

Gas sensing for space: Health and environmental monitoring

Journal Article**Author(s):**

Elias Abi-Ramia Silva, Tiago; Burisch, Federico; [Güntner, Andreas](#) 

Publication date:

2024-08

Permanent link:

<https://doi.org/10.3929/ethz-b-000675685>

Rights / license:

[Creative Commons Attribution 4.0 International](#)

Originally published in:

TrAC Trends in Analytical Chemistry 177, <https://doi.org/10.1016/j.trac.2024.117790>

Funding acknowledgement:

MB22.00041 - Wearable health monitors enabled by flame-aerosol engineering (SBFI)



Gas sensing for space: Health and environmental monitoring

Tiago Elias Abi-Ramia Silva^a, Federico Burisch^a, Andreas T. Güntner^{a,b,*}

^a Human-centered Sensing Laboratory, Department of Mechanical and Process Engineering, ETH Zürich, CH-8092, Zürich, Switzerland

^b Department of Endocrinology, Diabetology, and Clinical Nutrition, University Hospital Zurich and University of Zurich, CH-8091, Zürich, Switzerland

ARTICLE INFO

Keywords:

Chemical analysis
Biomedical analysis
Environmental monitoring
Breath analysis
Gas analysis
Electrochemical sensor
Chemoresistive sensor
Mass-sensitive sensor
Optical sensor
Biosensor

ABSTRACT

Humanity endeavors to resume crewed missions to the Moon and prepares for the exploration of Mars. These missions will require sustained human presence in space for longer periods than ever before. Space exposes astronauts to demanding conditions, including microgravity, radiation, rapid light-dark cycles, and hazardous chemicals. Gas sensors will be pivotal in preserving astronaut health by providing critical health data (e.g., through breath analysis) and space-resolved environmental information. Here, we explore the recent progress of gas sensors to meet the key needs of space exploration. First, the fundamental sensing principles of electrochemical, chemoresistive, mass-sensitive, and optical sensors are briefly introduced. Then, we connect space-related health challenges with suitable breath markers and sensor solutions, encompassing areas like gut microbiome, muscle activity, cardiovascular health, hepatic and renal function, and circadian rhythm. Finally, environmental exposure guidelines and suitable sensor innovations for distributed air quality monitoring in space vehicles and habitats are presented.

1. Introduction

The space age was inaugurated in 1957 with the launch of Sputnik 1, which was followed by the first human in space in 1961 and the first landing of a man on the Moon in 1969. Gas analysis has played a critical role in tracking astronaut's health and safety in space exploration ever since. For instance, experiments to analyze the metabolic activity of crew members through breath have been carried out at least since the Skylab Program in the 1970s when enclosed atmospheres were characterized [1]. Also, environmental air quality has been of concern: NASA has sampled spacecraft air for off-site analysis since Project Gemini in the 1960s to ensure astronaut safety and proper functioning of the ECLSS [2,3].

Now, a new era of space exploration is dawning: China's Chang'e [4] and India's Chandrayaan [5] lunar missions will survey the Moon's south pole and test technologies for a lunar science base, and the NASA-led Artemis program aims at returning humans to the Moon and sending crewed missions to Mars [6]. Vital to the latter's plan is sustainable lunar exploration, which will serve as a training ground for the eventual long-term habitation and life support of humans on Mars. The expected 30-month mission duration and longer communication lag (up to 40 min for the round-trip) [7] impose stricter requirements than ever before and require higher astronaut autonomy. As it will not be possible to transport crew members back to Earth easily, missions will rely on point-of-care devices, and the early detection of physiological disorders might mean avoiding the evolution of life-threatening illnesses [8].

Abbreviations: ANITA, Analysing interferometer for ambient air; AQM, Air quality monitor; BAW, Bulk acoustic wave; COL, Columbus Laboratory Module; CPA, Combustion products analyzer; ECLSS, Environmental Control and Life Support System; E-Nose, Electronic nose; ESA, European Space Agency; FAIMS, High-field asymmetric-waveform ion-mobility spectrometry; FeNO, Fractional exhaled nitric oxide; FTIR, Fourier transform infrared; GC/DMS, Gas chromatography/Differential mobility spectrometry; GC/IMS, Gas chromatography/Ion mobility spectrometry; GC/MS, Gas chromatography/Mass spectrometry; ISS, International Space Station; JAMSS, Japan manned space systems; JPL, Jet Propulsion Laboratory; JPM, Japanese Pressurized Module; LAB, U.S. Laboratory Module; LLOD, Lower limit of detection; LSPR, Localized surface plasmon resonance; MEMS, Micro-electromechanical systems; MIP, Molecularly imprinted polymer; MOF, Metal-organic framework; MSS, Membrane-type surface-stress sensor; NASA, National Aeronautics and Space Administration; NDIR, Non-dispersive infrared; NRC, National Research Council; PANI, Polyaniline; PID, Photoionization detector; ppb, Parts per billion; ppm, Parts per million; ppq, Parts per quadrillion; ppt, Parts per trillion; PTR-ToF-MS, Proton-transfer reaction time-of-flight mass spectrometry; PUMA, Portable Unit for Metabolic Analysis; QCM, Quartz crystal microbalance; QCN, Quartz crystal nanobalance; RH, Relative humidity; RSS, Respiratory sensor system; SAW, Surface acoustic wave; SIFT-MS, Selected-ion flow-tube mass spectrometry; SMACs, Spacecraft maximum allowable concentrations; TMA, Trimethylamine; VOA, Volatile organic analyzer; VOC, Volatile organic compound.

* Corresponding author. Human-centered Sensing Laboratory, Department of Mechanical and Process Engineering, ETH Zürich, CH-8092 Zürich, Switzerland.

E-mail address: andreas.guentner@hsl.ethz.ch (A.T. Güntner).

<https://doi.org/10.1016/j.trac.2024.117790>

Received 15 February 2024; Received in revised form 16 May 2024; Accepted 23 May 2024

Available online 24 May 2024

0165-9936/© 2024 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Prolonged mission durations will also decrease the threshold of a chemical compound's safety limit due to the possibility of chronic exposure.

Gas sensors will play a pivotal role as they can provide health information on demand and without effort, for instance, through automated breath analysis [9]. Also, they are capable of monitoring air quality continuously [10] to ensure adherence to safety limits and control decontamination units at minimal energy consumption. Yet, space-validated breath analysis remains limited to O₂, CO₂, and flow sensing [11,12]. Missing is the capability to quantify other relevant analytes, such as VOCs, that bear most of the physiological and pathological information in exhaled breath [13]. Furthermore, sensor solutions must meet the constraints brought by space missions, such as compactness, minimal weight, and low resource (e.g., power) consumption. This is usually not fulfilled by available technologies like the AQM onboard the ISS, which weighs 3 kg and draws up to 100 W [2]. Recent advances in gas sensors have moved the field towards addressing these needs. To name a few examples: Chemoresistive gas sensors can have their sensitivity and selectivity improved through nanostructuring [14], surface engineering [15], appropriate filter integration on the system [16], or even chip [17] level. Mass-sensitive sensors (e.g., BAW devices) offer low-power solutions [18], while plasmonic sensors may provide visual warnings [19,20]. Advancements in electrochemical [21, 22] and laser spectroscopy [23] sensors have also been achieved with regard to miniaturization.

Previous reviews reported archival and real-time air monitoring protocols and devices used by NASA from the Gemini program to the ISS [2]. The authors argued that more extensive real-time monitoring of major VOCs, combustion products, and spacecraft-specific compounds would be required in longer missions without, however, covering sensors that would be suitable for such. Also, air quality on board Mir and the ISS were compared, and the most significant contributors to the total VOC concentration were identified [24]. Concerning health, previous patents for in-flight medical analysis devices were elaborated [25], and the need to develop biomarker detection technologies for FeNO, carbon monoxide, and hydrocarbons was identified as critical to carrying out deep-space missions. Point-of-care diagnostics for niche applications were also reviewed [26], including space, highlighting the challenges of translating traditional solutions to such an environment. The lack of understanding of the effects of long-term microgravity environments on humans and which biomarkers are appropriate were identified as challenges as well. Also, the sensing capabilities of in-flight devices were investigated, and the authors called for the adoption of real-time molecular sensing, which could be applied to non-invasive health monitoring [26]. The current state-of-the-art of astronaut's health monitoring in space was analyzed, urging the expansion of knowledge on the effects of extended stays and highlighting the need for leveraging new technologies to overcome the challenges of the new space age [27]. Much has also been done concerning gas sensors outside of the space domain; recently, advances in the fabrication methods to prepare nanostructured gas sensors, for instance, by printing [28], chemical vapor deposition [29], or flame-aerosols [30], were reviewed and their application for breath sensors in health monitoring explored [9]. Also, arrays [31] and filters/columns (e.g., catalytic [32] or sorption [33]) that enable odor recognition and selectivity enhancement for molecule-selective sensors have been discussed.

Here, we analyze the needs and opportunities for gas sensors brought about by the upcoming deep space exploration. First, a brief description of gas sensor types and their working principles is provided. This is followed by a detailed analysis of health monitoring through breath analysis, where we provide a historical overview of already implemented technologies, discuss unexploited but critical biomarkers and connect these with promising sensor solutions that are suitable for compact integration, enabling effortless and routine testing. Finally, environmental monitoring for spacecraft and habitation safety are discussed with particular emphasis on air pollutants that can threaten the

immediate safety and health of astronauts during prolonged presences in space. Thereby, we also suggest promising sensing concepts and materials. The objective of this review is to furnish both the space and sensor science communities with a comprehensive outline of challenges, significant technological advancements, and collaborative research opportunities.

2. Gas sensing concepts: brief overview

Few gas/volatile detection concepts have already been tested in space. Most established are GC/IMS (e.g., VOA), GC/DMS (e.g., AQM), and FTIR spectroscopy (e.g., ANITA) [2]. Despite their high performance [34] and the significant advances in their miniaturization [35], such detectors are not yet, and may not become, sufficiently compact for wearable health or distributed air quality monitoring, limiting their adoption in deep space exploration. Other mobility spectrometry techniques, however, may become an option in the future, such as FAIMS, due to their high miniaturization potential [36–39]. More promising are electrochemical sensors (e.g., CPA and RSS), albeit for a reduced number of analytes, chemoresistive sensors (e.g., JPL's E-noses [40]), and mass-sensitive (e.g., JAMSS' QCM [41]) sensors. This chapter only introduces their sensing concepts (Fig. 1) and provides pertinent literature, as the cited reviews have comprehensively covered them already.

Electrochemical gas sensors work based on redox reactions [45]. Such sensors consist of a working, a counter, and possibly a reference electrode that are immersed in an electrolyte. Usually, a gas-permeable membrane connects the electrochemical cell to its gaseous surroundings. There are three classes of electrochemical gas sensors based on their operational concept: conductometric, amperometric [45], and potentiometric [46]. In the case of amperometric gas sensors, the reaction of an analyte at the working electrode generates a current that is measured at fixed [47] or variable potential [48]. Selectivity is typically achieved by modification of the electrodes (e.g., functionalization with MIPs [49] or aptamers [50]), electrolyte [51], or membrane [52].

Chemoresistive gas sensors (or chemistors) consist of solid-state semiconductors that change their resistance upon analyte exposure [53]. Usually, such sensors consist of a micromachined μ -hotplate [54] covered by a compact [55] or porous [56] sensing layer of metal oxides

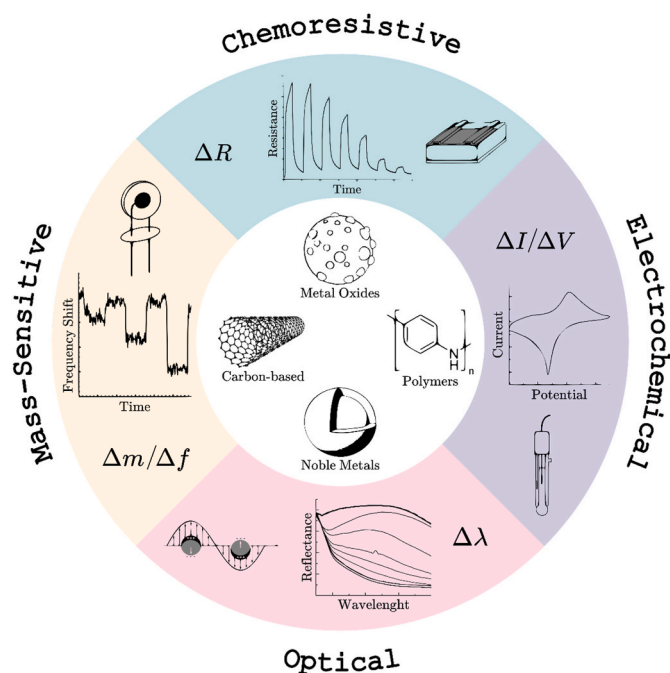


Fig. 1. Overview of gas sensing principles and some used sensing materials. Adapted from Refs. [20,42–44].

