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Skin microbiota interact with microbes on office surfaces

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ABSTRACT

The indoor environment is recognized as a potential contributor to human health impacts through resident microbiomes. Indoor surface microbial communities are formed from several sources, environmental and anthropogenic. In this study, we characterized the bacterial and fungal communities from various sources typical of a working office environment including dust, fingers, and computer keyboards and mice. The composition of the dust bacterial community was significantly different from the other tested surfaces ($P < 0.05$), whereas the dust fungal community was only significantly different from fingers ($P < 0.05$). Bacterial and fungal communities were both shaped by deterministic processes, and bacterial communities had a higher migration rate. Results of a network analysis showed that the microbial community interactions of keyboards and mice were mainly competitive. Fast expectation–maximization microbial source tracking (FEAST) identified the sources of > 70 % of the keyboard and mouse microbial communities. Biomarkers for each sample types were identified by LDA Effect Size (LEfSE) analysis, some of which were soil-derived and potential anthropogenic pathogens, indicating the potential for exchange of microbes among outdoor, human and indoor surfaces. The current study shows that the source of microorganisms at the office interface is highly traceable and that their migration is linked to human activity. The migration of potentially pathogenic microbes were identified, emphasising the importance of personal hygiene.

1. Introduction

It is estimated that humans spend >80 % of their time in indoor environments (Klepeis et al., 2001; Liu et al., 2020). Prolonged time indoors has potential health impacts (Li et al., 2019) through interactions with resident microbiomes (Lewis, 2021). For example, indoor dusts have been reported to carry various harmful pathogenic virus, bacteria and fungi (Garber, 2001; Seppanen and Fisk, 2004) and have potential to lead to respiratory diseases including asthma that has a deleterious effect on human health (Maciag and Phipatanakul, 2022). Conversely, studies suggested that exposure to certain indoor bacteria in early life stages is beneficial for health (Dannemiller et al., 2016; Lynch et al., 2014). For example, exposure to high abundance of fungal genus *Cryptococcus*, bacterial Firmicutes and Bacteriodetes in very early life stages might decrease potential threats (e.g., asthma) to human health (Stephens and Gibbons, 2016).

Dust microbes vary according to the type of indoor environment (Rintala et al., 2012) and their community composition is influenced, for example, by human activities, building environment, and pet ownership (Canha et al., 2018; Gupta et al., 2019; Lee et al., 2002). Furthermore, microbes from external sources such as climbing plants growing on building facades (Zhou et al., 2021d), and microbes carried by outdoor airborne particles such as PM 2.5 and PM 10 (Grydaki et al., 2021; Happo et al., 2013), can also be a source for the indoor microbiome.

The human skin is inhabited by a diversity of microbes and is in constant contact with microbial-rich interfaces (Byrd et al., 2018). Skin microbes have unique characteristics that distinguish them from other body microbiomes (Hannigan et al., 2015; Oh et al., 2016), with skin bacteria more abundant and diverse than skin fungal communities (Oh et al., 2016). The composition of the skin microbiota is related to both

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the humidity and physiological characteristics of the skin area and the associated sebaceous microenvironment (Jo et al., 2017). It is also influenced by a variety of external environmental factors, such as lifestyle, indoor environment, and pets (Gupta et al., 2019; Lax et al., 2014; Martin-Sanchez et al., 2021). Skin is relatively poor in nutrients (Byrd et al., 2018), thus resident microbes utilize available resources present in sweat, the cortex and stratum corneum (Scharschmidt and Fischbach, 2013). The resident skin microbial community actively prevent the colonization of pathogenic bacteria in a process known as 'anti-colonization', so that human skin acts as a barrier between the body and the environment (Kang et al., 2018; Sanford and Gallo, 2013). Where the barrier is broken or the balance between beneficial and pathogenic microbes is disturbed, the skin is a potential route for infection (Fitz-Gibbon et al., 2013). In susceptible individuals, the colonization of pathogenic bacteria often results in skin disease (Wiśniewska et al., 2019). In addition, pathogenic bacteria may help other pathogens to colonize the skin by modulating the host's immune response (Cogen et al., 2010).

