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## **Indoor Bioaerosol Dynamics**

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### **Abstract**

Inhaling indoor air is the primary means by which humans are exposed to bioaerosols. Considering bacteria, fungi, viruses, this paper reviews the dynamic processes that govern indoor concentrations and fates of biological particulate material. Bioaerosol behavior is coupled to particle size; this paper emphasizes the range 0.1-10  $\mu\text{m}$  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 ventilation plus indoor emission from occupants, occupant activities, and moldy materials. Important mechanisms that remove bioaerosols from indoor air include ventilation, 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.

**Keywords:** bacteria, deposition, emission, fungi, ventilation, virus

### **Practical Implications**

Bioaerosol exposure indoors is an important factor influencing human health. Understanding the dynamic behavior of biological particles can help 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.

## 1. 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 the present paper derives from three primary concerns. First, exposure to bioaerosol material can cause or contributes 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 lacking. However, 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 our health might in fact be influenced by attributes of the spaces we inhabit, including their microbiology generally and their bioaerosol aspects specifically.

Following the introduction, the paper is organized into two main sections. In §2, I define a framework for considering indoor bioaerosol dynamics. This section 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 are strongly influenced by measurement technology, so some of the key measurement methods are briefly summarized. Evidence regarding infectious disease transmission by airborne routes is also assembled.

The second primary section (§3) summarizes the information available 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 ventilation, an important removal mechanism for indoor bioaerosols and also a means by which outdoor bioaerosol particles are brought indoors. Then, we go on to investigate several additional processes that can affect the 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 in further studies of indoor bioaerosol dynamics are described along with several opportunities for near-term progress.

## 2. Framing the Issues

### 2.1. 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, peptidoclycans,  $\beta(1 \rightarrow 3)$ -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 is challenging to define. For the purposes of this paper, 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.

The indoor environments to be considered are those ordinarily and commonly occupied by humans. Of particular interest are 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 exposures potential, such as those associated with food systems.

This review also emphasizes the human-bioaerosol nexus in indoor environments. Densely occupied indoor spaces are of special interest. Conversely, environments such as archives, which may have indoor microbiomes of a specialized character, are not a focus of this study.

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. The microbiological composition of indoor dust is not a primary focus of this paper.

The overall approach employed 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 (Gregory, 1971; Spendlove and Fannin, 1983; Burge, 1990; Douwes et al., 2003). However, none of these earlier reviews is as strongly grounded in indoor aerosol science as the present article.

## *2.2. 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 approximately 1700 buildings in the US (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 made. The cumulative probability distribution functions (Figure 1) show that the data are well fit by lognormal distributions. The geometric mean outdoor concentration ( $493 \text{ CFU/m}^3$ ) are about  $6\times$  higher than the geometric mean indoor concentration ( $79 \text{ CFU/m}^3$ ). The indoor levels show considerably broader range than do the outdoor levels (GSD of 5.5 compared to 3.3). These data support an important general finding, that outdoor air is a major source of indoor fungi.

Culture-based analyses reflect 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.

Although it is common for fungi concentrations to be higher in outdoor air than indoors, in occupied spaces the reverse is true for bacteria. 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)- $\beta$ -D-glucans (a marker of fungi) in outdoor air was almost  $2\times$  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 are not appear 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 the degree of occupancy in the room where sampling was conducted during sampling (Chen and Hildemann, 2009b). Occupancy is used here as a surrogate measure of the intensity of human activity. Across all measures, 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 daycare 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 hours. Eight of these samples (50%) contained influenza A virus, with concentrations ranging from 5800 to 37,000 genomes per m<sup>3</sup>, and a substantial proportion of the detected virus was associated with fine particles (< 2.5 µm) that can remain airborne for extended periods and that can also penetrate and deposit deeply in the respiratory tract when inhaled.

### ***2.3. 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 ( $E$ ). Three processes can remove bioaerosol material: (i) ventilation ( $[Q_N + Q_L] \times C$ ); (ii) filtration in the recirculating air flow ( $\eta_R \times Q_R \times C$ ); and (iii) deposition onto room surfaces ( $\beta VC$ ).

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

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 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, i.e., 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 paper. A third feature of this

equation is that 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.

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

#### 2.4. Particle size

Most indoor airborne microbial material is found on particles in the diameter range 0.1 - 10  $\mu\text{m}$ . 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  $\mu\text{m}$  as compared with particles with diameters in the range 1-10  $\mu\text{m}$ .

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 approximately 0.1  $\mu\text{m}$  in size (Noda, 2012). The cells of *Staphylococcus aureus*, a common pathogenic species, have diameters of approximately 1  $\mu\text{m}$  (<http://textbookofbacteriology.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).

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).

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

## 2.5. 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 presented, the high deposition efficiency 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 and so it is most important only in the smallest airways: deposition efficiency 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  $\mu\text{m}$  in diameter, a size that is can be important for bacterial and fungal bioaerosol particles.

## *2.6. 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 measuring 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. 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 taxa specific. Disadvantages include that only viable organisms are measured and only a subset of airborne organisms is culturable. A further important limitation is that the commonly employed method of direct impaction onto an agar substrate is well suited for only a short sampling period. The common application of this method provides a short-term 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, e.g. associated with occupancy and activity.

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 potential for adverse health consequences. Examples include endotoxin and (1→3)- $\beta$ -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.

### ***2.7. 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 is from a source that 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.

## **3. 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 7.

### ***3.1. Ventilation: Source and sink***

Building ventilation is the replacement of indoor air with outdoor air. Ventilation 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 rate of ventilation consistently improves indoor air quality. However, when climate conditions are not comfortable, then the ventilation 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, ventilation can be an important source of indoor pollution.

Building ventilation 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 component of ventilation. Although practices vary and are changing with time, it is common in the United States for single-family dwellings to be ventilated by a combination of natural ventilation plus infiltration. Mechanical ventilation plus infiltration is common in commercial buildings.

One metric for characterizing ventilation rates is the air-exchange rate (AER). 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 schematic (a) and  $(Q_M + Q_L)/V$  for the commercial schematic (b). 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 with a range that spans about an order of magnitude, from 0.2 to 3 per hour. The BASE study of approximately 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 ventilation will have a characteristic residence time of one to two hours in the building air.

### *3.2. Bioaerosol deposition onto room surfaces*

Across the aerodynamic diameter range of 0.1-10  $\mu\text{m}$ , 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,  $\beta$ . The importance of deposition as a removal mechanism for airborne bioaerosol particles can be explored by comparing  $\beta$  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  $\mu\text{m}$ , the deposition loss rate coefficient is  $\sim 0.2$ -0.3 per hour, a value that is comparable to the lower end of range of air-exchange rates discussed in §3.1. Under low ventilation conditions, deposition of these submicron particles is competitive with air-exchange as a removal process, but in well-ventilated indoor spaces, deposition of these smaller particles is less important than ventilation. For larger particles, in the range 3-10  $\mu\text{m}$  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 Figure 9 also illustrate that enhanced air movement increases the rate of particle deposition 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 would 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  $\text{m}^{-3}$  (Figure 1) and assume they are associated with 6  $\mu\text{m}$  particles for which the deposition velocity is 30  $\text{mm h}^{-1}$  ( $= 0.03 \text{ m h}^{-1}$ ), then the resulting deposition flux to vertical walls would be  $80 \times 0.3 = 2.4 \text{ CFU m}^{-2}$



$\text{h}^{-1}$ . This process would represent a small contribution to the total loss rate of fungi from indoor air, but could be an important mechanism for fungal colonization of walls.

