

GEOSCIENCES

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

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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 govern-

ment released the 'Atmospheric Pollution Prevention and Control Action Plan' (http://www.gov.cn/zwggk/2013-09/12/content_2486773.htm in Chinese), in which it announced its aim of achieving a reduction in PM_{2.5} (particulate matter with an aerodynamic diameter of less than or equal to 2.5 μm; $D_p \leq 2.5 \mu\text{m}$) 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

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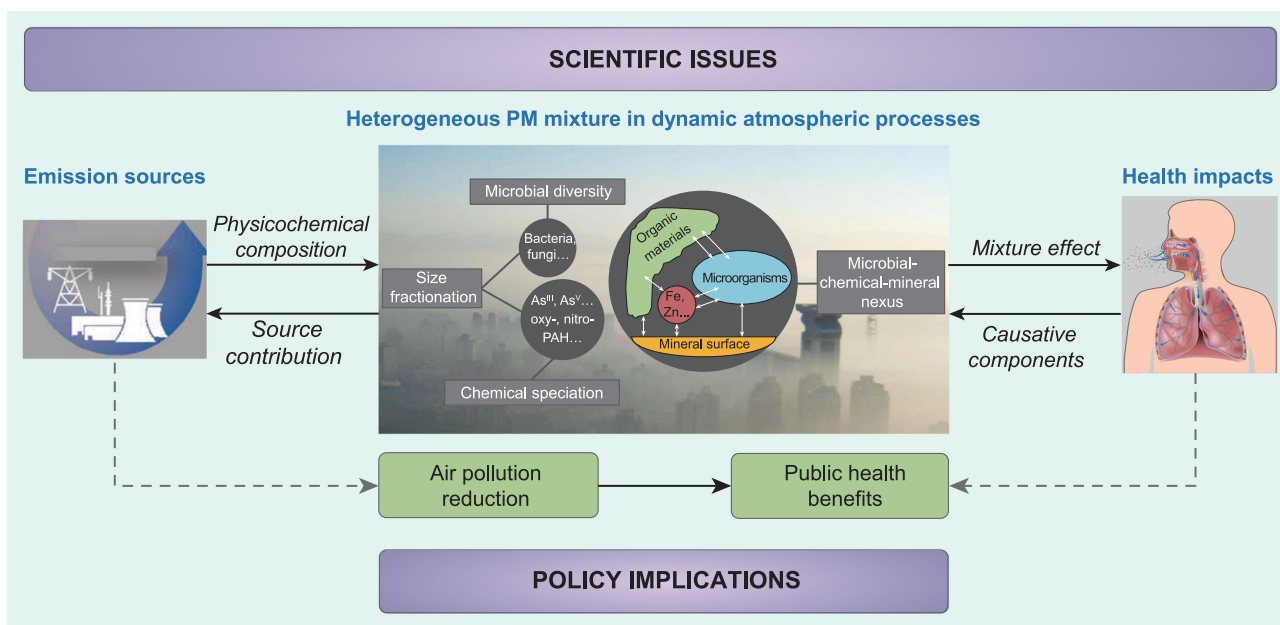


Figure 1. Scope of the review covering key scientific issues surrounding PM mixtures with high regulatory and public health relevance.

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 $10\ \mu\text{m}$ (PM_{10} ; $D_p \leq 10\ \mu\text{m}$). According to their type of source and mode of generation, PM_{10} are further stratified into different size fractions, including coarse ($\text{PM}_{2.5-10}$; $2.5 < D_p < 10\ \mu\text{m}$), fine ($\text{PM}_{2.5}$; $D_p \leq 2.5\ \mu\text{m}$) and ultrafine ($\text{PM}_{0.1}$; $D_p \leq 0.1\ \mu\text{m}$) 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

