



Airborne transmission of biological agents within the indoor built environment: a multidisciplinary review

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Abstract

The nature and airborne dispersion of the underestimated biological agents, monitoring, analysis and transmission among the human occupants into building environment is a major challenge of today. Those agents play a crucial role in ensuring comfortable, healthy and risk-free conditions into indoor working and leaving spaces. It is known that ventilation systems influence strongly the transmission of indoor air pollutants, with scarce information although to have been reported for biological agents until 2019. The biological agents' source release and the trajectory of airborne transmission are both important in terms of optimising the design of the heating, ventilation and air conditioning systems of the future. In addition, modelling via computational fluid dynamics (CFD) will become a more valuable tool in foreseeing risks and tackle hazards when pollutants and biological agents released into closed spaces. Promising results on the prediction of their dispersion routes and concentration levels, as well as the selection of the appropriate ventilation strategy, provide crucial information on risk minimisation of the airborne transmission among humans. Under this context, the present multidisciplinary review considers four interrelated aspects of the dispersion of biological agents in closed spaces, (a) the nature and airborne transmission route of the examined agents, (b) the biological origin and health effects of the major microbial pathogens on the human respiratory system, (c) the role of heating, ventilation and air-conditioning systems in the airborne transmission and (d) the associated computer modelling approaches. This adopted methodology allows the discussion of the existing findings, ongoing research, identification of the main research gaps and future directions from a multidisciplinary point of view which will be helpful for substantial innovations in the field.

Keywords Indoor air quality · Building ventilation · Airborne transmission · Bioaerosols · CFD models · Droplets

Introduction

Release, circulation and dispersion of chemical (harmful pollutants) and biological agents within confined indoor spaces can be easily inhaled. For that reason, it is considered

a serious threat for public health and therefore there is a continuous effort for preventing or controlling their release (Jones 1999). Such agents may include from toxic chemicals, pathogenic microorganisms (e.g. fungal and bacterial spores) and microbe-bearing air particles, such as droplets to various types of solids such as dust (Ghosh et al. 2015). Those are responsible for chemical poisoning or serious respiratory infections via the spread of infectious biological agents at hospitals, long-term care facilities (Vogazianos et al. 2021), schools and office areas (Taylor et al. 2012). The main route of human infection by biological agents is usually via the human respiratory system. This takes place by inhalation of tiny particles or droplets, commonly referred as particulates, however, in the case of pathogens those can be also contracted from touching infected surfaces, such as door handles, taps and furniture (Madigan 2009; Prat and Lacoma 2016).

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The shape, size and formation–dispersion mechanisms of these particulates when especially are in a liquid place (droplets) as well as their physicochemical properties affect significantly their potential to cause respiratory diseases. Those characteristics determine biological agents transmission patterns and how easy it is to be inserted into the human body via inhalation and further penetrating into the tissues of the lower respiratory system. Usually, only the micron-sized particulates can reach our lungs and the alveoli, leading to serious respiratory diseases (Bansal et al. 2018; Jones 1999). More information on which particle/droplet sizes are deposited in which part of the human respiratory tract, depending on the nature of the particulates, can be found in the following sections.

New respiratory pathogens have emerged during the last couple of years, with the most notorious being SARS-CoV-2, a novel coronavirus which is responsible for the infectious disease COVID-19 that has caused more than a million of deaths worldwide in 2019–2020 according to Rothan and Byrareddy (2020). Another coronavirus, MERS (Middle East respiratory syndrome), also caused many deaths in the Middle East in 2017 (Hageman 2020).

In addition, traditional pulmonary infectious agents, such as influenza virus (causing common flu), *Streptococcus pneumoniae* (causing pneumonia), *Mycobacterium tuberculosis* (causing tuberculosis) and *Aspergillus fumigatus* (causing lung aspergillosis) are still considered major health hazards (Hunter 2016; Latgé and Chamilos 2019; Murray et al., 2013; Pleschka 2013).

In order to rapidly detect and identify these infectious biological agents in the air or on surfaces, an arsenal of sophisticated new technologies is necessary to be developed. Those technologies will provide real-time accurate information about the presence of particulates in an indoor environment. Several such approaches have been developed (Huffman et al. 2020; Nasir et al. 2019; Usachev et al. 2013); however, most of them are still at low technology readiness level, an experimental level, and they are not routinely applied.

In addition, Heating, Ventilation and Air-Conditioning (HVAC) systems can be employed to control the transmission of harmful particles (solids or droplets). Different types of HVAC methods can reduce the spread of such agents in buildings or even eliminate the threat posed by pathogenic infectious microorganisms (Li et al. 2007; Shajahan et al. 2019).

Also, factors like the ventilation rate and heating/cooling settings of such systems can significantly influence the indoor transmission of hazardous agents (Li et al. 2007; Zhang et al. 2020a, b, c, d).

Moreover, computer modelling approaches have been used for predicting transmission patterns of chemical and biological agents in confined indoor areas. The most predominant methods are multi-zone and CFD modelling that are often used in combination for obtaining more robust

results (Wang and Chen 2008a). Numerous such studies have been carried out in key close space areas such as hospitals and offices and have helped in designing new effective sanitation approaches (Chen et al. 2011; Emmerich et al. 2013; Karakitsios et al. 2020; Lim et al. 2011).

The aim of this multidisciplinary review is to examine the critical issue of harmful particles control, with the emphasis drawn on biological agents, within indoor environments from four different angles (physical, biological, HVAC and computer modelling), highlighting key research gaps in each area and suggest solutions that could lead to substantially improved indoor health strategies in the near future.

This manuscript is organised in seven sections. The ‘**Introduction**’ section presents a short introduction to the reviewed topic. The ‘**Methods—literature review approach**’ section includes the classification of the present review and methodology of the collection and analysis of the relevant research works in the field. In the ‘**Droplet formation mechanisms**’ section, the effect of the physicochemical nature (chemical characteristics, size and shape) of particulates such as dust and droplets of water, the most characteristic formation mechanisms of droplets and aerosols and their dispersion into indoor space environment are discussed. The ‘**Aerosols and bioaerosols**’ section includes the most characteristic microbiological agents that are carried within aerosols with an account on the methods that are currently used for their detection and identification. In the ‘**The role of heating, ventilation and air-conditioning systems**’ section, the role of heating, ventilation and air-conditioning (HVAC) systems in association with the alternative ventilation patterns regarding the dispersion of pollutants and biological agents into indoor spaces is presented. The ‘**Computer modelling of particles and biological agents’ airborne transmission into indoor built environment**’ section exhibits the available computational modelling techniques for the prediction of biological agents’ airborne transmission routes. Finally, in the ‘**Conclusions—future directions**’ section, the major findings, remarks and recommendations for future research are presented.

Methods—literature review approach

The present review is classified as a semi-systematic review, designed for the topic of dispersion of biological agents and pollutants in indoor air environments. This type of literature review studies is suitable for works of multidisciplinary group of researchers within diverse disciplines of engineering and other sciences as described in (Snyder 2019). The adopted literature review strategy focused on how the research in the field of the indoor air pollutants of biological origin, the latest often underestimated, has progressed and developed over time. The authors attempt to identify the

potentially relevant research aspects which are important for the corresponding topic and synthesise these instead of measuring effect size, by using meta-narratives.

The importance of contribution of the present work is (a) mapping the recent trends of biological agents and pollutant dispersion in the indoor air research, (b) synthesise the current status of knowledge from different perspectives of a variety of disciplines and (c) create an updated agenda for further multidisciplinary research on the topic of indoor air pollution from biological agents, the main focus of this study, in which the current literature is scarce.

The research methodology used in the present semi-systematic review is composed of three primary and independent steps:

Step 1: Database selection. Scopus, Google Scholar, PubMed, Web of Science and database platforms were used to retrieve the relevant literature related to the scope of the study.

Step 2: Searching Keywords. Due to the multidisciplinary context of this work, four different keyword families were used to identify the relevant articles per section. In the ‘[Droplet formation mechanisms](#)’ section, the words “particles”, “particulates”, “size”, “shape”, “indoor air pollution”, “transmission”, “dispersion droplets”, “formation”, “technology”, “mechanism”, “suspension”, “re-suspension”, “particle size distribution”, “atomisation” and “coalescence”, as well as any combination among them, was used. The research works found were further narrowed down to the engineering aspects of the particles and droplets formation and airborne dispersion in the field of indoor air quality. In the ‘[Aerosols and bio-aerosols](#)’ section, the names of the microbial agents and the relevant methods were used as keywords, in addition to biomedical terms such as “bio-aerosols”, “dust”, “pollen”, “transmission”, “air microbiology”, “microbial identification”, “airborne disease”, “respiratory disease”, “lung infection”, “infectious dose” and “immunity”, used to identify the relevant articles. The terms “ventilation”, “natural ventilation”, “personal ventilation”, “mixed ventilation”, “underfloor ventilation”, “mechanical ventilation”, “air distribution” and combined with the Boolean operators “OR” and “AND” with the associated terms “airborne transmission”, “thermal plume”, “droplet”, “contaminant removal efficiency” “heating”, “cooling” and “bioaerosol” were adopted in the ‘[The role of heating, ventilation and air-conditioning systems](#)’ section. In the ‘[Computer modelling of particles and biological agents’ airborne transmission into indoor built environment](#)’ section, regarding turbulence, modelling techniques terms such as “Reynolds-Averaged Navier–Stokes (RANS)”, “Unsteady Reynolds-Averaged Navier–Stokes (URANS)”, “Detached Eddy Simulation (DES)”, “Reyn-

olds stress models (RSM)” and “Large Eddy Simulation (LES)” were used, in addition, to terms such as “indoor dispersion”, “dilution” “multiphase flows”, “Eulerian–Lagrangian techniques”, “Eulerian–Eulerian techniques”, multizone models”, “CFD—Physiologically Based Pharmacokinetic (PBPK)” or “CFD—Physiologically Based Toxicokinetic (PBTK)”. Furthermore, the combination of the aforementioned terms/ keywords from the ‘[Droplet formation mechanisms](#)’ and ‘[Aerosols and bioaerosols](#)’ sections along with “CFD” was also used to identify relevant papers.

Step 3: Article screening and reviewing. Articles were preliminary analysed through title, keywords, abstract and conclusions. This analysis was later on followed by an extensive reviewing of the articles selected from the screening process. The available material is certainly too much to be reviewed in a single paper. For this reason, regarding the modelling papers, the authors give special attention to what they consider the better established or more promising modelling approaches, such as single- and multi-zone models, CFD, coupling of CFD and multi-zone models, CFD-PKTE or CFD-PTBK models. No disrespect is therefore implied for studies with other models. It should be noted that extensive use has been made of the published literature on the field and of previous reviews.

Droplet formation mechanisms

The challenging nature of biological agents’ transmission in indoor environment

The importance of indoor air quality (IAQ) and spreading of pollutants and biological agents into indoor air, ranges from new types of chemicals and particulates released to infectious droplets spreading several kinds of diseases, and those are well known threats for the societies (Brundage et al. 1988; Cooke 1991; Jones 1999; Mutuku et al. 2020a). At the opening of the twentieth century (1918–2019), the outbreak of Spanish flu (H1N1) caused more than 1 billion infections and was then considered as the most lethal flu pandemic. Recently, Ni et al. (2020) reported that people spend approximately 90% of their time indoors with minimum time for outdoor activities. It is then obvious that staying long periods of time in a contaminated indoor environment increases the risk of respiratory diseases triggered due to the poor IAQ.

The nature, characteristics, behaviour and release mode of different pollutants and more importantly biological agents in indoor environment are still some of the areas which cause confusion among the researchers. This might be happening for reasons expanding from, for instance, the volatilisation or release of new types of chemicals emerging

from new types of processes such as construction materials (Salthammer 2020) to recently developed unknown types of respiratory diseases. From all respiratory diseases, the severe acute respiratory ones are deemed to be the most important due to the nature of the disease spreading and infection via the ‘invisible’ airborne routes.

Nowadays, there is a good understanding of pollutants’ nature and their impact on human health. The way also the modern types of indoor air purification systems and processes are operating to more efficiently trap and separate indoor air pollutants, as well as their spreading mode (Luen-gas et al. 2015) is better understood. For the most common, old-generation indoor polluting agents such as chemicals ranging from asbestos, tar droplets of tobacco products, carbon monoxide (CO), volatile organic compounds (VOCs) to dust, coal and pollen particulates, there is a much thorough and better understanding of their transmission to humans when these released into indoor air. The same good level of understanding exists of their associated health problems, causes and effects for those well-known pollutants which are studied for more than two decades (Domingo et al. 2020; Jones 1999; Monn 2001).

How the recently appeared droplets of infectious diseases occur, it is still though unclear to the global scientific community, as well as how they spread into indoor air and infect human occupants. Two very characteristic examples are the infectious severe acute respiratory syndrome (SARS) or SARS-CoV-2 variant or subvariant respiratory system diseases. Such types of biological agents are dispersed and, most importantly, among infected to non-infected individuals, resulting in alarming public health problems.

Lately, there is also an increasing concern of companion animal-to-human transmission risk (Yin et al. 2020) and other animals infected by coronaviruses (Carducci et al., 2020). There is also a lively discussion around transmission of such diseases by contaminated droplets of human saliva, along with a discussion on the origin and nature of the new infectious diseases which proved to lead to epidemic crisis, such the one caused by SARS-CoV-2.

Today, the general understanding is that the infectious saliva droplets are transmitted in indoor spaces via two prevailing modes: (1) the direct and (2) indirect mode of transmission between the occupants of a confined indoor space environment (Dhand and Li 2020; Galvin et al. 2020). The alarming and yet urgent need for better understanding of the above-mentioned transmission routes have led the scientific community to classify and further investigate such biological agents transmitting modes, focusing especially on the most risky ones to be released in indoor environments.

The importance of not only better understanding, but also hindering the transmission of such airborne, either biological agents or hazardous chemicals inhaled, and targeting the human respiratory system, can be showcased by the SARS

outbreak which first appeared in 2002–2003, (Morawska 2006) causing 774 deaths worldwide [www.nhs.uk/conditions/sars/, last accessed on 14.10.2022] (Lauxmann et al. 2020; Razzini et al. 2020). SARS-CoV-2 has recently been declared a pandemic by the World Health Association (WHO) and during the 21 months of 2020–2021 (January 2019–November 2021) killed more than 6,586,200 patients around the globe [<https://www.worldometers.info/coronavirus/>, last accessed on 26.10.2022].

According to Zhang et al. (2020a, b, c, d), the lower respiratory infections remain the primary cause of patients mortality worldwide, accounting for 650,000 deaths each year. This fact makes the issue of shading light and better understanding the pollutants and biological agents’ transmission through the droplet formation during inhalation and retention in the human tracheobronchial system, an area of research which necessitates further investigation as a matter of urgency. On the other hand, the chemical pollutants’ transport and deposition in the respiratory system have been studied excessively (Lauxmann et al. 2020; Mittal et al. 2020; Rothan and Byrareddy 2020) and as a result the main focus of this study will mainly be on the biological agents nature, spreading and transmission.

The human respiratory system

The anatomy and physiology of the human respiratory system both play an important role in either short (~2 m) or long distance transmission (> 2 m) of the airborne infectious diseases. During the accidental release of pollutants and/or biological agents in a sick building environment (Jones 1999) or unintentional release by a patient of a contaminant and inhalation of droplets from other healthy adults, there is a direct relevance of the human respiratory system’s role and especially the lungs’ operation (Bansal et al. 2018).

The human respiratory system is very complex and is constituted from many compartments of different shapes and sizes. It has the ability to absorb the indoor air’s droplets or solid particulates by inhalation (Steiner et al. 2020). When a person talks, coughs and sneezes spreads a cloud of tiny saliva droplets (aerosol) in a very short period, of a couple of hundreds of milliseconds (200 ms) (Bourouiba et al. 2014; Scharfman et al. 2016). Sneezes especially, which in fact are described as violent exhalation incidents, have received much less attention in the scientific literature and it is a field which needs further investigation. A sneeze leads to an extremely short (in the order of 150 ms) incident of aerosols formation and spreads at extremely high speed in the order of 35 m/s (Scharfman et al. 2016). The occurrence of such events is very similar to that of the well know liquid atomisation process of the liquid fuels (Vadivukkarasan et al. 2020). It is also important to note that aerosols of infectious respiratory diseases like SARS-CoV-2 survives for at

least 3 h (Netz 2020), while similar viruses might survive for days. When those droplets land on open surfaces substantially increasing the risk of indirect transmission to humans via touches. As aerosol is defined the suspension of fine solid particles or liquid droplets in a gaseous medium. Both droplets and particulates, commonly known in engineering science as particles can be potentially carried away by indoor air flows, in either short or long distances. How far those aerosol droplets or any other infected solid nanoparticles can be transported depends mainly on their size, which only in the case of solids is a stable characteristic. This is much more complicated for the case of different transport mechanisms of droplets of infectious diseases and particulates taking place simultaneously. For example, in an air-conditioned environment convective mass transfer (enhanced by the air currents) is taking place when a patient sneezes or coughs then an aerosol formed which can be dispersed in the indoor space. At the same time the infected saliva droplets might be unstable in size as a result of the effect of room temperature, humidity or their droplet breaking up tendency due to hydrodynamics (behaviour of droplets in air). It has been found that a sneeze releases approximately 40,000 droplets, while a cough produces a considerably lower number of droplets at around 3,000 (Dhand and Li 2020). Similarly, when a person walking or touching areas full of dust infected solid particles can spread in air. However, the size of the solid particles is not changing as a result of the indoor environment conditions and thus understanding of this mode of transmission is less complicated compared to the airborne droplets transmission mechanism. Regardless their behaviour though, both saliva droplets and/or any infected solid particulates are inevitably and unconsciously inhaled by the occupants of confined indoor spaces. Both those agents, infectious or not, and depending on their size, they are diffused at different concentrations in the many different compartments of the human respiratory system. Additionally, it is widely known from engineering studies that the airflow inside a specific geometry is strongly influenced by the geometric shape of the air flow pathways. Similar rules are applied in the human respiratory system and its compartments. Therefore, understanding the human's inhalation/exhalation geometry route is a useful step towards simulation studies of the inhaled/and exhaled pollutants and biological agents (Mutuku et al. 2020a; Mutuku et al. 2020b).

On the other hand, and for the purpose of computational modelling studies, it is useful to know that the lung of an adult man offers the incredible air exchange surface area of approximately 100 m². The mean lung capacity of an adult man is of 1.5 L (Scharfman et al. 2016) and he is able to inhale and exhale over 10,000 L of air per day while resting (Ni et al. 2020). This huge permeable membrane surface, the lungs, is the means by which the indoor air pollutants are absorbed and diffused by mainly the air mass transfer

mechanism into the human body. Specifically, air mass transfer by diffusion via membranes is the key engineering mechanism for not only transmitting viruses trapped in saliva droplets, but also, a variety of other aerosol particles and droplets into the human body (Jayaweera et al. 2020). It is also known that the air mass transfer is enhanced by the increased surface areas available to diffusion and the physiology of a human respiratory system is not only quite complicated in anatomical characteristics, but also offers an excessive total surface to enhance any such transmission of biological agents hosted in indoor air. This creates more serious respiratory problems as penetration of pollutants and biological agents can affect every other organ of the human body via their diffusion in veins and the human blood circular system.

The human respiratory system consists of and connects also the mouth, throat and pharynx with the trachea, all of them often known as Generation 0, according to the human tracheobronchial tree. After inhalation, the larger pollutants or biological agents are filtered by the nose or deposit in the oropharynx, whereas smaller particles, droplets and nuclei are possible to penetrate the deeper than Generation 0 parts of the human respiratory system. The Generation 0 system is further leading to two bronchi, commonly known as Generation 2, with then the different branches of the lungs' system to be continued down to smaller and smaller compartments of, in total, 23 different generations. The lowest and deeper of them, Generation 23, counting at some millions of the smallest lung compartments, being the alveolar sacks and alveoli (Mutuku et al. 2020a). For example, an adult man's lung is made from approximately 300,000,000 alveoli (~200 µm in diameter) where the supply of oxygen takes place through a rich network of blood vessels (Rhodes 2008). Concerning their characteristic lengths, each of the respiratory system compartments, starting from the nose and mouth and ending in the tiniest lung compartments the alveoli, has substantial different sizes. Those sizes range from 30 to 150 µm, with total lengths between 120 mm and 150 µm. Typical air velocities in the respiratory system are ranging from 9 to 4×10^{-5} m/s, with corresponding residence times of contaminated air being between 0.021 s in mouth and the incredible high residence time of 4 s in alveoli (Mutuku et al. 2020a; Rhodes 2008).

The face anatomy though of each individual person varies and at the same time plays a major role to the biological agents' transmission. For example, the nasal airways of an adults' narrowest section is ranging from 5 to 9 mm with a resulting cross-sectional area ranging between 20 and 60 mm², without taking into account the unique face anatomy of each individual. The nose anatomy, for instance, accounts for the 50% of the indoor airflow resistance and creates a natural resistance to biological agents' and other pollutants inhalation (Rhodes 2008). The typical airflow through the

nasal canals ranges from 0.18 to 1 l/s, from normal breathing to strongly sniffing, respectively (Rhodes 2008). The typical airflow from mouth during normal breathing is 3 m/s and depends, as previously stated, on the physiology of the face and lungs of a person (Rhodes 2008).

Table 1 depicts the main characteristics of the human respiratory tract (size (mm), velocity of air (m/s) and residence time (s)). The specific information might be proven useful for studies on lung damage during inhalation of pollutants and biological agents. In Table 1, it can be seen that by decreasing the characteristic length size of the geometry (higher Generation) of the respiratory system part, there is an incredible increase of the residence time of the biological agents which remain in the different generation parts of the human respiratory system.

It is also generally accepted that the respiratory droplets are formed from the fluid lining of the human respiratory track (Mittal et al. 2020), while the biological agents which are dispersed into indoor environments pose a new challenge. This challenge is mainly focused on the understanding of deposition/ diffusion patterns and efficiencies of the infectious aerosols generated from symptomatic and especially asymptomatic patients of infectious diseases (Mutuku et al. 2020a). Shao et al. (2021) stressed out the importance of indoor ventilation system design. More specifically, a properly designed and selected ventilation system is critical for decreasing the transmission risk of infectious diseases, while an inappropriate design can significantly limit the efficiency of droplets removal from indoor air. The local hot spots of biological agents with several orders of magnitude posing higher risks, and at the same time enhancing the droplets deposition causing surface contamination.

The site of droplet nuclei deposition in the lower Generation parts of lungs depends strongly on the droplet shape, size and mass. This transmission route is also dependent on the droplets which are carried in stable and small enough size via indoor air as respiratory droplets of some considerable size or as fine droplet nuclei (Dhand and Li 2020). The very fine droplets and particulates, entering and remaining in the lungs are often an approximate size of up

to 7 μm (Jones 1999). In addition, Cheng et al. (2016) found that there was a probability of 50% for the influenza infected nuclei of sizes from 0.3 to 0.4 μm to promote influenza reproduction number (R_0) at values higher than 1, known to increase the risk of transmission of the disease. This only indicates the importance of indoor air biological agents' size, and how influences their ability to be highly infectious. On the other side, Han et al. (2020) reported that the total dust and the respirable dust should be below 4.0 mg/m^3 and 2.5 mg/m^3 , respectively, to ensure the health and safety of people staying in indoor environments within their usual working timeframe of 8 h. Bourouiba et al. (2014) also reported that tiny droplets and particulates can easily penetrate the respiratory tract, reaching the deeper targeted tissues of the lungs during inhalation of hazardous agents, as shown in Fig. 1.

According to Scheuch (2020), the very fine particles are extremely difficult to separate from the indoor air environment. Those cannot even be effectively deposited in the human respiratory tract compartments, reporting that only 30% of the inhaled particles (0.1–0.5 μm) are deposited in lungs. This means that the rest 70% of the inhaled droplets/particles are exhaled back to the indoor air again. He also claims that while the deposition occurs to a small extent throughout the entire respiratory tract, ranging from nose, mouth to throat, bronchi, bronchiole and alveoli, the preferred site of biological particles deposition is the peripheral area of the lungs.

