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How do indoor environments affect air pollution exposure?

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Air pollution in urban areas is associated with adverse human health outcomes, including cardiopulmonary disease and premature death. The relationships, determined largely through epidemiological studies, drive regulatory policies for setting air pollution standards that are designed to protect human health. Breathing predominantly occurs indoors and especially at home. Therefore, indoor environments mediate the link between outdoor air pollution and human exposure. In this perspective, we explore current understanding about the relationship between air pollution, as characterized in monitoring networks, and inhalation exposures, which occur largely indoors. Recognizing substantial and important gaps in knowledge, we suggest research directions for advancing understanding at the nexus of outdoor air pollution, indoor environments and exposure. We conclude with key points to consider when evaluating the

influence of indoor environments on air pollution exposure.

To illustrate the scale of concern, consider the most recent Global Burden of Disease study. "Ambient particulate matter" (referring to PM_{2.5}) ranked as the environmental factor with the highest adverse health consequences, with 2.9 million attributable premature deaths and 83 million disability-adjusted life years (DALYs) lost per year globally in 2017. "Ambient ozone pollution" contributed an additional 0.5 million premature deaths and 7.4 million DALYs per year.

Buildings offer partial protection against pollutants of outdoor origin but enhance exposures to particles and gases that are emitted or produced indoors. A survey of time apportionment for the United States indicated that 87% of time on average is spent indoors (mostly in one's own residence), more than 10× higher than the proportion of time spent outdoors.² Consequently,

most "ambient particulate matter" and "ambient ozone pollution" is breathed indoors, albeit at concentration levels below outdoors. Furthermore, epidemiological studies of the link between outdoor air pollution and health generally do not effectively address the often-substantial exposure to air pollutants of indoor origin (e.g., emissions from cooking, cleaning, furnishings or the inhabitants themselves). Indoor organic compounds are of particular note, since their concentrations tend to be much larger than those outdoors and include species with known adverse health effects (e.g., carcinogens, teratogens, endocrine disruptors), as well as persistent organic pollutants and ozone reactive compounds.

How do buildings modulate exposures to outdoor particulate matter, outdoor ozone, and hazardous organic air pollutants, and what additional exposures are attributable to indoor sources? In other words, how different is the exposure that happens because we mainly breathe indoor air, not outdoor air? We contribute toward answering these broad questions by posing and commenting on three more focused questions.

Question 1. What chemical and physical transformations occur indoors that alter the form and composition of outdoor air pollution?

Airborne particles can span a diameter range covering about five orders of magnitude (0.001-100 μm). As outdoor particles penetrate building envelopes and deposit on indoor surfaces, the smallest (ultrafine) and largest (coarse) particles are removed to a greater extent than particles in the intermediate size range (fine).³⁻⁶ Hence, as illustrated in Figure 1, indoor particles of outdoor origin have a narrower distribution, centered about the most penetrating and persistent airborne particles. When inhaled indoors, a larger proportion of these fine particles can travel deep into

the respiratory tract. Being exposed to particles of outdoor origin while indoors shifts the pattern of deposition in the respiratory tract owing to the effect of size-selective filtering of buildings.

The chemical composition of particles also changes with transport from outdoors to indoors (Figure 1). Consider the partitioning of ammonia and nitric acid between the gas phase and particle-phase ammonium nitrate. Transport to indoors is accompanied by several factors that can each shift the gas-particle balance: change in temperature, loss of HNO₃ to indoor surfaces, and increased NH₃ from indoor sources. Altering the abundance of NH₄NO₃ in particles can shift particle pH. Also, given that outdoor and indoor relative humidity routinely differ, it is anticipated that the water content of outdoor airborne particles would change when transported indoors, which can also modify particle pH and size distribution. A change in pH can substantially influence the partitioning of acidic and basic gas-phase species to particulate water. In the change in pH can

Another chemical transformation that occurs with outdoor-to-indoor transport is the shift in the abundance and composition of semivolatile organic compounds (SVOCs) sorbed to airborne particles. ¹³⁻¹⁸ Certain SVOCs that are prominent in outdoor air, such as polycyclic aromatic hydrocarbons (PAHs), can desorb from outdoor particles transported indoors. ¹⁹ Other SVOCs, which are prominent indoors, can sorb to particles that are transported into buildings. Common examples of abundant indoor SVOCs are phthalate ester plasticizers, brominated flame retardants, and perfluorinated surfactants. ²⁰ Under conditions with minimal indoor particle emissions, particles of outdoor origin have been shown to quickly sorb indoor SVOCs, ¹⁶ resulting in larger mass fractions of particulate SVOCs indoors than outdoors. ¹⁷

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In summary, several features of indoor environments result in physical and chemical transformations such that indoor particles of outdoor origin differ meaningfully in size distribution and chemical composition from their outdoor precursors. Such changes might well influence the health consequences associated with inhaling them.

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Ozone reacts with surfaces it encounters as it is transported indoors and, subsequently, with compounds on exposed indoor surfaces. Ozone also reacts, to a lesser extent, in indoor air. The aggregate effect is that indoor ozone concentrations are commonly lower than those found outdoors. The reactions that consume ozone generate both gaseous and condensed-phase products. The indoor concentration of gas-phase reaction products can be larger than the indoor concentration of ozone itself.²¹⁻²³ Indoors, humans inhale both ozone of outdoor origin and indoor-generated oxidation products derived from outdoor ozone. Given the large fraction of time spent indoors, the amount of ozone inhaled indoors is approximately equal to ozone inhaled outdoors, and inhalation of products derived from outdoor ozone is comparable to or larger than the total inhalation of ozone itself.²¹⁻²³ Notably, there is a strong link between indoor moisture and the products of indoor ozone chemistry. As the indoor water vapor concentration increases, ozone reactions with skin oil constituents have been shown to yield fewer secondary ozonides, more carbonyls and an overall increase in gas-phase products. ^{24,25} Many studies address ozone's toxicity. However, the toxicity of many of its oxidation products is poorly characterized. This is especially true for stabilized Criegee intermediates, secondary ozonides, epoxides, and hydroperoxides. When considering ozone pollution and its health consequences, most studies

overlook the coincident indoor exposure to ozone-derived products and their potential contribution to the mortality and morbidity attributed to outdoor ozone.

Organic air pollutants that are almost exclusively gaseous outdoors partition between the gas phase and indoor surfaces, ²⁶ reflecting surface-to-volume ratios that are markedly larger indoors than outdoors. ²⁷ Sorption serves to reduce indoor exposure to outdoor organic pollutants during the peak of an outdoor episodic emission but extends the overall time of exposure to pollutants. The indoor mixture of organic air pollutants results from a combination of indoor and outdoor sources depending on ventilation and infiltration conditions. Importantly, there are many strong indoor sources of organic pollutants (e.g., buildings and their contents, cooking, cleaning, occupant metabolic emissions, personal care products, skin oil oxidation, consumer products, indoor combustion), resulting in indoor concentrations that are commonly an order of magnitude larger and chemically distinct from those outdoors (e.g., compounds emitted from vegetation, motor vehicles, solid fuel combustion, industry or fires). Coupled with the large fraction of time people spend indoors, inhalation of organic pollutants can be orders of magnitude larger indoors than outdoors and is generally dominated by indoor sources.

Question 2: How do building and human factors influence the nature and extent of modulation of air pollution exposures?

