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Citation (APA)
Jeong, S., Kim, K. E., Han, C. H., Sung, B., & Abelmann, L. (2026). Automated small-scale devices and robotic systems for analyzing the cellular impact of ambient aerosol particles. *iScience*, *29*(11), Article 118066. https://doi.org/10.1016/j.isci.2026.118066

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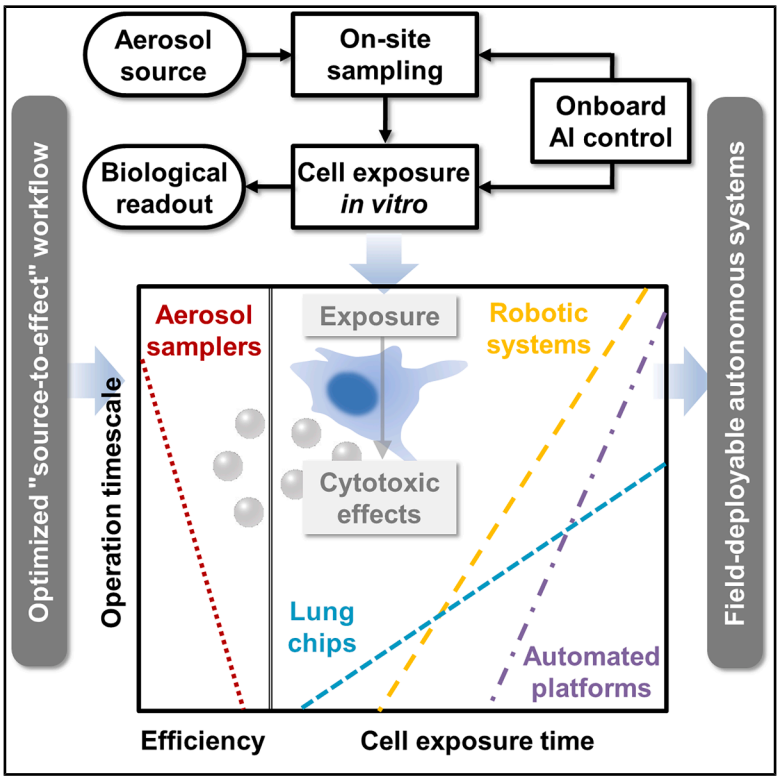
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Article

Automated small-scale devices and robotic systems for analyzing the cellular impact of ambient aerosol particles

Graphical abstract



Highlights

- We develop a conceptual framework of mobile systems for aerosol toxicity testing
- A workflow is provided to automate the aerosol bio-analysis at the cellular level
- We emphasize the applications of robotic platforms and artificial intelligence
- Future directions are discussed based on recent progress and current limitations

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In brief

Atmospheric science; Environmental health; Robotics

Jeong et al., 2026, iScience *29*, 118066
November 20, 2026 © 2026 The Authors. Published by Elsevier Inc.
https://doi.org/10.1016/j.isci.2026.118066

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Automated small-scale devices and robotic systems for analyzing the cellular impact of ambient aerosol particles

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https://doi.org/10.1016/j.isci.2026.118066

SUMMARY

In response to emerging threats associated with natural disasters, environmental pollution, and infectious diseases, the detrimental influences of airborne aerosols on humans have been investigated at the cellular level. Especially, intensive efforts have been devoted to system automation in order to enhance the efficiency, precision, and machine intelligence of aerosol cytotoxicity analysis. In this context, we combine the concepts of small-size automated and robotic platforms used for monitoring the harmful effects of aerosols. A conceptual framework is provided with a focus on mobile and field-deployable platforms that enable automated operation of (bio-)engineered systems on-site. Particular attention is given to the principles of biomimetic device design and the underlying physical and engineering mechanisms, to provide a system-level estimation on the complete "source-to-effect" workflow. In view of workflow integration, additional emphasis is placed on data acquisition and processing, as well as the extension of these technologies to autonomous system-supported environmental health applications.

INTRODUCTION

Aerosol particles are solid- and/or liquid-phase particles suspended in the air that originate from diverse natural and anthropogenic sources, and their size may vary from a few nanometers to hundreds of micrometers.[1,2] They include various particle types such as airborne particulate matter (PM), dust, smoke, fume, spray, and bioaerosols. Once emitted into the air, aerosols undergo growth, evaporation, chemical reaction, and removal processes through continuous interactions with humans and animals. Naturally occurring aerosols may act as a source of (micro-)nutrients, particularly for plants and marine microorganisms.[3–5] Nevertheless, aerosol particles generally exert adverse effects on human and animal health, especially in the case of aerosols associated with anthropogenic air pollution[6–8] and natural disasters such as wildfire[9] and volcanic eruptions.[10] Examples of detrimental aerosol particles also include coastal spray aerosols containing toxic cyanobacteria[11] and SARS-CoV-2-laden respiratory aerosols.[12]

Cellular responses induced by aerosol exposure can vary depending on the source and concentration of aerosol particles, as well as the duration of exposure. The most common interface between ambient aerosols and living organisms, especially terrestrial vertebrates including humans, is the respiratory tract epithelium.[13] Upon entering the lung airways through inhalation, aerosol particles undergo rapid changes in ambient conditions, including increased temperature and humidity, which may affect their properties and transport mechanisms.[14] The mucosal layer maintained at the epithelial surface represents the initial site of contact between aerosols and cells. Particle deposition may subsequently induce inflammation and other immune responses.

Skin and eyes constitute additional routes of epithelial deposition of ambient aerosols, in which deposition and adsorption are mediated by diffusion and convective transport. Exposure of the epidermis to hazardous aerosols may cause local allergic skin reactions and/or systemic toxicity through transcutaneous absorption.[15,16] Upon contact with airborne PM, the ocular surface may exhibit adverse responses such as redness and irritation.[17]

Automation and robotics have been emerging as main topics in the field of environmental technology.[18,19] In spite of a significant overlap, there is a subtle difference between the

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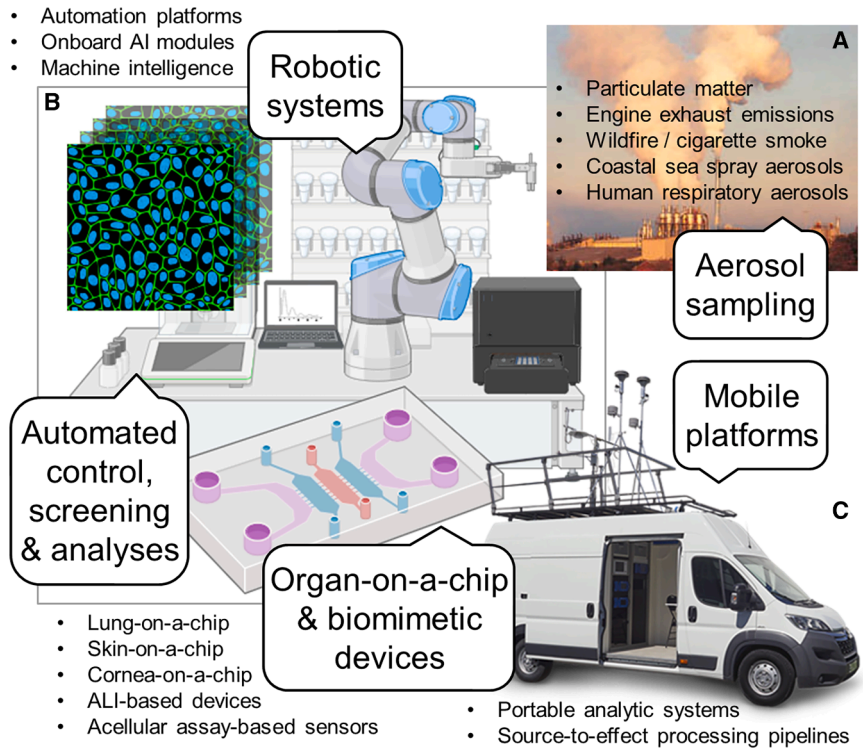


Figure 1. Schematic illustration of the technological elements covered in this paper

(A) Ambient aerosols are sampled/collected near their generation sources. [Credit: European Space Agency (©ESA)] (B) The aerosols are analyzed *in vitro* using (partially) automated/robotic systems incorporating biochips and air-liquid interface (ALI) cell culture devices. [Image created with BioRender.com] (C) These elements can be integrated into an autonomous (or semi-autonomous) system, for example, equipped in a mobile lab for on-site applications. [Credit: ENVIRA].

two interconnected concepts[20]: While automation emphasizes long-term efficiency in structured environments, robotics focuses on machine intelligence operating in unstructured environments. However, they share a wide range of common engineering principles for autonomous systems and are often used interchangeably in the industrial sector. In many cases, both characteristics are highly fused in developing (semi-)autonomous (bio-)mechatronic devices and platforms applied to aerosol science and technology.

Efficient estimation of the cell-level impact of ambient aerosols using automated (or partially automated) systems implemented in compact formats is required. Two different *in vitro* approaches, namely, acellular and cellular assays, are employed to identify and analyze the effects of aerosol particles on cell physiology and metabolism. Acellular assays recapitulate key biochemical events involved in aerosol-cell interactions. In contrast, cellular assays rely on the development of *in vitro* cell exposure methods that are necessary to emulate *in vivo* microenvironments. In the former approach, electrochemical and optical techniques for endpoint readout are essential for device operations. In this context, programmability or automation constitutes a core factor in device design to enable rapid readout of *in vitro* outcomes for advanced data processing and prediction. In the latter approach, tissue-mimetic device design plays a key role in simulating exposure conditions under *in vivo*-like environments. The implementation of airflow types within the *in vitro* device is directly related to the physiological relevance of the exposure system. This article will focus more on the cellular assay-based approaches because of their higher relevance to biological systems.

In particular, the necessity for automated or robotized bioassay platforms has increased with the growing importance of environmental toxicity monitoring. Considering the variability in cellular responses according to aerosol source characteristics, device miniaturization and inherent portability represent additional important aspects, as they facilitate analysis of the cellular impact of aerosols at the site of aerosol generation. In addition, integration of aerosol characterization modules into the *in vitro* platform enables correlation of physicochemical particle properties with biological outcomes. Current *in vitro* toxicity testing systems are generally bulky and are unsuitable for on-site measurements, resulting in the significant limitations in portability and mobility. Furthermore, certain environmental toxicants possess short lifetimes, necessitating rapid cell exposure testing in proximity to the emission source.

In this article, we provide a brief overview of recent progress toward automated and robotic platform-based aerosol analytic systems. We focus on the emerging technologies for assessing aerosol toxicity at the cellular level by assembling the methods of aerosol sampling, microfluidic devices, lung-on-a-chip systems, and robotic platforms. Unlike existing literature that treated these disciplines in isolation, this article offers a conceptual roadmap for mobile biological monitoring, addressing the critical need to link physical sampling with biological impact assessment. A qualitative perspective on future autonomous systems is described for implementing the continuous evaluation and prediction of adverse effects of airborne particles on cells and tissues (Figures 1 and 2). Particular emphasis is placed on the development of small-scale devices and systems with potential for on-site deployment. Current limitations and future outlook are discussed with a focus on unsupervised and intelligent high-throughput analysis of the cellular impact of atmospheric aerosols.

This paper is structured as follows: (1) To synthesize overarching technological trends, we will first introduce background knowledge and a framework for autonomous system-based aerosol research. (2) Small-scale platforms for aerosol sampling and analysis will be briefly reviewed as the first part of the technical elements applicable to automated systems. (3) Biomimetic

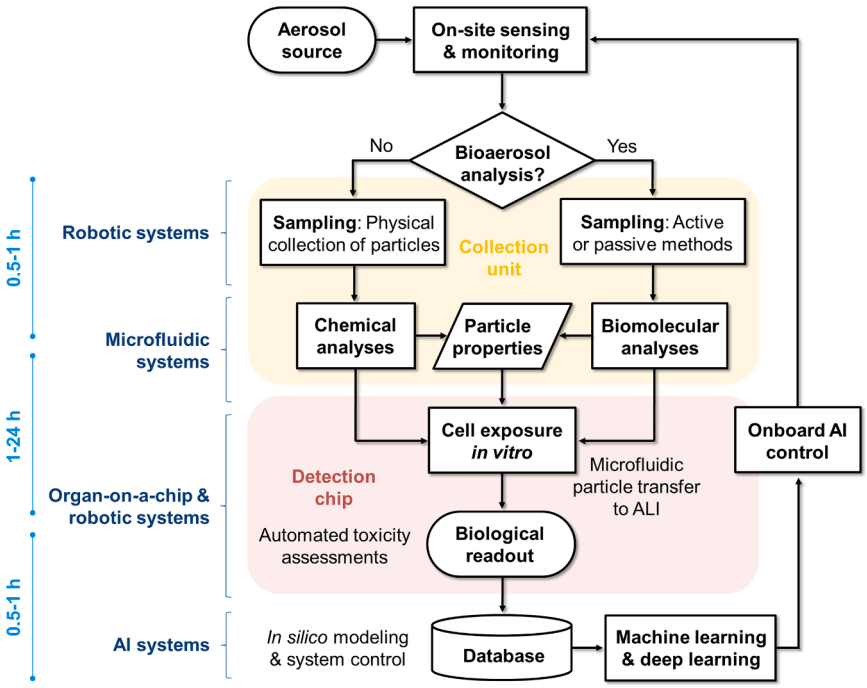


Figure 2. System-level flowchart illustrates the conceptual "source-to-effect" workflow and timeline

The workflow combines all technological elements, covering everything from aerosol collection to biological readout. One or two steps in the suggested workflow may be omitted depending on the system design requirements. (Here, the represented sampling procedures do not include the filter-based aerosol collection techniques due to their limitations for being integrated in (semi-)automated systems. The organ-on-a-chip and robot-assisted analyses may take longer than 24 h depending on the emulation scenarios of environmental exposure).

microdevices and autonomous robots for cytotoxicity testing—focused on two *in vitro* models: Air-liquid interface (ALI) cell culture and lung-on-a-chip systems—will be reviewed as the second part of the whole system. (4) We will discuss the opportunities and limitations in the state-of-the-art technologies for combining the two aspects explored in the preceding sections. (5) Finally, concluding remarks will be provided to summarize the discussions. Perspectives will be given regarding the future developments toward full automation with mobile platforms, especially in the context of a unified "source-to-effect" framework integrating robotic sampling/handling, lung-on-a-chip systems, and artificial intelligence (AI).