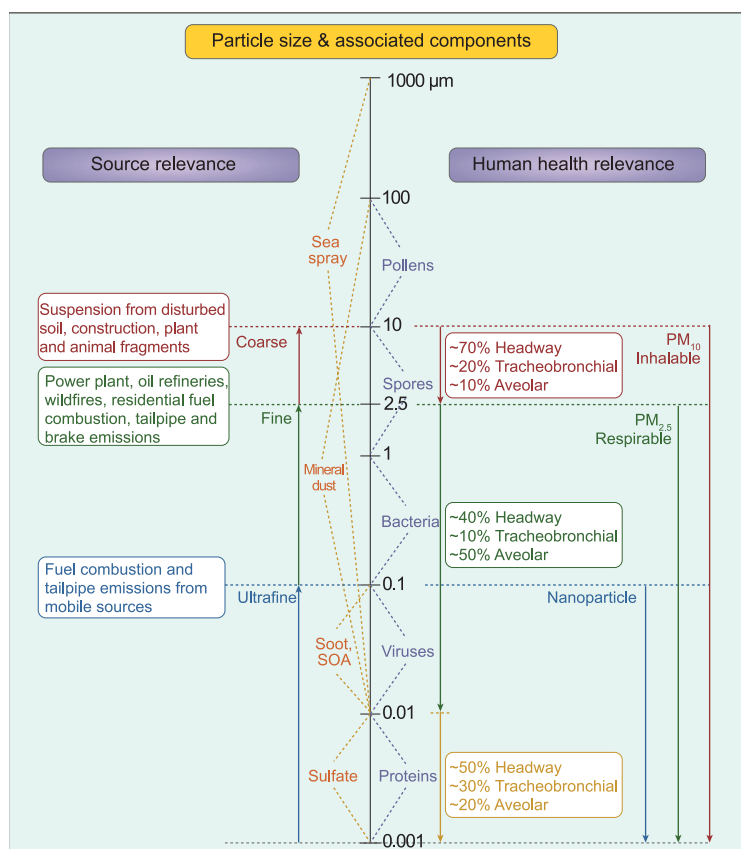


Figure 2. Size distribution of atmospheric PMs and associated components with implications for emission sources and inhalation exposure.

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 $\sim 2 \mu\text{m}$ 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, $\text{PM}_{0.1}$, 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 C_1 and C_2 compounds, to high-molecular-weight (HMW) compounds (e.g. humic-like substances (HULIS) and proteins) with a few to tens of thousands of Dalton [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 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 (α -Fe₂O₃) and aluminosilicate minerals in the subway of Shanghai, China, and magnetite (Fe₃O₄) 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 cur-

rent 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 10⁴–10⁸ 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 PM₁₀ 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	Inductively coupled plasma–atomic emission spectrometer (ICP–AES)/mass spectrometer (ICP–MS)	Trace and major elements [57,58]
	Ion chromatography	Water-soluble inorganic ions (e.g. SO_4^{2-} , NO_3^- , NH_4^+ , Na^+ and K^+); low-molecular-weight (LMW) organic acids; sugar alcohols [59–61]
	Gas chromatograph–mass spectrometer (GC–MS)	POA and SOA tracers (e.g. <i>n</i> -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 (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 AeRosol 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 microbially 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]
	Dehydroabiestic acid	Conifer resin products		
	HMW-alkanes	Epicuticular waxes and lipids	A strong correlation between levoglucosan and plant wax <i>n</i> -alkanes, suggesting the burning of biomass as a significant source of aliphatic lipids	[100]
Fossil fuel combustion	LMW-alkanes, hopanoid hydrocarbons (hopanes), PAHs	Petroleum and coal combustion	Concentrations in urban aerosols: India > China > Japan > New Zealand	[41,62,101,102]
Plastic emissions	Phthalates	Plasticizers in synthetic polymers or softeners in polyvinylchlorides	High levels of phthalates ubiquitously occurring in Chinese megacities; summer > winter supported by the ambient-temperature dependence of phthalates	[62,100]
	Triphenylbenzene	Plasticizer		
	Bisphenol A	Production of epoxy resins and polycarbonate plastics		
Primary biological aerosol	Primary saccharides	Produced by microorganisms, plants and animals)	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]
	Amino acids	Free amino acids from sea spray aerosols and terrestrial emissions; combined amino acids from emissions from the burning of biomass and bioaerosol emissions		
Biogenic SOA	2-Methyltetrols, 2-methylglyceric acid, pinic acid, pinonic acid, 3-hydroxyglutaric acid, 3-methyl-1,2,3-butanetricarboxylic acid, β -caryophyllinic acid, and many others	Secondary products of biogenic volatile organic compounds released from vegetation	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 understand-

ing 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_{2.5–10}) in PM₁₀ 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 characteris-

tic 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 $\mu\text{g}/\text{m}^3$) [3] is about three times higher than the global population-weighted mean (20 $\mu\text{g}/\text{m}^3$) [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 ($\text{SO}_4^{2-}/\text{NO}_3^-/\text{NH}_4^+$) source. Based on accurate $\text{PM}_{2.5}$ sampling, a chemical analysis and SA models, the major primary sources of $\text{PM}_{2.5}$ 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 $\text{PM}_{2.5}$ [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

reactions seem to be of fundamental importance. In addition to the direct generation of oxidants, cellular responses also contribute to oxidative stress after exposure to PM. ROS production occurs in the mitochondria, cell membranes, phagosomes and endoplasmic reticulum. Oxidative stress following exposure to PM initiates a cascade of cellular reactions. These include the activation of kinase cascades and transcription factors, and the release of inflammatory mediators, which ultimately lead to cell injury or apoptosis. Consequently, oxidative stress in cells and tissues is a central mechanism by which exposure to PM leads to injury, disease and mortality [148–150].