The *infiltration factor* quantifies the extent to which buildings are protective against airborne particles of outdoor origin. This term represents the indoor-to-outdoor particle concentration ratio when all indoor particles originate outdoors. The infiltration factor is controlled by loss processes that occur passively (deposition to surfaces) or by design (filtration in mechanical

ventilation systems). A central-tendency estimate for the infiltration factor of PM_{2.5} is 0.5 and studies report average values ranging from 0.3 to 0.8.²⁸ Buildings are much more effective at limiting the outdoor-to-indoor transport of ultrafine and coarse-mode particles.²⁹ Overall, in central tendency, buildings provide substantial but imperfect protection from outdoor particles. Furthermore, there is considerable variability in infiltration factors across the building stock.

Buildings are also protective against outdoor ozone exposure, largely because ozone reacts chemically with indoor surface materials. A compilation of empirical results studying the indoor/outdoor ratio for ozone in buildings without known indoor sources suggests a central tendency of about 0.25 with variation commonly spanning the range 0.1-0.6.^{23,30}

Important consequences ensue from the partial and variable protection provided by buildings against outdoor air pollution. In epidemiological studies, actual inhalation intake of outdoor air pollutants such as fine particles and ozone is lower than monitoring networks would indicate. Furthermore, exposures are variable across populations owing to differences in the factors that influence the degree of protection provided by buildings. For example, because of climate-associated variation in building design and operation, systematic spatial differences occur in the indoor-outdoor relationship of outdoor pollutants. Accounting for variability from location to location in air change rates, augmented by the fraction of time spent indoors, has partially explained observed regional differences in associated health effects for ozone, ²² PM_{2.5}, ³¹ and PM₁₀. ³² Furthermore, there can be systematic variation in infiltration factors in the buildings occupied by subpopulations, which may correlate with factors such as age, socioeconomic conditions, and health status.

Prominent epidemiologic and risk assessment studies commonly overlook the roles of buildings attenuating and modulating inhalation exposures of occupants. For example, Brauer et al.³³ did not account for attenuation in exposures associated with buildings in their extensive effort to estimate population exposures to outdoor PM_{2.5} and ozone for the Global Burden of Disease 2013 study. Burnett et al.³⁴ constructed an integrated exposure-response model for PM_{2.5}, synthesizing exposure and disease outcome information for "ambient air pollution, secondhand tobacco smoke, household solid cooking fuel, and active smoking." That effort neglected building-associated attenuation of outdoor air pollution exposure, therefore biasing the outcome. An assessment of how global mortality might shift with changes in outdoor PM_{2.5} concentrations likewise neglects the role of buildings as attenuators and modulators of exposure.³⁵ Efforts to incorporate the effects of buildings in health risk assessments for outdoor air pollution have been reported,^{36,37} but these issues have not yet taken root to influence major epidemiological studies.

The uneven ability to characterize exposures well may influence the outcomes of air-pollution epidemiology studies. For particles, the connection between PM_{2.5} and health effects understood through epidemiological studies is superior to the knowledge for health effects of ultrafine and coarse-mode particles. Part of the reason is that smoother spatial gradients occur outdoors for PM_{2.5}, which is largely secondary with a longer atmospheric persistence time than coarse-mode or ultrafine particles. Consequently, monitoring networks provide a more accurate representation of the spatial and temporal distribution of outdoor PM_{2.5} than would be possible for other particle size modes. Given that buildings generally provide a high degree of protection against ultrafine and coarse particles, combined with significant indoor sources of these modes, we are currently

in a state of near blindness about actual inhalation exposure to ultrafine and coarse particles. The same level of poor understanding applies to many of the pollutants for which indoor emissions are the dominant contributors to exposure, such as most organic pollutants.

Question 3: Which air pollutants have indoor sources leading to generally higher concentrations and exposures indoors than outdoors, and which of these may be particularly important for health?

The mix of indoor, outdoor, primary and secondary chemicals is modulated through buildings and the ways in which we construct and operate them. Since people spend ~70% of their time at home, we focus here on residences. Every home may have a unique combination of smells and activities, but in fact they have much in common that is generalizable. At their most basic, houses are boxes, constructed out of a relatively small range of materials, that exchange mass and energy with their surroundings. Buildings are operated to meet the requirements for thermal comfort and respiratory metabolism of their occupants. With global supply chains, there is more commonality in building materials and operations than might have been the case historically. Standardized building materials and furniture are now available worldwide from rapidly growing international vendors. Ventilation, filtration, and thermal comfort provisions are achieved through a few core technologies. Thus, whereas the nexus between outdoor environments, indoor air quality, and indoor exposure is richly complex, there are a core set of reasonably well-defined scientific principles and engineering tools with which to make generalizable progress.

To elaborate, notwithstanding the wide variety of buildings, sources, human occupancy, and activities, there is surprising commonality in indoor composition of organic chemicals in

residences.³⁸⁻⁴¹ Ample sources of VOCs and SVOCs cause their abundance in indoor air to be greatly enhanced above what is present in outdoor air for a broad suite of chemical classes. Typical sources include plastics and polymers (emitting plasticizers, flame retardants, antioxidants), pressed wood products (formaldehyde, organic acids), synthetic carpets (flame retardants, anti-stain agents, antioxidants), cleaning products, fragrances (terpenoids readily oxidized to undesirable products), appliances (flame retardants, particles, thermal greases, oils), other building materials, and common consumer products.⁴²⁻⁴⁸ Remarkably, it is now becoming recognized that the ventilation of these chemicals from indoor environments can make significant contributions to outdoor air pollutant loadings in cities.^{49,50}

Human beings are themselves potent mobile sources of volatile organic compounds (VOCs), inorganic compounds and particles in indoor environments. So-53 We shed skin flakes and microbes and we transfer skin oils to indoor surfaces. Several hundred bioeffluent VOCs are known to be emitted via breath and skin. Emissions of VOCs from personal care products are ubiquitous. In the presence of oxidants such as ozone, a multitude of chemical byproducts can be formed, some of which (e.g., 4-OPA) are known irritants. As well as innately emitting into their immediate environment, various human activities indoors, such as cooking, cleaning, smoking, have been shown to introduce large quantities of gases and particles to indoor air.

Indoor sources are uncommon (although not rare) for ozone and include devices that produce a corona discharge (e.g., electrostatic precipitators, photocopiers, and "ozone generators").⁵⁷ For particles, indoor sources are common and contribute substantially to exposures both acute and chronic, with differing impacts on immune system responses.⁵⁸⁻⁶¹ Among the prominent important indoor sources of particles are smoking⁶² and cooking.⁶³ Candle use has been

identified as an important source of indoor ultrafine particles.⁶⁴ Resuspension⁶⁵ and shedding⁶⁶ contribute to airborne coarse-mode particles indoors. While PM_{2.5} abundance inside residences is often lower than outdoors, during specific types of events (e.g., smoking, cooking, candle use), and via resuspension, much higher concentrations can occur indoors than outdoors.

