Airborne particulate matter pollution in urban China: a chemical mixture perspective from sources to impacts

Ling Jin¹, Xiaosan Luo², Pingqing Fu³ and Xiangdong Li¹,∗

ABSTRACT

Rapid urban and industrial development has resulted in severe air-pollution problems in developing countries such as China, especially in highly industrialized and populous urban clusters. Dissecting the complex mixtures of airborne particulate matter (PM) has been a key scientific focus in the last two decades, leading to significant advances in understanding physicochemical compositions for comprehensive source apportionment. However, identifying causative components with an attributable link to population-based health outcomes remains a huge challenge. The microbiome, an integral dimension of the PM mixture, is an unexplored frontier in terms of identities and functions in atmospheric processes and human health. In this review, we identify the major gaps in addressing these issues, and recommend a holistic framework for evaluating the sources, processes and impacts of atmospheric PM pollution. Such an approach and the knowledge generated will facilitate the formulation of regulatory measures to control PM pollution in China and elsewhere.

Keywords: particle size, source apportionment, molecular tracer, chemical speciation, airborne microbiome, bioavailability, mixture toxicity, cohort study

INTRODUCTION

Due to China’s rapid industrialization and urbanization, air-pollution problems of a magnitude comparable to those that took a century to develop in many developed countries have emerged in China over a relatively short span of three decades [1]. Because of China’s distinct development trajectory, the country’s air-pollution problems are unique and complex. The situation is further complicated by global climate change, resulting in frequent episodes of air pollution driven by weather events [2]. Episodes of haze or smog have occurred frequently in China in recent years on a national scale, especially in the most developed and highly populated urban clusters [3]. These pollution events are long-lasting and exhibit a high intensity of pollution and a broad geographical coverage, thus jeopardizing air quality [4], regional and global climates [5] and human health [6].

In response to the increasingly extreme episodes of haze, for example, in 2013, the Chinese government released the ‘Atmospheric Pollution Prevention and Control Action Plan’ (http://www.gov.cn/zwgk/2013–09/12/content_2486773.htm in Chinese), in which it announced its aim of achieving a reduction in PM₂.₅ (particulate matter with an aerodynamic diameter of less than or equal to 2.5 μm; \(D_p \leq 2.5 \mu m\)) levels of up to 25% from the 2012 levels by 2017. To this end, scientific issues of high regulatory relevance regarding what to control to protect human health and where to control the sources of emission need to be addressed (Fig. 1). These issues center on the key characteristics of PM as complex physicochemical and biological mixtures that evolve with regionally specific spatial features and temporal dynamics [7]. To effectively reduce air pollution, it is imperative to dissect the complex PM compositions, on the basis of which the quantitative contribution of natural and/or anthropogenic activities can be determined to devise targets and control measures. For effective public health interventions, it is equally vital to
address the health consequences of complex PM mixtures and to delineate the quantitative roles of various components in PM that are the major causative agents.

In view of these critical research needs, we have provided a synthesis of the current know-how on several interlinked aspects of the science surrounding PM mixtures, and on the associated methodological and technological advances, with a particular reference to China. With such a vision, we have further attempted to identify major gaps in knowledge and methodology regarding the sources, processes and impacts of PM mixtures, so as to be able to make recommendations on a holistic assessment framework and contribute to a comprehensive understanding of the subject.

**PM AS HETEROGENEOUS MIXTURES**

PM is a highly condensed mixture comprising a myriad of components in varying physicochemical states, which define the heterogeneous nature of air PM [8]. This heterogeneity is intrinsically embodied in the size segregation, chemical speciation and microbiological diversity that contribute to the compositional complexity of the atmospheric particles. Interactions between abiotic and biotic factors would further modify the characteristics of PM compositions. Therefore, it is important to understand these factors that govern the dynamically heterogeneous PM compositions.

**Particle sizes**

The size distribution characteristics of urban PM are shaped by size-specific chemical and biological components from primary emissions or by secondary formation processes depending on prevailing meteorology (Fig. 2). These characteristics determine the fate of differently sized particles in human respiratory tracts and the subsequent effects on human health. Of relevance to human health are ‘inhalable particles’ with an aerodynamic diameter of less than or equal to 10 μm (PM$_{10}$; $D_p \leq 10$ μm). According to their type of source and mode of generation, PM$_{10}$ are further stratified into different size fractions, including coarse (PM$_{2.5-10}$; 2.5 < $D_p$ < 10 μm), fine (PM$_{2.5}$; $D_p \leq 2.5$ μm) and ultrafine (PM$_{0.1}$; $D_p \leq 0.1$ μm) particles [9]. As the main contributors to urban ambient PM loads, anthropogenic particles may be further transformed with naturally occurring particles that have undergone long-range transport from a range of natural sources, such as volcanoes, sea spray, grassland fires, desert dust and biological emissions [10].

Chemical and microbial components constitute different size-specific fractions of airborne PM. Crustal elements (e.g. Al and Fe) are generally accumulated in coarse particle fractions, whereas those of anthropogenic origin (e.g. As, Cd, Cu, Ni, Pb, Se, Zn and V) are more associated with fine particles [11,12]. Particle-bound organic compounds are featured by modal peak distribution in fine and coarse particle fractions [13,14]. Compounds
Figure 2. Size distribution of atmospheric PMs and associated components with implications for emission sources and inhalation exposure.

with lower molecular weight are more easily redistributed amongst coarse particles by rapid volatilization and condensation, and those with higher molecular weight and hence lower vapor pressure tend to be more enriched in fine fractions than in coarse fractions [15–17]. Coarse and fine particles dominate the dry and wet deposition fluxes of these chemicals, respectively [13]. The typical size of airborne bacteria is approximately 1 μm. By contrast, the size of the particles associated with such bacteria is much larger, at about 4 μm in the count median diameter at continental sites and ~2 μm at coastal sites [18]. Recent studies conducted in China [19,20] have demonstrated that the size distributions of microorganisms during non-haze days are dominated by the coarse particle fraction, but shifts toward fine particle fractions have been shown to occur during haze days. In part, this reflects the fact that bacterial cells are often associated with larger particles (e.g. soil or leaf fragments) and are sometimes found as cell clumps [18].

Particle size distribution is one of the critical parameters used in assessing the health risks posed by inhaled particles [21,22]. The sized particles and associated components undergo an aerodynamically quantitative fractionation upon inhalation into the human respiratory tract (Fig. 2). In the model put forward by the International Commission on Radiological Protection, size-specific deposition efficiencies have been established for different regions of the human respiratory tract [23]. In general, smaller particles can penetrate into deeper regions of the lung and pose a greater risk to human health than larger particles. For instance, PM0.1, which makes up only 1–2% of the total mass of particles, contributes 10–30% of the polycyclic aromatic hydrocarbons (PAHs) deposited in the alveolar region of the lung [24]. The deposition efficiency of sized particles in the airway in part determines the bioavailability of particle-borne components, thus reconstructing the effective mixture composition in exposed subjects from the original ambient PM sample. For toxicological assessments, it is therefore essential to establish the de facto dosimetry of particles and associated components in lieu of total concentration-based measurements. The role of particle sizes in toxic and health effects will be further discussed in the ‘Role of particle sizes and chemical compositions’ section below.

Chemical speciation

Considerable efforts have been devoted to elucidating the elemental and molecular identities and compositions of PM, which offer traceable chemical fingerprints for source origins and various toxicologically active mixture combinations. A suite of offline, on-site to online instrumental techniques have been developed for structural elucidation of PM compositions on the elemental and molecular levels (Table 1) [25,26]. This is particularly the case for organic aerosols ranging from low-molecular-weight (LMW) species, such as C1 and C2 compounds, to high-molecular-weight (HMW) compounds (e.g. humic-like substances (HULIS) and proteins) with a few to tens of thousands of Daltons [27–29].

Organic aerosols (OA), which are essential components in the atmosphere [30], make up a large fraction of mass (20–90%) of atmospheric fine particles in urban and industrial sites on a global scale [31]. Generally, organic particles consist of primary organic aerosols (POA) and secondary organic aerosols (SOA). POA are directly emitted from sources, such as higher plants, soil dust, biomass and the burning of fossil fuels [30,32,33]. SOA are formed by the oxidation of gas-phase species in situ or through long-range transport in the atmosphere [34–37] and account for a large fraction of the OA burden [38,39]. With regard to the recent 2013 haze episode in China, the event was primarily driven by the formation of secondary aerosols, which
contributed 30–77% of the mass of the PM$_{2.5}$. The contribution from secondary inorganic aerosols (SIA) to the mass of the PM$_{2.5}$ was found to be similar [40]. At the chemical species level, the compositions of inorganic aerosols have been relatively well characterized, with the dominant mass contribution coming from sulfate and nitrate ions, and a minor contribution from ammonium, elemental carbon, chloride and metal ions [40]. Within OA, however, less than 30% of organic carbon has been identified at a molecular level [41,42]. The resolved fractions are characterized by the abundant presence of dicarboxylic acids, $n$-alkanes, fatty acids, sugars and phthalates. In contrast, fatty alcohols, polyols/polyacids, lignin and resin products, sterols, PAHs, hopanes and others are relatively minor components. It should be noted that the molecular compositions of atmospheric aerosols vary significantly among different geographical locations [30].