### 3.3. 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 ventilation-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 ventilation flow rates (§3.1) 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,  $\eta_M$ . 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  $\eta_M$  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 penetration factor varies with particle size for idealized crack geometry. Different 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  $\mu\text{m}$  for any crack whose minimum dimension exceeds  $\sim 1$  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 isn't known. However, it seems likely that a normal case would feature most of the 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 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, 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.

### *3.4. 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 versus 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 and the ventilation system as the dominant contributors 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.

#### 3.4.1. 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 microbic 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 has 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× more intensely. Bernard et al. (1965) observed that the shedding of airborne bacteria from humans was markedly elevated during a period 10-45 minutes 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).

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 a material-balance approach 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  $\mu\text{m}$  and a geometric standard deviation of 1.39. Bhangar et al. (in press) 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  $\mu\text{m}$  and that the average emissions 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. 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 4 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.

### 3.4.2. 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)- $\beta$ -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) since most fungal spores are smaller than 10  $\mu\text{m}$  in diameter and since cracks and gaps between a wall cavity and the indoor space would commonly be larger than 1 mm in minimum dimension.

### 3.4.3. 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. Bollin et al. (1985) showed that showerheads and hot-water faucet use could produce aerosols containing *Legionella pneumophila*. Thomson et al. (2013) found nontuberculous 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 prevalence of NTM in showerhead biofilms. Toilet flushing can produce aerosol droplets and,

since 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). The use of vacuum cleaners also is associated with the release of bioaerosols (Veillette et al., 2013). Not clear is the net effect, since presumably vacuum cleaner use would also reduce the floor burden available for later resuspension by walking.

### 3.5. *Other factors*

#### 3.5.1. Bioaerosol exposure control

Let's 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 in §2.3, there are two broad options: (a) reduce sources and/or (b) 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): (a) increase ventilation rate (typically either  $Q_N$  or  $Q_M$ ); (b) use recirculating air filtration (i.e., introduce or enhance  $\eta_R Q_R$ , where  $\eta_R$  is the filtration efficiency, as illustrated in Figure 12, and  $Q_R$  is the recirculating flow rate through the filter; or



(c) enhance the rate of deposition or degradation of the bioaerosol attribute (thereby increasing  $\beta$ ). Miller-Leiden et al. (1996) explored the effectiveness of in-room recirculating filtration for controlling the transmission of tuberculosis. 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 done well — can reduce the inhalation intake by an order of magnitude or more for a given airborne concentration,  $C$ . Nicas (1995) presents an illustrative example for the case of respiratory protection of healthcare workers against *Mycobacterium tuberculosis* bacilli.

### 3.5.2. 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,  $\beta$ , in equations (1) and (2).

### 3.5.3. Transport and mixing

Throughout this paper, 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 flow 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 (Brohus and Nielsen, 1996; Bjørn and Nielsen, 2002).

#### **4. 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 that aspects of the human microbiome may be 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.

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  $\mu\text{m}$ . 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 health care settings, contains 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 rapidly 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 paper, 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 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.

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## References

- Azimi, P. and Stephens, B. (2013) HVAC filtration for controlling infectious airborne disease transmission in indoor environments: Predicting risk reductions and operational costs, *Build. Environ.*, **70**, 150-160.
- Beck, J.M., Young, V.B. and Huffnagle, G.B. (2012) The microbiome of the lung, *Transl. Res.*, **160**, 258-266.
- Bernard, H.R., Speers, R., O'Grady, F.W. and Shooter, R.A. (1965) Airborne bacterial contamination: Investigation of human sources, *Arch. Surg.*, **91**, 530-533.
- Bhangar, S., Huffman, J.A. and Nazaroff, W.W. (in press) Size-resolved fluorescent biological aerosol particle concentrations and occupant emissions in a university classroom, *Indoor Air*, doi:10.1111/ina.12111.
- Bjørn, E. and Nielsen, P.V. (2002) Dispersal of exhaled air and personal exposure in displacement ventilated rooms, *Indoor Air*, **12**, 147-164.
- Bloch, A.B., Orenstein, W.A., Ewing, W.M., Spain, W.H., Mallison, G.F., Hermann, K.L. and Hinman, A.R. (1985) Measles outbreak in a pediatric practice: Airborne transmission in an office setting, *Pediatrics*, **75**, 676-683.
- Bollin, G.E., Plouffe, J.F., Para, M.F. and Hackman, B. (1985) Aerosols containing *Legionella pneumophila* generated by shower heads and hot-water faucets, *Appl. Environ. Microb.*, **50**, 1128-1131.
- Brohus, H. and Nielsen, P.V. (1996) Personal exposure in displacement ventilated rooms, *Indoor Air*, **6**, 157-167.
- Burge, H. (1990) Bioaerosols: Prevalence and health effects in the indoor environment, *The J. Allergy Clin. Immun.*, **86**, 687-701.
- Chen, Q. (2009) Ventilation performance prediction for buildings: A method overview and recent applications, *Build. Environ.*, **44**, 848-858.
- Chen, Q. and Hildemann, L.M. (2009a) Size-resolved concentrations of particulate matter and bioaerosols inside versus outside of homes, *Aerosol Sci. Tech.*, **43**, 699-713.
- Chen, Q. and Hildemann, L.M. (2009b) The effects of human activities on exposure to particulate matter and bioaerosols in residential homes, *Environ. Sci. Technol.*, **43**, 4641-4646.
- Davies, R.R. and Noble, W.C. (1962) Dispersal of bacteria on desquamated skin, *Lancet*, **280**, 1295-1297.
- Douwes, J. (2005) (1 → 3)- $\beta$ -D-glucans and respiratory health: a review of the scientific evidence, *Indoor Air*, **15**, 160-169.
- Douwes, J., Thorne, P., Pearce, N. and Heederik, D. (2003) Bioaerosol health effects and exposure assessment: Progress and prospects, *Ann. Occup. Hyg.*, **47**, 187-200.
- Duguid, J.P. (1946) The size and the duration of air carriage of respiratory droplets and droplet nuclei, *J. Hyg. Cambridge*, **44**, 471-479.
- Duguid, J.P. and Wallace, A.T. (1948) Air infection with dust liberated from clothing, *Lancet*, **252**, 845-849.
- Fabian, P., McDevitt, J.J., Lee, W.M., Houseman, E.A. and Milton, D.K. (2009) An optimized method to detect influenza virus and human rhinovirus from exhaled breath and the airborne