[57], polymers [58], or carbon-based [59] materials. By nanostructuring sensing layers, detection limits down to ppt have been achieved [60]. While assemblies of chemoresistive sensors to arrays [61] enable odor discrimination, recent advances in selective material design provide orthogonality [62] for targeted multi-tracer quantification [63]. Also of interest, and closely related to chemoresistors, are thermoelectric gas sensors, that consist of a thermopile that generates a Seebeck voltage when heated up by exothermic catalytic oxidation of target analytes (e.g., H₂ [64] or VOCs [65]).

Capacitive gas sensors are produced with dielectric materials that change their capacitance when exposed to analytes [66]. The sensing layer can consist of polymers [67–69], metal oxides [70,71], or MOFs [72,73], for example. Nanostructured capacitive gas sensors capable of quantifying gas concentrations down to low ppm (e.g., benzene [74] and ethanol [75]) and ppb levels (e.g., H₂ [76]) have been reported.

Mass-sensitive gas sensors recognize resonance frequency changes of their sensing element upon adsorption of analyte molecules [77]. Most relevant for space applications are the BAW devices, such as the QCM. In QCMs, a thin quartz crystal is placed between two electrodes across which an alternating potential is applied, causing the crystal to oscillate due to its piezoelectric properties [78]. When an analyte adsorbs on the device's surface, the mass increase results in a shift of the QCM's resonant frequency that is correlated to analyte concentration [42]. Selectivity is achieved through surface coating (e.g., functional [79] or molecularly-imprinted layers [80]) of the sensing element. As the crystal's properties from which the resonant frequency is derived are temperature dependent, QCMs require temperature control and compensations if precise measurements are to be obtained [81]. SAW oscillations propagate on the material's surface, in contrast to the bulk wave propagation in QCMs. These devices can be operated at lower powers and are generally more compact than BAWs [82]. Acoustic-wave-based sensors can also operate by propagating sound through the gas sample itself, as done in, e.g., audible range acoustic gas sensors [83]. Closely related to these mass-sensitive devices is the MSS. In these sensors, the analyte adsorbs onto a membrane suspended by piezoresistive beams, which in turn have their resistance altered by the stress induced in the sensing layer [84]. As a micromechanical device, the MSS is also a compact and low-power sensing solution [85,86].

A broad range of optical sensor concepts is also available. These are based, for instance, on the absorption of molecule-characteristic wavelength [87], fluorescence [88], or plasmonic [19] effects. More specifically, in the case of LSPR, the presence of analytes is detected through changes in the dielectric environment in the vicinity of plasmonic nanoparticles [19]. The sensitivity and selectivity of LSPR sensors can be enhanced through a chemical reaction between the analyte and the plasmonic surface [20]. Related to these optical sensors is the PID, which exposes gas samples to light (typically UV), ionizing molecules with ionization energy below the light source's energy, rendering PIDs inherently non-specific. Electrons and positive ions are then collected by the sensor's electrodes, generating a measurable current proportional to the concentration of ionizable analytes [89]. Similarly, photoacoustic sensors use light to excite molecules into higher energy states; as the molecules relax through non-radiative processes, local heat generation leads to temperature and pressure increases that are detected by an acoustic transducer [90]. A widely adopted photoacoustic sensing method is NDIR [91], although limited by its non-specific nature [92] and high LLOD (e.g., tens of ppm [93]).

Finally, also important to the development of gas sensing systems is the pre-processing of the gas mixtures. Exhaled human breath [94] and indoor air [95] are complex, with hundreds of different molecule types. Adsorption filters can enhance the selectivity of a system by separating the constituents of gas mixtures through their different interaction with a stationary phase (the adsorbent), where the analyte is temporarily retained in the column by adsorption [33]. They have found applications in diverse configurations, such as packed beds [96] and overlayers [97]. Catalytic filters operate continuously by selectively converting

confounders to species to which the sensing system is not sensitive while the target analyte exits the filter unscathed [32,98]. Sensitivity and LLOD can be enhanced with preconcentrators, which operate by accumulating analytes over fixed intervals and then releasing a concentrated stream for analysis [99] to achieve concentration factors in the range of, e.g., a few hundred [100]. Microfabricated preconcentrators can yield highly compact and integrated MEMS-based gas sensors [101]. While such pre-processing components increase system complexity and, in some cases, compromise performance (e.g., increase in response time caused by microporous membranes [102]) and inhibit continuous operation (e.g., pre-concentrators), they are still compatible with compact device integration [103].

3. Monitoring astronaut health through breath analysis

Astronauts face several health challenges in space due to its unique environment. More specifically, microgravity may lead to space motion sickness [104], muscle atrophy [105], loss of bone tissue [106], cardiovascular alterations [107,108], imbalance of body fluids [109], and visual impairment [110]. The enhanced exposure to radiation yields a higher risk for neurodegenerative diseases (e.g., Alzheimer's disease) and cancer, while variable light and dark cycles may disturb circadian rhythm and lead to sleep deprivation [111] and psychological stress [112]. Furthermore, an altered diet may result in dehydration and undernutrition [113], and altered microbiota has been associated with microbiota dysbiosis, skin hypersensitivity [114], and immune system dysregulation [115]. While regular exercise and balanced nutrition may mitigate some of these health issues, longer presence in space will require continuous health monitoring tools to recognize negative health developments early and guide personalized treatment.

Traditional methods bear risks of complication (e.g., biopsy) and require bulky equipment (e.g., MRI), specialized personnel, or supporting infrastructure (e.g., clinical laboratory). More practical are sensor-based techniques that astronauts can use autonomously. Promising in this regard is breath analysis [116] since it is non-invasive, thus inherently safe, and rich in physiological and pathological information [13]. In breath analysis, exhalation flow rate, airway pressure, and, most importantly, the concentrations of biomarkers are analyzed online [117, 118] or, for the case of the latter, also offline (e.g., through sampling bags [119]). Established in earth-based research settings for biomarker quantification are the GC/MS [120], PTR-ToF-MS [121], and the SIFT-MS [122], but these are too bulky [123] and power-consuming for space, also featuring limited miniaturization potential due to inevitable components (e.g., vacuum pumps and quadrupole mass filters). When performed with compact gas sensors [9], these may be integrated into astronaut suits (e.g., helmets) or headsets to provide automated/effortless analyses with full timeline transparency (Fig. 2). Thereby, the sensors or assembled arrays convert the chemical information contained in exhaled breath into measurable signals (Fig. 2). Processing these signals through advanced algorithms or machine learning [124, 125] yields biomarker quantification and longitudinal profiles that may be matched to physiological or pathological conditions. This information can be displayed in real-time to provide the astronauts with feedback or transmitted for remote health assistance from earth-based mission control.

Some breath analysis systems have already been developed for space applications. Specifically, NASA's PUMA (Fig. 3a) is a wearable device [126] based on indirect calorimetry to quantify fatty acid and carbohydrate oxidation rates [127]. More specifically, the device featured a breathing mask to collect breath and measure the expiratory gas flow rate [11]. The CO₂ concentration in the exhaled breath was quantified with an optical sensor based on NDIR spectroscopy, while oxygen-induced quenching of the fluorescence from ruthenium-based dyes was exploited for O₂ measurement [11]. The PUMA device was tested during cycling (Fig. 3b) at various loads (i.e., 0–200 W), and the increasing O₂ and CO₂ uptake rates were detected in good agreement

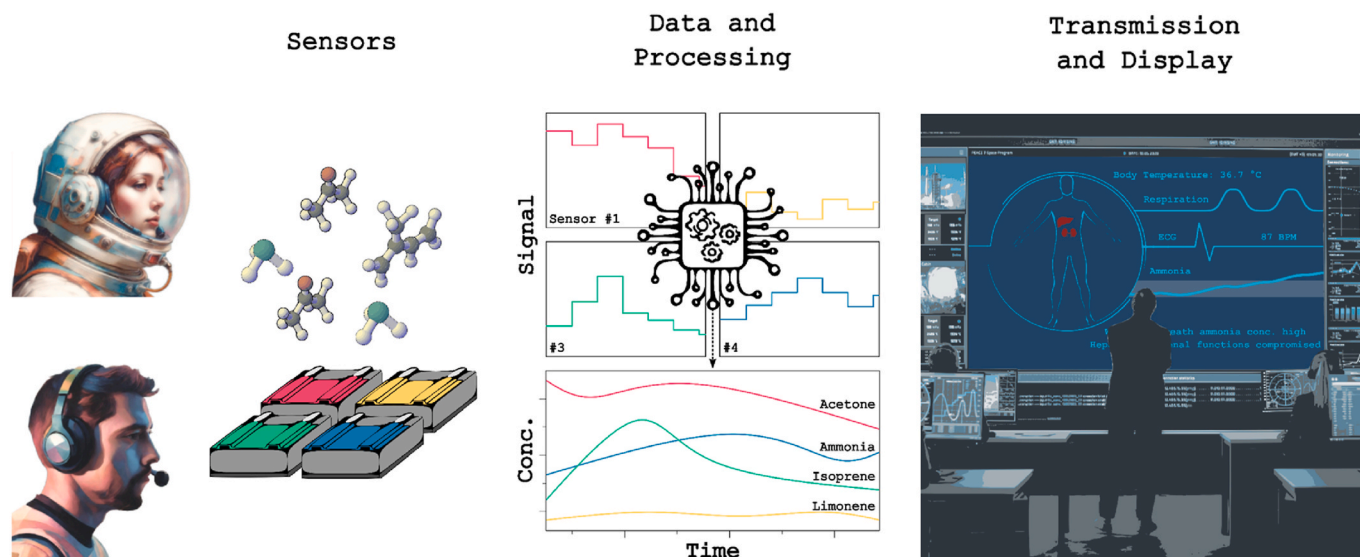


Fig. 2. Strategy for health monitoring through breath analysis: Breath is accumulated in space suit helmets or exhaled directly onto a headset. Embedded sensors, or an array of them, interact with the molecules contained in breath, leading to a signal (e.g., electrical or optical). Algorithms convert these signals into biomarker concentration profiles that provide the astronaut with on-demand information on critical health parameters, which can also be continuously relayed to mission control. Adapted from Ref. [42].

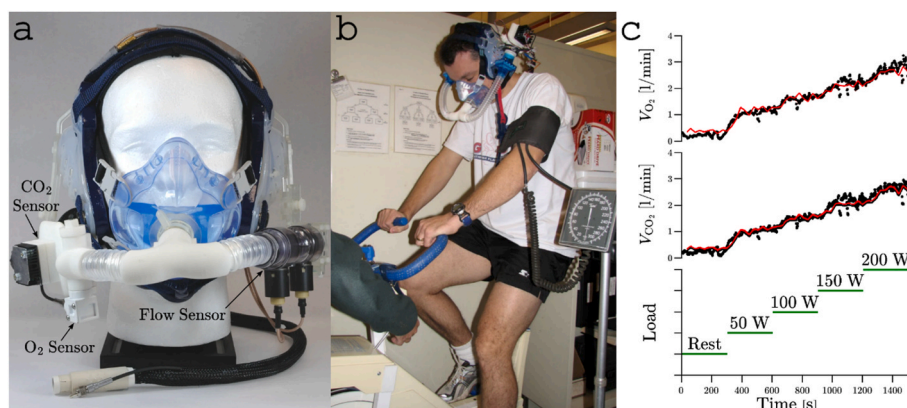


Fig. 3. NASA's PUMA measures a user's O_2 inhalation rate, CO_2 exhalation rate, and total exhalation flow. (a) PUMA on a mannequin head with selected components indicated [126]. Image courtesy of NASA. (b) PUMA load tests on a volunteer at the Glenn Research Center. Adapted from Ref. [11]. (c) Volumetric O_2 and CO_2 flows of a volunteer during cycling under different loads as measured by PUMA (black symbols) and a commercial solution by ParvoMedics (red lines). Adapted from Ref. [11].

(Fig. 3c, black symbols) with a commercial instrument by ParvoMedics (red lines, mostly overlapping with symbols). Further tests were conducted to measure the resting metabolic rate. An analog development based on indirect calorimetry, the RSS, was launched by ESA and aimed to include H_2 and CO measurements [12]. While RSS and PUMA demonstrated the first merits and the immediate practical impact of breath analysis, their focus on a few breath markers restricted the provided health information to metabolic activity. These devices were also rather bulky (Fig. 3a) and thus hardly compatible with being seamlessly integrated into the daily routine of astronauts on board spaceships/stations or during extravehicular activities (Fig. 2).