The chemical forms and composition of PM are strongly linked to the sources of emission. For trace metals, as with other solid environmental samples, a conventional way to investigate their chemical speciation in PM is to sequentially extract the different species as the adsorbed—the exchangeable, carbonate phase, the reducible phase, the oxidizable phase and the residual fraction [43–46]. The first three of those species, especially the adsorbed-exchangeable and carbonate phase, are considered to be more mobile in the environment and more bioavailable to organisms, and thus to pose greater health risks to human health. It has been observed in China that higher proportions of Zn, As, Cu, Cd and Pb are commonly present in the potentially mobile phases [44–46]. Advances in non-destructive techniques, such as synchrotron-based X-ray spectroscopy (XAS), have enabled the in situ characterization of the solid-phase speciation (e.g. the oxidation state and coordination chemistry) of metallic elements in environmental samples [47]. These tools have recently gained acceptance for metal speciation in air PM samples [48–51]. Extended X-ray absorption fine structure (EXAFS), for example, revealed that Pb-humate predominated the speciation of Pb in recent urban ambient airborne PM in El Paso, Texas, USA, and established the surrounding soil with legacy leaded gasoline as the dominant source [51]. X-ray absorption near-edge fine structure spectra (XANES), for example, demonstrated that Fe existed mainly in the form of hematite ($\alpha$-Fe$_2$O$_3$) and aluminosilicate minerals in the subway of Shanghai, China, and magnetite (Fe$_3$O$_4$) was found only in the aboveground metro line [50]. Such insights into the speciation of metals in airborne PM would assist future design of studies on their mixture toxicity and health impacts, as current efforts are solely based on total elemental concentrations.

Out of the broad spectrum of chemicals identified in PM mixtures, certain chemicals serve as useful indicators in that they correspond to specific types of sources of emissions (Table 2). A large fraction of OA is water-soluble organic matter (WSOM) including LMW mono- (e.g. formic and acetic acids), di-carboxylic (e.g. oxalic and succinic acids), poly-carboxylic (e.g. citric and tri-carboxylic acids) and hydroxy-acids (e.g. glycolic, glyceric and malic acids) [27,41,52–55]. The characteristic of water solubility would make these chemical components highly bioavailable upon inhalation, whereupon they can be extracted and dissolved in human lung fluid, hence increasing effective exposure doses. While the bioavailability/bioaccessibility of trace elements has been extensively studied, particularly by using a predictive methodology, such as artificial lung fluid [56], similar approaches have yet to be used to explore the largely untouched area of the bioavailability of organic fractions upon inhalation. Toxicity profiling and chemical identification are warranted to understand the toxicological relevance of the bioavailable chemical mixtures and the relative contribution of individual components thereof.

**Microbial composition and chemical–biological interplay**

In contrast to the extensive physicochemical characterization of PM, there is a surprisingly limited understanding of the inhalable biological particles associated with PM, including bacteria, fungi, viruses, pollens and cell debris. Materials of biological origin have been estimated to contribute as much as 25% to atmospheric aerosol, and bioaerosols constitute about 5–10% of atmospheric PM [107]. Thus, biological particles may have an important role to play in atmospheric events and have a significant impact on human health [108].

The abundance of airborne bacteria has been measured at $10^4$–$10^8$ cells per cubic meter, depending on the environment [18], with a diversity of taxa resembling the soil assemblage [109] and the bacteria consistently identified as the most abundant prokaryotic microorganisms in urban PM [109,110]. Owing to recent advances in airborne metagenomics [111–113], the deep sequencing of airborne DNA has made it possible to reach the level of species. This has been of particular benefit to the identification of respiratory pathogens (e.g. *Streptococcus pneumoniae, Aspergillus fumigatus* and human adenovirus C) in PM$_{2.5}$ and PM$_{10}$ samples from...
Table 1. Summary of current instrumental techniques for offline and online analyses of PM compositions.

| Type of instrument | Analytical targets/application | References |
|--------------------|--------------------------------|------------|
| **Offline analyses** |                                |            |
| ICP–AES/mass spectrometer (ICP–MS) | Trace and major elements | [57,58] |
| Ion chromatography | Water-soluble inorganic ions (e.g. $\text{SO}_4^{2-}$, $\text{NO}_3^-$, $\text{NH}_4^+$, $\text{Na}^+$ and $\text{K}^+$); low-molecular-weight (LMW) organic acids; sugar alcohols | [59–61] |
| Gas chromatograph–mass spectrometer (GC–MS) | POA and SOA tracers (e.g. $n$-alkanes, fatty acids, fatty alcohols, sugars and sugar alcohols, lignin and resin acids, terpenoid biomarkers, sterols, aromatic acids, plasticizers, hopanes, polycyclic aromatic hydrocarbons, amino acids and biogenic SOA tracers) | [41,62–65] |
| Gas chromatograph–flame ionization detector (GC–FID) | Typical method to measure dicarboxylic acids, oxocarboxylic acids and dicarbonyls such as glyoxal in atmospheric aerosols, with the predominance of oxalic acid ($\text{C}_2$) | [53,55,66–69] |
| Comprehensive two-dimensional gas chromatography (GC×GC) | Separation of thousands of organic species, including alkanes, alkenes, PAHs and OH-PAHs | [70–73] |
| Liquid chromatograph-mass spectrometer (LC–MS), MS/MS, Quadrupole time-of-flight mass spectrometer (Q-TOF MS) | Determination of organic acids and organosulfates | [74–76] |
| Fourier transform ion cyclotron (FTICR), Orbitrap | Characterization of humic-like substances (HULIS) and brown carbon | [77–81] |
| Nuclear magnetic resonance spectroscopy; fluorescence spectroscopy; UV-vis spectroscopy | Elucidation of the structure of HULIS or water-soluble organic carbon (WSOC) | [82–86] |
| Aerodyne aerosol mass spectrometer | Size-resolved compositions of non-refractory inorganic and organic components in the 50–1000-nm size range | [69,87–89] |
| **Online analyses** |                                |            |
| Metrohm Monitor for AerSol and GAses in ambient air (MARGA) instrument; particle-into-liquid sampler (PILS) | Time-resolved elemental composition of individual ions at the same nominal mass, enabling calculation of the elemental ratios (O/C, H/C, N/C) of the organic aerosols | [90,91] |
| Ultraviolet aerodynamic particle sizer, wideband integrated bioaerosol sensor (WIBS) | Time-resolved gases and aerosol inorganic species | [90,92–96] |
| | Bioaerosol particles (e.g. bacteria, fungi, pollens) | [97–99] |

severe wintertime haze episodes in Beijing [110]. In spite of unfavorable temperatures, the microorganisms still appear to have become more abundant as PM particle concentrations increased. The survival of microbes may have been favored by the high relative humidity that concurrently promotes particle growth through water uptake and facilitating aqueous redox reactions (e.g. oxidation of sulfur dioxide to sulfate) [114]. The summertime highs and wintertime lows in the content of airborne microbial DNA in the subtropical metropolis of Hong Kong clearly demonstrate that temperature is an important factor in controlling the microbial life in air [115].

Chemical or physical processes are believed to account for the transformation of aerosols, with little consideration for microbiologically mediated processes. Indirect evidence is emerging that airborne microorganisms may play an active role in atmospheric events [108,116]. Recently, a large portion of the bacteria found in cloud water demonstrated metabolic activity using an assay of tetrazolium dye uptake [117]. High concentrations of inorganic and dissolved organic nitrogen have been found in cloud water containing nitrifying bacteria, suggesting that the bacteria in cloud water play a role in the cycling of organic nitrogen in the atmosphere [117]. Airborne microbes existing in the boundary layer have demonstrated an ability to efficiently transform and utilize an important class of organic aerosols—dicarboxylic acids as nutrients [118,119]. Through the biodegradation of organic matter in the atmosphere, airborne microorganisms
**Table 2. Summary of organic molecular tracers for tracing emission sources.**

| Source type                | Representative tracer compounds | Source description                      | Observations and implications in China                                                                 | Reference |
|----------------------------|---------------------------------|------------------------------------------|--------------------------------------------------------------------------------------------------------|-----------|
| Burning of biomass         | Levoglucosan                    | Pyrolysis of cellulose                   | The most abundant compound (88–1210 ng/m$^3$) in the Mt. Tai aerosols collected in early June, indicating active burning of wheat straw in the North China Plain | [100]     |
| Vanillic acid, syringic acid | Lignin derivatives from burning wood | Winter (8.4–333 ng/m$^3$) > Summer (1.3–53 ng/m$^3$) across 14 Chinese cities, indicative of higher biomass-burning activity in cold seasons | [62]      |
| Dehydroabietic acid        | Conifer resin products           |                                          | A strong correlation between levoglucosan and plant wax n-alkanes, suggesting the burning of biomass as a significant source of aliphatic lipids | [100]     |
| HMW-alkanes                | Epicuticular waxes and lipids    |                                          | Concentrations in urban aerosols: India > China > Japan > New Zealand                                 | [41,62,101,102] |
| Fossil fuel combustion     | LMW-alkanes, hopanoid hydrocarbons (hopanes), PAHs | Petroleum and coal combustion            | High levels of phthalates ubiquitously occurring in Chinese megacities; summer > winter supported by the ambient-temperature dependence of phthalates | [62,100] |
| Plastic emissions          | Phthalates                      | Plasticizers in synthetic polymers or softeners in polyvinylchlorides | Arabitol and mannitol are specific tracers for fungal spores; elevated fungal tracers (arabitol and mannitol) in atmospheric aerosols due to the dissemination of spores from the burning of biomass in Chengdu | [103,104] |
| Triphenylbenzene Bisphenol A | Plasticizer                     | Production of epoxy resins and polycarbonate plastics | Low- to mid-level contributions of biogenic SOC to OC in urban China compared with other geographical locations as influenced by local vegetation cover, meteorological conditions, the oxidative capacity of the troposphere, and so on | [42,105,106] |

