

Understanding Building-Occupant-Microbiome Interactions toward Healthy Built Environments: A Review

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Running Title: Building-Occupant-Microbiome Interactions in the Built Environment

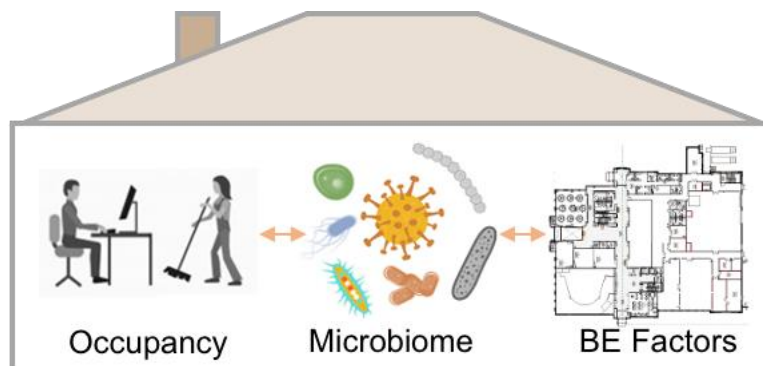
Highlight

The built environment, occupants, and microbiomes constitute an integrated ecosystem

This review summarizes research progress which has focused primarily on microbiomes

Critical research needs include studying impacts of occupant behaviors on microbiomes

Graphical abstract



Abstract

Built environments, occupants, and microbiomes constitute a system of ecosystems with extensive interactions that impact one another. Understanding the interactions between these systems is essential to develop strategies for effective management of the built environment and its inhabitants to enhance public health and well-being. Numerous studies have been conducted to characterize the microbiomes of the built environment. This review summarizes current progress in understanding the interactions between attributes of built environments and occupant behaviors that shape the structure and dynamics of indoor microbial communities. In addition, this review also discusses the challenges and future research needs in the field of microbiomes of the built environment that necessitate research beyond the basic characterization of microbiomes in order to gain an understanding of the causal mechanisms between the built environment, occupants, and microbiomes, which will provide a knowledge base for the development of transformative intervention strategies toward healthy built environments. The pressing need to control the transmission of SARS-CoV-2 in indoor environments highlights the urgency and significance of understanding the complex interactions between the built environment, occupants, and microbiomes, which is the focus of this review.

Keywords

Microbiome, Built Environment, Occupant, Health.

1. Introduction

The built environment (BE) harbors diverse microbial populations including viruses, bacteria, fungi, and protozoa (Adams et al., 2016; Gilbert and Stephens, 2018; Dannemiller, 2019), which collectively constitute the microbiomes of the built environment (MoBE). Humans have extensive interactions with the microbiomes that are in the air circulating in buildings, in the water flowing in plumbing systems, and on the surfaces from the most inaccessible to the most touched objects (NASEM, 2017). In developed countries, people spend about 90% of their time indoor (Klepeis et al., 2001). Increasing urbanization and modernization will likely make people in developing countries spend more time indoors (Popkin, 1999). Thus, the majority of microbiomes encountered by most humans during their lifetime are those present in the BE (Leung and Lee, 2016). There are diverse taxonomic groups in MoBE, which has been revealed by the rapid development and application of culture-independent, high-throughput sequencing techniques. Evidently, it is essentially impossible to characterize MoBE with conventional culture-dependent techniques, which are capable of targeting only a small portion of the MoBE that can be cultivated under laboratory conditions. Common bacterial genera in indoor environments include *Pseudomonas*, *Acinetobacter*, *Staphylococcus*, *Corynebacterium*, *Sphingomonas*, and *Clostridium*, while common fungi may be represented by populations associated with *Cladosporium*, *Penicillium*, and *Aspergillus* (Wilkins et al., 2016). The MoBE differs considerably in built environments with different functionalities, such as residential homes, hospitals, schools and daycare centers, transit systems, shopping malls, public restrooms, offices, museums, food processing facilities, fitness centers, aircraft, and even the international space station (Tringe et al., 2008; Kembel et al., 2014; Leung et al., 2014; Mukherjee et al., 2014; Checinska et al., 2015; Kettleson et al., 2015; Nordahl Petersen et al., 2015; Bokulich et al., 2016; Brooks et al., 2017; Täubel and Leppänen, 2017). Most studies are focused on bacteria and fungi, because of methodological limitations to profiling viruses. The few reports studying viral constituents of the MoBE targeted specific viruses in distinct BE such as intensive care units (ICUs) (Bramley et al., 2012).

MoBE has profound impacts on human health and well-being. Microbial pathogens are responsible for more than 400 million years of life lost annually worldwide (Fitzpatrick et al., 2019), some of which are results of transmission of pathogens via air, water, and surface contact in the BE (Madhav et al., 2017). It should be noted that the BE is considered as a major venue that facilitates the transmission of the novel coronavirus (SARS-CoV-2) (Allen and Marr, 2020; Prather et al., 2020), which is a pandemic that has infected millions and is still spreading rapidly. The resulting economic losses will be unprecedented. In addition, transmission in the BE is also responsible for the spread of influenza (e.g. by contacting contaminated objects) and *Legionella* (e.g. via inhalation of contaminated water droplets), leading to significant human and economic losses. Flu alone costs the US healthcare system an average of \$11.2 billion each year (Putri et al., 2018). During the 2019-2020 flu season, an estimated 16,000 people have died of flu. The case-fatality rate of Legionnaires' disease, caused by *Legionella*, can be as high as 50% in certain outbreaks (Prussin et al., 2017). The transmission of microbial pathogens in the BE is also manifested by the fact that every year there are 1.7 million hospital acquired infections (HAIs) in the US, resulting in 99,000 related deaths every year (Curtis, 2008). Moreover, about 21% of asthma cases in the US can be attributed to dampness and mold in the BE, particularly residential homes, costing \$3.5 billion annually (Mudarri and Fisk, 2007). It was found that reduced microbial diversity in the BE is associated with the development of asthma (Ege et al., 2011). In addition, MoBE may affect immune system functions through interactions with the host-associated microbiota, and further impact occupants' mental health (Hoisington et al., 2015). Having the simplistic assumption that microbiomes are "bad," people conventionally have attempted to suppress microbial growth and eradicate microorganisms from the BE. However, the MoBE research community has become increasingly aware of the beneficial roles "good" microbiomes play in preventing diseases (Turnbaugh et al., 2006; Round and Mazmanian, 2009; Bultman, 2014; Hsiao et al., 2013; Ridaura et al., 2013; Lowry et al., 2016; Dai et al., 2017). One example is that exposure to microbiomes from dogs (Liu et al., 2015) and traditional farm-type environments (Kirjavainen et al., 2019) early in life has been linked to reduced probability of developing asthma.