Beyond its main constituents, N_2 , O_2 , CO_2 , and water, exhaled breath contains over 1400 VOCs [128] that usually occur at extremely low concentrations, ranging typically from ppq to ppm [129]. Yet, they contain most of the physiological and pathological information. Table 1 connects space-relevant health challenges with promising breath biomarkers and their physiological/pathological origin and relevance. To demonstrate feasibility, some possible sensor solutions with proven functionality in human breath are also provided, including the number

of tested volunteers.

For instance, breath acetone is interesting for detecting undernutrition in astronauts. Formed after the β -oxidation of fatty acids in the hepatic mitochondria [130], breath concentration increases when metabolic fuel preference switches from carbohydrate to fatty acids [131]. In fact, rising acetone concentrations have been observed during exercise [132] that correlated with cardiorespiratory fitness [133], while glucose intake leads to a prompt decrease in expired acetone levels in healthy volunteers (Fig. 4a, green triangles). Also, the development of metabolic diseases may be detected, as different breath acetone patterns were recognized for diabetes type-1 patients (yellow circles). Primarily chemoresistive and optical sensors have demonstrated promising performance when detecting breath acetone in small-cohort human testing (Table 1). For instance, a $Si:WO_3$ sensor prescreened by a $Pt:Al_2O_3$ catalytic [32] filter quantified breath acetone with bias and precision of 25 and 169 ppb, respectively, in 146 breath samples [134] with stable performance for 145 days [135]. This is sufficiently low as breath acetone ranges typically between 148 and 2744 ppb in people following a normal Western diet [136].

Table 1

Space-relevant health challenges and promising breath markers for their monitoring. Also listed are suitable sensors that have been tested on humans but not yet implemented for space applications.

Breath Compound	Space-Related Health Challenge	Physiological Origin and Relevance	Sensing Principle	Material or Device	Human Test Conditions (Number of Volunteers)
Acetone	Nutritional deficiencies and metabolic diseases [153] Cardiac atrophy [107,108]	Acetyl-CoA Metabolism [154,155] ↑ Fasting [156] ↑ Ketoacidosis [157] ↑ Ketogenic Diet [131] ↑ Exercise [132] Diabetes [158] ↑ Heart Failure [159]	Chemoresistive	Si:WO ₃	Constant-load Cycling (5) [160] and (20) [132] Ketogenic Diet (11) [161] Diabetes (19) [158] Rest (4) [162]
				GC – SnO ₂	Constant-load Treadmill (6) [163]
			Optical	Pt/Al ₂ O ₃ – Si:WO ₃	Ramped-load Cycling (9) [134]
				H ₈ N ₂ O ₆ S NADH/S-ADH ^a	Rest (2) [164] Constant-load Cycling (3) [165]
Ammonia	Hepatic and renal dysfunction [109,168,169]	Protein Metabolism [170,171] ↑ Chronic liver disease [172] ↑ Renal dysfunction [150] ↑ Liver injury [173]	Chemoresistive	CuBr	Hypocaloric diet (58) [167] Chronic Liver Disease (39) [174]
				PANI TFB ^b	Hemodialysis (20) [151] Hemodialysis (40) [152]
			Optical	Poly (3-hexylthiophene) Cavity ring-down spectroscopy	Hemodialysis (2) [175] Hemodialysis (40) [176]
Hydrogen	Gut microbiome dysbiosis [177] Circadian desynchronization [111]	Gut microbiome [178] ↑ Carbohydrate intolerance [142,143] ↑ Intestinal bacterial overgrowth [179] ↑ Circadian rhythm [180]	Thermoelectric	Pt/Al ₂ O ₃	Post-meal (4) [181]
Isoprene	Muscle atrophy [105] Circadian desynchronization [111]	Muscular lipolytic cholesterol metabolism [182] ↑ Muscle activity [183] ↓ Muscle dystrophy [184] Circadian rhythm [185]	Chemoresistive	Activated alumina – Si:WO ₃ Polyoxometalate/Co ₃ O ₄	Cycling and rest (6) [186] Constant-load treadmill (1) [187]
Limonene	Hepatic and renal deterioration [109,168,169]	Dietary [188] (metabolized by CYP2C9 and CYP2C19 in healthy livers) [189] ↑ Hepatic encephalopathy [188]	Chemoresistive	Tenax – Si:WO ₃	Rest (4) [190]
Methane	Gut microbiome dysbiosis [177]	Hydrogenation of carbon dioxide by methanogens [191,192] ↑ Carbohydrate intolerance [191,193]	Optical	Tunable diode laser spectroscopy	Rest (3) [194]
FeNO	Inflammatory Infections [195]	Eosinophilic airway inflammation [196] ↑ Asthma [196] Circadian rhythm [197]	Electrochemical	NOBreath and NIOX MINO	Rest (36) [198]
Short-chained Fatty Acids	Gut Microbiome Dysbiosis [177]	Gut microbiome [199–201]	–	–	–
TMA	Gut Microbiome Dysbiosis [177]	Gut microbiome [202]	–	–	–

^a NADH/S-ADH: nicotinamide-adenine-dinucleotide-dependent secondary alcohol dehydrogenase.

^b TFB: poly [(9,9-dioctylfluorenyl-2,7-diyl)-co-(4,4'-(N-(4-s-butylphenyl)diphenylamine)].

Altered microbiomes may be recognized through the monitoring of short-chained fatty acids [137], and first sensors with detection limits at the relevant [138,139] ppb range are available [140]. Also H₂ and CH₄ are of relevance, being already established in clinical practice [141] for the diagnosis of lactose [142] or fructose intolerance [143] and bacterial overgrowth in the small intestine [144]. Specifically, expired H₂ concentrations in intolerant volunteers (Fig. 4b, blue squares) increase significantly upon lactose intake (e.g., 160 ppm), while they remain below 30 ppm in normal people (green triangles). Various research-level [145] and commercial breath hydrogen and methane sensors are available (e.g., QuinTron [146], H2 Check [147], and LactoFAN2 [148]).

Hepatic or renal impairment may be recognized through elevated breath ammonia concentrations, a protein metabolism product [149]. For instance, normal mouth-exhaled ammonia levels are 248–2935 ppb [136] but can exceed 10 000 ppb in end-stage renal disease patients (Fig. 4c, red diamonds) and drop, for instance, during hemodialysis treatment [150]. Several sensors have been successfully tested for ammonia quantification in exhaled human breath (Table 1). For example, chemoresistors based on PANI recognized reduced breath ammonia levels in 20 volunteers after hemodialysis and showed a strong correlation (i.e., a Pearson correlation coefficient of 0.97) to

photoacoustic laser spectroscopy [151]. Also, such sensors demonstrated a 2% drift over a three-week period, while other ammonia sensors have been tested for stability for periods surpassing two months [152].

Despite some promising examples and first functional prototypes, breath analysis and suitable sensor development are still in their infancy, and various challenges remain to implementing such technologies for comprehensive astronaut health monitoring during space missions. Upcoming research may focus on clarifying the medical relevance of breath markers for space-related challenges to support the connections delineated in Table 1. Furthermore, the design and optimization of molecular-specific sensor concepts may be targeted, especially for those breath markers where no sensor solutions with proven performance with humans exist yet (e.g., short-chained fatty acids or TMA, Table 1). More information on sensor stability is also needed as the expected mission duration of 30 months [7] has not yet been tested [135,151,152]. Orthogonal sensor arrays consisting of constituent sensors with high selectivity to target analytes [62] enable multi-tracer breath analysis [63] and seem promising to detect, for instance, the “breath print” of the circadian rhythm that some compounds (e.g., isoprene, Fig. 4d) are known to follow [204].

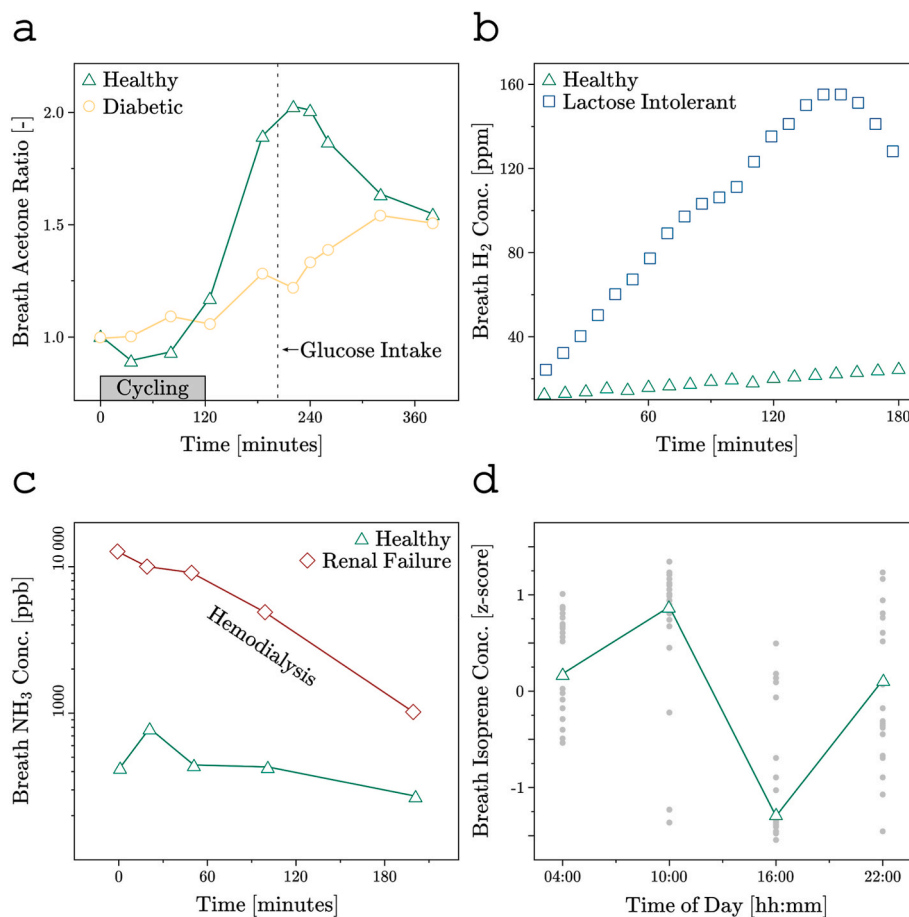


Fig. 4. (a) Breath acetone during exercising and fasting in healthy (green triangles) and type-1 diabetic (yellow circles) subjects. Adapted from Ref. [158]. (b) Breath hydrogen of healthy and lactose intolerant (blue squares) subjects following oral lactose ingestion. Adapted from Ref. [203]. (c) Breath ammonia of healthy and end-stage renal failure (red diamonds) subjects during hemodialysis. Adapted from Ref. [150]. (d) Breath isoprene of healthy subjects throughout the day. Adapted from Ref. [197].

4. Environmental monitoring: spacecraft and habitation safety

Manifold are also the challenges in environmental control in space missions. Outgassing (e.g., siloxanes [205]), for example, can hinder the performance of optical equipment and heat exchangers [206], while thermal degradation (e.g., from fires or equipment overheating) can introduce unsafe concentrations of gaseous contaminants [207]. Leaks from vital spacecraft systems (e.g., ammonia from thermal control systems [208]), commonly used chemicals (e.g., ethanol and isopropanol), and contaminants emitted by crew members (e.g., acetone, methane, methanol, hydrogen sulfide, and acetaldehyde [209]) are also unavoidable sources of air contaminants. Despite the thorough characterization of spacecraft-material outgassing and the adoption of strict quality control standards minimizing the risk of non-intentional combustion and leaks from containment vessels, sensing and controlling airborne contaminants is a critical aspect of space missions.

Environmental gas sensing has been crucial in previous and ongoing space missions. For instance, efforts to set chemical exposure guidelines for astronauts began with the NRC's guidelines in 1968 [210]. Soon after, a revised guideline for atmospheric contaminants in manned spacecraft was requested by NASA to guide the improvement of the ECLSS, which also contemplated 6-month periods [211]. The Skylab space station demonstrated that humans could live and work in space for extended periods (i.e., three months). While it had intermittent carbon dioxide monitoring by an electrochemical sensor [212], real-time monitoring of air aboard spacecraft was only extended beyond major constituents (i.e., O₂, N₂, CO₂, H₂, humidity, and CH₄) on NASA's Space

Shuttle, when the CPA, an electrochemical sensor, was tested [207]. The need for real-time air monitoring was reinforced during the ISS development because of the extension of typical mission durations. As off-site analyses became too infrequent, the ISS employed the VOA (Fig. 5a), a GC/IMS, to monitor VOCs of concern on spacecraft selectively (Fig. 5b) [213]. NASA advanced its VOC monitoring by developing E-noses [214], sensor arrays that extend the capability of non-specific sensors through pattern recognition [30], albeit still with a high susceptibility to confounders [62]. ESA adopted another strategy, developing an FTIR-based system, ANITA. More recently, the AQM (Fig. 5c), a GC/DMS, was deployed at the ISS [215]; its compactness and battery-powered operation allowed for longitudinal measurements of the air quality in different modules of the ISS (Fig. 5d).