could play a role in transforming PM-bound chemical components. It should, however, be noted that these studies are culture-dependent, and therefore may not truly reflect the in situ environmental realm. Fully mapping the PM-associated microbiome community and their function in situ is a step that would need to be taken before a mechanistic understanding of the involvement of microbes in interactions with other PM components and their joint effects on human health can be achieved. Despite the challenges, the current limited understanding of airborne microbiome calls for future research to be conducted on this overlooked biological dimension of complex PM mixtures.
SPATIOTEMPORAL VARIATIONS AND SOURCE APPORTIONMENT

Spatiotemporal patterns

As a vast country, China exhibits huge spatial disparities in PM pollution—a situation that is influenced by both anthropogenic/natural emissions and meteorological conditions in different regions. The levels of PM$_{2.5}$ that were observed were generally higher in cities of the north than in cities of the southeast, and highest in winter and lowest in summer [120]. The highest annual average concentration was observed in the Beijing–Tianjin–Hebei (BTH) region, which includes the two megacities of Beijing and Tianjin and Hebei Province, which has the highest density of coal-based industries in China [121]. With fewer coal-based industries and more favorable weather conditions for the dispersion of pollutants, PM$_{2.5}$ concentrations in the Pearl River Delta (PRD) region in the south are generally lower than those in the two other largest city clusters in China, namely the BTH and Yangtze River Delta (YRD) regions. The nationwide distribution suggests that the degree of urbanization has had a tremendous impact on PM$_{2.5}$ concentrations [122].

With regard to seasonal patterns, the wintertime maximum occurs as a result of intense fossil-fuel combustion and the burning of biomass for domestic heating as well as because of the presence of stagnant weather unfavorable for the dispersion of pollutants; with the reduction of these anthropogenic emissions, PM$_{2.5}$ levels are much lower in summer [123]. However, there is spatial variability to this seasonal trend because of specific environmental characteristics and human activities in some regions. In western China, the most polluted season is spring, not winter, because of the increased contribution of dust particles in this desert-like region [124,125]. The abundant coarse particle fraction (PM$_{3.5-10}$) in PM$_{10}$ and the high mineral content (e.g., Si and Al) of the particles [126] suggests a significant contribution from local fugitive dust emissions and the regional transport of dust. In eastern China, which is the country’s agricultural heartland, relatively high PM$_{2.5}$ levels are also found in autumn due to the enhanced open burning of biomass during the agricultural harvest. Such intense burning events lead to higher concentrations of PM$_{2.5}$ and of chemical tracers related to biomass burning in, for example, the cities of the PRD and northeast China in autumn than in spring—even higher than in winter in a few cases [127]. It is also noted that biomass burning in the wheat-harvest season in North China deteriorates the regional air quality significantly [100,128]. Overall, the spatially and seasonally varied sources of emissions shape the chemical profiles characteristic of different regions, with strong implications for variable toxicological consequences and/or health effects upon inhalation.

Zooming in from the regional scale, intra-city variability is also an important aspect that infers that sources of emissions are specific to functional zones according to the designated uses for land within a city (e.g., residential, commercial, industrial, etc.). Because of the lack of such fine-scale intra-urban studies, a generalized mechanistic consensus has yet to be reached on how PM abundance and composition profiles vary with the functional categorizations of different zones within a city. Most existing studies focus on comparisons of urban and rural areas. A range of chemical species, such as major and trace elements, sulfate, nitrate, ammonium, and organic and elemental carbon, have been found to be higher in urban than in rural sites by a factor of 1.5–2.5 [129]. A typical exception is PAHs [130], which showed similar levels in rural sites with the widespread combustion of biomass and domestic coal, as in urban sites with sources from industry and traffic.

On the global scale, the population-weighted mean of PM$_{2.5}$ in Chinese cities (61 μg/m$^3$) [3] is about three times higher than the global population-weighted mean (20 μg/m$^3$) [131]. Compared with global cities, the levels of atmospheric heavy metals in China are much higher than those of developed countries, such as the USA and the countries of the European Union, and slightly lower than those of cities in developing countries like India and Pakistan. Cr, As and Cd pollutants are highly elevated compared with the guideline values of the World Health Organization (WHO) [132]. The concentrations of total identified organic compounds detected in China, particularly in megacities (e.g., Chongqing and Xi’an) where industrialization/urbanization is actively occurring, are several orders of magnitude higher than those reported from developed countries [62]. In comparison with the global pattern, the intra- and inter-urban and regional spatiotemporal variability of PM loadings and compositions in China implies site-specific human exposure to the evolving PM mixtures in the long term. Therefore, there is a pressing need to capture these fine-scale spatial patterns by looking beyond regulatory monitoring data to better categorize community-level exposure and the related health risks.

Source apportionment

Depending on their origin, aerosols may come from a wide range of natural or anthropogenic sources [9]. It is important to identify and quantify the different sources of PMs using source apportionment (SA) techniques if policy makers are to develop effective...
control strategies. There are three major groups of SA methods [133]: (1) methods based on the evaluation of monitoring data, the main advantage of which is the simplicity and the consequent low impact of mathematical artifacts due to the treatment of data; (2) methods based on emission inventories and/or dispersion models to simulate the emission, formation, transport and deposition of aerosols, the significant advantage of which is that they may be used in scenario studies to evaluate the impact of emission abatement strategies on the anthropogenic contribution to ambient PM concentrations; and (3) methods based on the statistical evaluation of PM chemical data acquired at receptor sites (e.g. receptor-oriented models, RMs), the fundamental principle of which is that mass and species conservation can be assumed and that a mass balance analysis can be used to identify and apportion sources of airborne PM. For instance, different approaches used in Europe [134] include: (1) chemical transport models based on pollutant emission rates and meteorological data; and (2) RMs based on statistical analyses of pollutant concentrations measured at a sampling site (receptor site) to infer the types of sources and estimate their contributions to the measured site concentrations. The commonly used RMs include explorative methods (an incremental concentrations approach, and enrichment factor and tracer-based methods), the Chemical Mass Balance model (CMB) and related methods (Non-Negative Least Squares and Partial Least Squares Regression), principal component analysis (PCA) and related methods (UNMIX model), factor analysis (FA; Positive Matrix Factorization, PMF) and hybrid methods (Constrained Physical Receptor Model, COPREM; extended FA models). The CMB, PMF and UNMIX models are also gaining popularity in China [135]. These models [136] use the chemical measurement of elements (divided into two groups—crustal: Na, Mg, Al, K, Ca, Fe and Si; and anthropogenic: S, Zn, Ni, Cu, Mn, Sr, Ag, Ba, Pb, V, Cr and Ti), water-soluble ions (Cl\(^{-}\), NO\(_3\)\(^{-}\), SO\(_4^{2-}\), NH\(_4^+\), Na\(^+\), K\(^+\) and Ca\(^{2+}\)) and carbon (OC and EC or BC), and organic molecular tracers (natural and anthropogenic).

Through these SA methods, four main types of sources were identified for PMs in Europe [133]: a vehicular source (traced by carbon/Fe/Ba/Zn/Cu), a crustal source (Al/Si/Ca/Fe), a sea-salt source (Na/Cl/Mg) and a mixed industrial/fuel–oil combustion (V/Ni/SO\(_4^{2-}\)) and a secondary aerosol (SO\(_4^{2-}/\)NO\(_3\)\(^{-}/\)NH\(_4^+\)) source. Based on accurate PM\(_{2.5}\) sampling, a chemical analysis and SA models, the major primary sources of PM\(_{2.5}\) in China were identified to be coal combustion, biomass burning, motor vehicle emissions and industrial sources [123,137–140]. Generally, primary particulate emissions from individual sources contribute a minor portion of the PM\(_{2.5}\) [141] with the exception of northwest China, where dust-related emissions play a significant role [142]. The extensive use of coal in northern and western China for heating residences during winter has resulted in a higher contribution from the burning of coal in the BTH (northern China) and Guanzhong (Central Shaanxi Plain) city clusters than in the YRD (eastern China) and PRD (southern China) city clusters [143,144]. The contribution from the burning of biomass is notably higher in the PRD, Guanzhong and Chengdu–Chongqing regions compared to that in the BTH and YRD regions [125,144,145].

