

Keynote: Indoor Air 2014

Indoor bioaerosol dynamics

Abstract Inhaling indoor air is the primary means by which humans are exposed to bioaerosols. Considering bacteria, fungi, and viruses, this study reviews the dynamic processes that govern indoor concentrations and fates of biological particulate material. Bioaerosol behavior is strongly coupled to particle size; this study emphasizes the range 0.1–10 μm in aerodynamic diameter. The principle of material balance allows concentrations to be determined from knowledge of important source and removal processes. Sources reviewed here include outdoor air introduced by air exchange plus indoor emission from occupants, occupant activities, and moldy materials. Important mechanisms that remove bioaerosols from indoor air include air exchange, deposition onto indoor surfaces, and active filtration. The review summarizes knowledge about size-dependent particle deposition in different regions of the respiratory tract, techniques for measuring indoor bioaerosols, and evidence for diseases caused by airborne exposure to bioaerosols. Future research challenges and opportunities are highlighted.

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Practical Implications

Bioaerosol exposure indoors is an important factor influencing human health. Understanding the dynamic behavior of biological particles can contribute to more incisive research to characterize exposure and associated health consequences. Such understanding is also essential in the design of effective engineering controls to reduce concentrations and to limit exposures.

Introduction

In our daily lives, we humans move through a sea of microbial life that is seldom perceived except in the context of potential disease and decay (Feazel et al., 2009).

It is by now well established that most humans spend most of their time indoors. Furthermore, it is also well known that the indoor environments occupied by humans contain abundant material of microbial origin. However, we have gained until now only partial understanding of the complexity and richness of the indoor microbiome and its significance for human well-being. While acknowledging the limitations, in this article, I

seek to summarize what is known or what can reasonably be inferred about an important subtopic of the microbiology of the built environment. The title 'indoor bioaerosol dynamics' is meant to imply that we seek a mechanistic, quantitative description of the processes and outcomes regarding the microbiology of the built environment, centering on what is, was, or will be airborne.

There are many reasons to be interested in the microbiology of the built environment. The context for this study derives from three primary concerns. First, exposure to bioaerosol material can cause or can contribute to many important diseases. Second, adverse

respiratory symptoms correlate well with indicators of indoor dampness (Fisk et al., 2007). It is a reasonable hypothesis, although not yet well established, that the underlying cause of these associations is microbial. Third, the microbiology of spaces we occupy may influence the human microbiome in ways that could confer health benefits. Evidence for this last point is admittedly thin. There is growing evidence that people influence the microbiology of the spaces they inhabit (e.g., Lax et al., 2014). Emerging evidence also indicates that some aspects of the human microbiome are important for health (Grice and Segre, 2012). We further know that aspects of our personal microbiome can be influenced by individual factors such as diet and illness. So, it is not a large stretch to imagine that elements of our personal microbiome that matter for health might in fact be influenced by attributes of the spaces we inhabit, including their microbiology generally and their bioaerosol aspects specifically. Hanski et al. (2012) reported evidence supporting an analogous suggestion: ‘rapidly declining biodiversity may be a contributing factor to ... the rapidly increasing prevalence of allergies and other chronic inflammatory diseases among urban populations. ...’

Following the introduction, the study is organized into two main sections. In ‘Framing the issues,’ I define a framework for considering indoor bioaerosol dynamics. That section also defines the scope and limitations of this study. It presents some empirical evidence about indoor bioaerosols to help establish a context for studying dynamics. The section outlines the use of a material balance as a first-principles method for linking process to outcome for indoor bioaerosols. The size of particles is described as a primary variable of concern. Regional deposition of bioaerosol particles in the respiratory tract is described as a process linking concentrations and exposure to dose. Opportunities and limitations for progress in understanding indoor bioaerosol dynamics are strongly influenced by measurement technology, so some of the key measurement methods are summarized. Evidence regarding infectious disease transmission by airborne routes is also assembled.

The second primary section (‘Dynamic processes’) summarizes available information on many important processes that affect the concentrations and fates of indoor bioaerosol particles. This section begins by reviewing the state of knowledge regarding building air exchange, an important removal mechanism for indoor bioaerosols and also a means by which outdoor bioaerosol particles are brought indoors. Then, the article proceeds to discuss several additional processes that can affect indoor bioaerosol levels: deposition onto room surfaces, bioaerosol intrusion from outdoor air, indoor emission sources, and other factors, including

bioaerosol control, airborne growth and decay, and indoor transport and mixing.

In the conclusion, important challenges facing further studies are described along with several opportunities for near-term progress advancing knowledge about indoor bioaerosol dynamics. Such progress is fundamental to efforts to better understand how the microbiome of indoor environments interacts with human health and well-being.

Framing the issues

Scope, limitations, and approach

Bioaerosols are usually defined as aerosols or particulate matter of microbial, plant or animal origin. ... Bioaerosols ... may consist of pathogenic or non-pathogenic live or dead bacteria and fungi, viruses, high molecular weight ... allergens, bacterial endotoxins, mycotoxins, peptidoglycans, $\beta(1\rightarrow3)$ -glucans, pollen, plant fibers, etc.—Douwes et al. (2003)

‘Bioaerosol’ is a contraction of ‘biological aerosol’, and ‘aerosol’ refers to a suspension of particles in a gas. The exact boundary for what should be included or excluded in the term ‘bioaerosol’ is challenging to define. For the purposes of this study, the central focus will be defined more narrowly. All microbes are included: viruses, bacteria, and fungi. Also included are microbe-associated chemicals such as endotoxins and mycotoxins. However, although they are part of bioaerosols, this article shall not explicitly address either pollen or pet- or pest-associated allergens such as cat dander or fecal pellets of dust-mites.

This review also emphasizes the human–bioaerosol nexus in indoor environments. The indoor environments to be considered are those ordinarily and commonly occupied by humans: residences, offices, schools, and other settings that are occupied a high proportion of the time, or in which occupant density is high. Not included are industrial environments that have high associated occupational exposure potential, such as those associated with food systems.

Much of the literature concerning microbiology in indoor environments focuses on dust as the sampled matrix (Rintala et al., 2012). Favoring this approach is that dust reflects a longer term average condition in the environment, whereas bioaerosols are more dynamically variable and therefore more challenging to sample in a manner that is representative of time-averaged conditions. The primary counterargument is that the relationship between dust and human exposure is much less clear than is the relationship between bioaerosol particles and inhalation exposure. Notwithstanding its prominence in the literature, the microbiological composition of indoor dust is not a primary focus of this study.

The overall approach employed in this review is to adapt and apply concepts from indoor aerosol science (e.g., as described in Nazaroff, 2004). In particular, material balance is utilized as a core principle. Particle size is a primary determinant of indoor bioaerosol behavior. We seek a mechanistic understanding because it provides a powerful basis for extrapolating from limited empirical evidence. We also seek to develop quantitative insight, because knowledge of the scale of processes and outcomes is essential as a basis for separating the important from the trivial. Some prior scholarly reviews cover similar topics (Burge, 1990; Douwes et al., 2003; Gregory, 1971; Spendlove and Fannin, 1983). However, none of these earlier reviews is as strongly grounded in indoor aerosol science as the present article.

Some empirical evidence

To provide context for the process-oriented discussion to follow, it is instructive to consider some of the important empirical evidence concerning indoor bioaerosols. In the summaries to follow, I highlight several field-sampling studies whose results provide important clues about bioaerosol concentrations, associated particle-size distributions, and potential influencing factors.

The largest published survey of indoor bioaerosol levels involved more than 12 000 fungi samples measured indoors and outdoors in ~ 1700 buildings in the United States (Shelton et al., 2002). The analysis was culture based, so the results reflect number concentrations of viable airborne spores. Little information was

reported on the sampling protocol; however, it seems likely that the measurements were based on short-term sample collection. Also, little information was reported about the buildings in which these measurements were taken. The cumulative probability distribution functions (Figure 1) show that the data are well fit by log-normal distributions. The geometric mean outdoor concentration (493 CFU/m^3) is about $6 \times$ higher than the geometric mean indoor concentration (79 CFU/m^3). The indoor levels show considerably broader range of concentration than do the outdoor levels (GSD of 5.5 compared to 3.3). These data support an important general finding that 'in the majority of cases, indoor fungal aerosols are controlled by outdoor concentrations' (Burge, 2002). Note that the ratio of geometric mean concentrations, 0.16, lies well within the range 0.04–0.46 predicted by Riley et al. (2002) to apply as the fraction of coarse-mode ($2.5\text{--}10 \mu\text{m}$) particles that would be found in indoor air when outdoor air was the sole source.