As the new era of space exploration extends mission duration times, lower contaminant quantification thresholds are necessary to protect crew health in long-term exposure scenarios, and selective and low-resource environmental monitoring tools will be critical [216]. Thereby, a wide range of analytes and concentrations need to be covered, as specified by NASA's current SMACs list [217]. Such networks will be essential in ensuring safety and habitability when establishing a sustainable human presence on the Moon and Mars. The possibility of further integration into other platforms, such as in exploration vehicles, is a highly valued asset in an application where resources (e.g., energy and payload) are scarce. On Earth, similar sensor technologies have already advanced environmental monitoring and industrial safety with efforts to integrate them into Internet of Things networks [10] and to control air cleaners [218], but the accuracy and

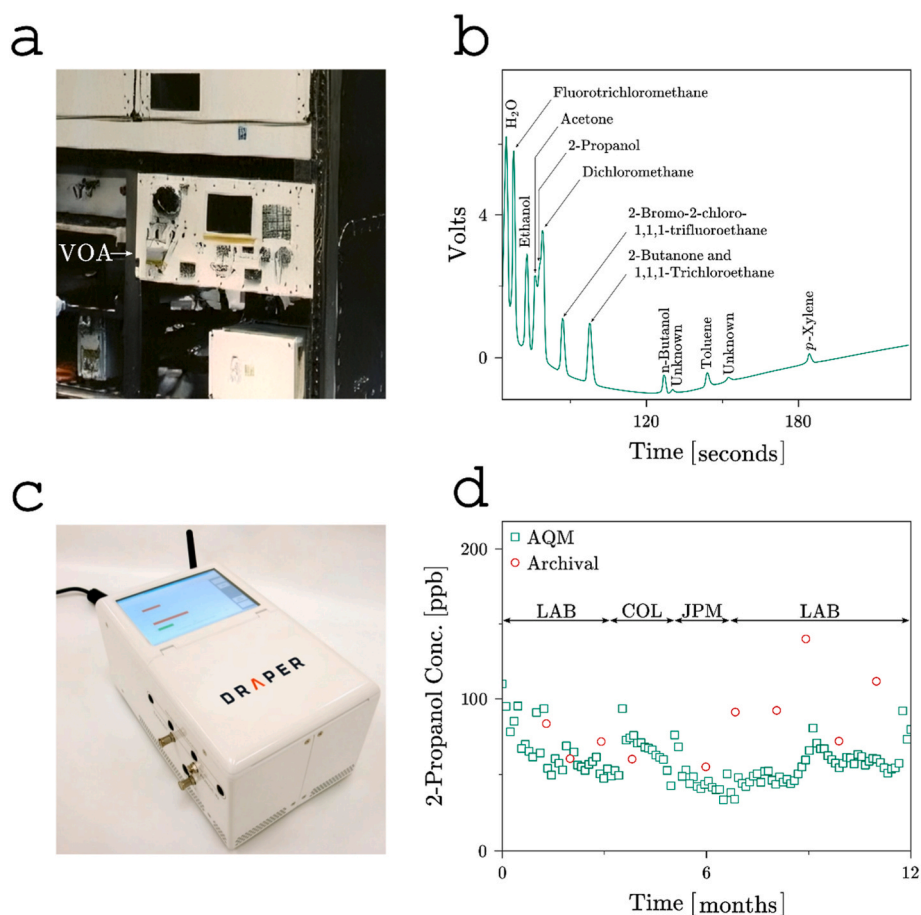


Fig. 5. Environmental monitoring devices deployed in space. (a) The VOA deployed at the ISS on space station racks on Earth. Adapted from Ref. [220]. (b) Measured compounds in an air sample as identified in the VOA's gas chromatograph by a thermal conductivity detector. Adapted from Ref. [213]. (c) Picture of the AQM. Adapted from Ref. [221]. (d) A time series of 2-propanol concentrations as measured by the AQM (green squares) and archival samples (red circles) in different sections of the ISS, i.e., the LAB, COL, and JPM. Adapted from Ref. [215].

stability of low-cost sensors have been long-lasting concerns [219].

Over 60 compounds are currently targeted by the SMACs, which defines short-term (i.e., 1 and 2 h) and long-term (i.e., 7, 30, 180 and 1000 days) exposure limits [217]. These include aldehydes (e.g., acetaldehyde and acrolein), alcohols (e.g., isopropanol and n-butanol), ketones (e.g., acetone and methyl ethyl ketone), aromatics (e.g., benzene and toluene), siloxanes, and esters (e.g., ethyl acetate and butyl acetate) [217]. Table 2 lists selected compounds from the SMACs as well as sensors suitable for their detection with miniaturization potential. Only sensors that meet the LLOD requirement set by the 1000-day exposure limit listed in the SMACs are reported, and most were tested under pertinent RH conditions.

Formaldehyde, for example, is a carcinogenic compound [222] that has been measured aboard the ISS (as a result of the thermal degradation of polymers and its occasional use in biological experiments [223]) and must be monitored to ensure crew safety. So critical it is to human health that national regulations are more restrictive than space guidelines (e.g., 8 ppb in France [224], considerably lower than the 100-ppb long-term SMAC [217]). Its monitoring in real room air has been achieved down to 5 ppb at a 2 min response time with micromachined, chemoresistive sensors preceded by a sorbent separation column, which was stably operated for two weeks (Table 2). Also of interest is the monitoring of propanol with a long-term SMAC of 60 ppm, which can potentially threaten the operation of the ECLSS and is off-gassed by spacecraft hardware and used as a disinfectant [225]. An optical terahertz sensor with a MIP as a receptor enabled its quantification down to 50 ppm at up to 80% RH [226]. While recovery relies on blowing nitrogen on the

sensor's surface, this gas is available, for instance, onboard the ISS [227].

Also carcinogenic is benzene [228], which has been occasionally detected onboard the ISS, probably outgasses from spacecraft materials or arises from the thermal degradation of electronic components [225]. Chemoresistive sensors meeting its 13 ppb LLOD requirements have been reported, with a gold-nanoparticle-decorated multiwall carbon nanotube sensor quantifying benzene at 2.5 ppb in air at 60% RH not showing significant drift over six months (Table 2). Also, their sensor exhibited selectivity towards benzene with respect to common confounders such as toluene and xylene (i.e., response ratios of 7 and 30, respectively, with all analytes at 100 ppb) [229]. Interesting as well are the various siloxanes listed in the SMACs, which have a diverse origin in spacecraft (e.g., outgassing from lubricants, heat transfer fluids and pads, and cosmetics [223]). Beyond the health risks posed by long-term exposure (e.g., to the central nervous and respiratory systems [217]), they may also compromise equipment by hindering heat transfer and the performance of optical equipment through the formation of opaque, insulating films [230]. A microcantilever array capable of discerning and quantifying distinct siloxanes down to 0.1 ppm has been reported (Table 2). The sensor's coating was stable during five weeks [231].

Leveraging the research and progress achieved in terrestrial applications, space exploration can pursue the same reliability, sensitivity, and operational efficiency but in the challenging conditions of space habitats. Ultimately, such sensor systems with the capacity to track various pollutants may be deployed as networks (Fig. 6) to map the chemical composition of the air in space habitats in real time to ensure

Table 2

Selected contaminants covered in the SMACs [217] and examples of sensors with miniaturization potential for their detection with proven performance at sufficient LLOD.

Contaminant	Origin	1000-day SMAC [217] [ppm]	Sensing Principle	Material or Device	LLOD [ppm]	RH [%]	Reference
Acetaldehyde	Outgassing, Crew Metabolism	2 ^a	Electrochemical	ALDH/H-PTFE ^c	0.11	Breath	[232]
Acetone	Outgassing, Crew Metabolism, Cleaning Agents	22 ^a	Chemoresistive	Si:WO ₃	0.02	0–90	[233]
				Nb:WO ₃	0.009	80	[234]
				Ru:SnO ₂	0.5	30	[235]
				Al:ZnO	0.1	0–90	[236]
				Pt:Al ₂ O ₃ – Si:WO ₃	0.05	30–90	[135]
				Pt:Al ₂ O ₃ – Pd:SnO ₂	0.05	30–90	[237]
Acrolein	Accidental Fire or Combustion	0.008	–	–	–	–	–
Ammonia	Life Support Systems, Waste Management Systems, Cleaning Agents	3	Chemoresistive	CuBr	0.005	90	[174]
					0.025	0–80	[238]
					0.0002	90	[239]
				Si:MoO ₃	0.4	90	[240]
Benzene	Propellant and Fuel System, Outgassing	0.013	Chemoresistive	WO ₃ – Pd:SnO ₂	0.013	10–80	[241]
				Cobalt porphyrin:TiO ₂	0.005	0–50	[242]
				Au/Multi-walled carbon nanotubes	0.0025	10–60	[229]
Butanol	Outgassing, Waste Management System, Experimental By-product	12	Chemoresistive	In ₂ O ₃ :ZnO	1	0	[243]
Butanone (Methyl Ethyl Ketone)	Outgassing	10 ^a	Mass-sensitive	Polyethylene glycol/QCN	5	0	[244]
Dichloroethane	Outgassing	0.4	–	–	–	–	–
Dichloromethane (Methylene Chloride)	Outgassing	1	Chemoresistive	Sm ₂ O ₃ :SnO ₂	0.1	0	[245]
Ethanol	Cleaning Agent, Experimental By-product	1000	Chemoresistive	Ga:NiO	10	0	[246]
				Tenax – Pd:SnO ₂	1000	0–90	[247]
Ethyl Acetate	Cleaning Agent, Outgassing, Experimental By-product	39	Chemoresistive	Al:In ₂ O ₃	5	30	[248]
Formaldehyde	Outgassing, Experimental By-product	0.1	Chemoresistive	Tenax – Pd:SnO ₂	0.005	45	[249]
				Zeolite – Pd:SnO ₂	0.03	50–90	[102]
				Array	0.003	90	[250]
				In ₂ O ₃	0.05	15–70	[251]
				Plasmonic	Ag – TiO ₂	0.005	50
	Mass-sensitive	PEI/BC/SAW ^d	0.1	30–84	[252]		
Hexane	Outgassing	2.4	–	–	–	–	–
Methanol	Propulsion System, Outgassing, Experimental By-product	10	Chemoresistive	Tenax – Pd:SnO ₂	1	10–90	[253]
Propanol	Cleaning Agent, Experimental By-product	60 ^a	Optical	MIP	50	5–80	[226]
Siloxanes	Outgassing, Experimental By-product, Thermal Control System	1–50 ^b	Mass-sensitive	Microcantilever	0.1	0	[231]
				MOF/QCM	0.01	0	[254]
Toluene	Outgassing	4	Chemoresistive	UV – In ₂ O ₃ /ZnO	1	0–80	[255]
Xylene	Outgassing	1.5	Chemoresistive	CuO/ZnO	0.01	0–40	[256]

^a 180-day SMAC; the 1000-day SMAC is not set.

^b Linear siloxanes have a 1000-day SMAC of 50 ppm; other siloxanes listed in the SMACs have a 1000- or 180-day SMAC of 1 ppm.

^c ALDH: Aldehyde dehydrogenase; H-PTFE: hydrophilic polytetrafluoroethylene.

^d PEI: polyethyleneimine; BC: bacterial cellulose.

adherence to set exposure limits and to alert personnel about hazardous pollutant concentrations.

5. Conclusions and outlook

By leveraging the capabilities of cutting-edge sensor technologies, the way can be paved for deep space exploration and habitation. We have elucidated the various types of gas sensors that have demonstrated their efficacy in detecting a wide array of breath markers or air pollutants. These hold immense promise to be applied in crewed space missions to ensure continuous health monitoring and safe environments. Beyond the needed technological advances in sensor performance (e.g., selectivity, sensitivity, and stability), seamless integration into established infrastructure, compliance with standard operational procedures, and adherence to resource constraints will be critical. Since space missions will endure over extended periods and target more remote places [6], sufficient longevity and durability must be ensured, as maintenance or even replacement of tools may not be possible. Looking ahead, collaborative interdisciplinary research and development efforts involving scientists and engineers from academia, space agencies, and

related industries will be instrumental in driving innovation and fostering the adoption of next-generation gas sensing technologies for space applications.