Sources of SIA are well defined in urban areas. The burning of coal is a primary source of SO\(_2\), which is subsequently oxidized to sulfate, while vehicle exhaust and power plants emit NO\(_x\), which is transformed to nitrate [146]. Sources of secondary organic aerosol are relatively complicated, depending on the anthropogenic activities characteristic of different urban clusters and biogenic emissions of volatile organic compounds, such as isoprene and monoterpenes. For example, the high traffic flow and/or widespread use of coal for domestic heating/cooking in the BTH and YRD regions have resulted in a high contribution from fossil-derived SOA to the total OA mass [40]. In contrast, the fraction of non-fossil SOA accounted for more of the OA mass in urban clusters, such as the PRD and Guanzhong regions [40], due to enhanced biomass-burning activities, as discussed in the ‘Spatiotemporal patterns’ section above.

**COMBINED EFFECTS OF PM MIXTURES**

**Mechanistic pathways of PM-induced toxicity**

Evidence of causality has been explored in exposed subjects (e.g. humans, animals or cells) to elucidate manner by which the toxic mechanisms of PM lead to diseases and health incidents. Several major mechanisms for PM-induced cardiopulmonary effects have been proposed, such as (1) the induction of pulmonary oxidative stress and inflammation with an indirect systemic ‘spill-over’ of inflammatory mediators; (2) the translocation of particles into the systemic circulation, where they may exert direct effects; and (3) the generation of imbalances of the autonomic nervous system [21,22,147]. These mechanisms are not likely to be mutually independent, and may have interactions leading to complementary effects, but oxidative stress through the generation of reactive oxygen species (ROS) and inflammatory...
Role of particle sizes and chemical compositions

Reiterating from the section on ‘Particle sizes’ above, there is compelling evidence of a strong association between the size of PM and their potential to cause health problems \[165,166\]. PM\(_{2.5}\), commonly regarded as ‘respirable’, can penetrate deeply into the respiratory system, often overwhelming the body’s intrinsic clearance mechanisms, and could quite possibly be retained and absorbed. PM\(_{10}\), referred to as ultrafine fractions (UFPs), has recently become a focus of research. It is suggested that these particles pose a great risk to health due to their high concentration in urban environments and strong ability to penetrate deep into the alveolar region of the lung and subsequently to enter the blood. There appears to be some agreement between experimental and epidemiological studies on the issue of PM size \[167,168\]. Epidemiological studies have most often pointed to a stronger exposure–response relationship in terms of mortality and morbidity outcomes with respect to PM\(_{2.5}\) than PM\(_{10}\). In general, the smaller the size of the PM, the higher the toxicity from mechanisms of oxidative stress and inflammation. For example, PM\(_{10}\) triggers lung inflammation and extrapulmonary adverse events in mice \[164\], while PM\(_{1}\) induces adverse effects on the lungs and cardiovascular system of mice \[169\]. The finest fraction (<0.45 µm) of urban air particles exhibits the highest mass, the highest active surface, the highest amount of associated PAHs, and also the highest direct and indirect genotoxic potential \[170\]. Recent toxicological studies suggest that UFPs may elicit a higher adverse response per unit of mass than PM\(_{2.5}\) and PM\(_{3.5-10}\) \[171\]. However, there have also been studies showing that PM\(_{2.5-10}\) is more strongly associated than PM\(_{2.5}\) with respiratory hospital admissions \[172\]. PMs not only exist in different sizes, but the chemical composition of these size fractions can also significantly influence health outcomes. The direct generation of oxidants by air PMs is usually attributed to organic and metal components \[173,174\]. Organic compounds (e.g. PAHs) generate oxidative stress through the redox cycling of quinone-based radicals, by complexing metals resulting in electron transport, or by depleting antioxidants via reactions between compounds containing quinones and thiol \[150\]. Metals directly support the transport of electrons to generate oxidants and also diminish levels of antioxidants \[175\]. The existing literature is unclear about the extent to which the toxicological properties of PM are attributed to particle sizes or to the chemical components associated with particular size fractions. Therefore, it is essential to quantitatively dissect the physical and chemical dimensions of the particle-
induced effects. A recent study [176] describes the dispersion of PM$_{2.5}$ in artificial lung fluid, which represents the toxicokinetic processes that occur prior to entry into cells. Proteins in the lung fluid facilitate the dispersion of particles by reducing the hydrodynamic diameter and sedimentation rate, while phospholipids act in the opposite manner. The dispersed PM$_{2.5}$ further sorbs onto the model cell membrane that contains positively-charged lipids but not neutrally and negatively charged lipids, suggesting the necessity for cationic sites for PM adhesion [177,178]. The subsequent disruption of the cell membrane appears to be a joint action of electrostatic forces and hydrogen bonds between oxygen-containing groups on the surface of PM and lipid phosphate groups [176–178]. These early toxicokinetic processes prior to the cellular internalization of particles and the subsequent apical events highlight the importance of major biomolecules in lung fluid and functional groups on the surface of PM to the development of PM pulmonary toxicity. Such mechanistic information can be incorporated in future models to establish the dosimetry of PM in vitro or in vivo exposed media to accurately decipher exposure–response relationships. This will improve our understanding of how the physical characteristics of particles, as differentiated from components associated with particles, contribute to the overall toxicity triggered by PM. Further broad-spectrum analyses of natural and anthropogenic chemicals can help to delineate the quantitative role of various components in the development of toxicity. In addition to various types of natural and anthropogenic chemicals, mixture toxicity modeling [179] using the concept of concentration addition/independent action and bio-analytical equivalent concentrations can be employed to quantify the fractional contribution of chemical and microbial components to PM-induced toxicity. Furthermore, PCA can also be applied to statistically rank the major toxicity-driving components in PM [180].

MAJOR GAPS AND FUTURE RESEARCH DIRECTIONS

Toxicological assessments under environmentally realistic scenarios

One of the current limitations in particle characterizations and exposure studies is associated with filter-based sampling strategies. Throughout the current literature, the most commonly used in vitro method of determining PM exposure involves collecting PM on filters, followed by their re-suspension in a liquid medium and subsequent addition onto a cell culture. This method has clear limitations relating to the intensity of exposure, and may modify the nature and composition of the particles. For example, the sampling process and post-treatment of filter-collected diesel exhaust PM may significantly modify the PM and likely lead to an underestimation of their toxicity (i.e. inflammatory response) in comparison with direct deposition/contact with PM from air to exposure media [160]. Recently, alternative sampling methods have been developed for collecting PM for toxicological investigations, such as the direct deposition of PM$_{0.02-10}$ onto cultured cells by the electrostatic aerosol in vitro exposure system (EAVES) [160,181]. This is accomplished by applying a charge to the PM in a flowing air stream, and then using a repelling electric field above the cells to rapidly, but gently, deposit the PM directly onto the air–liquid interface of the cells. EAVES can be used to expose cells directly to particles without prior collection in another sampling medium.

Another typical sampling procedure for size-fractionated PMs is the versatile aerosol concentration enrichment system (VACES). In VACES, a super-saturation/condensation system is used to rapidly enlarge particles to super-micrometer droplets, which are concentrated by means of a dichotomous virtual impactor. The particles are then obtained by a liquid impinge as liquid (water) suspension or on filters [182,183], or collected by an efficient electrostatic precipitator (ESP) on a Petri dish containing cell cultures or on any other desirable substrate suitable for particle collection and analysis [184,185]. VACES is capable of concentrating ambient ultrafine (PM$_{0.15}$), accumulation (PM$_{2.5}$), and coarse particles (PM$_{2.5-10}$) by several fold. This makes it possible to collect samples at short time intervals, which favors cell viability and the characterization of exposure. The in vitro electrostatic collector has the potential to perform hourly, direct, solvent-free collections of PM for toxicological studies. Such field PM exposure systems can be further coupled to the online instruments reviewed in the ‘Chemical speciation’ section above for real-time characterizations of chemical components associated with PM that may account for toxicity, thus providing an integrative toxicity-based metric tool for investigating ambient PM pollution in urban areas.

Linking toxicological and epidemiological data to delineate the multi-factorial effect of PM mixtures

Despite a growing body of literature linking toxic and/or health effects to certain components, a full
picture of the relative quantitative contribution of various components remains elusive, in contrast to the more comprehensive dissection of source contributions. As emphasized above, the identification of key toxic causative components would shed further light on how to control the sources of PM, by taking into consideration a vision oriented towards human health that goes beyond haze-formation mechanisms. The current inconclusive understanding of the subject is very much due to current methodological constraints that have resulted in incoherent extrapolations linking in vitro, in vivo and epidemiological studies.