To develop strategies for sustainable management of the BE to promote public health and well-being, it is essential to understand the processes underlying the interactions between the microbiomes, BE, and occupants. To this end, numerous studies have been conducted to characterize the MoBE and subsequently its linkages to the attributes of BE design and operation, as well as occupant behaviors. BE, occupants, and microbiomes constitute a system of ecosystems with extensive interactions that impact one another. The composition and dynamics of the MoBE, which is a frequent target for microbial control, have been found to be impacted considerably by the occupants as well as BE design and operation. This review summarizes our current understanding of how BE design and operation, and occupant behaviors and activities interact to shape MoBE. The review also discusses the opportunities, challenges and future research directions in the field of MoBE to move beyond the basic characterization of MoBE in order to gain mechanistic understanding of the interactions between BE, occupants, and microbiomes at various spatiotemporal resolutions, which would support the development of transformative and effective intervention strategies toward healthy BE.

2. Bibliographic Overview

Co-authorship Network by Country

To include relevant literature in the field of MoBE in this review, we searched and collected all published items in Web of Science (WOS) having the term “built environment” and “microbi*” in the abstract/title/keywords. A total of 1,403 publications related to MoBE were collected from 1991 to February 2020. Since MoBE is likely distinct geographically, the publication data was uploaded to VOSviewer to create a co-authorship network by country (van Eck and Waltman, 2010), showing that authors who published work in the field of MoBE are from 95 countries. The number of countries with 5 or more MoBE-related publications is 46, indicating the concentration of MoBE research in a small number of countries (Fig. 1). Among the countries represented in the network, authors from the US contributed to more than 25% of all the publications on MoBE. More revealing is the observation that research collaboration is stronger between countries already with high levels of MoBE research, which are mostly conducted in developed countries (Fig. 1). For example, the US has a very high level of collaboration with Germany and Belgium in MoBE research. Given the potential differences in MoBE between developed and developing countries, it is necessary to expand MoBE search in developing countries to address issues of global impact, such as the transmission of pathogens in BE, which may differ considerably in countries with distinct BE design and operation attributes.

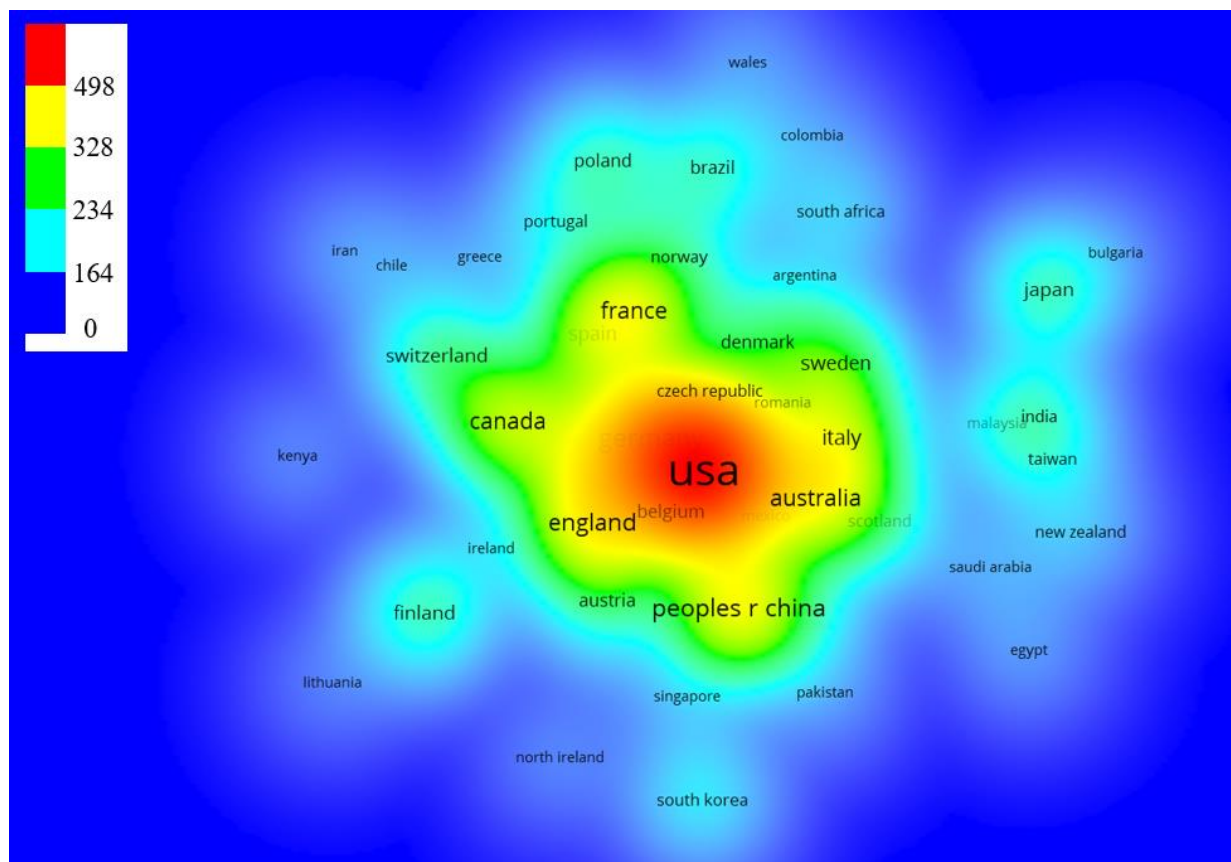


Fig. 1 Bibliometric map based on the network of co-authorship relationships among 46 countries, with the color of the network representing publication count by country. The distance between countries in the network represents the level of collaboration, i.e. the smaller the distance between the two countries, the greater number of publications contributed by authors from both countries.

Keyword Co-occurrence Network

VOSviewer was also used to create a keywords co-occurrence network, which could be used to identify key components included for MoBE analysis (Lee and Su, 2010). A total of 3,989 author keywords were identified in 1,403 publications on the topic of MoBE. These keywords were reduced to 110 by using minimum occurrences of 5, which was used to develop a co-occurrence network consisting of 110 keywords and 563 links (Fig. 2). As expected, microbiome, built environment, bacteria, and fungi are the four dominant keywords in the published items. In comparison, keywords related to specific BE attributes, such as air, surface, and water quality, have received less research attention and are not frequently investigated together with the microbiomes, indicated by the long distance between these keywords and the center of the network (Fig. 2). Given the significant impact of BE attributes on MoBE, the general lack of research efforts to linking BE attributes to MoBE indicates an important gap that needs to be closed in future studies (Kembel et al., 2012; Leung et al., 2014). Moreover, virus is absent as a keyword in the network, indicating that, despite the significance of viruses as a part of MoBE, few studies have investigated viruses as constituents of MoBE.