RESULTS

Aerosol generation, monitoring, and sampling techniques

Investigation of aerosol-induced biological responses requires aerosol generation, detection, and/or sampling techniques that provide stable aerosol sources and characterization information for cellular or acellular bioassays. A brief summary of commonly applied aerosol sampling methods with conventional alternatives on key operational parameters is presented in Table 1.

Atmospheric aerosols typically exist at low and unstable concentrations and often cannot retain their inherent physical and chemical properties when collected on a filter, particularly due to drying, aggregation, and loss of (semi-)volatile compounds. As a result, collected particles may exhibit physical and chemical properties different from those measured by continuous monitoring instruments. In addition, atmospheric aerosols are complex mixtures of diverse chemical compounds, which complicates direct correlation between particle characteristics and cytotoxicity outcomes. Therefore, stable and controlled aerosol generation, together with high-resolution characterization techniques, is essential for emulating both natural and anthropogenic aerosols. Diesel exhaust and cigarette smoke are the most common examples of outdoor/indoor air-pollution sources that are controllable and can be readily generated using benchtop mechanical setups. Conventional techniques for aerosol generation are summarized in Table S1.

Typical aerosol measurement methods are based on gravimetric (filters and impactors), optical (optical particle counters and aerodynamic particle sizers), and electrical (diffusion size classifiers and nanoparticle surface area monitors) approaches.[28] In addition, various spectroscopic techniques, including fluorescence spectroscopy, Raman spectroscopy, and breakdown spectroscopy, can be applied to real-time aerosol detection, in which microfluidics may play a fundamental role in enhancing sensitivity and bioassay kinetics.[29]

Aerosol sampling methods need to be properly adjusted depending on the type of target aerosols. For example, the sampler design concepts for PM and bioaerosols can be considerably different from each other. In general, techniques for collecting aerosol particles include filtration, condensation, electrostatic precipitation, liquid impingement, acoustic collection, and centrifugation.[30] The bioaerosol sampling methods are classified as passive and active sampling, where the former employs settle plates and surface sampling techniques, and the latter includes agar plate-based impactors, impingers, filters, and wetted cyclones.[31] During bioaerosol collection, it is critical to preserve the microbial bioefficiency by maintaining the viability of aerosol-contained microorganisms as much as possible.

Personal aerosol samplers, on one hand, have long been investigated for applications in the polluted air, related to environmental and occupational health.[32] On the other hand, portable aerosol impactors have been developed for bioaerosol sampling, particularly as small-size devices used in airborne pathogen monitoring.[33] Furthermore, nanostructure-based optical microdevices, where the nanomaterials have been engineered through metal-organic and covalent organic

Table 1. Sampling methods of airborne particles: A summary table for the comparison of typical aerosol samplers with key operational parameters

Sampling method	Sampling time	Preservation of sample integrity	Automation ease	Compatibility with downstream biological assays	Main limitation	Typical application
Filtration[21,22]	hours (typically 8–24 h)	low to moderate (loss of volatile and semi-volatile compounds, particle agglomeration)	low to moderate (filter cutting, extraction, concentration, solvent exchange)	moderate to high (post-preparation of samples, suitable for multiple biological assays)	loss of volatile and semi-volatile compounds, sample alteration during extraction, particle aggregation	ambient PM monitoring, chemical and toxicological analysis
Liquid impingement[23,24]	minutes (typically 10–30 min)	high (liquid collection minimizes dehydration and preserves viability)	moderate (liquid handling with media replacement and evaporation control)	high (direct liquid sample suitable for culture, PCR, and cell-based assays)	limited efficiency for ultrafine particles, sample dilution, evaporation during long sampling	bioaerosol monitoring, microbial viability assays
Cyclone sampling[24–26]	minutes (typically 5–30 min)	moderate-high (minimal processing; viability generally preserved)	high (direct liquid collection, minimal sample preparation)	moderate-high (direct liquid transfer for PCR/ culture, suitable for biological assays with minimal processing)	reduced collection efficiency for ultrafine particles, performance depends on flow rate and particle size	portable bioaerosol monitoring, pathogen surveillance, automated environmental sampling
Condensation-based collection[27]	minutes (typically 5–15 min)	high (gentle condensational growth preserves viral infectivity and minimizes sampling stress)	moderate (requires condensation unit and temperature control	high (direct liquid collection with minimal sample processing)	specialized instrumentation, higher system complexity	viable virus collection, infectious bioaerosol monitoring, respiratory virus surveillance

The items are sorted in a manner that the method with a longer sampling time appears nearer to the top.

frameworks, could enhance bioaerosol detection and sampling capability with efficient signal transduction modes.[34] These developments are motivated by the importance of airborne microbes deposition and downstream quantification in respiratory infectious disease research.[35–37]

Robotic systems for aerosol collection and physicochemical analysis

Small-scale autonomous platforms for the collection and removal of indoor airborne particles have been developed using mobile robot concepts. For example, Sagona et al.[38] reported an autonomous PM collection system termed the pretoddler inhalable particulate environmental robotic sampler (PIPER). The system was mechanically designed to mimic the postures and movements of young children on the floor and was used to estimate children's exposure to PM generated in home environments. This approach could be further combined with acellular assay-based exposure modules that are designed to be mountable on mobile platforms.

Robotic systems have been applied to high-throughput sampling and analysis of aerosol particles in indoor, outdoor, and occupational environments. L'Orange et al.[39] reported an automated air analysis facility, termed AIRLIFT, for filtered aerosol samples, which employed a programmable robotic arm-based control system for gravimetric and optical analyses of airborne particles. Li et al.[25] developed a robot-assisted portable bioaerosol sampler capable of achieving high microbial collection efficiency. Furthermore, Feld-Cook et al.[40] demonstrated that a programmable humanoid platform can perform volatile organic compound (VOC) monitoring during robotic motions mimicking human workers, thereby enabling automated and realistic exposure data acquisition under simulated workplace environments.

In a different approach, a mobile robot-sensor system was developed to detect indoor PM and collect data on-line through computer-programmed autonomous identification of PM hotspots.[41] This is an interesting approach for the future development of smart mobile systems in environmental technology, because the autonomous machine intelligence could be directly associated with the field-deployable small-scale exposure modules.

Microfluidic devices used for aerosol research

Microfluidic devices refer to microfabricated fluid channel systems in which miniaturized sensors and actuators are integrated. Fluid flow behavior in microfluidic systems can be finely controlled and is commonly coupled with physicochemical detection modules and/or optical microscopy units. Airflow in microfluidic devices can be precisely regulated through physical

interconnections with liquid microflow architectures and integrated soft material components. In addition, the devices support bubble/droplet manipulation and microflow parallelization, which enable particle-into-liquid sampling and high-throughput chemical screening. The microfluidic platforms have been widely employed, particularly for on-site bioaerosol detection, collection, and analysis.[42,43] Applications of microfluidic tools in aerosol science have been concisely summarized by Metcalf et al.[44] More recently, aerosol transport mechanisms in lung-mimicking microfluidic devices were reviewed by Sznitman.[45]

Incorporation of microchambers and soft compartments for 2D and 3D cell culture models into microfluidic devices and sensor-embedded systems is an active area of research in biomedical and environmental technologies.[46–50] Interactions between airborne particles and airway epithelia have typically been modeled by implementing an interface between aerosol-laden airflow and mono- or multilayer epithelial cells (the 1st part of Methods S1): The *in vitro* lung epithelia are usually exposed to the aerosol-containing airflows formed in small-scale geometries. Such air-liquid interface (ALI)-based microdevices enable reconstitution of *in vivo*-like phenomena and biological signal transduction through electromechanical systems integrated into the platforms.

Here, the core idea is that (1) the ALI models are used for *in vitro* cell exposure to aerosols and (2) the ALI-based microfluidic devices support automated or semi-automated aerosol delivery, biosensing, and cytological analyses. For example, at the individual device level, a portable ALI microfluidic system has been developed to allow PM deposition on human bronchial epithelial cells, which enabled gene analysis and apoptosis pathway studies.[51] It is notable that the microfluidic *in vitro* systems have already been exploited for automated compound screening platforms in the pharmaceutical industry, due to the systems' capabilities of continuous chemical testing and quasi-autonomous operations.[52,53]

Lung-on-a-chip systems for studying the adverse effects of aerosols

Lab-on-a-chip systems are multicomponent integrated and functionally advanced microfluidic devices that incorporate complex microchannel and microchamber geometries, physical and chemical microsensors, and miniature valves and actuators.[54] Lab-on-a-chip platforms offer advantages in miniaturization and digitalization, especially when small-size organ mimics are integrated into the platforms to function as microphysiological systems (i.e., "organ-on-a-chip" systems).[55] In the area of aerosol research, (semi-)automated lung-on-a-chip devices have been extensively developed to investigate the cell- and tissue-level impact of airborne particles and smokes. In those systems, through microfluidic airways implemented on-chip, the on-site collected aerosols can be easily transferred to the miniature ALI modules (for *in vitro* exposure) without contamination.

Cellular *in vitro* assays provide essential information linking aerosol properties with cellular endpoints based on cell signaling and damage mechanisms. Various chip-embedded sensors have been employed to measure metabolic and biochemical analytes produced as a consequence of exposure to airborne PM, and both acellular and cellular toxicity assays can be integrated with microfluidic platforms.[56] Lung-on-a-chip systems are specialized biomimetic microfluidic devices that reconstitute pulmonary microphysiology by recapitulating key functions of the human lung, including pulmonary cilia and directional mucociliary clearance.[57] Because the ALI combined with culture medium flow (referred to as the dynamic ALI) can be implemented in lung chips, these cell biology-based, miniaturized, and programmable microdevices function as the 3D lung tissues maintained under near-physiological conditions.[58,59] In particular, on-chip mimicry of alveolar airflow dynamics has been optimized to emulate the transport and deposition of aerosol particles, as well as their effects on lung tissues. A summary of selected relevant studies is presented in Table 2.

For example, lung chips may recapitulate the airway tree and gravitation-driven deposition behavior of airborne PM.[58] Lung chips incorporating 3D bifurcating airway structures can be utilized to investigate PM-induced dysfunction of the alveolar-capillary barrier, which may ultimately contribute to the mechanism-based understanding of neuroinflammation and neurodegeneration in the human brain. Further improvements in the complexity of on-chip reconstructed aerosol exposure systems may facilitate mechanistic studies of particle transport through the epithelial mucus layer and migration of particles and leukocytes across air-blood barriers.

Rapid readout and continuous on-chip analysis can be achieved through the integration of multichannel biosensors into lung chips. These devices are designed to reproduce the morphological traits and mechanical characteristics of the lung, including cyclic breathing motions, within artificial microsystems.[71] Lung chips support multifaceted monitoring and assessment of the biological effects of inhaled aerosols, including PM, noxious gases, and bacteria or viruses. Cellular- and tissue-level endpoints may include cell viability, cytokine secretion, gene expression, and epithelial barrier properties, which may ultimately influence systemic responses.[72]

A variety of device types has been developed to investigate the biological effects of PM exposure on-chip. The 3D lung chip model developed by Xu et al.[60] demonstrated microfluidically integrated cellular components. The microscale extracellular niche could effectively mimic the alveolar-capillary barrier and recapitulate interactions between immune cells and sites of tissue damage induced by PM exposure. Sakolish et al.[65] devised an on-chip exposure system that recreated the parenchymal-vascular interface within a lung chip, thereby enabling physiologically relevant flow conditions and mechanical stimuli. The airway-on-a-chip was based on an ALI cell culture platform and could be directly exposed to physical, chemical, and biological stressors to produce quantitative and high-content data.

Robotic systems for cell exposure

Application of robotic systems in aerosol-related environmental health has recently emerged as a focus in control engineering (Figure 3). A summary of relevant developments is shown in Table 3. In particular, commercialized smoking robots integrated with ALI modules have been widely used in tobacco smoke toxicity studies under various exposure doses and chemical mixture conditions using lung epithelial cultures. These studies have generally focused on the biological impact of electronic

Table 2. Lung-on-a-chip and related microphysiological systems for studying adverse effects of aerosols

Exposure agent	Exposure modality	Cell/tissue model	Device architecture	Physiological features	Biological endpoints/ readouts	Operation/ Readout timescale	Automation and system-integration feature	References
PM2.5	PM2.5 exposure in alveolar channel	alveolar epithelial cells, endothelial cells, monocyte interaction	3D alveolar-capillary lung-on-chip	alveolar-blood barrier mimicry, immune-cell interaction	permeability, ROS, apoptosis, IL-6, TNF-α, monocyte adhesion	72 h exposure (daily medium replacement) and analysis	microfluidic PM2.5 exposure with perfused barrier model	Xu et al.[60]
PM2.5	direct aerosolized ALI exposure	HBE cells and HFL-1 fibroblasts	portable all-in-one lung-mimicking ALI exposure platform	integrated aerosol generator, ALI culture, perfusion	DNA methylation, RNA sequencing, ErbB signaling, drug-response assay	210 s exposure & 24 h post-exposure	portable all-in-one PM2.5 generator-ALI exposure platform	Zheng et al.[51]
Urban particulate matter	suspension-based urban PM treatment on chip	nasal epithelial cells, fibroblasts, endothelial cells	3D respiratory mucosa-on-chip	multicellular mucosal barrier mimicry	RNA sequencing, cytokines, ZO-1, VE-cadherin, inflammatory markers	24 h exposure & analysis	miniaturized multicellular chip with offline endpoint analysis	Byun et al.[61]
Indoor airborne nanoscale particles	perfusion-based vascular exposure	HUVEC-based 3D microvascular network	human microvessel-on-chip	vascular response to airborne nanoscale particles	ROS, inflammatory signaling, coagulation-related markers	24 h exposure & analysis	flow-perfused vascular chip; no integrated aerosol generator	Li et al.[62]
PM2.5	direct ALI PM2.5 exposure	BEAS-2B cells and HPMECs	organ-level lung microfluidic platform with aerosol exposure	ALI, perfusion, epithelial-endothelial interaction	RNA sequencing, iTRAQ proteomics, TEM, IL-6, AKT1-related pathway	24 h exposure & analysis	integrated ALI aerosol exposure with perfused lung chip	Zheng et al.[63]
Ambient fine PM	perfusion-based vascular exposure	3D HUVEC microvascular network	microfluidic vascular chip	perfusable human microvasculature	ROS, NO dysregulation, IL-6, procoagulant response	24 h exposure & analysis	flow-perfused vascular chip with microscopy/ biochemical readouts	Li et al.[64]
Dry air, LPS, particulate matter, iodomethane	direct gas/aerosol exposure at ALI	primary small airway epithelial cells and lung microvascular endothelial cells	multilayer small-airway chip	ALI, epithelial-endothelial interface, ciliary function	LDH, permeability, ciliary beating, mucin, ZO-1	5 h exposure & next day analysis	controlled gas/ aerosol ALI exposure with perfused channel	Sakolish et al.[65]