While in vitro cell tests offer a rapid tool to screen the molecular and cellular effects of PM exposure, they only provide a snapshot of one-off short-term effects (e.g. 24-h exposure to a PM sample), and do not capture the cumulative effects of long-term exposure. Thus, there is clearly a missing link to the environmental realm of human exposure scenarios, especially considering the repeated cycles of air-pollution episode periods and non-episode periods over the seasonal and annual cycle, for example, in large urban regions of China. For in vivo animal models, the mechanistic grounds for making interspecies extrapolations to human health are still lacking, and there are ethical, budgetary and logistical limitations to conducting large-scale in situ investigations on exposure. Epidemiological associations require a more quantitative approach to eliminating confounding factors (e.g. different lifestyles constituting other sources of exposure) and mechanism-based experimental evidence to establish principal causal links. Therefore, there is a pressing need for an integrated approach to close these gaps. Here, we propose a methodological framework for a holistic assessment of PM-associated health effects and causative components (Fig. 3).

To overcome the current limitations of in vitro tests, it would be desirable to devise a system of exposure that offers the various advantages of in vitro systems while also allowing for in vivo-like evaluations of the cumulative effects arising from long-term and intermittent exposure to various air pollutants [186]. Using ‘omics’ approaches, the in vitro exposure can generate system-level insights into the dynamics of molecular and cellular responses to chronic exposure [187,188]. Upon calibrating the in vivo animal model, useful biomarkers of effect (e.g. protein or DNA adducts of relevance to disease) may be identified from complex molecular signaling networks in response to PM exposure [189–191]. On the other hand, key biomarkers of exposure linked to biomarkers of effect need to be identified out of the population-based exposome [191,192]. Using molecular epidemiology approaches, these biomarkers can then be employed in population-based cohort studies to establish the principal link between PM exposure and population health risks [193].

The less explored frontier of the airborne microbiome

As compared to the physical and chemical aspects of airborne PM, the nature and implications of the biological dimension (i.e. the airborne microbiome) remain largely unexplored. Current exploratory efforts often focus on the identity and diversity of the microbial community with less emphasis on the interactions within the community and the functions it manifests on PM.

In the last decade, metagenomics has revolutionized our efforts beyond traditional culture-dependent approaches to achieve unbiased, non-targeted identifications of microbial compositions. However, an often overlooked question in current scientific investigations is how much of the microbial mass is viable; yet the ability to answer this question is a pre-requisite to addressing the atmospheric functions and health implications of such microbial masses. Towards this end, a fluorescence-activated cell sorting (FACS) technique coupled with a fluorescent staining technique [194] can be applied to purify, separate and concentrate viable cells/spores from urban PM samples (Fig. 4).

As introduced in the ‘Microbial composition and chemical–biological interplay’ section above,
while metagenomics reveals the genetic potential of the PM-borne microbial community, it alone cannot reveal the finer-level details of actual expression and function (e.g. RNA and proteins) in response to environmental forces or biotic interactions [195]. Other meta-omics approaches, including metatranscriptomics, metaproteomics and metabolomics, can provide system-level insights into the molecular machinery network involved in the life processes occurring on PM [108,196]. In addition, synchrotron X-ray techniques may enrich our observations of the microbes adhering to the mineral surface on PM. This will enhance our understanding of the elemental compositions of microbial cells in their interactions with trace element speciation in the biofilms [197]. All of these tools will enhance our ability to solve the overarching question ‘What do those microbes do?’ beyond current efforts that focus on the primary question ‘Who are they?’.

As far as human health implications are concerned, future research needs to focus on airborne pathogens and hazardous microbial components. For example, similarly to the efforts to study human gut microbiome, lung microbiome can be explored in parallel with airborne microbiome in population-based cohort studies. Within the metageneome, more data mining can be conducted to analyse hazardous genetic elements, such as antibiotic resistance genes, to trace resistomes shared between airborne microbiome and human lung microbiome. In addition, clinically relevant microbial allergens (e.g. endotoxins and β-glucans) can be targeted to enrich the database of PM-borne components to which the multiple factors underlying the toxicological and health consequences of urban PM can be attributed.

Influence of changing urban landscape and climate scenarios on PM pollution and the impact on human health

Evolving urban landscape and climate scenarios reflect the outermost dimensions of spatiotemporal variables with global implications that can determine the features of PM pollution. From China’s past experience, the projections on urban expansion and land-use changes in the country are expected to continue to have an impact on air pollution. Spatial information remains critical in such a context, but further improvement is required in terms of predictive values. Beyond current efforts focusing on phenomenological ‘hotspot’ pattern recognition or urban–rural comparisons, more fine-scale transect studies need to be conducted to generate predictive insights on how the abundance and composition of PM change according to functional categorizations within a city. In such a sense, land-use regression models have emerged as a useful tool for characterizing long-term, local-scale spatial variability in PM and associated chemical components (e.g. metals and volatile organic compounds) [198–201]. With a bird’s-eye view of high-resolution data on PM loadings and the associated components, such modeling approaches may shed light on site-specific risks to the population of exposure to PM [202–205].

In addition to the static spatial scale, dynamic transport models enhance the temporal dimension of the power to predict the polluting effect of regional transport via the movement of cloud masses. This is important for assessing levels of pollution and their associated health implications, particularly under climate change scenarios indicating that the forces that are driving episodes of regional pollution in China will continue to gather momentum [206,207]. There are emerging signs that a range of air pollutants (e.g. PM, ozone, allergens derived from animals and plants, smoke from wildfire events) along with the distribution of weather patterns known to be conducive to air-pollution episodes (e.g. stagnating high pressure systems) will respond sensitively to future changes in climate [208,209]. These influences may have implications for the health of the population arising from long-term, intermittent exposure to seasonal cycles of air-pollution episodes. As such, there is a pressing need to devise an integrated model of future air quality under projected climate change scenarios, in order to reach quantitative conclusions on the extent to which such changes would modify the occurrence
and distribution of airborne pollutants, and the effect of these changes on human health.

All of these predictive tools would make it possible to more accurately quantify the health effects associated with PM pollution and their distribution among the population on a large but fine spatiotemporal scale [205]. They would also facilitate attempts to attribute air quality and the impact on health to specific sources and types of pollutants that together shape the characteristic mixtures of PM. Such an advanced understanding would in turn inform regulatory control measures that could be adapted to future urban planning and climate scenarios to better protect public health.

FUNDING
This work was financially supported by the Research Grants Council of Hong Kong (PolyU 152095/14E), The Hong Kong Polytechnic University (Projects of Strategic Importance and the PolyU Postdoctoral Fellowship Scheme) and the National Natural Science Foundation of China (41471418, 41475117 and 91543205).

Conflict of interest statement. None declared.

REFERENCES
1. Chan CK and Yao XH. Air pollution in mega cities in China. Atmos Environ 2008; 42: 1–42.
2. Kan HD, Chen RJ and Tong SL. Ambient air pollution, climate change, and population health in China. Environ Int 2012; 42: 10–19.
3. Zhang YL and Cao F. Fine particulate matter (PM2.5) in China at a city level. Sci Rep 2015; 5: 14884.
4. Ma ZW, Hu XF and Sayer AM et al. Satellite-based spatiotemporal trends in PM2.5 concentrations: China, 2004–2013. Environ Health Perspect 2016; 124: 184–92.
5. Menon S, Hansen J and Nazarenko L et al. Climate effects of black carbon aerosols in China and India. Science 2002; 297: 2250–3.
6. Lelieveld J, Evans JS and Fnais M et al. The contribution of outdoor air pollution sources to premature mortality on a global scale. Nature 2015; 525: 367–71.
7. West JJ, Cohen A and Dentener F et al. What we breathe impacts our health: improving understanding of the link between air pollution and health. Environ Sci Technol 2016; 50: 4985–904.
8. Pöschl U and Shiraiwa M. Multiphase chemistry at the atmosphere–biosphere interface influencing climate and public health in the anthropocene. Chem Rev 2015; 115: 4440–75.
9. Calvo AI, Alves C and Castro A et al. Research on aerosol sources and chemical composition: past, current and emerging issues. Atmos Res 2013; 120–121: 1–28.
10. Pope CA and Dockery DW. Health effects of fine particulate air pollution: lines that connect. J Air Waste Manage Assoc 2006; 56: 709–42.
11. Song F and Gao Y. Size distributions of trace elements associated with ambient particular matter in the affinity of a major highway in the New Jersey–New York metropolitan area. Atmos Environ 2011; 45: 6714–23.
12. Pan YP, Tian SL and Li XR et al. Trace elements in particulate matter from metropolitan regions of Northern China: sources, concentrations and size distributions. Sci Total Environ 2015; 537: 9–22.
13. Luo P, Ni HG and Bao LJ et al. Size distribution of airborne particle-bound polybrominated diphenyl ethers and its implications for dry and wet deposition. Environ Sci Technol 2014; 48: 13793–9.
14. Chrysikou LP and Samara CA. Seasonal variation of the size distribution of urban particulate matter and associated organic pollutants in the ambient air. Atmos Environ 2009; 43: 4557–69.
15. Lya Y, Xu TT and Li X et al. Size distribution of particle-associated polybrominated diphenyl ethers (PBDEs) and their implications for health. Atmos Meas Tech 2016; 9: 1025–37.
16. Shen GF, Wang W and Yang YF et al. Emission factors and particulate matter size distribution of polycyclic aromatic hydrocarbons from residential coal combustions in rural Northern China. Atmos Environ 2010; 44: 5237–43.
17. Degrendele C, Okonski K and Melymuk L et al. Size specific distribution of the atmospheric particulate POCDFs, dl-PCBs and PAHs on a seasonal scale: Implications for cancer risks from inhalation. Atmos Environ 2014; 98: 410–16.
18. Burrows SM, Elbert W and Lawrence MG et al. Bacteria in the global atmosphere—Part 1: Review and synthesis of literature data for different ecosystems. Atmos Chem Phys 2009; 9: 5263–80.
19. Li YP, Fu HL and Wang W et al. Characteristics of bacterial and fungal aerosols during the autumn haze days in Xi’an, China. Atmos Environ 2015; 122: 439–47.
20. Gao M, Jia RZ and Qiu TL et al. Seasonal size distribution of airborne culturable bacteria and fungi and preliminary estimation of their deposition in human lungs during non-haze and haze days. Atmos Environ 2015; 118: 203–10.
21. Araujo JA and Nel AE. Particulate matter and atherosclerosis: role of particle size, composition and oxidative stress. Part Fibre Toxicol 2009; 6: 24.
22. Valavanidis A, Fiotakis K and Vlachoglanni T. Airborne particulate matter and human health: toxicological assessment and importance of size and composition of particles for oxidative damage and carcinogenic mechanisms. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev 2008; 26: 339–62.
23. Oberdörster G, Oberdörster E and Oberdörster J. Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles. Environ Health Perspect 2006; 113: 823–39.
24. Kawanaka Y, Tsuchiya Y and Yun SJ et al. Size distributions of polycyclic aromatic hydrocarbons in the atmosphere and estimation of the contribution of ultrafine particles to their lung deposition. Environ Sci Technol 2009; 43: 6851–6.
63. Ding X, He QF and Shen RQ et al. Spatial distributions of secondary organic aerosols from isoprene, monoterpenes, β-caryophyllene, and aromatics over China during summer. J Geophys Res Atmos 2014; 119: 11877–91.