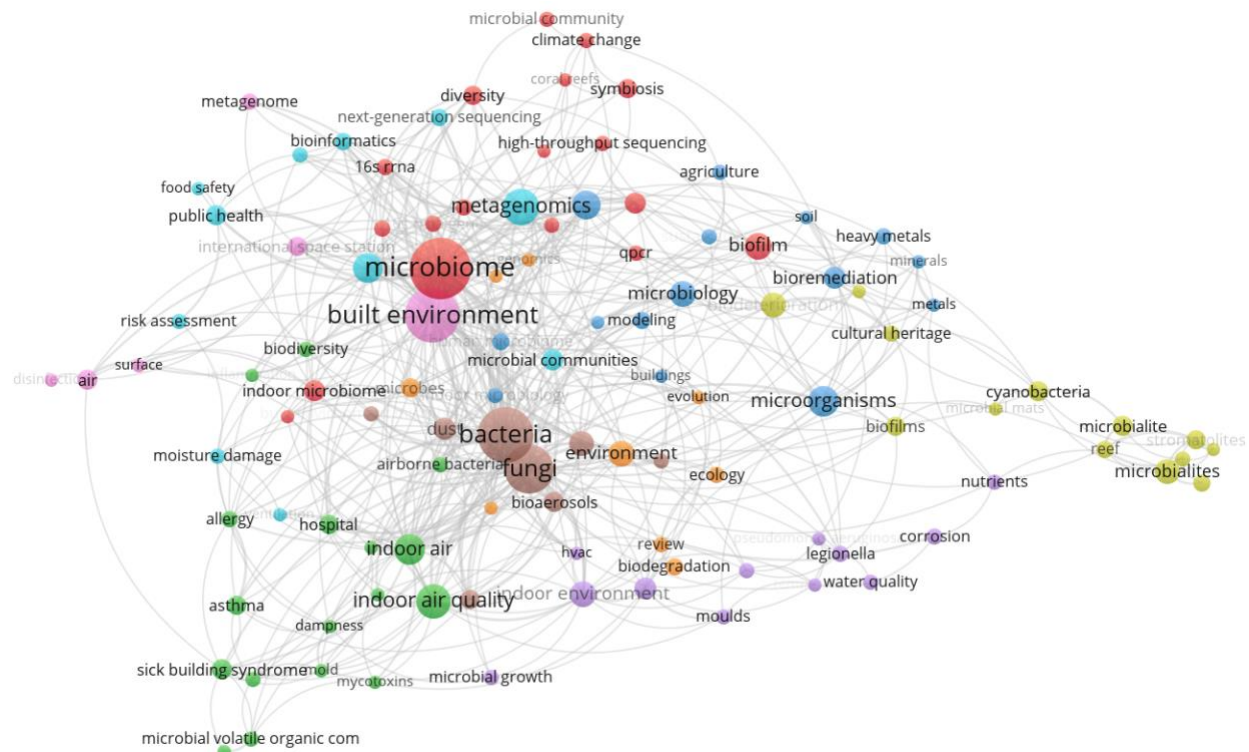


Fig. 2 Author keyword co-occurrence patterns in MoBE literature. Each circle represents a keyword. The size of the circle is defined as the occurrence frequency of the keyword measured in terms of publications. The distance between the circles is an indication of the number of co-occurrences – the shorter the distance between two keywords, the stronger the relationship is.

3. Impacts of Occupancy on MoBE

The occupants of BE play an important role in shaping MoBE (Smith et al., 2013; Nice and Bole, 2016). It has been demonstrated that high occupancy increases the accumulation of human-associated microorganisms (Hospodsky et al., 2012; Kembel et al., 2012; Qian et al., 2012; Kembel et al., 2014; Meadow et al., 2014a; Meadow et al., 2014b; Miletto and Lindow, 2015; Ross and Neufeld, 2015; Dannemiller et al., 2016; Kang et al., 2018) and potential microbial transmission through increased social interactions, direct or indirect contact with surfaces, and air flow (Salathe et al., 2010; Andrews et al., 2014; Wood et al., 2014). The MoBE associated with indoor dust and surfaces are specifically enriched with microbial populations originated from the human skin, gut, oral, and urogenital microbiomes (Flores et al., 2011; Jeon et al., 2013; Adams et al., 2014; Lax et al., 2014; Leung et al., 2014; Meadow et al., 2014a; Afshinnnekoo et al., 2015; Gibbons et al., 2015). This is expected as it is estimated that humans emit in the order of 10^6 particles and 10^7 bacterial genome copies per hour (Qian et al., 2012; You et al., 2013). It is worth noting that the microbial clouds emitted from individual human occupants could be different. For instance, people with contrasting health conditions exhibit distinct microbiomes (Hoisington et al., 2015; Lloyd-Price et al., 2016). The distribution of occupant-associated indoor microbiomes can also be linked to the duration that individuals spend in the BE and the type of activities performed (Dunn et al., 2013; Lax et al., 2014; Adams et al., 2015b; Meadow et al., 2015; Karkman et al., 2017; Luongo et al., 2017; Ross et al., 2017), which could partially explain the differences in MoBE of different functionalities including hospitals, residences, and schools (Meadow et al., 2015).

Occupant-associated microbiomes may disperse into the BE via three pathways (Fig. 3): 1) direct human contact with surfaces; 2) emission of bioaerosols and particulates from human breath, skin, and hair; and 3) resuspension of indoor dust containing human-emitted microbiomes (Meadow et al., 2015). Previous studies have shown that occupants affect MoBE through desquamation and physical contacts with indoor surfaces (Lax et al., 2014; Adams et al., 2015a; Wood et al., 2015) as the primary pathways. Both the frequency (Flores

et al., 2013) and the nature of human contact (e.g. with skin, or with shoes on floor or carpet, or release of gut-associated microbiomes in washrooms) (Flores et al., 2011; Kembel et al., 2014; Meadow et al., 2014b; Mukherjee et al., 2014; Gibbons et al., 2015; Wood et al., 2015) can affect the composition of microbiomes in different indoor areas and on different surfaces within a single BE. For instance, desk surfaces in classroom are associated with indicator taxa related to *Streptococcus* species that are more commonly found in human skin and oral samples. Walls are found to be associated with indicator taxa from airborne bacterial assemblages such as *Sphingomonas* and *Alicyclobacillus* species, while floors are more likely to harbor non-human environmental bacterial populations (Meadow et al., 2014b). Revealed by longitudinal analysis, surfaces in public areas (e.g. fitness centers, airplanes, public transit, etc.) with more frequent contacts exhibit greater temporal variations in their microbial communities (Wood et al., 2015), as compared with a private BE (e.g. residential unit). In addition, occupant movements may cause re-suspension of settled dust particles (Hospodsky et al., 2012; Qian et al., 2012; Adams et al., 2015a; Yamamoto et al., 2015), and introduce exogenous microbial populations from outdoor environments (Fujimura et al., 2010; Heydenreich et al., 2012; Adams et al., 2015b; Barberán et al., 2015), which can redistribute and reshape MoBE. These findings reveal considerable variations in MoBE at fine spatiotemporal resolutions, pointing to the need for surveying MoBE at much finer resolutions than those of individual rooms and seasons, which are typically lacking in MoBE studies in the literature.