- environment, *J. Environ. Monitor.*, **11**, 314-317.
- Feazel, L.M., Baumgartner, L.K., Peterson, K.L., Frank, D.N., Harris, J.K. and Pace, N.R. (2009) Opportunistic pathogens enriched in showerhead biofilms, *P. Natl. Acad. Sci. USA*, **106**, 16393-16399.
- Feustel, H.E. (1999) COMIS — an international multizone air-flow and contaminant transport model, *Energ. Buildings*, **30**, 3-18.
- Fields, B.S., Benson, R.F. and Besser, R.E. (2002) Legionella and Legionnaires' disease: 25 years of investigation, *Clin. Microbiol. Rev.*, **15**, 506-526.
- Fisk, W.J., Lei-Gomez, Q. and Mendell, M.J. (2007) Meta-analyses of the associations of respiratory health effects with dampness and mold in homes, *Indoor Air*, **17**, 284-296.
- Fox, A., Harley, W., Feigley, C., Salzberg, D., Sebastian, A. and Larsson, L. (2003) Increased levels of bacterial markers and CO<sub>2</sub> in occupied school rooms, *J. Environ. Monitor.*, **5**, 246-252.
- Fox, A., Harley, W., Feigley, C., Salzberg, D., Toole, C., Sebastian, A. and Larsson, L. (2005) Large particles are responsible for elevated bacterial marker levels in school air upon occupation, *J. Environ. Monitor.*, **7**, 450-456.
- Górny, R.L., Reponen, T., Grinshpun, S.A. and Willeke, K. (2001) Source strength of fungal spore aerosolization from moldy building material, *Atmos. Environ.*, **35**, 4853-4862.
- Górny, R.L., Reponen, T., Willeke, K., Schmechel, D., Robine, E., Boissier, M. and Grinshpun, S.A., (2002) Fungal fragments as indoor air biocontaminants, *Appl. Environ. Microb.*, **68**, 3522-3531.
- Gralton, J., Tovey, E.R., McLaws, M.L. and Rawlinson, W.D. (2013) Respiratory virus RNA is detectable in airborne and droplet particles, *J. Med. Virol.*, **85**, 2151-2159.
- Gregory, P.H. (1971) The Leeuwenhoek Lecture, 1970: Airborne microbes: Their significance and distribution, *P. Roy. Soc. Lond. B Bio.*, **171**, 469-483.
- Grice, E.A. and Segre, J.A. (2012) The human microbiome: Our second genome, *Annu. Rev. Genom. Hum. G.*, **13**, 151-170.
- Gustafson, T.L., Lavelly, G.B., Brawner, Jr., E.R., Hutcheson, Jr., R.H., Wright, P.F. and Schaffner, W. (1982) An outbreak of airborne nosocomial varicella, *Pediatrics*, **70**, 550-556.
- Hall, G.S., Mackintosh, C.A. and Hoffman, P.N. (1986) The dispersal of bacteria and skin scales from the body after showering and after application of a skin lotion, *J. Hyg. Cambridge*, **97**, 289-298, 1986.
- Heikkinen, T. and Järvinen, A. (2003) The common cold, *Lancet*, **361**, 51-59.
- Hernandez, M., Miller, S.L., Landfear, D.W. and Macher J.M. (1999) A combined fluorochrome method for quantitation of metabolically active and inactive airborne bacteria, *Aerosol Sci. Tech.*, **30**, 145-160.
- Hoge, C.W., Reichler, M.R., Dominguez, E.A., Bremer, J.C., Mastro, T.D., Hendricks, K.A., Musher, D.M., Elliott, J.A., Facklam, R.R. and Breiman, R.F. (1994) An epidemic of pneumococcal disease in an overcrowded, inadequately ventilated jail, *New Engl. J. Med.*, **331**, 643-648.
- Hoisington, A.J., Maestre, J.P., King, M.D., Siegel, J.A. and Kinney, K.A. (2014) Impact of sampler selection on the characterization of the indoor microbiome via high-throughput sequencing, *Build. Environ.*, **80**, 274-282.

- Hospodsky, D., Qian, J., Nazaroff, W.W., Yamamoto, N., Bibby, K., Rismani-Yazdi, H. and Peccia, J. (2012) Human occupancy as a source of indoor airborne bacteria, *PLoS ONE*, **7**, e34867.
- Hospodsky, D., Yamamoto, N. and Peccia, J. (2010) Accuracy, precision, and method detection limits of quantitative PCR for airborne bacteria and fungi, *Appl. Environ. Microb.*, **76**, 7004-7012.
- Johnson, D.L., Mead, K.R., Lynch, R.A. and Hirst, D.V.L. (2013) Lifting the lid on toilet plume aerosol: A literature review with suggestions for future research, *Am. J. Infect. Control*, **41**, 254-258.
- Lai, A.C.K. and Nazaroff, W.W. (2005) Supermicron particle deposition from turbulent chamber flow onto smooth and rough vertical surfaces, *Atmos. Environ.*, **39**, 4893-4900.
- Lax, S., Smith, D.P., Hampton-Mercell, J., Owens, S.M., Handley, K.M., Scott, N.M., Gibbons, S.M., Larsen, P., Shogan, B.D., Weiss, S., Metcalf, J.L., Ursell, L.K., Vázquez-Baeza, Y., Van Treuren, W., Hasan, N.A., Gibson, M.K., Colwell, R., Dantas, G., Knight, R. and Gilbert, J.A. (2014) Longitudinal analysis of microbial interaction between humans and the indoor environment, *Science*, **345**, 1048-1052.
- Liu, D.L. and Nazaroff, W.W. (2001) Modeling pollutant penetration across building envelopes, *Atmos. Environ.*, **35**, 4451-4462.
- Liu, L.J.S., Krahmer, M., Fox, A., Feigley, C.E., Featherstone, A., Saraf, A. and Larsson, L. (2000) Investigation of the concentration of bacteria and their cell envelope components in indoor air in two elementary schools, *J. Air Waste Manage.*, **50**, 1957-1967.
- Luckey, T.D. (1972) Introduction to intestinal microecology, *Am. J. Clin. Nutr.*, **25**, 1292-1294.
- Marks, P.J., Vipond, I.B., Regan, F.M., Wedgwood, K., Fey, R.E. and Caul, E.O. (2003) A school outbreak of Norwalk-like virus: Evidence for airborne transmission, *Epidemiol. Infect.*, **131**, 727-736.
- Melikov, A.K. (2004) Personalized ventilation, *Indoor Air*, **14** (Suppl. 7), 157-167.
- Miller, J.D. and Young, J.C. (1997) The use of ergosterol to measure exposure to fungal propagules in indoor air, *Am. Ind. Hyg. Assoc. J.*, **58**, 39-43.
- Miller-Leiden, S., Lobascio, C., Nazaroff, W.W. and Macher, J.M. (1996) Effectiveness of in-room air filtration and dilution ventilation for tuberculosis infection control, *J. Air Waste Manage.*, **46**, 869-882.
- Mortimer, E.A., Wolinsky, E., Gonzaga, A.J. and Rammelkamp, C.H. (1966) Role of airborne transmission in staphylococcal infections, *Brit. Med. J.*, **1**, 319-322.
- Muise, B., Seo, D.C., Blair, E.E. and Applegate, T. (2010) Mold spore penetration through wall service outlets: A pilot study, *Environ. Monit. Assess.*, **163**, 95-104.
- Nazaroff, W.W. (2004) Indoor particle dynamics, *Indoor Air*, **14** (Suppl. 7), 175-183.
- Nicas, M. (1995) Respiratory protection and the risk of *Mycobacterium tuberculosis* infection, *Am. J. Ind. Med.*, **27**, 317-333.
- Noda, T. (2012) Native morphology of influenza virions, *Front. Microbio.*, **2**, article 269.
- Noris, F., Siegel, J.A. and Kinney, K.A. (2011) Evaluation of HVAC filters as a sampling mechanism for indoor microbial communities, *Build. Environ.*, **45**, 338-346.
- Novoselac, A. and Srebric, J. (2002) A critical review on the performance and design of combined cooled ceiling and displacement ventilation systems, *Energ. Buildings*, **34**, 497-



509.