64. Quintana JB, Rodil R and Reemtsma T et al. Organophosphorus flame retardants and plasticizers in water and air II: analytical methodology. TrAC Trends Anal Chem 2008; 27: 904–15.

65. Fu PQ and Kawamura K. Ubiquity of bisphenol A in the atmosphere. Environ Pollut 2010; 158: 3138–43.

66. Kawamura K, Kasukabe H and Barrie LA. Source and reaction pathways of dicarboxylic acids, ketoacids and dicarbonyls in Arctic aerosols: one year of observations. Atmos Environ 1996; 30: 1709–22.

67. Fu PQ, Kawamura K and Usukura K et al. Dicarboxylic acids, ketoacids and glyxol in the marine aerosols collected during a round-the-world cruise. Mar Chem 2013; 148: 22–32.

68. Zhang YL, Wang XM and Blake DR et al. Aromatic hydrocarbons as ozone precursors before and after outbreak of the 2008 financial crisis in the Pearl River Delta region, south China. J Geophys Res 2012; 117: D15306.

69. Liu T, Wang X and Deng W et al. Secondary organic aerosol formation from photochemical aging of light-duty gasoline vehicle exhausts in a smog chamber. Atmos Chem Phys 2019; 15: 9949–62.

70. Xu X, Williams C and Plass-Dülmer H et al. GC×GC measurements of C7-C11 aromatic and n-alkane hydrocarbons on Crete, in air from Eastern Europe during the MINOS campaign. Atmos Chem Phys 2003; 3: 1461–75.

71. Hamilton JF, Webb PJ and Lewis AC et al. Partially oxidised organic components in urban aerosol using GCXGC-TOF/MS. Atmos Chem Phys 2004; 4: 1279–90.

72. Xu X, van Stee LLP and Williams J et al. Comprehensive two-dimensional gas chromatography (GC×GC) measurements of volatile organic compounds in the atmosphere. Atmos Chem Phys 2003; 3: 665–82.

73. Weggler BA, Ly-Verdu S and Jemmerwein M et al. Untargeted identification of wood type-specific markers in particulate matter from wood combustion. Environ Sci Technol 2015; 50: 10073–81.

74. Inumai Y, Muller C and Berndt T et al. Evidence for the existence of organosulfates from β-pinene ozonolysis in ambient secondary organic aerosol. Environ Sci Technol 2007; 41: 6678–83.

75. Huang DD, Li YJ and Lee BP et al. Analysis of organic sulfur compounds in atmospheric aerosols at the HKUST supersite in Hong Kong using HR-ToF-AMS. Environ Sci Technol 2015; 49: 3672–9.

76. He QF, Ding X and Wang XM et al. Organsulfates from pinene and isoprene over the Pearl River Delta, South China: seasonal variation and implication in formation mechanisms. Environ Sci Technol 2014; 48: 9236–45.

77. Lin P, Liu JM and Shilling JE et al. Molecular characterization of brown carbon (BrC) chromophores in secondary organic aerosol generated from photooxidation of toluene. Phys Chem Chem Phys 2015; 17: 23312–25.

78. Lin P, Rincon AG and Kalberer M et al. Elemental composition of HULIS in the Pearl River Delta Region, China: results inferred from positive and negative electrospray high resolution mass spectrometric data. Environ Sci Technol 2012; 46: 7454–62.

79. Mazzoleni LR, Ehrmann BM and Shen XH et al. Water-soluble atmospheric organic matter in fog: exact masses and chemical formula identification by ultrahigh-resolution fourier transform ion cyclotron resonance mass spectrometry. Environ Sci Technol 2010; 44: 3690–7.

80. Lin P, Laskin J and Nickorodov SA et al. Revealing brown carbon chromophores produced in reactions of methylyglyoxal with ammonium sulfate. Environ Sci Technol 2015; 49: 14257–66.

81. Chen QC, Ikemori F and Higo H et al. Chemical structural characteristics of HULIS and other fractionated organic matter in urban aerosols: results from mass spectral and FT-IR analysis. Environ Sci Technol 2016; 50: 1721–30.

82. Paglione M, Kiemeld-Scharr A and Mensah AA et al. Identification of humic-like substances (HULIS) in oxygenated organic aerosols using NMR and AMS factor analyses and liquid chromatographic techniques. Atmos Chem Phys 2014; 14: 25–45.

83. Fu PQ, Kawamura K and Chen J et al. Fluorescent water-soluble organic aerosols in the High Arctic atmosphere. Sci Rep 2015; 5: 9845.

84. Schmitt-Kopplin P, Gelencsér A and Dabek-Zlotorzynska E et al. Analysis of the unresolved organic fraction in atmospheric aerosols with ultrahigh-resolution mass spectrometry and nuclear magnetic resonance spectroscopy: organosulfates as photochemical smog constituents. Anal Chem 2010; 82: 9017–26.

85. Havers N, Burba P and Lambert J et al. Spectroscopic characterization of humic-like substances in airborne particulate matter. J Atmos Chem 1998; 29: 45–54.

86. Deescasri S, Facchinii MC and Fuzzi S et al. Characterization of water-soluble organic compounds in atmospheric aerosol: a new approach. J Geophys Res 2000; 105: 1481–9.

87. Zhang Q, Ramí Alfarra M and Worsnop DR et al. Deconvolution and quantification of hydrocarbon-like and oxygenated organic aerosols based on aerosol mass spectrometry. Environ Sci Technol 2009; 43: 4538–52.

88. Sun YL, Du W and Wang DQ et al. Real-time characterization of aerosol particle composition above the urban canopy in Beijing: insights into the interactions between the atmospheric boundary layer and aerosol chemistry. Environ Sci Technol 2015; 49: 11340–7.

89. Zhou W, Jiang JK and Duan L et al. Evolution of submicrometer organic aerosols during a complete residential coal combustion process. Environ Sci Technol 2016; 50: 7861–9.

90. Dong HB, Zeng LM and Hu M et al. Technical Note: The application of an improved gas and aerosol collector for ambient air pollutants in China. Atmos Chem Phys 2012; 12: 10519–33.

91. Wang JF, Ge XL and Chen YF et al. Highly time-resolved urban aerosol characteristics during springtime in Yangtze River Delta, China: insights from soot particle aerosol mass spectrometry. Atmos Chem Phys 2016; 16: 9109–27.

92. Orsini DA, Ma YL and Sullivan A et al. Refinements to the particle-into-liquid sampler (PILS) for ground and airborne measurements of water soluble aerosol composition. Atmos Environ 2003; 37: 1243–59.

93. Thomas RM, Trebs I and Otjes R et al. An automated analyzer to measure surface-atmosphere exchange fluxes of water soluble inorganic aerosol compounds and reactive trace gases. Environ Sci Technol 2009; 43: 1412–18.

94. Violaki K, Fang T and Mihalopoulos N et al. Real-time, online automated system for measurement of water-soluble reactive phosphate ions in atmospheric particles. Anal Chem 2016; 88: 7163–70.

95. Weber RJ, Orsini D and Daun Y et al. A particle-into-liquid collector for rapid measurement of aerosol bulk chemical composition. Aerosol Sci Technol 2001; 35: 718–27.