Aliabadi et al. (2011) indicated that the humidity and temperature of the human respiratory tract varies with the anatomical location of the targeted compartment of the human respiratory system. A temperature, for example, of 37 $^{\circ}\text{C}$ and a relative humidity of 99.5% may be assumed for nasal respiration. For oral respiration the same temperature of 37 $^{\circ}\text{C}$ but lower relative humidity (90%) can be assumed, as well as an increase of the relative humidity by 1% per each Generation of the human airway (branching) until a maximum of 99.5% can be assumed for modelling studies. Varying temperature and relative humidity which prevail in the human respiratory tract are both very important factors due to the impacts on the characteristics of the hygroscopic aerosols, carrying biological or any other chemical agents. As those aerosols inhaled and

Table 1 Main characteristics of the human respiratory tract of an adult (basis 60 l/min) along with the generated number of saliva droplets (adapted from Rhodes (2008))

Characteristics—body part	Diameter range (mm)	Length range (mm)	Typical air velocity range (m/s)	Typical residence time range (s)
Nasal airways, mouth and pharynx, trachea	5–30	70–120	1.4–4.4	0.021–0.027
Bronchi (main, lobar and segmental)	5–13	28–60	2.9–4.0	0.010–0.007
Bronchioles (main, secondary and terminal)	0.7–2.0	5–20	0.2–0.6	0.023–0.036
Alveolar ducts and sucks	0.3–0.8	0.5–1.0	2.3×10^{-3} – 7.0×10^{-4}	0.44–0.75
Alveoli	0.15	0.15	4×10^{-5}	4.0

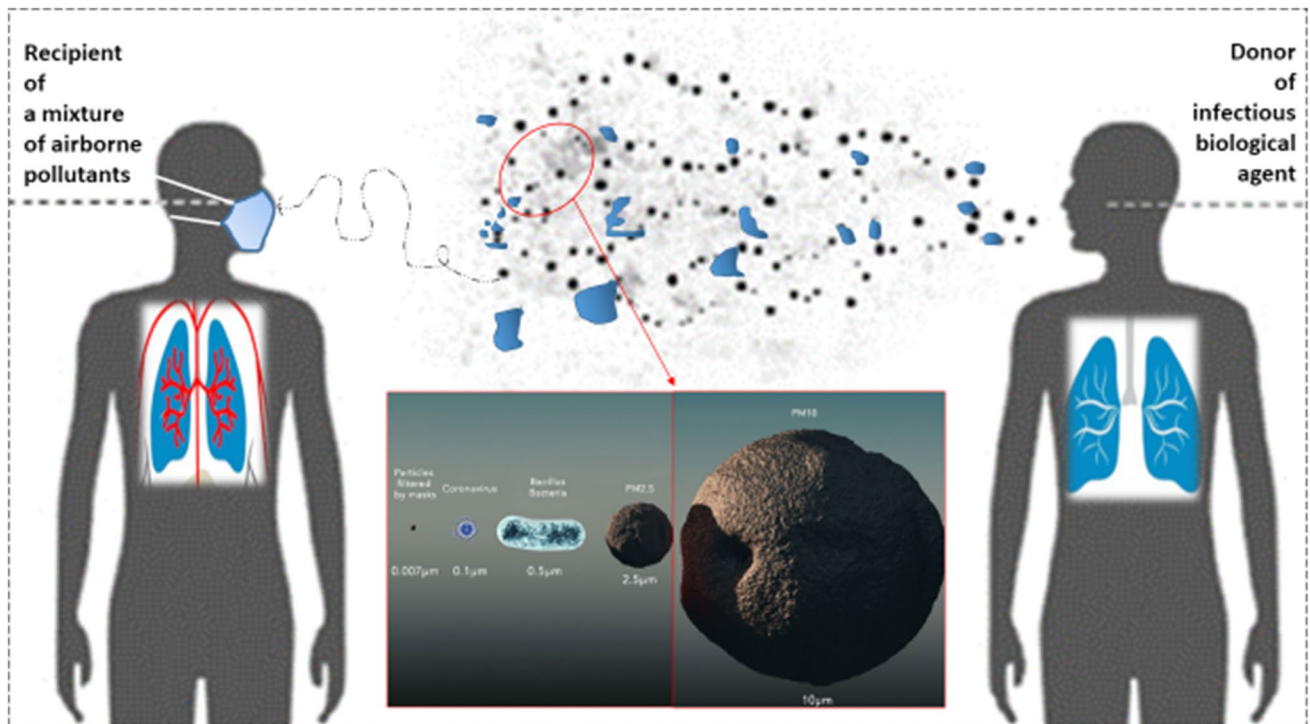


Fig. 1 Schematic representation of a variety of biological (infectious) and chemical agents' transmission between humans via the airborne route

move along the respiratory tract, their diameter and density might be changing. This is affecting their fate: either those aerosols will be exhaled or end up in deeper Generation part of the human's respiratory system.

To better understand the importance of the temperature and humidity especially in the survival of biological agents, Zhang et al. (2020a, b, c, d) reported that MERS-CoV exhibited a very strong ability of surviving in air. They indicated that those agents surviving even 1 h after of their atomisation, via a violent for example sneezing, at relative humidity of 79% and ambient temperature of 25 °C. However, when the temperature increased by roughly 10 °C at 38 °C, only 5% survival rate occurred in 1 h when the relative humidity was 27%.

Chemical composition of particles and biological agents

It is widely known that different contaminants and mixtures of droplets present varying physicochemical properties, and those properties affect both the droplets' and solid particles' behaviour. The physicochemical characteristics of droplets such as viscosity (μ), density (ρ) and/ or surface tension (σ) affect their shape and characteristic size, among others parameters of the aerosol system (Mandato et al. 2012). Aerosols of human saliva which are infected with viruses, for instance, are primarily composed by water (more than

99% wt), and secondary by traces of enzymes, mucus, white blood cells, enzymes amylase, lipase and antimicrobial agents lysozymes (Al Assaad et al. 2020; Sarkar et al. 2019). Galton et al. (2011) reported that an increase in the droplets' size made from saliva and release in indoor air environment is directly related to an increased mucus viscosity.

In the literature as already mentioned it is common to simulate the aerosol droplets of saliva including water (Bourouiba et al. 2014; Liu et al. 2019a, b, c, d, e). However, water has a density of 1,000 kg/m³, viscosity of 10⁻³ Pa·s and an interfacial surface tension of 0.0728 N/m (Viswanathan 2019) at ambient indoor air conditions, while the saliva has a viscosity 86 to 150 × 10⁻³ Pa·s and interfacial surface tension of 0.05898 N/m (Sarkar et al. 2019). In the case of droplets' formation during a coughing incident, the quality of saliva, which is different between a healthy person and a patient, will impact the droplets behaviour. This is done by strengthening the elasticity of the droplets and their resistance into their breaking up to smaller nuclei droplets and residuals, while releasing in the indoor air. As a result the saliva droplets will be more resistant to break, forming a lowest number of fine droplets and fewer droplets of a large size (Zayas et al. 2012). The droplets formed by a respiratory event of a patient can unfortunately be at the same time carriers of a biological agent due to their illness. In addition, contaminated droplets travelling in air might attract other (i.e. chemical contaminants being present in the confined

indoor environment). As a result, another healthy person (recipient) can be infected via the unconscious inhalation process (Fig. 1) (Vadivukkarasan et al. 2020).

Similarly, for other types of indoor air contaminants, chemical analyses and characterisation play an important role on understanding their physicochemical characteristics. For example, droplets of tobacco smoke are made only from 20% wt water among the rest several thousands of different traces of their tar constituents (Ni et al. 2020). It is obvious that such properties will be different in nature biological agents and those should be taken into account when modelling the routes of transmission for indoor air agents. Balachandar et al. (2020) claim that although the surface tension of saliva droplets measured similar to that of water, their viscosity can be 1 to 2 orders of magnitude larger than that of water, resulting in making those droplets less coalescence prone.

Shape of particles and biological agents

Another important characteristic of pollutants and biological agents is their shape which has a strong influence on droplets' and particles' size (Rhodes 2008). The shape of a particle affects its properties such as the surface area per unit volume (m^2/m^3) and/or the rate at which particles in general settle in indoor air environments (Rhodes 2008). Defining the droplet, and especially the solid particles' shape, is dependent on their real shape, the availability and suitability of the analytical methods for their shape determination. More specifically, in the case of droplets their chemical composition has a great impact on their characteristics such as density, viscosity and the forces imparted on particles, while they are expelled and move in the indoor air.

Particles in general, and for the sake of modelling and simulation studies, are usually assumed to be represented by spheres in a 3-D system or circles in a 2-D system, respectively. However, very rarely particles maintain a spherical shape and a uniform size. In practice particles' shape, either those being plain chemical pollutants such as ash or biological agents, their shape is usually far away from that of a perfect sphere. Simulating solid particles as spheres might not be realistic and thus the dimensionless number of sphericity (φ) is used to determine how far away the shape of a real particle is from the perfect spherical one. Sphericity is defined as the ratio of the surface area of an equal in volume sphere with the real particle to the surface area of the real particle. Sphericity values of particles are always ranging between 0 and 1, with the value of 1 to represent the sphericity of the perfect shape that of the sphere (Rhodes 2008).

When also a droplet or a particle falls freely in air, under the action of gravity, and an indoor air stream blows at an angle, several forces acting on the droplet/particle. Those are the gravitational force due to the mass of the particle,

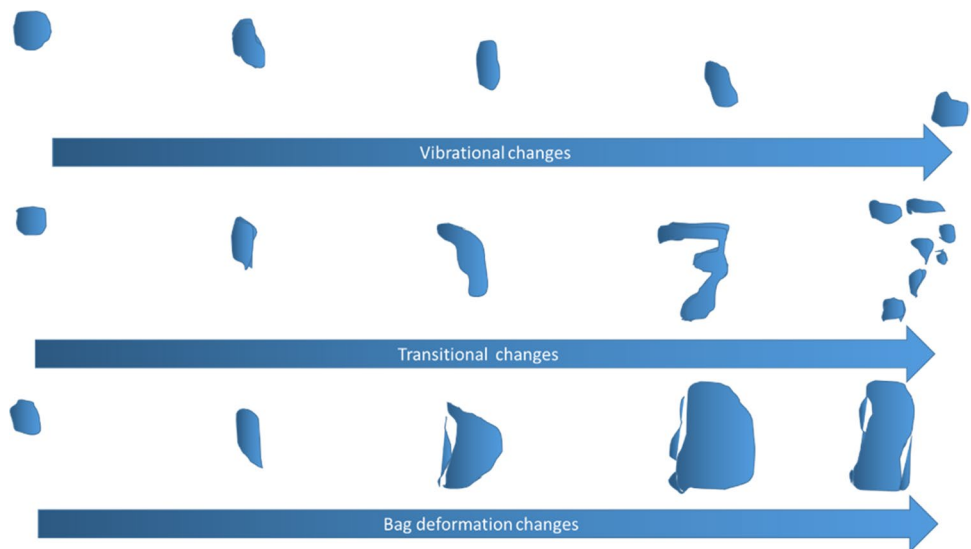
the buoyancy force due to the movement of the particle in a fluid, as well as the inertia and drag forces which oppose the travel direction of the particle. The balance of all these forces imparted on a particle will dictate the terminal velocity by which the particle or droplet of a final stable size, for the latter, will settle in indoor air (Soni et al. 2020).

In fluid dynamics studies, the dimensionless numbers are very useful in analysing the fluid flows, especially the multi-phased ones, where there is an interface between different fluids (gas–gas, gas–liquids). A widely used dimensionless number for this type of flows is the Weber number (We). We number indicates how the shape of a droplet will be in a certain fluid system or when deposited on a surface. Thus, it measures the relative importance of the inertia over the surface tension force and is mainly used to demonstrate the different break-up modes of the droplets and, as the result, the shape of the droplets. We number can also be used in describing the influence on the surface wettability under the effect of droplets. According to Liu et al. (2019e), when the value of We number is less than 0.5, droplets impact differently processes on hydrophobic, hydrophilic and super-hydrophilic surfaces which are dominated by the spreading stage and retraction is not evident.

At low We number, a droplet undergoes shape oscillations at a certain frequency (Fig. 2). As the We number increases slowly, by increasing the aerodynamic force applied on a droplet and keeping the surface tension force constant, the droplet exhibits a transition from the vibrational mode to the 'bag' break-up mode of droplets. When the We number is low the droplet tends to maintain its shape. On the other hand, high values of We number along with increasing the aerodynamic forces imparted on the droplet lead to the loss of the almost spherical shape of the droplet and create a 'bag' deformation and breakage, which also forms several smaller satellite droplets of smaller dimensions (Soni et al. 2020).

During the release and travelling of the formed droplets in the air, they interact with their host medium and alter their shape as move along with air, especially at high speed airflows. It is also known that high speeds prevailing when a person coughs or sneezes. Hence, the droplet shape changes depend on different mechanisms such as the vibrational changes of droplets ($We = 5.13$), transitional towards a bag shape, bag-stamen, dual-bag, multi-mode, shear and catastrophic break-up ($We = 6.35$) modes, according to the work of Soni et al. (2020). Those transitional areas of the droplet shape-change depend on the conditions under which the experiment is taking place. This spherical shape is changing rapidly in a 'bag' shape and breaking via ligaments with the production of finer satellite droplets based on the surface tension and the aerodynamic forces applied on droplets. Relatively little attention has been given though to the instabilities associated with the dynamics of respiratory droplets

Fig. 2 Schematic representation of the vibrational, transitional and bag deformation shape changes of water droplets traveling in air adapted from (Soni et al. 2020)



creation and expelling during especially the coughing or sneezing incidents (Vadivukkarasan et al. 2020).

Size of particles and biological agents

The size of particles, either being solid particulates or liquid droplets, is determined by their characteristic length (size). The size of solid particles very rarely depends on the ambient indoor conditions (temperature, humidity). It also depends on their natural shape and morphology, and their chemical composition (Rhodes 2008). In addition, the particulates found in nature or produced by processes very rarely possessing the perfect shape of a sphere. Real particles quite often have irregular shapes such as acicular, flaky, spongy or any other shape.

As a result, the size characterisation of solid particles is easier compared to droplets even though their shape is not spherical. The most appropriate characteristic length then for solid particles, instead of the diameter of a perfect sphere, it might be a different size such as the equivalent circle diameter or the surface to volume diameter and Sauter mean diameter and others (Rhodes 2008). All these characteristic lengths are used to describe the real size of a particle in conjunction with their non-spherical shape and real surface area, while they are moving in a fluid under aerodynamic forces. The measurement of the characteristic diameters is achieved by analytical methods such as the scanning electron microscopy (SEM), electro zone sensing, permeability and other less known analytical and optical methods (Morawska et al. 2009; Rhodes 2008).

On the contrary of the stable size of solid particulates, droplets' size is not unfortunately remaining stable upon released in indoor air and the droplet size is highly dependent on indoor air conditions. When a liquid is atomised an aerosol of droplets is produced, with those droplets to

usually keeping their initial spherical shape for only a short period of time after their formation. Their shape depends on several factors which have to do with the droplet's physico-chemical characteristics and environmental conditions of the indoor space where they are dispersed and move.

The size of droplets highly depends on their formation process with fine ones of less than 1 μm to be produced from engineering manufacturing processes and larger up to 100 μm from mechanical processes (Morawska 2006). It also depends on especially the humidity and temperature (Dhand and Li 2020; Gralton et al. 2011) of the indoor air. The diameter of the droplet is a dynamic property due to the liquid evaporation under certain indoor air conditions. Those conditions are resulting in droplet shrinking by time which finally leads to the formation of the stable droplet nuclei (Ji et al. 2018; Li et al. 2018; Liu et al. 2019a, b, c, d, e; Liu et al. 2017; Morawska et al. 2009; Wang et al. 2019a, b; Wei and Li 2015; Xie et al. 2007; Yang et al. 2018).

In the case of droplets, it should be also considered the effect of droplet's evaporation (Ji et al. 2018; Li et al. 2018; Liu et al. 2019a, b, c, d, e; Liu et al. 2017; Morawska et al. 2009; Wang et al. 2019a, b; Wei and Li 2015; Xie et al. 2007; Yang et al. 2018). A characteristic example of the effect of the relative humidity (RH) of air in water droplets of 50- μm diameter is that they will evaporate at $RH = 50\%$ in less than 3 s (Vuorinen et al. 2020). Droplets also under favourable humidity conditions may even increase in size due to attachment of the surrounding humidity of air on them. As a result, the droplet size varying not only with time, but also depends highly on the environmental conditions of temperature and humidity.

On another aspect the initial formation mechanism of an aerosol of droplets occurs due to mainly water vapour condensing onto the cloud of initial nuclei. This condensation occurs only when air contains slightly more water vapour

than it normally holds for a given temperature. Vuorinen et al. (2020) indicated to the importance of understanding what are the humidity supersaturation conditions of atmospheric air and their nuclei, which promote cloud droplet nucleation and growth. Carducci et al. (2020) reported that the different expiratory events such as coughing, sneezing, speaking, singing and simple breathing release droplets of sizes ranging between 1 and 2000 μm noticing, however, that the majority of them has a size between 2 and 100 μm .

Recently, Dhand and Li (2020) indicated that the size of the droplets expelled by a patient mainly depends on their site of origin from their respiratory systems. For example, droplets which are produced by the mouth (oral cavity) have a large size ($\sim 100 \mu\text{m}$), while smaller droplets ($\sim 1 \mu\text{m}$) are formed during talking and coughing. The difference in size of droplets is due to the fact that the smaller droplets originate from the bronchioles, while the larger droplets are generated during normal breathing and from the larynx during talking and coughing. It was also reported that the particle size distribution could be altered by the presence of viruses (Dhand and Li 2020).

The droplet size determination is usually taking place via optical methods and laser analysis (Stadnytskyi et al. 2020; Tang et al. 2009). Ni et al. (2020) reported that recent studies have demonstrated that particulate matter ($\text{PM}_{2.5}$) is closely associated with the chronic lung diseases and special attention should be given to biological pollutants of this specific size range. However, special attention should also be given to the fact that only few studies have conducted with modern techniques, capable of detecting sub-micrometric size particles. Thus, it is necessary to undertake further studies in order to develop a better understanding of the formation mechanisms of fine droplets (Morawska 2006).

Size distribution of a large population of particles and biological agents

The accurate characterisation of a large population of droplets/particulates can be done by investigating their size distribution within the multi-phase cloud of particles. This size distributions changes with time and distance from the source of generation depending on environmental factors, too (Dhand and Li 2020). This can be achieved by three ways and depends on the nature of droplets/ particles. For example, a droplet of an agent, infectious or not, in equilibrium with the environment has a stable size as cannot shrinks or increases in size. The later can be determined as per their particle size distribution based on mass, or surface area or number of particles (Rhodes 2008).

Concerning the aerosols and the size distribution of particles there is a threshold distance of approximately 1.5 m, which distinguishes the two basic droplet and droplet nuclei transmission processes, namely (a) the short-range mode and

(b) the long-range airborne route. The short-range mode of transmission includes the conventional, large droplet routes of parabolic travel under the effect of gravity, as well as the newly defined short-range airborne transmission (Liu et al. 2016a, b). However, Pendar and Páscoa (2020) reported lately that the infectious saliva droplets can travel up to 6 m at a wind speed of 15 km h^{-1} and a safe distance of 2 m is not appropriate for outdoor activities.

A large number of studies highlights the importance of the size distribution regarding the particles and biological agents, as well as the occupants in indoor environments (Choi et al. 2015; Cole and Cook 1998; Dhand and Li 2020; Faridi et al. 2020; Faulkner et al. 2015; Feng et al. 2020a, b; Fernstrom and Goldblatt 2013; Ghosh et al. 2015; Gralton et al. 2011; Lv et al. 2018; Milton et al. 2013; Monn 2001; Morawska et al. 2009; Nicas 1996; Nielsen 2015; Phu et al. 2020; Sajjadi et al. 2016); Scheuch 2020; Schroeter et al. 2012; Vianello et al. 2019; Wang and Yoneda 2020; Yang et al. 2016).

Lv et al. (2018) indicated that the supply flowrate of fresh air per unit of closed space volume, defined as air changes per hour (ACH) is also an important factor which influences the indoor particle distribution. They found that the free settling of particles into indoor space for particles ranging from 0.5 μ to 1.0 μm , 1.0 to 3.0 μm and 3.0 to 5.0 μm , presenting a sedimentation rate of 0.086 h^{-1} , 0.122 h^{-1} and 0.173 h^{-1} , respectively. The same researchers reported that an increase of ACH from 0 to 2.5 yields significantly different values on the sedimentation. Recently though, special attention is given to studies with reference to the size distribution of droplets and the improvement of measurement accuracy for small scales below micrometre range. For instance, a droplet size distribution for coughing indicates a peak drop size of almost 15 μm while the associated settling speed obtained at 6.5 mm/s in an ambient winter indoor air (Bourouiba et al. 2014).

Han et al. (2020) stated that there are several empirical equations to characterise the droplet size distribution such as Nukiyama-Tanasawa, Rosin–Rammler, log-normal, root-normal and log-hyperbolic. Poon et al. (2020) found that the droplets produced by coughing present a wide size distribution of droplets ranging from 0.6 to 16 μm , with a mode of around 6 μm . Lately several studies have been devoted to the size distribution of small droplets expelled during talking, coughing and sneezing; however, uncertainties on the droplet size distribution are still present (Asadi et al. 2019; Scharfman et al. 2016).

The airborne route of transmission of particles and biological agents

The droplet or aerosol airborne transmission route seems to be the most complicated mode of dispersion of particles, droplets and biological agents into indoor environment (Dhand and

Li 2020; Ai et al. 2019a, b; Ai and Melikov 2018; Aliabadi et al. 2011; Beggs 2003; Booth et al. 2005; Drossinos and Stilianakis 2020; Monn 2001) and as a result remains one of the most difficult aspects to study. Aerosols of particulates and droplets pose a major challenge: being invisible in human eye, they are transported as a cloud of submicron-sized particles generated especially by coughing and sneezing via a process which is called atomisation in engineering practise, or trapped in liquid micro-sized water droplets (Vuorinen et al. 2020) or even drifted away by being attached on solid particulates (e.g. dust and pollen) (Griffin 2007).

The airborne transmission is further classified as short and long range, with most of the scientific community to be still unclear on the determination of the safety distances need to be kept to avoid infections. This becomes even more unclear considering especially infectious diseases which have the ability to spread in short and long diseases (Bourouiba et al. 2014) and under the two most widely known modes of transmission the short and long one. It seems that the most common indirect transmission route is occurring via spreading of an infected cloud of small saliva droplets (aerosols) during talking, coughing, sneezing or breathing (Gralton et al. 2011; Tang et al. 2009; Zhao et al. 2005). Lately, Godri Pollitt et al. (2020) demonstrated that the short-range airborne route of infection may be the most common transmission way of infectious diseases. Carducci et al. (2020) also refer that droplets up to 5 μm , fall next to the donor source, within a distance of approximately 1–2 m, due to the effect of the gravitational force prevailing on the large droplets. The smaller aerosols though can remain suspended and travel at greater distances in the indoor air environment. More information on the aerosol's nature, generation and behaviour can be found in next sections.