- Park, J.H., Spiegelman, D.L., Gold, D.R., Burge, H.A. and Milton, D.K. (2001) Predictors of airborne endotoxin in the home, *Environ. Health Persp.*, **109**, 859-864.
- Persily, A.K. and Gorfain, J. (2008) Analysis of ventilation data from the U.S. Environmental Protection Agency Building Assessment Survey and Evaluation (BASE) Study, NISTIR 7145-Revised, National Institute of Standards and Technology, Washington, DC.
- Pitkäranta, M., Meklin, T., Hyvärinen, A., Paulin, L., Auvinen, P., Nevalainen, A. and Rintala, H. (2008) Analysis of fungal flora in indoor dust by ribosomal DNA sequence analysis, quantitative PCR, and culture, *Appl. Environ. Microb.*, **74**, 233-244.
- Qian, J., Hospodsky, D., Yamamoto, N., Nazaroff, W.W. and Peccia, J. (2012) Size-resolved emission rates of airborne bacteria and fungi in an occupied classroom, *Indoor Air*, **22**, 339-351.
- Qian, J., Peccia, J. and Ferro, A.R. (2014) Walking-induced particle resuspension in indoor environments, *Atmos. Environ.*, **89**, 464-481.
- Reed, N.G. (2010) The history of ultraviolet germicidal irradiation for air disinfection, *Public Health Rep.*, **125**, 15-27.
- Reponen, T., Willeke, K., Ulevicius, V., Reponen, A. and Grinshpun, S.A. (1996) Effect of relative humidity on the aerodynamic diameter and respiratory deposition of fungal spores, *Atmos. Environ.*, **30**, 3967-3974.
- Riley, R.L. (1974) Airborne infection, *Am. J. Med.*, **57**, 466-475.
- Rintala, H., Pitkäranta, M. and Täubel, M. (2012) Microbial communities associated with house dust, *Adv. Appl. Microbiol.*, **78**, 75-120.
- Robertson, O.H. (1943) Air-borne infection, *Science*, **97**, 495-502.
- Rylander, R., Reeslev, M. and Hylander, T. (2010) Airborne enzyme measurements to detect indoor mould exposure, *J. Environ. Monitor.*, **12**, 2161-2164.
- Seo, S.C., Reponen, T., Levin, L., Borchelt, T. and Grinshpun, S.A. (2008) Aerosolization of particulate (1→3)- $\beta$ -D-glucan from moldy materials, *Appl. Environ. Microb.*, **74** 585-593.
- Shelton, B.G., Kirkland, K.H., Flanders, W.D. and Morris, G.K. (2002) Profiles of airborne fungi in buildings and outdoor environments in the United States, *Appl. Environ. Microb.*, **68**, 1743- 1753.
- Sippola, M.R. and Nazaroff, W.W. (2003) Modeling particle loss in ventilation ducts, *Atmos. Environ.*, **37**, 5597-5609.
- Spendlove, J.C. and Fannin, K.F. (1983) Source, significance, and control of indoor microbial aerosols: Human health aspects, *Public Health Rep.*, **98**, 229-244.
- Spengler, J., Neas, L., Nakai, S., Dockery, D., Speizer, F., Ware, J. and Raizenne, M. (1994) Respiratory symptoms and housing characteristics, *Indoor Air*, **4**, 72-82.
- Stelzer-Braid, S., Oliver, B.G., Blazey, A.J., Argent, E., Newsome, T.P., Rawlinson, W.D. and Tovey, E.R. (2009) Exhalation of respiratory viruses by breathing, coughing, and talking, *J. Med. Virol.*, **81**, 1674-1679.
- Tellier, R. (2009) Aerosol transmission of influenza A virus: A review of new studies, *J. R. Soc. Interface*, **6**, S783-S790.
- Thatcher, T.L., Lai, A.C.K., Moreno-Jackson, R., Sextro, R.G. and Nazaroff W.W. (2002)

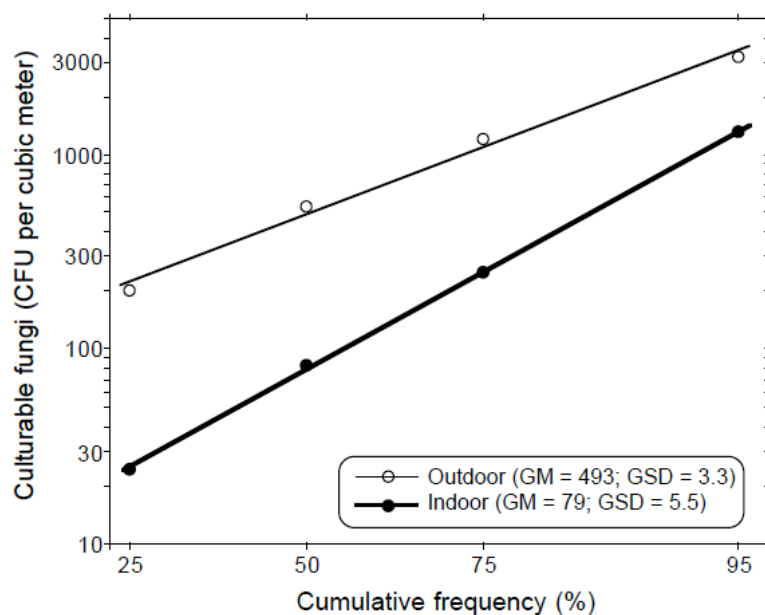
- Effects of room furnishings and air speed on particle deposition rates indoors, *Atmos. Environ.*, **36**, 1811-1819.
- Thomson, R., Tolson, C., Carter, R., Coulter, C., Huygens, F. and Hargreaves, M. (2013) Isolation of nontuberculous mycobacteria (NTM) from household water and shower aerosols in patients with pulmonary disease caused by NTM, *J. Clin. Microbiol.*, **51**, 3006-3011.
- Toivola, M., Nevalainen, A. and Alm, S. (2004) Personal exposures to particles and microbes in relation to microenvironmental concentrations, *Indoor Air*, **14**, 351-359.
- Tsai, F.C. and Macher, J.M. (2005) Concentrations of airborne culturable bacteria in 100 large US office buildings from the BASE study, *Indoor Air*, **15** (Suppl. 9), 71-81.
- Tsai, F.C., Macher, J.M. and Hung, Y.Y. (2007) Biodiversity and concentrations of airborne fungi in large US office buildings from the BASE study, *Atmos. Environ.*, **41**, 5181-5191.
- Veillette, M., Knibbs, L.D., Pelletier, A., Charlebois, R., Lecours, P.B., He, C., Morawska, L. and Duchaine, C. (2013) Microbial contents of vacuum cleaner bag dust and emitted bioaerosols and their implications for human exposure indoors, *Appl. Environ. Microb.*, **79**, 6331-6336.
- Warfel, J.M., Beren, J. and Merkel, T.J. (2012) Airborne transmission of *Bordetella pertussis*, *J. Infect. Dis.*, **206**, 902-906.
- Waring, M.S. and Siegel, J.A. (2008) Particle loading rates for HVAC filters, heat exchangers, and ducts, *Indoor Air*, **18**, 209-224.
- Weber, T.P. and Stilianakis, N.I. (2008) Inactivation of influenza A viruses in the environment and modes of transmission: A critical review, *J. Infection*, **57**, 361-373.
- Wehrle, P.F., Posch, J., Richter, K.H. and Henderson, D.A. (1970) An airborne outbreak of smallpox in a German hospital and its significance with respect to other recent outbreaks in Europe, *B. World Health Organ.*, **43**, 669-679.
- Womack, A.M., Bohannon, B.J.M. and Green, J.L. (2010) Biodiversity and biogeography of the atmosphere, *Philos. T. R. Soc. B*, **365**, 3645-3653.
- Yamamoto, N., Shendell, D.G., Winer, A.M. and Zhang, J. (2010) Residential air exchange rates in three major US metropolitan areas: Results from the Relationship among Indoor, Outdoor, and Personal Air study 1999-2001, *Indoor Air*, **20**, 85-90.
- Yang, W., Elankumaran, S. and Marr, L.C. (2011) Concentrations and size distributions of airborne influenza A viruses measured indoors at a health centre, a day-care centre and on aeroplanes, *J. R. Soc. Interface*, **8**, 1176-1184.
- Yeh, H.C., Cuddihy, R.G., Phalen, R.F. and Chang, I.Y. (1996) Comparisons of calculated respiratory tract deposition of particles based on the proposed NCRP model and the new ICRP66 model, *Aerosol Sci. Tech.*, **25**, 134-140.
- Yooseph, S., Andrews-Pfannkoch, C., Tenney, A., McQuaid, J., Williamson, S., Thiagarajan, M., Bami, D., Ziegler-Allen, L., Hoffman, J., Goll, J.B., Fadrosch, D., Glass, J., Adams, M.D., Friedman, R. and Venter, J.C. (2013) A metagenomic framework for the study of airborne microbial communities, *PLoS ONE*, **8**, e81862.
- Yu, I.T.S., Li, Y., Wong, T.W., Tam, W., Chan, A.T., Lee, J.H.W., Leung, D.Y.C. and Ho, T. (2004) Evidence of airborne transmission of the severe acute respiratory syndrome virus, *New Engl. J. Med.*, **350**, 1731-1739.