Culture-based analyses measure only a small portion of bioaerosols. Figure 2 presents data from a personal monitoring study of elementary school teachers in Finland (Toivola et al., 2004). For each of the 81 subjects, air was sampled through filters throughout two 24-h periods using personal sampling pumps. Particles were extracted from the filters and analyzed for both fungi and bacteria, using culture-based methods and also using microscope-assisted visual counting. A key point is that the total number concentrations of fungal spores and bacterial cells determined microscopically were a few orders of magnitude higher than the corresponding number concentrations of colony forming units, as determined by culture-based assessment. If

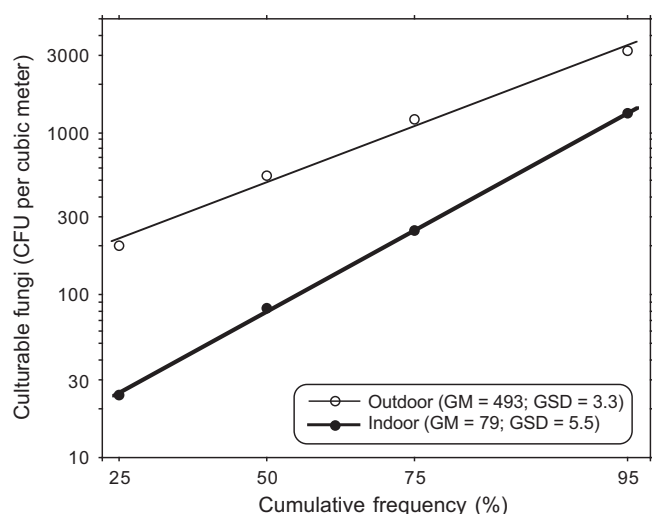


Fig. 1 Cumulative probability distribution of indoor and outdoor airborne concentrations of culturable fungi measured in 1717 US buildings (Shelton et al., 2002). In all, 9619 indoor and 2407 outdoor samples were collected during indoor air quality investigations

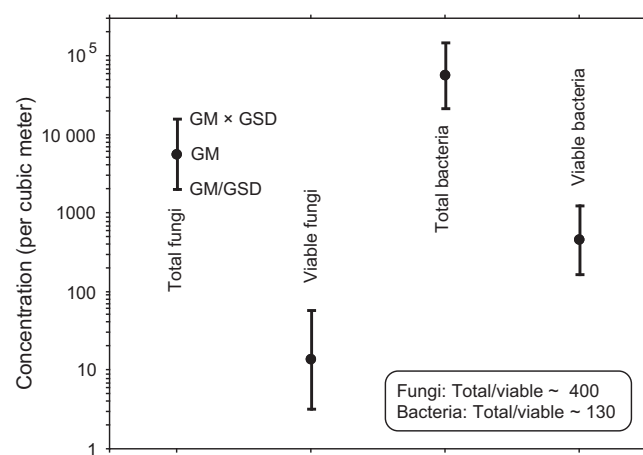


Fig. 2 Results from personal sampling of 81 elementary school teachers in eastern Finland (Toivola et al., 2004). For each subject, 24-h filter samples were collected twice during winter. Total fungi and bacteria were determined by microscopic analysis. Viable fungi and bacteria were evaluated by culture-plate assay. The ratios in the lower right box are based on geometric means (GM)

culture-based sampling methods only measure a tiny fraction of indoor bioaerosols and if what they do measure is not representative of what is airborne, then culture-based investigations cannot completely characterize indoor bioaerosol attributes that might influence human health and well-being.

Although it is common for fungi concentrations to be higher in outdoor air than indoors, in occupied spaces the reverse is commonly true for bacteria (Bartlett et al., 2004; Fox et al., 2005; Hospodsky et al., 2015). Figure 3 (Chen and Hildemann, 2009a) illustrates this point. The plotted results are geometric mean concentrations based on filter samples of 9–12 h duration collected inside and outside of ten occupied residences in California. Summing across all particle sizes, the GM level of endotoxin (associated with Gram-negative bacteria) was about 50% higher indoors than outside, whereas the GM level of (1–3)- β -D-glucans (a marker of fungi) in outdoor air was almost twice the corresponding indoor level.

An important point is that human occupancy and activities are major factors influencing indoor microbiology. Humans are important primary sources of certain bacteria and viruses. Even for fungi, for which humans do not appear to be a major primary source, human activities play an important role, for example, in shedding particulate matter from our clothing or in suspending settled dust that can contain materials of fungal origin. Figure 4 illustrates this point using samples collected in the same ten houses as discussed in connection with Figure 3. In this case, only indoor air

samples are considered. The ten houses are divided into two equal-sized groups, sorted according to degree of occupancy (Chen and Hildemann, 2009b). Occupancy is used here as a surrogate measure of the intensity of human activity. Across all measures displayed in the figure—that is, airborne concentrations of particulate matter, protein, endotoxin, and glucans—the geometric mean level in the high activity homes was considerably higher than in the low activity homes.

Measurement of airborne viruses in indoor environments has lagged behind measurement of bacteria and fungi. The recent development of quantitative polymerase chain reaction (qPCR) and other DNA-based measurement technologies has facilitated studies that measure pathogenic viruses in indoor air. Data from one study targeting the influenza A virus are presented in Figure 5. During the flu season, size-resolved particle samples were collected on filters in three different environment types: a day care center, a health center, and (three) airplanes. In all, 16 samples were collected by means of sampling at a rate of 9 l/min for periods of 6–8 h. Eight of these samples (50%) contained influenza A virus, with concentrations ranging from 5800 to 37 000 genomes per m³, and a substantial proportion of the detected virus was associated with fine particles (< 2.5 μ m) that can remain airborne for extended periods and that can also penetrate and deposit deeply in the respiratory tract when inhaled.

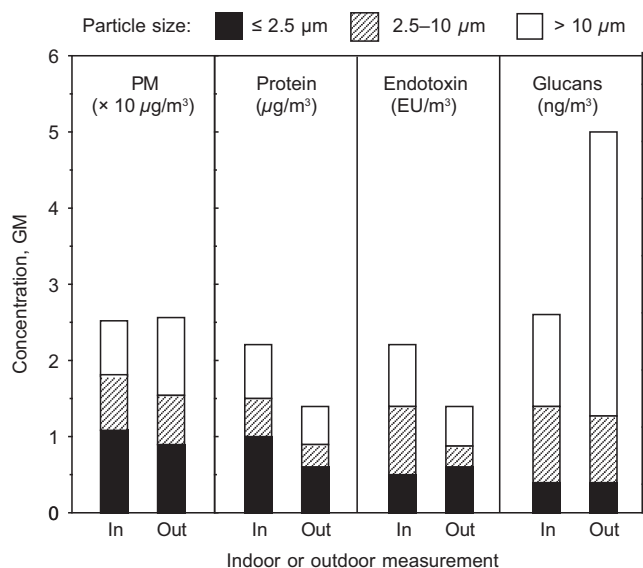


Fig. 3 Aerosol and bioaerosol parameters sampled inside and outside ten homes in northern California. At each house, 4 daytime samples were obtained (9–12 h each), using size-segregated, filter-based collection. Plotted results are the geometric mean concentrations for indoors ($N = 39-40$) and outdoors ($N = 20$). Data source: Chen and Hildemann (2009a)

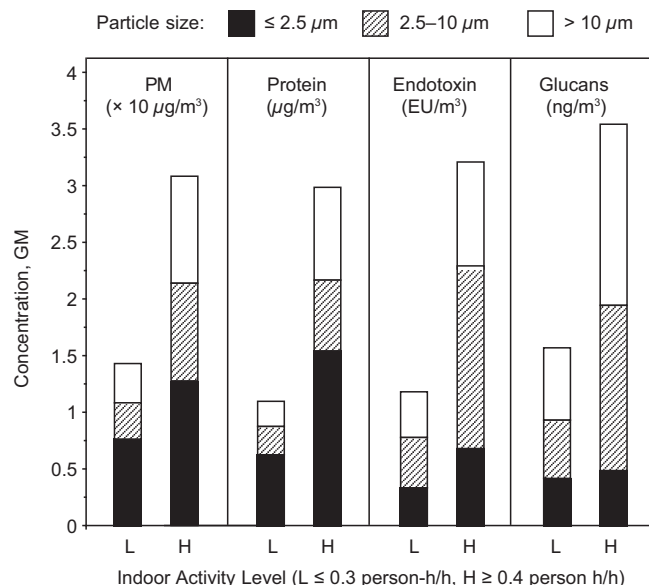


Fig. 4 Aerosol and bioaerosol parameters sampled inside ten homes in northern California. At each house, 4 daytime samples were obtained (9–12 h each), using size-segregated, filter-based collection. Houses were sorted into two groups according to the degree of occupancy in the living room during sampling. Data source: Chen and Hildemann (2009b)

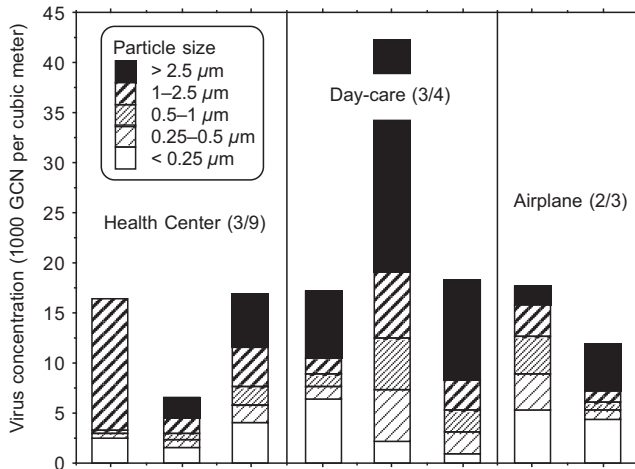


Fig. 5 Size-resolved influenza A virus concentrations measured in filter samples collected in indoor environments during the 2009–2010 flu season (Yang et al., 2011). In all, eight of sixteen samples collected (3 of 9 in a health center, 3 of 4 in a day care center, and 2 of 3 in an airplane) tested positive for influenza A. Abbreviation: GCN = genome copy number

Material balance

A fundamental principle that is usefully applied in quantitative, mechanistic studies of indoor environmental quality is material balance: Stuff is conserved. On a time-averaged basis, the sum of the rates of supply of a bioaerosol component to the indoor air must balance the sum of the rates of removal. This quantitative balance provides a basis for connecting rates of processes to concentrations of bioaerosol components.