Given the significance of occupants in shaping MoBE, it is fundamentally important to incorporate occupant behaviors and activities into the analysis of MoBE. Up till now, few studies have attempted to link occupants to MoBE, which is likely due to the lack of technologies suitable for the monitoring and characterization of occupant movements.

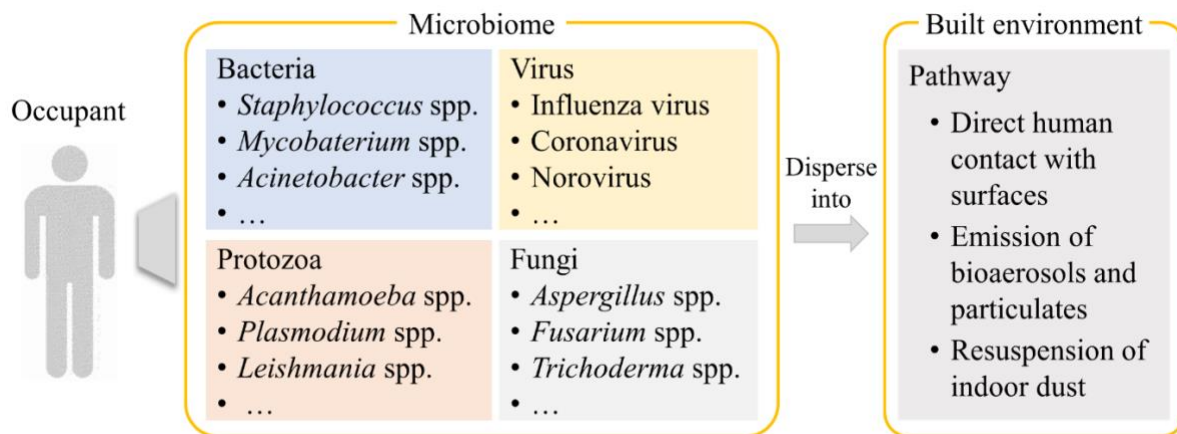


Fig. 3 Impacts of Occupancy on MoBE

Previous studies have further shown that the impacts of occupants on MoBE are mediated by the design and operation of the BE. For instance, architectural design attributes influence occupant behaviors and activities such as the contact and use patterns (Beans, 2016; Brown et al., 2016), human interactions (Purcell, 1987; Dunn et al., 2013), how and where occupant-associated microbiomes are emitted and deposited (Kembel et al., 2014; Meadow et al., 2014a), properties of building surface materials (affecting the colonization of human-emitted microbiomes), and temperature (affecting occupant behaviors). Next, a detailed review of how the design and operation attributes of BE would influence MoBE is presented.

4. Impacts of BE Attributes on MoBE

The built environment is a reservoir of diverse microorganisms and provides an environment for microbial colonization, succession, and transmission. The attributes of BE design and operation have a direct influence on the MoBE (Fig. 4). Further, these attributes indirectly affect MoBE via impacts on occupant behaviors and activities. For instance, the building layout directly affects the movements and activities of occupants, which subsequently influences how occupant-associated microbiomes are dispersed in the BE (Hathway et al., 2011).

The choice of design will also influence sunlight exposure, which could play roles in the inactivation of microorganisms (Couret et al., 2013). Ventilation (e.g., the exchange with outdoor air) may also have impact on indoor microbiomes in both diversity and abundance. The direction of airflow will dictate the distribution of aerosols and particulates which are the carriers of microorganisms. Temperature and moisture represent two interrelated attributes in the built environment as temperature differences are typically linked to humidity gradients. Controlling moisture and temperature in the BE is believed to be important to suppress the growth of molds, which are significant constituents of MoBE. More importantly, the coupled influence of moisture and building material properties (e.g. surface roughness and pH of material), together with human contact and activities, will significantly influence microbial growth. Often neglected is the contribution of plumbing systems to MoBE, as bacteria such as *Legionella* can be transported from the water in plumbing systems to the air, and subsequently transmitted further via the ventilation systems.