**Table 1.** Analytical methods applied for study of indoor bioaerosols.

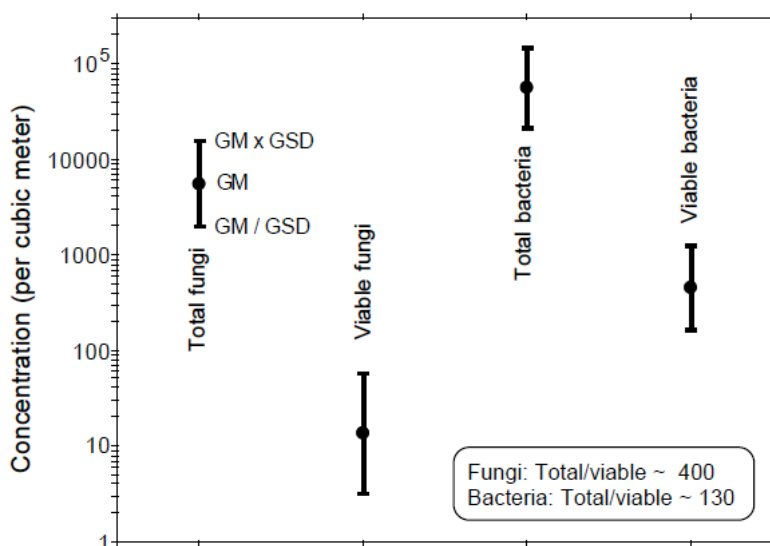
<b>Method/Analyte</b>	<b>Comment</b>	<b>References</b>
Culture-based	Most indoor bioaerosol data have been collected in this manner; limited to culturable species and (typically) short-term sampling	Shelton et al. (2002); Tsai and Macher (2005); Tsai et al. (2007)
Microscopy	Labor-intensive but can generate 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	Pitkaranta et al. (2008); Noris et al. (2011); Hospodsky et al. (2012); Hoisington et al. (2014)
Metagenomic DNA sequencing	Constructs genetic sequencing information for bioaerosol without amplification; requires large volume of air to collect enough 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)

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

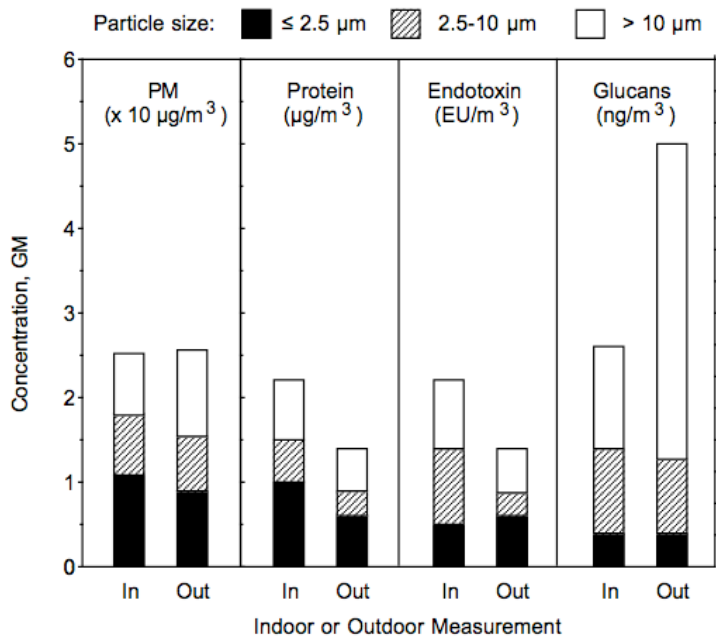
<b>Disease</b>	<b>Microbial agent</b>	<b>Taxa</b>	<b>Reference</b>
Chickenpox	Varicella zoster virus	Virus	Gustafson et al. (1982)
Cold (common)	Rhinovirus	Virus	Heikkinen and Järvinen (2003)
Gastroenteritis	<i>Norovirus</i>	Virus	Marks et al. (2003)
Influenza	Influenza virus A	Virus	Tellier (2009)
Legionnaires'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



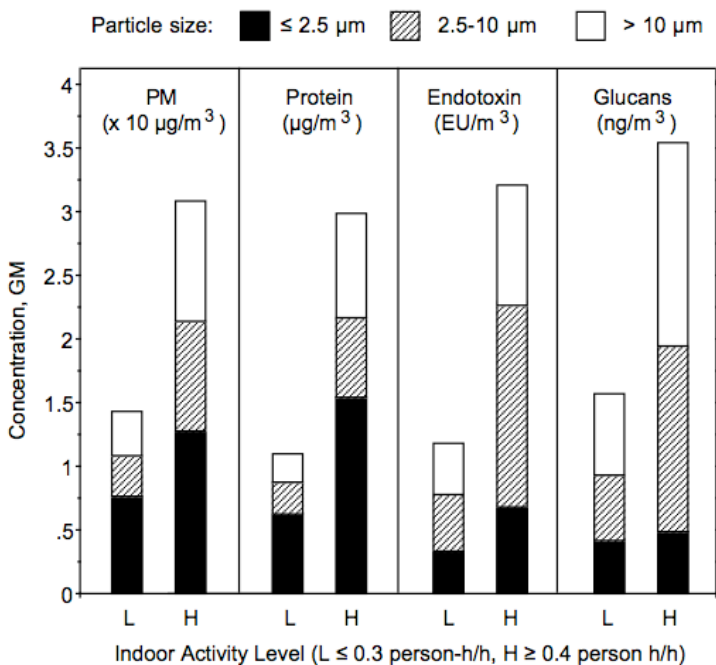
**Figure 1.** Cumulative probability distribution of indoor and outdoor airborne concentrations of culturable fungi measured in 1717 US buildings (Shelton et al., 2002). In all, 9619 indoor and 2407 outdoor samples were collected during indoor air quality investigations.