Aerosols of particles and biological agents

An aerosol is defined as a population of submicron particles or a suspension of droplets and droplet nuclei in the air. An aerosol of droplets is usually created by a violent respiratory event such as a cough or sneeze (Sakharov and Zhukov 2020). Jayaweera et al. (2020) claimed that up to 90% of the aerosol droplets generated by a human expiratory activities. Since aerosols are particles or biological agents of less than 50 μm , they remain suspended into indoor air due to their small size for extended periods of time. The larger airborne particles (> 50 μm) are too heavy to become suspended in the air for longer periods of time (Marui et al. 2019). In addition, the droplet nuclei residuals remain into indoor air at a fine and stable size, in the range of 5–10 μm (Bourouiba et al. 2014). This final stable size of the residual droplets/nuclei is determined by the equilibrium with the moisture of ambient indoor air (Vuorinen et al. 2020). The dynamic reduction in the size of the infectious droplets leads to a change in the pattern of

transporting in air, depending also in the indoor air currents, humans moving and talking, coughing or sneezing all known to be able to create a laminar or event transient and turbulent flow of the aerosols in confined spaces.

Many researchers study how the diameter of the liquid droplets changes dynamically and strongly affected by the temperature and relative humidity (RH) of indoor air (Aliabadi et al. 2011; Dedesko and Siegel 2015; Faridi et al. 2020; Shajahan et al. 2019; Verijkazemi et al. 2018; Zhang et al. 2019). Aerosols of less than 1 μm , with the lowest density are generated by nasal breathing, while the highest density by coughing in very short time (up to 500 ms) (Bourouiba et al. 2014). Exhaled breath is also more responsible for transmitting viruses of size of approximately 0.1 μm , compared to the bacteria transmission with particle size over 1 μm (Zhang et al. 2019). From the above-mentioned, it is evident that all the above factors, chemical composition, shape and size of droplets are interconnected.

The main characteristics of an aerosol depend on the characteristics of the single droplet and the forces imparted on them as they move along with the air currents (Rhodes 2008). The shape, and as a result size, of droplets depends on the spray/aerosol angle, covering of surface, droplet velocity distribution, volume distribution and pattern is different for different aerosol systems (Broniarz-Press et al. 2009). Some physicochemical properties of the droplets, such as viscosity, might vary, and depend on the fluid environment where the droplets are hosted (other liquid or air environments). For an aerosol of droplets in air, for instance, the relative viscosity of the liquid compared to the surrounding gas viscosity is high (50%), while in a liquid host is relatively low (Ben-Tzvi and Rone 2010).

In general, the larger the droplets and particles are, the quicker they settle and in a shortest distance they travel, as this will determine how far the particles will be dispersed. This is based on the force by which they are expelled from the source, either the source being a person or a ventilation equipment. It is widely acceptable that the respiratory droplets evaporate to form smaller droplet nuclei, remain then suspended in air due to Brownian motion, and susceptible individuals from the source could inhale them even when stand far away. Scheuch (2020) indicated that for small particles, the main mechanism of their transport in air is the Brownian motion and this mechanism works relatively effectively with droplets size in the range of 5–100 nm. Scheuch (2020) stated that the second important physical mechanism of eliminating particles from the indoor air is sedimentation. This mechanism is effective for aerosol particles above 0.5 μm – 1 μm . Stilianakis and Drossinos (2010) indicated that all droplets generated by an expiratory event, either this being coughing, sneezing, laughing, talking or breathing cover a large size range from approximately 0.6 to more than 1000 μm .

Atomisation of liquids

Atomisation is the process of formation of fine droplets, or an aerosol of droplets or biological agents in the case of indoor environments (Morawska 2006). The atomisation as a process creates small fractions of the liquid droplets affecting considerably other pollutants emission and spreading (Urbán et al. 2017), especially in indoor spaces. Ai and Melikov (2018) reported that the techniques of producing aerosols are increasingly been used to investigate airborne transmission of biological and chemical agents.

For example, a sneezing or violent coughing incident in terms of engineering is a large-scale atomisation process and formation of an aerosol of saliva droplets and nuclei. The atomisation as a mechanical process is affected by the geometry of the source, the aerodynamic forces imparted on particles, the surface tension and viscosity of the droplet. The aerodynamic forces are of considerable effect on the droplet or particle, while travelling in the air with the dominant being the gravitational forces or mass body forces which are imparted on relatively large particles. Thus, larger droplets settle quickly and the smaller airborne droplet nuclei are travelling over longer distances by the indoor air streams (Dhand and Li 2020). The drag force being also opposite to the gravitational force leading to the resistance in motion of droplets/particles in air. The surface tension, too, is the natural tendency of a liquid droplet to stabilise the shape of a droplet of a certain volume, offering the minimum surface area possible. The surface tension has a consolidating influence, which contradicts with the opposite tendency of the surface of the droplet to extent and wet a surface. The viscosity is a property which describes the rheological properties-behaviour of a fluid, and is opposing any change of the shape of the liquid droplets as they flow (Morawska 2006).

Atomisation is further classified as primary, upon injection of droplets and particles i.e. by a person sneezing, and secondary atomisation (Kuznetsov et al. 2019). The secondary atomisation takes place by the droplet size disruption due to interference of a solid surface such as a collision with a wall or a substrate (e.g. hand in front of the mouth while sneezing). This creates a second wave of atomisation due to the fact that the single cloud of droplets colliding with each other, a micro-explosive break-up of droplets is taking place, especially under the effect of the increased temperature and heat, as well as the interference of an existing indoor air stream flow. Han et al. (2020) indicated that increasing the mean air velocity results in larger aerodynamic forces which reduce the droplet sizes, while an increase in air pressure reduces the droplet size. The same researchers (Han et al. 2020) reported that the droplet size distribution is a crucial parameter of the atomisation process besides the mean diameter of droplets.

Suspension and resuspension of particles and biological agents

Suspension time of indoor pollutants is defined as the time that small droplets or particles remain suspended on air, carried away at short or long distances due to airflow motion and without necessary settling on horizontal surfaces such as the floor. Their velocity also plays an important role on the analysis and simulation of the aerosol systems and their suspension time. The effects of gravity or inertia forces on droplets of less than 30 μm are negligible as they are too small in size; their transmission then is mainly influenced by the indoor airflow as those particles remain suspended for long time and as a result the risk to be inhaled is high (Zhu et al. 2006). Results of studying a coughing incident showed that more than 6.7 mg of saliva are expelled as droplets exhibiting a velocity up to 22 m/s, while at the same time a travel distance of more than 2 m has been reported (Zhu et al. 2006). On the other hand, droplets with their size range varying from 50 to 200 μm are of significant size in terms of importance. Those are affected by gravity and fall on the ground as the indoor air flow streams are weakening. Droplets of diameter of 300 μm or larger, which are mostly affected by inertia forces rather than gravitational, rarely fall (Zhu et al. 2006).

In general, the evaporation rate of droplets depends mainly on the ambient temperature and humidity. It was found that droplets of size less than 100 μm will typically become droplet nuclei before settling on the floor. Small droplets of sizes between 5 and 10 μm will rapidly evolve into droplet nuclei with extremely low settling speeds (> 0.003 m/s). As a result those droplet nuclei are able to remain suspended for longer periods of time, however, the fate of droplets are determined by the competing effect of inertia, gravity and evaporation (Mittal et al. 2020). At the same time the nuclei are expected to be crucial in the long-range airborne transmission route. Bourouiba et al. (2014) also highlighted the synergistic effect of Brownian motion in the phenomenon of suspension and resuspension of particles, where air currents are absent. The same mechanism may keep the stable in size droplet nuclei suspended for very long periods of time in such environments.

The resuspension of particles into indoor spaces is the phenomenon of the detachment of deposited particles and droplets of other pollutants or biological agents from the surfaces into the bulk air (Al Assaad et al. 2020). The reason of resuspension is usually the human activities such as walking and natural or mechanical ventilation. All these actions cause the aerodynamic and mechanical vibration disturbances of the particles. It seems that particle resuspension takes places within a very narrow time frame of less than 25 s, since the initial disturbance, prior further decreasing to negligible values (Al Assaad et al. 2020).

For different indoor open surfaces, it was found that the resuspension was the lowest for smooth surfaces such as glass, followed by marble and linoleum. When though the aerodynamic disturbances applied on those surfaces were accompanied with vibrations the resuspension of particles increased by more than 45% for all cases (Al Assaad et al. 2020). It also seems that a decrease in the roughness of the indoor space surfaces can increase the particles and droplets adhesive forces reducing considerably the vibration effects which are responsible for enhancing the resuspension in air (Al Assaad et al. 2020). For example, dust is re-suspended when people walking on carpets and has been found that the mass load of dust is generally greater in carpets than the hardwood floors (Haines et al. 2020). They reported other pollutants such as stain-protectors which were found not only in the carpet, attached to dust, but were also detected in the blood serum of the occupants (Haines et al. 2020). The same researchers found that the man-driven resuspension of particles previously settled on carpets and hard flooring is a source of coarse-mode biological agents' pollution. When an adult, for instance, is walking across the floor, this can create a resuspension of 10 to 100 million particles per minute, many of which are likely to be of biological origin. For particles thought of less than 10 μm mass resuspension rates can exceed 10 mg/min (Haines et al. 2020).

In addition, indoor environmental conditions of temperature, humidity and air streams should not be underestimated, as it was found that 50% of the airborne biological agents could originate from the resuspension of fungi grown at equilibrium relative humidity of more than 85% on dust floor (Dannemiller et al. 2017). You and Wan (2014) based their findings both on experimental and modelling results. They showed that *Bacillus anthracis* particles' concentration becomes 1.5 to 3 times and 4 to 8 times higher after the initiation of airflow for particle of sizes between 2 and 4.75 μm . Their study indicated clearly the importance of the airflow to the resuspension of particles.

Evaporation, coalescence and growth of droplets

The evaporation of droplets plays an important role in the later fate of the droplet and competing effects of inertia and gravity. The evaporation rate depends on the difference between the droplet surface saturation vapour pressure and the vapour pressure of the surrounding air, which also depends on the humidity (Mittal et al. 2020). The diffusion mechanism strongly affects the droplets surface-to-temperature difference, and the relative velocity between the droplet and surrounding gas. Thus, dimensionless numbers such as the Sherwood (Sh), Nusselt (Nu) and Reynolds (Re_p) for the droplets are important to determine the evaporation phenomenon. It seems that higher temperature and lower relative humidity lead to larger evaporation rates that increase the

critical droplet size (Mittal et al. 2020). The temperature effect initiates the evaporation of atomised liquid droplets affecting the overall motion and distribution of droplets. Sakharov and Zhukov (2020) indicated that smaller droplets, 5 μm , would evaporate in less than 3 s, at typical indoor relative humidity of 50%.

Evaporation is a very fast molecular process, for instance, a 20- μm droplet evaporates to 1- μm diameter droplet within only a rate of 0.24 s^{-1} at 50% ambient relative humidity (Yang et al. 2018; Ai and Melikov 2018). Due to the evaporation phenomenon, the size of the droplets is affected by time, as they are shrinking and this is prominent for droplets with an initial diameter of 100 μm (Yang et al. 2018). Wells (1934) although has already found that by the beginning of the twentieth century, droplets with characteristic diameter larger than 100 μm settle to the ground in less than 1 s, without being significantly affected by evaporation. Similarly Morawska et al. (2009) did not detect droplet evaporation for particle sizes varied between 0.5 and 20 μm , and, if any evaporation occurs, take place at less than 1 s. Studies of water droplets with diameters of 10 to 240 μm indicated that the medium-sized droplets vary from 50 to 170 μm , as the thermal stratification weaken the evaporation of droplets due to less heat and mass transfer between the droplets and air. When the ambient relative humidity increased to 60%, a possible condensation phenomenon occurred on droplets, increasing the suspending time of droplets in the air (Liu et al. 2019a, b, c, d, e). In addition, vapours generated due to evaporation and super-saturated wet air exhaled from the respiratory tracks form a *vapour plume* in front of the nose and mouth of a person, which, despite the short life time enhances significantly the evaporation of the droplets captured in it (Li et al. 2018). Due to the evaporation and density of airborne droplets and mass concentration of inhalable pathogens, the process can result in a higher risk of infection (Li et al. 2018). The study of Li et al. (2018) demonstrated the importance of considering inhomogeneous humidity field when modelling the evaporation and dispersion of cough droplets.

Droplets might collide with each other and can undergo coalescence. Droplet coalescence is the process of merging of two or more droplets during contact to form a single larger droplet. If droplets are hydroscopic they grow in size or while transported in air might trap particulates such as dust (Han et al. 2020; Morawska 2006). As a result, the coalescence mechanism leads to a change of the particle size distribution with the mode value of droplets to increase as the total number of particles decrease (Morawska 2006). Shao et al. (2021) reported that the viscosity and surface tension of droplets might be of significant importance. They influence the droplet size distribution as both controlling the coalescence and breakage of larger droplets to smaller. However, these mechanisms are important only during

the ejection stage of the infected saliva droplets. Once the infected saliva droplets are below 50 μm, the coalescence and break up mechanisms are hindered. Occasionally, the particles may shatter apart into numerous smaller particles; however, this process usually occurs primarily in large particle size droplets, which cannot be considered as aerosols (Shao et al. 2021).

Aerosols and bioaerosols

An overview of airborne particle types that affect respiratory health

As previously discussed, the vast variety of abiotic (chemical agents) and biotic (biological agents) particles being

present in air at considerable concentrations can have a negative effect on human respiratory system or human health in general. Such particles are usually present in the form of aerosols which either travelling or being suspended in air. As defined in the ‘Aerosols of particles and biological agents’ section, an aerosol is a suspension of fine solid or liquid particles of varying sizes in air (Fig. 3).

Bioaerosols can be defined as the particulate matter usually associated with compounds of pure biological origin. This definition includes all pathogenic or non-pathogenic media ranging from live or dead fungi and bacteria, viruses, high molecular weight allergens, pollens and many others (Ghosh et al. 2015). The main type of aerosols being of a significant concern for human health is the plume of droplets of micron size that are scattered in the air during breathing, talking, coughing or sneezing (see the ‘The human

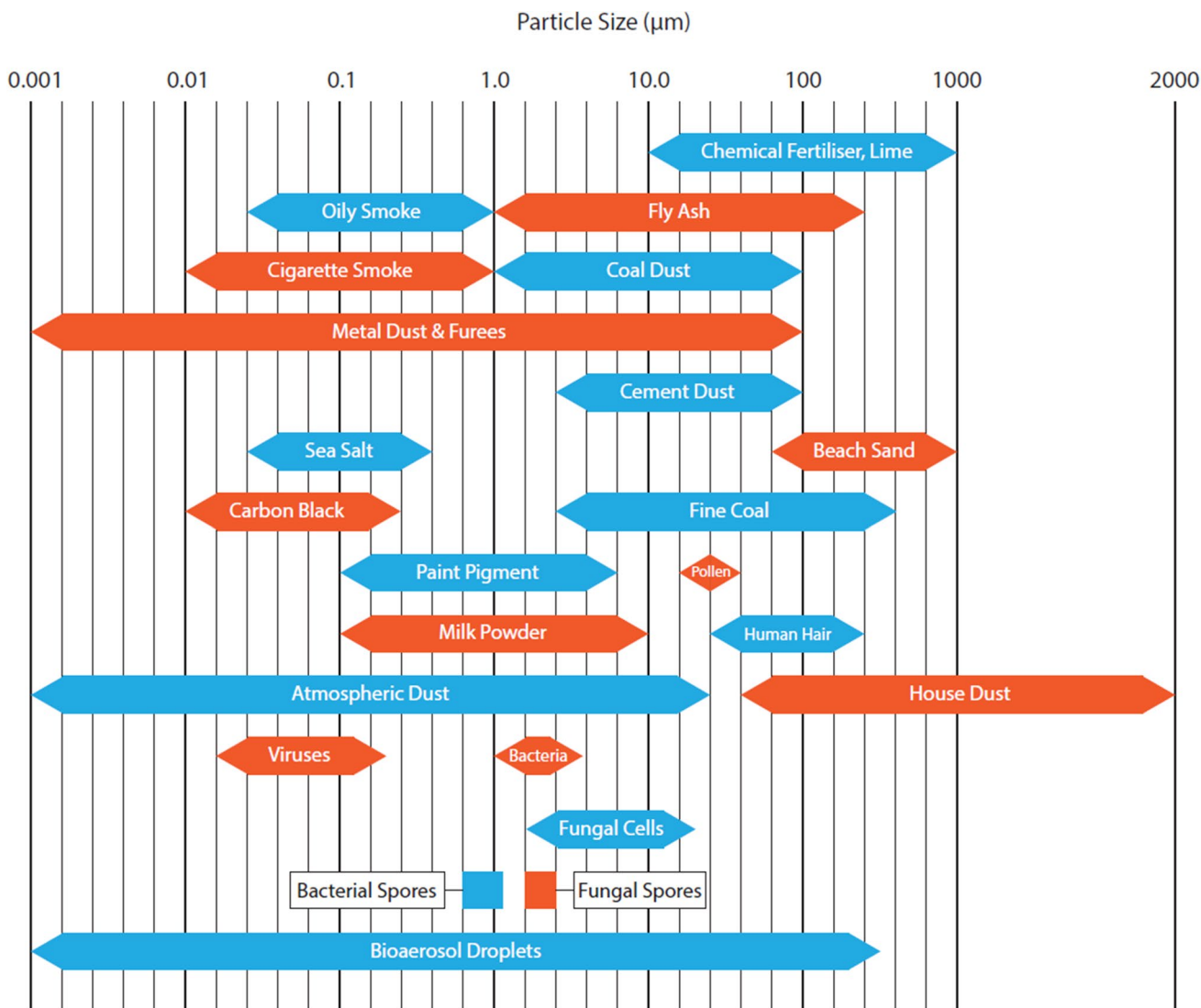


Fig. 3 The size ranges of air particles and microorganisms

respiratory system' section). As these droplets can stay suspended in the air for many minutes and contain pathogenic microorganism that can lead to respiratory diseases (Bourouiba et al. 2014; Cole and Cook 1998) (Fig. 4). Aerosols of biological agents can be also created mechanically by other ways such as emerging from water fountains, shower heads, surgical or dental procedures, as well as faulty air-conditioning or ventilation systems (Tran et al. 2012).

As discussed previously, the size of these droplets is a very important factor affecting the transmission of respiratory diseases. Usually droplets' size range from 0.01 to 500 μm , although larger droplets have also been reported (Gralton et al. 2011). According to Guzman (2020), only droplets smaller than 5 μm are able to reach the trachea of the recipient, while droplets below 2.5 μm can penetrate to the lower respiratory system and reach the bronchioles and alveoli inside the lungs (see **'The human respiratory system**' section). Aerosols smaller than 5 μm are considered to be airborne means of disease transmission, since they stay in the air for long periods of time, while larger aerosols are linked with droplet-associated transmission of diseases (Gralton et al. 2011).

The spread of pulmonary aerosols is a major public health concern, especially for indoor environments of hospitals and other healthcare units, where patients often have a weak immune system and at the same time multi-drug microbial pathogens might be present (Stockwell et al. 2019); Tang et al. 2006).

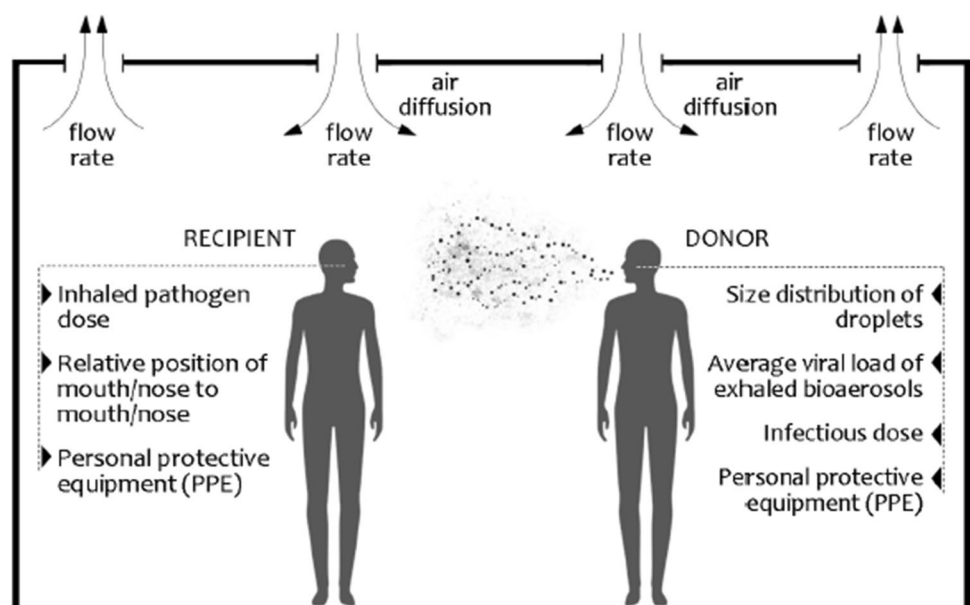
A second type of particles that could be potentially harmful, even though not of biological origin, is related with dust. Dust particles in domestic surfaces, such as floors, furniture or carpets (Haines et al. 2020), may also be contaminated by microbial pathogens (Dannemiller et al. 2017), inducing

allergic reactions or worsen the symptoms of an already pre-existing asthma condition. Inhalation of household dust, which contains a variety of aeroallergens, can worsen the symptoms of allergies and asthma. House dust particle sizes range from 2 μm to 63 μm , with approximately 33% of the dust being smaller than 500 μm (Lanzerstorfer 2017). Examples of such allergens include the house dust mite (HDM) protein Der p 1, Can f 1 (associated with dogs) and Fel d 1 (associated with cats). Dust particles < 5 μm tend to remain suspended in the air for a number of days, whereas larger particles (> 5- μm diameter), which remain airborne for a shorter period after disturbance (Hussain et al. 2019). The dust mite itself has a diameter of 200 μm and it is considered too large for penetrating the lungs, however a small proportion of its faeces that are rich in Der p 1 can enter the lungs and cause allergy symptoms (Wilson and Platts-Mills 2018).

House dust particles can also absorb harmful microbial volatile organic compounds (MVOCs). Exposure to low levels of MVOCs in indoor air is related to a range of non-specific symptoms, including redness of the eyes and irritation of the nose and skin, that are known as the sick building syndrome (Wady and Larsson 2005). Other types of dust that could enter inside buildings via open doors or windows include sand particles, farm and coal mine dust and they can all lead to serious lung damage (Khan and Strand 2018; Penconek et al. 2019; Schuijs et al. 2015).

Fungal and bacterial spores can also lead to development of serious lung disease (Cutting and Ricca 2014; Foster et al. 2017; Han and Weiss 2017). Several microorganisms such as fungi (e.g. *Aspergillus fumigatus*) and bacteria (e.g. *Bacillus anthracis*) form spores. These are resistant structures with thick cell walls of several layers that provide resistance against extreme environmental conditions, such

Fig. 4 A donor-recipient model of transmission of respiratory pathogens within droplets



as adverse temperatures, drought and chemical biocides (Leggett et al. 2012; Madsen et al. 2016). These spores can be easily dispersed in the air, outside aerosols and become inhaled by humans. After inhalation, they end up in the lungs where they germinate and colonise the tissues of the human respiratory system, if they are not controlled by the immune system (Husman 1996). Bacterial spore sizes vary from 0.8 to 1.2 μm (Carrera et al. 2007), while fungal spores range from 2 to 4 μm (Madsen et al. 2016). Fungal spores and vegetative fragments can also be allergenic, bearing a variety of allergens such as Asp f 1, Alt a 1 and Cop c 1 (Cramer et al. 2006; Green et al. 2006). Anthrax spores formed by *Bacillus anthracis* are considered to be a highly persistent and lethal type of bioterrorism agent, therefore they are a major biosecurity concern, especially for indoor environments, such as offices or schools (Taylor et al. 2012).