(*Continued on next page*)

Table 2. *Continued*

Exposure agent	Exposure modality	Cell/tissue model	Device architecture	Physiological features	Biological endpoints/ readouts	Operation/ Readout timescale	Automation and system-integration feature	References
Cytotoxic airborne surrogate particles	airflow-mediated aerosol deposition	differentiated NHBE airway epithelium	bronchial tree-on-chip exposure platform	airway branching geometry, physiologically relevant airflow	particle deposition mapping, viability, apoptosis	5 min exposure & cytotoxicity assays (30 min exposure for particle deposition analysis)	parallel airway-chip exposure under controlled respirator airflow	Elias-Kirma et al.[66]
Inhaled toxicants/ aerosol-relevant compounds	ALI exposure combined with recirculating microfluidic flow	NHBE airway tissue and HepaRG liver spheroids	lung/liver-on-chip with shared circulation	multi-organ crosstalk, long-term co-culture	TEER, ATP, LDH, albumin, CYP activity, tissue viability	N/A	pump-driven shared circulation; no direct aerosol module	Bovard et al.[67]
100 nm nanoparticles and 1,000 nm microparticles	ALI exposure under cyclic stretch	A549 and 16HBE14o- cells	breathing bioreactor with elastic membrane	ALI, cyclic mechanical stretch, basal perfusion	particle uptake, transepithelial transport, barrier-related readouts	N/A	programmable cyclic stretch with real-time membrane monitoring	Doryab et al.[68]
Cigarette smoke; SARS-CoV-2 pseudovirus	ALI smoke exposure and viral challenge	primary human alveolar epithelial cells	3D alveolar lung-on-chip with inverse-opal structure	alveolar sac-like geometry, cyclic breathing motion	viability, ZO-1, 4-HNE, cytokines, ACE2, infection assay	N/A	cyclic strain actuation with staged smoke/ viral challenge	Huang et al.[69]
Viral aerosols/ poly I:C aerosol surrogate	regional airway aerosol transmission	nasal, bronchial, and acinar epithelial chips	modular airways-on-chip system	nose-to-acini respiratory tract connectivity	viral/aerosol transmission, cytokines, barrier response	N/A (endpoint viral transmission and cytokine analysis)	modular regional airway chips with connected airflow routing	Nof et al.[70]

The items are sorted in a manner that the device of longer operation/readout timescale appears nearer to the top. 4-HNE: 4-hydroxynonenal; 16HBE14o-: human bronchial epithelial cell line 16HBE14o-; A549: human alveolar basal epithelial adenocarcinoma cell line A549; ACE2: angiotensin-converting enzyme 2; AKT1: AKT serine/threonine kinase 1; ALI: air-liquid interface; ATP: adenosine triphosphate; COPD: chronic obstructive pulmonary disease; BEAS-2B: human bronchial epithelial cell line BEAS-2B; CYP: cytochrome P450; DNA: deoxyribonucleic acid; e-cigarette: electronic cigarette; ErbB: erythroblastic oncogene B receptor family; HBE: human bronchial epithelial cell; HFL-1: human fetal lung fibroblast cell line HFL-1; HPMEC: human pulmonary microvascular endothelial cell; HUVEC: human umbilical vein endothelial cell; IL-6: interleukin-6; IL-8: interleukin-8; IL-13: interleukin-13; iTRAQ: isobaric tags for relative and absolute quantitation; LDH: lactate dehydrogenase; LPS: lipopolysaccharide; MUC5AC: mucin 5AC; NHBE: normal human bronchial epithelial cell; NO: nitric oxide; PM: particulate matter; poly I:C: polyinosinic:polycytidylic acid; RNA: ribonucleic acid; ROS: reactive oxygen species; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; TEER: transepithelial electrical resistance; TEM: transmission electron microscopy; TNF-α: tumor necrosis factor alpha; VE-cadherin: vascular endothelial cadherin; ZO-1: zonula occludens-1. The deposition mechanisms of inhaled aerosols and the human airway structure and cell types are concisely described in the 2nd and 3rd parts of Methods S1, respectively.

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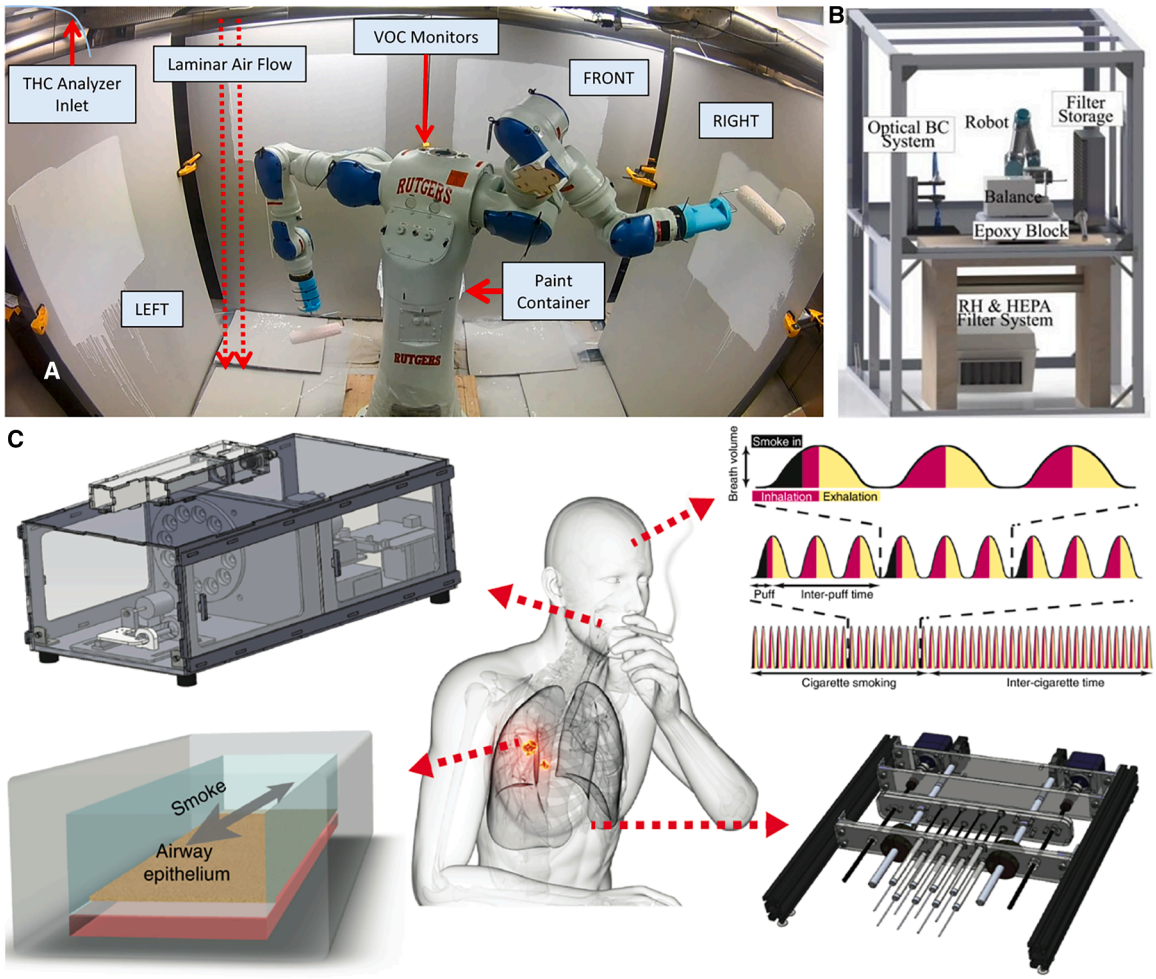


Figure 3. Robotic systems used for atmospheric and occupational aerosol monitoring, (semi-)automated analysis, and inhalation toxicity assessment

(A) Humanoid-based volatile organic compound (VOC) sensing system programmed to simulate human exposure to VOC aerosols during painting motions.[40] [Credit: Springer Nature, CC BY 4.0 license] (B) Robotic platform for black carbon (BC) filter analysis.[39] (RH, relative humidity; HEPA, high-efficiency particulate air). [Credit: Springer Nature, CC BY 4.0 license] (C) Bio-inspired automated exposure system incorporating a vaping robot and a breathing emulator connected to a lung-on-a-chip platform.[73] [Credit: Elsevier, CC BY NC ND license].

nicotine delivery systems, in which vapors generated from e-liquids composed of nicotine, propylene glycol, glycerin, and other compounds were transported to epithelial cultures through controlled airflow.

To investigate the toxic effects of e-liquid chemical composition on lung cells, Sassano et al.[81] developed a high-throughput screening assay that enabled parallel assessment of e-liquid aerosols across multiple cell cultures. The system was based on a VC10 smoking robot used for automated vapor exposure of primary human bronchial epithelial cells.

The Cultex Radial Flow System (CULTEX RFS; CULTEX Laboratories, Hannover, Germany) was developed for efficient *in vitro* simulation of inhalation toxicity under exposure to cigarette smoke and particulate atmospheres.[82] The system adopted a modular design strategy integrating an aerosol-generating robot, a CULTEX RFS module containing ALI cell supports with automatic medium supply pumps and a temperature controller, and a mixing chamber for aerosol dilution. The Vitrocell VC10 smoking robot was also employed to evaluate the genotoxicity of e-cigarette and cigarette smoke aerosols using standard bacterial mutagenicity tester strains (TA98 and TA100) in the Ames assay.[83] A Vitrocell smoking robot integrated with the Vitrocell exposure system (VITROCELL Systems GmbH) was further utilized to assess e-cigarette aerosol toxicity in EpiAirway tissue, a 3D reconstructed model based on primary human tracheobronchial epithelium.[84] These commercialized devices could be further integrated into robot-assisted benchtop exposure systems.

Robotization of lung-on-a-chip systems for aerosol exposure has recently emerged as a developing area in *in vitro* respiratory toxicity testing, by combining robotic aerosol generators and sensors with lung-mimicking microphysiological systems. The Ingber group has contributed extensively to this field[76,79] through integration of critical aspects of *in vivo*-like lung airway

Table 3. Robotic and programmable systems for cell exposure

Exposure agent	Exposure system	Cell/tissue model	Robotic/ programmable component	Exposure control features	Biological endpoints/readouts	Operation/Readout timescale	References
PM10	lung chip with integrated monitoring	distal airway epithelial model	automated TEER monitoring and portable microscopy	continuous barrier monitoring during repeated PM exposure	TEER, ROS, cytokines, mucus marker expression	repeated 8 h/day exposure over 4 days (96 h experimental duration) & analysis	Jabbar et al.[74]
Cigarette smoke and tobacco-heating-system aerosol	direct aerosol exposure module linked to multi-organ chip	bronchial tissue and liver spheroids	instrument-integrated repeated exposure module	repeated aerosol exposure; comparison with aqueous aerosol fraction	CYP induction, metabolic signatures, tissue viability	1–28 min aerosol exposure (2–56 puffs) & 48 h post-exposure analysis	Bovard et al.[75]
Whole cigarette smoke; e-cigarette aerosol	biomimetic smoking robot compatible with organ chips	organ-chip airway epithelium	smoking robot, microrespirator, programmable control interface	controlled puff profile, breathing motion, dynamic aerosol exposure	protocol platform for imaging, molecular assays, and omics	programmable (typically 75 min exposure) + 24 h post incubation & analysis	Benam et al.[76]
Whole-smoke conditioned medium; e-cigarette vapor conditioned medium	BioFlux microfluidic cardiovascular model	HAECs and THP-1 monocytes	automated perfusion and wash cycles	controlled shear flow and adhesion assay	monocyte adhesion, ICAM-1, CD11b	24 h exposure & analysis (after 10–40 min)	Makwana et al.[77]
Cigarette smoke and environmental airborne agents	real-time cell exposure examination device	NHBE cells	instrument-integrated exposure chamber with live imaging	direct exposure with *in situ* microscopy	TEER, permeability, ciliary beat frequency, migration, mass deposition	~90 min operation +12 h post incubation & analysis	Chandrala et al.[78]
Whole cigarette smoke; e-cigarette aerosol	small-airway chip coupled to smoke exposure and microrespirator system	primary human small airway epithelium	programmable breathing-like airflow and smoke delivery	dynamic bidirectional flow, smoking topography simulation	ciliary function, oxidative stress genes, IL-8, COPD-specific responses	75 min exposure & next day analysis	Benam et al.[79]
Cigarette smoke	automatic smoking machine with direct ALI exposure module	A549 and HFBE cells	programmable smoking machine and dilution unit	controlled puff generation, dilution, and online smoke monitoring	ATP/ADP, glutathione, viability, particle deposition	1 h exposure +2 h post incubation & analysis	Aufderheide et al.[80]

The items are sorted in a manner that the system of longer operation/readout timescale appears nearer to the top. ADP: adenosine diphosphate; A549: human alveolar basal epithelial adenocarcinoma cell line A549; ALI: air-liquid interface; ATP: adenosine triphosphate; CD11b: cluster of differentiation molecule 11b; COPD: chronic obstructive pulmonary disease; CYP: cytochrome P450; DNA: deoxyribonucleic acid; e-cigarette: electronic cigarette; ErbB: erythroblastic oncogene B receptor family; HAEC: human aortic endothelial cell; HBE: human bronchial epithelial cell; HFL-1: human fetal lung fibroblast cell line HFL-1; HFBE: human fetal bronchial epithelial cell; ICAM-1: intercellular adhesion molecule 1; IL-8: interleukin-8; LDH: lactate dehydrogenase; NHBE: normal human bronchial epithelial cell; PM: particulate matter; RNA: ribonucleic acid; ROS: reactive oxygen species; TEER: transepithelial electrical resistance; THP-1: human monocytic leukemia THP-1 cell line.