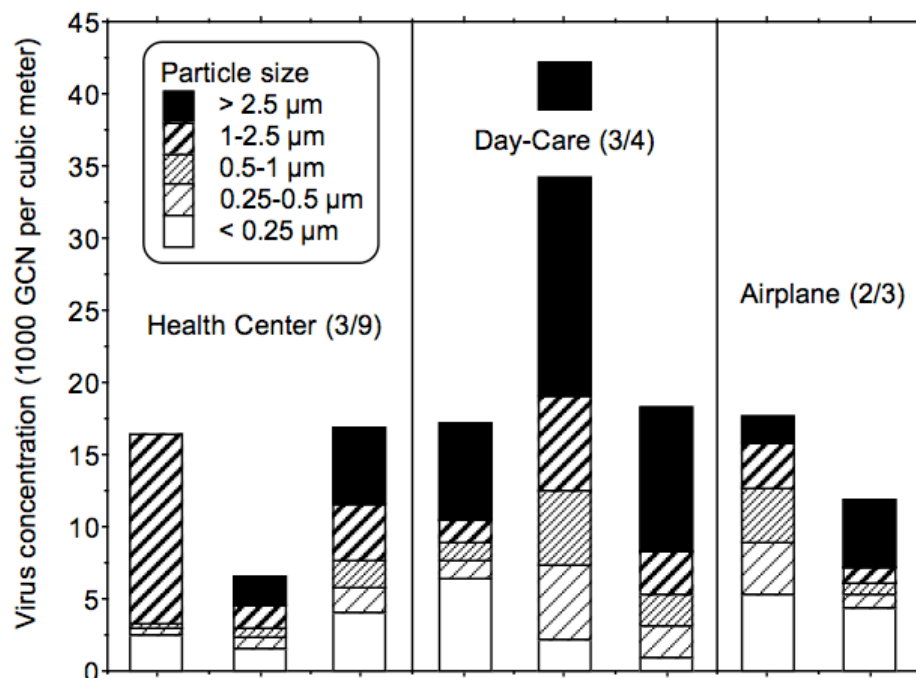
**Figure 2.** Results from personal sampling of 81 elementary school teachers in eastern Finland (Toivola et al., 2004). For each subject, 24-h filter samples were collected twice during winter. Total fungi and bacteria were determined by microscopic analysis. Viable fungi and bacteria were evaluated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



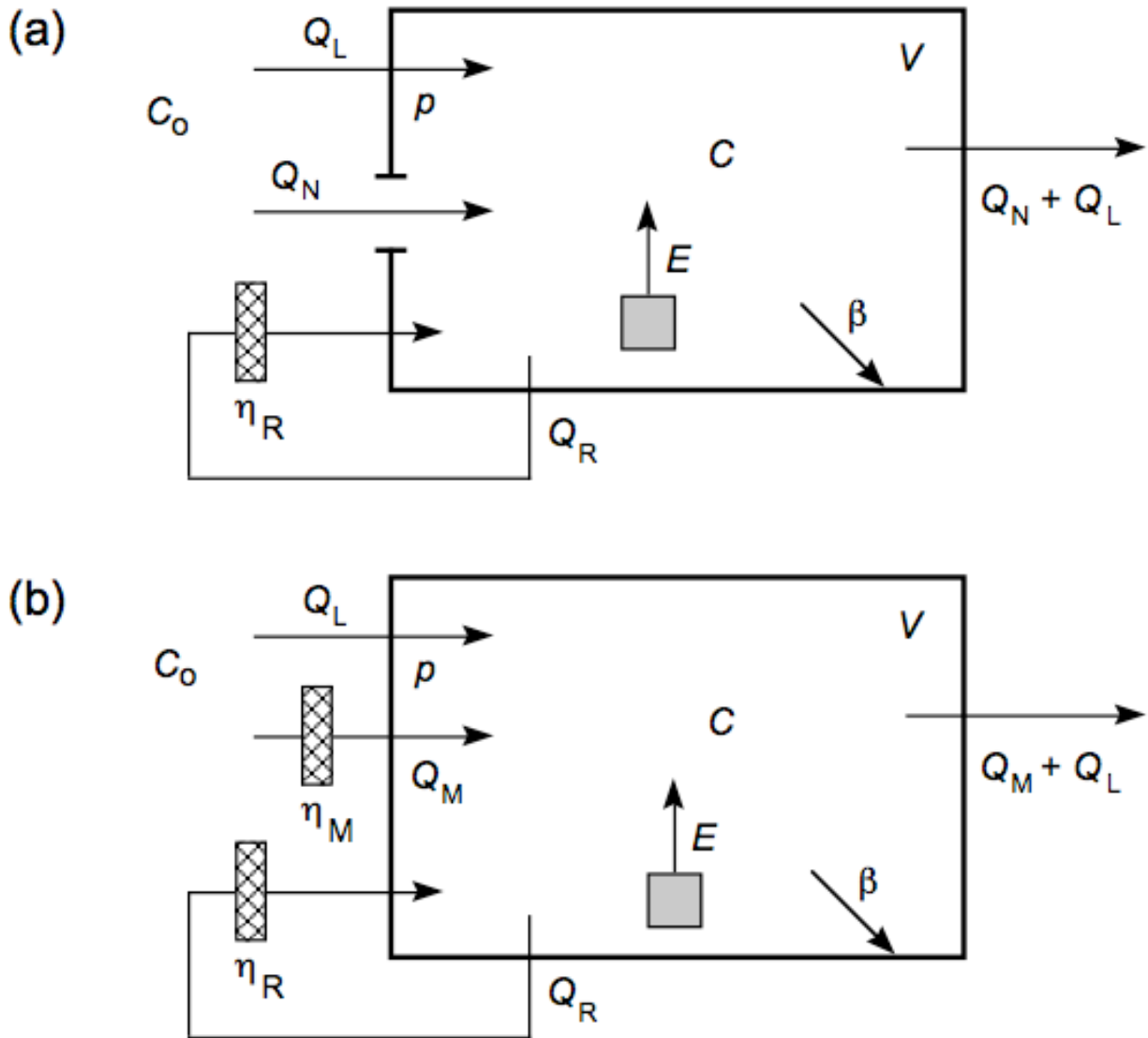
**Figure 3.** Aerosol and bioaerosol parameters sampled inside and outside ten homes in northern California. At each house, four daytime samples were collected (9-12 h each), using size-segregated, filter-based sample collection. Plotted results are the geometric mean concentrations for indoors ( $N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



**Figure 4.** Aerosol and bioaerosol parameters sampled inside ten homes in northern California. At each house, four daytime samples were obtained (9-12 h each), using size-segregated, filter-based sample 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).