Finally, plants produce pollen, which is a powdery substance consisting of pollen grains that contain the male gametes (sperm cells) of the plant. Such particles have a rigid thick exterior layer which protects the genetic material of the gamete. Pollen size ranges generally from 20 to 60 μm (Mander 2016; Rantio-Lehtimäki et al. 1994; Soares et al. 2018). There are, however, exceptions such as *Pinaceae* pollen which can be of size over 80 μm (Smith et al. 2014). Pollen grains can also travel long distances in air and are known to contain allergenic proteins inducing hay fever and asthma exacerbations. More than 150 different pollen allergens have been identified so far (Mothes and Valenta 2004; Rodríguez et al. 2007); White and Bernstein 2003). The most common ones are the Phl p 1 and Lop p 1. Unfortunately, allergic reactions to pollen represent the most frequent type I allergies affecting up to 30% of the industrialised population (Biedermann et al. 2019; D'Amato et al. 2007; D'Amato et al. 1998). Climatic

changes are expected to influence the duration as well as the intensity of pollen seasons which might in hand with air pollution contribute to increased numbers of respiratory allergy and asthma (Pablos et al. 2016).

Major respiratory microbial pathogens and health effects

Numerous infectious agents lead to serious respiratory illness or even death. These belong to three major classes of microorganisms, namely viruses, bacteria and fungi (King and Auger 2002; Prat and Lacoma 2016; Rath et al. 2017) (Fig. 5). Viruses are not considered to be living organisms, as they do not have a metabolism and are unable to replicate outside a host cell. Their viral genetic material is usually protected by a protein capsule. Several viruses are also surrounded by a lipid envelope (Weber and Stilianakis 2008). Bacteria and fungi are living organisms. The morphology of these microbes is extremely diverse in nature, but again the genetic material is enclosed by a lipid membrane and a polysaccharide cell wall. On their surface, these agents have receptors enabling them to attach to human cells and potentially invade into the human cells. In terms of pathogens sizes viruses typically range between 20–300 nm, bacteria 1.0–5.0 μm and fungal cells 2–30 μm (Choudoir et al. 2018; Shi and Tarabara 2018; Weiser 2013) (Table 2). Some bacteria and fungi are able to build long filaments up to several centimetres (cm), while some fungi can form much larger structures in nature (e.g. mushrooms). As discussed in the previous section, the respiratory pathogens usually spread through the air via coughing or sneezing (Barmby and Larguem 2009; Srivastav et al. 2018; Xie et al. 2009), as well as being transmitted by touching contaminated surfaces and then touching the eyes, nose or mouth (Deacon 2006; Madigan 2009).



Fig. 5 Images of key respiratory pathogens: **a** SARS-CoV-2, **b** *Mycobacterium tuberculosis* and **c** *Aspergillus fumigatus*. Source: Public Health Image Library, CDC-USA

Table 2 Details of key respiratory pathogens in relation to their pathogenicity

Species name	Size (µm) (Collier et al. 2000; Murray et al. 2013)	Disease(s) (Collier et al. 2000; Murray et al. 2013)	Duration of survival on surfaces (h) (Kramer et al. 2006)	Minimal infectious dose (# of particles/cells) (Yezli & Otter 2011)
Rhinovirus	0.03	Common cold	Up to 7 days	10
Influenza virus	0.08–0.12	Flu	24–48 h (Bean et al. 1982)	1,000
SARS virus	0.05–0.20	Respiratory syndrome	24 h (M. Y. Y. Lai et al. 2005)	280 (Watanabe et al. 2010)
MERS virus	0.10 (Hajjar et al. 2013)	Respiratory syndrome	8–48 h (Kampf et al. 2020)	1,000 (Douglas et al. 2018)
SARS-CoV2 (COVID19)	0.60–0.14 (Dhama et al. 2020)	Respiratory syndrome	84 h (Hirose et al. 2020)	100 (Ryan et al. 2020)
Respiratory syncytial virus	0.15–0.25	Common cold	6 h	Unknown
Parainfluenza virus	0.15–0.25	Respiratory illness in children	4–10 h (Henrickson 2003)	Unknown
<i>Streptococcus pneumoniae</i>	0.5–1.25	Pneumonia	20 days	5 × 10 ⁶ (Dietert et al. 2017)
<i>Haemophilus influenzae</i>	1.00	Pneumonia	12 days	Unknown
<i>Legionella pneumophila</i>	3.00–5.00	Legionnaire's Disease	2 h (Katz & Hammel 1987)	100,000 (Gama et al. 2012)
<i>Mycobacterium tuberculosis</i>	2.00–4.00	Tuberculosis	Up to 4 months	10 (Gama et al. 2012)
<i>Acinetobacter baumannii</i>	0.90–1.60	Lung infection; wound infection	Up to 5 months	10 ⁶ (Breslow et al. 2011)
<i>Bordetella pertussis</i>	0.40–0.80	Whooping cough	3–5 days	10,000 (Vidlak & Kielian 2016)
<i>Klebsiella pneumoniae</i>	0.50–2.00	Pneumonia	Up to 30 months	Unknown
<i>Pseudomonas aeruginosa</i>	1.50–3.00	Lung infection; wound infection	Up to 5 weeks	10 ¹⁰ (Gama et al. 2012)
<i>Staphylococcus aureus</i>	1.00–1.50	Lung infection; wound infection; toxic shock syndrome	Up to 7 months	100,000 (Vidlak & Kielian 2016)
<i>Bacillus anthracis</i>	3.00–10.00	Highly fatal lung infection; skin infection	56 days	8,000 (Gama et al. 2012)
<i>Aspergillus fumigatus</i>	10.00–20.00 (Loures et al. 2015)	Allergic bronchopulmonary aspergillosis (ABPA); allergic <i>Aspergillus</i> sinusitis; Aspergilloma; chronic pulmonary aspergillosis; invasive aspergillosis	30 days (Neely & Orloff 2001)	Unknown
<i>Candida albicans</i>	10.00–12.00	Lung infection; oral and vaginal infections	Up to 3 months	Unknown
<i>Cryptococcus</i> spp.	4.00–6.00	Lung infection; meningitis	Unknown	Unknown
<i>Pneumocystis</i> spp.	2.00–6.00	Pneumonia	Unknown	Unknown

Viruses

One of the most frequently encountered viral pathogens is the rhinovirus, which is the primary cause of common cold in humans, closely related to respiratory diseases. There are three species of rhinovirus (A, B and C) that include around 160 serotypes (Glanville and Johnston 2015; Pomeranz et al. 2019; Taylor-Robinson and Tyrrell 1962). The symptoms that they cause upon human infection include sore throat, runny nose, nasal congestion, sneezing and cough, muscle aches, fatigue, malaise, headache, muscle

weakness and loss of appetite. However, this virus can also cause exacerbation of underlying lung disease, for instance, in critically ill patients with pneumonia, with or without co-pathogens. In terms of particle size, they are among the smallest viruses, with diameters of about 30 nm (Collier et al. 2000; To et al. 2017).

Another very common respiratory viral infectious agent is the influenza virus, which causes the common flu. There are four types of this virus (A, B, C and D) (Iwasaki and Pillai 2014; Kim et al. 2018; Lyons and Luring 2018). Types A, B and C are known to infect humans (Kumar 2017; Peteranderl

et al. 2016; Webster and Govorkova 2014), while D affects cattle. Normally, flu is characterised by systemic symptoms such as fever, myalgia, headaches and severe malaise, and respiratory symptoms such as coughing, sore throat and rhinitis. Those occur after approximately 2 days of an incubation period and can last for up to 7 to 10 days. Coughing and tiredness symptoms though can persist for even up to two weeks. If the virus reaches the alveoli of the lungs, it can result to serious viral pneumonia and interstitial pneumonitis. The influenza virus especially consist a major health risk and hazard for the elderly or immunocompromised individuals (Pleschka 2013).

Coronaviruses is another group of viruses causing diseases in humans, mammals and birds. When humans are infected by coronaviruses, this leads to respiratory infections that can range from mild effect to detrimental for the human health and even lead to death. Mild symptoms are similar to these of common cold, while more lethal strains can result in severe respiratory illnesses such as SARS, MERS and SARS-CoV-2 syndrome (de Wit et al. 2016; Hageman 2020; Yin and Wunderink 2018). The mortality rates range from 5 to 15% (Chan et al. 2003; Singh 2016; Weiss and Murdoch 2020). The SARS-CoV virus pandemic (2002–2004) resulted in 926 deaths worldwide, while the newly identified SARS-CoV-2 virus led to 279,000 deaths worldwide by 21/05/2021, only 6 months after the first outbreak (Lauxmann et al. 2020; Rothan and Byrareddy 2020). As of July 2017, 2040 MERS-CoV laboratory confirmed cases, resulting in 712 deaths, were reported globally, with a majority of these cases from the Arabian Peninsula (Chafekar and Fielding 2018). There are as yet no vaccines or antiviral drugs to prevent or treat human coronavirus infections. Finally, other airborne viral pathogens include respiratory syncytial virus (RSV) and parainfluenza virus (Collier et al. 2000).

Bacteria

Streptococcus pneumoniae is asymptotically carried in healthy individuals, typically colonising various tissues of the upper respiratory system, as well as the sinuses. However, in susceptible individuals with weaker immune systems, such as the elderly and young children, *S. pneumoniae* can lead to serious pneumonia. Moreover, several strains of this species have developed resistance to many of the traditional antibiotics, which makes such infections difficult to treat (Feldman and Anderson 2016). This bacterium also causes bronchitis, rhinitis, acute sinusitis, otitis media, conjunctivitis, meningitis, sepsis, osteomyelitis, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis and brain abscess (Murray et al. 2013).

Haemophilus influenzae is a bacterium that is responsible for a wide range of topical and systemic infections. Most strains of *H. influenzae* are opportunistic pathogens,

as they usually grow on the mucosal layers of the respiratory tract without causing any disease. However, when other factor such as a viral infection, impaired immune function or chronic inflammation create the appropriate conditions, then a disease can occur. In infants and children, *H. influenzae* type b (Hib) causes bacteraemia, pneumonia and acute meningitis. More rarely, it can also lead to cellulitis, osteomyelitis and infectious arthritis (Butler and Myers 2018).

Legionella pneumophila is a bacterial pathogen which invades and replicates inside macrophages via phagocytosis. Inside the macrophages, the bacteria are enclosed into a membrane-bound vacuole that protects them from degradation by cellular enzymes and allows them to multiply in large numbers. *Legionella* is most commonly transmitted by inhalation of contaminated aerosols produced by water sprays, jets or mists. This bacterium can cause Legionnaires' disease and the less severe form, Pontiac fever. The common clinical symptoms of *Legionella* infection include high fever, cough, chills, difficulty in breathing, neurological problems, muscle weakness, diarrheal, chest pain, headache, nausea and vomiting. Legionnaires' disease, which is a form of atypical pneumonia, has a mortality rate in the range of ~10–50% (Murray et al. 2013; Prussin et al. 2017).

Mycobacterium tuberculosis is the causative agent of tuberculosis. Although this type of lung disease was widely controlled after the discovery of antibiotics, new emerging multidrug-resistant (MDR) strains are still a great concern in many areas of the world. Symptoms include chest pain and a prolonged productive cough. Approximately 25% of tuberculosis patients remain asymptomatic, but they can still spread the pathogen (Hunter 2016, 2018; Wang 1999). From time to time, patients may cough up blood in small amounts, while in rare cases, the infection may damage the pulmonary artery, resulting in massive bleeding (Bansal et al. 2018; Beggs et al. 2003). Other bacteria that can lead to serious lung disease are *Acinetobacter baumannii*, *Bordetella pertussis* and *Klebsiella pneumoniae* *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Bacillus anthracis* (Murray et al. 2013).

Fungi

Aspergillus fumigatus is a fungal pathogen that it is ambiguously found both indoors and outdoors. It forms thousands of tiny spores (2–3 µm) which readily become airborne and after inhalation they can easily penetrate the tissues of the lower respiratory system. The fungus is capable of growth at temperatures up to 50 °C, with spores surviving at 70 °C (Dijksterhuis 2019; Grishkan 2018; Pitt and Christian 1970). Typically, inhaled spores are quickly eliminated by the immune system in healthy individuals. However, in immunocompromised people, such as transplant recipients, AIDS or cancer patients, the fungus is more likely to become

pathogenic and lead to more serious lung illnesses such as allergic bronchopulmonary aspergillosis (ABPA), aspergilloma, chronic pulmonary aspergillosis and invasive aspergillosis. Due to the extended use of immune suppressants for treating human diseases, it is estimated that *A. fumigatus* is the cause of over 600,000 deaths annually, with mortality rates ranging from 25 to 90% (Latgé and Chamilos 2019; Murray et al. 2013). Other important fungi that can cause respiratory disease in immunocompromised patients are *Candida albicans*, *Cryptococcus* spp. and *Pneumocystis* spp. (Murray et al. 2013).

Microbiological and molecular methods for microbial enumeration and identification

Nowadays science innovation arises from the multidisciplinary approach of a variety of scientific fields. Analytical methods often applied in biomedical sciences find applications in engineering. Below, the main microbial and molecular methods for identification or biological agents are reported, and might be proved very useful in engineering applications such as determination of the biological load of indoor air.

Air samplers

The microbiological quality of the air is usually determined by sampling small volumes of air, which contain various bioaerosols. Then the process of enumerating and identifying the microbes within the sample is taking place. Such microbial monitoring is done routinely at healthcare-related areas for assessing environmental quality and deciding if corrective intervention is necessary or not (Napoli et al. 2012; Razzini et al. 2020). Air samplers are the most frequently used devices for such purposes, mainly because of their low costs and easiness of handling. Air samplers draw in air and force the various particles in it to get impacted over collecting surfaces or impinged into a liquid. These samples can also utilise filters for selecting a specific range of particles, while different impaction rates can be used by adjusting the vacuum settings (Ghosh et al. 2015).

Air filtration

Another method for collecting airborne bioaerosols is filtration. During this procedure, air is drawn through a filter with a 0.2- μm pore size, trapping all particles apart from small viruses. This can be facilitated by a vacuum system. The filter can be then used for enumerating the microbes or culturing them before identification with traditional or molecular techniques. One important advantage of filtration is that the captured microorganisms remain viable. Also, the filter can be directly used for nucleic acid extraction (Ferguson

et al. 2019). However, such filters are prone to overloading or damage and also desiccation can result in low recovery efficiency of the trapped microbes (Ghosh et al. 2015). Such method of air sampling by filtration was used for sampling of bioaerosols by (Predicala et al. 2002) at a swine farm environment.

Other bio-aerosol precipitation approaches

More laboratory-based approaches are available for precipitating bioaerosols or other particles from the indoor air. Those however are not used as frequently as the ones mentioned above. These include sedimentation and centrifugation, as well as electrostatic or thermal precipitation (Ghosh et al. 2015).

Cotton swabs

Medical-type swabs are often used for taking biological samples from surfaces, for subsequent microbiological or molecular analysis. The procedure is very simple, as the swab is rubbed onto or into the contaminated area and then wiped across a culture medium, such as an agar plate, where the bacteria and fungi from the swab may grow. This has to be done quickly and aseptically, in order to avoid contamination of the sample with other environmental microbes. It has been suggested that if the swab is mildly sonicated after sampling, the microbial recovery rate on the culture media is increased (Ahnrud et al. 2018).

A combination of air sampling and cotton swabs was used this year at a Milanese hospital for detecting SARS-CoV-2 genetic material (RNA) in the air and on key surfaces of the building (Razzini et al. 2020). The most contaminated surfaces were hand sanitizer dispensers (100%), medical equipment (50%), medical equipment touch screens (50%), shelves for medical equipment (40%), bedrails (33.3%) and door handles (25%) (Haun et al. 2016; Kurgat et al. 2019; D. J. Weber et al. 2019). Other recent studies that used cotton swab sampling approaches for microbiological monitoring are these by Lee et al. (2018) and Luksamijarulkul and Pipitsangjan (2015). According to these studies, it was shown that such swabs remain the easiest and most widely used method for surface sampling. A variety of more effective swabbing products, such as nylon, rayon and polyester swabs, has been lately developed (Bruijns et al. 2018).

Microscopy

One of the most traditional methods for microbial identification is observation of the microbe's physical characteristics, such as shape, size and the types of dyes that absorbs, under a light microscope. For example, the Gram stain can

distinguish different bacterial species to Gram-positive or Gram-negative, according to their cell wall structure. Other types of staining can provide information about production of spores (Schaeffer-Fulton staining), capsules (India ink or nigrosine) and mycolic acids (acid-fast staining). Light microscopy can also be used for enumeration of cells, by using of a haemocytometer. For virus identification, the use of electron microscopy is required (Ahmed et al. 2016).

Use of selective and differential culture media for microbial enumeration and identification

The method that is most frequently used for isolating bacteria and fungi involves culturing them on the surface of solid nutrient media (Brugger et al. 2012; Burmølle et al. 2009; Wiegand et al. 2008). Such media contain all the necessary nutrients for the growth of a wide range of microbes, including carbon (C), nitrogen (N) and phosphate (P) sources, amino acids, inorganic salts and trace elements. It also contains 1.5% agar, which is a polysaccharide that gives a gel-like structure to the solid medium. After incubation for 24 h at 37 °C, colonies appear on the surface of the agar, which can be counted and identified based on their morphological characteristics (Collins et al. 1989).

There is a wide range of selective and differential media that are used in clinical microbiology laboratories for microbial enumeration and identification (Bonnet et al. 2020; Reddy et al. 1972; Yoo et al. 2014). Selective media contain compounds that inhibit the growth of some microorganisms, permit however others to grow. Differential media contain ingredients making the colonies of a certain group of microorganisms appear in a different colour than this of other groups. Some differential media are also selective, for instance, MacConkey agar, which is selective for Gram-negative coliforms and can also differentiate between lactose-fermenting and non-lactose-fermenting bacteria (Ahmed et al. 2016; Nigro and Steward 2015). Such traditional microbiological culture-based approaches have been followed recently for indoor bioaerosol characterisation (Yasmeen et al. 2020; and Nasir et al. 2018).

Use of biochemical tests for microbial identification

A plethora of biochemical tests is also available for identifying microbial species. These tests usually determine the ability of a species to grow in media containing certain carbon or nitrogen sources, such as glucose, lactose and urea. As the microbes metabolise these substrates, they produce products leading to a medium colour change, which is regarded as a positive test result. Based on the results from many such tests, a microbiologist can use specific charts for identifying a bacterial pathogen. Automated identifying systems are today available for running these tests in a high-throughput

mode, e.g. VITEK2® and FAME, and those have been very useful for bioaerosol profiling (Duquenne 2017). Similar approaches can be used for identifying fungi, but not viruses as they do not have a metabolism activity (Spiegelman et al. 2005).

Polymerase chain reaction

The polymerase chain reaction (PCR) is a widely used method for rapidly amplifying a specific area of the DNA of a sample (Gadsby et al. 2019; Liu et al. 2019a, b, c, d, e; Siqueira and Rôças 2003). The PCR product is then analysed by gel electrophoresis and a final result can be obtained about the identity of microbe, based on whether it contained the targeted area in its DNA or not (Järvinen et al. 2009). Real-time quantitative (qPCR) is a more advanced method and can be used for both identification and quantification of a microbial pathogen in a clinical sample. Real-time qPCR utilises fluorescent chemicals that can be detected by a detection system when amplification of the desired DNA area begins. As a result, there is not a need for gel electrophoresis. This method is more sensitive and precise than the standard PCR method (Kralik and Ricchi 2017). Real-time quantitative and standard PCR methods have been recently applied in several indoor bioaerosol surveillance studies (Coleman and Sigler 2020; Razzini et al. 2020).

Matrix-assisted laser desorption/ionisation

Matrix-assisted laser desorption/ionisation (MALDI) is an ionisation technique for mass spectrometry that uses a laser energy absorbing matrix to create ions from large molecules (Dingle and Butler-Wu 2013; Jang and Kim 2018; Singhal et al. 2015). Biological macromolecules such as DNA, proteins and peptides tend to be fragile and fragment when ionised by more conventional ionisation methods. The advantage of matrix-assisted laser desorption/ionisation (MALDI-TOF) is that it does not lead to such fragmentation, something which makes it suitable for clinical use. Colony material of the microbe in question is placed onto the sample target and overlaid with matrix. The resulting spectra are used for the identification of micro-organisms, after analysis by dedicated software and compared with stored profiles. MALDI-TOF is much faster, more accurate and cheaper than traditional methods (Madsen et al. 2015; Murray 2012; White et al. 2019).

Nucleic acid sequencing

Next-generation sequencing (NGS) is a highly advanced technology that via which millions of DNA fragments can be simultaneously and independently sequenced (Huang

et al. 2020; Lin et al. 2019; Sung et al. 2018). In clinical microbiology laboratories, metagenomic NGS (mNGS) is most frequently used for detection of certain pathogens. The cost of such analyses is still very high, and most hospitals cannot afford them even when the results are obtained faster and are much more reliable.

Another advantage of NGS is that analyse DNA or RNA in a clinical sample are surveyed *en masse*, in contrast to PCR that can only analyse few specific targets per run (Gu et al. 2019; Madsen et al. 2015; White et al. 2019). MALDI-TOF and NGS are definitely the most promising advanced technologies for microbial identification at the moment. This year's "Viruses in the Built Environment (VIBE) meeting in Arlington, Virginia, USA, highlighted the importance of constructing bioinformatic tools and databases that will ensure a quick and accurate microbiological monitoring within buildings (Prussin et al. 2020). Other methods that can also help with microbial identification include DGGE, serological approaches, epifluorescent microscopy and flow cytometry (Ghosh et al. 2015).

New novel approaches for real-time monitoring of bioaerosols

The last few years, several novel approaches have been tested and applied for real-time monitoring and characterisation of bioaerosols. These include fluorescence spectroscopy, elastic scattering, microscopy and holography, Raman spectroscopy, mass spectrometry, breakdown spectroscopy, remote sensing, microfluidic techniques and paired aqueous techniques (Huffman et al. 2020; Nasir et al. 2019). Examples of such modern applications are provided below. In 2013, Usachev et al. (2013) applied a surface plasmon resonance-based immunosensor for real-time bioaerosol detection. The collected viral particles were mixed with a target-specific antibody and the positive aggregates were efficiently detected in less than 2 min.

Choi et al. (2015) developed and tested a micro-optofluidic platform that proved able to accurately detect, quantify and characterise bacterial aerosols, by use of fluorescent dye detection, fluidics and optical microscopy. Furthermore, an adenosine triphosphate (ATP) bioluminescence assay was developed by detecting and measuring the concentration of bacterial aerosols. This assay was coupled with a continuous aerosol sampling device. The collected bacteria were charged, added to a liquid buffer and their numbers were estimated by measurement of the ATP levels generated via microbial metabolism (Park et al. 2016).

Finally, laser-based bio-detectors were applied for characterising a great number of individual particles in seconds, by analysing optical scattering and fluorescence characteristics. Data analysis by use of Artificial Neural Networks led to construction of decision trees for aerosol classification

(Leskiewicz et al. 2018). All these approaches seem extremely promising and are expected to be more widely applied for characterisation of medically important aerosols in the near future.

Survival of respiratory microbial pathogens

The duration of survival of different microbial pathogens in the environment is a major public health parameter that has significantly attracted the interest of most epidemiologists worldwide. The main factor that affects this is the structural composition of the pathogen. For instance, fungal and bacterial spores can survive for years due to their thick cell walls and dormant metabolism. Non-enveloped viruses are also very tolerant due to their resistant protein capsule. Enveloped viruses are less resistant, because their lipid bilayer is susceptible to heat, dryness and chemical agents. Finally, fungi are usually better at survival than bacteria due to their stronger cell walls (Table 2). Both bacteria and fungi often require high water activity and nutrient availability in order to survive and grow (Dedesko and Siegel 2015; Mendell et al. 2018). Furthermore, the type of surface is also important for determining the survival of microbial pathogens. For example, moist, porous and soft surfaces such as carpets and curtains are more likely to accommodate microbial growth than dry non-porous hard surfaces such as wood, plastic or metal (Thompson and Bennett 2017).