CRedit authorship contribution statement

Tiago Elias Abi-Ramia Silva: Writing – review & editing, Writing – original draft, Visualization, Investigation, Data curation, Conceptualization. **Federico Burisch:** Writing – review & editing, Visualization, Investigation, Conceptualization. **Andreas T. Güntner:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

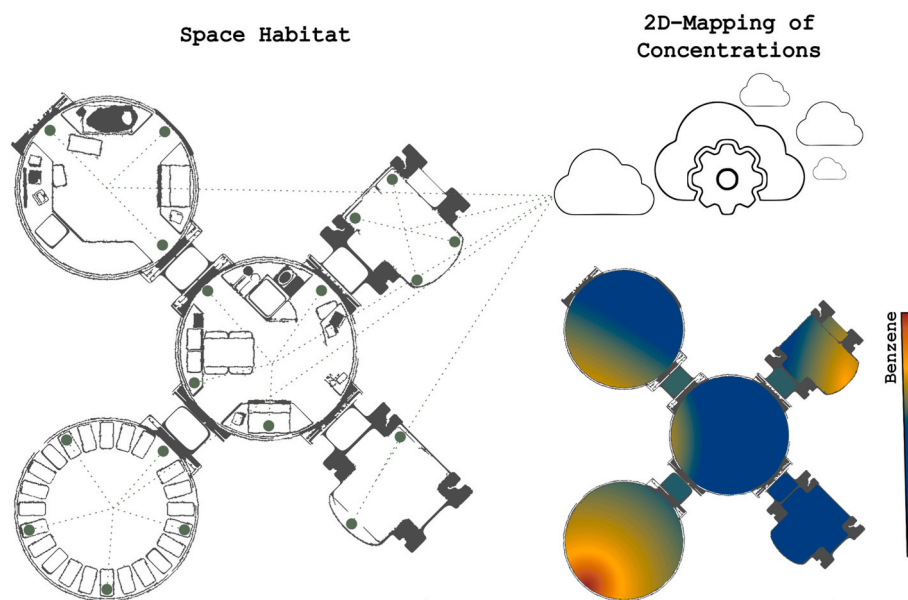


Fig. 6. Environmental air monitoring. Efficient and miniaturized sensors will allow for deploying distributed sensing networks within the constraints posed by space missions (e.g., modularity and minimal resource consumption). When combined with proper data processing methods, such networks can measure time- and space-resolved concentration profiles. Adapted from Refs. [42,257].

Data availability

No data was used for the research described in the article.

Acknowledgment

This study was financially supported by the Swiss State Secretariat for Education, Research and Innovation (SERI) under contract number MB22.00041 (ERC-STG-21 “HEALTHSENSE”), and partially by the European Space Agency (contracts 4000144484 and 4000144357).

References

- [1] C. Sawin, The Skylab medical experiments altitude test (SMEAT), *Aerospace Medicine and Human Performance* 92 (1) (2021) 58–60.
- [2] T.F. Limero, W.T. Wallace, What air and water quality monitoring is needed to protect crew health on spacecraft? *New Space* 5 (2) (2017) 67–78.
- [3] National Academies of Sciences, Engineering, and Medicine, *Refinements To the Methods For Developing Spacecraft Exposure Guidelines*, The National Academies Press, Washington, DC, 2016, p. 64.
- [4] Williams, D.R. Future Chinese Lunar Missions. [cited 2024 February 10]; Available from: https://nssdc.gsfc.nasa.gov/planetary/lunar/cnsa_moon_future.html.
- [5] ISRO, Chandrayaan-3. [cited 2024 February 10], Available from: https://www.isro.gov.in/Chandrayaan3_Details.html.
- [6] Office of the Federal Register, National Archives and records administration, DCPD-201700902 - Memorandum on Reinvigorating America’s Human Space Exploration Program (2017). Office of the Federal Register, National Archives and Records Administration.
- [7] D.L. Baisden, et al., Human health and performance for long-duration spaceflight, *Aviat Space Environ. Med.* 79 (6) (2008) 629–635.
- [8] B.A. Houtchens, Medical-care systems for long-duration space missions, *Clin. Chem.* 39 (1) (1993) 13–21.
- [9] A.T. Güntner, et al., Breath sensors for health monitoring, *ACS Sens.* 4 (2) (2019) 268–280.
- [10] M. Mayer, A.J. Baumner, A megatrend challenging analytical chemistry: biosensor and chemosensor concepts ready for the Internet of Things, *Chem. Rev.* 119 (13) (2019) 7996–8027.
- [11] D.L. Dietrich, Development of a portable unit for metabolic analysis (PUMA) [cited 2024 February 5]; Available from: <https://nescacademy.nasa.gov/downloadFile/1255>, 2023.
- [12] U. Hoffmann, et al., Development and application of a miniaturised sensor system for respiratory investigations (MAP-RSS), *Life in Space for Life on Earth* 553 (2008) 102.
- [13] W. Miekisch, J.K. Schubert, G.F.E. Noeldge-Schomburg, Diagnostic potential of breath analysis—focus on volatile organic compounds, *Clin. Chim. Acta* 347 (1) (2004) 25–39.
- [14] N. Yamazoe, New approaches for improving semiconductor gas sensors, *Sensor. Actuator. B Chem.* 5 (1) (1991) 7–19.
- [15] S.-Y. Jeong, J.-S. Kim, J.-H. Lee, Rational design of semiconductor-based chemiresistors and their libraries for next-generation artificial olfaction, *Adv. Mater.* 32 (51) (2020) 2002075.
- [16] A.T. Güntner, I.C. Weber, S.E. Pratsinis, Catalytic filter for continuous and selective ethanol removal prior to gas sensing, *ACS Sens.* 5 (4) (2020) 1058–1067.
- [17] S.-Y. Jeong, et al., Exclusive detection of volatile aromatic hydrocarbons using bilayer oxide chemiresistors with catalytic overlayers, *Nat. Commun.* 14 (1) (2023) 233.
- [18] Y. Yang, C. Dejous, H. Hallil, Trends and applications of surface and bulk acoustic wave devices: a review, *Micromachines* 14 (1) (2023) 43.
- [19] A. Tittl, H. Giessen, N. Liu, Plasmonic gas and chemical sensing, *Nanophotonics* 3 (3) (2014) 157–180.
- [20] A.T. Güntner, F.M. Schenk, Environmental formaldehyde sensing at room temperature by smartphone-assisted and wearable plasmonic nanohybrids, *Nanoscale* 15 (8) (2023) 3967–3977.
- [21] A. Barhoum, et al., Modern designs of electrochemical sensor platforms for environmental analyses: principles, nanofabrication opportunities, and challenges, *Trends in Environmental Analytical Chemistry* 38 (2023) e00199.
- [22] F.T.G. van den Brink, et al., Miniaturization of electrochemical cells for mass spectrometry, *TrAC, Trends Anal. Chem.* 70 (2015) 40–49.
- [23] Z. Yang, et al., Miniaturization of optical spectrometers, *Science* 371 (6528) (2021) eabe0722.
- [24] A.V. Macatangay, J.L. Perry, Cabin Air Quality on Board Mir and the ISS - A Comparison, 2007.
- [25] T. Straume, et al., Biomarker-detection technologies for comprehensive medical diagnosis during deep-space missions, *Recent Pat. Space Technol.* 3 (1) (2013).
- [26] B.M. Cummins, F.S. Ligler, G.M. Walker, Point-of-care diagnostics for niche applications, *Biotechnol. Adv.* 34 (3) (2016) 161–176.
- [27] A. Roda, et al., Advanced biosensors for monitoring astronauts’ health during long-duration space missions, *Biosens. Bioelectron.* 111 (2018) 18–26.
- [28] J. Dai, et al., Printed gas sensors, *Chem. Soc. Rev.* 49 (6) (2020) 1756–1789.
- [29] R. Kumar, et al., Strategic review on chemical vapor deposition technology-derived 2D material nanostructures for room-temperature gas sensors, *J. Mater. Chem. C* 11 (3) (2023) 774–801.
- [30] A.T. Güntner, N.J. Pineau, S.E. Pratsinis, Flame-made chemoresistive gas sensors and devices, *Prog. Energy Combust. Sci.* 90 (2022) 100992.
- [31] S.M. Majhi, et al., Recent advances in energy-saving chemiresistive gas sensors: a review, *Nano Energy* 79 (2021) 105369.
- [32] I.C. Weber, A.T. Güntner, Catalytic filters for metal oxide gas sensors, *Sensor. Actuator. B Chem.* 356 (2022) 131346.
- [33] J. van den Broek, et al., Highly selective gas sensing enabled by filters, *Mater. Horiz.* 8 (3) (2021) 661–684.
- [34] P. Mochalski, et al., Monitoring of selected skin- and breath-borne volatile organic compounds emitted from the human body using gas chromatography ion mobility spectrometry (GC-IMS), *J. Chromatogr. B* 1076 (2018) 29–34.
- [35] H. Borsdorf, et al., Recent developments in ion mobility spectrometry, *Appl. Spectrosc. Rev.* 46 (6) (2011) 472–521.
- [36] I.A. Buryakov, et al., A new method of separation of multi-atomic ions by mobility at atmospheric pressure using a high-frequency amplitude-asymmetric strong electric field, *Int. J. Mass Spectrom. Ion Process.* 128 (3) (1993) 143–148.