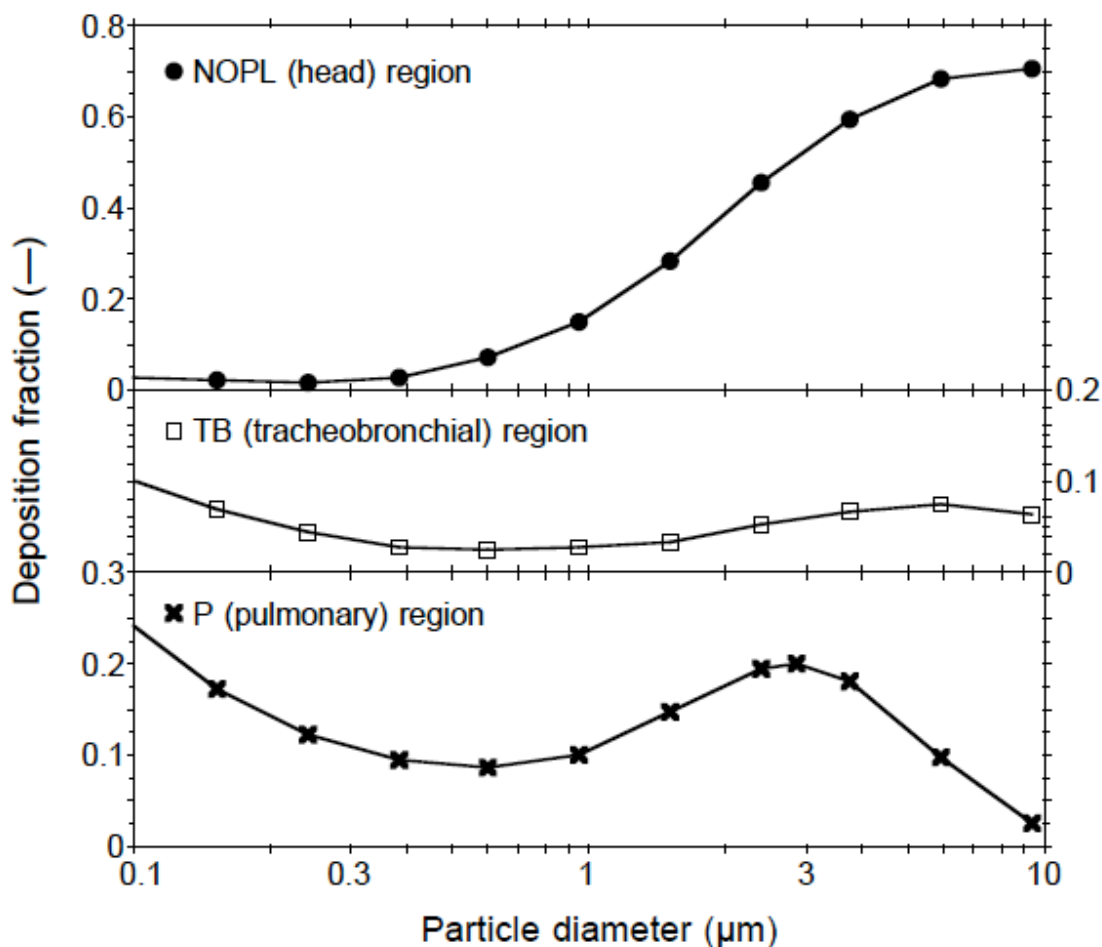


**Figure 5.** Size-resolved influenza A virus concentrations measured in filter samples collected in indoor environments during the 2009-2010 flu season (Yang et al., 2011). In all, eight of sixteen samples collected (3 of 9 in a health center, 3 of 4 in a daycare center and 2 of 3 in an airplane) tested positive for influenza A.

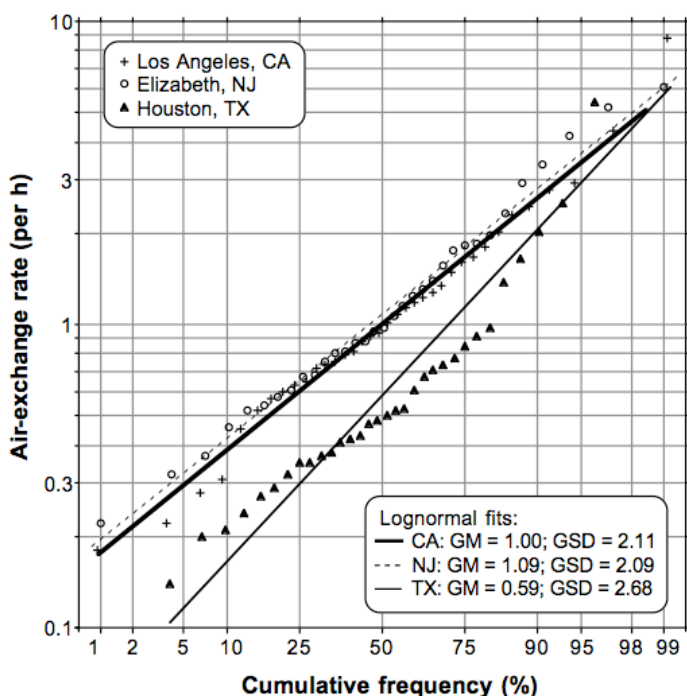


**Figure 6.** Schematic representation of indoor environments for quantitatively relating influencing processes to resulting concentrations of bioaerosol parameters: (a) residence; (b) commercial building. Symbols (associated units) are as follows:  $C_o$  — outdoor concentration of bioaerosol parameter (quantity  $\text{m}^{-3}$ );  $C$  — indoor concentration of bioaerosol parameter (quantity  $\text{m}^{-3}$ );  $V$  — interior volume ( $\text{m}^3$ );  $Q_N$  — natural ventilation rate ( $\text{m}^3 \text{h}^{-1}$ );  $Q_L$  — ventilation rate associated with infiltration ( $\text{m}^3 \text{h}^{-1}$ );  $Q_R$  — recirculation air flow rate ( $\text{m}^3 \text{h}^{-1}$ );  $Q_M$  — mechanical ventilation rate ( $\text{m}^3 \text{h}^{-1}$ );  $p$  — penetration efficiency of bioaerosol parameter associated with infiltration (—);  $\eta_R$  — single-pass filtration plus deposition efficiency in recirculating airflow (—);  $\eta_M$  — single-pass filtration plus deposition efficiency in mechanical ventilation supply flow (—);  $\beta$  — rate coefficient for deposition on indoor surfaces ( $\text{h}^{-1}$ );  $E$  — emission rate from indoor sources (quantity  $\text{h}^{-1}$ ).

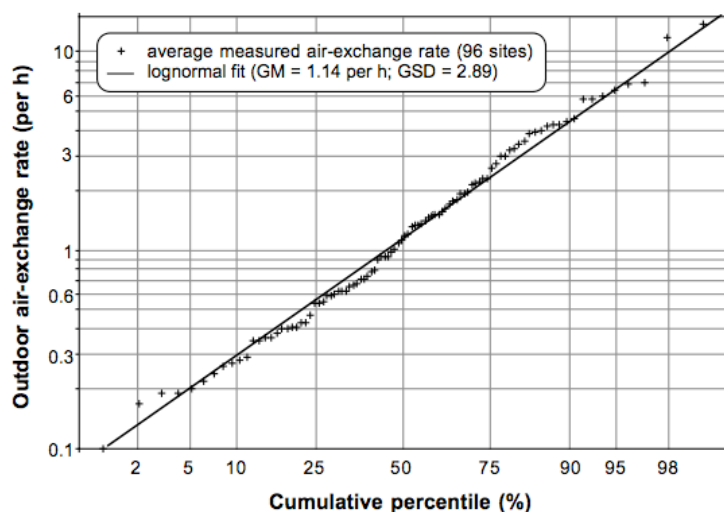




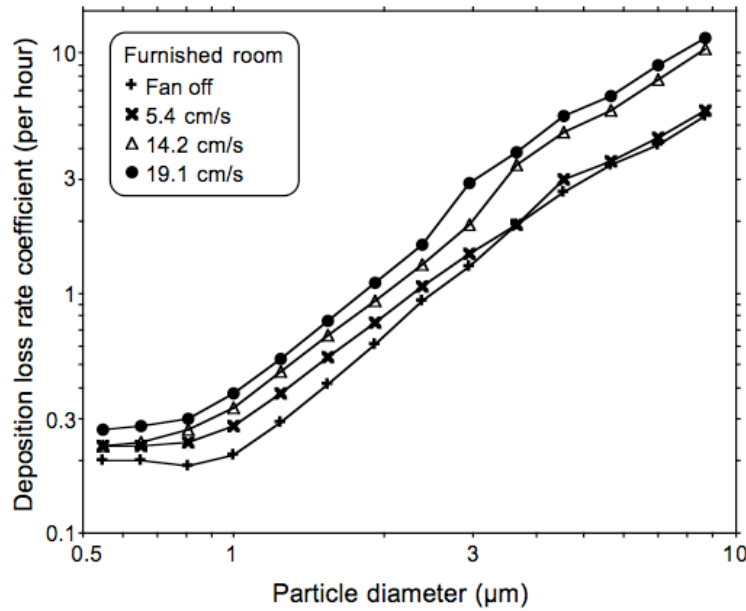
**Figure 7.** Fractional particle deposition in different regions of the respiratory tract as functions of particle size. The results are from the NCRP/ITRI semi-empirical model (Yeh et al., 1996). Particle density is assumed to be  $1 \text{ g cm}^{-3}$ . The results assume nose breathing, tidal volume of 0.77 L, breathing frequency of  $13 \text{ min}^{-1}$ , 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.