Some types of surface material such as copper, silver or antibacterial polymers can lead to microbial death and prevention of colonisation (Muller et al. 2016). Finally, environmental factors such as heat, pH, humidity, UV radiation and chemicals can affect microbial viability. Some bacteria are tolerant to adverse environmental condition (Walsh and Camilli 2011), while many bacteria and fungi can form biofilms, slimy layers made of polysaccharides and proteins that protect them from hazardous conditions (Hall-Stoodley et al. 2004). Environmental factors such as humidity and ambient temperature can also affect the survival of microbes in the air, either within or outside bioaerosol droplets, with a subsequent importance for respiratory disease (Prussin et al. 2020; Pyankov et al. 2018; Tang et al. 2006).

Transmission of respiratory microbial pathogens

Microbial pathogens can be transmitted via a variety of routes, including person-to-person (touch, saliva), airborne, foodborne/waterborne, via blood, sex, insects or fomites (non-living objects, such as door handles or towels, etc.). When it comes to airborne transmission, this can be classified as long and short range, depending on the viability of a pathogen in the air or the stability and size of the droplet that might carry it. Large-droplet diameter is considered to be > 50 to 60 μm , small droplet diameter is < 50 to 60 μm

and droplet nuclei diameter < 5 to $10\ \mu\text{m}$ (Tang et al. 2006) (see the ‘Size of particles and biological agents’ section). An example of short-range airborne transmission is the inhalation of droplets from a coughing or sneezing infected donor (from a < 1 -m distance), while long-range airborne transmission can include inhalation of fungal or bacterial spores that have travelled a long distance in the air via the wind (see ‘The challenging nature of biological agents’ transmission in indoor environment’ section). However, several non-spore bioaerosols can also travel long distances, if certain environmental conditions permit it (e.g. indoor air circulation) or if they are inside small droplets or droplet nuclei.

Many respiratory pathogens can be also transmitted via personal contact, via dust or from fomites, if the recipient touches a contaminated area and then touch facial, oral or nasal areas, allowing the entry of the pathogen into the respiratory tract (Wei and Li 2016a, b). Even if the pathogen enters the upper respiratory system, it might not be able to cause disease unless it penetrates the lower respiratory tract (trachea, bronchi, bronchioles and the alveoli). As it was mentioned in the ‘The human respiratory system’ section, this depends on the size of the infectious agent or the droplet that carries it ($< 5\ \mu\text{m}$ are able to penetrate lungs).

Factors that affect the development of respiratory infectious disease

Pathogen-related factors

Several microbe-related factors can affect its ability to cause respiratory disease. Some infectious agents are more pathogenic than others and even within the same species there are often sub-species, serovars or strains that are more virulent than others. This depends on the weaponry of virulent factors that a strain carries, such as toxins, super-antigens and degradative enzymes that destroy the tissues and cause localised damage and inflammation. Moreover, some strains have the ability to form filaments, spores and biofilms that make them more invasive and tolerant to the attacks of the immune system. Finally, the ability of a strain to mutate is an additional factor that affects its virulence (Davidson 2018; Murray et al. 2013).

In addition, the number of the initial infectious agents that enter the site of infection (e.g. lungs) is very important. Usually, low numbers, e.g. 50–150 cells or virus particles, can be easily dealt by the immune system which represses the infection before it leads to disease. Higher infectious doses can be difficult to control. However, this also depends on the type of pathogen that reaches the site of infection. The infectious doses of certain infectious agents that can lead to death have been experimentally measured by use of mice or other laboratory animals (Prussin et al. 2020; Tang et al. 2006) (Table 1).

Host-related factors

There are also many different host-related factors that can determine if a respiratory disease such as pneumonia will develop or not and how severe it will be. Firstly, the age of the patient is important. Young children do not have a fully developed immune system and the elderly have a weakened one that is often unable to eradicate the infectious agent. Vaccination against agents such as the influenza virus, *Mycobacterium tuberculosis* or *Streptococcus pneumoniae* can also prevent development of respiratory disease.

Immunocompromised individuals, such as cancer patients, transplant recipients or HIV patients, are also more vulnerable to infectious agents that cannot cause respiratory disease in healthy individuals (e.g. *Cryptococcus neoformans*, *Candida albicans*). Moreover, smoking and air pollution destroy the ciliated cells of the respiratory system that are a physical defence mechanism against microbes and push mucous-trapped microorganisms out of the body. This makes smokers more susceptible to lung and airway disease. Finally, underlying disease such as diabetes, obesity or cystic fibrosis can affect the potency of the immune system (Engin et al. 2020; Lacoma et al. 2019; Murray et al. 2013).

The role of heating, ventilation and air-conditioning systems

Heating, ventilation and air-conditioning (HVAC) systems are widely recognised as the most influential engineering approach to control the airborne transmission of the pollutant agents in the internal spaces (Bhagat et al. 2020; Li et al. 2007; Luongo et al. 2016; Qian and Zheng 2018; Shajahan et al. 2019; Wei and Li 2016a, b) as their operation is associated with the movement/ flow of the indoor air due to the introduced buoyancy forces and pressure differences. The operation patterns of these systems have been analysed in several engineering and epidemiological studies in last decades, resulting in the suggestion of three individual characteristics, (a) ventilation rate, (b) airflow direction and (c) thermal plume, to be the main parameters that significantly determine the transportation and the infectious mechanisms.

Adequate ventilation rate is pointed out as an important factor for removing the pollutants in general and especially the less studied biological agents from the indoor spaces. Airflow direction leads the air from the clean zone into the pollutant source area and consequently from the polluted space to outdoors. Thermal plume influences the space stratification conditions and the kinetics of the pollutant agent. The following sections summarise and criticise the results of previous studies related to the aforementioned parameters regarding the control of the airborne

transmission of the contaminant agents, and on minimising the risk of cross-infection between the occupants.

The role of ventilation

Ventilation is the supply of the outdoor air into internal building spaces, and can be categorised as natural and mechanical or forced ventilation. Both ventilation options induce different advantages and disadvantages while their combination could provide mixed characteristics (Cao et al. 2014; Gilkeson et al. 2013). Natural ventilation is of low cost and maintenance and allows the ambient air to be entered into the building by various and mixing routes. In contrast, the use of natural ventilation is directly linked with fluctuating ventilation rates that under specific outdoor and indoor conditions the air movement could be inadequate or overabundant. In addition, the intake air is unfiltered and depending on the ambient environmental conditions it may transport a variety of undesirable contaminants (e.g. dust, fumes and microbes, among others).

Mechanical ventilation could supply filtered fresh air and especially in combination with high efficiency minimum efficiency reporting value (MERV) 13–16 filters, the risk of the airborne disease transmission can be significantly reduced (Rui et al. 2008). Although the mechanical ventilation systems offer better control capability of the indoor environment characteristics, however, they introduce significant financial expenditures (Azimi and Stephens 2013; Escombe et al. 2019; Hobday and Dancer 2013). Weather using natural or mechanical ventilation the quantity of pathogens and the quality of the indoor air are not necessarily higher in case of the first or second alternative, e.g. (Qian et al. 2010; Short and Al-Maiyah 2009; Stockwell et al. 2019). This is due to the fact that in both cases the airflow rate and the airflow movement pattern are the most prominent characteristics that determine the efficacy of each option to provide the desirable indoor atmosphere. In general, the use of ventilation in buildings is associated with a dual positive and negative effect against the airborne transmission (Noakes and Andrew Sleight 2009). The positive role is the dilution of the concentration or the dispersion of the biological agents and particulates leading to minimising the occupants' risk. In parallel, the transportation of the bio-aerosols and particulates among adjacent spaces is a non-negligible undesirable effect.

Mechanical systems of ventilation

In mechanical ventilation systems, two different airflow patterns are commonly used such as the displacement ventilation (DV) and the entrainment or mixed ventilation (MV)

flow (ASHRAE 2017b). There are also advanced mechanical systems such as personalised ventilation (PV) and personalised exhaust which can be installed stand alone or in combination with other ones in spaces with or without specific requirements (Melikov 2004). The application of PV systems in common indoor spaces becomes more attractive, as many recent studies indicate the benefits on the indoor air quality (IAQ) improvement and minimising the airborne transmission risk (Al Assaad et al. 2018; Habchi et al. 2016; Lipczynska et al. 2015; Melikov et al. 2013; Yang et al. 2015).

Except for the fact that any stand-alone or conjugated ventilation system under controlled conditions is able to supply fresh air, however, the differentiation of the airflow direction and pattern-based on the design characteristics of each system in association with ventilation rate- are the most important parameters that influence the (a) contaminant concentration; (b) contaminant removal effectiveness; (c) infection risk; and (d) human's exposure to pollutants in general and biological agents.

Displacement and entrainment/mixed ventilation systems

Displacement ventilation (DV) system or displacement airflow describes the air movement in one direction by a piston type motion. Ideally, the air is not mixed and the pollutants are totally removed out from the indoor space. The airflow in DV systems could be either downward (ceiling-to-floor) (see Fig. 6) or upward (floor-to-ceiling) (see Fig. 7), based on the design requirements of each space. In both cases, the idea is to supply fresh and clean air with low velocity leading to a laminar airflow which intent to sweep air across the space with the minimum possible mixing (ASHRAE 2017b).

Due to that characteristics, the downward DV system is considering as the ideal system for removing the contaminated indoor air, and is expected to minimise the cross-infection risk (Qian and Zheng 2018; Tang et al. 2006). However,

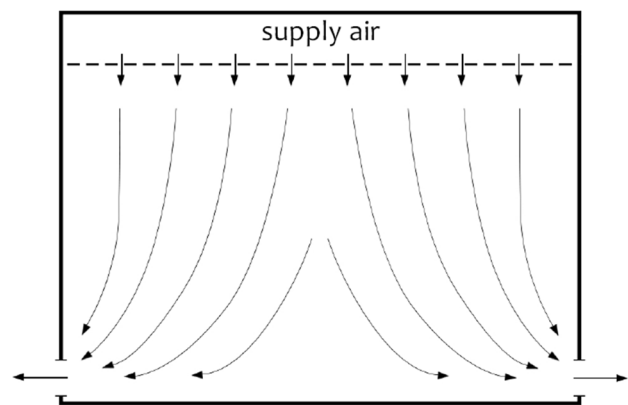


Fig. 6 Displacement downward ventilation pattern

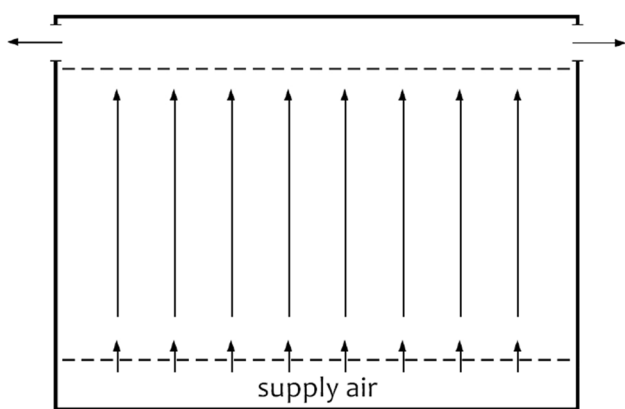


Fig. 7 Displacement upward ventilation pattern

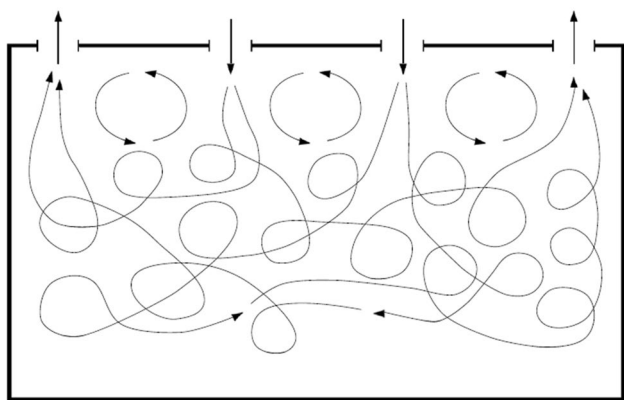
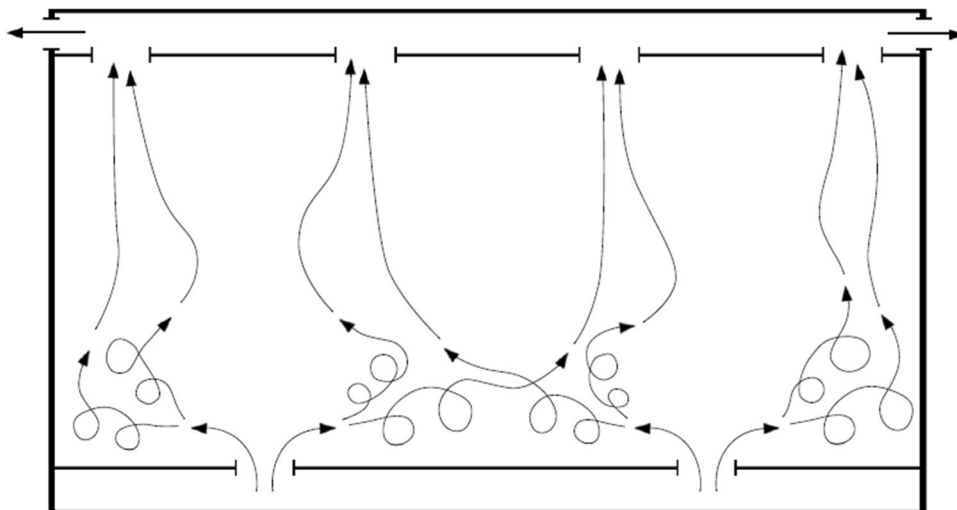


Fig. 8 Mixed ventilation (MV) pattern

either the design of DV systems with airflow pattern about 4.0 ACH or the synergies with the humans' thermal plume are impossible to produce laminar flow, thus mixed ventilation airflows occur (Qian et al. 2008).

Fig. 9 Underfloor air distribution pattern



Entrainment/ mixed ventilation (MV) system or airflow, Fig. 8, refers to a circular pattern of air flow in which the intake fresh air is conventional mixed with the internal air and finally the mixture leaves the space.

In this case, the pollutants are removed by dilution. Entrainment flows, according to mixing conditions are characterised as short-circuit flow or complete/ uniform mixing (well-mixed). In the first case, the supply air leaves the space without mixing with the indoor air as a result of very poor mixing conditions, while in the second one the supply air is instantly and evenly distributed in the space leading to a perfect mixing with the room air (ASHRAE 2017b).

Underfloor air distribution (UFAD or UAD), in Fig. 9, is a hybrid ventilation method that combines the characteristics of both displacement and mixing ventilation schemes. Outdoor air is introduced into a plenum floor and supplied to the indoor space throughout floor-mounted diffusers. The diffusers produce a turbulent flow near to the floor level and the supplied air is mixing with the indoor one. Then the mixed air moves to the ceiling in a laminar flow without mixing phenomena and exhausted from the space through outtake diffusers.

The ventilating performance of the underfloor distribution system is thus between upward DV and MV systems (ASHRAE 2017b). The effectiveness of the DV, MV and UAD systems on minimising the airborne transmission of the infectious agents has been evaluated in several studies using experimental and numerical approaches. A detailed analysis on these studies indicated that the majority of them deal with the assessment of cross-infection risk, while some of them focused on the assessment of the droplet dispersion mechanisms and behaviour.

Qian et al. (2006) performed a series of experiments to understand the interaction of the exhaled bio-aerosols in downward and upward DV and MV airflows in a hospital ward. They reported that downward DV with an airflow

rate of 4 ACH has similar behaviour as the MV, due to the turbulent characteristics of the flow. In addition, they do not suggest the installation of upward DV system in hospital wards due to the possibility of increase the exposure level, if an occupant is located in the exhalation jet.

Olmedo et al. (2012) studied the human exposure to the contaminants of the exhaled bio-aerosol among two persons taking into consideration between other parameters the use of upward displacement and mixing ventilation. They found that in the case of upward DV, the exhaled air flows transport for longer distance with higher concentration. Lin et al. (2012) assessed the risk of pathogen inhalation under stratum and upward DV and concluded that the risk was higher when upward DV system was used.

Chen et al. (2014) analysed the person-to-person bio-aerosol transport under upward displacement and mixing ventilation and UAD systems. They indicated that the upward DV and underfloor air distribution have the same performance in reducing the contaminant exposure and were about 20% better than the MV. Although this study presents contradictory behaviour compared to the similar ones, the authors, however, reported that in cases of upward DV and UAD, significant variations in the relative effect on exposure have been noticed. This phenomenon indicates that under certain circumstances, the pointed out relationship among the alternative ventilation systems may be altered (Chen et al. 2014). Similar results and recommendations have also been reported in many studies (Ai et al. 2019a, b; Friberg et al. 1996; Jurelionis et al. 2015; Keshavarz et al. 2017; Li et al. 2012; Lin et al. 2013; Mazumdar et al. 2010; Salmanzadeh et al. 2012; Villafrauela et al. 2019; Wu and Lin 2015; Yang 2013; Yin et al. 2009).

Lai and Cheng (2007) studied the droplet's dispersion in a space under upward displacement and well-mixed ventilation flows. They concluded that for the well-mixed ventilation system, the dispersion pattern is driven by the velocity airflow. High-velocity airflow produces within 1 min a homogeneous bio-aerosol. In contrast, when upward DV with low-velocity airflow is used, the dispersion pattern is dominated by the droplets' size. In this case, 10- μm droplets begin to settle at the lower areas of the located space.

Gao et al. (2008a, b) simulate the dispersion characteristics of an exhaled bio-aerosol consisted with droplets in the range of 1 to 10 μm in an office space using upward DV, MV and UAD systems. The obtained results showed that in MV system the exhaled droplets were uniformly distributed. However, in all ventilation systems, the exhaled flow was trapped in the breathing zone of the occupant.

Mui et al. (2009) stated that the droplet dispersion and mixing in case of DV is poorer, compared to the MV. Sun and Ji (2007) proved again that the efficiency of the upward DV is higher in removing small droplets, while MX has

equal efficiency for removing droplets in the range of 80 to 100 μm and higher efficiency in removing large size droplets. They concluded that this behaviour is subjected to the equilibrium between gravitational and buoyancy forces. High gravitational forces occur in the case of large droplets, while the buoyancy forces become significant in the case of small-sized droplets and high-velocity airflow. DV introduce low-velocity airflow, and for the case of upward airflow pattern, the large size particles tend to settle in the lower part of the space. However, for the case study of downward airflow systems, these particles can be efficiently removed by the outlet vents. MV systems are characterised by high airflow patterns leading to a well-mixed bio-aerosol which can be efficiently removed from the space, regardless of the droplet sizes. It is worth noticing that similar results have also been reported in the following studies (Berlanga et al. 2018; Chao and Wan 2006; Gao et al. 2012a, b; Lai and Wong 2011; Seepana and Lai 2012; Li et al. 2011; Yin et al. 2011).

Personalised ventilation systems

Personalised ventilation (PV) system or personalised airflow intends to provide fresh air into breathing zone of an occupant. The system uses air terminal devices that consist of nozzle/s allowing the control of airflow rate by the occupant to the desirable level and direction. The PV system has two main advantages: it improves the quality of the inhaled air and allows the user to control the temperature, velocity and direction of the supplied airflow (Melikov 2004). The contribution of PV systems on the mitigation of the airborne cross-infection risk has been analysed in several studies. Cermak and Melikov (2007) conducted a series of measurements to examine the capability of two PV systems in association with an UAD system to protect occupants from exhaled infectious aerosols and emissions from the floor materials. They found that the conjugated systems protect the occupants from inhaling the aerosols, while the concentration of the pollutants into the indoor air was increased. Pantelic et al. (2009) studied the protective role of a PV system against the infectious cough droplets released near the PV occupant. They addressed that the PV system significantly reduced the bio-aerosol concentration in the breathing area of the occupant. It had also reduced the risk of cross-infection particularly in cases that the source point of the bio-aerosol infection and the occupant were at a distance less than 1.75 m. He et al. (2011) assessed the airborne transmission of an exhaled bio-aerosol between two occupants under three ventilation systems, namely MV, upward DV and UAD working autonomous and in conjugation with PV. They concluded that for PV scenarios the quality of the inhaled air has been improved. A study of Mazej and Butala (2012) proved that by using a PV system, the amount of the re-inhaled bio-aerosol is extremely

low; however, the dispersion of bio-aerosol to the indoor air increases the risk of cross-infection onto the occupants who are not using personalised ventilation. Li et al. (2013) analysed the exposure of occupants to the exhaled pollutants under two different conjugated ventilation systems. They concluded that the upward DV combined with PV provides better inhaled air quality compared to the alternative option of MV with personalised one. Pantelic et al. (2015) evaluated the effectiveness of a PV system to reduce the inhalation intake fraction of an infectious bio-aerosol against to MV system. The obtained results indicated that the PV system substantially reduces the intake fraction for the all analysed cases. In addition to the above studies, it is worth mentioning that similar results have also been addressed in many other cases (Bolashikov et al. 2015; Bolashikov and Melikov 2009; Cermak et al. 2006; Nielsen 2009; Nielsen et al. 2007a, b; Nielsen et al. 2007b; Pantelic and Tham 2011; Pantelic and Wai 2009; Tham and Pantelic 2011; Wai and Pantelic 2009; Yang et al. 2015; Zheng et al. 2011). Moreover, detailed reviews on the personalised ventilation systems have been published on (Liu et al. 2019d; Melikov 2004; Zhai and Metzger 2019).

Natural ventilation

Natural ventilation is the physical flow of the external air through the building vents into indoor spaces caused by a thermal and/or wind pressure difference. Under certain circumstances, it can be provided an adequate level of pollutants' removal, which is not always controlled and acceptable. There are two types of natural ventilation airflow patterns: the cross and the single-sided ventilation. Cross ventilation is achieved using openings in both sides of the space and it is driven by the pressure difference. Single-sided ventilation occurs when one or more openings in the same façade of the building are open. Thus, the airflow could be driven by temperature and/or pressure difference. Although the role of natural ventilation on indoor air quality and comfort levels has been well studied and documented (e.g. (Allocca et al. 2003; Brager and De Dear 1998; De Dear and Brager 2002)), however, the effect on the airborne transmission of pollutants and bio-aerosols between the adjusted building units and their dispersion in lower or higher building floors has attracted the research interest mainly after the SARS pandemic in 2003. Li et al. (2005) studied the SARS virus transmission between adjusted flats in a high-rise residential building in Hong Kong. They concluded that in the natural ventilated high-rise apartment buildings it is difficult to control the air leakage between flats as the flow is driven by the air-tightness and the pressure difference. This phenomenon leads to carry bio-aerosols between the apartments of the building. A study by Gao et al. (2008a, b) proved again the airborne transmission across apartments in a high-rise

natural ventilated building through open windows between flats caused by buoyancy effect. They reported that the gaseous pollutant's concentration in the immediate upper flat is 2 orders lower compared to the lower flat in which the gaseous pollutant is generated, while the risk of infection is 1 order lower, respectively. They also noticed the importance of wind speed and concluded that high-speed winds act like air-curtain reducing the pollutants' spread. However, they clearly reported that in natural ventilated multi-family buildings the infection control of bio-aerosols should consider the role of this airflow.

