final approval to the manuscript.

Additional information

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Competing interests: A patent application based on this manuscript has been submitted by J.v.d.B., S.A., S.E.P., and A.T.G.

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