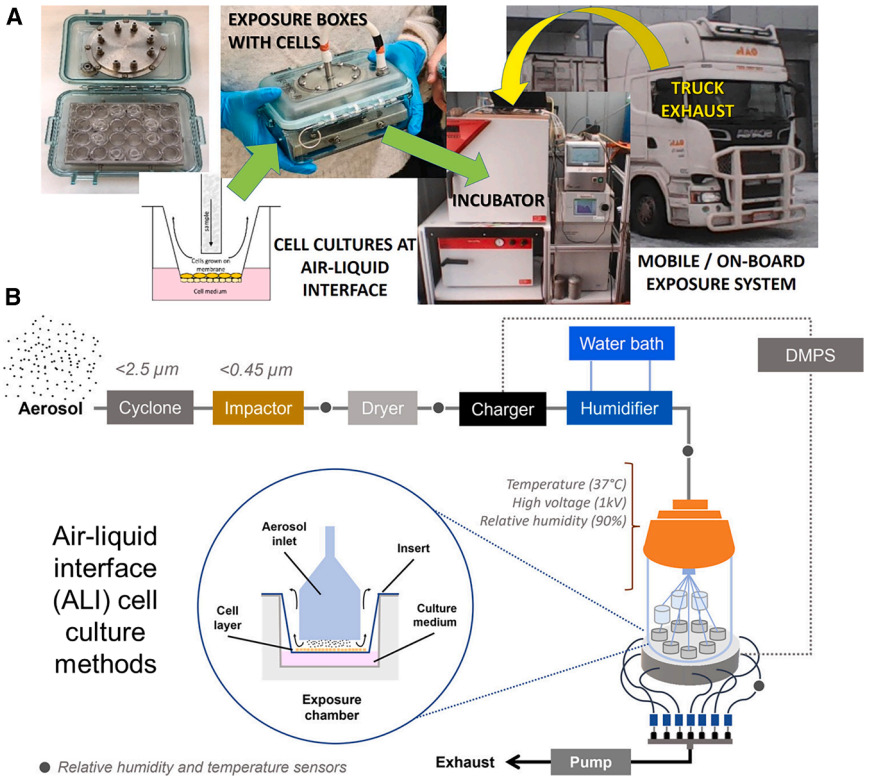


Figure 4. Recent examples of the portable platforms developed for *in vitro* cell exposure to ambient aerosols

(A) Compact mobile ALI cell culture setup for testing emission toxicity.[85] [Credit: Elsevier, CC BY 4.0 license] (B) ALI-based cell exposure system for assessing environmental aerosol toxicity.[86] (DMPS, differential mobility particle sizer) [Credit: Taylor & Francis, CC BY 4.0 license].

microphysiology into a miniaturized platform, including (1) bioengineered human lung mimics on-chip, (2) microrespirator-driven breathing, (3) simulated smoking behavior, and (4) a programming-based breathing control interface. The device incorporated bidirectional airflow within the lung-on-a-chip system, together with programmable dynamic aerosol exposure. Under exposure to tobacco smoke and e-cigarette aerosols, the system demonstrated the capability to identify clinical biomarkers of cellular oxidative stress and associated ciliary micropathological outcomes. In the same line of research, the Benam group subsequently developed a biologically inspired robotic system utilized as an automatically controlled inhalation exposure chamber.[73]

Automated and/or miniaturized cytotoxicity assessment

On-site aerosol sampling and cell exposure are essential procedures for *in vitro* evaluation of aerosol toxicity (Figure 4). Representative aerosol exposure methods for cell cultures are summarized in Table S2. Diverse types of small-size or portable devices have been developed for this purpose, as shown in Table 4. For instance, Secondo et al.[89] reported a portable cassette-format exposure device that supported ALI-based *in vitro* nanotoxicity testing using the A549 cell line.

Automated systems for assessing the cytotoxicity of ambient aerosols are in high demand because of (1) their applicability to field measurements and (2) the simplicity and readiness of system operation. Programmed instrument operation, often under software control, enables rapid toxicity analysis and high-throughput measurement of biological endpoints.

The developed devices have been implemented as partially or fully automated systems, some of which employ miniaturized platforms. For example, a semi-automatic aerosol dispenser and cell exposure system, termed RHINOCON, was developed in the early 2000s based on the human airway epithelial cell line HFBE21.[93] Shaking and actuation of the dispenser unit were controlled through a computer program. The dispenser was designed to accommodate six pump-spray units, enabling realistic aerosol deposition onto cells at the ALI. Shaking stroke actuation and time intervals between exposures were regulated through a computerized control panel. More recently, other types of automated systems have been developed for cell-free cytotoxicity assays of aerosols.

Ferro et al.[94] developed an organic electrochemical tool for monitoring the integrity of human bronchial epithelium *in vitro*. Using this method, electrical conductivity across the mucus layer at the ALI could be continuously measured *in situ*, and the detrimental effects of e-cigarette aerosols on the epithelium were confirmed in a dose-dependent manner.

The acellular assays for assessing aerosol cytotoxicity have largely relied on the measurement of oxidative potential (OP), which is the airborne particle's capability of generating endogenous reactive oxygen species (ROS).[95] A concise summary on the automated OP assessment systems has recently been provided, focusing on atmospheric PM.[96] In general, acellular assay-based devices are simple and easy to use, but may exhibit lower biological relevance when compared to the cell-based *in vitro* toxicity assessment tools. Representative quasi-autonomous cell-free systems may include the following examples.

Fang et al.[97] developed a semi-automated system for quantifying the OP of aerosols. The analytical system employed programmable syringe pumps with selector valves to efficiently perform the dithiothreitol (DTT) assay, a widely used method for OP measurement. The system could operate continuously for 24 h and be monitored remotely. Berg et al.[98] presented an automated DTT assay liquid-handling device combined with either ultraviolet-visible absorbance or electrochemical detection. This system employed an autosampler programmed to mix reagents and inject aliquots for analysis of the OP of ambient PM2.5. More recently, Salana et al.[99] developed a

Table 4. Automated and miniaturized platforms for aerosol exposure and cytotoxicity testing

Exposure agent	Toxicant form	Platform type	Exposure/ operation mode	Automation/ miniaturization features	Biological model	Main endpoints	Operation/Readout timescale	Reference
PM2.5	fine particle suspension	microfluidic gradient chip	liquid-phase gradient exposure	concentration-gradient generation; integrated migration assay	16HBE cells and macrophage chemotaxis module	Viability, EMT markers, NF-κB, PI3K, macrophage migration	24,48, and 72 h exposure & analysis	Cui et al.[87]
Airborne particles	ultrafine aerosol after condensational growth	portable ALI deposition device	condensational particle growth and deposition	multi-jet deposition system; four ALI cultures exposed simultaneously	A549 ALI cultures	deposited mass, deposition uniformity, LDH/ viability	20 min exposure & 24 h post-exposure	Tilly et al.[88]
Copper nanoparticles; field aerosols	nanoparticle aerosol; field aerosol	portable *in vitro* exposure cassette	personal/portable ALI aerosol sampling	wearable cassette format; field-deployable exposure	A549 cells	LDH, oxidative stress, cytotoxicity	10 min exposure & up to 24 h analysis	Secondo et al.[89]
Aerosol particles	submicron/ ultrafine aerosol	electrostatic ALI deposition chamber	electrostatic particle deposition	six parallel exposure positions; controlled temperature, humidity, and CO_2	BEAS-2B cells, macrophages, tracheal explants	deposition efficiency, ciliary beat frequency, cytokines, LDH	2 h exposure & 2–24 h post-exposure analysis	Savi et al.[90]
Engineered particles; diesel soot	nanoscale aerosol/soot aggregates	microfluidic exposure chamber	continuous ALI aerosol exposure	dose-controlled multiculture exposure chamber; CFD-optimized design	A549 lung epithelial cells	deposition efficiency, ROS, fluorescence-based readout	1 h exposure & analysis (3 h exposure for deposition efficiency calculation)	Asimakopoulou et al.[91]
Sidestream cigarette smoke	particle-gas smoke mixture	CULTEX ALI exposure module	direct smoke exposure at ALI	controlled dilution and exposure module	HFBE21 bronchial epithelial cells	cell number, metabolic activity, glutathione	1 h exposure and analysis	Aufderheide et al.[92]

The items are sorted in a manner that the platform of longer operation/readout timescale appears nearer to the top. 16HBE: human bronchial epithelial cell line 16HBE; A549: human alveolar basal epithelial adenocarcinoma cell line A549; ALI: air-liquid interface; Bax: BCL2-associated X protein; Bcl-2: B-cell lymphoma 2; BEAS-2B: human bronchial epithelial cell line BEAS-2B; CFD: computational fluid dynamics; CO_2: carbon dioxide; CULTEX: commercial air-liquid interface exposure system; EMT: epithelial-mesenchymal transition; HaCaT: human keratinocyte cell line HaCaT; HFBE21: human fetal bronchial epithelial cell line 21; IL-6: interleukin-6; LDH: lactate dehydrogenase; NF-κB: nuclear factor kappa-light-chain-enhancer of activated B cells; PI3K: phosphoinositide 3-kinase; PM: particulate matter; p53: tumor protein p53; ROS: reactive oxygen species; TNF-α: tumor necrosis factor alpha.

semi-automated cell-based device, termed SCOPE, that incorporated alveolar macrophages derived from the murine cell line NR8383 and was capable of rapidly analyzing the cellular OP of PM extracts. The instrument showed potential as a field-deployable device through rapid measurement of cellular OP. An online system (termed ROS-Online) enabling quasi real-time OP measurement of PM has been recently developed that could continuously operate for 48 h with a temporal resolution of 1 h.[100]

Recent progress has also been made in automated and portable systems designed to evaluate OP of environmental aerosol particles using acellular assays. Wragg et al.[101] reported a portable instrument, termed OPROSI, that enabled continuous online measurement of aerosol ROS through automated fluorescence spectroscopy. OPROSI employed a cell-free fluorescent assay based on 2′,7′-dichloro-fluorescein (DCFH) and horseradish peroxidase (HRP) to quantify aerosol-bound ROS and was optimized for field deployment. Within the same research group, Utinger et al.[102] developed a different type of device capable of performing a physiologically relevant acellular ascorbic acid assay for continuous quantification of the OP of aerosol particles. The instrument, termed OOPAAI, was designed to be portable and capable of automated operation for up to 3 days.

DISCUSSION

Relevance to *in vivo* mechanisms and pathophysiology

The various *in vitro* cytotoxicity endpoints/readouts covered in this article (Tables 2, 3, and 4) provide insight into the applications of the devices and systems in the aerosol-involved healthcare domain. The most important cellular toxicity outcome is oxidative stress, which is often related to inflammatory diseases.[103] With a close relationship to OP, oxidative stress in living systems induces perturbations in subcellular oxidation-reduction (redox) homeostasis and causes oxidation of lipids and nucleic acids. DNA methylation is known to be triggered by oxidative stress and is an extensively studied biomarker for cancer diagnosis.[104] Cytochrome P450 (CYP) induction is the typical enzyme-related source of endogenous ROS, and NF-κB and p53 are the redox-sensitive transcription factors that regulate molecular redox switching.[105,106] In mitochondrial bioenergetics, upregulated ATP/ADP production can be linked to the lowered antioxidant defense in pathological metabolic states. These mechanisms and endpoints are closely connected to the human biomarkers that are well-established in clinical medicine.[107]

The inflammatory response is a main mechanism of *in vivo* host defense against airborne particles and bioaerosols.[108,109] Cytokines play a central role in the tissue-level inflammatory reactions in humans and animals by interacting with membrane receptors and regulating cell signaling. Interleukins (ILs) and tumor necrosis factor alpha (TNF-α) are major classes of cytokines secreted by leukocytes, such as macrophages and neutrophils resident in lung epithelia. The oxidative stress may mediate the cytokine production upon tissue exposure to ambient particles. The exposure-response relationships for assessing the links between bioaerosol-contained endotoxins and pro-inflammatory biomarkers may provide crucial information on the pathological mechanisms *in vivo*.

Lactate dehydrogenase (LDH) and glutathione redox status are widely employed as cytotoxicity and oxidative metabolic outcomes, respectively, particularly for aerosol toxicity tests *in vitro* (e.g., Pariselli et al.[110]). The transepithelial electrical resistance (TEER) is a biophysical indicator that represents the integrity of epithelial layers *in vitro*.[111] These *in vitro* model-based outcomes are regarded to be indirectly related to the airborne particle-induced pulmonary dysfunctions. Biomarker discovery for narrowing the *in vitro-in vivo* data gap would be needed to facilitate translational research.

Technological opportunities and limitations

Automated (or partially automated) pipelines for ambient aerosol analysis, including autonomous robotic systems, have emerged as a developing direction in environmental technology. Simultaneously, miniaturization of aerosol analytical systems enhances mobility, on-site adaptability, and suitability for field deployment. From an environmental health perspective, rapid high-throughput screening of aerosol toxicity using cellular and acellular assays has gained increasing importance, particularly in relation to the development of alternatives to animal testing.

Mobile and unsupervised platforms may enable long-term aerosol monitoring and collection through integration of on-board cell exposure modules, ultimately supporting the realization of on-site air pollutant exposure systems.[57] In particular, lab-on-a-chip tools for airborne microbial sampling can enhance the analytical efficiency of bioaerosols[35] and may be integrated with lung-on-a-chip exposure models.

Despite current progress in the aforementioned technologies, several limitations remain to be addressed. First, aerosol sampling systems typically exhibit limited performance in terms of the quantity of collected PM and the capability to precisely measure such tiny masses, which may be a hurdle particularly for reducing time intervals in continuous PM analysis systems. The monitoring devices may quantify airborne particles with sizes from nanometers to micrometers, and can detect from a few hundred to thousands of particles per cubic centimeter. In contrast, estimation of the particle mass from particle size information generally requires several assumptions regarding particle shape and density.