In-line with the previous study, the same research team simulated the airborne transmission of particle pollutants (Gao et al. 2009a, b). They found that the concentration of the particle pollutant in the upper floor is between two to three orders lower than in the lower source floor. They also concluded that particles up to 1- μm disperse like gaseous pollutants, while particles larger than 20 μm show a strong deposition on the source space and limit their transport to the up-floor area. Ai and Mak (2014) studied the dispersion characteristics of infectious aerosols exhausted from a building unit in association with the hypothesis that the exhausted aerosol can re-enter into another unit of the building through opened windows. They reported that the re-entry ratios can be reach up to 10% based on the wind direction and façade characteristics, non-flush walls or balconies. The high re-entrer ratio is observed in the windward site following by the leeward site both in case of 45° wind direction. In addition, the balconies enhance the re-entering phenomenon of the exhausted bioaerosols, except the case of the normal incident wind direction. Wu et al. (2018) studied the role of infiltration on the airborne transmission route and evaluate the associated infection risk in a high-rise building, under different wind directions and leakage characteristics of doors and windows. They found that infiltration rates below 0.7 ACH increase the cross-infection risk up to 20% compared to the risk of 9% in case of air change rates over 3 ACH. The increase of infiltration rate along the building height leads to the increase of the cross-infection risk in the lower building floors. They also reported that the wind direction is a significant parameter that influence the cross-infection risk. The higher cross-infection risk observed in case of the contaminant source is placed on the windward site and on the adjacent units. Finally, they concluded that improving the air-tightness of the internal openings and increasing the airflow on the external ones is an effective solution for the control of inter-unit airborne transmission. The effect of natural ventilation in the airborne transmission of bio-aerosols in multi-family buildings (in both vertical and horizontal directions) together with the role of wind characteristics has also been investigated by many scientist (Ai and Mak 2016; Ai et al. 2013; Cui et al. 2018; Liu and Niu 2011; Liu et al. 2007; Liu et al. 2008; Liu et al. 2011a, b; Liu et al. 2010,

2011a, b; Mu et al. 2016; Mu et al. 2017; Niu et al. 2005; Niu and Tung 2008; Wang et al. 2010a, b; Wu et al. 2019a, b; Zhou et al. 2014), who finally conclude to similar results and suggestions.

The role of ventilation rate

A minimum level of ventilation rate is recommended by relevant Standards (ASHRAE 2017a, 2019a, b; CEN 2019), in order to maintain the quality of the indoor air to a pre-defined acceptable level and minimise the risk of human exposure to pollutants in general and biological threats. In general, there are three methods for the calculation of the ventilation rate, that based on the: (a) perceived air quality, (b) criteria for individual substances and (c) pre-defined ventilation air flow rates. According to the perceived air quality method, the ventilation rate is found by adding the required air volume for people and emissions. This method is mainly used in residential and non-residential buildings in which critical contaminant sources are not identified. In spaces with essential pollutant sources the ventilation rate is calculated based on the generation rate of the pollutant, the concentration of the pollutant on the supply air, the guideline concentration of the pollutant in the indoor air and on the effectiveness of the ventilation system. The third method introduces pre-defined ventilation air flow rates based on the local climate and building characteristics, and is also used in residential and non-residential buildings. It is worth noticing that the first and third method in case of the non-occupied hours of the building, lower the ventilation rate to a minimum air flow needed to maintain the concentration of the non-human related pollutants to the guided level (CEN 2019). In line with the above strategy, Gao et al. (2012a, b), estimate that increasing the ventilation rate up to 10 ACH in schools led to a reduction of the peak infection to influenza up to 9% and postponed the peak of outbreak by 3 days. However, they noticed that ventilation rates over 5 ACH may be difficult to reach and suggest to be used in conjunction with alternative prevention policies. A similar study (Gao et al. 2016), regarding the potential outbreak of influenza in Hong Kong, concluded that even in cases that the airborne transmission is 20% of the total infection the increase of ventilation rate has strong influence on transmission pathways similar to other control measures. Nardell et al. (1991) studied the air borne infection caused by the operation of building's ventilation and concluded that of increasing the ventilation rate by 67% and 133%, reducing the infection risk by 33% and 52% respectively. The relationship between ventilation rate and infection risk has also been studied in the work of Fennelly and Nardell (1998). They found that the infection risk decreases exponentially with the increase of ventilation rate, for instance, in a moderate-exposure space operated with 6 ACH the probability of infection is 0.42 and

decreasing to 0.21 by increasing the ventilation rate to 12 ACH. Similar conclusions regarding the influence of ventilation rate to the infection risk and on the associated concentration of airborne pathogen bioaerosols into indoor air have also been reported (Beggs et al. 2003; Bergeron et al. 2011; Cao et al. 2015; Chen et al. 2014; Escombe et al. 2007; Escombe et al. 2019; Gao et al. 2009a, b; Knibbs et al. 2014; Knibbs et al. 2011; Lim et al. 2010; Lindsley et al. 2012; Menzies et al. 2000; Milton et al. 2000; Myatt et al. 2004; Nielsen et al. 2010; Qian and Li 2010; Qian et al. 2010; Stockwell et al. 2019; Sun et al. 2011; Tung and Hu 2008).

Although these conclusions led into significant revisions and changes of the recommended ventilation rates on relevant standards and guidelines, over the last years, new findings indicate that the increase of ventilation rate might lead to the increase of the cross-infection risk. This is due to the fact that higher ventilation rates under specific conditions increasing the buoyancy forces of the airborne infectious droplets resulting in the increase of aerosol transmission and associated cross-infection risk. Bolashikov et al. (2012) examined the exposure of a health professional and a patient to the airborne pathogen caused by an infected patient in a hospital isolation room under different ventilation rates. They performed a series of experiments and concluded that at the distance of 1.1 m for the infected patient the peak concentration of the pathogen is much higher at the ventilation rate of 12 ACH compared to the ventilation rates of 6 and 3 ACH. Pantelic and Tham (2013) evaluated the capability of the ventilation rate to act as a sole indicator of the effectiveness of an air distribution system on the mitigation of airborne infectious disease transmission. They concluded that the increase of ventilation rate can lead to the increase of exposure risk under certain circumstances (e.g. upward airflow, characteristics of local airflow patterns and airflow quality). This evidence indicates that the use of ventilation rate as a sole indicator for the evaluation of the air distribution system's effectiveness on the control of the infectious airborne transmission is not possible. Mousavi and Grosskopf (2015) noticed again that increasing the ventilation rate is not proportionately effective for reducing the aerosol concentrations in patient rooms. Ai et al. (2019a, b) studied the airborne transmission between an infected and a healthy person under exposed to a horizontal air flow. They also confirmed that the influence of ventilation rate is not straightforward to the exposure index. The obtained experimental results indicated a decrease of the exposure index when the ventilation rate was increased from 2 to 3 ACH and from 6 to 9 ACH, while the increase from 3 to 6 ACH resulted a decrease of exposure index. Similar findings have also been reported (Marshall et al. 1996; Memarzadeh and Xu 2012). It is worth noticing that the above-mentioned studies did not neglect neither the role and the importance of ventilation rate nor the contribution on minimising the

airborne transmission. In general, the ventilation rate based on the quantity dilutes the concentration of the infectious airborne bio-aerosols and decreases the risk of transmission. However, based on the velocity and on the air flow pattern, the ventilation rate may lead to the increase of transmission risk. These contradictory effects need to be further studied and evaluated in parallel during the design stage of the ventilation system considering the specific requirements and/or operations of the serviced space.

In addition to the above-mentioned studies, reviews on the role of ventilation rate to the transmission of the airborne infection may be found (Li et al. 2007; Memarzadeh and Xu 2012; Sundell et al. 2011).

The role of space heating and cooling emission system

Space heating and cooling emission units are used to provide energy to end-use space in order to maintain the desirable thermal environment. In general, and considering the main heat transfer mechanism, these units are categorised as free-convection or convector unit, forced-convection or fan-coil unit and radiator or radiant panel unit, or radiant floor/ceiling/wall system. The operation of a convector/radiator unit or system is associated with thermal plumes that affect the air movement, while a forced-convection unit increases the air velocity in the occupied zone. Both phenomena in conjunction with the ventilation type introduce different temperature and pressure stratification conditions on horizontal and vertical directions; which finally affect the contaminants distribution and the dispersion of the airborne agents into the internal spaces. Several studies analyse the effect of space heating and cooling terminal units in association with different mechanical ventilation systems on the dispersion of pollutants and biological agents. Causone et al. (2010a, b) studied the effect of floor heating system in conjunction with upward displacement ventilation in an experimental chamber. They found that due to the influence of the thermal plume, the actual airflow pattern was between mixing and displacement ventilation, and in case of contaminants production from a heat source, high ventilation rates are required to achieve high ventilation effectiveness. Wu et al. (2014) analysed the ventilation effectiveness of mixing and upward displacement ventilation patterns with floor and ceiling heating systems. They reported that both systems have slightly similar ventilation effectiveness that ranges between 0.97 for the ceiling heating with mixing ventilation system up to 1.14 for the floor heating with displacement ventilation one. Lipczynska et al. (2015) compared the effectiveness of a personalised ventilation with chilled ceiling system against to mixing ventilation, chilled ceiling combined with mixing ventilation and chilled ceiling combined with mixing ventilation and personalised ventilation.

They concluded that evaluated personalised ventilation systems was up to 10 time more efficient compared to mixing ventilation ones, and resulted a strongest protection of the occupants from the cross-infection. Jurelionis et al. (2018) accessed the capability of a conjugated floor heating and mixing ventilation system on the dispersion of the air pollutants. They reported that the use of floor heating increased the effectiveness of pollutant dispersion by 5% and reduced the exposure of the occupants by 22% on average. Choi et al. (2019) measured the contaminants concentration profiles in a hospital ward equipped with radiant panel and displacement ventilation. They stated that the heat plume generated by the vertical radiant panel strongly affects the diffusion of the contaminated air. In case of heating operation, the use of radiant panel increases the exposure of a lying patient as the contaminant air is trapped above the lying level. In contrast, during the cooling operation the downward plume drives the exhaled contaminant to the lower high than that of the lying patient, and thus increasing the contaminants concentration in the near to floor levels of the ward. These results proved that the location of the radiant panel and its thermal operation are import parameters which strongly influence the contaminants concentration on the specific levels of the hospital ward. Similar results have also been reported (Causone et al. 2010a, b; Cetin et al. 2020b; Jurelionis et al. 2016; Liu et al. 2019a, b, c, d, e; Olesen et al. 2011; Ouazia et al. 2012; Ouazia et al. 2011; Schiavon et al. 2015; Shi et al. 2019; Wu et al. 2015; Wu et al. 2019a, b; Wu et al. 2020; Zhou et al. 2017). In addition to that, a comprehensive review on the integrated radiant heating and cooling systems in conjunction with the ventilation ones has been reported by Zhang et al. (2020a, b, c, d).

Computer modelling of particles and biological agents' airborne transmission into indoor built environment

Undoubtedly, mathematical models have proven their value for predicting the high risk and impact of the chemical-biological agents' exposure on building environment and public health (Argyropoulos et al. 2016, 2018; Bongers et al. 2008). According to Milner et al. (2011) in order to investigate numerically the indoor exposure, a selection of the three following types of IAQ models, namely statistical regression (Valero et al. 2009), micro-environmental (Duan 1982) and CFD models (Béghein et al. 2005; Choi and Edwards 2008, 2012), should be made. The first type involves models employing empirical and semi-empirical approaches to associate indoor environment exposure with significant parameters such as building characteristics, contaminant concentration levels and source strength. The second type of model, adopts the 'well-mixed' zone simplification assumption (Axley 2007,

1989; Emmerich 2001) at the building interior for the temperature and contaminant concentration levels and can be further classified into the mass balance (Gerharz et al. 2009; Shrubsole et al. 2012), measurement-based (Kornartit et al. 2010; Ozkaynak et al. 2007), sub-zonal (Megri and Haghighat 2007; Stewart and Ren 2006) and multi-zone models (Argyropoulos et al. 2017a, b; Ashraf et al. 2016; Zhu et al. 2020).

CFD models could be a superior alternative approach to surpass the limitation of the ‘well-mixed’ assumption which does not always hold true especially for non-uniform concentrations in large spaces and transient state (Wang and Chen 2007, 2008a; Wang et al. 2010a, b). CFD models are capable of predicting the airborne transmission of aerosols in indoor spaces, by providing valuable insights into a number of driving factors of the phenomenon such as ventilation system, droplet formation mechanisms, concentrations, turbulence effects, ambient temperature, relative humidity for the survival capability of the agent and on airflow and agent deposition in human airways. However, these models are more computational demanding but more accurate.

A coupling approach of multi-zone and CFD models is preferable for a compromise between computational demands and accuracy (Argyropoulos et al. 2017b; Argyropoulos et al. 2020; Srebric et al. 2008; Wang and Chen 2008a). For detailed evaluation of the all above models, the interested reader is directed to the review papers by Milner et al. (2011) and Wang and Zhai (2016). In the following two subsections, it is presented a review of numerical studies focused mainly on the use of multi-zone and CFD models, as well as its coupling, for investigating the dispersion of airborne pathogens within indoor spaces. Numerical studies related to aircraft and vehicle cabins fall out of the scope of the present study. Finally, few numerical studies based on CFD-PBTK (Physiologically-Based Toxicokinetic) models are also mentioned. This class of models is capable of approximating the kinetic behaviour of contaminants and as a result can assess the internal dose at targeted tissues/organs (Argyropoulos et al. 2018; Feng et al. 2021; Mumtaz et al. 2012).

Single-zone and microenvironment models

This class of models is based on semi-empirical and empirical approaches which include empirical correction factors for a great variety of ingress and egress configurations, as well as different room characteristics. Mass balance models also known as dilution models are deterministic and can be also used for the prediction of indoor contaminant concentrations in different rooms or buildings both spatially and over time.

Chao and Tung (2001), developed an empirical model for the investigation of I/O ratio based on the ventilation influence using a non-steady-state mass balance approach.

They found that the air exchange rate has a crucial role to the penetration of outdoor pollutants into residential buildings.

Özkaynak et al. (2008) performed numerical simulations using HAPEM model for estimating the inhalation exposures for over 30 gaseous and particulate pollutants, by examining 37 microenvironments (MEs). The numerical results obtained showed that the predictions are appear to be influenced by the exposure concentration levels due to their dependence on the pollutant type, activity and site. Similarly, Borrego et al. (2006) studied numerically the exposure of concentration levels using an indoor/outdoor function (additional source term) to their model.

A large number of numerical studies has also been devoted to investigate PM (Dimitroulopoulou et al. 2001; Dimitroulopoulou et al. 2006; Nazaroff 2004), element PM (Lunden et al. 2003a, b), airborne bacteria and fungi (Nazaroff 2016), among other contaminants such as CO, Rn, NO₂, VOCs and O₃ (Briggs et al. 2003; Hicklin et al. 2018; Lee et al. 2004; Li and Niu 2007; Lunden et al. 2003a, b; Mölter et al. 2012).

Multi-zone models

Multi-zone airflow modelling is characterised by great capabilities for simulating the building infiltration, exfiltration and ventilation effects into indoor spaces. Multi-zone models are constituted by a network of elements which represents flow paths (e.g. fans, doorways, opening, cracks and HVAC ducts) among different zones of a building (Fig. 10). Consequently, the air flow rate is calculated from one zone to another as a function of pressure drop along a flow path.

There are many multi-zone simulation programmes such as AIRNET (Walton 1989), CONTAM (Dols and Polidoro 2015; Walton and Dols 2005), COMIS (Feustel 1999; Feustel et al. 1989), BREEZE (Evers and Waterhouse 1978) and CBSAIR (Haghighat and Rao 1991) to name only a few; however, the most popular are CONTAM by the US National Institute of Standards and Technology (NIST) and COMIS by Lawrence Berkeley National Laboratory (LBNL). The first is the most widely used, while a validation study of the last two multi-zone models can be found in the work of Haghighat and Megri (1996). More details for the multi-zone models, the interested reader is directed to the comprehensive reviews by Axley (2007; 1989), Feustel and Dieris (1992) and Emmerich (2001).

According to Dols and Polidoro (2015), the transient partial differential equations for the description of airflow in CONTAM are specified as follows in Eq. (1):

$$\frac{\partial m_i}{\partial t} = \rho_i \frac{\partial V_i}{\partial t} + V_i \frac{\partial \rho_i}{\partial t} = \sum_j F_{ji} + F_i \quad (1)$$

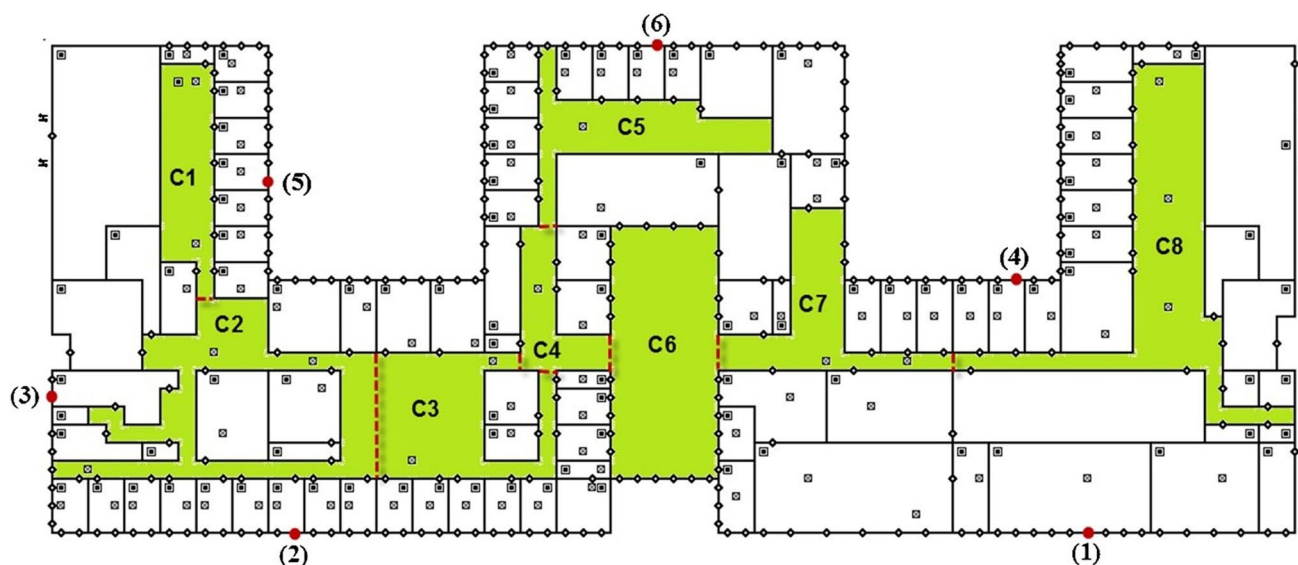


Fig. 10 Building layout produced by CONTAM according to available HVAC data Reproduced from Reference (Argyropoulos et al. 2017a, b) with permission from Elsevier

where t is the time, m_i the mass of air for zone i , V_i the volume for zone i , ρ_i the density for zone i , F_{ij} the air flow rate from zone j to i and F_i non-flow processes for zone i (remove or add significant amounts of air from i zone). The above terms F_{ij} and m_i can be calculated by using the following formulas (Dols and Polidoro (2015)):

$$F_{ij} = f(P_j - P_i) \quad (2)$$

$$m_i = \rho_i V_i = \frac{P_i V_i}{RT_i} \quad (3)$$

where P_i is the pressure for zone i , P_j the pressure for zone j , $f(P_j - P_i)$ the function of pressure drop n along the flow path, T_i the temperature for zone i and R the ideal gas constant.

Kowalski et al. (2003) performed a multi-zone analysis using CONTAMW (Dols et al. 2000) software for predicting concentration levels and inhaled doses against intentional releases of biological agents into a 40-story commercial office building. They investigated the performance of different cleaning systems such as air-cleaning and air-disinfection systems. They concluded that the combination of ultraviolet germicidal irradiation (UVGI) and filtration as air-cleaning strategy can provide encouraging protection for the occupants and there is no significant improvement beyond the following selected characteristics, i.e. 15% outside air ventilation, filtration of MERV 13–15 and UVGI dose of $1000 \mu\text{W}\cdot\text{s}/\text{cm}^2$, for the considered 40-story commercial office building.

An early attempt to conduct multi-zone airflow simulations using CONTAM for studying the severe acute

respiratory syndrome (SARS) virus airborne transmission among flats in Block E of the Amoy Gardens was undertaken by Li et al. (2004a, b) and Yu et al. (2004). The numerical results, which describe the evolution of virus spread, presented encouraging agreement with the observed spatial infection data. They concluded that the airborne transmission route was the main reason of SARS spread and building infiltration along with natural ventilation have a positive influence on the infection control. Few years later, Chen et al. (2011) using multi-zone modelling in conjunction with experimental measurements in an environmental chamber found that the air exchange which caused by small temperature differences between cubicles has also significant effect on the transmission of the SARS virus.

Ren and Stewart (2005) modified COMIS with sub-zones (COwZ) for investigating the occupational personal exposure to pollutant sources in a ventilated room. The numerical results were validated by available experimental measurements and CFD data, exhibiting good agreement. They found that the impact of occupant's location and orientation has significant influence and should be considered for the personal exposure assessment.

Some years later, Lim et al. (2011) performed field measurements of pressure and numerical simulations using CONTAMW to predict both concentration levels and airflow evaluation of virus (H1N1) spread in tall Hospital buildings. Their numerical results showed the possibility of airborne transmission of pathogens through the stack effect within high-rise hospital buildings, presenting encouraging agreement with measurements excluding a few floor cases.

Preventive and protection measures were also suggested for minimising the virus spread.

Emmerich et al. (2013) conducted numerical simulations using CONTAM for assessing different control strategies to reduce the dispersion of airborne pathogens (e.g. tuberculosis and squame cells) into a hypothetical hospital. The obtained numerical results indicated that the use of HEPA or MERV-15 filtration have a positive effect on the protection of occupants over pollutant dispersion, as well as UVGI systems. Finally, they also observed that increasing the interior wall leakage by a factor of 5 leads to decrease of pressure difference by a factor of 2.

Recently, numerical simulations were undertaken by Karakitsios et al. (2020) using CONTAM for a hypothetically release of a contaminant within a high-rise building. The simulations examined different scenarios for meteorological conditions, building operational characteristics and source types and location. The obtained results showed that all rooms with ventilation appeared pollutants and there was also transfer of pollutants through leakages towards the stairwell and elevators. Finally, they suggested potential locations for the installation of sensor technologies in order to detect indoor chemical-biological agents.

The same year, Zhu et al. (2020) investigated experimentally and numerically the ventilation effect in two actual building geometries (residence halls) during an entire flu season. By collecting CO₂ measurements, they calibrated multi-zone models (CONTAM) in order to simulate airborne transmission of influenza A within adjacent rooms and predict the concentration levels (exposure) for room occupants. The opening doors and windows of dormitory rooms within low ventilated building can improve the ventilation rates, however, this operation sacrifices the thermal comfort (e.g. low outdoor temperatures) of the room occupants. Their numerical results indicated that there is a strong trend between the low outdoor air supply and respiratory infection rates into dormitory rooms; however, more studies are needed to confirm their findings. They also concluded that the cross-infection risk for airborne transmission of *influenza A* should be considered based on the airflow map rather than the spatial distribution among the occupants' rooms.

Computational fluid dynamics models

In many cases, computational fluid dynamics (CFD) modelling is the best alternative for investigating the airborne transmission in indoor ventilated spaces, as well as the transmission from human body motion, talking, coughing and breathing.

The mathematical representation of air flow in indoor spaces, based on the set of elliptic, partial differential equations, expressing the mass conservation, momentum,

continuity, energy, chemical species concentration and turbulence parameters can be all written in the following general form (Eq. (4)) (Patankar 1980):

$$\frac{\partial(\rho\phi)}{\partial t} + \text{div}(\rho\mathbf{u}\phi) = \text{div}(\Gamma_{\phi}\text{grad}\phi) + S_{\phi} \quad (4)$$

where ρ is the air density, t the time, ϕ the dependent variable (u , v or w for momentum, 1 for continuity, h for enthalpy, c for chemical species concentration, k the kinetic energy of turbulence and ε the eddy dissipation rate), \mathbf{u} is the velocity vector of air, Γ_{ϕ} the effective exchange coefficient of variable ϕ (1 for continuity) and S_{ϕ} the source/sink term of variable ϕ . The four terms in Eq. (4) represent the unsteady, convection, diffusion and source terms, respectively.