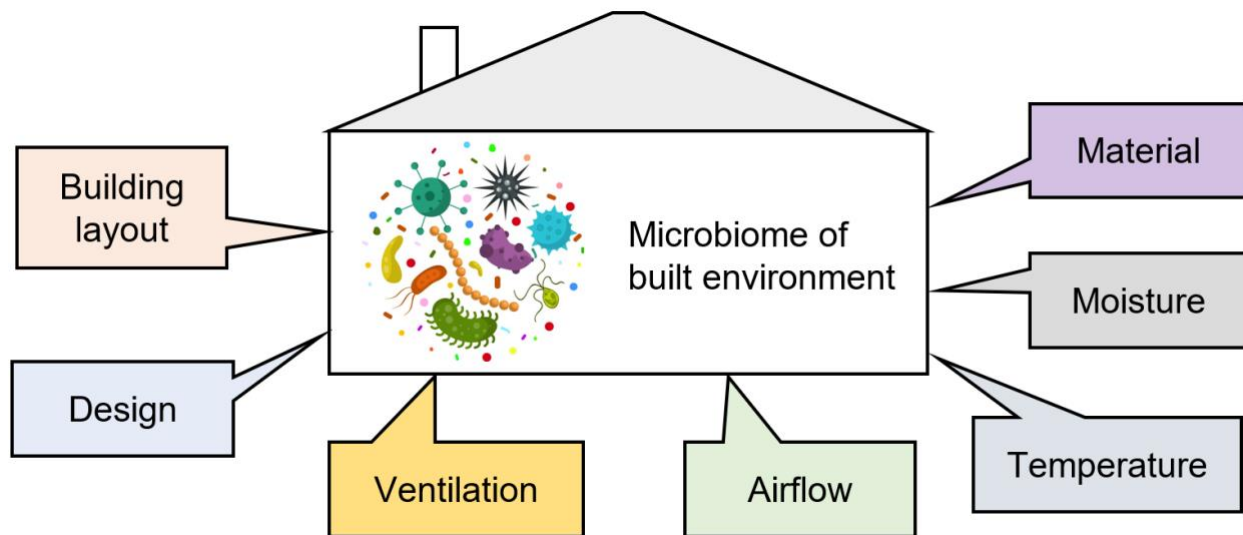


Fig. 4 Impacts of BE attributes on MoBE

4.1 Functional Characteristics of BE

The functionalities of BE have been found to directly impact the composition of MoBE. Previous studies analyzed bacterial communities in dust samples collected from 155 BE locations to reveal how BE design attributes impact the MoBE (Kembel et al., 2012; Kembel et al., 2014). It was found that bacterial communities in restrooms were dramatically different from those in other rooms. Further, the set of bacterial taxa found in spaces with high occupancy and high degree of connectedness to other spaces exhibit significant differences from those found in spaces with low occupancy and low degree of connectedness. Another study examined microbiome data acquired from various built environments with different functionalities, including apartment buildings, food processing facilities, hospitals, residential kitchens, art museums, and university buildings (Adams et al., 2015a). The analysis identified variations in microbial communities among different building types, which supports the hypothesis that the function of BE would impact the indoor microbial communities.

Despite the numerous studies on MoBE, it remains unclear how the functions of BE would impact MoBE. This ambiguity may stem from two aspects. First, the functional characteristics of BE likely impact the MoBE through many interrelated processes. The functionality of a particular BE would typically dictate various design attributes of the BE, including the choices of sunlight admission, ventilation pattern, building materials, and heating, ventilation, and air conditioning (HVAC) systems. These choices collectively would influence the environmental conditions (e.g. temperature, humidity, lighting, and airflow) critical for the colonization, succession, and also transmission of the MoBE. Second, the functional characteristics of BE would likely also impact occupant activities (e.g. specific user groups, occupant density, and movement) (Zifferblatt, 1972). Given the significance of occupants and building characteristics in shaping MoBE, it is important to study the

building, occupant, and microbiome as an integrated system to identify processes involved in the development of MoBE. In the following sections, we will review the scientific literature focusing on the linkages between design and operational attributes and MoBE.

4.2 Building Material

All building materials may be subject to microbial colonization (Warscheid and Braams, 2000; Cutler and Viles, 2010; Jurado et al., 2014; Coutinho et al., 2015; Dedesko and Siegel, 2015; Guerra et al., 2019; Hu et al., 2019). Studies have been conducted to identify the microorganisms readily present on building materials in the BE. One group of microbial populations most frequently identified in building materials are those belonging to *Penicillium* (Andersson et al., 1997; Tuomi et al., 2000; Doll, 2002; Hyvärinen et al., 2002; Rintala et al., 2002; Andersen et al., 2011; Verdier et al., 2014). *Aspergillus* species are often found on ceramic-type materials as well as surfaces of paint and glue (Hyvärinen et al., 2002; Andersen et al., 2011). Gypsum-type materials may facilitate the development of *Stachybotrys*, another indication of the selectivity of microbial colonization on building materials (Pasanen et al., 1992; Andersson et al., 1997; Hyvärinen et al., 2002; Andersen et al., 2011).

As a result, the susceptibility of different building materials to microbial colonization has been evaluated. Among bio-based construction materials, chipboard was found to be the most susceptible to mold growth and wood the least (Stefanowski et al., 2017), while plant aggregates would make earth-based materials more sensitive to fungal growth (Laborel-Préneron et al., 2018; Simons et al., 2019). Compared with cement-stabilized earth blocks, bricks as wall materials were shown to be more susceptible to fungal growth (Udawattha et al., 2018). Some studies suggest that high levels of copper in pipe materials inhibit *Legionella* survival and growth in indoor plumbing systems (van der Kooij et al., 2005; Proctor et al., 2017), while others found increased persistence of *Legionella* in biofilms formed on copper plumbing materials (Buse et al., 2014). A significant portion of indoor surfaces, including textiles, have incorporated metal nanoparticles to discourage fungal and bacterial growth (Chen et al., 2018; da Silva et al., 2019). Recently, the green wall and green roof concepts have also been introduced into buildings. The plants may introduce source microorganisms, moisture, and nutrition that support microbial growth. It is known that indoor plants can contribute substantially to the microbial abundance and diversity in the BE (Mahnert et al., 2015). It is thus important that new materials being continuously developed for applications in the BE need to be evaluated for their impact on MoBE as part of the product evaluation process.

The properties of the materials, coupled with lighting, heating, cooling, humidity and ventilation as well as the occupants and their activities, can considerably affect MoBE. Building material properties may contribute to the microbial colonization via two ways. First, the ingredients of the building materials can provide potential substrates and nutrients for the colonized microbiomes (Lugauskas et al., 2003; Vacher et al., 2010). For instance, because cellulose-based materials can be metabolized by a number of microbial populations (Gutarowska, 2010; Hoang et al., 2010), they are more susceptible to microbial colonization and growth than inorganic materials such as gypsum, mortar, and concrete. Addition of carbon sources (e.g. carboxymethyl cellulose) or emulsion paint is known to provide potential substrates for microbial growth (Ayerst, 1969; Grant et al., 1989). Second, most building materials, such as wallpaper glue, paint, grease, paper, textile, and wood products, are characterized with high porosity and surface roughness. The rough and porous surface may facilitate the adherence of dust and organic compounds resulting from the activities in the buildings. In addition, porous material may also retain sufficient moisture (Hoang et al., 2010). As a result, in rough and porous building materials could facilitate microbial growth due to increased levels of organics and moisture (Lax et al., 2019). However, it is suggested that microorganisms retained by porous materials may be immobilized, making it less likely for these microorganisms to subsequently interact with the BE (Abrishami et al., 1994; Ak et al., 1994). Therefore, the influence of porous materials on MoBE needs further investigation.

4.3 Heating, ventilation, and air conditioning (HVAC)

4.3.1 Temperature

Indoor air temperature has been shown to have impacts on the abundance of indoor microbial community. However, the relationship between temperature and MoBE is unclear as some studies found positive correlations as greater abundance of indoor was associated with higher temperature (Ponsoni and Raddi, 2010; Frankel et al., 2012; Kembel et al., 2012) while other studies observed inverse correlations (Frankel et al., 2012; Dannemiller et al., 2016). The potential explanation to the conflicting findings is twofold. First, most BE are maintained at a temperature range between 60- and 80- degrees Fahrenheit for human comfort. Although different types of microbial populations have different temperature ranges for growth, many microorganisms grow well in this indoor temperature range (Tang, 2009). As a result, the temperature alone in the BE may not be considered as a factor to explain the variations in MoBE. Second, temperature may impact other parameters in BE such as moisture, as well as occupant behaviors and activities, which exert indirect impacts on microbial colonization and transmission. These indirect impacts made it very difficult to quantify the impact of temperature on MoBE.