Figure 6 presents schematic representations of indoor environments that can be used to formulate material balance equations. Consider a residential space (Figure 6a). In this representation, three processes can add bioaerosol material to the indoor air: (i) natural ventilation through designed openings (at rate $Q_N \times C_o$); (ii) infiltration through leaks in the building envelope ($p \times Q_L \times C_o$); and (iii) direct indoor emissions (E). (To the extent that tracked-in microbes contribute to the indoor bioaerosol load, this process would be included in the direct indoor emission term, E .) Three processes can remove bioaerosol material: (i) ventilation airflow out of the building ($[Q_N + Q_L] \times C$); (ii) filtration in the recirculating airflow ($\eta_R \times Q_R \times C$); and (iii) deposition onto room surfaces (βVC).

$$C \sim \frac{(Q_N + pQ_L) C_o + E}{Q_N + Q_L + \eta_R Q_R + \beta V} \quad (1)$$

Some important observations should be made about equation (1). First, the symbol ‘ $\sim$ ’ is used instead of an equal sign because the expression is only approximately true. Among the considerations that limit its strict

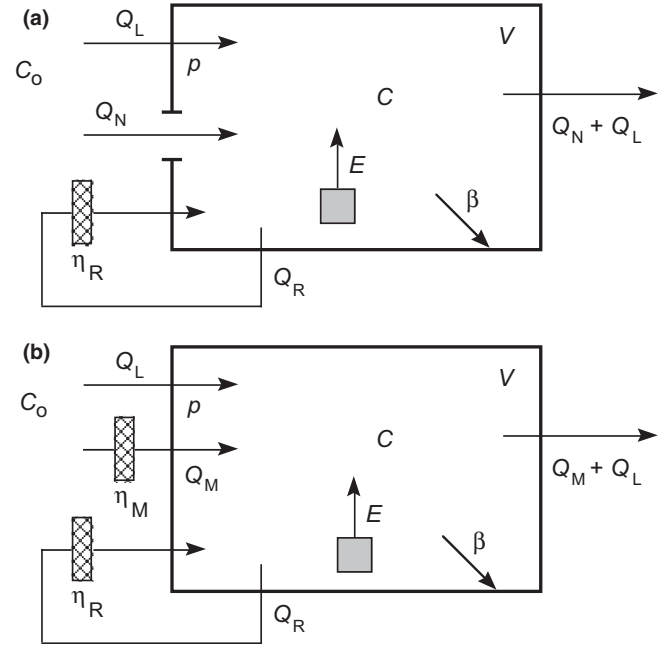


Fig. 6 Schematic representation of indoor environments for quantitatively relating influencing processes to resulting concentrations of bioaerosol parameters: (a) residence; (b) commercial building. Symbols (associated units) are as follows: C_o —outdoor concentration of bioaerosol parameter (quantity/m³); C —indoor concentration of bioaerosol parameter (quantity/m³); V —interior volume (m³); Q_N —natural ventilation rate (m³/h); Q_L —ventilation rate associated with infiltration (m³/h); Q_R —recirculation airflow rate (m³/h); Q_M —mechanical ventilation supply flow rate (m³/h); p —penetration efficiency of bioaerosol parameter associated with infiltration (—); η_R —single-pass filtration plus deposition efficiency in recirculating airflow (—); η_M —single-pass filtration plus deposition efficiency in mechanical ventilation supply flow (—); β —rate coefficient for deposition on indoor surfaces (h^{−1}); and E —emission rate from indoor sources (quantity/h)

applicability are that some of the parameters on the right-hand side are time dependent. If applied over short time intervals, one must also be concerned that accumulation, that is, the increase or decrease in the amount of bioaerosol in the indoor space, is not incorporated in equation (1). Also, on a time-averaged basis, the equation is only approximately correct because it does not account for the possibility that time-varying parameters may correlate in such a way that the average of the product is not the same as the product of the averages. A second key point is that some of the processes exhibit strong dependence on particle size. This aspect is addressed in detail in subsequent sections of the study. A third feature of this equation is that it implicitly assumes that the indoor space can be represented as well mixed. That is not always the case. Finally, the equation is specific to the particular schematic representation of the indoor environment depicted in Figure 6a. This configuration accommodates some common conditions in residences, such as air exchange by a combination of natural ventilation

(Q_N) and infiltration (Q_L), and the potential presence of a central air distribution system (with flow rate Q_R) for heating and cooling. On the other hand, the schematic and the resulting equation would need to be modified to accommodate mechanical ventilation.

For a commercial building space, the schematic representation in Figure 6b is more common, with mechanical ventilation (Q_M) and no natural ventilation. The appropriate material balance in this case is presented in equation (2). Similar caveats as in equation (1) apply.

$$C \sim \frac{[(1 - \eta_M) Q_M + p Q_L] C_o + E}{Q_M + Q_L + \eta_R Q_R + \beta V}. \quad (2)$$

Particle size

Most indoor airborne microbial material is found on particles in the diameter range 0.1–10 μm . This range of diameters corresponds to six orders of magnitude in particle mass. In part because of the large range, size is a major determinant of indoor airborne particle behavior (Nazaroff, 2004). The behavior of larger particles is strongly influenced by their mass. Gravitational settling and inertial impaction are important deposition mechanisms. The smaller particles in this size range follow airstreams more closely. Transport mechanisms leading to the departure of smaller particles from air streamlines include Brownian motion. Generally, the efficiency of filtration, the likelihood of deposition somewhere in the respiratory tract, and the rate of deposition onto indoor surfaces are all considerably smaller for particles with diameters in the range 0.1–1 μm as compared with particles with diameters in the range 1–10 μm .

Whole microbial agents vary widely in size and mainly follow this pattern: Viruses are much smaller than bacterial cells or endospores, which are smaller than fungal spores. For example, the influenza A virion is $\sim 0.1 \mu\text{m}$ in size (Noda, 2012). The cells of *Staphylococcus aureus*, a common opportunistic pathogenic species, have diameters of $\sim 1 \mu\text{m}$ (<http://textbookof-bacteriology.net/staph.html>). Common indoor fungal spores have been measured to have aerodynamic diameters of $\sim 1.8 \mu\text{m}$ (*Cladosporium cladosporioides*), $\sim 2.2 \mu\text{m}$ (*Aspergillus fumigatus*), and $\sim 2.7 \mu\text{m}$ (*Penicillium melinii*) (Reponen et al., 1996). Spores of other species such as *Alternaria alternata* and *Epicoccum nigrum* are considerably larger (McGinnis, 2007).

Bioaerosol particles can be larger or smaller than the size of whole microbial agents. For example, bacteria have been observed to occur in clusters or attached to other material such as fragments of human skin (Davies and Noble, 1962). Fungal fragments have also been measured in indoor air (Górny et al., 2002). Based on samples of outdoor air, Yamamoto et al.

(2014) found that the geometric mean size of fungal DNA associated with particular taxa was considerably larger than individual cultured spores.

Theoretical and experimental evidence support an expectation that microbial airborne particles behave similarly to abiotic particles of the same aerodynamic size. Consequently, powerful tools and theories from aerosol mechanics can be applied to study indoor bioaerosols.