An important factor of CFD modelling for examining the airborne transmission in indoor built environments is the effect of turbulence motion on the pathogen spread and mean flow field. In the literature, the most of the relevant CFD studies are based on Reynolds-Averaged Navier Stokes (RANS) models (Satheesan et al. 2020; Tao et al. 2020; Wang et al. 2020; Ye et al. 2020; Zhang et al. 2020a) for treating turbulence, and only several Large Eddy Simulation (LES) studies (Berrouk et al. 2010; Liu and You 2011; Tian et al. 2007; Vuorinen et al. 2020; Zhang et al. 2019) have been conducted the previous decades, however, an increasing number of new LES articles due to the SARS-CoV-2 pandemic period is published, as well as an integrated DNS approach for the prediction of cough/sneeze flows by Diwan et al. (2020).

In general, the selection of the appropriate turbulence model for predicting airflow and cross-infection risk in ventilated spaces including the dispersion of airborne pathogens among occupants (e.g. through talking, sneezing, breathing, coughing) is of great challenge due to the complexity of the physical phenomenon (e.g. human body micro-environment, buoyancy, contaminant concentrations, convection, circulation, reattachment and vortices (Zhai et al. 2007)). Regarding RANS models for human body micro-environment, the most used are the RNG $k-\varepsilon$ and low Reynolds number $k-\varepsilon$ (Gao and Niu 2005; Nielsen 2015). An interesting evaluation and comparison of eight different turbulence modelling approaches (i.e. RNG $k-\varepsilon$, SST $k-\omega$, low Reynolds number Launder & Sharma (LRN-LS) $k-\varepsilon$, v^2-f), detached Eddy simulation (DES) and LES) and available experimental data from the literature for the prediction of airflow in enclosed environments can be found in the work of Zhang et al. (2007). Subsequently, Phuong and Ito (2015) compared four different turbulence models (LRN-LS $k-\varepsilon$, LRN-AKN (Abe-Kondoh-Nagano) $k-\varepsilon$, RNG $k-\varepsilon$ and SST $k-\omega$) against PIV measurements for investigating the flow distribution in upper human airway including oral and nasal inhalation. More details about the

equations, advantages, limitations and implementation of different turbulence modelling approaches, the interested reader is directed to the review paper by Argyropoulos and Markatos (2015). Finally, a recent paper by Foster and Kinzel (2021) also presents a useful comparison between CFD models and Wells–Riley mathematical models for SARS-CoV-2 spread into classrooms.

Another important parameter to investigate pathogens transport and trajectory using advanced CFD techniques is the selection of the suitable multiphase model in order to study phenomena such as droplet evaporation, turbulence dispersion forces, droplet breakup and coalescence, among others (Dbouk and Drikakis 2020a; Löhner et al. 2020). It is common practice to choose an Eulerian approach for the gas phase, while the particle (bioaerosol) transport can be simulated using both a Lagrangian or an Eulerian method (Crowe et al. 1996). According to Eulerian–Lagrangian approach, the liquid phase is treated by a Discrete Droplet model; while for the Eulerian–Eulerian method, a Continuum Formulation model is adopted (Novozhilov 2007). Both methods have advantages and drawbacks, while many researchers have investigated extensively their limitations and applications (Zhang and Chen 2007). The mathematical formulation of the aforementioned models along with useful information for their implementation is not repeated herein, due to space limitations, but it may be found in the classical textbooks by Yeoh and Tu (2010), Brennen (2005), and Azzopardi (2006) and review papers by Crowe et al. (1996), Peng et al. (2020). Finally, the equations for the motion of particles/droplets and virus loads may be found (Löhner and Antil 2020; Löhner et al. 2020).

Numerical studies focused on the infection spread into chambers and offices

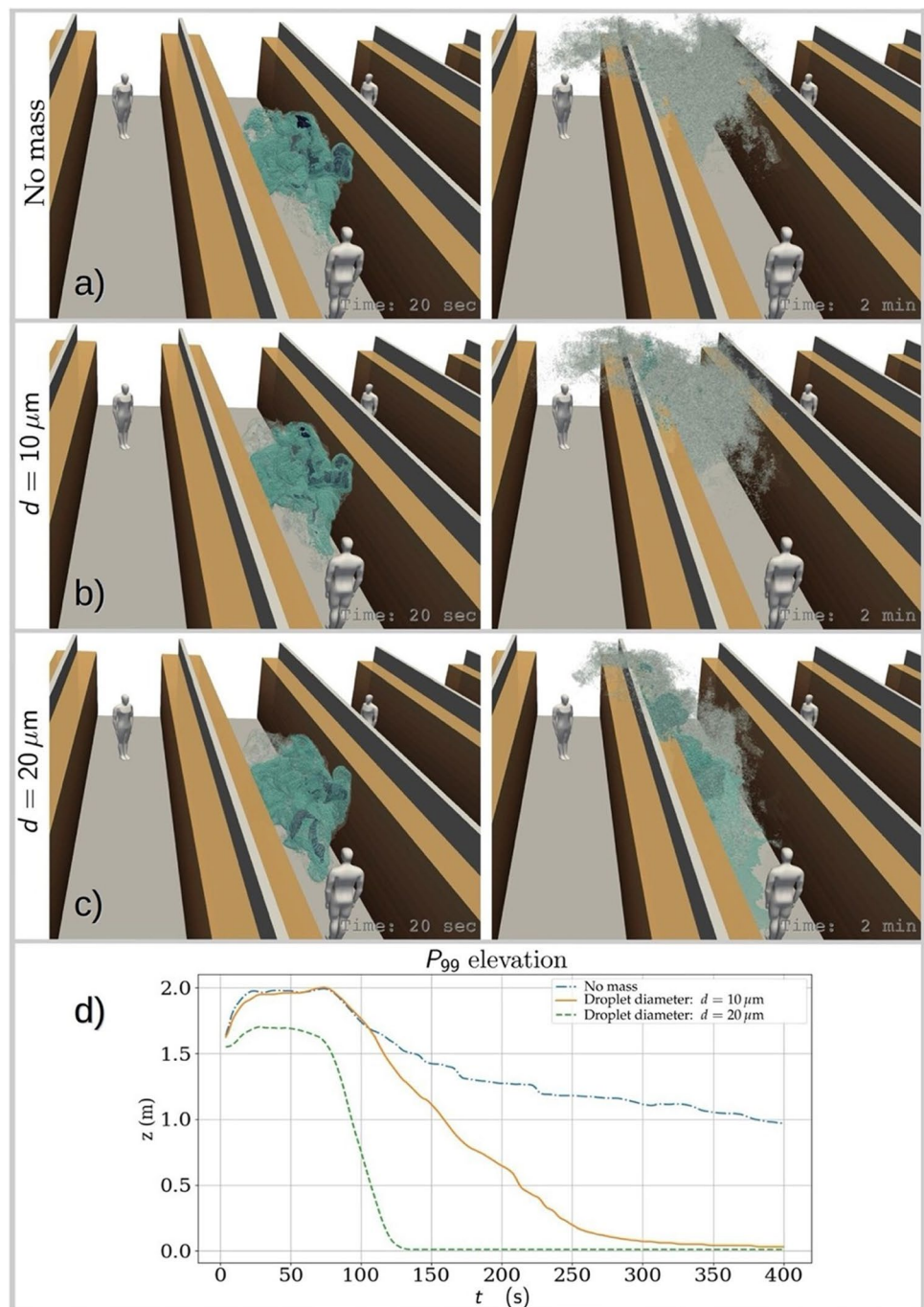
SHAO et al. (2021) performed CFD simulations using OpenFOAM in conjunction with in-situ measurements to investigate the airborne transmission risk of SARS-CoV-2 by asymptomatic individuals into small classroom, elevator and supermarket. They found that the design of ventilation system in confined spaces plays a major role in the particle removal and deposition. Bad design of ventilation system results in decreasing of particle removal efficiency and increasing of particle deposition in which both increase the risk of contamination. Similarly, Vuorinen et al. (2020) investigated numerically the dispersion and inhalation of droplets in relation to SARS-CoV-2 for open office and supermarket, using an LES approach (Fig. 11). They examined four different open sources CFD codes, namely, PALM, FDS, OpenFOAM and NS3dLab, while a number of Monte Carlo simulations was also conducted to investigate susceptible and infected individuals.

Several relevant LES studies, including ventilation effects, different sub-grid scale models (e.g. WALE, Deardorff model, Smagorinsky) and CFD codes (e.g. ANSYS FLUENT and CFX, PHOENICS, OpenFOAM, Star-CCM+), have also published in the literature (Béghein et al. 2005; Berrouk et al. 2010; Choi and Edwards 2008, 2012; Dudalski et al. 2020; Feng et al. 2020a, b; Fontes et al. 2020; Karakitsios et al. 2020; Pendar and Páscoa 2020; Tian et al. 2007; Zhang et al. 2019). It is worth mention that Diwan et al. (2020) also developed a DNS approach for the prediction of cough/sneeze flows. According to their temperature profile results, the dry cough (without liquid droplets) flow was dispersed very fast (cough duration of 0.58 s) at a distance of more than 1 m.

Pendar and Páscoa (2020) proposed a fully coupled Eulerian–Lagrangian method based on the OpenFOAM code for investigating the dispersion of saliva microdroplets generated by sneeze and cough in indoor environment. Their numerical results showed that the use of mask and a full bending of our head during sneeze can reduce significantly the risk of infection. More specifically, the latter action can cause decreasing of the microdroplets travelling distance by > 22%, while the first action can restrict the risk infection in a transmission sphere area of 0.6 m diameter. They also claimed that the social safety distance of 2 m should be increased to 4 m for providing more effective protection.

Feng et al. (2020a, b) conducted LES using ANSYS 17.0 in order to investigate the influence of human micro-environment on the transmission of infection diseases via microbial particles during human respiratory. They showed that an increase of heat flux leads to increase of the air flow flux of the thermal plume, resulting in a further increase of thermal plume ability to transfer particles upward. One year later, Zhang et al. (2019) employed an LES model combined with Lagrangian approach for studying the spread and transmission of bacteria and virus in a ventilated room. The numerical results obtained compared with experimental data from a climate chamber, presenting good agreement. They concluded that the droplet cloud velocity, which is characteristic for respiratory activities such as coughing and breathing, has great influence on the accuracy of the simulation. Choi and Edwards (2012) investigated via LES combined with an Immersed Boundary Method, the contaminant spread in room compartments. The immersed boundary method used for considering heat transfer effects and passive scalar advection. The numerical results obtained were validated by available experimental and CFD data, exhibiting good agreement. Fontes et al. (2020) performed DES for the investigation of human physiology factors (e.g. nasal and buccal passages, with or without teeth) during the human respiratory event of sneezing on the airborne virus transmission. They found that saliva properties have significant effect on the spray

Fig. 11 Visualisations demonstrating the effect of particle size (and mass) on the modelled spreading of the cough-released aerosol cloud. For better sense of scale, bystanders are placed 8 m from the coughing person. Instantaneous views on the state of the cloud are shown for realisations where the particles have **a** no mass, **b** 1000 kg m^{-3} density and $10\text{-}\mu\text{m}$ diameter and **c** 1000 kg m^{-3} density and $20\text{-}\mu\text{m}$ diameter. Images on the left column are at $t=20 \text{ s}$ and on the right column at $t=120 \text{ s}$. Below, **d** presents the time evolution of the mean elevation of the 99th percentile concentration highlighting the different descent rates. Droplets in these size scales have $\tau_{\text{evap}} < 1 \text{ s}$ and they would become aerosol-like droplet nuclei very rapidly. Reproduced from Reference (Vuorinen et al. 2020) with permission from Elsevier



formation (i.e. droplet distribution, primary and secondary break-up mechanisms). They also claimed that women seem to be less effective on the transmission of airborne pathogens.

Special attention has also been given to pathogen transmission using Reynolds-averaged Navier Stokes (RANS), unsteady Reynolds-averaged Navier Stokes (URANS) and Reynolds Stress (RS) models associated with ventilation strategies for particle removal and dispersion (Cetin et al. 2020a; He et al. 2011; Katramiz et al. 2020; Murga et al.

2020; Park and Chang 2019; Shao et al. 2020; Wang et al. 2020), human movement (Li et al. 2020; Tao et al. 2020; Tao et al. 2019), comparison of Eulerian-Eulerian and Eulerian-Lagrangian approaches for the pathogens transport and trajectory (Yan et al. 2020) and human expiratory events (e.g. coughing, sneezing, speaking) (Chen and Zhao 2010; de Oliveira et al. 2021; Kang et al. 2015; Li et al. 2018; Licina et al. 2015; Liu et al. 2016a, b; Yan et al. 2019; Zhang et al. 2020a, b, c, d; Zhu et al. 2006), among others.

Ji et al. (2018) investigated numerically the effects of evaporation process of pure water droplet under different *RHs* (0%, 30%, 90%) and ventilation strategies (displacement and mixing). They concluded that the evaporation process for small droplets occurs rapidly and it is difficult to observe differences between mixing and displacement ventilation. However, *RH* has small effect on large droplets' deposition, while displacement ventilation can delay evaporation similar to high *RH*.

Al Assaad et al. (2018) and Katramiz et al. (2020) performed numerical simulations using the RNG *k-ε* turbulence model for the investigation of intermittent personalised ventilation with respect to the protection of occupants from indoor contaminants. Their results showed that a selected average flowrate of 7.5 L/s along with an operating frequency of 0.86 Hz are acceptable for providing good ventilation and thermal comfort conditions in order to protect occupants. They also extended their study for the effect of walking occupant on the personalised ventilation in an office (Al Assaad et al. 2019a) and particle resuspension in a prayer room related to human prostration cycle (Al Assaad et al. 2019b). They concluded that the human prostration cycle due to prayers plays an important role in the particle spread from the floor to the upper levels of the confined space, while higher risk of contamination in the breath zone was found in the case of 1 μm particle concentration compared to 10 μm, according to the examined scenarios.

Dbouk and Drikakis (2020a) conducted RANS simulations combined with the *k-ω* turbulence model, by using the open-source code OpenFOAM. They investigated the spread of saliva droplets generated from a human cough in order to predict the influence of wind on social distancing. Their results showed that in the absence of wind effect the majority of exhaling saliva droplets during a cough can travel up to 1-m distance, while a small number can be travelled further. However, these droplets present low risk due to the low trajectory (< 1 m height). On the other hand, with the presence of wind speed in the range of 4–15 km/h, the travelled distance of the saliva droplets can reach up to 6 m, which is much farther than the recommended social safety distance of 2 m. Dbouk and Drikakis (2020c) presented a continuation of their previous study (Dbouk and Drikakis 2020a) with the aim at extending their work to consider the unsteady evaporation process of the saliva droplets, relative humidity, temperature and wind speed. They concluded that the low relative humidity combined with high temperature foster the droplet evaporation rate, resulting in significant reduction of virus viability. Similarly, Feng et al. (2020a, b) examined the transmission of SARS-CoV-2 droplets between two human bodies by means of RANS approach including evaporation and condensation effects (Fig. 12). They showed that the recommended social distance of 1.83 m (6 ft) is not sufficient to provide protection to people, under different wind conditions and static air environment (exposure at 3.05 m (10 ft)), from SARS-CoV-2 during coughing. Moreover, deposition

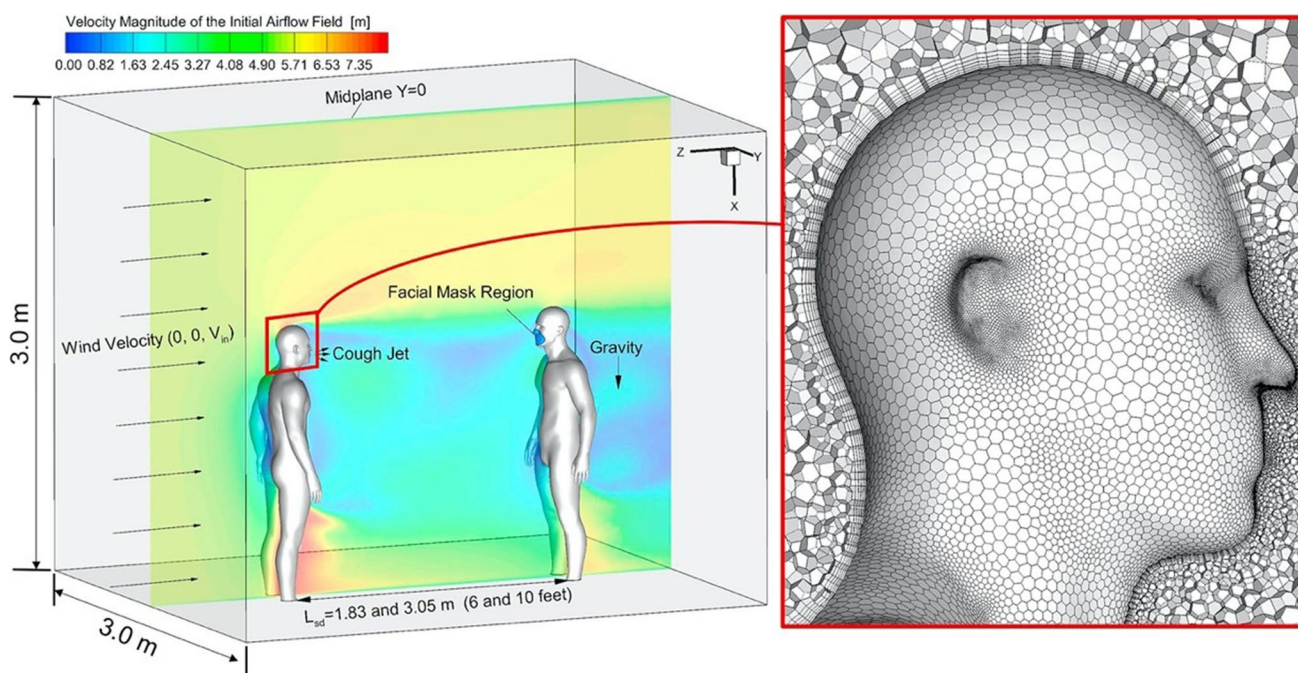


Fig. 12 Schematic of the computational domain with two virtual humans and the hybrid mesh details. Reproduced from Ref (Feng et al. 2020a, b) with permission from Elsevier

and transport of droplets are dependent on the wake flow patterns and secondary flow between the two human bodies. Their results also indicated that high RH (99.5%) increases the deposition of droplets in the space, however, without increasing necessarily the risk of exposure. On the other hand, medium RH (40%) fosters the water evaporation phenomenon, resulting in decreasing of droplet diameter and remaining airborne for longer times. Similar studies including evaporation and condensation effects results obtained for coughing from one person have also been reported (Chen and Zhao 2010; Li et al. 2018; Yan et al. 2019).

Numerical studies focused on the infection spread in hospitals and patient wards

A large number of numerical studies have been undertaken by many scientists and engineers for preventing the nosocomial airborne infection in hospitals and patient wards including ventilation and turbulence effects (Qian and Li 2010; Saarinen et al. 2015; Seymour et al. 2000; Shajahan et al. 2019; Wan et al. 2007; Yang 2013), while the current number of relative published papers (Anghel et al. 2020; Borro et al. 2020; Gu et al. 2020; Satheesan et al. 2020; Villafruela et al. 2019; Wang et al. 2021) is continuously increasing due to SARS-CoV-2 pandemic. This is mainly attribute to the strong interest in the SARS-CoV-2 Coronavirus modes transmission among patients, visitors and healthcare personnel in order to protect them.

An early attempt to perform RANS computations using a $k-\varepsilon$ turbulence model for the prediction of airborne pathogens transmission in a hospital isolation room, including the effects of ventilation systems, was undertaken by Seymour et al. (2000). Furthermore, Li et al. (2004a, b) conducted CFD simulations to investigate the spread of virus-laden bio-aerosols in a hospital ward during SARS outbreak in Hong Kong, by using the commercial CFD code Fluent 6.1. The numerical results showed that the predicted spread of the viral respiratory disease is in good agreement with the reported SARS cases. Chau et al. (2006) also examined the effects of the local exhaust ventilation system in a hospital patient ward for the protection of healthcare workers from virus diseases such as SARS.

Huang and Tsao (2005) presented numerical and experimental results for the removal of airborne pathogens in negative pressure isolation rooms. Their results showed that the buoyancy effects play an important role to flow and the removal of bacteria, while the redesign of the isolation room can improve the pathogen's removal. Qian and Li (2010) performed numerical simulations and experiments for studying the ventilation and deposition effects in a six-bed room. They presented CFD simulations using the RNG $k-\varepsilon$ turbulence model along with a Lagrangian method for the prediction of particles trajectory. The numerical results, which

describe the characteristics of the flow and the distribution of exhaled particles, indicated that the removal of particles is achieved more efficiently by ceiling-level exhausts compared to floor-level exhausts. In a similar way, Yang (2013) investigated the different types of ventilation in a four-bed sickroom using the commercial CFD code Star CD, while Chao et al. (2008) presented numerical and experimental results for the characteristics of the expiratory droplets in a three-bed hospital ward. Recently, Satheesan et al. (2020) presented numerical results for the Middle East respiratory syndrome coronavirus (MERS-CoV) in a six-bed inpatient ward.

King et al. (2015) also exhibited CFD simulations using an RSM closure model in conjunction with particle deposition data for predicting the cross-contamination risk among healthcare workers in single- and four-bed isolation rooms. Their results showed that the cross-infection risk in a single-patient room can be decreased significantly, while the ventilation, infection patients' location, type of patient's care and room layout may also affect the infection spread inside four-bed rooms (Sadrizadeh et al. 2014a, b; Sadrizadeh et al. 2018; Sadrizadeh et al. 2014a, b) and Wang et al. (2019a, b) studied numerically the effects of door opening on airborne particle movement, as well as the ventilation and stuff number in operating rooms during simulated surgery. They concluded that the use of a positive-pressure system can be more effective to reduce the airborne particle spread, while the door opening combined with the ventilation system and increased number of staff may expand the contamination risk for the patient into the surgical site.

Borro et al. (2020) performed URANS simulations combined with a Lagrangian approach for the investigation of ventilation system at the Vatican State Children's hospital (Fig. 13). The numerical results indicated that the proposed methodology is capable of predicting the contamination risk and optimising the ventilation flow in hospitals. They also showed that the installed HVAC system can diffuse the formed droplets from a coughing event, while the turbulence effects of the flow also enhance the pathogens spread and particle suspension for longer time in the room. Finally, they concluded that the use of a LEV unit placed above the face of patients can remove the particles and infected air in just a few seconds after the cough event.