The pathophysiological mechanisms for PM-induced human health effects are still not fully understood, and there are multiple mechanistic pathways that are complex and interactive. To date, assessments of the public health consequences of air pollution have largely focused on a single-pollutant approach [151]. Thus, there is an emerging need for more specific metrics of exposure that account for the composition or origin of ambient PMs. This could be an effect-based metric, such as one that measures the oxidative potential of ambient particles, the advantage of which is that it effectively integrates differences in the size distribution, surface area and chemical composition of PM into a simple, quantitative, unitary expression of toxicity [152,153]. Oxidative potential based on dithiothreitol (DTT) activity [154] or antioxidant depletion [155] has been applied to PM and successfully linked to cause-specific mortality. This has provided a more meaningful integrated metric of toxicology that can be applied to epidemiological findings. With regard to pulmonary toxicity and its relevance to health, both complementary chemical acellular assays (e.g. DTT test: consumption of dithiothreitol in a cell-free system) and *in vitro* biological assays of common PM target cells (e.g. macrophages or respiratory epithelial cells, ROS analysis) are generally used to measure PM-induced oxidative stress [156–158]. *In vitro* cell assays include cytotoxicity [159], inflammation assays [160], intracellular ROS generation [161] and DNA damage [162]. Furthermore, *in vivo* animal exposure experiments [163,164] are also often conducted to evaluate the *in vivo* pulmonary and systemic cytotoxicity and inflammatory activity induced by PM, by analysing bronchoalveolar lavage fluid (BALF) and blood samples. However, the precise components and mechanisms responsible for the toxicological consequences following exposure to PM have yet to be studied. It is imperative from a regulatory control perspective to dissect the PM mixture to arrive at a quantitative characterization of the major drivers of toxicity—a subject that warrants future well-structured investigations.

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_{0.1}, 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 PM₁₀. In general, the smaller the size of the PM, the higher the toxicity from mechanisms of oxidative stress and inflammation. For example, PM₁₀ triggers lung inflammation and extrapulmonary adverse events in mice [164], while PM₁ 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_{2.5–10} [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 *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

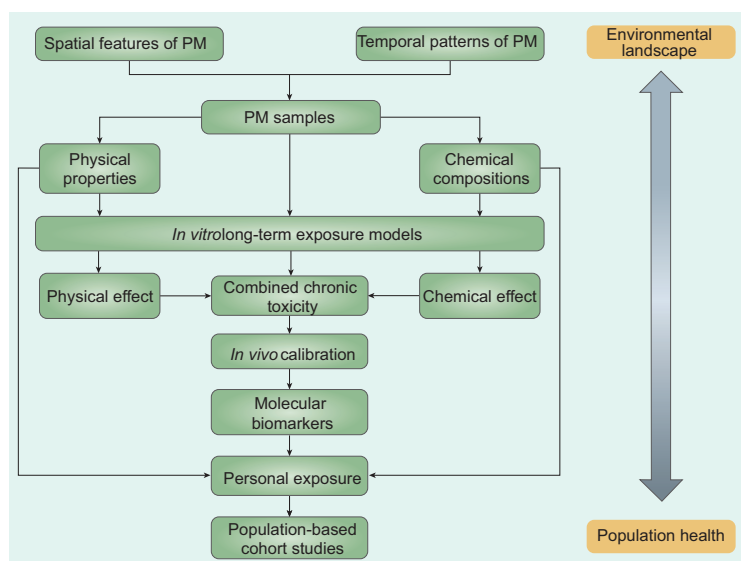


Figure 3. Proposed methodological framework for holistic assessments of airborne PM linking evolving urban landscape and climate scenarios to population health adaptations and consequences.

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,

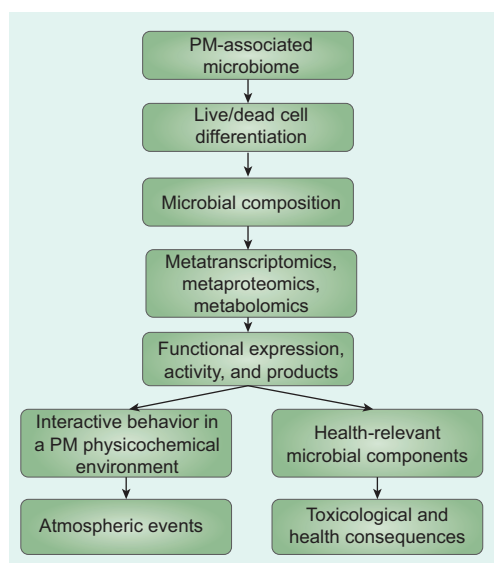


Figure 4. Proposed research needs and approaches in future function-centered investigations of the airborne microbiome.

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 metagenome, 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 wild-fire 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.

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