4.3.2 Moisture

Moisture significantly influences the survival (Jump et al., 2007; Tang, 2009; Zhao et al., 2012; Hoeksma et al., 2015), activity (Dannemiller et al., 2017; Hegarty et al., 2018), and composition of the MoBE (Pessi et al., 2002; Kembel et al., 2012; Dannemiller et al., 2016). The moisture in BE may come from a variety of sources including indoor water vapor content, weather events, plumbing problems, and leaks from building envelopes and roof systems. Temperature gradients are a less obvious source of moisture, which is often overlooked and ignored. However, at locations where relatively warm and moist air is in contact with relatively cold surfaces, water condensate may occur on building surfaces (Hänninen, 2011), which might occur frequently in air-conditioned buildings.

Moisture in the air and on the surface may impact the MoBE in different ways. Relative humidity is often used to measure moisture saturation in the air. Low relative humidity will increase the possibility of aerosolization of microorganisms on indoor surfaces and the resuspension into air due to occupant movements (Frankel et al., 2014; Hyytiäinen et al., 2018; Wu et al., 2018). Low relative humidity will also increase the potential for the aerosols to stay aloft longer and travel longer (Wolkoff, 2018). On the other hand, high relative humidity is conducive to microbial survival and activity on surfaces (Jump et al., 2007; Tang, 2009; Zhao et al., 2012; Hoeksma et al., 2015), and facilitates the direct contact transfer of microorganisms from fomite to occupants (Lopez et al., 2013). Microenvironments within surfaces, e.g., high relative humidity in the carpet, can create niches for microbial growth and further influence their transfer from surfaces (Dannemiller et al., 2017). In this sense, localized relative humidity in a building needs to be effectively controlled to reduce the dispersal and transmission of microorganisms in the BE (Wolkoff, 2018).

Moisture at the material surface is assessed as equilibrium relative humidity (ERH). When the ERH reaches certain thresholds, the surface of building materials could become the target of microbial growth. For instance, it is more conducive for microbial growth when the ERH is greater than 70% for wooden materials, 85% for gypsum-board, and around 90-95% for cementitious and concrete materials (Riva et al., 2014; Adams and Lymeropoulou, 2018). High ERH will facilitate the germination and proliferation of mold on building materials (Pasanen et al., 1992; Kembel et al., 2012; Green, 2014; Lau and Chamberlain, 2016; Dade-Robertson et al., 2017). The surface relative humidity is seldom the same as that of the air since the temperature of surface is usually not the same as that of the air. Therefore, efforts to control the indoor air relative humidity alone will not likely guarantee optimal control of mold growth on surfaces (Tsongas and Riordan, 2016).

4.3.3 Ventilation

Ventilation affects indoor temperature, humidity, airflow rates, and carbon dioxide levels which could influence the compositions of MoBE and may select for the survival of specific microbial taxa (Kembel et al.,

2012; Kembel et al., 2014; Leung et al., 2014; Kettleson et al., 2015). The most direct impact of ventilation on MoBE is to facilitate or impede outdoor microbiomes from entering the BE. This argument is supported by studies showing microbial communities in mechanically ventilated rooms exhibit significant differences from those with natural ventilation (Kembel et al., 2012; Adams et al., 2013; Adams et al., 2014; Meadow et al., 2014a). For example, differences in microbial community composition were apparent between dust samples collected from a mixed-use building with half of the offices using natural ventilation and those of the other half using a conventional mechanical system (Brągoszewska et al., 2018). Compared with mechanically ventilated rooms, naturally ventilated rooms had indoor microbiomes more similar to those of the outdoor environment (Kembel et al., 2012; Meadow et al., 2014a), because microbes from the outdoors are more likely to enter the naturally ventilated rooms (Adams et al., 2013; Robertson et al., 2013; Meadow et al., 2014a).

In contrast, mechanical ventilation usually uses filters to prevent some of the outdoor microbes and particulates from entering the BE. Conventional air filters are effective in removing particles less than 0.1 μm in diameter via diffusion and particles larger than 1 μm in diameter with impaction, which makes it effective against bacterial and fungi (Hospodsky et al., 2015) but less effective against some viruses such as influenza due to their size ranges (Lindsley et al., 2010). It has been shown that appropriate ventilation with sufficient air exchanges and/or directed air flow can effectively reduce the overall concentrations of airborne microbial pathogens (Memarzadeh, 2013), thus reducing disease transmission risks (Chartier and Pessoa-Silva, 2009; Hobday and Dancer, 2013). However, inappropriate ventilation, such as high ventilation rates with high turbulence, can retain particulates and associated microbial populations in the air, thus may negatively impact health (Carlton et al., 2019).

Natural ventilation introduces extra outdoor air to the BE and is proven to mitigate the sick building syndrome (Seppanen and Fisk, 2002). This is likely due to the introduction of more diverse indoor bacterial communities into BE, which has shown positive health effects (Kembel et al., 2012). However, natural ventilation also introduces undesirable contaminants such as allergens, which is a challenge to the broader application of natural ventilation, particularly in BE with vulnerable occupants (Kovesi et al., 2009).

4.4 Sunlight

The antiseptic effect of sunlight was discovered in the late 1800s (Downing and Blunt, 1878; Bazzoni, 1914). Such an effect has been particularly studied in healthcare facilities (Nightingale, 1863; Kundsins, 1988; Medeiros et al., 2015). Studies have also been conducted to illustrate how sunlight (full-spectrum) and light of specific spectrum affect mono-culture microorganisms as well as complex microbial communities. It was found that the survival and activity of bacterial or fungal monocultures were negatively affected by exposure to sunlight (Fonseca and Tavares, 2011; Hobday and Dancer, 2013; Hessling et al., 2017), ultraviolet light (Kundsins, 1988; Besaratinia et al., 2011; Goldman and Travisano, 2011; Dai et al., 2012; Oppizzo, 2012; Takada et al., 2017), and light of blue or red wavelengths (Ondrusch and Kreft, 2011; Deng et al., 2012; Lins de Sousa et al., 2015; Maclean et al., 2016).