- [37] R. Guevremont, High-field asymmetric waveform ion mobility spectrometry: a new tool for mass spectrometry, *J. Chromatogr. A* 1058 (1) (2004) 3–19.
- [38] A. Wilks, et al., Characterization of a miniature, ultra-high-field, ion mobility spectrometer, *International Journal for Ion Mobility Spectrometry* 15 (3) (2012) 199–222.
- [39] M.T. Costanzo, et al., Portable FAIMS: applications and future perspectives, *Int. J. Mass Spectrom.* 422 (2017) 188–196.
- [40] A. Shevade, et al., Development of the Third Generation JPL Electronic Nose for International Space Station Technology Demonstration, 2007. SAE Technical Paper.
- [41] JAMSS, Odor in space? Surveying odors inside the ISS - technical demonstration of acquiring odor data with the “odor sensor” was conducted on the ISS, Available from: <https://www.jamss.co.jp/en/news/detail.php?id=v9f5fzb-g/>, 2023.
- [42] P. Gründler, *Chemical Sensors: an Introduction for Scientists and Engineers*, Springer Science & Business Media, 2007.
- [43] M. D’Andria, et al., Structure-function relationship of highly reactive CuOx clusters on Co3O4 for selective formaldehyde sensing at low temperatures, *Adv. Sci.* 11 (10) 2308224.
- [44] D. Lange, et al., Complementary metal oxide semiconductor cantilever arrays on a single chip: mass-sensitive detection of volatile organic compounds, *Anal. Chem.* 74 (13) (2002) 3084–3095.
- [45] J.R. Stetter, J. Li, Amperometric gas Sensors A review, *Chem. Rev.* 108 (2) (2008) 352–366.
- [46] P. Pasierb, M. Rekas, Solid-state potentiometric gas sensors—current status and future trends, *J. Solid State Electrochem.* 13 (1) (2009) 3–25.
- [47] A. Amine, H. Mohammadi, Amperometry, *Ref. Modul. Chem. Mol. Sci. Chem. Eng* 10 (2018) 70–79.
- [48] M. Aliramezani, C.R. Koch, R. Patrick, A variable-potential amperometric hydrocarbon sensor, *IEEE Sensor. J.* 19 (24) (2019) 12003–12010.
- [49] T. Cowen, M. Cheffena, Molecularly imprinted polymer real-time gas sensor for ambient methanol vapor analysis developed using principles of sustainable chemistry, *ACS Sustain. Chem. Eng.* 11 (29) (2023) 10598–10604.
- [50] A. Frutiger, et al., Nonspecific binding—fundamental concepts and consequences for biosensing applications, *Chem. Rev.* 121 (13) (2021) 8095–8160.
- [51] G. Jiang, et al., Free-standing functionalized graphene oxide solid electrolytes in electrochemical gas sensors, *Adv. Funct. Mater.* 26 (11) (2016) 1729–1736.
- [52] P. Prasertying, et al., Disposable microchamber with a microfluidic paper-based lid for generation and membrane separation of SO₂ gas employing an in situ electrochemical gas sensor for quantifying sulfite in wine, *Anal. Chem.* 94 (22) (2022) 7892–7900.
- [53] T. Seiyama, et al., A new detector for gaseous components using semiconductive thin films, *Anal. Chem.* 34 (11) (1962) 1502–1503.
- [54] I. Simon, et al., Micromachined metal oxide gas sensors: opportunities to improve sensor performance, *Sensor. Actuator. B Chem.* 73 (1) (2001) 1–26.
- [55] C. Marichy, N. Pinna, Atomic layer deposition to materials for gas sensing applications, *Adv. Mater. Interfac.* 3 (21) (2016) 1600335.
- [56] A. Tricoli, M. Righettoni, A. Tekei, Semiconductor gas sensors: dry synthesis and application, *Angew. Chem. Int. Ed.* 49 (42) (2010) 7632–7659.
- [57] H. Shin, et al., Rational design approaches of two-dimensional metal oxides for chemiresistive gas sensors: a comprehensive review, *MRS Bull.* 46 (11) (2021) 1080–1094.
- [58] J. Janata, M. Josowicz, Conducting polymers in electronic chemical sensors, *Nat. Mater.* 2 (1) (2003) 19–24.
- [59] F.-L. Meng, Z. Guo, X.-J. Huang, Graphene-based hybrids for chemiresistive gas sensors, *TrAC, Trends Anal. Chem.* 68 (2015) 37–47.
- [60] K. Suematsu, et al., One-trillionth level toluene detection using a dual-designed semiconductor gas sensor: material and sensor-driven designs, *ACS Appl. Electron. Mater.* 2 (12) (2020) 4122–4126.
- [61] K. Persaud, G. Dodd, Analysis of discrimination mechanisms in the mammalian olfactory system using a model nose, *Nature* 299 (5881) (1982) 352–355.
- [62] N.J. Pineau, et al., Orthogonal gas sensor arrays by chemoresistive material design, *Microchim. Acta* 185 (12) (2018) 563.
- [63] A.T. Güntner, et al., Sniffing entrapped humans with sensor arrays, *Anal. Chem.* 90 (8) (2018) 4940–4945.
- [64] J.F. McAleer, et al., Tin dioxide gas sensors: use of the seebeck effect, *Sensor. Actuator. B Chem.* 8 (3) (1985) 251–257.
- [65] S. Masoumi, et al., Zinc oxide-based direct thermoelectric gas sensor for the detection of volatile organic compounds in air, *Sensor. Actuator. B Chem.* 294 (2019) 245–252.
- [66] T. Ishihara, S. Matsubara, Capacitive type gas sensors, *J. Electroceram.* 2 (4) (1998) 215–228.
- [67] M.F. Hassan, P.K. Giesbrecht, M.S. Freund, Capacitive polymer sensors: factors influencing performance and design principles, *Sensor. Actuator. B Chem.* 393 (2023) 134211.
- [68] Y.A. Anisimov, et al., Polyaniline/biopolymer composite systems for humidity sensor applications: a review, *Polymers* 13 (16) (2021) 2722.
- [69] A. Koll, et al., Discrimination of volatile organic compounds using CMOS capacitive chemical microsensors with thickness-adjusted polymer coating, in: *Proc. SPIE Symposium on Smart Structures and Materials*, 1999.
- [70] M. Senapati, P.P. Sahu, Meat quality assessment using Au patch electrode Ag-SnO₂/SiO₂/Si MIS capacitive gas sensor at room temperature, *Food Chem.* 324 (2020) 126893.
- [71] M.A. Dwiputra, et al., The enhanced performance of capacitive-type humidity sensors based on ZnO nanorods/WS₂ nanosheets heterostructure, *Sensor. Actuator. B Chem.* 310 (2020) 127810.
- [72] Z. Zhai, et al., MOFs/nanofiber-based capacitive gas sensors for the highly selective and sensitive sensing of trace SO₂, *Appl. Surf. Sci.* 613 (2023) 155772.
- [73] B. Niu, et al., Preparation of MOF-199/polyacrylonitrile nanofiber membrane and its application in the preparation of flexible VOC gas sensors, *Microchem. J.* 191 (2023) 108815.
- [74] K. Dutta, A. Hazra, P. Bhattacharyya, Ti/TiO₂ nanotube array/Ti capacitive device for non-polar aromatic hydrocarbon detection, *IEEE Trans. Device Mater. Reliab.* 16 (2) (2016) 235–242.
- [75] K. Dutta, et al., Performance improvement of Pd/ZnO-nr/Si MIS gas sensor device in capacitive mode: correlation with equivalent-circuit elements, *IEEE Trans. Electron. Dev.* 63 (3) (2016) 1266–1273.
- [76] K. Shubham, R.U. Khan, P. Chakrabarti, Characterization of Pd/TiO₂/Si metal-Insulator/Semiconductor sensors for hydrogen detection, *Sens. Lett.* 11 (10) (2013) 1950–1955.
- [77] S. Fanget, et al., Gas sensors based on gravimetric detection—a review, *Sensor. Actuator. B Chem.* 160 (1) (2011) 804–821.
- [78] Q.a. Zhou, et al., A review on rapid detection of modified quartz crystal microbalance sensors for food: contamination, flavour and adulteration, *TrAC, Trends Anal. Chem.* 157 (2022) 116805.
- [79] F. Fauzi, et al., Gas and humidity sensing with quartz crystal microbalance (QCM) coated with graphene-based materials – a mini review, *Sensor Actuator Phys.* 330 (2021) 112837.
- [80] J. Wackerlig, P.A. Lieberzeit, Molecularly imprinted polymer nanoparticles in chemical sensing – synthesis, characterisation and application, *Sensor. Actuator. B Chem.* 207 (2015) 144–157.
- [81] F. Dirri, et al., A review of quartz crystal microbalances for space applications, *Sensor Actuator Phys.* 287 (2019) 48–75.
- [82] J. Devkota, P.R. Ohodnicki, D.W. Greve, SAW sensors for chemical vapors and gases, *Sensors* 17 (4) (2017) 801.
- [83] T. Yildirim, et al., Audible sensing of low-ppm concentration gases, *Sensor Actuator Phys.* 370 (2024) 115215.
- [84] S. Sang, et al., Surface stress-based biosensors, *Biosens. Bioelectron.* 51 (2014) 124–135.
- [85] H.P. Lang, et al., An electronic nose based on a micromechanical cantilever array, in: *Micro Total Analysis Systems '98*, Springer, Netherlands, 1998. Dordrecht.
- [86] K. Minami, et al., Recent advances in nanomechanical membrane-type surface stress sensors towards artificial olfaction, *Biosensors* 12 (9) (2022) 762.
- [87] B. Tuzson, et al., Highly selective volatile organic compounds breath analysis using a broadly-tunable vertical-external-cavity surface-emitting laser, *Anal. Chem.* 89 (12) (2017) 6377–6383.
- [88] R. Paolesse, et al., Fluorescence based sensor arrays, in: L. Prodi, M. Montalti, N. Zaccheroni (Eds.), *Luminescence Applied in Sensor Science*, Springer Berlin Heidelberg, Berlin, Heidelberg, 2011, pp. 139–174.
- [89] J.N. Driscoll, Review of photoionization detection in gas chromatography: the first decade, *J. Chromatogr. Sci.* 23 (11) (1985) 488–492.
- [90] S. Palzer, Photoacoustic-based gas sensing: a review, *Sensors* 20 (9) (2020) 2745.
- [91] K. Luft, Über eine neue Methode der registrierenden Gasanalyse mit Hilfe der Absorption ultraroter Strahlen ohne spektrale Zerlegung, *Z. tech. Phys* 24 (5) (1943) 97–104.
- [92] T.-V. Dinh, et al., A review on non-dispersive infrared gas sensors: improvement of sensor detection limit and interference correction, *Sensor. Actuator. B Chem.* 231 (2016) 529–538.
- [93] X. Wang, et al., High performance CO₂ measurement based on pressure modulation, *Procedia Eng.* 5 (2010) 1208–1211.
- [94] B. de Lacy Costello, et al., A review of the volatiles from the healthy human body, *J. Breath Res.* 8 (1) (2014) 014001.
- [95] C. Rösch, et al., Relationship between sources and patterns of VOCs in indoor air, *Atmos. Pollut. Res.* 5 (1) (2014) 129–137.
- [96] R. JordanL, P.C. Hauser, G.A. Dawson, Portable trap-sensor system for monitoring low levels of ethylene, *Analyst* 122 (8) (1997) 811–814.
- [97] J. Brunet, et al., All-organic device with integrated chemical filter dedicated to the selective measurement of NO₂ in air, *Org. Electron.* 11 (7) (2010) 1223–1229.
- [98] M. Fleischer, H. Meixner, Selectivity in high-temperature operated semiconductor gas-sensors, *Sensor. Actuator. B Chem.* 52 (1) (1998) 179–187.
- [99] I. Voiculescu, M. Zaghoul, N. Narasimhan, Microfabricated chemical preconcentrators for gas-phase microanalytical detection systems, *TrAC, Trends Anal. Chem.* 27 (4) (2008) 327–343.
- [100] B. Han, et al., Micro-fabricated packed metal gas preconcentrator for enhanced monitoring of ultralow concentration of isoprene, *J. Chromatogr. A* 1572 (2018) 27–36.
- [101] M.M. McCartney, et al., An easy to manufacture micro gas preconcentrator for chemical sensing applications, *ACS Sens.* 2 (8) (2017) 1167–1174.
- [102] A.T. Güntner, et al., Zeolite membranes for highly selective formaldehyde sensors, *Sensor. Actuator. B Chem.* 257 (2018) 916–923.
- [103] A.T. Güntner, M. D’Andria, J. van den Broek, The road to commercializing the mobile methanol detector Alivion Spark M-20, *Nature Reviews Bioengineering* 1 (6) (2023) 385–387.
- [104] G.G. De la Torre, Cognitive neuroscience in space, *Life* 4 (3) (2014) 281–294.
- [105] D.G. Chang, et al., Lumbar spine paraspinal muscle and intervertebral disc height changes in astronauts after long-duration spaceflight on the international space station, *Spine* 41 (24) (2016) 1917–1924.
- [106] M.F. Holick, Perspective on the impact of weightlessness on calcium and bone metabolism, *Bone* 22 (5) (1998) 105S–111S. Supplement 1.
- [107] B. Baselet, et al., Cardiovascular diseases related to ionizing radiation: the risk of low-dose exposure, *Int. J. Mol. Med.* 38 (6) (2016) 1623–1641.