96. Runsey IC, Cowen KA and Walker JT et al. An assessment of the performance of the Monitor for AeRosols and GAses in ambient air (MARGA): a semi-continuous method for soluble compounds. Atmos Chem Phys 2014; 14: 5639–58.

97. Pöhler C, Huffman JA and Pöschl U. Auto fluorescence of atmospheric bioaerosols: fluorescent biomolecules and potential interferences. Atmos Meas Tech 2012; 5: 37–71.
98. Yue SY, Ren H and Fan SY et al. Springtime precipitation effects on the abundance of fluorescent biological aerosol particles and HULIS in Beijing. Sci Rep 2016; 6: 29618.

99. Pan YL. Detection and characterization of biological and other organic-carbon aerosol particles in atmosphere using fluorescence. J Quant Spectrosc Radiat Transf 2015; 150: 12–35.

100. Fu PQ, Kawamura K and Chen J et al. Diurnal variations of organic molecular tracers and stable carbon isotopic composition in atmospheric aerosols over Mt. Tai in the North China Plain: an influence of biomass burning. Atmos Chem Phys 2012; 12: 8939–75.

101. Kawamura K, Kosaka M and Sempere R. Distributions and seasonal changes of hydrocarbons in urban aerosols and rainwaters. Chikyukagaku (Geochemistry) 1995; 29: 1–15.

102. Wang HB, Kawamura K and Shooter D. Wintertime organic aerosols in Christchurch and Auckland, New Zealand: contributions of residential wood and coal burning and petroleum utilization. Environ Sci Technol 2008; 40: 5257–62.

103. Yang YH, Chan CY and Tao J. Observation of elevated fungal tracers due to biomass burning in the Sichuan Basin at Chengdu City, China. Sci Total Environ 2012; 431: 68–77.

104. Bauer H, Cleeves M and Vermeylen R et al. Arabitol and mannitol as tracers for the quantification of airborne fungal spores. Atmos Environ 2008; 42: 589–93.

105. Guo S, Hu M and Guo QF et al. Primary sources and secondary formation of organic aerosols in Beijing, China. Environ Sci Technol 2012; 46: 9646–53.

106. Hu D, Bian QJ and Li TWY et al. Contributions of isoprene, monoterpenes, β-carotene, and toluene to secondary organic aerosols in Hong Kong during the summer of 2006. J Geophys Res 2008; 113: D22206.

107. Jaenicke R. Abundance of cellular material and proteins in the atmosphere. Science 2005; 308: 73.

108. Führlich-Nowosyj K, Kampf CJ and Weber B et al. Bioaerosols in the Earth system: climate, health, and ecosystem interactions. Atmos Res 2016; 182: 346–76.

109. Brodie EL, DeSantis TZ and Parker JPM et al. Urban aerosols harbor diverse and dynamic bacterial populations. Proc Natl Acad Sci USA 2007; 104: 299–304.

110. Cao C, Jiang WJ and Wang BY. Contributions of isoprene, monoterpenes, and biomass burning and its influence on regional aerosol properties during the wheat harvest season in North China. Atmos Environ 2015; 107: 153–63.

111. Jiang WJ, Liang P and Wang BY et al. Optimized DNA extraction and metagenomic sequencing of airborne microbial communities. Nat Protoc 2010; 5: 768–79.

112. Yooseph S, Andrews-Pfannkoch C and Tenney A et al. Metagenomic framework for the study of airborne microbial communities. PloS One 2013; 8: e61862.

113. Behzad H, Gojobori T and Mineta K. Challenges and opportunities of airborne metagenomics. Genome Biol Evol 2015; 7: 1216–26.

114. Chapleski RC, Zhang YF and Troya D et al. Heterogeneous chemistry and reaction dynamics of the atmospheric oxidants, O3, NO2, and OH, on organic surfaces. Chem Soc Rev 2016; 45: 3731–46.

115. Woon AC, Brar MS and Chan Y et al. Temporal variation in airborne microbial populations and microbially-derived allergens in a tropical urban landscape. Atmos Environ 2013; 74: 291–300.

116. Deguillaume L, Leriche M and Amato P et al. Microbiology and atmospheric processes: chemical interactions of primary biological aerosols. Biogeosciences 2008; 5: 1073–84.

117. Hill KA, Shepson PB and Galbavy ES et al. Processing of atmospheric nitrogen by clouds above a forest environment. J Geophys Res 2007; 112: D13011.

118. Arita PA. Microbiological degradation of atmospheric organic compounds. Geophys Res Lett 2002; 29: 2077.

119. Côté V, Kos G and Mortazavi R et al. Microbial and ‘de novo’ transformation of dicarboxylic acids by three airborne fungi. Sci Total Environ 2008; 390: S30–7.

120. Cheng Z, Jiang JK and Fajardo O et al. Characteristics and health impacts of particulate matter pollution in China (2001–2011). Atmos Environ 2013; 65: 186–94.

121. Hu M, Guo S and Peng JF et al. Insight into characteristics and sources of PM2.5 in the Beijing–Tianjin–Hebei region, China. Natl Sci Rev 2015; 2: 257–8.

122. Han LJ, Zhou WQ and Li WF et al. Impact of urbanization level on urban air quality: a case of fine particles (PM2.5) in Chinese cities. Environ Pollut 2014; 194: 163–70.

123. Cao JJ, Shen ZK and Chow JC et al. Winter and summer PM2.5 chemical compositions in fourteen Chinese cities. J Air Waste Manage Assoc 2012; 62: 1214–26.

124. Shen ZK, Arimoto R and Cao JJ et al. Seasonal variations and evidence for the effectiveness of pollution controls on water-soluble inorganic species in total suspended particulates and fine particulate matter from Xi’an, China. J Air Waste Manage Assoc 2012; 58: 1456–70.

125. Tao J, Zhang LM and Engling G et al. Chemical composition of PM2.5 in an urban environment in Chengdu, China: importance of springtime dust storms and biomass burning. Atmos Res 2013; 122: 270–83.

126. Wang GH, Zhou BH and Cheng CL et al. Impact of Gobi desert dust on aerosol chemistry of Xi’an, inland China during spring 2009: differences in composition and size distribution between the urban ground surface and the mountain atmosphere. Atmos Chem Phys 2013; 13: 819–35.

127. Ho KF, Engling G and Ho SSH et al. Seasonal variations of anhydrosugars in PM2.5 in the Pearl River Delta Region, China. Tellus B 2014; 66: 22577.

128. Wang LL, Xin JY and Li XR et al. The variability of biomass burning and its influence on regional aerosol properties during the wheat harvest season in North China. Atmos Res 2015; 157: 153–63.

129. Zhang XY, Wang YQ and Niu T et al. Atmospheric aerosol compositions in China: spatial/temporal variability, chemical signature, regional haze distribution and comparisons with global aerosols. Atmos Chem Phys 2012; 12: 779–99.

130. Liu SZ, Tao S and Liu WX et al. Atmospheric polycyclic aromatic hydrocarbons in North China: a winter-time study. Environ Sci Technol 2007; 41: 8256–61.

131. van Donkelaar A, Martin RV and Brauer M et al. Global estimates of ambient fine particulate matter concentrations from satellite-based aerosol optical depth: development and application. Environ Health Perspect 2010; 118: 847–55.

132. Duan JC and Tan JH. Atmospheric heavy metals and arsenic in China: situation, sources and control policies. Atmos Environ 2013; 74: 93–101.

133. Viana M, Kuhlbusch TAJ and Querol X et al. Source apportionment of particulate matter in Europe: a review of methods and results. J Aerosol Sci 2008; 39: 827–49.

134. Belis CA, Karagulian F and Larsen BR et al. Critical review and meta-analysis of ambient particulate matter source apportionment using receptor models in Europe. Atmos Environ 2013; 69: 94–108.
135. Pui DYH, Chen SC and Zuo ZL. PM2.5 in China: measurements, sources, visibility and health effects, and mitigation. *Paticcology* 2014; 13: 1–28.

136. Pant P and Harrison RM. Critical review of receptor modelling for particulate matter: a case study of India. *Atmos Environ* 2012; 46: 1–12.

137. Yang F, Tan J and Zhao Q et al. Characteristics of PM2.5 speciation in representative megacities and across China. *Atmos Chem Phys* 2011; 11: 5207–19.

138. Zhang ZS, Engling G and Lin CY et al. Fossil vs. non-fossil sources of fine carbonaceous aerosols in four Chinese cities during the extreme winter haze episode of 2013. *Atmos Chem Phys* 2015; 15: 1299–312.

139. Liu JW, Li J and Liu D et al. Source apportionment and dynamic changes of carbonaceous aerosols during the haze bloom-decay process in China based on radiocarbon and organic molecular tracers. *Atmos Chem Phys* 2016; 16: 2985–96.

140. Pan YP, Tian SL and Liu DW et al. Fossil fuel combustion-related emissions dominate atmospheric ammonia sources during severe haze episodes: evidence from 15N-stable isotope in size-resolved aerosol ammonium. *Environ Sci Technol* 2018; 50: 8049–56.

141. Huang Y, Shen HZ and Chen H et al. Quantification of global primary emissions of PM2.5, PM10, and TSP from combustion and industrial process sources. *Environ Sci Technol* 2014; 48: 13834–43.