Beyond the sampling process, reliable aerosol transfer between sampling, characterization, and biological exposure modules represents another important challenge in integrated systems. Aerosol particles transported through sampling probes, tubing, connectors, and other interfaces may be lost through deposition mechanisms that depend on particle properties, airflow conditions, and transport geometry.[14] Such size-dependent losses may alter not only the particle concentration but also the physiological representativeness of the aerosol delivered downstream. This is particularly relevant to biological exposure studies because particle size influences respiratory deposition and interactions with airway epithelia.[13] Particle losses have also been experimentally observed within ALI exposure systems. For example, Tilly et al.[88] attributed discrepancies between theoretical and experimental deposition efficiencies partly to particle losses within the exposure device. Consequently, the aerosol dose delivered to cells may differ from that measured at an upstream characterization point, potentially

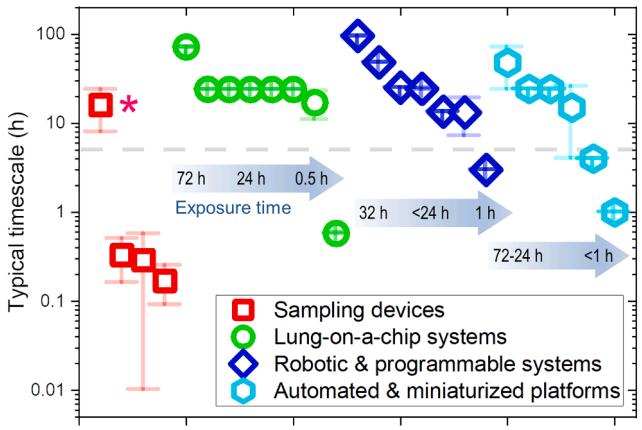


Figure 5. Typical operational timescale of the devices and modules summarized in Tables 1, 2, 3, and 4

(References with no timescale information are not reflected.) The starred point represents the filter-based aerosol sampling devices. The horizontal dotted line indicates the timescale of 5 h. Each point and error bar in the plot represents a median with min/max values, respectively.

complicating interpretation of source-to-effect relationships.[89] Transfer efficiency should therefore be characterized when coupling individual modules, while transport distances, bends, and unnecessary interfaces should be minimized where possible.

Next, the application of lung chips in environmental toxicology largely remains at the proof-of-concept stage,[112] partly because of the limited degree of lung mimicry. Recapitulation of the biological complexity of pulmonary structures and functions on-chip may be enhanced through the use of induced pluripotent stem cells (iPSCs).[113] However, *in vitro* methods for iPSC-based toxicological screening remain at an early stage with respect to their application in exposure systems for ambient and laboratory-generated aerosols. In addition to these biological and physiological challenges, further advances are needed to improve the automation and analytical throughput of lung-on-a-chip and ALI-based systems. Current systems incorporating (semi-)automated functions may still need manual procedures for cell preparation, medium handling, system operation, and/or endpoint analysis. Moreover, biological readouts may require several hours to days depending on the exposure model and endpoints, which may constrain the overall throughput of integrated workflows.

Lastly, most existing *in vitro* methods for evaluating aerosol-induced adverse effects are confined to lung toxicity, and the skin and ocular toxicities have not been sufficiently addressed. It is only recently that bioengineered constructs of human skin and corneal epithelia have been applied to investigations of cellular adverse effects of airborne PM (e.g., Simpson et al.,[114]; Ko et al.,[115]). The combination with *in silico* toxicity prediction methods could further strengthen their translational capabilities, in the context of increasing concerns about air pollution and the need for alternatives to animal testing.

Optimization of the workflow integration

Different on-site environmental scenarios require different combinations of aerosol collection and detection techniques. Long-term ambient PM monitoring generally benefits from continuous particle sizing and chemical characterization coupled with high-capacity sampling (Table S3), whereas infectious bioaerosol surveillance requires sampling methods that preserve particle viability together with rapid biological detection techniques (Table 1). Consequently, the optimal configuration of automated source-to-effect platforms should integrate complementary sampling and detection strategies depending on the target aerosol characteristics, sampling duration and temporal resolution, workflow automation, and downstream (biological) readout. Importantly, the sampling strategy needs to be selected so that the sampling duration (typically a few minutes, except for the filter-based methods; Table 1) is compatible with the analytical throughput and readout timescale (typically ranging from 0.5 h to days; Tables 2, 3, and 4) required for the intended monitoring application.

Beyond selecting an appropriate sampling strategy, the preservation of the physicochemical integrity of collected aerosols is another critical requirement, especially for reliable downstream bio-analyses. Although filter-based sampling methods have been widely used, they are time consuming (8–24 h; Table 1) and the filter-collected particles usually require elution or extraction, which may introduce particle losses, incomplete recovery, or extraction bias during post-collection processes.[35] Especially, for bioaerosols, collection-induced dehydration is known to reduce microbial viability or viral infectivity.[31] Recent advances in aerosol collection techniques have largely focused on improving time-efficiency and preserving the intrinsic properties of airborne particles while improving compatibility with downstream bioassays.[35,116]

It is critical to compare the performance of individual modules that can be integrated into a single workflow: Figure 5 represents the devices' operational timescales listed in Tables 1, 2, 3, and 4. On one hand, the aerosol sampling time range generally corresponds to 5–30 min, except for the case of filtration methods. The filter-based collection techniques would not be compatible with the workflow because they largely rely on manual procedures. On the other hand, the cell exposure-based systems (including the lung chips and robotic/automated platforms) require much longer operation time, usually hours to days. Figure 5 shows that the operation time decreases with a shorter period of *in vitro* cell exposure to aerosol particles. As is summarized in Tables 2, 3, and 4, the exposure/incubation time of culture cells to particles typically spans from 24 h to 72 h, depending on the cytotoxicity outcomes that are aimed to be obtained using a specific method of toxicity assessment. The exposure time is a fundamental biological factor required for performing *in vitro* cell toxicity testing regardless of whether the systems are automated/robotized or not. Although 24 h of particle exposure to cells has mostly been adopted as the cytotoxicity testing condition, the exposure time can be reduced to 1 h (or less) depending on the instrumentation. Figure 5 implies that it is technically possible to reduce the operation timescale of each module down to <5 h.

Automated exposure platforms have also been developed to minimize sample handling (and its required time) between aerosol generation/exposure and cellular assessments. In these approaches, aerosols are delivered directly to culture cells,

typically under ALI conditions, to eliminate intermediate collection and preparation steps that may alter particle properties. Overall, if we rule out filter-based aerosol samplers, the analytic microdevices for *in vitro* exposure and cytotoxicity testing remain the main bottlenecks that prevent enhanced turnaround time of future autonomous analytic systems. For an automated framework to be feasible, whole system-level optimization will be indispensable for the timescale matching between sampling rate and exposure module throughput.

Device and system standardization

Standardization represents a major challenge in the development of airborne pollutant exposure systems, encompassing aerosol samplers, sensor calibration and operation, organ-on-a-chip design and fabrication, and automated data analysis algorithms.[29,58] Regarding aerosol samplers, establishment of the device performance criteria and standardized test procedures have been considered essential milestones.[117,118] One of the key parameters in PM sampler standardization is the air flow rate because the flow calibration methods vary with device types.[119] For bioaerosol collectors, the need to standardize analytical methods for airborne endotoxins and microbial nucleic acids has been raised to reduce inter-laboratory data variability at the international level.[120,121]

Various research-level and low-cost aerosol sensors have been utilized for monitoring airborne particles and aerosol-related gases due to their compact size and low power consumption, compared to the lab-scale monitoring instruments (Tables S3 and S4). Although there is still a lack of standardized protocols and programs for calibration and operation, the commercially available sensors are portable and highly suitable to be coupled with mobile exposure systems. Since the protocols for device testing and calibration are rapidly progressing,[122–125] the system integration of sensors with optimized control (e.g., Frijns et al.[126]) could improve the standardization of cell culture-based exposure systems.

Standardization of lung-on-a-chip, skin-on-a-chip, and cornea-on-a-chip devices has been a critical bottleneck hindering their translation to industrial and clinical sectors.[127–129] The devices are designed and fabricated to recapitulate the core physiological processes in the human organs that are closely relevant to ambient aerosol exposure. Therefore, it is strongly needed to develop standardized and international guidelines for both instrumentation and evaluation procedures, particularly related to the chip integration into exposure systems.

The inter-laboratory consensus on the common data treatment algorithms is required to promote automated and standardized data analysis throughout the workflow of aerosol detection, sampling, exposure, and biological readout. Lightweight computational toolkits for managing big data and large-scale databases will be a fundamental component to be incorporated in future mobile exposure systems.

Application of artificial intelligence

The AI technologies, including machine learning and deep learning techniques, provide effective approaches for handling large and complex datasets generated from aerosol sensing, sampling, and characterization systems.[30] For instance, in dust aerosol research, the AI algorithms have shown potential robustness in intelligent monitoring, automatic extraction of multi-scale features, and rapid assessment of health effects.[130] Furthermore, in bioaerosol detection, the air sampler-combined sensor devices equipped with AI-assisted signal processing have been emerging as the next-generation biosensing tools.[131] AI-based predictive toxicology has also attracted interest for applications in public and environmental health.[132] The implementation of *onboard* AI software for field-deployable health risk predictions remains a future development.

System-level AI techniques for air quality analysis and control have recently been developed.[133] Machine learning modeling has been enhancing the systems' capabilities in source-based classification, chemical characterization, and oxidant prediction of aerosols.[134] AI-based toxicity assessment models are required to be embedded in the systems. Integration of data-driven modeling modules into mobile analytical systems could prominently strengthen the quantitative predictability of aerosol toxicity for both humans and ecosystems. Additionally, mathematical and computational methods (associated with AI) can improve mechanistic understanding of various aerosol-associated physical, chemical, and biological phenomena, including aerosol generation, transport, deposition, and toxicity.[36,135,136] Finally, integration of AI and soft robotics may enable lung-on-a-chip systems to exhibit more *in vivo*-like behavior.[137,138] Still, these recent approaches support only partial automation of present platforms developed for environmental bio-analyses.

Future research directions should include (1) development of AI-assisted biochips for assessing PM toxicity in skin and eyes, (2) biophysical mechanism-related machine learning methods that could efficiently connect aerosol characterization data and in-depth cell biology approaches, and (3) autonomous microdevices for screening the cellular effects of natural and anthropogenic aerosol particles on ecological species. Ultimately, the AI-empowered devices and systems should be properly evaluated and translated into regulatory sectors.

Concluding remarks

Recent acceleration in climate change caused by human activities has been noticeably facilitating the generation of detrimental aerosols (e.g., wildfire smoke). In parallel, anthropogenic airborne particles have been progressively threatening public health. In this context, we have reviewed the state-of-the-art and future directions in the field for developing mobile and automated platforms based on the overarching technologies of aerosol collectors, microfluidic devices, lung-on-a-chip, and robotic platforms. The prospects for a system-level "source-to-effect" workflow have been provided by combining the technological elements covering from airborne particle sampling to biological readout *in vitro*.

In our viewpoint, however, there are still several limitations in implementing the vision. (1) The current on-device cytotoxicity endpoints have rather indirect relevance to *in vivo* toxicological outcomes, and novel methods for *in vitro-in vivo* data gap filling are required. (2) Aerosol sampling devices usually exhibit limited performance, and there may be particle losses during transfer to the connected analytic modules. Thus, the system-level design should carefully consider the aerosol transfer efficiency by minimizing the interface between the devices and instruments. (3) For

applications to environmental health sectors, the current lung-on-a-chips are able to recapitulate the *in vivo* lungs only to a limited degree. Furthermore, fully automated lung chips need to be developed to achieve rapid biological readout capabilities. In addition to the lungs, bioengineered human skin and corneal epithelia need to be considered for embedding in the suggested workflow.

For the optimization of workflow integration, the aerosol sampling duration should be adjusted to be compatible with the downstream devices' operation timescales. The preservation of the physicochemical integrity and viability of collected particles is another crucial requirement. In these reasons, filter-based sampling methods are not recommended for the workflow implementation. The standardization of individual devices and whole systems remains a main hurdle preventing their translation to practical domains. AI-driven control systems, data analyses, and toxicity predictions will be essential techniques that support the automation and/or robotization of the mobile ''source-to-effect'' framework.

Limitations of the study

Although we propose a unified ''source-to-effect'' framework for mobile and automated analysis of aerosols, the practical strategies on system-level implementation are not provided in detail. Additionally, we do not suggest any potential solutions for overcoming technical problems that may occur when developing the conceptualized workflow as a real system. Mathematical analysis or computational modeling may be an efficient approach to quantitatively validate the feasibility of the proposed framework, which is predominantly missing in this study.

RESOURCE AVAILABILITY

Lead contact

Further information should be requested to the lead contact, Dr. Baeckkyoung Sung (sung@kist-europe.de).

Materials availability

No new materials were generated in this work.

Data and code availability

- This paper analyzes previously published studies, and no data were newly generated.
- This paper does not report original code.
- Any additional information required to reanalyze the data reported in this paper are available from the lead contact upon request.

ACKNOWLEDGMENTS

This work was supported by the KIST-Europe Basic Research Program (project no 12603). We thank Dr. Jihoon Park (KIST Europe) for his valuable comments and discussions.

AUTHOR CONTRIBUTIONS

Conceptualization, B.S. and L.A.; methodology, S.J. and K.E.K.; investigation, B.S., S.J., and C.-H.H.; writing – original draft, B.S., S.J., K.E.K., and C.-H.H.; writing – review and editing, B.S., S.J., C.-H.H., and L.A.; funding acquisition, B.S.; supervision, B.S.

DECLARATION OF INTERESTS

The authors declare no competing interests.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

- KEY RESOURCES TABLE
- METHOD DETAILS
  - Literature selection
  - Information extraction
  - Operational timescale analysis
- QUANTIFICATION AND STATISTICAL ANALYSIS

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.isci.2026.118066.