Secondary sources of air pollutants can also be important indoors. Specifically, oxidation products from outdoor ozone infiltrating and reacting with alkenes on exposed indoor surfaces,⁶⁷ in skin oil, and in the gas-phase are ubiquitous. Reactions with terpenes and terpene alcohols used as scenting agents in a variety of indoor cleaners and "air fresheners" are common.⁴⁸ Additional reactions in the gas phase and on surfaces can occur sporadically because of occupant activities.^{68,69} Noteworthy examples include addition of oxidants such as hypochlorite in bleach and related products (chlorine chemistry), changing surface pH via cleaning with ammonia or vinegar, and changing surface moisture through intentional humidification. Oxidants such as OH and NO₃ are assumed to be at generally low concentrations indoors making them typically less important as sources of secondary organics than is the case outdoors during daytime.^{70,71}

Kirk Smith aptly advised, that to advance scientific understanding and improve the human condition, we need to "follow the risk". ⁷² Research is needed to determine which of the numerous organic chemicals or chemical classes found indoors may be particularly important as health risks. Among known candidates, PM_{2.5}, acrolein, and formaldehyde have been identified as accounting for the vast majority of DALY losses caused by indoor air pollutants, with impacts equal to or larger than those estimated for radon and secondhand tobacco smoke. ⁷³ In current morbidity and mortality studies, PM_{2.5} is assumed to be equitoxic, despite known dependencies on chemical composition. ⁷⁴ How indoor emissions and processes affect PM_{2.5} toxicity is a key

question for future research. Indoor sources of formaldehyde, as well as the health impacts of this smallest aldehyde, have been extensively studied. 75 Carcinogenic chemicals (e.g., benzene, benzo[a]pyrene (BaP), radon, nitrosamines) are another category of concern for indoor air exposure. ⁷⁶ Although PAHs may be elevated in outdoor particles, indoor combustion is also a source, including of the carcinogenic benzo(a)pyrene. Nitrous acid has been shown to react with nicotine and other third-hand smoke components to generate carcinogenic nitrosamines.⁷⁷ When chemicals enter the human body, some interact with our regulatory system disrupting the autoregulatory processes that rely on chemical signaling.^{78,79} More than 100,000 new chemicals have been introduced as constituents of commercial products in recent decades, including many used deliberately or inadvertently in indoor environments. 80,81 An emerging body of evidence suggests some widely used commercial chemicals are endocrine disruptors. 82,83 Some chemicals of concern as endocrine disruptors have substantially higher concentrations indoors compared to outdoors. Phthalates are a prime example. 17 Human exposures to semivolatile organic compounds are dominated by indoor environments both through inhalation and dermal uptake. 84,85 Diseases believed to be influenced by environmental exposures to endocrine disrupting chemicals have increased over time, including asthma, allergy, Alzheimer's disease, psychogenic processes, eating disorders, chronic obesity, and possibly autism. 86-88 While indoor exposure to many SVOCs that are suspected endocrine disruptors has increased, the clinical relevance of these indoor exposures and the molecular basis for increased adverse health risks

remain subjects for future multidisciplinary investigations.

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Challenges and opportunities at the nexus of outdoor air pollution, indoor environments and exposure.

Human exposure to harmful air pollutants results from a combination of outdoor and indoor sources. These are difficult to delineate since exposure occurs mostly indoors and especially within the home. Although outdoor measurements of ozone and PM_{2.5} are used to link air pollution to health effects, they are proxies for more complex chemical and physical processes that act at the intersection of outdoor air pollution, indoor environments and exposure.

Understanding these processes should be a research focus to ensure future wellbeing.

Global trends show that the world's population is migrating from the countryside to cities. By 2050, some 70% of humanity will live in urban areas. 89,90 This shift is occurring despite the per capita mortality rate attributable to air pollution being approximately 50% higher in urban than in rural areas. 91 The resulting increased demand for urban housing and potential for rising levels of outdoor pollutants including ozone 92 will likely lead to smaller living spaces and tighter structures in which indoor sources and chemical processing increase in importance. Lower indoor-outdoor air-change rates are also anticipated as housing becomes more energy efficient and heat exchange restricted. With continued warming of urban atmospheres, 93 air conditioning will become more prevalent. In some of the world's hottest regions, such as the Eastern Mediterranean and Middle East, home to over 400 million people, most already reside in urban areas where life without active cooling is barely tenable. 94 Therefore, it seems likely that future homes will tend to be increasingly isolated from the outside. Living and working conditions described by temperature, humidity, and chemical exposure will be more directly influenced by buildings and inhabitants. While effectively designed and operated mechanical ventilation

systems coupled with air-cleaning technologies can attenuate their impact, building occupants will remain susceptible to exposures that originate from pollutants emitted indoors.

Improvements in outdoor and indoor air quality can improve human health. Landrigan et al. 95 estimated that in 2015, polluted air was responsible for 6.4 million deaths and economic losses of US\$21 billion worldwide. Lowering urban and regional air pollution requires the concerted action of a population that possesses considerable societal inertia. The continued use of the outside atmosphere as a repository for pollutant emissions is therefore a lamentable but also likely future condition as a modern-day tragedy of the commons. 96 A further complication for air pollution control strategies is that the sources of outdoor PM2.5, which is our clearest link to premature mortality, vary considerably with location. In Asia, where most premature deaths attributed to air pollution occur, residential energy use for heating and cooking is a substantial source of emissions, while in Europe, parts of the USA, Russia and East Asia agriculture plays an important role, and in large sections of the USA traffic and power generation are dominant sources. 91

People have more direct control over their exposure indoors than outdoors, and this potential for control is especially germane in parts of the world that have serious outdoor air pollution issues, such as India and China. Opportunities to intervene exist, modifying building systems to deliberately reduce air pollution exposure and thereby improve occupant health. Activated carbon filters have been demonstrated to be effective in controlling ozone.⁹⁷ High-quality particle filters can substantially reduce indoor particle levels⁹⁸ and can be cost effective.⁹⁹⁻¹⁰¹ Intervention studies have documented improved outcomes for biomarkers of health through

building-level air-pollution mitigation, ^{102,103} although overall health improvements have been judged to be relatively modest compared to the substantial reduction in indoor PM using filtration. ¹⁰⁴ Nonetheless, building-level interventions can be applied with local control on a much faster time scale than interventions for improving outdoor air pollution.

As isolation of the home environment from outside air is common and likely increasing, architectural innovations have potential to play an important role in mediating chemical exposure between our lungs and the environment. Cleansing facilities and practices (e.g., doormats, shoe brushes, shoe removal) at the home entrance to limit importation of particles and chemicals into the home, efficient range hoods, transitioning from gas to electric stoves, use of lower emitting materials, frequent cleaning of clothing as protection from indoor exposure, and increased air cleaning via filtration of recirculated air in whole-house HVAC systems or portable units in selected rooms¹⁰⁴ are all possible adaptions. Such protective strategies can be adopted by individuals, even while community-wide emission reductions of outdoor pollutants are pursued.