Respiratory tract deposition

For bioaerosol particles, arguably the most important exposure pathway is inhalation followed by deposition in the respiratory tract. The probability of deposition varies with particle size, with lung morphology, and with breathing characteristics. Figure 7, which is based on semi-empirical modeling originally developed for radiological protection (Yeh et al., 1996), illustrates some of these features. In these model calculations, the respiratory tract is divided into three zones: the head region (NOPL), the tracheobronchial or conducting airways (TB), and the pulmonary or gas-exchange region (P). The information presented in this figure reflects two dominant characteristics of the system. First, the three regions of the respiratory tract are exposed to bioaerosol particles sequentially. For the largest particles considered, the high deposition effi-

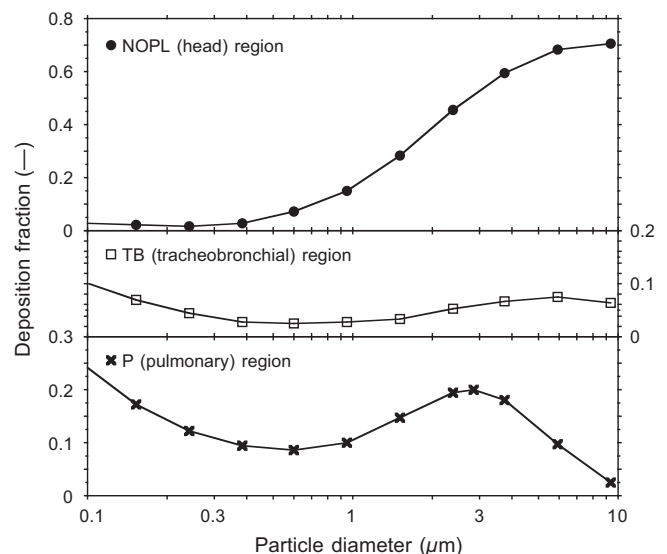


Fig. 7 Fractional particle deposition in different regions of the respiratory tract in relation to particle size. The results are from the NCRP/ITRI semi-empirical model (Yeh et al., 1996). Particle density is assumed to be 1 g/cm^3 . The results assume nose breathing, tidal volume of 0.77 l, breathing frequency of 13/min, and a functional residual capacity of 3 l. In each frame, the deposition fraction is referenced to particle concentrations in the inhaled air. Total deposition fraction in the respiratory tract for a given particle size would be obtained by summing results for the three regions

ciency in the head protects the distal airways from exposure. Second, two different mechanism classes control particle deposition. The behavior of the larger particles is dominated by their inertia. Larger particles have a higher mass-to-drag ratio, and so the larger the particle, the more efficient the deposition. However, for submicron particles, inertial processes are relatively unimportant. For the smallest particles in this figure, Brownian diffusion is the dominant transport mechanism. This is a slow process, important only in the smallest airways: Deposition efficiency of 0.1–1 μm particles is small in the head region, yet substantial in the pulmonary region. Similarly, the deposition efficiency increases with decreasing particle size when Brownian diffusion dominates.

Worth noting is that the combination of these effects leads to two important modes of particle deposition in the pulmonary region. Not only are the smallest particles deposited with reasonable efficiency, but there is also an important mode that peaks in efficiency at about 3 μm in diameter, a size that is important for bacterial and fungal bioaerosol particles.

Measurement technologies

Measure what is measurable, and make measurable what is not so.—Galileo Galilei

Many important aspects of indoor bioaerosols must be determined by experiment rather than from theory. Experimental capabilities are intrinsically linked to technologies available for measurement. While many methods have been developed for mea-

suring bioaerosol attributes, the availability of suitable methods remains an important constraint on research progress.

Table 1 provides a summary of many methods that have been used for bioaerosol sampling and analysis. (See also the reviews by Henningson and Ahlberg, 1994 and Verreault et al., 2008). The most widely applied methods have been culture based. These are subject to the limitations noted in connection with Figure 2. Culture-based methods offer the virtues of being relatively inexpensive, well developed, quantitative, and taxon specific. Disadvantages include that only viable organisms are measured and only a subset of airborne organisms is culturable. A commonly employed method of direct impaction onto an agar substrate utilizes a short sampling period, which provides only a snapshot of the viable organism concentration at the time of sampling. Relating these results to longer term exposure conditions is challenging because of the high degree of temporal variability, for example, associated with occupancy and occupant activities.

Effective bioaerosol sampling and analysis for studies of indoor environmental conditions must address two key challenges: specificity and temporality. No method is well suited to address both of these challenges well. The nature and significance of these issues varies according to the specific concern. In studies of airborne infection, specificity is essential. Pathogenic strains may be closely related to nonpathogenic organisms of the same species.

Some of the chemical analytes that can be used in bioaerosol studies are of interest because of their direct

Table 1 Analytical methods applied for studying indoor bioaerosols

Method/Analyte	Comment	References
Culture based	Most indoor bioaerosol data have been collected in this manner; limited to culturable species and (typically) short-term sampling	Shelton et al. (2002); Tsai and Macher (2005); Tsai et al. (2007)
Microscopy	Labor intensive but can generate high-quality results; combine with staining to highlight features such as metabolic competence	Hernandez et al. (1999)
Quantitative PCR	Suitable for quantification of total fungal DNA or total bacterial DNA using universal probes and primers	Hospodsky et al. (2010)
High-throughput DNA sequencing	Characterize bacterial and fungal taxa using PCR-amplified DNA abundance employing universal probes and primers	Pitkäranta et al. (2008); Noris et al. (2011); Hospodsky et al. (2012); Hoisington et al. (2014)
Metagenomic DNA sequencing	Construct genetic sequencing information for bioaerosol without amplification; has required large volumes of air to collect sufficient DNA	Yooseph et al. (2013)
Endotoxin	Lipopolysaccharide cell wall component of the outer membrane of Gram-negative bacteria	Park et al. (2001)
Beta glucans	Glucose polymers found in cell wall of most fungi and some bacteria	Douwes (2005)
Ergosterol	Analog of cholesterol, found in fungi, but not plants or animals; suitable for total airborne characterization of fungi, not species specific	Miller and Young (1997)
3-Hydroxy fatty acids	Chemical marker of lipopolysaccharide in Gram-negative bacteria	Fox et al. (2005); Liu et al. (2000)
N-acetylhexosaminidase (NAHA)	Fungal enzyme	Rylander et al. (2010)
Muramic acid	Derivative of glucosamine, found in bacterial cell walls	Fox et al. (2003)
Fluorescence of airborne particles	Real-time capability, but not biologically specific	Bhangar et al. (2014)
Quantitative reverse-transcriptase polymerase chain reaction	Airborne viruses such as influenza A	Fabian et al. (2009); Yang et al. (2011)

potential for adverse health consequences. Examples include endotoxin and (1→3)-β-D-glucans. Other analytes, such as ergosterol or muramic acid, are not of direct health concern, but rather can be valuable as quantitative indicators of broad bioaerosol categories.

Dynamic processes can influence indoor bioaerosol concentrations by an order of magnitude or more over time scales that are as short as minutes. Consequently, it is important to have measurement tools that permit sampling and analysis with high time resolution. There are no methods for bioaerosol sampling and analysis that are suitable for routine research application, that are highly specific, and that exhibit good time resolution. Because of these limitations, process-oriented studies that are discussed in the next section have largely used abiotic particles as surrogates. The recent advent of real-time fluorescence-based instruments enhances capabilities for studying dynamic behavior of bioaerosols. These instruments offer excellent time and size resolution, but typically provide no biological specificity, even at the level of differentiating between bacteria and fungi.

Diseases associated with bioaerosol exposure

...there is a growing body of data in support of the conclusion that air transmission within enclosed spaces plays an important role in the communication of many bacterial and viral diseases, especially those of the respiratory tract.—Robertson (1943)

There are two noteworthy points to make about the quote from Robertson: (i) It was published more than 70 years ago and (ii) the role of airborne routes in the transmission of disease remains controversial today for many infectious agents. Table 2 provides a list of many diseases for which there is published evidence indicating that airborne exposure indoors makes a meaningful contribution to the occurrence or spread of disease.

Dynamic processes

This section summarizes evidence concerning the dynamic processes that influence indoor bioaerosol levels. The emphasis is on those processes depicted schematically in Figure 6.

Air exchange: source and sink

Building air exchange is the replacement of indoor air with outdoor air. Air exchange is needed to limit the accumulation of carbon dioxide and other bioeffluents from human occupants. It is also used to limit the concentrations of pollutants emitted from inanimate indoor sources. When outdoor air is uncontaminated, then increasing the air exchange rate consistently improves indoor air quality. However, when climate conditions are not comfortable, then the air exchange rate is limited to avoid excessive energy use. In many circumstances, outdoor air is polluted to levels that exceed health-based standards. In these cases, by introducing pollutants from outdoor air, air exchange can be an important contributor to indoor pollution.

Building air exchange may be divided into three modes: Infiltration refers to the uncontrolled leakage of air through the building envelope; natural ventilation occurs through windows and other designed openings; and fans induce mechanical ventilation. Buildings generally leak, so infiltration is regularly a contributor to air exchange. Although practices vary and are changing with time, it is common in the United States for air exchange in single-family dwellings to occur by a combination of natural ventilation plus infiltration. Mechanical ventilation plus infiltration is common in commercial buildings.