Received: June 16, 2026
Revised: September 18, 2026
Accepted: October 13, 2026

REFERENCES

1. Hinds, W.C. (1999). Aerosol Technology: Properties, Behavior, and Measurement of Airborne Particles, 2nd ed. (Wiley).
2. Kwon, H.-S., Ryu, M.H., and Carlsten, C. (2020). Ultrafine particles: unique physicochemical properties relevant to health and disease. Exp. Mol. Med. *52*, 318–328. https://doi.org/10.1038/s12276-020-0405-1.
3. Boucher, O. (2015). Atmospheric aerosols. In Atmospheric Aerosols: Properties and Climate Impacts, O. Boucher, ed. (Springer), pp. 9–24. https://doi.org/10.1007/978-94-017-9649-1_2.
4. Griffin, D., and Kellogg, C. (2004). Dust storms and their impact on ocean and human health: dust in earth's atmosphere. EcoHealth *1*, 284–295. https://doi.org/10.1007/s10393-004-0120-8.
5. Ito, A., Ye, Y., Baldo, C., and Shi, Z. (2021). Ocean fertilization by pyrogenic aerosol iron. npj Clim. Atmos. Sci. *4*, 30. https://doi.org/10.1038/s41612-021-00185-8.
6. Highwood, E.J., and Kinnersley, R.P. (2006). When smoke gets in our eyes: the multiple impacts of atmospheric black carbon on climate, air quality and health. Environ. Int. *32*, 560–566. https://doi.org/10.1016/j.envint.2005.12.003.
7. Losacco, C., and Perillo, A. (2018). Particulate matter air pollution and respiratory impact on humans and animals. Environ. Sci. Pollut. Res. Int. *25*, 33901–33910. https://doi.org/10.1007/s11356-018-3344-9.
8. Zhang, Y., Dong, S., Wang, H., Tao, S., and Kiyama, R. (2016). Biological impact of environmental polycyclic aromatic hydrocarbons (ePAHs) as endocrine disruptors. Environ. Pollut. *213*, 809–824. https://doi.org/10.1016/j.envpol.2016.03.050.
9. Bolan, S., Sharma, S., Mukherjee, S., Isaza, D.F.G., Rodgers, E.M., Zhou, P., Hou, D., Scordo, F., Chandra, S., Siddique, K.H.M., and Bolan, N. (2025). Wildfires under changing climate, and their environmental and health impacts. J. Soils Sediments *25*, 3173–3197. https://doi.org/10.1007/s11368-025-04020-y.
10. Stewart, C., Damby, D.E., Horwell, C.J., Elias, T., Ilyinskaya, E., Tomašek, I., Longo, B.M., Schmidt, A., Carlsen, H.K., Mason, E., et al. (2022). Volcanic air pollution and human health: recent advances and future directions. Bull. Volcanol. *84*, 11. https://doi.org/10.1007/s00445-021-01513-9.
11. Plaas, H.E., and Paerl, H.W. (2021). Toxic cyanobacteria: a growing threat to water and air quality. Environ. Sci. Technol. *55*, 44–64. https://doi.org/10.1021/acs.est.0c06653.

12. Zuo, Y.Y., Uspal, W.E., and Wei, T. (2020). Airborne transmission of COVID-19: aerosol dispersion, lung deposition, and virus-receptor interactions. ACS Nano *14*, 16502–16524. https://doi.org/10.1021/acsnano.0c08484.

13. Cooper, D.M., and Loxham, M. (2019). Particulate matter and the airway epithelium: the special case of the underground? Eur. Respir. Rev. *28*, 190066. https://doi.org/10.1183/16000617.0066-2019.

14. Morawska, L., Buonanno, G., Mikszewski, A., and Stabile, L. (2022). The physics of respiratory particle generation, fate in the air, and inhalation. Nat. Rev. Phys. *4*, 723–734. https://doi.org/10.1038/s42254-022-00506-7.

15. Semple, S. (2004). Dermal exposure to chemicals in the workplace: just how important is skin absorption? Occup. Environ. Med. *61*, 376–382. https://doi.org/10.1136/oem.2003.010645.

16. Lee, R.K., and Sung, B. (2026). Computational modelling of skin sensitisation of chemicals. In Cheminformatic Modelling and Data Gap Filling for a Green and Sustainable Environment, K. Roy and A. Banerjee, eds. (Elsevier), pp. 589–606. https://doi.org/10.1016/B978-0-443-36474-7.00024-7.

17. Jung, S.J., Mehta, J.S., and Tong, L. (2018). Effects of environment pollution on the ocular surface. Ocul. Surf. *16*, 198–205. https://doi.org/10.1016/j.jtos.2018.03.001.

18. Dunbabin, M., and Marques, L. (2012). Robots for environmental monitoring: Significant advancements and applications. IEEE Robot. Automat. Mag. *19*, 24–39. https://doi.org/10.1109/MRA.2011.2181683.

19. Duffy, G., and Regan, F. (2017). Recent developments in sensing methods for eutrophying nutrients with a focus on automation for environmental applications. Analyst *142*, 4355–4372. https://doi.org/10.1039/c7an00840f.

20. Goldberg, K. (2012). What is automation? IEEE Trans. Automat. Sci. Eng. *9*, 1–2. https://doi.org/10.1109/TASE.2011.2178910.

21. Lichtveld, K.M., Ebersviller, S.M., Sexton, K.G., Vizuete, W., Jaspers, I., and Jeffries, H.E. (2012). In vitro exposures in diesel exhaust atmospheres: Resuspension of PM from filters versus direct deposition of PM from air. Environ. Sci. Technol. *46*, 9062–9070. https://doi.org/10.1021/es301431s.

22. Roper, C., Delgado, L.S., Barrett, D., Massey Simonich, S.L., and Tanguay, R.L. (2019). PM2.5 filter extraction methods: Implications for chemical and toxicological analyses. Environ. Sci. Technol. *53*, 434–442. https://doi.org/10.1021/acs.est.8b04308.

23. Chen, Y.-C., Wang, I.-J., Cheng, C.-C., Wu, Y.-C., Bai, C.-H., and Yu, K.-P. (2021). Effect of selected sampling media, flow rate, and time on the sampling efficiency of a liquid impinger packed with glass beads for the collection of airborne viruses. Aerobiologia *37*, 243–252. https://doi.org/10.1007/s10453-020-09683-3.

24. Raynor, P.C., Adesina, A., Aboubakr, H.A., Yang, M., Torremorell, M., and Goyal, S.M. (2021). Comparison of samplers collecting airborne influenza viruses: 1. Primarily impingers and cyclones. PLoS One *16*, e0244977. https://doi.org/10.1371/journal.pone.0244977.

25. Li, X., Chen, H., Qi, X., Peng, Y., Zhou, L., Ma, J., and Yao, M. (2021). A robot assisted high-flow portable cyclone sampler for bacterial and SARS-CoV-2 aerosols. Aerosol Air Qual. Res. *21*, 210130. https://doi.org/10.4209/aaqr.210130.

26. Verreault, D., Moineau, S., and Duchaine, C. (2008). Methods for sampling of airborne viruses. Microbiol. Mol. Biol. Rev. *72*, 413–444. https://doi.org/10.1128/MMBR.00002-08.

27. Lednicky, J., Pan, M., Loeb, J., Hsieh, H., Eiguren-Fernandez, A., Hering, S., Fan, Z.H., and Wu, C.-Y. (2016). Highly efficient collection of infectious pandemic influenza H1N1 virus (2009) through laminar-flow water-based condensation. Aerosol Sci. Technol. *50*, i–iv. https://doi.org/10.1080/02786826.2016.1179254.

28. Lowther, S.D., Jones, K.C., Wang, X., Whyatt, J.D., Wild, O., and Booker, D. (2019). Particulate matter measurement indoors: a review of metrics, sensors, needs and applications. Environ. Sci. Technol. *53*, 11644–11656. https://doi.org/10.1021/acs.est.9b03425.

29. Huffman, J.A., Perring, A.E., Savage, N.J., Clot, B., Crouzy, B., Tummon, F., Shoshanim, O., Damit, B., Schneider, J., Sivaprakasam, V., et al. (2020). Real-time sensing of bioaerosols: review and current perspectives. Aerosol Sci. Technol. *54*, 465–495. https://doi.org/10.1080/02786826.2019.1664724.

30. Gao, T., Wang, K., Shen, X., Cao, Y., and Xue, B. (2025). Collection and characterization of aerosol particles. Mater. Res. Express *12*, 042002. https://doi.org/10.1088/2053-1591/adc4c2.

31. Haig, C.W., Mackay, W.G., Walker, J.T., and Williams, C. (2016). Bioaerosol sampling: sampling mechanisms, bioefficiency and field studies. J. Hosp. Infect. *93*, 242–255. https://doi.org/10.1016/j.jhin.2016.03.017.

32. Baron, P.A. (1998). Personal aerosol sampler design: a review. Appl. Occup. Environ. Hyg *13*, 313–320. https://doi.org/10.1080/1047322X.1998.10390088.

33. Kabir, E., Azzouz, A., Raza, N., Bhardwaj, S.K., Kim, K.-H., Tabatabaei, M., and Kukkar, D. (2020). Recent advances in monitoring, sampling, and sensing techniques for bioaerosols in the atmosphere. ACS Sens. *5*, 1254–1267. https://doi.org/10.1021/acssensors.9b02585.

34. Batool, S.S., Batool, S.M., DeSutter, T., Meehan, M., and Oduor, P.G. (2026). Smart bioaerosol monitoring: Advanced sampling and sensing across environmental, clinical, and industrial domains. ACS Omega *11*, 4868–4902. https://doi.org/10.1021/acsomega.5c09151.

35. Mainelis, G. (2020). Bioaerosol sampling: classical approaches, advances, and perspectives. Aerosol Sci. Technol. *54*, 496–519. https://doi.org/10.1080/02786826.2019.1671950.

36. Alsved, M., Bourouiba, L., Duchaine, C., Löndahl, J., Marr, L.C., Parker, S.T., Prussin, A.J., II, and Thomas, R.J. (2020). Natural sources and experimental generation of bioaerosols: challenges and perspectives. Aerosol Sci. Technol. *54*, 547–571. https://doi.org/10.1080/02786826.2019.1682509.

37. Pan, M., Lednicky, J.A., and Wu, C.-Y. (2019). Collection, particle sizing and detection of airborne viruses. J. Appl. Microbiol. *127*, 1596–1611. https://doi.org/10.1111/jam.14278.

38. Sagona, J.A., Shalat, S.L., Wang, Z., Ramagopal, M., Black, K., Hernandez, M., and Mainelis, G. (2015). Evaluation of particle resuspension in young children's breathing zone using stationary and robotic (PIPER) aerosol samplers. J. Aerosol Sci. *85*, 30–41. https://doi.org/10.1016/j.jaerosci.2015.03.001.

39. L'Orange, C., Neymark, G., Carter, E., and Volckens, J. (2021). A high-throughput, robotic system for analysis of aerosol sampling filters. Aerosol Air Qual. Res. *21*, 210037. https://doi.org/10.4209/aaqr.210037.

40. Feld-Cook, E., Shome, R., Zaleski, R.T., Mohan, K., Kourtev, H., Bekris, K.E., Weisel, C.P., and Shin, J.M.K. (2021). Exploring the utility of robots in exposure studies. J. Expo. Sci. Environ. Epidemiol. *31*, 784–794. https://doi.org/10.1038/s41370-019-0190-x.

41. Cashkar, A., Li, J., and Biswas, P. (2019). Particulate matter sensors mounted on a robot for environmental aerosol measurements. J. Environ. Eng. *145*, 04019057. https://doi.org/10.1061/(ASCE)EE.1943-7870.0001569.

42. Lee, I., Jeon, E., and Lee, J. (2023). On-site bioaerosol sampling and detection in microfluidic platforms. Trends Analyt. Chem. *158*, 116880. https://doi.org/10.1016/j.trac.2022.116880.

43. Aryal, P., Hefner, C., Martinez, B., and Henry, C.S. (2024). Microfluidics in environmental analysis: advancements, challenges, and future prospects for rapid and efficient monitoring. Lab Chip *24*, 1175–1206. https://doi.org/10.1039/d3lc00871a.

44. Metcalf, A.R., Narayan, S., and Dutcher, C.S. (2018). A review of microfluidic concepts and applications for atmospheric aerosol science. Aerosol Sci. Technol. *52*, 310–329. https://doi.org/10.1080/02786826.2017.1408952.

45. Sznitman, J. (2022). Revisiting airflow and aerosol transport phenomena in the deep lungs with microfluidics. Chem. Rev. *122*, 7182–7204. https://doi.org/10.1021/acs.chemrev.1c00621.

46. Silvani, S., Figliuzzi, M., and Remuzzi, A. (2019). Toxicological evaluation of airborne particulate matter. Are cell culture technologies ready to replace animal testing? J. Appl. Toxicol. *39*, 1484–1491. https://doi.org/10.1002/jat.3804.

47. O'Connor, J.S., Kim, H., Gwag, E., Abelmann, L., Sung, B., and Manz, A. (2021). 3D printing for microgel-based liver cell encapsulation. In 2021 IEEE 34th International Conference on Micro Electro Mechanical Systems (MEMS) (IEEE), pp. 1023–1026. https://doi.org/10.1109/MEMS51782.2021.9375385.

48. Mohizin, A., Won, Y., and Sung, B. (2023). Thermally driven sol-gel transition of gelatin in a 3D-printed microfluidic chip. In 2023 IEEE SENSORS (IEEE), pp. 1–4. https://doi.org/10.1109/SENSORS56945.2023.10324960.

49. Abelmann, L., Gwag, E., and Sung, B. (2024). Permanent magnet systems to study the interaction between magnetic nanoparticles and cells in microslide channels. J. Magn. Magn Mater. *591*, 171696. https://doi.org/10.1016/j.jmmm.2023.171696.

50. Delafosse, M., Regnault, E., Gebauer-Barrett, J., Manz, A., and Sung, B. (2026). Cell-embedded microgels as emerging miniature 3D tissue-mimics toward biochip-based toxicity screening. Bioeng. Transl. Med. *11*, e70061. https://doi.org/10.1002/btm2.70061.

51. Zheng, L., Wang, Y., Zhang, Y., Fu, Y., Yang, Z., Fan, Y., Sun, Z., Zhao, M., Zhu, L., Dai, B., et al. (2021). EGFR inhibitors regulate Ca2+ concentration and apoptosis after PM2.5 exposure based on a lung-mimic microfluidic system. Sci. Total Environ. *761*, 143200. https://doi.org/10.1016/j.scitotenv.2020.143200.

52. Schneider, G. (2018). Automating drug discovery. Nat. Rev. Drug Discov. *17*, 97–113. https://doi.org/10.1038/nrd.2017.232.

53. Shibuta, M., Tetsuka, K., Kawabe, T., Namatame, I., Asano, H., Heijmans, J., Wevers, N.R., and Sasaki-Iwaoka, H. (2026). End-to-end automation of organ-on-a-chip culture and drug testing: Enhancing scalability and expandability. SLAS Technol. *39*, 100434. https://doi.org/10.1016/j.slast.2026.100434.

54. Manz, A., Neužil, P., O'Connor, J.S., and Simone, G. (2021). Microfluidics and Lab-On-A-Chip (Royal Society of Chemistry).

55. Leung, C.M., de Haan, P., Ronaldson-Bouchard, K., Kim, G.-A., Ko, J., Rho, H.S., Chen, Z., Habibovic, P., Jeon, N.L., Takayama, S., et al. (2022). A guide to the organ-on-a-chip. Nat. Rev. Meth. Prim. *2*, 33. https://doi.org/10.1038/s43586-022-00118-6.