Computer keyboards and mice are essential office items and are surfaces with a high degree of contact with hands and transfer microbes from indoor dust and human skin (Dayane et al., 2019; Gibbons, 2016). Thus, keyboards, through high frequency contact and deposition of skin microbes, become an extension of the skin environment (Fonseca et al., 2016; Lax et al., 2015). However, little is known about the assemblage of microbial communities at these interfaces and how they interact with the skin microbiota. Potentially, these surfaces may also contain pathogenic microbes that threaten human health (Gebel et al., 2013). Whereas the species of these pathogenic bacteria and their potential sources remain unclear. In this study, we conducted high-throughput sequencing of microbial communities from a range of sample types (finger, mice, keyboard, and their surrounding environment) associated with 40 office workers with the aim of 1) characterizing microbial communities from tested surfaces; 2) exploring the pattern of microbial colonization of office surfaces through human interaction; and 3) identifying whether pathogenic bacteria were present.

2. Material and methods

2.1. Experiment design and DNA extraction

A total of 40 people (20 males and 20 females) from an office located in Xiamen city, Fujian, China (24°36′ N, 118°03′E) were selected for study. The offices were cleaned and vacuumed weekly. Samples were taken from their keyboard, mouse, dust surrounding their workstation and all ten digits. Prior to sampling hand washing had not occurred within 2 h. Workstation dust samples were taken as being representative of deposited aerosols. To collect microbes from each surface, sterilized cotton swabs were first dipped in Tween-20 reagent (Beyotime, China) and each surface swabbed 5 times. Post sampling, swabs were stored in individual sterile 2.0 ml centrifuge tubes and at −20 °C prior to DNA extraction. The cotton from the swabs was stripped and DNA extracted using a QIAamp® BiOstic® Bacteremia DNA Kit (Germany) following the manufacturer's instructions. DNA quality control was assessed using a Qubit 3.0 fluorometer (Zhou et al., 2021b). Extracted DNA was stored at −20 °C prior to high-throughput sequencing.

2.2. High-throughput sequencing

Bacterial (16 s rRNA; 338F/806R, region V3-V4) (Fadrosh et al., 2014) and fungal (ITS; fITS7/ITS4) (Karlsson et al., 2014) primer sets were used to evaluate the composition of microbial communities from different sample types. The PCR amplification mixture contained 12.5 μL of Phusion Hot Start Flex Master Mix (Li et al., 2021), 0.1 μM each of forward and reverse primer, 3.0 μL DNA and sterile ddH_2O to make a final volume of 25 μL. PCR conditions were as previously described for bacteria (Li et al., 2021) and fungi (Zhao et al., 2020). Amplification products were purified using a universal DNA purification kit (DP214-3 Tiangen, China). The quality and quantity of purified amplicons were analyzed by Qubit Fluorometer 3.0 and sent to LC-BIO Bio-tech ltd (Hangzhou, China) for high-throughput sequencing using an Illumina Miseq PE300 platform.

Bacterial and fungal sequences were analyzed by Quantitative Insights Into Microbial Ecology 2 (QIIME 2) (Bolyen et al., 2019). "USEARCH" was used to identify and discard chimeric sequences (Edgar, 2013). Amplicon sequence variants (ASVs) were generated using a DADA2 pipeline. Silva (v138) and Unite (v8.2) databases were used to annotate bacterial and fungal taxonomy, respectively. Alpha and beta diversity of samples were calculated using QIMME 2. Identification of potential bacterial pathogens used 16Spip software with an identity threshold of 100 % (Miao et al., 2017). Sequencing data for this study are openly accessible at the Science Data Bank using the following links for bacteria (https://www.doi.org/10.11922/sciencedb.01595) and fungi (https://resolve.pid21.cn/31253.11.sciencedb.01595).