The effect of light on microbial communities including those in house dust or on human skin were also reported in the literature (Patra et al., 2016; Prescott et al., 2017; Fahimipour et al., 2018). Visible or UV light can reduce the number of live bacteria and lead to less human-associated bacterial communities in the BE (Fahimipour et al., 2018). Similarly, increased illumination in hospital rooms was found to reduce human-associated taxa in indoor surface bacterial communities (Hartmann et al., 2004). In particular, sunlight/UV was found to be effective in the inactivation of viruses (Sandhu and Singh, 2009; Tang, 2009; Hobday and Dancer, 2013). Compared with viruses, bacteria may be more resistant to sunlight/UV exposure (Goldman and Travisano, 2011).

Given the disinfection effect of sunlight, it could be expected that areas of BE with greater sunlight exposure would have lower microbial activity, which is a desirable outcome when microbial control is a priority. BE design and operation can take advantage of the disinfection capacity of sunlight by strategically enhancing sunlight exposure in areas with greater risks of microbial contamination and transmission, such as conference rooms and bathrooms. The effectiveness of the strategy to exploit sunlight for the control of MoBE, however, needs to be further validated in field studies.

4.5 Premise Plumbing Systems

Premise plumbing systems include the portions of the potable water distribution system in the building beyond the connection to the water mains. A front line of human exposure, premise plumbing, is also an ideal ecological niche for opportunistic pathogens such as *Legionella*, *Mycobacterium*, and *Pseudomonas*. As a result, bacterial levels in the premise plumbing systems were found to be orders of magnitude higher than in the water main (NRC, 2006).

Colonization of opportunistic pathogens was reported in various locations in premise plumbing systems including cold and hot water reservoirs (Falkinham et al., 2008), tap and shower (Feazel et al., 2009; Perkins et al., 2009), eye wash stations (Paszko-Kolva et al., 1998), and water filters (Falkinham, 2010). The presence of microbial colonization in premise plumbing systems are also documented in hospital buildings (Thomas et al., 2006; Rivera et al., 2007; Arvand et al., 2011; Brown-Elliott et al., 2011) and hotels (Borella et al., 2005; Mouchtouri et al., 2007; Bonetta et al., 2010). The additional growth time during overnight water stagnation, which is characteristic of premise plumbing, was found to significantly increase the abundance of *Legionella*, *Mycobacteria*, and other bacterial populations in premise plumbing (Wang et al., 2012). The microbial populations in premise plumbing systems can spread across the building through drains (Kotay et al., 2017) and aerosolized water droplets generated at faucets and showerheads (Kline et al., 2004; Falkinham et al., 2008; Thomson et al., 2013). Once entering the BE, pathogens such as *Legionella pneumophila* can persist in building ventilation systems and infect building occupants (Yu and Stout, 2000; Borella et al., 2004).

The colonization and growth of opportunistic pathogens in premise plumbing systems are also affected by water treatment in the building. Point-of-use filtration, albeit being relatively costly and require maintenance (Marchesi et al., 2011), was found to be very effective in reducing *L. pneumophila* and *M. avium* concentrations in filtered water (Sheffer et al., 2005; Marchesi et al., 2011; Williams et al., 2011). However, filters were found to be a potential source of microbial growth after saturation (Falkinham, 2010). Other features of the premise plumbing were also found to influence microbial colonization. For example, the presence of *Legionella* was found to be less prevalent in newly constructed buildings (Mathys et al., 2008). Electronic faucets prevent the touching of the contaminated taps and therefore are often considered less susceptible to microbial growth compared with the manual faucets. However, it was found that the electronic faucets were more commonly contaminated with *Legionella* species (Sydnor et al., 2012), *P. aeruginosa* (Yapicioglu et al., 2012), and other bacteria in hospitals. Evidently, much remains to be learned how MoBE is linked to the premise plumbing systems.

4.6 Cleaning and Disinfection

Cleaning and disinfection practices are routinely performed with reducing occupants' exposure to harmful microorganisms in BE as one of the primary goals. These practices include removal of airborne microbes through ventilation and filtration, and inactivation of microbes in indoor air and on surfaces through the application of UV irradiation and chemical disinfectants.

UV irradiation has been shown as an effective technology for the inactivation of microbes in the BE. The mechanism of UV disinfection is attributed to the damage of UV irradiation to the DNA of living organisms and render them unable to replicate, thus noninfectious. Typically, UV disinfection of indoor air is conducted by irradiation of the upper-level of a room and taking advantage of rapid vertical mixing of air for complete disinfection of the air in that environment (Brickner et al., 2003). To prevent accidental exposure to UV by occupants, the UV lamps need to be specially louvered for in-room use (Sliney, 2013). In addition to the exposure risk to radiation, UV with wavelength below 242 nm generates ozone which also imposes exposure risks to occupants, requiring UV application to follow established guidelines (ASHRAE, 2019).

UV irradiation is also effective in the inactivation of microorganisms on indoor surfaces to achieve comprehensive disinfection of the BE, which is practiced mostly in healthcare and laboratory settings. The effectiveness of UV disinfection has been demonstrated by significant reductions in healthcare-associated infections (HAIs) when UV irradiation was added to the standard cleaning regimen in hospitals (Levin et al., 2013; Miller et al., 2015; Nagaraja et al., 2015; Weber et al., 2016; Anderson et al., 2017). UV irradiation has

also been applied on cooling coils to reduce microbial growth and endotoxin production in the ventilation system (Menzies et al., 2003), again supporting its effectiveness in microbial control in the BE.

Chemical disinfectants are also effective in inactivating microbial populations on indoor surfaces. It should be noted that the cleaning/disinfecting chemicals could be potential sources of volatile organic compounds (VOCs) and secondary aerosols in the indoor air (Nazaroff and Weschler, 2004). These aerosolized chemical disinfectants may present acute exposure risks to indoor occupants. Another potential issue with the use of chemical disinfectants is that the very presence of antimicrobial chemicals increases the risk of producing resistance strains (Aiello and Larson, 2003), which is an emerging public health concern. Moreover, due to the lack of selectivity in inactivating microbes, common disinfection practices would indiscriminately kill beneficial microorganisms, which demands the development of disinfection strategies that specifically target harmful microbial populations.

With the ongoing pandemic of COVID-19, the deployment of chemical disinfectant and UV irradiation has increased dramatically in various BE. It is important to investigate the impacts of intensified disinfection on MoBE and subsequent effects on the health of occupants.

5. Discussion

There are tremendous opportunities in the fledging research area of MoBE that will benefit disciplines including public health and building engineering in particular. In this section, we discuss the challenges and possible solutions to in-depth understanding of the complex interactions between the built environment, occupants, and microbiomes.