Synthesis

- We highlight key points to consider when evaluating the influence of indoor environments on air pollution exposure:
 - Most of our inhalation of outdoor PM occurs indoors, and when indoors we are exposed
 preferentially to outdoor fine PM, the size range that is most efficient at penetrating deeply
 into our lungs.
- Buildings most effectively attenuate the ingress of outdoor ultrafine- and coarse-mode
 particles. Indoor sources can make large contributions to inhalation exposures of the smallest

- and largest particles. Epidemiological studies that rely on outdoor air concentrations have elicited consistent associations (but not demonstrated causation) between PM_{2.5} and adverse health outcomes. Studies that rely on outdoor concentrations as proxy measures of exposure are likely to be less successful in assessing health consequences of exposure to ultrafine and coarse mode particles.
- Inhalation of outdoor ozone occurs almost equally indoors and outdoors. Indoor inhalation of
 the products of indoor reactive chemistry initiated by ozone originating outdoors can be
 larger than the aggregate inhalation of ozone itself.
- The concentration of gas-phase organic compounds is commonly an order of magnitude larger indoors than outdoors. In part, this reflects contributions from scenting agents, cyclic and linear siloxanes, plasticizers, flame retardants, perfluorinated surfactants, pesticides and cooking emissions. Given the large fraction of time spent indoors, cumulative inhalation of gas-phase organics occurs at approximately two orders of magnitude higher daily rate from breathing indoor air rather than outdoor air.
- Outdoor PM_{2.5} transported indoors sorbs semivolatile organic compounds released from indoor sources. When inhaled, these particles carry the sorbed organics deeper into the respiratory tract than would be the case for the gas-phase counterparts.

Implications from our perspective include these three points:

- Science might be missing some of the important health consequences associated with air pollution by failing to properly understand how buildings modulate air pollution exposures.
- The apparently equitoxic nature of PM_{2.5} might reflect inadequate understanding of inhaled particle composition, in contrast to particle composition in outdoor air. Future studies that

- aim to elucidate the most health-harmful components of inhaled PM_{2.5} should take account of indoor modulation and modification of PM_{2.5} constituents.
- Indoor environments materially alter the link between outdoor air pollution and human

 exposure. Core elements of understanding were identified several decades ago, 105 but the

 lessons have not been widely learned. In failing to account for how indoor environments

 affect air pollution exposure, epidemiologists are overlooking critical elements needed to

 make the important transition from association to causation.

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References

- 1. Stanaway, J. D.; Afshin, A.; Gakidou, E.; et al. Global, regional, and national comparative
- risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or
- clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the
- 353 Global Burden of Diseases Study 2017. *Lancet*. **2018**, *392*, 1923–1994.
- 2. Klepeis, N. E.; Nelson, W. C.; Ott, W. R.; Robinson, J. P.; Tsang, A. M.; Switzer, P.; Behar,
- J. V.; Hern, S. C.; Engelmann, W. H. The National Human Activity Pattern Survey
- 356 (NHAPS): a resource for assessing exposure to environmental pollutants. *Journal of*
- Exposure Analysis and Environmental Epidemiology. 2001, 11, 231–252.
- 358 3. Long, C. M.; Suh, H. H.; Catalano, P. J.; Koutrakis, P. Using Time- and Size-Resolved
- Particulate Data to Quantify Indoor Penetration and Deposition Behavior. *Environmental*
- *Science & Technology.* **2001**, *35*, 2089–2099.
- 4. Riley, W. J.; McKone, T. E.; Lai, A. C. K.; Nazaroff, W. W. Indoor Particulate Matter of
- Outdoor Origin: Importance of Size-Dependent Removal Mechanisms. *Environmental*
- *Science & Technology.* **2002**, *36*, 200–207.

- 5. Thatcher, T. L.; Lunden, M. M.; Revzan, K. L.; Sextro, R. G.; Brown, N. J. A Concentration
- Rebound Method for Measuring Particle Penetration and Deposition in the Indoor
- Environment. Aerosol Science & Technology. 2003, 37, 847–864.
- 6. Rim, D.; Wallace, L.; Persily, A. Infiltration of Outdoor Ultrafine Particles into a Test House.
- 368 Environmental Science & Technology. **2010**, 44, 5908–5913.
- 7. Zhang, Q.; Jimenez, J. L.; Canagaratna, M. R.; Allan, J. D.; Coe, H.; Ulbrich, I.; Alfarra, M.
- R.; Takami, A.; Middlebrook, A. M.; Sun, Y. L.; Dzepina, K.; Dunlea, E.; Docherty, K.;
- DeCarlo, P. F.; Salcedo, D.; Onasch, T.; Jayne, J. T.; Miyoshi, T.; Shimono, A.; Hatakeyama,
- S.; Takegawa, N.; Kondo, Y.; Schneider, J.; Drewnick, F.; Borrmann, S.; Weimer, S.;
- Demerjian, K.; Williams, P.; Bower, K.; Bahreini, R.; Cottrell, L.; Griffin, R. J.; Rautiainen,
- J.; Sun, J. Y.; Zhang, Y. M.; Worsnop, D. R. Ubiquity and dominance of oxygenated species
- in organic aerosols in anthropogenically-influenced Northern Hemisphere midlatitudes.
- 376 Geophysical Research Letters. 2007, 34, L13801.
- 8. Lunden, M. M.; Revzan, K. L.; Fischer, M. L.; Thatcher, T. L.; Littlejohn, D.; Hering, S. V.;
- Brown, N. J. The transformation of outdoor ammonium nitrate aerosols in the indoor
- environment. *Atmospheric Environment*. **2003**, *37*, 5633–5644.
- 9. Nazaroff, W. W.; Weschler, C. J. Indoor acids and bases. *Indoor Air.* **2020**, *30*, 559–644.
- 381 10. Nguyen, J. L.; Schwartz, J.; Dockery, D. W. The relationship between indoor and outdoor
- temperature, apparent temperature, relative humidity, and absolute humidity. *Indoor Air*.
- **2014**, *24*, 103–112.
- 11. Collins, D. B.; Wang, C.; Abbatt, J. P. D. Selective Uptake of Third-Hand Tobacco Smoke
- 385 Components to Inorganic and Organic Aerosol Particles. *Environmental Science &*
- *Technology.* **2018**, *52*, 13195–13201.

- 12. DeCarlo, P. F.; Avery, A. M.; Waring, M. S. Thirdhand smoke uptake to aerosol particles in
- the indoor environment. *Science Advances*. **2018**, *4*, eaap8368.
- 13. Avery, A. M.; Waring, M. S.; DeCarlo, P. F. Seasonal variation in aerosol composition and
- concentration upon transport from the outdoor to indoor environment. *Environmental*
- 391 *Science: Processes & Impacts.* **2019**, *21*, 528–547.
- 392 14. Hodas, N.; Turpin, B. J. Shifts in the Gas-Particle Partitioning of Ambient Organics with
- Transport into the Indoor Environment. *Aerosol Science and Technology.* **2014**, *48*, 271–281.
- 15. Johnson, A. M.; Waring, M. S.; DeCarlo, P. F. Real-time transformation of outdoor aerosol
- components upon transport indoors measured with aerosol mass spectrometry. *Indoor Air*.
- **2017**, *27*, 230–240.
- 16. Lunderberg, D. M.; Kristensen, K.; Liu, Y.; Misztal, P. K.; Tian, Y.; Arata, C.; Wernis, R.;
- Kreisberg, N.; Nazaroff, W. W.; Goldstein, A. H. Characterizing Airborne Phthalate
- 399 Concentrations and Dynamics in a Normally Occupied Residence. *Environmental Science &*
- 400 *Technology.* **2019**, *53*, 7337–7346.
- 401 17. Lunderberg, D. M.; Kristensen, K.; Tian, Y.; Arata, C.; Misztal, P. K.; Liu, Y.; Kreisberg, N.;
- Katz, E. F.; DeCarlo, P. F.; Patel, S.; Vance, M. E.; Nazaroff, W. W.; Goldstein, A. H.
- 403 Surface Emissions Modulate Indoor SVOC Concentrations through Volatility-Dependent
- Partitioning. *Environmental Science & Technology*. **2020**, *54*, 6751–6760.
- 405 18. Meng, Q. Y.; Turpin, B. J.; Lee, J. H.; Polidori, A.; Weisel, C. P.; Morandi, M.; Colome, S.;
- Zhang, J.; Stock, T.; Winer, A. How Does Infiltration Behavior Modify the Composition of
- 407 Ambient PM_{2.5} in Indoor Spaces? An Analysis of RIOPA Data. *Environmental Science &*
- 408 *Technology.* **2007**, *41*, 7315–7321.