2.3. Statistical analysis

Microsoft Excel 2018 was used to calculate the sum, standard errors and means of the relative abundance of bacterial and fungal communities. SPSS 22 (IBM, USA) was used to calculate ANOVA and significance level (only $P < 0.05$ was considered) of each sample. Principal Coordinate Analysis (PCoA) based on Bray-Curtis distances were conducted by the R package, "Vegan" (Oksanen et al., 2019). To assess whether community composition differed between sample types, PCoA scores were analysed using the "ANOSIM" function in "Vegan". Null hypotheses were determined by previous study (Clarke, 1993). A neutral community model (NCM) (Burns et al., 2016) was determined as previously described (Zhou et al., 2021c). For each sample a normalized stochasticity ratio (NST) was calculated using the R package, "NST", to quantify the assembly mechanism of microbial communities (Ning et al., 2019). A 50 % threshold was set to evaluate whether assembly was dominated by deterministic or stochastic proccesses. Bar chart, PCoA, NCM, NST, LDA Effect Size (LEfSe) and Venn analysis were visualized using online OmicStudio tools (https://www.omicstudio.cn/tool). A network analysis based on Random matrix theory (RMT) was determined using an online tool, Molecular Ecological Network Analysis Pipeline (MENAP), http://ieg4.rccc.ou.edu/MENA/. Following the protocol provided by the developers, network parameters, such as average clustering coefficient (avgCC, the average percentage of interconnections between pairs of nodes that are connected to the same node.), density (Measurement of network integrity) and modulity (potential microbial community detection algorithms) were calculated (Deng et al., 2012) and visualized via Gephi 0.9.2. The positive (collaboration) and negative (competition) correlations between the two nodes are indicated by different colours, respectively. Fast expectation-maximization microbial source tracking (FEAST) quantified the contribution of different microbial sources for each sampled surface type (Shenhav et al., 2019) and visualized by Originlab 2018.

3. Results

3.1. Microbial community profiles

A total of 8,011,287 and 11,739,507 high-quality bacterial and fungal sequences were obtained ranging from 32,810 to 68,513 and 65,772 to 91,929 per sample, respectively. From these sequences, a total of 3615 and 1305 ASVs were identified. Compared to other sample types, bacterial and fungal communities from dust samples had a significantly higher alpha-diversity ($p < 0.05$) (Fig. S1a-b). Proteobacteria, Firmicutes, Actinobacteria, Bacteroidetes and Cyanobacteria were the dominant bacterial phyla detected from all samples, whereas, Ascomycota and Basidiomycota were the dominant fungi detected from office surface and skin samples (Fig. S1c-d). The composition of bacterial

communities from dust samples significantly differed from finger ($P = 0.002$), keyboard ($P = 0.001$) and mouse ($P = 0.001$) samples (Fig. 1a-g). Furthermore, bacterial communities from fingers separated from both keyboard ($P = 0.003$), and mouse ($P = 0.014$) samples along the PCoA1 axis (Fig. 1e and f). No significant difference was observed between keyboard and mouse samples (Fig. 1g). The composition of fungal communities from dust samples was significantly different from finger samples ($P = 0.019$), but not from the other sample types (Fig. 1i-k).

Both bacterial and fungal communities from dust, keyboard and mouse samples were fitted to a neutral community model (NCM) (Fig. 2a-e). Bacterial and fungal communities from keyboard and mouse samples had a better goodness fit than dust samples, and bacterial communities had a better goodness fit than fungal communities in dust for all sample types. The migration rate (m) of either bacterial or fungal communities from keyboard and mouse samples was greater than dust samples. A normalized stochasticity ratio (NST) quantified the assembly mechanisms of bacterial and fungal communities for each surface type, indicating that a deterministic process dominated in all samples with an average NST value lower than the 50 % threshold (Fig. 2f). Dust samples had a significantly lower NST value than either keyboard ($P < 0.001$) or mouse ($P < 0.001$) samples for both bacterial and fungal communities.