The air exchange rate (AER) is an important metric for characterizing air quality aspects of buildings. This measure is the volume-normalized flow rate of air from the building to outdoors. As depicted in Figure 6, the AER would be $(Q_N+Q_L)/V$ for the residential sche-

Table 2 Some diseases for which a contribution to transmission is associated with indoor bioaerosols

Disease	Microbial agent	Taxa	Reference
Chickenpox	Varicella zoster virus	Virus	Gustafson et al. (1982)
Cold (common)	Rhinovirus	Virus	Heikkinen and Järvinen (2003)
Gastroenteritis	Norovirus	Virus	Marks et al. (2003)
Influenza	Influenza virus A	Virus	Tellier (2009)
Legionnaires' disease	Legionella pneumophila	Bacteria	Fields et al. (2002)
Measles	Measles virus	Virus	Bloch et al. (1985)
Pneumonia	Streptococcus pneumoniae	Bacteria	Hoge et al. (1994)
Pulmonary disease	Non-tuberculous mycobacteria (NTM)	Bacteria	Thomson et al. (2013)
SARS	SARS coronavirus	Virus	Yu et al. (2004)
Smallpox	Variola major or Variola minor	Virus	Wehrle et al. (1970)
Staphylococcal infection	Staphylococcus aureus	Bacteria	Mortimer et al. (1966)
Tuberculosis	Mycobacterium tuberculosis	Bacteria	Riley (1974)
Whooping cough	Bordetella pertussis	Bacteria	Warfel et al. (2012)

matic (i) and $(Q_M + Q_L)/V$ for the commercial schematic (ii). Figure 8 presents a summary of AER data from two large studies conducted in the United States. The measurements in residences (Figure 8a) show a median in the approximate range of 0.5–1 per hour. Considering individual households, most of the data lie within a

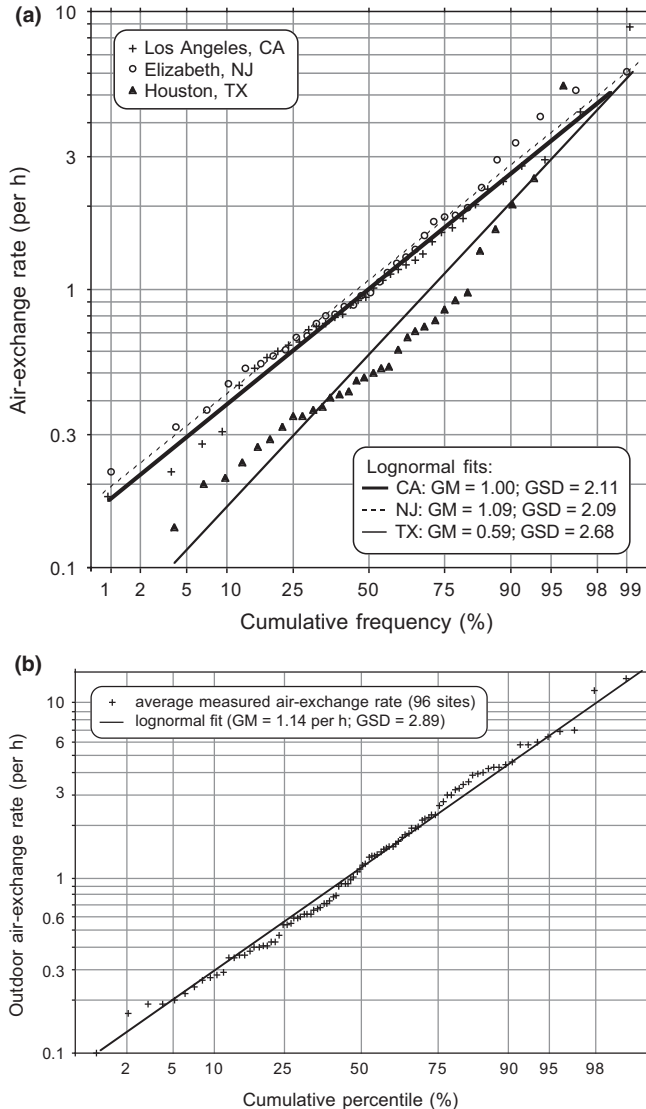


Fig. 8 (a) Air exchange rates (AER) measured in samples of houses in Los Angeles, CA ($N = 105$), Elizabeth, NJ ($N = 96$), and Houston, TX ($N = 100$). For each house, one or two measurements of air exchange rate were taken over a few-day period using perfluorocarbon tracers. Analysis is based on treating each house as a single unit; in cases where two AER measurements were taken, the results were averaged. Yamamoto et al. (2010) have also published an analysis of these data. (Data source: <https://riopa.aer.com/login.php>). (b) Air exchange rates (AER) measured in 96 US commercial buildings during the US Environmental Protection Agency's BASE Study. At each site, up to four determinations of outdoor AER were made over periods of several hours each, while the building ventilation system was operating. All measurements for any given site were averaged; the distribution of the averaged results is presented in the figure. (Data source: Persily and Gorfain, 2008)

range that spans about an order of magnitude, from 0.2 to 3 per hour. The BASE study of ~ 100 commercial buildings (Figure 8b) shows a similar central tendency and a somewhat larger range, especially at the high end of the distribution. Each of these data sets conforms reasonably well to a lognormal distribution.

The AER sets a time scale for one of the main removal processes for impurities in indoor air. An AER of 0.5–1 per hour means that any airborne species removed primarily by air exchange will have a characteristic residence time of one to two hours in the building air.

Bioaerosol deposition onto room surfaces

Across the aerodynamic diameter range of 0.1–10 μm , particle deposition onto room surfaces is an important fate. In equations (1) and (2), the deposition loss rate is parameterized by a size-dependent rate constant, β . The importance of deposition as a removal mechanism for airborne bioaerosol particles can be explored by comparing β to the air exchange rate.

Figure 9 presents some data on size-dependent particle loss rates by means of deposition to room surfaces. These data show that, for particles in the size range 0.5–1 μm , the deposition loss rate coefficient is ~ 0.2 –0.3 per hour, a value that is comparable to the lower end of range of air exchange rates discussed in the previous subsection. Under low air exchange conditions, deposition of these submicron particles is competitive with air exchange as a removal process, but in indoor

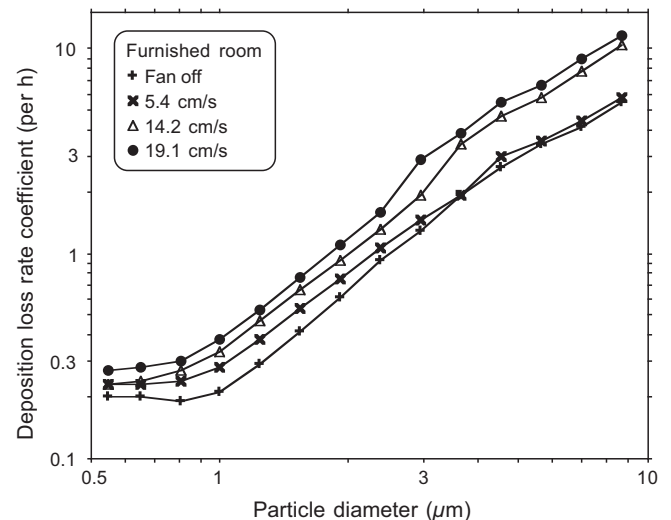


Fig. 9 Particle deposition loss rate coefficient (β) measured in a 14-m³ room as a function of particle diameter. Three of four experiments were conducted with four small fans operating to induce different degrees of air motion. As noted in the key, the mean measured speed in the room with the fans on ranged between 5.4 and 19.1 cm/s. The room was furnished with carpeting, chairs, table, bookcase, and curtains. Source: Thatcher et al. (2002)

spaces with high air exchange rates, deposition of these smaller particles is less important than air exchange. For larger particles, in the range 3–10 μm in diameter, the deposition loss rate coefficient is much higher, in the range 2–10 per hour. For these larger particles, deposition is an important mechanism influencing the fate of bioaerosols even for buildings with relatively high air exchange rates.

The data in Figure 9 also illustrate that enhanced air movement increases the rate of particle deposition, at least over the range of conditions studied (up to air speeds of about 20 cm/s). The effect of such air movement is to more rapidly deliver particles to surfaces to which they deposit. These air speeds are too low to cause particles to be resuspended from surfaces onto which they had previously deposited.

Most of the particle loss reflected in Figure 9 is attributable to gravitational settling onto upward facing surfaces. However, some deposition also occurs to vertical and even downward facing surfaces. Figure 10 shows results from a study that measured particle deposition to chamber walls under stirred conditions. The deposition velocity, plotted on the vertical axis of the figure, multiplied by the airborne concentration yields the deposition flux. So, for example, if we consider as a typical indoor air value for viable fungal spores of 80 CFU/m³ (Figure 1) and assume they are associated with 6- μm particles for which the deposition velocity is 30 mm/h (= 0.03 m/h), then the resulting deposition flux to vertical walls would be

$80 \times 0.03 = 2.4 \text{ CFU/m}^2/\text{h}$. This process would represent a small contribution to the total loss rate of fungi from indoor air, but could be an important step in the process of fungal colonization of walls. Such colonization would also require sufficient quality and quantity of nutrients, appropriate surface pH, and sufficient water activity in the substrate (Pasanen et al., 1992).