- [108] M.A. Perhonen, et al., Cardiac atrophy after bed rest and spaceflight, *J. Appl. Physiol.* 91 (2) (2001) 645–653.
- [109] R.H.G. Olde Engberink, et al., The kidney, volume homeostasis and osmoregulation in space: current perspective and knowledge gaps, *npj Microgravity* 9 (1) (2023) 29.
- [110] T.H. Mader, et al., Optic disc edema, globe flattening, choroidal folds, and hyperopic shifts observed in astronauts after long-duration space flight, *Ophthalmology* 118 (10) (2011) 2058–2069.
- [111] L.K. Barger, et al., Prevalence of sleep deficiency and use of hypnotic drugs in astronauts before, during, and after spaceflight: an observational study, *Lancet Neurol.* 13 (9) (2014) 904–912.
- [112] N. Kanas, Psychiatric issues affecting long duration space missions, *Aviat Space Environ. Med.* 69 (12) (1998) 1211–1216.
- [113] M. Heer, et al., Body mass changes, energy, and protein metabolism in space, *Am. J. Kidney Dis.* 38 (3) (2001) 691–695.
- [114] A.A. Voorhies, et al., Study of the impact of long-duration space missions at the International Space Station on the astronaut microbiome, *Sci. Rep.* 9 (1) (2019) 9911.
- [115] R. Siddiqui, N. Akbar, N.A. Khan, Gut microbiome and human health under the space environment, *J. Appl. Microbiol.* 130 (1) (2021) 14–24.
- [116] J. Beauchamp, C. Davis, J. Pleil, *Breathborne Biomarkers and the Human Volatilome*, 2020.
- [117] T. Bruderer, et al., On-line analysis of exhaled breath, *Chem. Rev.* 119 (19) (2019) 10803–10828.
- [118] S. Schon, S.J. Theodore, A.T. Güntner, Versatile breath sampler for online gas sensor analysis, *Sensor. Actuator. B Chem.* 273 (2018) 1780–1785.
- [119] J. Beauchamp, et al., On the use of Tedlar® bags for breath-gas sampling and analysis, *J. Breath Res.* 2 (4) (2008) 046001.
- [120] A. Mashir, R.A. Dweik, Exhaled breath analysis: the new interface between medicine and engineering, *Adv. Powder Technol.* 20 (5) (2009) 420–425.
- [121] E. Hartungen, et al., Proton transfer reaction-mass spectrometry: fundamentals, recent advances and applications, *Eur. Phys. J. Appl. Phys.* 61 (2) (2013) 24303.
- [122] D. Smith, P. Španěl, SIFT-MS and FA-MS methods for ambient gas phase analysis: developments and applications in the UK, *Analyst* 140 (8) (2015) 2573–2591.
- [123] C. Davis, J. Beauchamp, *Volatile Biomarkers: Non-invasive Diagnosis in Physiology and Medicine*, Newnes, 2013.
- [124] A. Paleczek, A. Rydosz, Review of the algorithms used in exhaled breath analysis for the detection of diabetes, *J. Breath Res.* 16 (2) (2022) 026003.
- [125] Y.Y. Broza, et al., Disease detection with molecular biomarkers: from chemistry of body fluids to nature-inspired chemical sensors, *Chem. Rev.* 119 (22) (2019) 11761–11817.
- [126] D.L. Dietrich, et al., Portable unit for metabolic analysis, Google Patents, United States Patent, in: The United States of America as Represented by the Administrator of, National Aeronautics and Space Administration, 2018.
- [127] A.E. Jeukendrup, G.A. Wallis, Measurement of substrate oxidation during exercise by means of gas exchange measurements, *Int. J. Sports Med.* 26 (S 1) (2005) S28–S37.
- [128] N. Drabińska, et al., A literature survey of all volatiles from healthy human breath and bodily fluids: the human volatilome, *J. Breath Res.* 15 (3) (2021) 034001.
- [129] M. Phillips, et al., Variation in volatile organic compounds in the breath of normal humans, *J. Chromatogr. B Biomed. Sci. Appl.* 729 (1) (1999) 75–88.
- [130] P. Puchalska, P.A. Crawford, Multi-dimensional roles of ketone bodies in fuel metabolism, signaling, and therapeutics, *Cell Metabol.* 25 (2) (2017) 262–284.
- [131] K. Musa-Veloso, S.S. Likhodii, S.C. Cunnane, Breath acetone is a reliable indicator of ketosis in adults consuming ketogenic meals, *Am. J. Clin. Nutr.* 76 (1) (2002) 65–70.
- [132] A.T. Güntner, et al., Noninvasive body fat burn monitoring from exhaled acetone with Si-doped WO₃-sensing nanoparticles, *Anal. Chem.* 89 (19) (2017) 10578–10584.
- [133] K. Königstein, et al., Breath acetone change during aerobic exercise is moderated by cardiorespiratory fitness, *J. Breath Res.* 15 (1) (2021) 016006.
- [134] I.C. Weber, et al., Monitoring lipolysis by sensing breath acetone down to parts-per-billion, *Small Science* 1 (4) (2021) 2100004.
- [135] I.C. Weber, et al., Superior acetone selectivity in gas mixtures by catalyst-filtered chemoresistive sensors, *Adv. Sci.* 7 (19) (2020) 2001503.
- [136] C. Turner, P. Španěl, D. Smith, A longitudinal study of ammonia, acetone and propanol in the exhaled breath of 30 subjects using selected ion flow tube mass spectrometry, SIFT-MS, *Physiol. Meas.* 27 (4) (2006) 321–337.
- [137] S. Sanna, et al., Causal relationships among the gut microbiome, short-chain fatty acids and metabolic diseases, *Nat. Genet.* 51 (4) (2019) 600–605.
- [138] D. Smith, et al., Breath concentration of acetic acid vapour is elevated in patients with cystic fibrosis, *J. Breath Res.* 10 (2) (2016) 021002.
- [139] K. Dryahina, et al., Exhaled breath concentrations of acetic acid vapour in gastroesophageal reflux disease, *J. Breath Res.* 8 (3) (2014) 037109.
- [140] N.J. Pineau, et al., Y-doped ZnO films for acetic acid sensing down to ppb at high humidity, *Sensor. Actuator. B Chem.* 327 (2021) 128843.
- [141] H.F. Hammer, et al., European guideline on indications, performance, and clinical impact of hydrogen and methane breath tests in adult and pediatric patients: European Association for Gastroenterology, Endoscopy and Nutrition, European Society of Neurogastroenterology and Motility, and European Society for Paediatric Gastroenterology Hepatology and Nutrition consensus, *United European Gastroenterology Journal* 10 (1) (2022) 15–40.
- [142] D.H. Calloway, E.L. Murphy, D. Bauer, Determination of lactose intolerance by breath analysis, *Am. J. Dig. Dis.* 14 (1969) 811–815.
- [143] Y.K. Choi, et al., Fructose intolerance: an under-recognized problem, *Am. J. Gastroenterol.* 98 (6) (2003) 1348–1353.
- [144] J.M. Rhodes, P. Middleton, D.P. Jewell, The lactulose hydrogen breath test as a diagnostic test for small-bowel bacterial overgrowth, *Scand. J. Gastroenterol.* 14 (3) (1979) 333–336.
- [145] W. Shin, Medical applications of breath hydrogen measurements, *Anal. Bioanal. Chem.* 406 (16) (2014) 3931–3939.
- [146] W. Lee, et al., Analysis of the breath hydrogen test for carbohydrate malabsorption: validation of a pocket-sized breath test analyser, *J. Paediatr. Child Health* 36 (4) (2000) 340–342.
- [147] MD Diagnostics. [cited 2024 February 3]; Available from: <https://www.mdd.org.uk/products/h2-check/>.
- [148] FAN. [cited 2024 February 4]; Available from: <https://fan-gmbh.de/en/home/products/lactofan2/>.
- [149] P. Španěl, D. Smith, What is the real utility of breath ammonia concentration measurements in medicine and physiology? *J. Breath Res.* 12 (2) (2018) 027102.
- [150] S. Davies, P. Španěl, D. Smith, Quantitative analysis of ammonia on the breath of patients in end-stage renal failure, *Kidney Int.* 52 (1) (1997) 223–228.
- [151] T. Hibbard, et al., Point of care monitoring of hemodialysis patients with a breath ammonia measurement device based on printed polyaniline nanoparticle sensors, *Anal. Chem.* 85 (24) (2013) 12158–12165.
- [152] M.-Y. Chuang, et al., Organic gas sensor with an improved lifetime for detecting breath ammonia in hemodialysis patients, *ACS Sens.* 2 (12) (2017) 1788–1795.
- [153] C. Krittanawong, et al., Human health during space travel: state-of-the-art review, *Cells* 12 (1) (2023).
- [154] M.P. Kalapos, On the mammalian acetone metabolism: from chemistry to clinical implications, *Biochim. Biophys. Acta Gen. Subj.* 1621 (2) (2003) 122–139.
- [155] J.C. Anderson, Measuring breath acetone for monitoring fat loss, *Obesity* 23 (12) (2015) 2327–2334.
- [156] M. Statheropoulos, A. Agapiou, A. Georgiadou, Analysis of expired air of fasting male monks at Mount Athos, *J. Chromatogr. B* 832 (2) (2006) 274–279.
- [157] M.J. Sulway, J.M. Malins, Acetone in diabetic ketoacidosis, *Lancet* 296 (7676) (1970) 736–740.
- [158] A.T. Güntner, et al., Monitoring rapid metabolic changes in health and type-1 diabetes with breath acetone sensors, *Sensor. Actuator. B Chem.* 367 (2022) 132182.
- [159] F. Gouzi, et al., Breath acetone concentration: too heterogeneous to constitute a diagnosis or prognosis biomarker in heart failure? A systematic review and meta-analysis, *J. Breath Res.* 16 (1) (2022) 016001.
- [160] M. Righettoni, et al., Breath acetone monitoring by portable Si: WO₃ gas sensors, *Anal. Chim. Acta* 738 (2012) 69–75.
- [161] A.T. Güntner, et al., Guiding ketogenic diet with breath acetone sensors, *Sensors* 18 (11) (2018) 3655.
- [162] M. Righettoni, et al., Monitoring breath markers under controlled conditions, *J. Breath Res.* 9 (4) (2015) 047101.
- [163] M.J. Kim, et al., Breath acetone measurement-based prediction of exercise-induced energy and substrate expenditure, *Sensors* 20 (23) (2020) 6878.
- [164] D. Wang, et al., Colorimetric sensor for online accurate detection of breath acetone, *ACS Sens.* 6 (2) (2021) 450–453.
- [165] M. Ye, et al., An acetone bio-sniffer (gas phase biosensor) enabling assessment of lipid metabolism from exhaled breath, *Biosens. Bioelectron.* 73 (2015) 208–213.
- [166] F. Bovey, et al., Breath acetone as a marker of energy balance: an exploratory study in healthy humans, *Nutr. Diabetes* 8 (1) (2018) 50.
- [167] S.K. Kundu, et al., Breath acetone analyzer: diagnostic tool to monitor dietary fat loss, *Clin. Chem.* 39 (1) (1993) 87–92.
- [168] A. Beheshti, et al., Multi-omics analysis of multiple missions to space reveal a theme of lipid dysregulation in mouse liver, *Sci. Rep.* 9 (1) (2019) 19195.
- [169] K.R. Jonscher, et al., Spaceflight activates lipotoxic pathways in mouse liver, *PLoS One* 11 (4) (2016) e0152877.
- [170] N.T. Brannelly, J.P. Hamilton-Shield, A.J. Killard, The measurement of ammonia in human breath and its potential in clinical diagnostics, *Crit. Rev. Anal. Chem.* 46 (6) (2016) 490–501.
- [171] M.M. Adeva, et al., Ammonium metabolism in humans, *Metabolism* 61 (11) (2012) 1495–1511.
- [172] R. Adrover, et al., Breath-ammonia testing of healthy subjects and patients with cirrhosis, *Dig. Dis. Sci.* 57 (1) (2012) 189–195.
- [173] M.-Z. Dai, et al., Highly sensitive ammonia sensor with organic vertical nanojunctions for noninvasive detection of hepatic injury, *Anal. Chem.* 85 (6) (2013) 3110–3117.
- [174] J. Ishida, et al., Real-time breath ammonia measurement using a novel cuprous bromide sensor device in patients with chronic liver disease: a feasibility and pilot study, *J. Breath Res.* 15 (2) (2021) 026010.
- [175] S.-Y. Yu, et al., A versatile method to enhance the operational current of air-stable organic gas sensor for monitoring of breath ammonia in hemodialysis patients, *ACS Sens.* 4 (4) (2019) 1023–1031.
- [176] G. Neri, et al., Real-time monitoring of breath ammonia during haemodialysis: use of ion mobility spectrometry (IMS) and cavity ring-down spectroscopy (CRDS) techniques, *Nephrol. Dial. Transplant.* 27 (7) (2012) 2945–2952.
- [177] F.E. Garrett-Bakelman, et al., The NASA Twins Study: a multidimensional analysis of a year-long human spaceflight, *Science* 364 (6436) (2019) eaau8650.
- [178] S.U. Christl, et al., Production, metabolism, and excretion of hydrogen in the large intestine, *Gastroenterology* 102 (4) (1992) 1269–1277.
- [179] S. Bamba, et al., Altered gut microbiota in patients with small intestinal bacterial overgrowth, *J. Gastroenterol. Hepatol.* 38 (1) (2023) 61–69.
- [180] M. Kagaya, et al., Circadian rhythm of breath hydrogen in young women, *J. Gastroenterol.* 33 (4) (1998) 472–476.
- [181] M. Nishibori, et al., Sensing performance of thermoelectric hydrogen sensor for breath hydrogen analysis, *Sensor. Actuator. B Chem.* 137 (2) (2009) 524–528.