56. Liu, F., Ng, N.L., and Lu, H. (2021). Emerging applications of microfluidic techniques for in vitro toxicity studies of atmospheric particulate matter. Aerosol Sci. Technol. *55*, 623–639. https://doi.org/10.1080/02786826.2021.1879373.

57. Lin, K.C., Yen, C.Z., Yang, J.W., Chung, J.H.Y., and Chen, G.-Y. (2022). Airborne toxicological assessment: The potential of lung-on-a-chip as an alternative to animal testing. Mater. Today Adv. *14*, 100216. https://doi.org/10.1016/j.mtadv.2022.100216.

58. Wang, H., Yin, F., Li, Z., Su, W., and Li, D. (2023). Advances of microfluidic lung chips for assessing atmospheric pollutants exposure. Environ. Int. *172*, 107801. https://doi.org/10.1016/j.envint.2023.107801.

59. Sung, B. (2023). Biomaterials and microfluidics systems used for modeling pathological tissues. In Functional Biomaterials: Advances in Design and Biomedical Applications, A. Kumar, D. Dhinasekaran, I. Savina, and S.S. Han, eds. (CRC Press), pp. 289–308.

60. Xu, C., Zhang, M., Chen, W., Jiang, L., Chen, C., and Qin, J. (2020). Assessment of air pollutant PM2.5 pulmonary exposure using a 3D lung-on-chip model. ACS Biomater. Sci. Eng. *6*, 3081–3090. https://doi.org/10.1021/acsbiomaterials.0c00221.

61. Byun, J., Song, B., Lee, K., Kim, B., Hwang, H.W., Ok, M.R., Jeon, H., Lee, K., Baek, S.K., Kim, S.H., et al. (2019). Identification of urban particulate matter-induced disruption of human respiratory mucosa integrity using whole transcriptome analysis and organ-on-a-chip. J. Biol. Eng. *13*, 88. https://doi.org/10.1186/s13036-019-0219-7.

62. Li, Y., Hu, C., Wang, P., Liu, Y., Wang, L., Pi, Q., Gong, Z., Yang, X., Mak, M., and Wu, Y. (2019). Indoor nanoscale particulate matter-induced coagulation abnormality based on a human 3D microvascular model on a microfluidic chip. J. Nanobiotechnol. *17*, 20. https://doi.org/10.1186/s12951-019-0458-2.

63. Zheng, L., Dong, H., Zhao, W., Zhang, X., Duan, X., Zhang, H., Liu, S., and Sui, G. (2019). An air-liquid interface organ-level lung microfluidics platform for analysis on molecular mechanisms of cytotoxicity induced by cancer-causing fine particles. ACS Sens. *4*, 907–917. https://doi.org/10.1021/acssensors.8b01672.

64. Li, Y., Pi, Q.-M., Wang, P.-C., Liu, L.-J., Han, Z.-G., Shao, Y., Zhai, Y., Zuo, Z.-Y., Gong, Z.-Y., Yang, X., and Wu, Y. (2017). Functional human 3D microvascular networks on a chip to study the procoagulant effects of ambient fine particulate matter. RSC Adv. *7*, 56108–56116. https://doi.org/10.1039/c7ra11357a.

65. Sakolish, C., Georgescu, A., Huh, D.D., and Rusyn, I. (2022). A model of human small airway on a chip for studies of subacute effects of inhalation toxicants. Toxicol. Sci. *187*, 267–278. https://doi.org/10.1093/toxsci/kfac036.

66. Elias-Kirma, S., Artzy-Schnirman, A., Das, P., Heller-Algazi, M., Korin, N., and Sznitman, J. (2020). In situ-like aerosol inhalation exposure for cytotoxicity assessment using airway-on-chips platforms. Front. Bioeng. Biotechnol. *8*, 91. https://doi.org/10.3389/fbioe.2020.00091.

67. Bovard, D., Sandoz, A., Luettich, K., Frentzel, S., Iskandar, A., Marescotti, D., Trivedi, K., Guedj, E., Dutertre, Q., Peitsch, M.C., and Hoeng, J. (2018). A lung/liver-on-a-chip platform for acute and chronic toxicity studies. Lab Chip *18*, 3814–3829. https://doi.org/10.1039/c8lc01029c.

68. Doryab, A., Taskin, M.B., Stahlhut, P., Schröppel, A., Orak, S., Voss, C., Ahluwalia, A., Rehberg, M., Hilgendorff, A., Stöger, T., et al. (2021). A bioinspired in vitro lung model to study particokinetics of nano-/microparticles under cyclic stretch and air-liquid interface conditions. Front. Bioeng. Biotechnol. *9*, 616830. https://doi.org/10.3389/fbioe.2021.616830.

69. Huang, D., Liu, T., Liao, J., Maharjan, S., Xie, X., Pérez, M., Anaya, I., Wang, S., Tirado Mayer, A., Kang, Z., et al. (2021). Reversed-engineered human alveolar lung-on-a-chip model. Proc. Natl. Acad. Sci. USA *118*, e2016146118. https://doi.org/10.1073/pnas.2016146118.

70. Nof, E., Zidan, H., Artzy-Schnirman, A., Mouhadeb, O., Beckerman, M., Bhardwaj, S., Elias-Kirma, S., Gur, D., Beth-Din, A., Levenberg, S., et al. (2022). Human multi-compartment airways-on-chip platform for emulating respiratory airborne transmission: from nose to pulmonary acini. Front. Physiol. *13*, 853317. https://doi.org/10.3389/fphys.2022.853317.

71. Artzy-Schnirman, A., Lehr, C.-M., and Sznitman, J. (2020). Advancing human in vitro pulmonary disease models in preclinical research: opportunities for lung-on-chips. Expert Opin. Drug Deliv. *17*, 621–625. https://doi.org/10.1080/17425247.2020.1738380.

72. Sung, B. (2022). In silico modeling of endocrine organ-on-a-chip systems. Math. Biosci. *352*, 108900. https://doi.org/10.1016/j.mbs.2022.108900.

73. Kaiser, A.J., Salem, C., Alvarenga, B.J., Pagliaro, A., Smith, K.P., Valerio, L.G., Jr., and Benam, K.H. (2021). A robotic system for real-time analysis of inhaled submicron and microparticles. iScience *24*, 103091. https://doi.org/10.1016/j.isci.2021.103091.

74. Jabbar, F., Kim, Y.S., and Lee, S.H. (2022). Biological influence of pulmonary disease conditions induced by particulate matter on microfluidic lung chips. Biochip J. *16*, 305–316. https://doi.org/10.1007/s13206-022-00068-x.

75. Bovard, D., Renggli, K., Marescotti, D., Sandoz, A., Majeed, S., Pinard, L., Ferreira, S., Pak, C., Barbier, A., Beguin, A., et al. (2022). Impact of aerosols on liver xenobiotic metabolism: a comparison of two

methods of exposure. Toxicol. Vitro *79*, 105277. https://doi.org/10.1016/j.tiv.2021.105277.

76. Benam, K.H., Novak, R., Ferrante, T.C., Choe, Y., and Ingber, D.E. (2020). Biomimetic smoking robot for in vitro inhalation exposure compatible with microfluidic organ chips. Nat. Protoc. *15*, 183–206. https://doi.org/10.1038/s41596-019-0230-y.
77. Makwana, O., Smith, G.A., Flockton, H.E., Watters, G.P., Lowe, F., and Breheny, D. (2021). Impact of cigarette versus electronic cigarette aerosol conditioned media on aortic endothelial cells in a microfluidic cardiovascular model. Sci. Rep. *11*, 4747. https://doi.org/10.1038/s41598-021-83511-7.
78. Chandrala, L.D., Afshar-Mohajer, N., Nishida, K., Ronzhes, Y., Sidhaye, V.K., Koehler, K., and Katz, J. (2019). A device for measuring the in-situ response of human bronchial epithelial cells to airborne environmental agents. Sci. Rep. *9*, 7263. https://doi.org/10.1038/s41598-019-43784-5.
79. Benam, K.H., Novak, R., Nawroth, J., Hirano-Kobayashi, M., Ferrante, T.C., Choe, Y., Prantil-Baun, R., Weaver, J.C., Bahinski, A., Parker, K.K., and Ingber, D.E. (2016). Matched-comparative modeling of normal and diseased human airway responses using a microengineered breathing lung chip. Cell Sys *3*, 456–466.e4. https://doi.org/10.1016/j.cels.2016.10.003.
80. Aufderheide, M., Knebel, J.W., and Ritter, D. (2003). An improved in vitro model for testing the pulmonary toxicity of complex mixtures such as cigarette smoke. Exp. Toxicol. Pathol. *55*, 51–57. https://doi.org/10.1078/0940-2993-00298.
81. Sassano, M.F., Davis, E.S., Keating, J.E., Zorn, B.T., Kochar, T.K., Wolfgang, M.C., Glish, G.L., and Tarran, R. (2018). Evaluation of e-liquid toxicity using an open-source high-throughput screening assay. PLoS Biol. *16*, e2003904. https://doi.org/10.1371/journal.pbio.2003904.
82. Rach, J., Budde, J., Möhle, N., and Aufderheide, M. (2014). Direct exposure at the air-liquid interface: evaluation of an in vitro approach for simulating inhalation of airborne substances. J. Appl. Toxicol. *34*, 506–515. https://doi.org/10.1002/jat.2899.
83. Thorne, D., Crooks, I., Hollings, M., Seymour, A., Meredith, C., and Gaca, M. (2016). The mutagenic assessment of an electronic-cigarette and reference cigarette smoke using the Ames assay in strains TA98 and TA100. Mutat. Res. *812*, 29–38. https://doi.org/10.1016/j.mrgentox.2016.10.005.
84. Neilson, L., Mankus, C., Thorne, D., Jackson, G., DeBay, J., and Meredith, C. (2015). Development of an in vitro cytotoxicity model for aerosol exposure using 3D reconstructed human airway tissue; application for assessment of e-cigarette aerosol. Toxicol. Vitro *29*, 1952–1962. https://doi.org/10.1016/j.tiv.2015.05.018.
85. Vojtisek-Lom, M., Dittrich, L., Pechout, M., Cervena, T., Vimrova, A., Sikorova, J., Zavodna, T., Ondracek, J., Aakko-Saksa, P., Topinka, J., and Rössner, P. (2025). Portable emissions toxicity system: evaluating the toxicity of emissions or polluted air by exposure of cell cultures at air-liquid interface in a compact field-deployable setup. Sci. Total Environ. *959*, 178010. https://doi.org/10.1016/j.scitotenv.2024.178010.
86. Juárez-Facio, A.T., Introna, M., Gustavsson, S.Å., Attergren, M., Lindwall, M., Olofsson, U., Steimer, S.S., and Elihn, K. (2025). A mobile air-liquid interface exposure system optimized for outdoor toxicity testing of aerosols. Aerosol Sci. Technol. *59*, 214–226. https://doi.org/10.1080/02786826.2024.2426487.
87. Cui, S., He, Z.Z., Zhu, Z.W., Sun, Z., Xu, Y.T., Wang, J.L., Bao, Y.Y., Ji, D.Y., Liu, S., Liu, J.T., et al. (2015). Microfluidic analysis of PM2.5-induced epithelial–mesenchymal transition in human bronchial epithelial 16HBE cells. Microfluid. Nanofluidics *19*, 263–272. https://doi.org/10.1007/s10404-014-1499-3.
88. Tilly, T.B., Ward, R.X., Luthra, J.K., Robinson, S., Eiguren-Fernandez, A., Lewis, G.S., Salisbury, R.L., Lednicky, J.A., Sabo-Attwood, T.L., Hussain, S.M., and Wu, C.Y. (2019). Condensational particle growth device for reliable cell exposure at the air–liquid interface to nanoparticles. Aerosol Sci. Technol. *53*, 1415–1428. https://doi.org/10.1080/02786826.2019.1659938.
89. Secondo, L.E., Wygal, N.J., and Lewinski, N.A. (2019). A new portable in vitro exposure cassette for aerosol sampling. J. Vis. Exp. *144*, e58916. https://doi.org/10.3791/58916.
90. Savi, M., Kalberer, M., Lang, D., Ryser, M., Fierz, M., Gaschen, A., Rička, J., and Geiser, M. (2008). A novel exposure system for the efficient and controlled deposition of aerosol particles onto cell cultures. Environ. Sci. Technol. *42*, 5667–5674. https://doi.org/10.1021/es703075q.
91. Asimakopoulou, A., Daskalos, E., Lewinski, N., Riediker, M., Papaioannou, E., and Konstandopoulos, A.G. (2013). Development of a dose-controlled multiculture cell exposure chamber for efficient delivery of airborne and engineered nanoparticles. J. Phys., Conf. Ser. *429*, 012023. https://doi.org/10.1088/1742-6596/429/1/012023.
92. Aufderheide, M., Ritter, D., Knebel, J.W., and Scherer, G. (2001). A method for in vitro analysis of the biological activity of complex mixtures such as sidestream cigarette smoke. Exp. Toxicol. Pathol. *53*, 141–152. https://doi.org/10.1078/0940-2993-00187.
93. Knebel, J.W., Ritter, D., Hoffmann, K., Lödding, H., Windt, H., Koch, W., and Aufderheide, M. (2001). Development and validation of a semiautomatic system for generation and deposition of sprays on isolated cells of the respiratory tract. Toxicol. Meth. *11*, 161–171. https://doi.org/10.1080/105172301316871581.
94. Ferro, M.P., Leclerc, L., Sleiman, M., Marchiori, B., Pourchez, J., Owens, R.M., and Ramuz, M. (2019). Effect of e cigarette emissions on tracheal cells monitored at the air-liquid interface using an organic electrochemical transistor. Adv. Biosyst. *3*, 1800249. https://doi.org/10.1002/adbi.201800249.
95. Elkaee, S., Miljevic, B., Stevanovic, S., Wang, R., Wang, H., and Ristovski, Z.D. (2025). Online monitoring of particle-bound reactive oxygen species (ROS) and oxidative potential (OP) in a changing atmosphere: A review. ACS EST. Air *2*, 2753–2775. https://doi.org/10.1021/acsestair.5c00261.
96. Carlino, A., Romano, M.P., Lionetto, M.G., Contini, D., and Guascito, M.R. (2023). An overview of the automated and on-line systems to assess the oxidative potential of particulate matter. Atmosphere *14*, 256. https://doi.org/10.3390/atmos14020256.
97. Fang, T., Verma, V., Guo, H., King, L.E., Edgerton, E.S., and Weber, R.J. (2015). A semi-automated system for quantifying the oxidative potential of ambient particles in aqueous extracts using the dithiothreitol (DTT) assay: results from the Southeastern Center for Air Pollution and Epidemiology (SCAPE). Atmos. Meas. Tech. *8*, 471–482. https://doi.org/10.5194/amt-8-471-2015.
98. Berg, K.E., Clark, K.M., Li, X., Carter, E.M., Volckens, J., and Henry, C.S. (2020). High-throughput, semi-automated dithiothreitol (DTT) assays for oxidative potential of fine particulate matter. Atmos. Environ. *222*, 117132. https://doi.org/10.1016/j.atmosenv.2019.117132.
99. Salana, S., Wang, Y., Puthussery, J.V., and Verma, V. (2021). A semi-automated instrument for cellular oxidative potential evaluation (SCOPE) of water-soluble extracts of ambient particulate matter. Atmos. Meas. Tech. *14*, 7579–7593. https://doi.org/10.5194/amt-14-7579-2021.
100. Barbero, A., Freche, G., Piard, L., Richard, L., Mhadhbi, T., Marsal, A., Houdier, S., Camman, J., Brezins, M., Golly, B., et al. (2025). Qualification of an online device for the measurement of the oxidative potential of atmospheric particulate matter. Atmos. Meas. Tech. *18*, 7085–7104. https://doi.org/10.5194/amt-18-7085-2025.
101. Wragg, F.P.H., Fuller, S.J., Freshwater, R., Green, D.C., Kelly, F.J., and Kalberer, M. (2016). An automated online instrument to quantify aerosol-bound reactive oxygen species (ROS) for ambient measurement and health-relevant aerosol studies. Atmos. Meas. Tech. *9*, 4891–4900. https://doi.org/10.5194/amt-9-4891-2016.
102. Utinger, B., Campbell, S.J., Bukowiecki, N., Barth, A., Gfeller, B., Freshwater, R., Rüegg, H.-R., and Kalberer, M. (2023). An automated online

field instrument to quantify the oxidative potential of aerosol particles via ascorbic acid oxidation. Atmos. Meas. Tech. *16*, 2641–2654. https://doi.org/10.5194/amt-16-2641-2023.