A network analysis assessed the co-occurrence patterns among skin

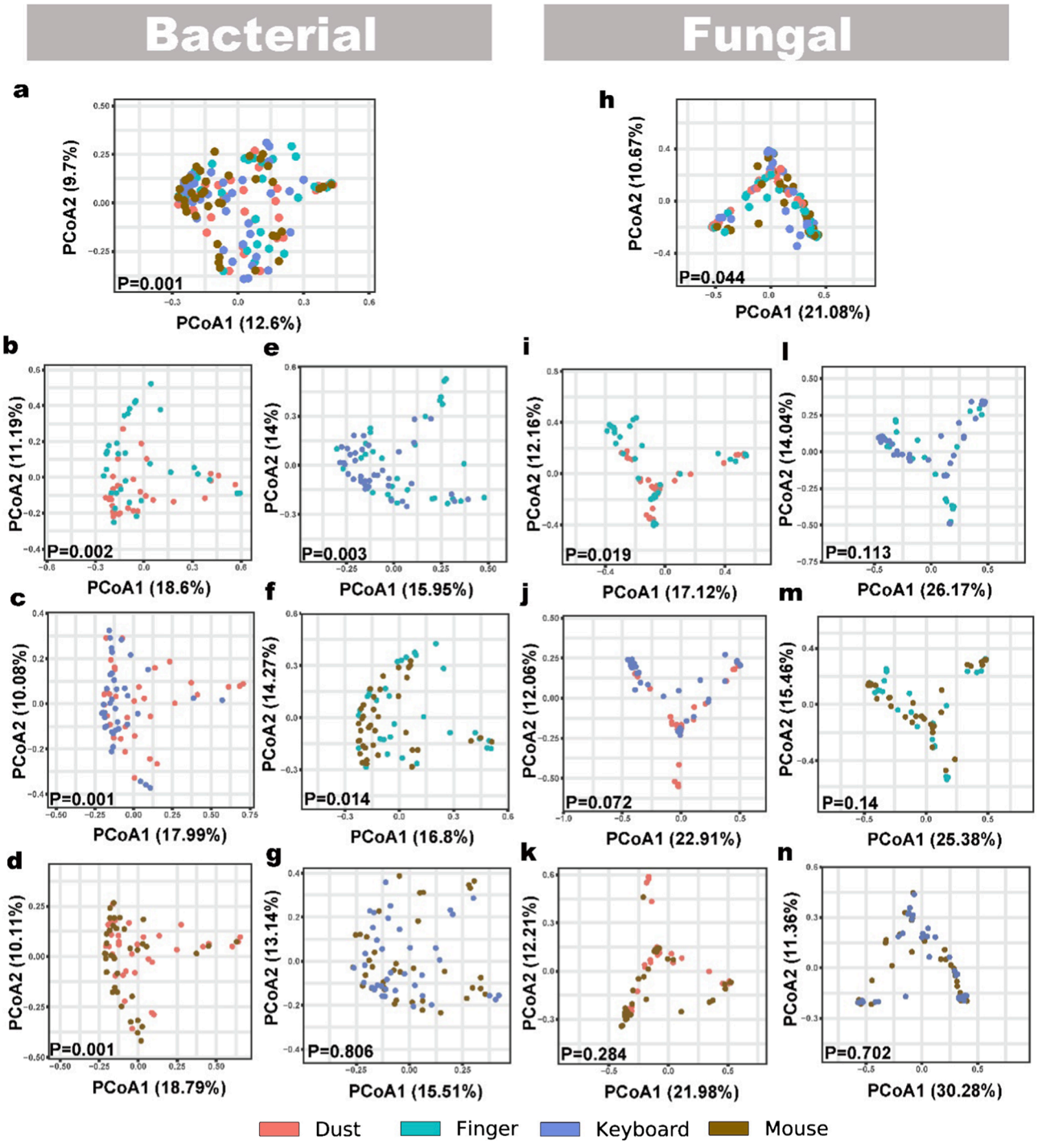

Fig. 1. Principal coordinate analysis (PCoA) of bacterial (a-g) and fungal communities (h-n) from dust, finger, keyboard, and mouse samples based on a Bray-Curtis dissimilarity matrix.