Bioaerosol sources: outdoor air

...the atmosphere is thronged with travellers: microbes using the wind, speaking teleologically, as a convenient transport from one place to another. Travellers mostly performing quite short journeys.—
Gregory (1971)

It is worthwhile to differentiate among the sources that contribute to indoor bioaerosols. Such differentiation can improve the basis for understanding concentrations, exposures, and influencing factors. It also serves as a basis for engineering interventions to alter exposures.

Among the major categories that can contribute to indoor bioaerosols is air exchange-induced supply from outdoor air. From equations (1) and (2), the rate of supply of bioaerosol material from outdoors is represented either by the term $(Q_N + pQ_L)C_o$ (for the residential schematic, Figure 6a) or by the term $[(1-\eta_M)Q_M + pQ_L]C_o$ (for the commercial building schematic, Figure 6b). We have discussed the various air exchange flow rates and—to an extent—the outdoor bioaerosol concentration, C_o . The new terms to address here are the fractional penetration of bioaerosols along with infiltration flow, p , and the efficiency of bioaerosol particle removal in the mechanical ventilation supply flow, η_M . An important point is that both of these efficiency terms are expected to exhibit significant particle-size dependence. Consequently, the relationship between outdoor bioaerosol concentrations and the source of indoor bioaerosols can vary with particle size.

The main principles that govern p and η_M are well understood. However, evaluation of proper values of these parameters for any particular building remains a challenge because uncontrolled and unknown details of construction and operation can influence the outcomes.

Consider particle penetration through leakage paths. As air flows into a building through a leak in the envelope, particles suspended in that airstream may contact a surface bounding the leak, adhere, and be lost from the airstream. The penetration factor, p , represents that portion of particles in the outside air that make it through the leaks to enter the indoor environment. Large particles may deposit because of gravitational settling or inertial impaction. Small particles may deposit because of Brownian motion. Figure 11 presents the results of model calculations showing how the

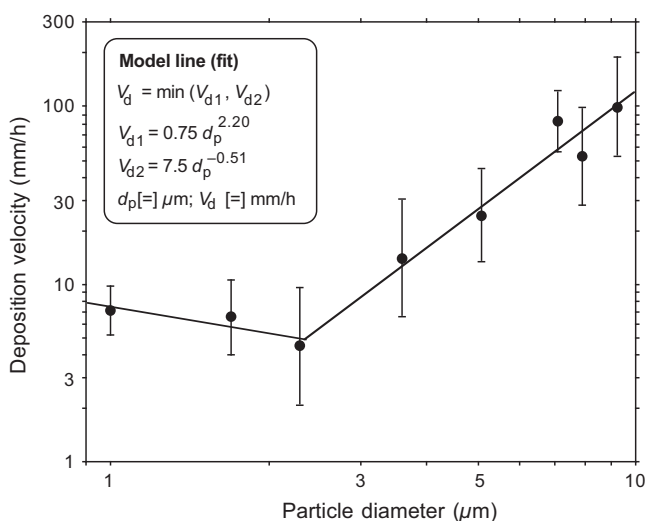


Fig. 10 Deposition velocity (v_d) measured to the vertical wall of a 2-m³ chamber as a function of particle diameter (d_p) (Lai and Nazaroff, 2005). The deposition velocity is linked to the loss rate coefficient as follows: $\beta_w = v_d S_w/V$, where β_w is the contribution to the total loss rate coefficient attributable to deposition on the walls (h^{-1}), S_w is the wall area, and V is the room volume. The model equations are linear regressions to the log-transformed data, utilizing three measured points (v_{d1}) and six measured points (v_{d2}), respectively

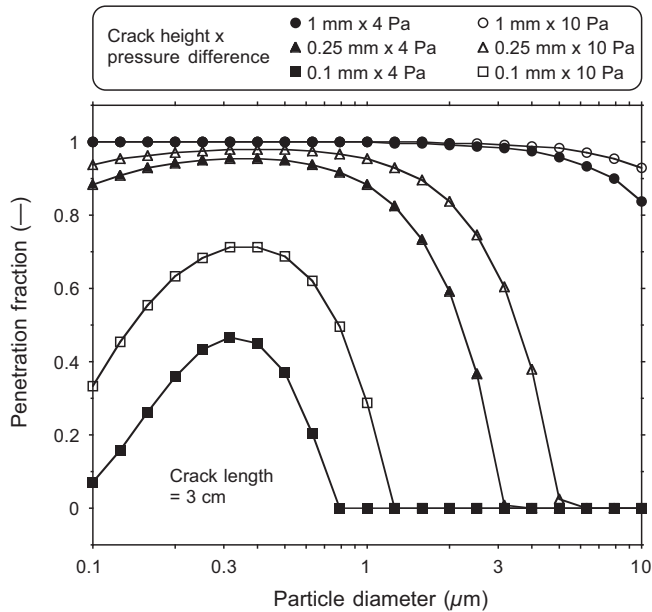


Fig. 11 Model prediction for size-dependent particle penetration (p) through a crack in the building envelope. Source: Liu and Nazaroff (2001)

penetration factor varies with particle size for idealized crack geometry. Different parameter values are assumed for the indoor–outdoor pressure drop (4 or 10 Pa) and the height of the crack (0.1, 0.4, and 1.0 mm). An important message from this figure is that cracks must be quite fine for any meaningful attenuation of the airborne particles during infiltration. Specifically, penetration is essentially complete across the full diameter range 0.1–10 μm for any crack whose minimum dimension exceeds ~ 1 mm (given a 4 Pa or higher pressure drop and assuming that the flow channel through the crack is no longer than 3 cm). The distribution of leak dimensions in any real building is not known. However, it seems likely that a normal case would feature most of the infiltrating air flowing through cracks larger than 1 mm in minimum dimension. Hence, there is an expectation that $p \sim 1$ for bioaerosol particles.

In the case of a mechanically ventilated building, a second important parameter is the efficiency of a particle filter in the flow path connecting outdoor air to the air supply registers. Figure 12 illustrates two important points about filter efficiency. First, it is highly variable with filter quality, ranging from low for filters with a MERV 4 rating to high for MERV 13 or MERV 16 filters. Second, filter efficiency can vary markedly with particle size. Across the range that is pertinent for bioaerosols, the filtration efficiency tends to be higher for larger particles than for smaller particles. A mechanically ventilated building with a high mechanical ventilation to infiltration flow rate ratio ($Q_M/Q_L \gg 1$) and a high-efficiency filter ($1 - \eta_M \ll 1$) can provide a high

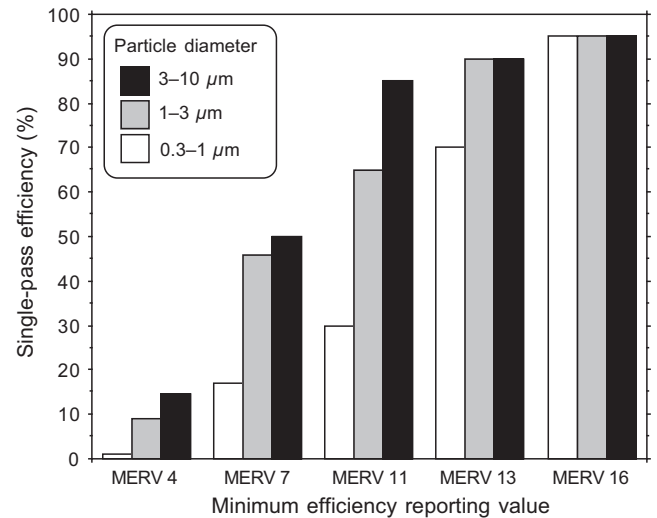


Fig. 12 Specified minimum single-pass particle removal efficiency of fibrous filters used in ventilation systems as a function of particle size (three shading styles) and MERV rating (horizontal axis). Source: Azimi and Stephens (2013)

degree of protection of the indoor environment from outdoor bioaerosols.

In mechanical ventilation systems, some bioaerosol deposition can occur on surfaces other than the filters, including ducts and heat-exchanger fins. Evidence suggests that such deposition is size dependent and much higher for the larger bioaerosol particles than for the smaller ones (Sippola and Nazaroff, 2003; Waring and Siegel, 2008). This deposition process might contribute to meaningful rates of removal from airstreams in some circumstances. However, a more significant concern is the risk of fouling and the degradation of system hygiene.