- 409 19. Naumova, Y. Y.; Offenberg, J. H.; Eisenreich, S. J.; Meng, Q.; Polidori, A.; Turpin, B. J.;
- Weisel, C. P.; Morandi, M. T.; Colome, S. D.; Stock, T. H.; Winer, A. M.; Alimokhtari, S.;
- Kwon, J.; Maberti, S.; Shendell, D.; Jones, J.; Farrar, C. Gas/particle distribution of
- polycyclic aromatic hydrocarbons in coupled outdoor/indoor atmospheres. *Atmospheric*
- 413 *Environment.* **2003**, *37*, 703-719.
- 20. Lucattini, L.; Poma, G.; Covaci, A.; de Boer, J.; Lamoree, M. H.; Leonards P. E. G. A review
- of semi-volatile organic compounds (SVOCs) in the indoor environment: occurrence in
- 416 consumer products, indoor air and dust. *Chemosphere*. **2018**, *201*, 466-482.
- 417 21. Weschler, C. J. Ozone's Impact on Public Health: Contributions from Indoor Exposures to
- Ozone and Products of Ozone-Initiated Chemistry. *Environmental Health Perspectives*.
- **2006**, *114*, 1489-1496.
- 420 22. Chen, C.; Zhao, B.; Weschler, C. J. Indoor Exposure to "Outdoor PM₁₀" Assessing Its
- Influence on the Relationship Between PM₁₀ and Short-term Mortality in U.S. Cities.
- 422 Epidemiology. 2012, 23, 870–878.
- 423 23. Yao, M.; Weschler, C. J.; Zhao, B.; Zhang, L.; Ma, R. Breathing-rate adjusted population
- exposure to ozone and its oxidation products in 333 cities in China. *Environment*
- 425 *International.* **2020**, *138*, 105617.
- 426 24. Arata, C.; Heine, N.; Wang, N.; Misztal, P. K.; Wargocki, P.; Bekö, G.; Williams, J.;
- Nazaroff, W. W.; Wilson, K. R.; Goldstein, A. H. Heterogeneous Ozonolysis of Squalene:
- 428 Gas-Phase Products Depend on Water Vapor Concentration. *Environmental Science &*
- 429 *Technology*. **2019**, *53*, 14441–14448.

- 430 25. Heine, N.; Houle, F. A.; Wilson, K. R. Connecting the Elementary Reaction Pathways of
- 431 Criegee Intermediates to the Chemical Erosion of Squalene Interfaces during Ozonolysis.
- 432 *Environmental Science & Technology.* **2017,** *51*, 13740–13748.
- 433 26. Wang, C.; Collins, D. B.; Arata, C.; Goldstein, A. H.; Mattila, J. M.; Farmer, D. K.;
- Ampollini, L.; DeCarlo, P. F.; Novoselac, A.; Vance, M. E.; Nazaroff, W. W.; Abbatt, J. P.
- D. Surface reservoirs dominate dynamic gas-surface partitioning of many indoor air
- constituents. Science Advances. 2020, 6, eaay8973.
- 437 27. Nazaroff, W. W.; Weschler, C. J.; Corsi, R. L. Indoor air chemistry and physics. *Atmospheric*
- 438 *Environment.* **2003**, *37*, 5451–5453.
- 439 28. Chen, C.; Zhao, B. Review of relationship between indoor and outdoor particles: I/O ratio,
- infiltration factor and penetration factor. *Atmospheric Environment.* **2011**, *45*, 275–288.
- 29. El Orch, Z.; Stephens, B.; Waring, M. S. Predictions and determinants of size-resolved
- particle infiltration factors in single-family homes in the U.S. *Building and Environment*.
- **2014**, *74*, 106–118.
- 30. Xiang, J.; Weschler, C. J.; Zhang, J.; Zhang, L.; Sun, Z.; Duan, X.; Zhang, Y. Ozone in urban
- China: Impact on mortalities and approaches for establishing indoor guideline
- 446 concentrations. *Indoor Air.* **2019**, *29*, 604–615.
- 447 31. Hodas, N.; Meng, Q.; Lunden, M. M.; Rich, D. Q.; Özkaynak, H.; Baxter, L. K.; Zhang, Q.;
- Turpin, B. J. Variability in the fraction of ambient fine particulate matter found indoors and
- observed heterogeneity in health effect estimates. *Journal of Exposure Science and*
- 450 *Environmental Epidemiology.* **2012**, *22*, 448–454.

- 451 32. Chen, C.; Zhao, B.; Weschler, C. J. Assessing the Influence of Indoor Exposure to "Outdoor
- Ozone" on the Relationship between Ozone and Short-term Mortality in U.S. Communities.
- 453 Environmental Health Perspectives. 2012, 120, 235–240.
- 454 33. Brauer, M.; Freedman, G.; Frostad, J.; van Donkelaar, A.; Martin, R. V.; Dentener, F.; van
- Dingenen, R.; Estep, K.; Amini, H.; Apte, J. S.; Balakrishnan, K.; Barregard, L.; Broday, D.;
- 456 Feigin, V.; Ghosh, S.; Hopke, P. K.; Knibbs, L. D.; Kokubo, Y.; Liu, Y.; Ma, S.; Morawska,
- L.; Sangrador, J. L. T.; Shaddick G.; Anderson, H. R.; Vos, T.; Forouzanfar, M. H.; Burnett,
- 458 R. T.; Cohen, A. Ambient Air Pollution Exposure Estimation for the Global Burden of
- 459 Disease 2013. *Environmental Science & Technology*. **2016**, *50*, 79–88.
- 460 34. Burnett, R. T.; Pope, C. A. III; Ezzati, M.; Olives, C.; Lim, S. S.; Mehta, S.; Shin, H. H.;
- Singh, G.; Hubbell, B.; Brauer, M.; Anderson, H. R.; Smith, K. R.; Balmes, J. R.; Bruce, N.
- G.; Kan, H.; Laden, F.; Prüss-Ustün, A.; Turner, M. C.; Gapstur, S. M.; Diver, W. R.; Cohen,
- A. An Integrated Risk Function for Estimating the Global Burden of Disease Attributable to
- Ambient Fine Particulate Matter Exposure. *Environmental Health Perspectives.* **2014**, *122*,
- 465 397–403.
- 466 35. Apte, J. S.; Marshall, J. D.; Cohen, A. J.; Brauer, M. Addressing Global Mortality from
- Ambient PM_{2.5}. Environmental Science & Technology. **2015**, 49, 8057–8066.
- 468 36. Ji, W.; Zhao, B. Estimating Mortality Derived from Indoor Exposure to Particles of Outdoor
- 469 Origin. *PLoS One.* **2015**, *10*, e0124238.
- 470 37. Azimi, P.; Stephens, B. A framework for estimating the US mortality burden of fine
- particulate matter exposure attributable to indoor and outdoor microenvironments. *Journal of*
- *Exposure Science and Environmental Epidemiology.* **2020**, *30*, 271–284.