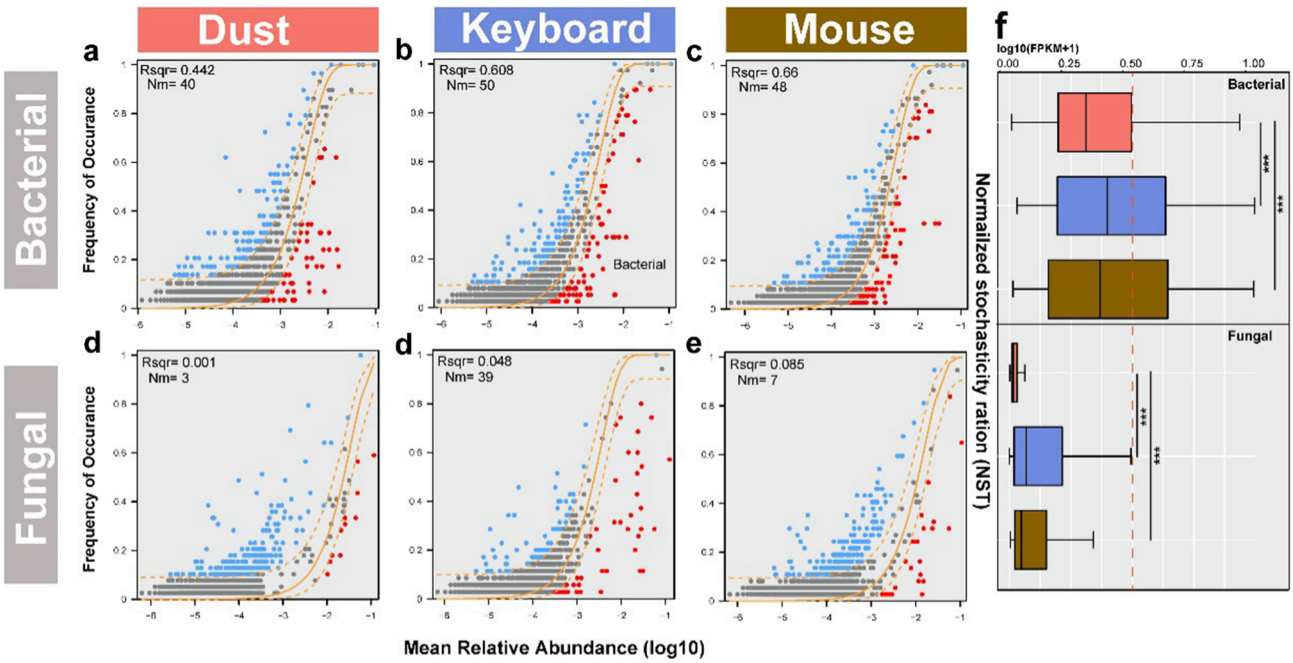

Fig. 2. Fit of a neutral community model (NCM) to bacterial and fungal communities from dust, keyboard, and mouse samples (a-e). Solid and dashed golden lines indicate the best fit to the model and the 95% of confidence intervals, respectively. The parameters, Rsqr and Nm, indicate the goodness of model prediction and estimated migration rate, respectively. Blue, grey and red dots indicate over-representation, best fit and under-representation of the model to the sample types. Normalized stochasticity ratio (NST) of bacterial and fungal communities among dust, keyboard, and mouse samples (f). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