103. Bates, J.T., Fang, T., Verma, V., Zeng, L., Weber, R.J., Tolbert, P.E., Abrams, J.Y., Sarnat, S.E., Klein, M., Mulholland, J.A., and Russell, A.G. (2019). Review of acellular assays of ambient particulate matter oxidative potential: Methods and relationships with composition, sources, and health effects. Environ. Sci. Technol. *53*, 4003–4019. https://doi.org/10.1021/acs.est.8b03430.

104. Franco, R., Schoneveld, O., Georgakilas, A.G., and Panayiotidis, M.I. (2008). Oxidative stress, DNA methylation and carcinogenesis. Cancer Lett. *266*, 6–11. https://doi.org/10.1016/j.canlet.2008.02.026.

105. Sies, H., Berndt, C., and Jones, D.P. (2017). Oxidative stress. Annu. Rev. Biochem. *86*, 715–748. https://doi.org/10.1146/annurev-biochem-061516-045037.

106. Liu, B., Chen, Y., and St. Clair, D.K. (2008). ROS and p53: A versatile partnership. Free Radic. Biol. Med. *44*, 1529–1535. https://doi.org/10.1016/j.freeradbiomed.2008.01.011.

107. Giustarini, D., Dalle-Donne, I., Tsikas, D., and Rossi, R. (2009). Oxidative stress and human diseases: Origin, link, measurement, mechanisms, and biomarkers. Crit. Rev. Clin. Lab. Sci. *46*, 241–281. https://doi.org/10.3109/10408360903142326.

108. Driscoll, K.E., Carter, J.M., Hassenbein, D.G., and Howard, B. (1997). Cytokines and particle-induced inflammatory cell recruitment. Environ. Health Perspect. *105*, 1159–1164. https://doi.org/10.1289/ehp.97105s51159.

109. Thorne, P.S. (2000). Inhalation toxicology models of endotoxin- and bioaerosol-induced inflammation. Toxicology *152*, 13–23. https://doi.org/10.1016/s0300-483x(00)00287-0.

110. Pariselli, F., Sacco, M.G., Ponti, J., and Rembges, D. (2009). Effects of toluene and benzene air mixtures on human lung cells (A549). Exp. Toxicol. Pathol. *61*, 381–386. https://doi.org/10.1016/j.etp.2008.10.004.

111. Rothen-Rutishauser, B., Blank, F., Mühlfeld, C., and Gehr, P. (2008). In vitro models of the human epithelial airway barrier to study the toxic potential of particulate matter. Expert Opin. Drug Metab. Toxicol. *4*, 1075–1089. https://doi.org/10.1517/17425255.4.8.1075.

112. Campana, O., and Wlodkowic, D. (2018). Ecotoxicology goes on a chip: Embracing miniaturized bioanalysis in aquatic risk assessment. Environ. Sci. Technol. *52*, 932–946. https://doi.org/10.1021/acs.est.7b03370.

113. Moreira, A., Müller, M., Costa, P.F., and Kohl, Y. (2022). Advanced in vitro models for drug and toxicity screening: the promising role of induced pluripotent stem cells. Adv. Biol. *6*, 2101139. https://doi.org/10.1002/adbi.202101139.

114. Simpson, A., DiColandrea, T., and Przyborski, S. (2025). Assessing the impact of airborne particulate pollution on human skin utilizing a novel human skin equivalent containing MUTZ-3-derived Langerhans cells. Bioeng. Transl. Med. *10*, e10738. https://doi.org/10.1002/btm2.10738.

115. Ko, R., Hayashi, M., Tanaka, M., Okuda, T., Nishita-Hara, C., Ozaki, H., and Uchio, E. (2021). Effects of ambient particulate matter on a reconstructed human corneal epithelium model. Sci. Rep. *11*, 3417. https://doi.org/10.1038/s41598-021-82971-1.

116. Li, W., Gao, H., Cheng, M., Lv, M., Han, Y., Yu, H., Lin, W., Huang, Y., Zhang, Q., Meng, D., et al. (2026). Ultrarapid collection of high-concentration viral samples from small-volume exhaled breath for respiratory virus surveillance. Anal. Chem. *98*, 7330–7341. https://doi.org/10.1021/acs.analchem.5c06572.

117. Kenny, L.C., Aitken, R., Chalmers, C., Fabriès, J.F., Gonzalez-Fernandez, E., Kromhout, H., Lidén, G., Mark, D., Riediger, G., and Prodi, V. (1997). A collaborative european study of personal inhalable aerosol sampler performance. Ann. Occup. Hyg. *41*, 135–153. https://doi.org/10.1016/S0003-4878(96)00034-8.

118. Vincent, J.H. (2005). Health-related aerosol measurement: a review of existing sampling criteria and proposals for new ones. J. Environ. Monit. *7*, 1037–1053. https://doi.org/10.1039/b509617k.

119. Patel, P., and Aggarwal, S.G. (2022). On the techniques and standards of particulate matter sampling. J. Air Waste Manag. Assoc. *72*, 791–814. https://doi.org/10.1080/10962247.2022.2048129.

120. Duquenne, P., Marchand, G., and Duchaine, C. (2013). Measurement of endotoxins in bioaerosols at workplace: A critical review of literature and a standardization issue. Ann. Occup. Hyg. *57*, 137–172. https://doi.org/10.1093/annhyg/mes051.

121. Mbareche, H., Brisebois, E., Veillette, M., and Duchaine, C. (2017). Bioaerosol sampling and detection methods based on molecular approaches: No pain no gain. Sci. Total Environ. *599–600*, 2095–2104. https://doi.org/10.1016/j.scitotenv.2017.05.076.

122. Holstius, D.M., Pillarisetti, A., Smith, K.R., and Seto, E. (2014). Field calibrations of a low-cost aerosol sensor at a regulatory monitoring site in California. Atmos. Meas. Tech. *7*, 1121–1131. https://doi.org/10.5194/amt-7-1121-2014.

123. Wang, Y., Li, J., Jing, H., Zhang, Q., Jiang, J., and Biswas, P. (2015). Laboratory evaluation and calibration of three low-cost particle sensors for particulate matter measurement. Aerosol Sci. Technol. *49*, 1063–1077. https://doi.org/10.1080/02786826.2015.1100710.

124. Sousan, S., Koehler, K., Thomas, G., Park, J.H., Hillman, M., Halterman, A., and Peters, T.M. (2016). Inter-comparison of low-cost sensors for measuring the mass concentration of occupational aerosols. Aerosol Sci. Technol. *50*, 462–473. https://doi.org/10.1080/02786826.2016.1162901.

125. Gäbel, P., and Hertig, E. (2026). Recalibration of low-cost O3 and PM2.5 sensors: Linking practices to recent air sensor test protocols. Atmos. Meas. Tech. *19*, 1293–1321. https://doi.org/10.5194/amt-19-1293-2026.

126. Frijns, E., Verstraelen, S., Stoehr, L.C., Van Laer, J., Jacobs, A., Peters, J., Tirez, K., Boyles, M.S.P., Geppert, M., Madl, P., et al. (2017). A novel exposure system termed NAVETTA for in vitro laminar flow electrodeposition of nanoaerosol and evaluation of immune effects in human lung reporter cells. Environ. Sci. Technol. *51*, 5259–5269. https://doi.org/10.1021/acs.est.7b00493.

127. Dichtl, S., Posch, W., and Wilflingseder, D. (2024). The breathtaking world of human respiratory in vitro models: Investigating lung diseases and infections in 3D models, organoids, and lung-on-chip. Eur. J. Immunol. *54*, 2250356. https://doi.org/10.1002/eji.202250356.

128. Zhang, J., Zhang, Q., Fang, X., Guo, G., and Wang, X. (2026). Advances in skin-on-a-chip technology: Functional innovations and translational challenges. TrAC, Trends Anal. Chem. *194*, 118500. https://doi.org/10.1016/j.trac.2025.118500.

129. Trujillo, S. (2025). Evolution of ocular organ-on-chip systems for disease modelling and drug testing: Where are we now? Adv. Therapeut. *8*, e00200. https://doi.org/10.1002/adtp.202500200.

130. Sha, T., Zheng, R., Cheng, Y., Yao, Z., and Chen, Q. (2026). Integrating traditional and artificial intelligence methods in dust aerosol research: A comprehensive review. Curr. Pollut. Rep. *12*, 9. https://doi.org/10.1007/s40726-026-00402-z.

131. Kumar, K. (2026). Next-generation biosensors for detecting bioaerosols: Challenges, innovations, and applications. J. Microbiol. Methods *244*, 107489. https://doi.org/10.1016/j.mimet.2026.107489.

132. Lee, Y.O., and Sung, B. (2022). In Silico Platforms for Predictive Ecotoxicology: From machine learning to deep learning. In Chemometrics and Cheminformatics in Aquatic Toxicology, K. Roy, ed. (Wiley), pp. 453–471.

133. Patel, D., Kulwant, M., Shirin, S., Kumar, A., Ansari, M.A., and Yadav, A.K. (2022). Artificial intelligence for air quality and control systems: Status and future trends. In Modeling and Simulation of Environmental Systems, S.P. Maurya, A.K. Yadav, and R. Singh, eds. (CRC Press), pp. 133–152.

134. Wang, Y., Xu, W., Zhong, H., Chen, B., Yang, L., Wang, L., Ren, J., Duan, J., Lin, C., and Huang, R.-J. (2025). Advancing aerosol chemistry with machine learning: A short review. ACS EST. Air *2*, 2323–2341. https://doi.org/10.1021/acsestair.5c00001.

135. Rostami, A.A. (2009). Computational Modeling of Aerosol Deposition in Respiratory Tract: A Review. Inhal. Toxicol. *21*, 262–290. https://doi.org/10.1080/08958370802448987.

136. Gupta, A.D., and Gupta, T. (2023). A review on potential approach for in silico toxicity analysis of respirable fraction of ambient particulate matter. Environ. Monit. Assess. *195*, 1216. https://doi.org/10.1007/s10661-023-11859-6.

137. Majidi, C. (2019). Soft-matter engineering for soft robotics. Adv. Mater. Technol. *4*, 1800477. https://doi.org/10.1002/admt.201800477.

138. Singh, A.V., Maharjan, R.S., Kromer, C., Laux, P., Luch, A., Vats, T., Chandrasekar, V., Dakua, S.P., and Park, B.-W. (2021). Advances in smoking related in vitro inhalation toxicology: a perspective case of challenges and opportunities from progresses in lung-on-chip technologies. Chem. Res. Toxicol. *34*, 1984–2002. https://doi.org/10.1021/acs.chemrestox.1c00219.

STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Software and algorithms		
OriginPro® 2019b	OriginLab Corporation	Version 2019b, https://www.originlab.com

METHOD DETAILS

Literature selection

Published studies were screened to select representative examples of technological developments relevant to aerosol generation, monitoring and sampling, microfluidic and organ-on-a-chip systems, aerosol exposure platforms, robotic systems, and AI-assisted aerosol analysis. Research articles were collected to describe and compare individual devices and experimental platforms, whereas review articles were used to provide broader technological and methodological contexts. The literature selection was intended to support a qualitative and comparative assessment of the technological components discussed in this article and was not conducted as a systematic review or meta-analysis.

Information extraction

Operational and analytical characteristics were extracted from the original publications and summarized in Tables 1, 2, 3, and 4. For aerosol sampling approaches, extracted characteristics included sampling duration, preservation of sample integrity, automation, compatibility with downstream biological assays, major limitations, and typical applications. For lung-on-a-chip, robotic, programmable, and miniaturized exposure systems, extracted information included exposure agents and modalities, biological models, device or platform architecture, biological endpoints, operation/readout timescales, and automation or system-integration features.

Operational timescale analysis

Operational timescale values, summarized in Tables 1, 2, 3, and 4, were extracted for the system performance comparison presented in Figure 5. Studies without relevant timescale information were excluded. Reported values were converted to the unit of hours where necessary and grouped according to the device categories shown in Figure 5.

QUANTIFICATION AND STATISTICAL ANALYSIS

No inferential statistical analysis or meta-analysis was performed. Descriptive statistics were used to summarize the operational timescales presented in Figure 5. For each device category, the median was used as the measure of central tendency and the minimum-to-maximum range was used to represent dispersion. Calculations and visualization were conducted using OriginPro 2019b (OriginLab Corp., Northampton, MA) software.