Bioaerosol sources: indoor emissions

An important and challenging feature of indoor bioaerosol dynamics is characterizing indoor emission sources. From a systematic research perspective, a core advantage of source characterization is that it is likely to provide more generalizable information than would phenomenological studies of concentrations or other outcome variables. The information sought in source characterization would include these factors for any particular bioaerosol analyte: the quantity emitted per time, the size distribution of particles with which the emitted analyte is associated, and the important parameters that influence the emission rate. Depending on the particular source, experiments to investigate emissions might suitably be conducted in a bench-scale laboratory apparatus, in a room scale chamber, or through controlled field monitoring.

There are many potential indoor sources of bioaerosols. Research that characterizes emissions is still in a relatively early stage of development, with limited

quantitative information available for most sources. In the following paragraphs, several studies that have investigated indoor bioaerosol sources are highlighted. Primary goals include indicating the breadth of source types that have been investigated and providing entry points into the literature for those interested in deeper study.

Among the merits of quantifying emissions from interior sources are these. First, such quantification allows for the assessment of the relative importance of indoor vs. outdoor sources as contributors to the indoor burden. Examine the numerators of equations (1) and (2), and note that in each case, there is a term that is proportional to the outdoor concentration and a term (E) that reflects indoor emissions. If, for a particular bioaerosol component of concern, the indoor emissions term is small compared to the outdoor source, then we can safely focus our attention on the outdoor environment transported via air exchange as the dominant contributor to indoor levels. Conversely, if the indoor emission source greatly exceeds the term associated with the outdoor level, then we can focus on indoor emissions and scale down our attention to the outdoor air as a significant contributor.

Second, if the indoor emissions are well-characterized, then (provided we have adequate additional information about the indoor environment) we can estimate the contribution of the indoor emissions to airborne concentrations. Equations (1) and (2) illustrate the relationship, and the additional required information is that needed to quantify the appropriate denominator.

Human occupants. Adult man carries 10^{12} microbes associated with his epidermis and 10^{14} microbes in his alimentary tract. . . . The 10^{13} cells in his body are a distinct numerical minority of the total being that we call man. If we abandon anthropomorphism for the microbial view, we must admire the efficiency of these microbes in using man as a vehicle to further their own cause.—Luckey (1972)

In the context of better understanding and controlling airborne infection, bioaerosol emissions from humans have been a topic of concern since at least the 1940s. For example, Duguid (1946) experimentally assessed the size distribution of particles and droplets emitted by sneezing, coughing, and talking. The likelihood that such particles would contain bacteria was estimated based on their prevalence in respiratory fluids. Duguid and Wallace (1948) experimentally investigated the ‘bacterial contamination of air produced by liberation of dust from the skin and personal clothing during bodily movement’. Using culture-based analysis methods, they found that dust particles carrying bacteria were liberated at a rate of about 1000 per minute from a ‘person making slight movements’ and that marching liberated culturable bacteria about

$10 \times$ more intensely. Bernard et al. (1965) observed that the shedding of airborne bacteria from humans was markedly elevated during a period 10–45 min after showering. The application of lanolin or alcohol to the skin reduced the effect, as did wearing a tightly woven fabric. Hall et al. (1986) did not find this showering effect to occur. However, they did observe that ‘men dispersed many more bacteria than women’ and that the emissions rate could be considerably lowered through the application of skin lotion. They also noted that friction between skin and clothing appeared to be an important factor inducing the release.

A second mechanism by which human activities may contribute to bioaerosol loading is through resuspension of biological particles that had previously settled on flooring or on other upward facing surfaces (Qian et al., 2014). Using a mechanical stepping apparatus that mimicked walking combined with artificially seeded flooring materials, Tian et al. (2014) found that the fractional resuspension of abiotic particles was $\sim 10^{-5}$ and $\sim 10^{-4}$ per step for particles with diameters 1–3 μm and 5–10 μm , respectively. Goebes et al. (2011) documented that foot traffic contributes to measureable concentrations of airborne *Aspergillus*; resuspension from flooring was demonstrated to be an important mechanism.

A few recent studies have aimed to quantify size-resolved biological particle emission rates associated with human occupants using modern analytical methods. Qian et al. (2012) studied a university classroom with bioaerosol sampling using a cascade impactor followed by quantitative PCR applied with universal bacterial and fungal primers. By applying material balance to the indoor and outdoor data under room-occupied and unoccupied conditions, they inferred the per-occupant effective emission rates of bacteria and fungi. For example, the bacterial emission rates were determined to average 37 million genome copy numbers per hour per occupant. Particle size conformed reasonably well to a lognormal distribution with a geometric mean aerodynamic diameter of 4.4 μm and a geometric standard deviation of 1.39. Bhangar et al. (2014) used real-time particle detection to quantify size-resolved emissions of fluorescent biological aerosol particles also in a university classroom. They concluded that the modal size was in the range 3–4 μm and that the average emission rates were 1.6 million particles per person per hour during the main portion of lecture classes plus 0.8 million particles per person emitted during transitions between classes.

Advanced analytical methods and ongoing concerns about the spread of infectious respiratory diseases have motivated a renewed effort to study bioaerosol release from the nose and mouth. Fennelly et al. (2004) measured the size distribution of cough-generated particles containing culturable *Mycobacte-*

rium tuberculosis emitted from patients with pulmonary tuberculosis. Stelzer-Braid et al. (2009) collected respiratory emissions from 50 subjects while breathing, talking, and coughing. They detected one or more of nine respiratory viruses in 21 of 33 subjects who had symptoms of upper respiratory tract infections and only in four among 17 asymptomatic subjects. Gralton et al. (2013) conducted an analogous study that focused on breathing and coughing, included children among the subjects, and investigated the size distribution of the emitted particles and droplets. They concluded that ‘individuals with symptomatic respiratory viral infections produce both large and small particles carrying viral RNA on coughing and breathing’.

Overall, human occupants are important contributors to the bioaerosol burden of indoor environments. They shed bacteria along with their skin; they emit viruses from their respiratory tract; and they resuspend particulate material that contains biological agents from floors and other surfaces that they contact.

Moldy materials. A second potentially important emission source category for indoor bioaerosols is moldy building materials. Dampness and mold is common in buildings. For example, Spengler et al. (1994) reported that half of surveyed households in 24 US and Canadian cities had a dampness-related condition (water damage, water in basement, and/or mold or mildew).

Several laboratory studies have investigated emissions of bioaerosols from moldy materials. For example, Górny et al. (2001) characterized the release of fungal spores—*Aspergillus versicolor*, *Cladosporium cladosporioides*, and *Penicillium melinii*—from ceiling tiles in relation to the air speed above the surface and the vibration of the contaminated material. Seo et al. (2008) investigated the release of (1→3)- β -D-glucan from moldy ceiling tiles and gypsum board. In many buildings, moisture intrusion or condensation occurs in wall cavities or in other hidden spaces that may be coupled by airflow pathways to the occupied building interior. Muise et al. (2010) demonstrated experimentally that mold spores could penetrate effectively through wall service outlets. That finding is consistent with expectations (see Figure 11) as most fungal spores are smaller than 10 μ m in diameter and as cracks and gaps between a wall cavity and the indoor space would commonly be larger than 1 mm in minimum dimension.

Housekeeping and hygiene. A third bioaerosol source category that is potentially important indoors is related to housekeeping and hygiene. Several examples are briefly mentioned here. Davies and Noble (1962) demonstrated that bedmaking increased the airborne concentrations of skin scales and bacteria. Wouters et al. (2000) reported increased levels of microbial markers

in house dust in homes in which household organic waste was separately stored indoors.

Floor dust or settled dust can be richly microbial (Rintala et al., 2012), and this can serve as a bioaerosol source through resuspension (Qian et al., 2014). In a laboratory study, substantial bacteria and mold emission rates were observed from the operation of household vacuum cleaners (Veillette et al., 2013). This finding is not a surprise: Vacuum cleaner use was already demonstrated to be a potent short-term generator of airborne particulate matter, both in the exhaust air (because of incomplete filtration) and through mechanical agitation of the floor (Corsi et al., 2008; Knibbs et al., 2012). The net effect of vacuuming on indoor bioaerosol levels is not clear, however, as presumably vacuum cleaner use would also reduce the floor load of microbes available for later resuspension.

Indoor surfaces that are frequently moist can harbor microbial growth; examples related to household hygiene include shower curtains (Kelley et al., 2004) and sink drains (Adams et al., 2013). Bollin et al. (1985) showed that showerheads and hot-water faucet use could produce aerosols containing *Legionella pneumophila*. Thomson et al. (2013) found non-tuberculous mycobacteria (NTM) in shower aerosols in homes of patients with pulmonary disease caused by NTM, a finding broadly consistent with evidence from Feazel et al. (2009) of enhanced NTM prevalence in showerhead biofilms. Toilet flushing can produce aerosol droplets, and as fecal material is rich in microbes, the toilet is a potentially important source of indoor bioaerosols, especially in connection with diarrheal diseases (Johnson et al., 2013).

Other factors

Bioaerosol exposure control. Let us acknowledge that the goal should not be to make indoor environments sterile. At the same time, elevated levels of airborne pathogens are to be avoided, as are excessive levels of many bioaerosol attributes. And in certain circumstances, we should be particularly concerned about protecting vulnerable people from even ordinary bioaerosol exposure, such as individuals who are immunocompromised.