Gu et al. (2020) developed and demonstrated a numerical simulation framework based on LES approach and FDS software, for assisting the design of ventilation systems in temporary hospitals, such as the first SARS-CoV-2 Wuhan Huoshenshan hospital in China. The numerical results showed that the proposed methodology is capable of assisting HVAC engineers to select and design the appropriate ventilation system in temporary hospitals. Finally, they claimed that there is no case for contamination risk to the surrounding buildings or the fresh-air intakes due to the

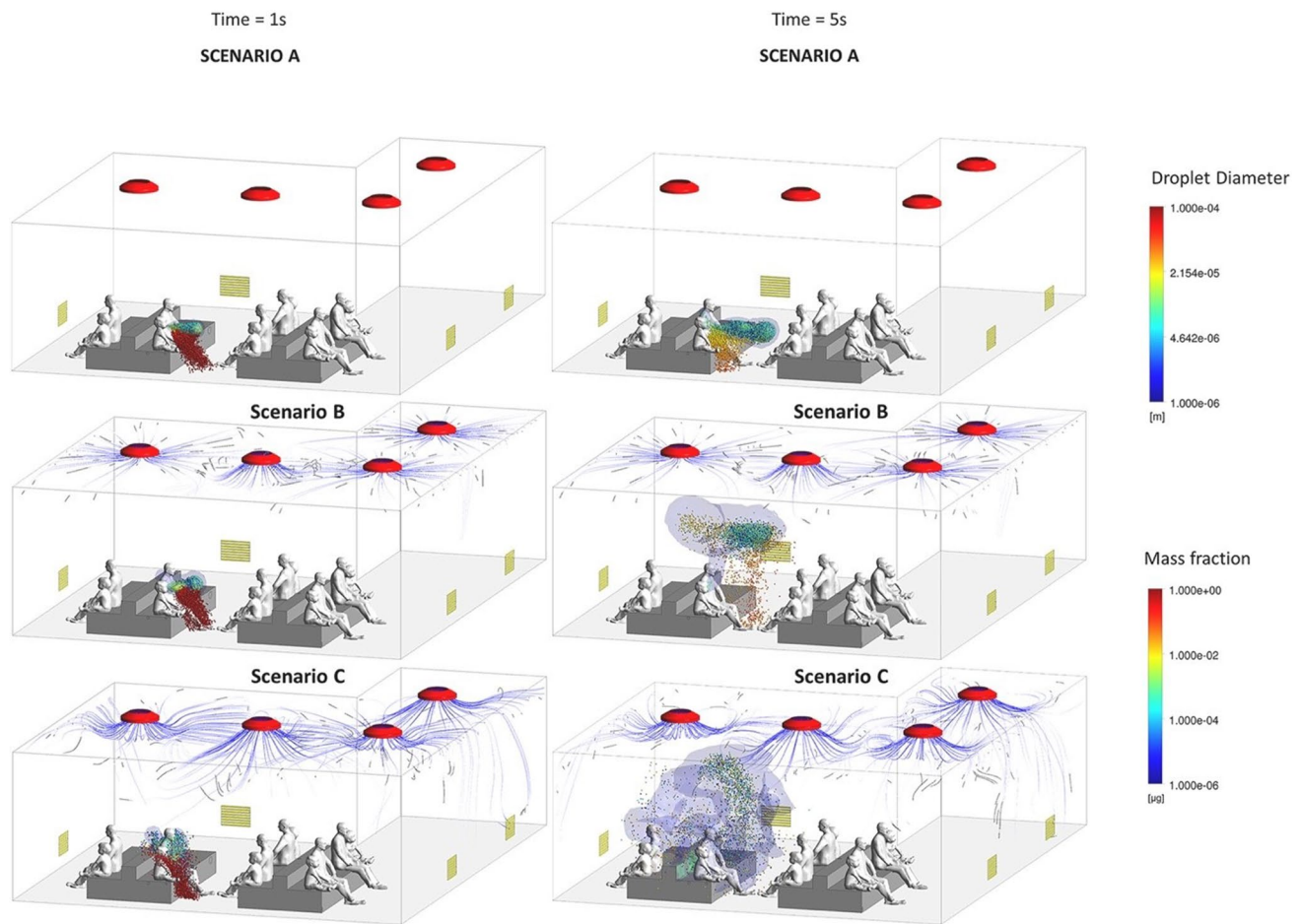


Fig. 13 Prospective view of the Scenarios A, B and C at $t=1$ s (left) and 5 s (right). The spheres represent the droplets coloured by the diameter size (top right legend). The contaminated air is represented

by different iso-surfaces coloured by mass fraction. Reproduced from Reference (Feng et al. 2020a, b) with permission from Elsevier

release of the infected air from the air outlets of the temporary hospital.

Numerical studies focused on the preventive role of mask against airborne droplet transmission

A significant number of concerns has been raised due to the SARS-CoV-2 pandemic for the efficacy of face masks and coverings in controlling and limiting the transport of infective droplets which are formed during cough and sneeze events. Special attention, therefore, is given to investigate the effectiveness of face masks regarding the transmission of respiratory droplets and the recommended social distancing guidelines, respectively.

An early attempt to investigate the aerodynamics of a gas mask canister numerically and experimentally was undertaken by Li (2009). The numerical and experimental results showed that the proposed methodology can be a useful tool for the design of gas mask canister, even though with a low respiratory drop.

Lei et al. (2012a, b) proposed a CFD approach for the investigation of studying the leakages between a headform and an N95-filtering facepiece respirator (FFR). The numerical results were compared with infrared images of respiratory leakage. Their results also indicated that the use of N95 FFR may cause thermal discomfort due to the temperature increase near the lip. They concluded that the most leak presented at the region of nose (40%), left (26%) and right (26%) cheek. The same group (Lei et al. 2012a, b) also investigated numerically and experimentally the effect of pressure contact on digital headforms.

Dbouk and Drikakis (2020b) performed multiphase CFD simulations for the prediction of the droplet transmission from a headform with and without a surgical mask. Their results showed that during a mild cough event the droplets can reach up to 70-cm distance without the use of surgical mask, and wearing mask the droplets may travel about the half above mentioned distance. They also observed that after 10 cough cycles the efficiency

of the surgical mask can be reduced by $\sim 8\%$, while for severe cough events the efficiency drops significantly. Finally, the diameter of the transmitted droplets without the presence of mask on the headform was larger across the cough cycles.

Khosronejad et al. (2020) performed LES using very fine grids for the investigation of saliva droplets transmission during a cough event with and without facial mask (Fig. 14). They also examined the effects of indoor and outdoor conditions during the cough event, namely stagnant background air and unidirectional mild breeze. Their numerical results showed that during a cough event without mask and stagnant background air condition the travelling distance of fine droplets can reach up to 2.62 m, while the larger in diameter droplets fall down in the area between the human and the previous mention distance in less than 2 min.

Furthermore, a number of fine droplets can also be remained suspended for several minutes in the air. They also observed that the wearing of a medical and non-medical mask can reduce the travelling distance of saliva droplets at 0.48 m and 0.73 m, respectively. Finally, the droplet

evaporation phenomenon can increase the travelling distance to 2.84 m without wearing mask and to 0.91 m for using non-medical mask.

Numerical studies focused on the airflow and aerosols deposition in human airways

CFD modelling can also be helpful to investigate the influence of airflow and aerosols deposition in human airflow. More details regarding the transport of particles and characteristics of the transitional flow mechanisms in the human lungs may be found in the recent review papers by Islam et al. (2020) and Mutuku et al. (2020a).

Ito (2014) proposed an integrated method for investigating the airborne infection transmission of pathogens in a hospital using a combination of CFD and SIR epidemiological models. This approach can allow the consideration of the hospital space in conjunction with the human nasal airway. As a result, the proposed methodology is capable of evaluating the exposure risk of occupants and estimate the contaminant dose. Phuong

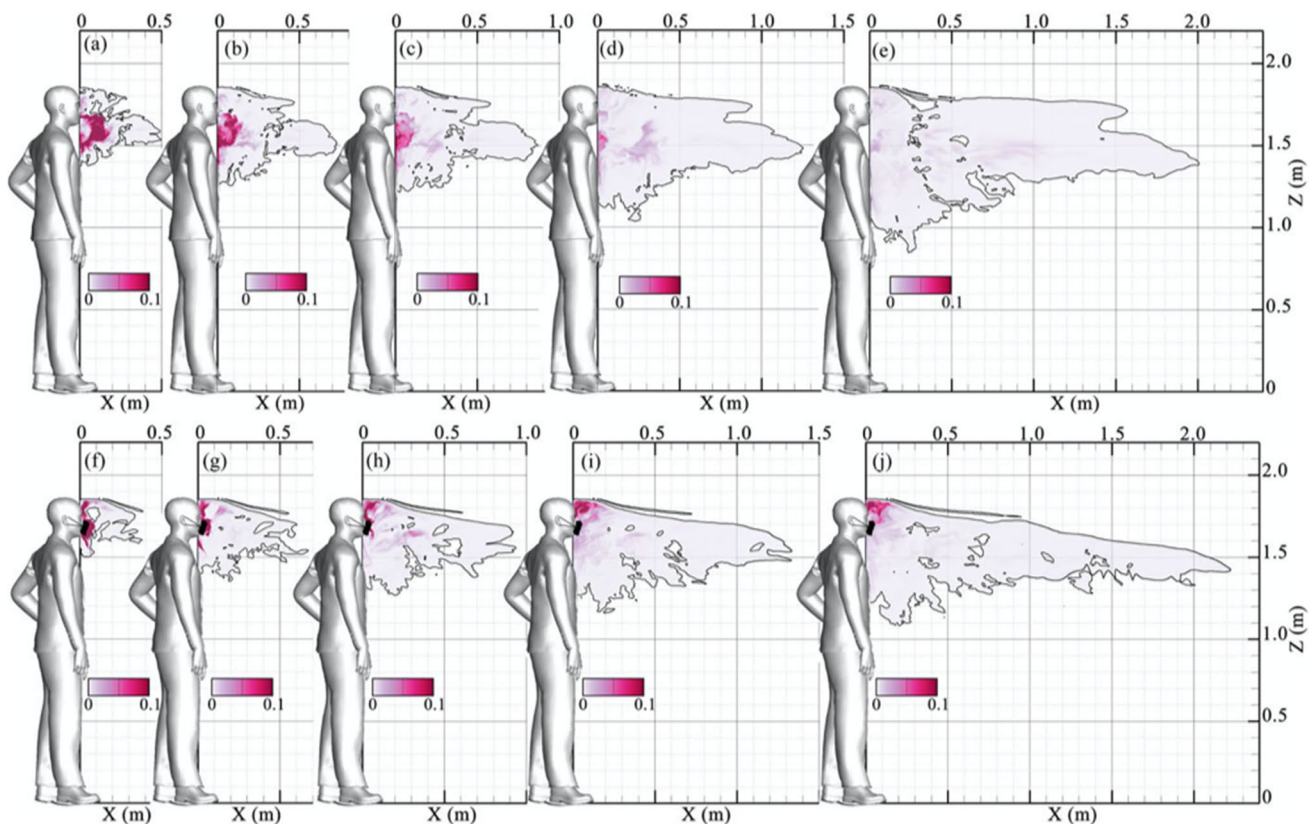


Fig. 14 Simulated evolution of the 10- μm saliva particulate concentration (volume fraction) after the cough under outdoor conditions (mild breeze) without (top) and with (bottom) the facial mask. [(a) and (f)], [(b) and (g)], [(c) and (h)], [(d) and (i)] and [(e) and (j)] show the simulated saliva particulate concentration fields after 0.24 s,

0.3 s, 0.4 s, 0.5 s and 0.6 s, respectively, on the sagittal plane. The outdoor simulations were stopped after 0.6 s, when the saliva particulates travel ~ 2.0 m and 2.2 m without (top) and with (bottom) the facial mask, respectively. Reproduced from Reference (Khosronejad et al. 2020) with permission from AIP

and Ito (2015) performed RANS simulations using four different turbulence models (i.e. two LRN $k-\epsilon$, RNG $k-\epsilon$ and SST $k-\omega$) to investigate the airflow in human realistic respiratory tract for three constant breathing conditions (7.5, 1.5 and 30 L/min). The numerical results obtained with LRN-AKN model were compared with PIV measurements, presenting better agreement. Recently, an extension of the previous work was proposed by Phuong et al. (2020).

Haghnegahdar (2019a) et al. developed a Computational Fluid Particle Dynamics (CFPD) model combined with Host Cell Dynamic (HCD) model (Fig. 15) for the prediction of influenza A virus droplets trajectory and deposition in the pulmonary tracts.

Their numerical results showed that the proposed model is capable of predicting the spread of virus and population variations in the upper airways tissues. They also predicted particle deposition fractions values of 26.4%, 23.7% and 24.1% for droplet mass fraction of 0, 0.068 and 0.104, respectively, in the oral cavity, while for the nasal cavity the fraction values are 48.1%, 45.2% and 47.6%, respectively. Finally, the average diameter of deposited droplets on the oral cavity is less than nasal cavity.

Mutuku et al. (2020b) performed CFD simulations for investigating the characteristics of airflow and particle deposition effects of $PM_{2.5}$ on healthy and Chronic Obstructive Pulmonary Disease (COPD) patients. The numerical results showed that the deposition fractions are between 0.12% and 1.18% for healthy case and between 0.05% and 0.49% for COPD case, while carina 5 was found to be the most important place of particle deposition.

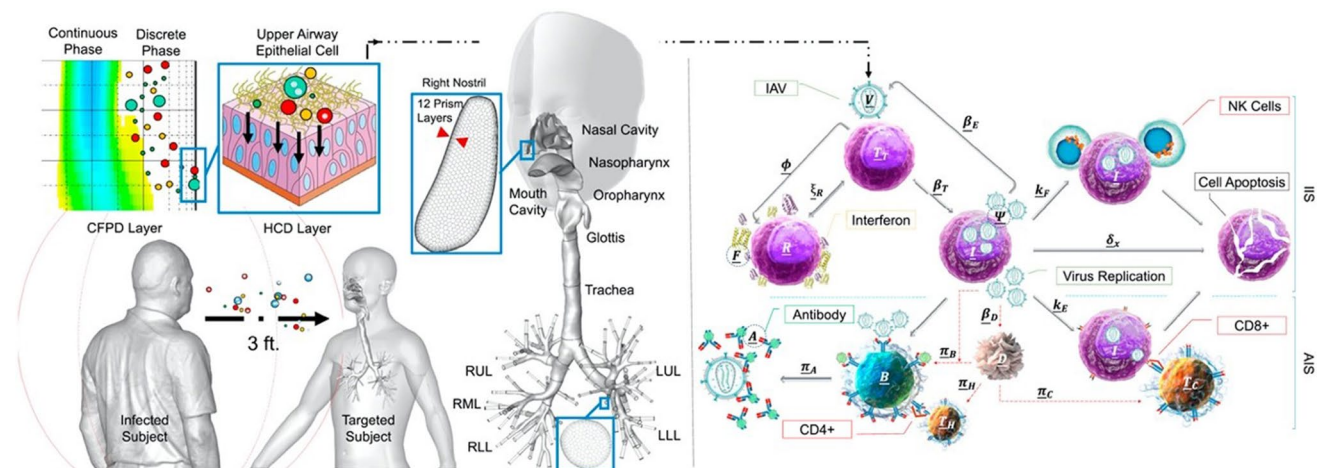


Fig. 15 The framework of the multiscale CFPD-HCD model for the human-to-human IAV infection with a subject-specific airway geometry. The description of the HCD model is given in the ‘The human respiratory system’ section of the original paper (Haghnegahdar et al. 2019a). The detail of the final polyhedral-core mesh is provided at the

Coupling of multi-zone and CFD models

Multi-zone models suffer from the well-mixing assumption which clearly is not valid in cases for Archimedes number (Ar) smaller than 400 and dimensionless temperature gradient (τ) greater than 0.03 (Wang and Chen, (2008b)). To surpass this issue, a combination of a multi-zone model and CFD model can be adopted which is superior for more realistic prediction of pollutant concentration levels and airflow characteristics. The coupling of the models provides a satisfactory compromise between accuracy and computational sources.

Wang and Chen (2008a) presented a coupling approach of CFD and multi-zone model for estimating the concentration levels in case of chemical-biological-radiological agent release within complex three-floor building. They showed that the combination of CFD and multi-zone models is superior and capable of identifying the optimal location of emergency sensors, ventilation strategies for emergency response, as well as to examine proposed routes for evacuation.

Jiang et al. (2009) performed multi-zone simulations for predicting the virus concentration and the required ventilation rate for sufficient air dilution in two Hospitals in Beijing and Guangzhou, respectively. It is worth mentioning that the pressure coefficient was predicted by the commercial CFD software PHOENICS 3.2. (Spalding 1981) and used as input parameter for CONTAM model. Their numerical results were validated against field experiments using tracer gas (SF_6), with promising and encouraging results.

Recently, Karakitsios et al. (2020) used COMIS for calculating the inflow and outflow conditions from the openings (windows and doors) and then induced them into ADREA-HF CFD code (Efthimiou et al. 2018; Kovalets et al. 2018) in

right nostril and an airway outlet (RUL: right upper lobe, RML: right middle lobe, RLL: right lower lobe, LUL: left upper lobe, LLL: left lower lobe). Reproduced from Reference (Haghnegahdar et al. 2019a with permission from Elsevier

order to investigate the release of a hazardous agent through the HVAC system in a large office.

CFD-PKTE or CFD-PTBK models

Another interesting combination of models for the investigation of the transport and deposition of particles into human airways is CFD-physiologically based pharmacokinetic (PBPK) or CFD-physiologically based toxicokinetic (PBTK) (Mumtaz et al. 2012), respectively. Recently, Feng et al. (2021) presented a detailed tutorial paper regarding the development, implementation and validation of CFD-PBPK and CFD-PBTK models for investigating the human lung aerosol dynamics numerically.

Yoo and Ito (2018) proposed a computational framework based on CFD, Computer Simulated Person (CSP) and PBPK models for the prediction of inhaled formaldehyde internal dose at human respiratory system. The numerical results indicated that the computational framework is capable of tackling many different types of pollutants and not only the examined formaldehyde. It is also important to mention that the proposed numerical methodology can also provide useful information regarding the exposure to pollutants and health risk assessment into indoor environments. The same group of researchers extended their work (Yoo and Ito (2018) for unsteady breath conditions using the aforementioned computational approach, predicting different concentration levels of formaldehyde inside the room and around the human zone, while for the person breathing zone the concentration values were lower than inside the room.

Murga et al. (2019) conducted health risk assessment in a working environment for the toxic inhalation of breathing air and how affects the human respiratory system, by means of CFD, CSP and PBTK models. The results revealed that the nose area is primarily influenced in all examined cases according to the considered working conditions and there is high risk of acute exposures during the working period.

Haghnegahdar et al. (2019b) also developed a CFD-PTBK model for investigating the transport of xenon gas and how the inhaled dose affects the human body. The numerical results obtained were compared with experimental data, exhibiting good agreement. Finally, the multiscale model is capable of predicting the concentration levels of xenon in the human respiratory system and can also be used for future non-invasive studies regarding patient specific pulmonary diseases.

Conclusions—future directions

The nature and physicochemical characteristics of particles, either those being solids or liquids forming droplets, play an important role in the mode of transmission of a variety of pollutants, contaminants and biological agents in indoor

air environments. Understanding the engineering aspects of particle technology plays a major role in designing better depollution or prevention of pollutants and biological agents' strategies and as a result minimising the risk of transmission in indoor air environments. The current study shade light on the possible gaps and directions for future research in the field of particles transmission in indoor air, focusing especially on biological agents' transmission:

- Only a handful of studies conducted with the application of modern techniques capable of detecting sub-micrometer-sized particles, it is important that more work is done in this area to develop a better understanding of the mechanism of droplet generation (Morawska 2006).
- It is evident that aqueous solution of mucin alone cannot fully represent various physicochemical and biophysical properties of saliva. Systematic studies on designing saliva targeted tribological properties have to be investigated in future (Sarkar et al. 2019).
- However, studies of how surface contamination is propagated by human touching are scare as there are no experimental data (Xiao et al. 2018).
- Both studies on the absolute and relative humidity which are known to affect the viral survival need to be further investigated (Poon et al. 2020).
- The fundamental science underlying the virus –microorganisms transfer mechanisms on soft matter domain (Poon et al. 2020).
- Studies of how the solid surfaces contamination is propagated by human touching are scarce due to mainly the lack of experimental data (Xiao et al. 2018) due to complexity of such types of experiments and quite intense health and safety protocols, laboratories mainly accessible by medical scientists and difficulties in introducing other disciplines in the field etc.
- Better understanding the pollutants in general and even more biological agents' mechanisms in the deeper generation parts of the human tracheobronchial system.
- The mechanisms of how the droplets are formed near the mouth has not been studied (Vadivukkarasan et al. 2020)
- Sneezes especially have received much less attention in literature and is a field which needs further investigation (Scharfman et al. 2016).
- Concentration of biological agents in the droplets (Zhang et al. 2020a, b, c, d).
- Viral survival on the skin (Zhang et al. 2020a, b, c, d).
- Dependence of evaporation on the temperature and humidity regarding seasonal and geographic variations in transmission rates (Tang et al. 2009).

The installed ventilation system plays significant role on the transmission of the pollutants and biological agents into indoor spaces. The positive and/ or negative influences of

either mechanical systems or natural one have been extensively analysed and documented in a series of studies. Hereafter some of the main conclusions regarding HVAC systems are summarised:

- Mixing ventilation leading to well-mixed homogeneous bio-aerosols and high dispersion rates, regardless of the droplet sizes.
- Upward displacement ventilation provides high efficiency removing of small size droplets.
- Downward displacement ventilation is ideally removing the contaminated indoor air, and minimise the cross-infection risk.
- Human's thermal plume and walking velocity are significantly influence the dispersion mechanism and kinetics of the bio-aerosols.
- Relative position and orientation among occupants are critical parameters that influence the cross-infection risk. Face-to-face position and upward exhaled bio-aerosol airflow are of high cross-infection risk.
- Personalised ventilation decreases the cross-infection risk of the user and increases the risk of cross-infection to the non-personalised occupants of the space.
- Natural ventilation minimises the cross-infection risk due to high airflow rates and mixed airflow distribution; however, in some cases, the concentration of pollutants in the unfiltered air is significant high.
- Thermal plumes from radiant heating and convective heating and cooling panels strongly influence the contaminants concentration and the associated cross-infection risk. In general, upward thermal plumes in-line with the airflow pattern have positive effect on the dispersion of airborne agents, while the downward of crossflow ones might need higher airflow rates in order to maintain the ventilation effectiveness.

In addition to the above reporting findings, it is worth noticing that today the main scientific interest on ventilation systems has been turn to the more sophisticated ones, such as personalised systems, which still remaining in a developing stage. The opportunities for future research and the still remaining open research questions in this area have been recently presented by Zhai and Metzger (2019).

Since the 1970's, the first documented attempts to use CFD in ventilation industry (Chow 1996; Nielsen 2015), the progress of CFD has been tremendous for indoor environments, with promising results for the prediction of pollutant dispersion and concentration levels, as well as for the design of ventilation strategies. Nowadays, the further development of CFD techniques along with the continuing progress of computer-hardware development has established the use of CFD as the main tool for the prediction of air movement and design of HVAC systems for the controlled ventilation

of indoor spaces. In the current pandemic of SARS-CoV-2, CFD simulations have played a major role to investigate the airborne saliva droplets transmission among people in enclosed spaces. Below, we present some final comments regarding the aforementioned computational approaches for the pollutants in general and biological agents' airborne transmission into indoor built environment:

- Human's thermal plume and walking velocity are significantly influenced by the dispersion mechanism and kinetics.
- More research should be devoted to evaluate the probability of droplet vs. viral transmission during airborne droplets transport and coughing (Dbouk and Drikakis 2020a).
- Regarding face masks and protection from the dispersion of airborne infected saliva droplets further research must be directed to the composition, properties of saliva droplets and mask high-filter efficiency for the prediction of airborne droplet transmission (Dbouk and Drikakis 2020b).
- LES seems to be the most appropriate method for practical computation for the investigation of droplet transmission, however, it is time consuming and computationally demanding. Furthermore, there are still challenges such as the development of advanced sub-grid scale models, high-order discretisation schemes for the elimination of the numerical errors, implementation on unstructured grids, and interaction with other physical mechanisms (Argyropoulos and Markatos 2015).
- The combination of CFD and multi-zone models can be very useful for more realistic prediction of pollutant concentration levels and airflow characteristics, and can provide a compromise between accuracy and computational sources.
- It is important to mention that the CFD-PKTE or CFD-PTBK models for the transport prediction of particles in human respiratory system exhibit many difficulties and should be further improved by developing the next generation of virtual lung computational framework (Feng et al. (2021).
- There is also a need for further improvement and validation of the current numerical methods in order to be fully capable of predicting accurately complex phenomena of the biopathogens' transmission mechanisms, such as evaporation, dispersion, droplet distribution, primary and secondary break-up mechanisms, coalescence, turbulence, inhalation and pulmonary transport.

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Declarations

Ethics approval and consent to participate Not applicable.

Conflict of interest The authors declare no competing interests.

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