- 473 38. Wallace, L. A.; Pellizzari, E. D.; Hartwell, T. D.; Sparacino, C.; Whitmore, R.; Sheldon, L.;
- Zelon, H.; Perritt, R. The TEAM Study: Personal Exposures to Toxic Substances in Air,
- Drinking Water, and Breath of 400 Residents of New Jersey, North Carolina, and North
- 476 Dakota. *Environmental Research*. **1987**, *43*, 290–307.
- 477 39. Weisel, C. P.; Zhang, J.; Turpin, B. J.; Morandi, M. T.; Colome, S.; Stock, T. H.; Spektor, D.
- 478 M.; Korn, L.; Winer, A.; Alimokhtari, S.; Kwon, J.; Mohan, K.; Harrington, R.; Giovanetti,
- R.; Cui, W.; Afshar, M.; Maberti, S.; Shendell, D. Relationship of Indoor, Outdoor and
- Personal Air (RIOPA) study: study design, methods and quality assurance/control results.
- Journal of Exposure Analysis and Environmental Epidemiology. **2005**, 15, 123–137.
- 482 40. Logue, J. M.; McKone, T. E.; Sherman, M. H.; Singer, B. C. Hazard assessment of chemical
- air contaminants measured in residences. *Indoor Air.* **2011**, *21*, 92–109.
- 41. Liu, Y.; Misztal, P. K.; Xiong, J.; Tian, Y.; Arata, C.; Weber, R. J.; Nazaroff, W. W.;
- Goldstein, A. H. Characterizing sources and emissions of volatile organic compounds in a
- 486 northern California residence using space- and time-resolved measurements. *Indoor Air*.
- **2019**, *29*, 630–644.
- 488 42. Levin, H. Building materials and indoor air quality. Occupational Medicine (Philadelphia,
- 489 *PA*). **1989**, 4, 667–693.
- 490 43. Hodgson, A. T.; Wooley, J. D.; Daisey, J. M. Emissions of Volatile Organic Compounds
- from New Carpets Measured in a Large-Scale Environmental Chamber. Journal of the Air &
- 492 *Waste Management Association.* **1993**, *43*, 316–324.
- 493 44. Hodgson, A. T.; Beal, D.; McIlvaine, J. E. R. Sources of formaldehyde, other aldehydes and
- terpenes in a new manufactured house. *Indoor Air.* **2002**, *12*, 235–242.

- 45. Hites, R. A. Polybrominated Diphenyl Ethers in the Environment and in People: A Meta-
- Analysis of Concentrations. *Environmental Science & Technology.* **2004**, *38*, 945–956.
- 497 46. Lamorena, R. B.; Jung, S.-G.; Bae, G.-N.; Lee, W. The formation of ultra-fine particles
- during ozone-initiated oxidations with terpenes emitted from natural paint. *Journal of*
- 499 *Hazardous Materials.* **2007**, *141*, 245–251.
- 500 47. Corsi, R. L.; Lin, C.-C. Emissions of 2,2,4-Trimethyl-1,3-Pentanediol Monoisobutyrate
- 501 (TMPD-MIB) from Latex Paint: A Critical Review. Critical Reviews in Environmental
- *Science and Technology.* **2009**, *39*, 1052–1080.
- 48. Nazaroff, W. W.; Weschler, C. J. Cleaning products and air fresheners: exposure to primary
- and secondary air pollutants. *Atmospheric Environment*. **2004**, *38*, 2841–2865.
- 49. McDonald, B. C.; de Gouw, J. A.; Gilman, J. B.; Jathar, S. H. Akherati, A.; Cappa, C. D.;
- Jimenez, J. L.; Lee-Taylor, J.; Hayes, P. L.; McKeen, S. A.; Cui, Y. Y.; Kim, S.-W.; Gentner,
- D. R.; Isaacman-VanWertz, G.; Goldstein, A. H.; Harley, R. A.; Frost, G. J.; Roberts, J. M.;
- Ryerson, T. B.; Trainer, M. Volatile chemical products emerging as largest petrochemical
- source of urban organic emissions. *Science*. **2018**, *359*, 760-764.
- 50. Li, M.; Weschler, C. J.; Bekö, G.; Wargocki, P.; Lucic, D.; Williams, J. Human Ammonia
- Emission Rates under Various Indoor Environmental Conditions. *Environmental Science &*
- 512 *Technology.* **2020**, *54*, 5419–5428.
- 51. Mochalski, P.; Unterkofler, K.; Teschl, G.; Amann, A. Potential of volatile organic
- compounds as markers of entrapped humans for use in urban search-and-rescue operations.
- 515 *Trends in Analytical Chemistry.* **2015**, *68*, 88–106.
- 516 52. Weschler, C. J. Roles of the human occupant in indoor chemistry. *Indoor Air.* **2016**, *26*, 6–
- 517 24.

- 53. He, J.; Zou, Z.; Yang, X. Measuring whole-body volatile organic compound emission by
- humans: A pilot study using an air-tight environmental chamber. *Building and Environment*.
- **2019**, *153*, 101–109.
- 54. de Lacey Costello, B.; Amann, A.; Al-Kateb, H.; Flynn, C.; Filipiak, W.; Khalid, T.;
- Osborne, D.; Ratcliff, N. M. A review of the volatiles from the healthy human body. *Journal*
- *of Breath Research.* **2014**, *8*, 014001.
- 524 55. Wisthaler, A.; Weschler, C. J. Reactions of ozone with human skin lipids: Sources of
- 525 carbonyls, dicarbonyls, and hydroxycarbonyls in indoor air. *Proceedings of the National*
- 526 Academy of Sciences of the U. S. A. 2010, 107, 6568–6575.
- 56. Anderson, S. E.; Franko, J.; Jackson, L. G.; Wells, J. R.; Ham, J. E.; Meade, B. J. Irritancy
- and Allergic Responses Induced by Exposure to the Indoor Air Chemical 4-Oxopentanal.
- 529 *Toxicological Sciences.* **2012**, *127*, 371–381.
- 530 57. Guo, C.; Gao, Z.; Shen, J. Emission rates of indoor ozone emission devices: A literature
- review. *Building and Environment*. **2019**, *158*, 302–318.
- 58. Bhangar, S.; Mullen, N. A.; Hering, S. V.; Kreisberg N. M.; Nazaroff W. W. Ultrafine
- particle concentrations and exposures in seven residences in northern California. *Indoor Air*.
- **2011**, *21*, 132–144.
- 59. Wallace, L. Indoor Particles: A Review. Journal of the Air & Waste Management
- *Association.* **1996**, *46*, 98–126.
- 60. Özkaynak, H.; Xue, J.; Spengler, J.; Wallace, L.; Pellizzari, E.; Jenkins, P. Personal Exposure
- to Airborne Particles and Metals: Results from the Particle TEAM Study in Riverside,
- California. *Journal of Exposure Analysis and Environmental Epidemiology.* **1996**, *6*, 57–78.