142. Shen ZX, Cao JJ and Arimoto R et al. Ionic composition of TSP and PM2.5 during dust storms and air pollution episodes at Xi’an, China. *Atmos Environ* 2009; 43: 2911–18.

143. Zheng M, Salmon LG and Schauer JJ et al. Seasonal trends in PM2.5 source contributions in Beijing, China. *Atmos Environ* 2005; 39: 3967–76.

144. Xu HM, Cao JJ and Chow JC et al. Inter-annual variability of wintertime PM2.5 chemical composition in Xi’an, China: evidences of changing source emissions. *Sci Total Environ* 2016; 545–546: 546–55.

145. Zhang ZS, Engling G and Lin CY et al. Chemical speciation, transport and contribution of biomass burning smoke to ambient aerosol in Guangzhou, a mega city of China. *Atmos Environ* 2010; 44: 3187–95.

146. Seinfeld JH and Pandis SN. *Atmospheric Chemistry and Physics: From Air Pollution to Climate Change*. Hoboken, New Jersey: John Wiley & Sons 2006.

147. Bhatnagar A. Environmental cardiology: studying mechanistic links between pollution and heart disease. *Circ Res* 2006; 99: 692–705.

148. Kelly FJ. Oxidative stress: its role in air pollution and adverse health effects. *Occup Environ Med* 2003; 60: 612–16.

149. Grahame TJ and Schlesinger RB. Oxidative stress-induced telomeric erosion as a mechanism underlying airborne particulate matter-related cardiovascular disease. *Part Fibre Toxicol* 2012; 9: 21.

150. Li N, Xia T and Niel AE. The role of oxidative stress in ambient particulate matter-induced lung diseases and its implications in the toxicity of engineered nanoparticles. *Free Radic Biol Med* 2008; 44: 1689–99.

151. Jahn HJ, Schneider A and Breitner S et al. Particulate matter pollution in the megacities of the Pearl River Delta, China: a systematic literature review and health risk assessment. *Int J Hyg Environ Health* 2011; 214: 281–95.

152. Kelly FJ and Fussell JC. Size, source and chemical composition as determinants of toxicity attributable to ambient particulate matter. *Atmos Environ* 2012; 60: 504–26.

153. Weichenthal SA, Godri-Pollitt K and Villeneuve PJ. PM2.5, oxidant defence and cardiorespiratory health: a review. *Environ Health* 2013; 12: 40.

154. Bates JT, Weber RJ and Abrams J et al. Reactive oxygen species generation linked to sources of atmospheric particulate matter and cardiorespiratory effects. *Environ Sci Technol* 2015; 49: 13605–12.

155. Weichenthal S, Crouse DL and Pinault L et al. Oxidative burden of fine particulate air pollution and risk of cause-specific mortality in the Canadian Census Health and Environment Cohort (CanCHEC). *Environ Res* 2016; 146: 92–9.

156. Boogaard H, Janssen NAH and Fischer PH et al. Contrasts in oxidative potential and other particulate matter characteristics collected near major streets and background locations. *Environ Health Perspect* 2012; 120: 195–91.

157. Verma V, Rico-Martinez R and Kotra N et al. Contribution of water-soluble and insoluble components and their hydrophobic/hydrophilic subfractions to the reactive oxygen species-generating potential of fine ambient aerosols. *Environ Sci Technol* 2012; 46: 11384–92.

158. Lin YH, Arashimo M and Martin E et al. Isoprene-derived secondary organic aerosol induces the expression of oxidative stress response genes in human lung cells. *Environ Sci Technol Lett* 2016; 3: 250–4.

159. Deme D, Cabral-Ndior M and Garçon G et al. Relationship between physicochemical characterization and toxicity of fine particulate matter (PM2.5) collected in Dakar city (Senegal). *Environ Res* 2012; 113: 1–13.

160. Lichtveld KM, Ebersviller SM and Sexton KG et al. In vitro exposures in diesel exhaust atmospheres: resuspension of PM from filters versus direct deposition of PM from air. *Environ Sci Technol* 2012; 46: 9062–70.

161. Loxham M, Cooper MJ and Gerlofs-Nijland ME et al. Physicochemical characterization of airborne particulate matter at a mainline underground railway station. *Environ Sci Technol* 2013; 47: 3614–22.

162. Wang WT, Jarjasopit N and Schrlau J et al. Concentration and photochemistry of PAHs, NPAHs, and OPAHs and toxicity of PM2.5 during the Beijing Olympic games. *Environ Sci Technol* 2011; 45: 8887–95.

163. Gerlofs-Nijland ME, Rummelhard M and Boere AJF et al. Particle induced toxicity in relation to transition metal and polyaromatic hydrocarbon contents. *Environ Sci Technol* 2009; 43: 4729–36.

164. Farina F, Sancini G and Battaglia C et al. Milano summer particulate matter (PM10) triggers lung inflammation and extra pulmonary adverse events in mice. *PloS One* 2013; 8: e66836.

165. Brunekeef B and Holgate ST. Air pollution and health. *Lancet* 2002; 360: 1233–42.

166. Dockery DW, Pope CA and Xu XP et al. An association between air pollution and mortality in six U.S. cities. *N Engl J Med* 1993; 329: 1753–9.

167. Schwarze PE, Ovrevik J and Lag M et al. Particulate matter properties and health effects: consistency of epidemiological and toxicological studies. *Hum Exp Toxicol* 2006; 25: 559–73.

168. Heal MR, Kumar P and Harrison RM. Particles, air quality, policy and health. *Chem Soc Rev* 2012; 41: 6606–30.

169. Farina F, Sancini G and Longhin E et al. Milan PM1 induces adverse effects on mice lungs and cardiovascular system. *Biomed Res Int* 2013; 2013: 538513.

170. Čupr P, Flegrová Z and Franců J et al. Mineralogical, chemical and toxicological characterization of urban air particles. *Environ Int* 2013; 54: 26–34.

171. Li N, Sioutas C and Cho A et al. Ultrafine particulate pollutants induce oxidative stress and mitochondrial damage. *Environ Health Perspect* 2003; 111: 455–60.

172. Qiu H, Yu ITS and Tian LW et al. Effects of coarse particulate matter on emergency hospital admissions for respiratory diseases: a time-series analysis in Hong Kong. *Environ Health Perspect* 2012; 120: 572–6.

173. Ghio AJ, Caraway MS and Madden MC. Composition of air pollution particles and oxidative stress in cells, tissues, and living systems. *J Toxicol Environ Health B Crit Rev* 2012; 15: 1–21.
174. Lakey PSJ, Berkemeier T and Tong HJ et al. Chemical exposure–response relationship between air pollutants and reactive oxygen species in the human respiratory tract. *Sci Rep* 2016; 6: 32916.

175. Jomova K and Valko M. Advances in metal-induced oxidative stress and human disease. *Toxicology* 2011; 283: 65–87.

176. Zhou OH, Wang LX and Cao ZY et al. Dispersion of atmospheric fine particulate matters in simulated lung fluid and their effects on model cell membranes. *Sci Total Environ* 2015; 542: 36–43.

177. Chen KL and Bothun GD. Nanoparticles meet cell membranes: probing nonspecific interactions using model membranes. *Environ Sci Technol* 2014; 48: 873–80.

178. Yi P and Chen KL. Interaction of multiwalled carbon nanotubes with supported lipid bilayers and vesicles as model biological membranes. *Environ Sci Technol* 2013; 47: 5711–19.

179. de Bruijne K, Ebersviller S and Sexton KG et al. Role of microbial and chemical composition in toxicological properties of indoor and outdoor air particulate matter. *Part Fibre Toxicol* 2014; 11: 60.

180. Kim S, Jaques PA and Chang M et al. Versatile aerosol concentration enrichment system (VACES) for simultaneous in vivo and in vitro evaluation of toxic effects of ultrafine, fine and coarse ambient particles Part II: Field evaluation. *J Aerosol Sci* 2001; 32: 1299–314.

181. Ning Z, Sillanpää M and Pakbin P et al. In vitro toxicity of particulate matter (PM) collected at different sites in the Netherlands is associated with PM composition, size fraction and oxidative potential—the RAPTES project. *Part Fibre Toxicol* 2008; 5: 15.

182. Chen KL and Bothun GD. Nanoparticles meet cell membranes: probing nonspecific interactions using model membranes. *Environ Sci Technol* 2014; 48: 873–80.

183. Rossner P, Binkova B and Rossnerova A et al. Molecular epidemiology and air pollution: current air quality issues. *InTech* 2015; 10:5772/59955.

184. Zhou QH, Wang LX and Cao ZY et al. Nanoparticles meet cell membranes: probing nonspecific interactions using model membranes. *Environ Sci Technol* 2014; 48: 873–80.

185. Jomova K and Valko M. Advances in metal-induced oxidative stress and human disease. *Toxicology* 2011; 283: 65–87.

186. Lakey PSJ, Berkemeier T and Tong HJ et al. Chemical exposure–response relationship between air pollutants and reactive oxygen species in the human respiratory tract. *Sci Rep* 2016; 6: 32916.