How can bioaerosol control be achieved? Conceptually, in the context of the material balance described earlier, there are two broad options: (i) reduce sources and/or (ii) increase removal rates. Equations (1) and (2) provide a basis for quantitatively estimating the benefit of a control measure.

Among the options for source control are to keep indoor environments dry, to maintain good hygienic conditions in ventilation systems, to apply effective filtration on mechanical supply ventilation, and to use masks in the event of respiratory illness.

Regarding removal processes, the primary control alternatives are three, which appear in the denominator of equations (1) and (2): (i) increase the outdoor air ventilation rate (typically either Q_N or Q_M); (ii) use recirculating air filtration (i.e., introduce or enhance η_R Q_R , where η_R is the filtration efficiency, as illustrated in Figure 12, and Q_R is the recirculating flow rate through the filter; or (iii) enhance the rate of deposition or degradation of the bioaerosol attribute (thereby increasing β). Miller-Leiden et al. (1996) explored the effectiveness of in-room recirculating filtration for controlling the transmission of tuberculosis. Cheng et al. (1998) have evaluated the use of portable air cleaners for reducing indoor concentrations of fungal spores. Ultraviolet germicidal irradiation can be applied to reduce the infectivity of air without actively removing the bioaerosol particles (Reed, 2010).

The control measures described in the preceding paragraphs all aim to reduce the airborne concentration of the bioaerosol agent, denoted C in equations (1) and (2). A complementary approach is to provide susceptible individuals with personal protective equipment, which—if performed well—can reduce the inhalation intake by an order of magnitude or more for a given airborne concentration. Nicas (1995) presents an illustrative example for the case of respiratory protection of healthcare workers against *Mycobacterium tuberculosis* bacilli.

Airborne growth and decay. The embodiment of the material balance principle in equations (1) and (2) does not account for microbial reproduction or for any other bioaerosol growth process during the period of suspension in the indoor air. There is some evidence supporting the possibility of airborne microbial life in the atmosphere, as reviewed by Womack et al. (2010). However, indoors, where the airborne residence time is limited to about a few hours or less, such processes have not been demonstrated and seem unlikely to be important.

Infectious agent viability may decay at a significant rate when airborne (Weber and Stilianakis, 2008). Incorporating the effects of such processes into model equations can be achieved through the decay parameter, β , in equations (1) and (2).

Transport and mixing. Throughout this study, it has been assumed that an indoor environment can be represented as a well-mixed space. At the level of an individual room, the size of a typical bedroom or private office, that description is often but not always reasonable. An entire residence, or a large building, might be appropriately represented as a network of well-mixed rooms or zones, interconnected by airflow paths (Feustel, 1999).

For some situations, the well-mixed conceptualization is inappropriate. For example, while much of

mechanical ventilation practice uses air diffusers designed to promote rapid mixing, other concepts aim to deliberately exploit incomplete mixing as a basis to improve efficiency. Such methods include displacement ventilation (Novoselac and Srebric, 2002) and personalized ventilation (Melikov, 2004). Understanding how sources relate to concentrations in the breathing zone of occupants in cases like these cannot be accurately accomplished using a well-mixed analysis framework; instead, more sophisticated methods are required, such as approaches based on computational fluid dynamics (Chen, 2009). Experimentally, investigations in such conditions require methods that can accommodate spatially varying contaminant concentrations (Björn and Nielsen, 2002; Brohus and Nielsen, 1996).

Conclusion

Although study of the normal human lung microbiome is still in its early stages, the bulk of published evidence demonstrates that phylogenetically diverse microbial communities in the lungs of healthy humans can be detected using high throughput sequencing.—Beck et al. (2012)

In a recent review, Grice and Segre (2012) articulate important ways in which microorganisms modulate human health: ‘The human microbiome is a source of genetic diversity, a modifier of disease, an essential component of immunity, and a functional entity that influences metabolism and modulates drug interactions’. They then summarize what has recently been learned about the microbiology of the human gastrointestinal tract, the oral cavity, the reproductive tract, and the skin. However, they do not comment on the microbiology of the respiratory tract. Beck et al. (2012), in their review, note that, ‘although the lungs were classically believed to be sterile, recently published investigations have identified microbial communities in the lungs of healthy humans’. Lax et al. (2014) document that the microbes found in a home are distinctively related to the people who live in that home and that ‘after a house move, the microbial community in the new house rapidly converged on the microbial community of the occupants’ former house, suggesting rapid colonization by the family’s microbiota’. What is not yet clear, but seems plausible, is whether aspects of the human microbiome are strongly influenced by microbiological and other conditions in inhabited indoor spaces.

Indoor bioaerosol behavior might play an important role in these stories. Almost certainly, the most important exposures of the human lung to environmental microorganisms occur via inhalation of bioaerosols. Furthermore, most of the air that is inhaled by humans is indoor air. Bioaerosols also are important vectors transporting microorganisms from outdoors to indoors and

from one indoor surface to another. It is feasible that airborne transport to and deposition on the human envelope influences skin microbiota (Adams et al., 2013).

Relative to the complexity and importance of the subject of indoor bioaerosol dynamics, our understanding is not yet mature. One might anticipate fundamental paradigm shifts to occur as our knowledge grows. Our ability to ask and answer incisive questions should improve.

Although the gap between what we know and what we would like to know is quite large, our current knowledge is substantial. For example, in considering the dynamic behavior of airborne biological particles in buildings, indoor aerosol science provides a good starting point. Mechanistically, bioaerosol particles behave like their abiotic counterparts. Particle size is a primordial determinant of behavior, and bioaerosol particles are mainly found in the aerodynamic diameter range 0.1–10 μm . Aerosol science has developed powerful tools and theories regarding emission processes, airborne behavior, and fate. Much of the understanding developed from aerosol science can be applied to indoor bioaerosol dynamics.

As we proceed in studying the microbiology of the indoor environment, we should maintain a central focus on people. Human occupants are a major source of indoor bacteria. Our activities influence the emissions and fate of other bioaerosols as well. The outcomes of primary concern are centered on human health and welfare.

Technological advances enable the acquisition and analysis of microbial data of phenomenal richness. As we conduct research with the new tools, it is important that we not lose sight of the knowledge gained by prior generations of scholars. Public health engineering studies conducted in the 1940s through 1970s, for example, on the theme of infection control in healthcare settings, contain particularly important insights that remain relevant to our current research agendas.

The diversity and complexity of the system will continue to pose great challenges for studies of indoor bioaerosol dynamics, especially in efforts to link microbiological abundance to exposure and to health outcomes. The measurement limitations continue to be daunting. Dust is an attractive sampling medium of questionable exposure relevance. Culture-based analysis methods have limited scope. Microscopic methods, DNA-based analysis, and methods using chemical markers are best suited for making time-integrated measurements with sampling periods of hours. These methods are not well suited for studying dynamic processes. The fluorescent particle-sampling and analysis methods have the advantage of offering excellent time and particle-size resolution. However, these methods lack specificity.

In recent years, we have seen benefits from efforts to fuse concepts and approaches from the indoor environmental sciences with the rapidly developing techniques

and evolving knowledge of microbial ecology. We can anticipate continuing opportunities from cooperation between scholars from these domains. As we gain empirical knowledge, it will be important to seek generalizable understanding from the specifics of particular investigations. We will never measure everything! Research that focuses on processes and that is framed in the context of well-established mechanistic knowledge can be a valuable way to proceed. In this review, the principle of material balance has served to structure a relationship between bioaerosol processes and indoor concentrations, an important intermediate outcome. Further studies can be fruitfully pursued to better understand each of the input parameters that appear in the material balance equations. Research could also be undertaken to test the accuracy of and to refine as necessary the model equations themselves. Benefits would especially be anticipated from studies to better characterize and quantify indoor bioaerosol emission sources and the influencing factors. This particular process has especially large influence on outcomes, it is difficult to characterize without direct experimental measurement, and it is subject to enormous variability.

The ultimate goal for improving knowledge about indoor bioaerosol dynamics is to contribute to a stronger knowledge base for the design, construction, operation, and maintenance of healthful buildings. This review has focused on the natural science and engineering aspects of the theme. This review has not addressed the complementary and comparably complex theme of how human health is influenced by bioaerosol exposure. Because we are at an early stage of understanding both themes and because of their complementarity, progress toward the ultimate goal would benefit from the development of synergistic interactions between the respective research communities. That is a challenging proposition for several reasons, including largely independent educational tracks and funding agencies that—at least in the United States—do not embrace the nexus between the built environment and health. The first steps to overcoming any challenge are recognizing its importance and making a commitment to the attempt. Perhaps the recent efforts to improve knowledge about the indoor microbiome and about the relationship between the human microbiome and health are establishing fertile ground for future synergistic efforts to better understand the relationship between the indoor microbiome and health.

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