- 540 61. Morawska, L.; Afshari, A.; Bae, G. N.; Buonanno, G.; Chao, C. Y. H.; Hänninen, O.;
- Hofmann, W.; Isaxon, C.; Jayaratne, E. R.; Pasanen, P.; Salthammer, T.; Waring, M.;
- Wierzbicka, A. Indoor aerosols: from personal exposure to risk assessment. *Indoor Air.* **2013**,
- *23*, 462–487.
- 62. Semple, S.; Creely, K. S.; Naji, A.; Miller, B. G.; Ayres, J. G. Secondhand smoke levels in
- Scottish pubs: the effect of smoke-free legislation. *Tobacco Control.* **2007**, *16*, 127–132.
- 63. Abdullahi, K. L.; Delgado-Saborit, J. M.; Harrison, R. M. Emissions and indoor
- concentrations of particulate matter and its specific chemical components from cooking: A
- 548 review. *Atmospheric Environment*. **2013**, 71, 260–294.
- 64. Bekö, G.; Weschler, C. J.; Wierzbicka, A.; Karottki, D. G.; Toftum, J.; Loft, S.; Clausen, G.
- Ultrafine Particles: Exposure and Source Apportionment in 56 Danish Homes.
- *Environmental Science & Technology.* **2013**, *47*, 10240–10248.
- 65. Qian, J.; Peccia, J.; Ferro, A. R. Walking-induced particle resuspension in indoor
- environments. Atmospheric Environment. 2014, 89, 464–481.
- 66. Licina, D.; Tian, Y.; Nazaroff, W. W. Emission rates and the personal cloud effect associated
- with particle release from the perihuman environment. *Indoor Air.* **2017**, *27*, 791–802.
- 556 67. Deming, B. L.; Ziemann, P. J. Quantification of alkenes on indoor surfaces and implications
- for chemical sources and sinks. *Indoor Air.* **2020**, *30*, 914-924.
- 558 68. Weschler, C. J.; Carslaw, N. Indoor Chemistry. *Environmental Science & Technology*. **2018**,
- *52*, 2419–2428.
- 560 69. Abbatt, J. P. D.; Wang, C. The atmospheric chemistry of indoor environments.
- Environmental Science: Processes & Impacts. 2020, 22, 25–48.

- 562 70. Arata, C.; Zarzana, K. J.; Misztal, P. K.; Liu, Y.; Brown, S. S.; Nazaroff, W. W.; Goldstein,
- A. H. Measurement of NO₃ and N₂O₅ in a Residential Kitchen. *Environmental Science &*
- 564 *Technology Letters.* **2018**, *5*, 595–599.
- 565 71. Waring, M. S.; Wells, J. R. Volatile organic compound conversion by ozone, hydroxyl
- radicals, and nitrate radicals in residential indoor air: Magnitudes and impacts of oxidant
- sources. *Atmospheric Environment*. **2015**, *106*, 382–391.
- 568 72. Seelye, K. Q. Kirk Smith, Towering Figure in Environmental Science, Dies at 73. New York
- *Times.* **2020**, June 24.
- 570 73. Logue, J. M.; Price, P. N.; Sherman, M. H.; Singer, B. C. A Method to Estimate the Chronic
- Health Impact of Air Pollutants in U.S. Residences. *Environmental Health Perspectives*.
- **2012**, *120*, 216–222.
- 573 74. Tuomisto, J. T.; Wilson, A.; Evans, J. S.; Tainio, M. Uncertainty in mortality response to
- airborne fine particulate matter: Combining European air pollution experts. *Reliability*
- *Engineering and System Safety.* **2008**, *93*, 732–744.
- 576 75. Salthammer, T.; Mentese, S.; Marutzky, R. Formaldehyde in the Indoor Environment.
- 577 *Chemical Reviews.* **2010**, *110*, 2536–2572.
- 578 76. Loh, M. M.; Levy, J. I.; Spengler, J. D.; Houseman, E. A.; Bennett, D. H. Ranking Cancer
- Risks of Organic Hazardous Air Pollutants in the United States. *Environmental Health*
- 580 *Perspectives.* **2007**, *115*, 1160–1168.
- 581 77. Sleiman, M.; Gundel, L. A.; Pankow, J. F.; Jacob, P. III; Singer, B. C.; Destaillats, H.
- Formation of carcinogens indoors by surface-mediated reactions of nicotine with nitrous
- acid, leading to potential thirdhand smoke hazards. Proceedings of the National Academy of
- *Sciences of the U.S.A.* **2010**, *107*, 6576–6581.

- 585 78. Colborn, T.; vom Saal, F. S.; Soto, A. M. Developmental Effects of Endocrine-Disrupting
- Chemicals in Wildlife and Humans. *Environmental Health Perspectives*. **1993**, *101*, 378–
- 587 384.
- 588 79. Rudel, R. A.; Fenton, S. E.; Ackerman, J. M.; Euling, S. Y.; Makris, S. L. Environmental
- Exposures and Mammary Gland Development: State of the Science, Public Health
- Implications, and Research Recommendations. *Environmental Health Perspectives*. **2011**,
- 591 *119*, 1053–1061.
- 592 80. Weschler, C. J. Changes in indoor pollutants since the 1950s. *Atmospheric Environment*.
- **2009**, *43*, 156–172.
- 81. Wang, Z.; Walker, G. W.; Muir, D. C. G.; Nagatani-Yoshida, K. Toward a Global
- 595 Understanding of Chemical Pollution: A First Comprehensive Analysis of National and
- Regional Chemical Inventories. *Environmental Science & Technology*. **2020**, *54*, 2575–2584.
- 82. Rudel, R. A.; Perovich, L. J. Endocrine disrupting chemicals in indoor and outdoor air.
- 598 *Atmospheric Environment.* **2009**, *43*, 170–181.
- 83. Bornehag, C. G.; Nanberg E. Phthalate exposure and asthma in children. *International*
- *Journal of Andrology.* **2010**, *33*, 333–345.
- 84. Weschler, C. J.; Nazaroff, W. W. Dermal Uptake of Organic Vapors Commonly Found in
- Indoor Air. Environmental Science & Technology. 2014, 48, 1230–1237.
- 85. Salthammer, T.; Zhang, Y.; Mo, J.; Koch, H. M.; Weschler, C. J., Assessing Human
- Exposure to Organic Pollutants in the Indoor Environment. *Angewandte Chemie* –
- 605 *International Edition.* **2018,** *57,* 12228–12263.
- 86. Birnbaum, L. S. State of the Science of Endocrine Disruptors. *Environmental Health*
- 607 *Perspectives.* **2013**, *121*, a107-a107.