BE, occupants, and MoBE constitute a system of ecosystems with extensive interactions that impact one another. Previous studies have demonstrated that a significant portion of MoBE originates from the occupants. The quantity and composition of occupant-associated microorganisms are dictated to a large extent by characteristics of occupant behaviors, which are greatly influenced by BE attributes including layout, function, and indoor environmental conditions. In addition to occupant behavior, BE attributes further influence the survival and dynamics of the MoBE, which subsequently determine the occupants' exposure to the MoBE. These interactions are evidently manifested in the transmission of SARS-CoV-2. In BE, SARS-CoV-2 is derived exclusively from occupants. Thus, the concentration of SARS-CoV-2 in BE is closely linked to occupant behaviors, such as facemask-wearing, hand-washing, and social distancing (Prather et al., 2020). Accordingly, these behavioral patterns could be influenced by BE attributes including indoor temperatures conducive to mask wearing, availability of handwashing facilities, and adequate occupant capacity (West et al., 2020). BE attributes, particularly ventilation and disinfection practices, further influence the viability and concentration of SARS-CoV-2, and subsequently the exposure risks of occupants (Allen and Marr, 2020). The ongoing COVID-19 pandemic highlights the significance of interactions between BE, occupants, and MoBE.

Despite the progress made in characterizing MoBE, significant gaps are identified in this review, including: 1) The need to extend MoBE studies to more developing countries in order to be representative of the potential diversity in MoBE related to socioeconomic disparities; 2) The need to characterize MoBE with linkages to building attributes in order to elucidate the mechanisms driving MoBE; 3) The need to characterize MoBE at a finer spatiotemporal resolution to capture the dynamics of MoBE, particularly under the influence of occupant behaviors; and 4) The need to determine the impacts of occupant behaviors on MoBE. These knowledge gaps stem from three major technical challenges: 1) lack of effective methods to monitor and model the built environment and occupant behaviors at fine resolutions to enable quantitative, sensitive, and reproducible experimental design and data analysis; 2) lack of efficient tools to monitor the spatiotemporal patterns of indoor microbiomes that are present in spatially and functionally distributed components of the built environments and occupants; and 3) lack of approaches to integrating data of the built environment, occupants, and microbiomes to identify transmission and exposure pathways. Monitoring the built environment and occupant activities is a prerequisite for understanding their influence on MoBE, which is critical for identifying transmission modes and exposure pathways of specific pathogens in the BE. Fine-resolution representations of the built environment and occupant behaviors are required for quantitative, sensitive, and reproducible modeling of MoBE, given its spatiotemporal dynamics at fine resolutions. Previous studies have fallen short of

closing these knowledge gaps largely because of these technical challenges. Therefore, as a critical first step, efforts should be devoted to developing capabilities for monitoring the built environment at sufficient resolutions so that understanding of fine-resolution processes that structure microbiome dynamics is possible.

The MoBE is an inherently transdisciplinary field at the nexus of building science, environmental microbiology, public health, material sciences, sensors, and data science, just to name a few. Given the multidimensional nature of data for MoBE characterization, we call for the development and application of the following approaches to address research challenges in this field: 1) data-driven approaches to monitor the built environment and occupants by integrating advanced techniques such as building information modeling and internet-of-things (IoT) based sensing; 2) modeling-informed approaches for spatiotemporal sampling and characterization of MoBE at optimized resolutions; and 3) approaches integrating transport modeling with metagenomics and metatranscriptomics profiling to predict microbial dynamics, metabolic activities, and transmission pathways. The integration of new tools for sensing, modeling, and monitoring will provide unprecedented data at fine resolutions to gain new insights by: 1) guiding sampling for meaningful data collection; 2) identifying linkages between the built environment attributes, occupant behaviors, and MoBE characteristics; and 3) linking the dynamics of the built environment, occupants, and microbiomes to transmission and exposure pathways. Future efforts are needed to advance MoBE research from basic characterization (e.g. what microorganisms are there) toward modeling and prediction (e.g. how built environment attributes and occupant activities contribute to the dynamics of specific microbial populations, and how it may reciprocally affect the built environment and occupants).

In today's society, the communities and cities are increasingly connected with the built environment and natural environment tightly coupled, making it necessary to study the microbiomes, environments, and human interactions at a broader scale to gain new knowledge and insights to promote the health of the society as a whole. This pertains to an interesting and important question: how do activities at the community- and city-scales impact MoBE, and how does MoBE influence the inhabitants ranging from small scales (individual people) to large scales (communities and cities). Findings at these scales will have greater significance beyond individual built environments as most public health concerns are better addressed at the community scale and beyond. There were attempts to investigate MoBE at larger scales. In one study (Robertson et al., 2013), a baseline assessment was conducted for the microbiomes in the New York subway system. Results from this study could lead to potentially important applications, including infectious disease surveillance, bioterrorism threat mitigation, and community-scale public health management. However, it remains a challenge to the application of high-dimensional microbiome data integrated with community behavioral information such as mobility as well as environment monitoring data.

Based on the review of current literature, we suggest developing the ability to predict the dynamics of MoBE to serve the needs of engineering practitioners, city planners, and public health professionals. Previous studies have identified potential correlations between the MoBE and attributes of the built environment (e.g. geographic location, design, occupancy, ventilation rate and type), with various levels of uncertainties and inconsistency notwithstanding. It remains very challenging, if not impossible, to predict MoBE profiles in even small-scale buildings with due accuracy in real-time. It would be an ambitious, yet beneficial, call to develop capabilities to predict MoBE dynamics aided with emerging technologies of real-time sensing and data analytics, which will have great significance in the understanding and control of microbial transmission pathways in the built environment, an urgent issue of current public health concern.

6. Conclusions

Humans spend most of their time in the built environment with a vast diversity of microorganisms. Activities of the occupants and attributes of the built environment will impact the colonization, succession, and transmission of these microorganisms, which will in turn influence the built environment and human health. This review summarizes our current understanding of the complex interactions among the built environment, human activities, and microbiomes of the built environment, with an emphasis on how the built environment coupled with human activities impact the microorganisms. This review highlights the importance of advancing our understanding of the interrelationships among microorganisms, the built environment, and its occupants. Further, we call for the development and application of transdisciplinary approaches for the sensing and

monitoring of building-occupant-microbiome Interactions at sufficiently fine spatiotemporal resolutions to enable capacity development for the modeling and prediction of MoBE. These capabilities will support the goal toward developing healthy built environments that are both sustainable and resilient to detrimental microorganisms, particularly infectious pathogens. Future efforts are also needed to expand MoBE research from individual rooms and buildings to the scales of communities and cities, which will advance our understanding of the microbiome-human-environment ecosystem at a scale more relevant for the development of sustainable, healthy, and resilient communities as an ultimate goal.

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