- [182] P. Sukul, et al., Origin of breath isoprene in humans is revealed via multi-omic investigations, *Commun. Biol.* 6 (1) (2023) 999.
- [183] J. King, et al., Physiological modeling of isoprene dynamics in exhaled breath, *J. Theor. Biol.* 267 (4) (2010) 626–637.
- [184] J. King, et al., Breath isoprene: muscle dystrophy patients support the concept of a pool of isoprene in the periphery of the human body, *Biochem. Biophys. Res. Commun.* 423 (3) (2012) 526–530.
- [185] J. King, et al., Measurement of endogenous acetone and isoprene in exhaled breath during sleep, *Physiol. Meas.* 33 (3) (2012) 413.
- [186] J. van den Broek, et al., Selective monitoring of breath isoprene by a portable detector during exercise and at rest, *Sensor. Actuator. B Chem.* 357 (2022) 131444.
- [187] S.J. Park, et al., Highly sensitive and selective real-time breath isoprene detection using the gas reforming reaction of MOF-derived nanoreactors, *ACS Appl. Mater. Interfaces* 15 (5) (2023) 7102–7111.
- [188] M. O'Hara, et al., Limonene in exhaled breath is elevated in hepatic encephalopathy, *J. Breath Res.* 10 (4) (2016) 046010.
- [189] M. Miyazawa, M. Shindo, T. Shimada, Metabolism of (+)- and (–)-Limonenes to respective carveols and perillyl alcohols by CYP2C9 and CYP2C19 in human liver microsomes, *Drug Metabol. Dispos.* 30 (5) (2002) 602–607.
- [190] I.C. Weber, et al., Dynamic breath limonene sensing at high selectivity, *ACS Sens.* 8 (7) (2023) 2618–2626.
- [191] B. de Lacy Costello, M. Ledochowski, N.M. Ratcliffe, The importance of methane breath testing: a review, *J. Breath Res.* 7 (2) (2013) 024001.
- [192] A.B. Sahakian, S.-R. Jee, M. Pimentel, Methane and the gastrointestinal tract, *Dig. Dis. Sci.* 55 (8) (2010) 2135–2143.
- [193] D. Polag, F. Keppler, Long-term monitoring of breath methane, *Sci. Total Environ.* 624 (2018) 69–77.
- [194] Y. Lin, et al., Real-time measurement of CH₄ in human breath using a compact CH₄/CO₂ sensor, *Sensors* 24 (4) (2024) 1077.
- [195] P.W. Taylor, Impact of space flight on bacterial virulence and antibiotic susceptibility, *Infect. Drug Resist.* (2015) 249–262.
- [196] R.A. Dweik, et al., An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications, *Am. J. Respir. Crit. Care Med.* 184 (5) (2011) 602–615.
- [197] M. Wilkinson, et al., Circadian rhythm of exhaled biomarkers in health and asthma, *Eur. Respir. J.* 54 (4) (2019) 1901068.
- [198] B. Antus, I. Horvath, I. Barta, Assessment of exhaled nitric oxide by a new handheld device, *Respir. Med.* 104 (9) (2010) 1377–1380.
- [199] J. Fernandes, et al., Adiposity, gut microbiota and faecal short chain fatty acids are linked in adult humans, *Nutr. Diabetes* 4 (6) (2014) e121–e121.
- [200] A. Smolinska, et al., Volatile metabolites in breath strongly correlate with gut microbiome in CD patients, *Anal. Chim. Acta* 1025 (2018) 1–11.
- [201] T. Sawabe, et al., Acetic acid production of *Vibrio halotiocoli* from alginate: a possible role for establishment of abalone–*V. halotiocoli* association, *Aquaculture* 219 (1) (2003) 671–679.
- [202] S. Rath, et al., Uncovering the trimethylamine-producing bacteria of the human gut microbiota, *Microbiome* 5 (1) (2017) 54.
- [203] D. Law, J. Conklin, M. Pimentel, Lactose intolerance and the role of the lactose breath test, *Official journal of the American College of Gastroenterology | ACG* 105 (8) (2010) 1726–1728.
- [204] P. Martinez-Lozano Sinues, et al., Circadian variation of the human metabolome captured by real-time breath analysis, *PLoS One* 9 (12) (2014) e114422.
- [205] L. Carter, et al., Process development for removal of siloxanes from ISS atmosphere. 45th International Conference on Environmental Systems, 2015.
- [206] T.J. Patrick, Outgassing and the choice of materials for space instrumentation, *Vacuum* 23 (11) (1973) 411–413.
- [207] T.F. Limero, et al., A Combustion Product Analyzer for Contingency Use during Thermodegradation Events on Spacecraft, 1991.
- [208] K.L. Fox, et al., Natural and induced environment around the international space station (ISS) as observed during on-orbit operations of the robotic external leak locator (RELL), in: *Proc. SPIE Systems Contamination: Prediction, Control, and Performance*, 2018.
- [209] A. Agapiou, et al., Trace detection of endogenous human volatile organic compounds for search, rescue and emergency applications, *TrAC, Trends Anal. Chem.* 66 (2015) 158–175.
- [210] National Research Council, Atmospheric Contaminants in Spacecraft, National Academy of Sciences, 1968.
- [211] National Research Council, Atmospheric Contaminants in Manned Spacecraft, National Academy of Sciences, 1972.
- [212] R.S. Johnston, L.F. Dietlein, Biomedical Results from Skylab, vol. 377, Scientific and Technical Information Office, NASA, 1977.
- [213] T.F. Limero, et al., A second generation volatile organic analyzer for the international space station, *SAE Technical Paper 1999-01-2059* (1999).
- [214] M.A. Ryan, et al., Operation of an electronic nose aboard the space Shuttle and directions for research for a second generation device, *SAE Technical Paper 2000-01-2512* (2000).
- [215] W.T. Wallace, et al., Monitoring of the atmosphere on the international space station with the air quality monitor, in: *47th International Conference on Environmental Systems*, 2017, Charleston, South Carolina.
- [216] National Research Council, NASA Space Technology Roadmaps and Priorities: Restoring NASA's Technological Edge and Paving the Way for a New Era in Space, The National Academies Press, Washington, DC, 2012, p. 376.
- [217] NASA, Spacecraft Maximum Allowable Concentrations for Airborne Contaminants, 2022.
- [218] M.Y. Rajapakse, et al., Controlled air exchange rate method to evaluate reduction of volatile organic compounds by indoor air cleaners, *Chemosphere* 313 (2023) 137528.
- [219] A. Lewis, P. Edwards, Validate personal air-pollution sensors, *Nature* 535 (7610) (2016) 29–31.
- [220] T. Limero, et al., A volatile organic analyzer for space station: description and evaluation of a gas chromatography/ion mobility spectrometer, *SAE Trans.* (1992) 1416–1424.
- [221] W.T. Wallace, et al., Monitoring of the atmosphere on the international space station with the air quality monitor [cited 2024 February 6]; Available from: <http://ntrs.nasa.gov/api/citations/20170006511/downloads/20170006511.pdf>, 2017.
- [222] C.G. Gatlin, IARC classifies formaldehyde as carcinogenic, *Oncol. Times* 26 (2004) 72.
- [223] National Research Council, Spacecraft Maximum Allowable Concentrations For Selected Airborne Contaminants: Volume 1, The National Academies Press, Washington, DC, 1994, p. 393.
- [224] S. Fable, L. Chiappini, Air intérieur : Métrologie du formaldéhyde, *Note du LCSQA*, 2011.
- [225] National Research Council, Spacecraft Maximum Allowable Concentrations For Selected Airborne Contaminants: Volume 2, The National Academies Press, Washington, DC, 1996, p. 408.
- [226] S. Lin, et al., Specific detection of n-propanol gas via terahertz metasurface sensor modified by molecularly imprinted polymer, *Spectrochim. Acta Mol. Biomol. Spectrosc.* 292 (2023) 122413.
- [227] B. Dick, Current status of the nitrogen oxygen recharge system, in: *41st International Conference on Environmental Systems*, 2011.
- [228] D. Loomis, et al., Carcinogenicity of benzene, *Lancet Oncol.* 18 (12) (2017) 1574–1575.
- [229] P. Clément, et al., Deep cavitand self-assembled on Au NPs-MWCNT as highly sensitive benzene sensing interface, *Adv. Funct. Mater.* 25 (26) (2015) 4011–4020.
- [230] D. Mossman, H. Bostic, J. Carlos, Contamination induced degradation of optical solar reflectors in geosynchronous orbit, in: *Proc. SPIE Technical Symposium Southeast on Optics, Electro-Optics, and Sensors*, vol. 777, 1987.
- [231] Z. Long, et al., Landfill siloxane gas sensing using differentiating, responsive phase coated microcantilever arrays, *Anal. Chem.* 81 (7) (2009) 2575–2580.
- [232] K. Mitsubayashi, et al., Bioelectronic sniffers for ethanol and acetaldehyde in breath air after drinking, *Biosens. Bioelectron.* 20 (8) (2005) 1573–1579.
- [233] M. Rightettoni, A. Tricoli, S.E. Pratsinis, Si:WO₃ sensors for highly selective detection of acetone for easy diagnosis of diabetes by breath analysis, *Anal. Chem.* 82 (9) (2010) 3581–3587.
- [234] H.J. Choi, et al., Highly selective, sensitive, and rapidly responding acetone sensor using ferroelectric e-WO₃ spheres doped with Nb for monitoring ketogenic diet efficiency, *Sensor. Actuator. B Chem.* 338 (2021) 129823.
- [235] X. Kou, et al., High-performance acetone gas sensor based on Ru-doped SnO₂ nanofibers, *Sensor. Actuator. B Chem.* 320 (2020) 128292.
- [236] R. Yoo, et al., Sensing of acetone by Al-doped ZnO, *Sensor. Actuator. B Chem.* 283 (2019) 107–115.
- [237] I.C. Weber, C.-t. Wang, A.T. Güntner, Room-temperature catalyst enables selective acetone sensing, *Materials* 14 (8) (2021) 1839.
- [238] S.-K. Kim, et al., Facile and rapid fabrication of porous CuBr films by solution oxidation and their application for the exclusive detection of NH₃ at room temperature, *J. Mater. Chem. A* 10 (2) (2022) 950–959.
- [239] A.T. Güntner, et al., Rapid and selective NH₃ sensing by porous CuBr, *Adv. Sci.* 7 (7) (2020) 1903390.
- [240] A.T. Güntner, M. Rightettoni, S.E. Pratsinis, Selective sensing of NH₃ by Si-doped α-MoO₃ for breath analysis, *Sensor. Actuator. B Chem.* 223 (2016) 266–273.
- [241] I.C. Weber, et al., Handheld device for selective benzene sensing over toluene and xylene, *Adv. Sci.* 9 (4) (2022) 2103853.
- [242] Y. Kang, et al., Highly sensitive detection of benzene, toluene, and xylene based on CoPP-functionalized TiO₂ nanoparticles with low power consumption, *ACS Sens.* 5 (3) (2020) 754–763.
- [243] F. Liu, et al., High response and selectivity of single crystalline ZnO nanorods modified by In₂O₃ nanoparticles for n-butanol gas sensing, *Sensor. Actuator. B Chem.* 277 (2018) 144–151.
- [244] A. Mirmohseni, et al., Selective determination of ethyl acetate, acetone, ethanol, and methyl ethyl ketone using quartz crystal nanobalance combined with principle component analysis, *Journal of Environmental Science and Health, Part A* 44 (9) (2009) 847–853.
- [245] H.M. Aliha, A.A. Khodadadi, Y. Mortazavi, The sensing behaviour of metal oxides (ZnO, CuO and Sm₂O₃) doped-SnO₂ for detection of low concentrations of chlorinated volatile organic compounds, *Sensor. Actuator. B Chem.* 181 (2013) 637–643.
- [246] Shailja, K.J. Singh, R.C. Singh, Highly sensitive and selective ethanol gas sensor based on Ga-doped NiO nanoparticles, *J. Mater. Sci. Mater. Electron.* 32 (8) (2021) 11274–11290.
- [247] S. Abegg, et al., A pocket-sized device enables detection of methanol adulteration in alcoholic beverages, *Nature Food* 1 (6) (2020) 351–354.
- [248] J. Shen, et al., Enhanced ethyl acetate sensing performance of Al-doped In₂O₃ microcubes, *Sensor. Actuator. B Chem.* 253 (2017) 461–469.
- [249] J. van den Broek, et al., Selective formaldehyde detection at ppb in indoor air with a portable sensor, *J. Hazard Mater.* 399 (2020) 123052.
- [250] A.T. Güntner, et al., E-nose sensing of low-ppb formaldehyde in gas mixtures at high relative humidity for breath screening of lung cancer? *ACS Sens.* 1 (5) (2016) 528–535.

- [251] Z. Tao, et al., Synthesis of urchin-like In₂O₃ hollow spheres for selective and quantitative detection of formaldehyde, *Sensor. Actuator. B Chem.* 298 (2019) 126889.
- [252] J.L. Wang, et al., Integrated sensing layer of bacterial cellulose and polyethyleneimine to achieve high sensitivity of ST-cut quartz surface acoustic wave formaldehyde gas sensor, *J. Hazard Mater.* 388 (2020) 121743.
- [253] J. van den Broek, et al., Highly selective detection of methanol over ethanol by a handheld gas sensor, *Nat. Commun.* 10 (1) (2019) 4220.
- [254] P. Iacomi, et al., MIL-101(Cr) MOF as an effective siloxane sensor, *ACS Appl. Mater. Interfaces* 14 (15) (2022) 17531–17538.
- [255] Z. Cai, J. Park, S. Park, Porous In₂O₃-ZnO nanofiber-based sensor for ultrasensitive room-temperature detection of toluene gas under UV illumination, *J. Mater. Res. Technol.* 24 (2023) 2482–2499.
- [256] L.M. Maebana, et al., Low-operational temperature for selective detection of xylene gas using a p-n CuO-ZnO heterostructure-based sensor, *J. Alloys Compd.* 960 (2023) 170683.
- [257] K.J. Kennedy, L.D. Toups, M. Rudisill, Constellation architecture team-lunar scenario 12.0 habitation overview, *Earth and Space 2010: Engineering, Science, Construction, and Operations in Challenging Environments* (2010) 989–1011.