- 87. Schug, T. T.; Johnson, A. F.; Birnbaum, L. S.; Colborn, T.; Guillette Jr, L. J.; Crews, D. P.;
- Collins, T.; Soto, A. M.; vom Saal, F. S.; McLachlan, J. A.; Sonnenschein, C.; Heindel, J. J.
- Endocrine Disruptors: Past Lessons and Future Directions. *Molecular Endocrinology*. **2016**,
- *30*, 833–847.
- 88. Egusquiza, R. J.; Blumberg, B. Environmental Obesogens and Their Impact on Susceptibility
- to Obesity: New Mechanisms and Chemicals. *Endocrinology*. **2020**, *161*, 1–14.
- 89. United Nations, Department of Economic and Social Affairs, Population Division. World
- 615 Urbanization Prospects: The 2018 Revision. Report ST/ESA/SER.A/420. New York: United
- Nations. **2019**. https://population.un.org/wup/Publications/Files/WUP2018-Report.pdf
- 617 90. Zhang, Y.; Mo, J.; Weschler, C. J. Reducing Health Risks from Indoor Exposures in Rapidly
- Developing Urban China. *Environmental Health Perspectives*. **2013**, *121*, 751–755.
- 619 91. Lelieveld, J.; Evans, J. S.; Fnais, M.; Giannadaki, D.; Pozzer, A. The contribution of outdoor
- air pollution sources to premature mortality on a global scale. *Nature.* **2015**, *525*, 367–371.
- 621 92. Zhong, L.; Lee, C.-S.; Haghighat, F. Indoor ozone and climate change. *Sustainable Cities*
- 622 and Society. 2017, 28, 466–472.
- 93. McCarthy, M. P.; Best, M. J.; Betts, R. A. Climate change in cities due to global warming
- and urban effects. *Geophysical Research Letters*. **2010**, *37*, L09705.
- 625 94. Lelieveld, J.; Proestos, Y.; Hadjinicolaou, P.; Tanarhte, M.; Tyrlis, E.; Zittis, G. Strongly
- increasing heat extremes in the Middle East and North Africa (MENA) in the 21st century.
- 627 *Climatic Change.* **2016**, *137*, 245–260.
- 628 95. Landrigan P.J.; Fuller, R.; Acosta, N. J. R.; Adeyi, O.; Arnold, R.; Basu, N.; Bibi Baldé, A.;
- Bertollini, R.; Bose-O'Reilly, S.; Boufford, J. I.; Breysse, P. N.; Chiles, T.; Mahidol, C.;
- 630 Coll-Seck, A. M.; Cropper, M. L.; Fobil, J.; Fuster, V.; Greenstone, M.; Haines, A.;

- Hanrahan, D.; Hunter, D.; Khare, M.; Krupnick, A.; Lanphear, B.; Lohani, B.; Martin, K.;
- Mathiasen, K. V.; McTeer, M. A.; Murray, C. J. L., Ndahimananjara, J. D.; Perera, F.;
- Potočnik, J.; Preker, A. S.; Ramesh, J.; Rockström, J.; Salinas, C.; Samson, L. D.; Sandilya,
- K.; Sly, P. D.; Smith, K. R.; Steiner, A.; Stewart, R. B.; Suk, W. A.; van Schayck, O. C. P.;
- Yadama, G. N.; Yumkella, K.; Zhong, M. The *Lancet* Commission on pollution and health.
- 636 *Lancet.* **2018**, *391*, 462–512.
- 637 96. Hardin, G.; The Tragedy of the Commons. *Science*. **1968**, *162*, 1243–1248.
- 638 97. Shair, F. H. Relating Indoor Pollutant Concentrations of Ozone and Sulfur Dioxide to Those
- Outside: Economic Reduction of Indoor Ozone Through Selective Filtration of the Make-up
- 640 Air. ASHRAE Transactions. 1981, 87 (Part I), 116–139.
- 98. Ben-David, T.; Wang, S.; Rackes, A.; Waring, M. S. Measuring the efficacy of HVAC
- particle filtration over a range of ventilation rates in an office building. *Building and*
- 643 Environment. 2018, 144, 648–656.
- 99. Bekö, G.; Clausen, G.; Weschler, C. J. Is the use of particle air filtration justified? Costs and
- benefits of filtration with regard to health effects, building cleaning and occupant
- 646 productivity. *Building and Environment.* **2008**, *43*, 1647–1657.
- 647 100. Zhao, D.; Azimi, P.; Stephens, B. Evaluating the Long-Term Health and Economic
- Impacts of Central Residential Air Filtration for Reducing Premature Mortality Associated
- with Indoor Fine Particulate Matter (PM_{2.5}) of Outdoor Origin. *International Journal of*
- *Environmental Research and Public Health.* **2015**, *12*, 8448–8479.
- 651 101. Fisk, W. J.; Chan, W. R. Effectiveness and cost of reducing particle-related mortality
- with particle filtration. *Indoor Air.* **2017**, *27*, 909–920.

- 653 102. Day D. B.; Xiang, J.; Mo, J.; Li, F.; Chung, M.; Gong, J.; Weschler, C. J.; Ohman-
- Strickland, P. A.; Sundell, J.; Weng, W.; Zhang, Y.; Zhang, J. Association of Ozone
- Exposure With Cardiorespiratory Pathophysiologic Mechanisms in Healthy Adults. *JAMA*
- 656 Internal Medicine. 2017, 177, 1344–1353.
- 657 103. Cui, X.; Li, F.; Xiang J.; Fang, L.; Chung, M. K.; Day, D. B.; Mo, J.; Weschler, C. J.;
- Gong, J.; He, L.; Zhu, D.; Lu, C.; Han, H.; Zhang, Y.; Zhang J. Cardiopulmonary effects of
- overnight indoor air filtration in health non-smoking adults: A double-blind randomized
- crossover study. *Environment International.* **2018**, *114*, 27–36.
- 661 104. United States Environmental Protection Agency. Residential Air Cleaners: A Technical
- 662 Summary, 3rd Edition. Portable Air Cleaners, Furnace and HVAC Filters. Report EPA 402-F-
- 663 09-002. EPA Indoor Environments Division. July 2018.
- 664 105. Dockery, D. W.; Spengler, J. D. Indoor-Outdoor Relationships of Respirable Sulfates and
- Particles. *Atmospheric Environment*. **1981**, *15*, 335–343.

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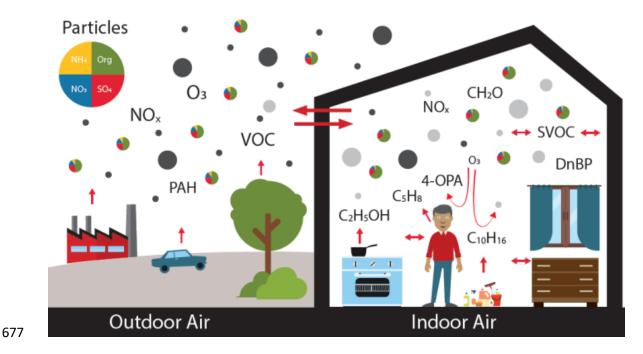


Figure 1. Schematic illustration of selected air pollutant transformations that occur between outdoor and indoor air. Pie charts indicate fine-mode particle composition (legend top left, following color scheme of Zhang et al.⁷). Note outdoor versus indoor differences in particle size distributions, particle composition, ozone, and sources. Solid black circles represent ultrafine-and coarse-mode particles of outdoor origin; buildings attenuate their outdoor-to-indoor transport. Solid light gray circles represent particles of indoor origin, some of which are transported outdoors. Ozone tends to have a much larger concentration outdoors than indoors (suggested by font size), reflecting reactions on indoor surfaces and in air that generate gaseous and condensed-phase products. Multiple indoor sources of organic compounds result in indoor concentrations much larger than those outdoors. Indoor organics partition among the air, airborne particles, room and human surfaces.