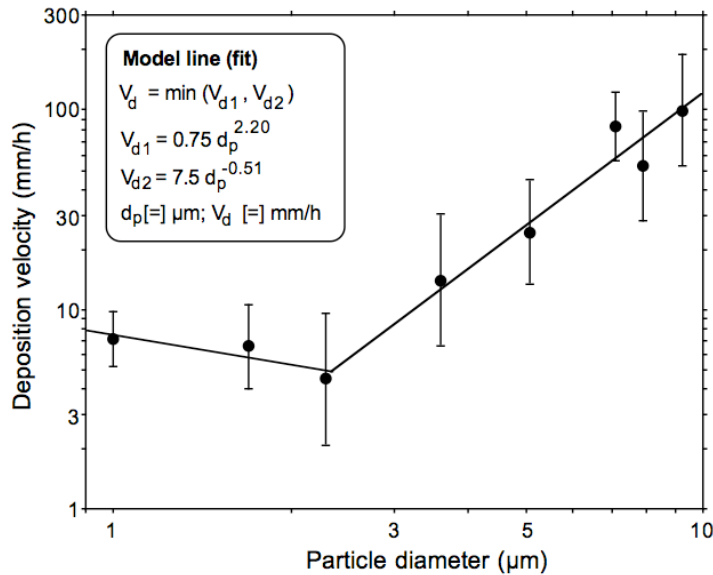
**Figure 8a.** Air-exchange rates (AER) measured in samples of houses in Los Angeles, CA ( $N = 105$ ), Elizabeth, NJ ( $N = 96$ ), and Houston, TX ( $N = 100$ ). For each house, one or two measurements of air-exchange rate were made over a few-day period using perfluorocarbon tracers. Analysis is based on treating each house as a single unit; in cases where two AER measurements were made, the results were averaged. Yamamoto et al. (2010) have also published an analysis of these data. (Data source: <https://riopa.aer.com/login.php>.)



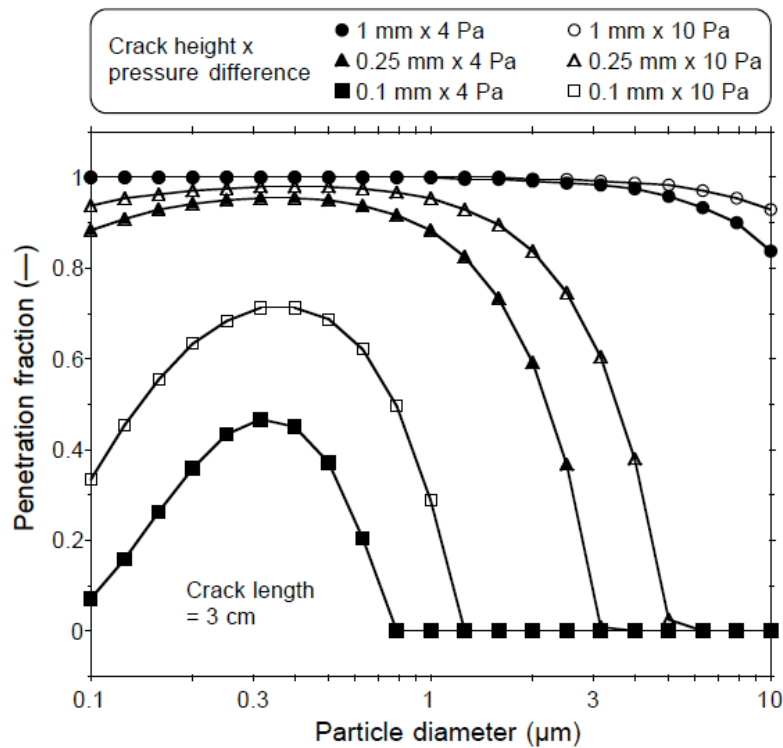
**Figure 8b.** Air-exchange rates (AER) measured in 96 US commercial buildings during the US Environmental Protection Agency's BASE Study. At each site, up to four determinations of outdoor AER were made over periods of several hours each while the building ventilation system was operating. All measurements for any given site were averaged; the distribution of the averaged results is presented in the figure. (Data source: Persily and Gorfain, 2008).



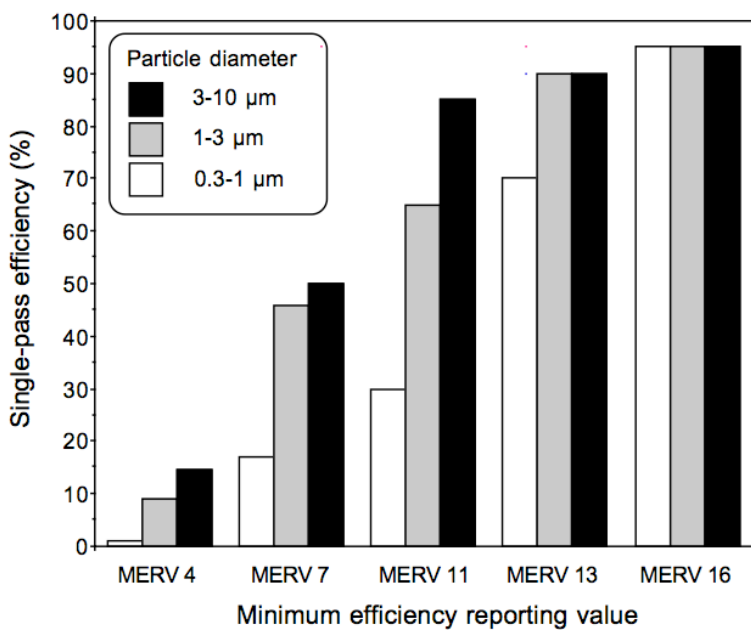
**Figure 9.** Particle deposition loss rate coefficient ( $\beta$ ) measured in a 14-m<sup>3</sup> room as a function of particle diameter. Three of four experiments were conducted with four small fans operating to induce different degrees of air motion. As noted in the key, the mean measured speed in the room with the fans on ranged between 5.4 and 19.1 cm/s. Source: Thatcher et al. (2002).



**Figure 10.** Deposition velocity ( $v_d$ ) measured to the vertical wall of a 2-m<sup>3</sup> 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  $\beta_w$  is the contribution to the total loss rate coefficient attributable to deposition on the walls (h<sup>-1</sup>),  $S_w$  is the wall area (m<sup>2</sup>), and  $V$  is the room volume (m<sup>3</sup>). The model equations are linear regressions to the log-transformed data, utilizing three measured points ( $v_{d1}$ ) and six measured points ( $v_{d2}$ ), respectively.



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



**Figure 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).