microbiota. Average clustering coefficients (avgCC) for the bacterial networks in dust, keyboard and mouse samples were 0.531, 0.472 and 0.444. For all sample types, the density of bacterial networks in dust samples was greatest, while modularity was lower than either keyboard or mouse samples (Fig. S2a-c). At least 70 % of network links across all sample types were positive (Fig. 2Sd). The avgCC for fungal networks from dust, keyboard and mouse samples were 0.795, 0.789 and 0.837. A higher density of fungal networks occurred with mouse samples whereas modularity was greatest in keyboard samples (Fig. S2e-g). Positive correlations predominated (>99 %) in fungal networks (Fig. S2h). Results of interactions between microbial taxa showed that dust samples had the highest avgCC and network density but lowest modularity (Fig. 3a-c). In contrast to bacterial communities, network links across all samples were at least 68 % negative (Fig. 3e).

3.2. *Source tracking of microbiota*

Dust, finger, keyboard, and mouse samples shared 707 bacterial ASVs (Fig. 4a). Dust samples had the most unique ASVs (784). Keyboard and mouse samples shared 1052 and 1096 bacterial ASVs with finger samples, and shared 1121 and 1063 ASVs with dust samples, respectively. For fungal communities, 470 ASVs were shared between all sample types (Fig. 4b). Keyboard samples had the most unique ASVs (529), while finger samples had the least (201). Keyboard and mouse samples shared 649 and 686 fungal ASVs with finger samples, and shared 936 and 803 ASVs with dust samples, respectively.

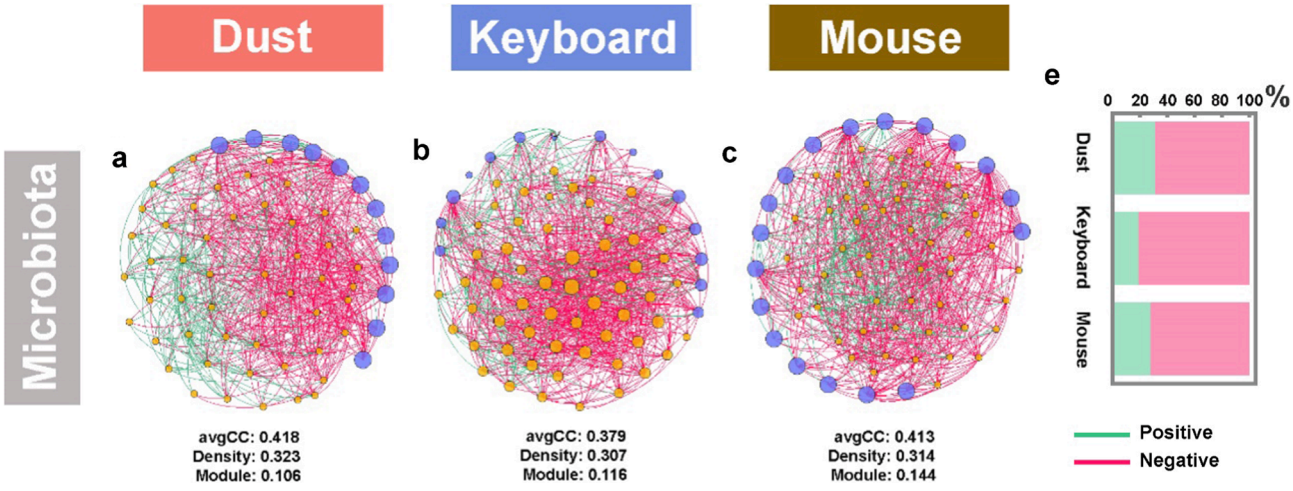

Fig. 3. Co-occurrence pattern of microbiota (a-c) from dust, keyboard and mouse samples based on random matrix theory. Average clustering coefficient (avgCC), network density and modularity are calculated to indicate the properties of network. Bar-charts (e) depict the percentages of positive and negative links between nodes.

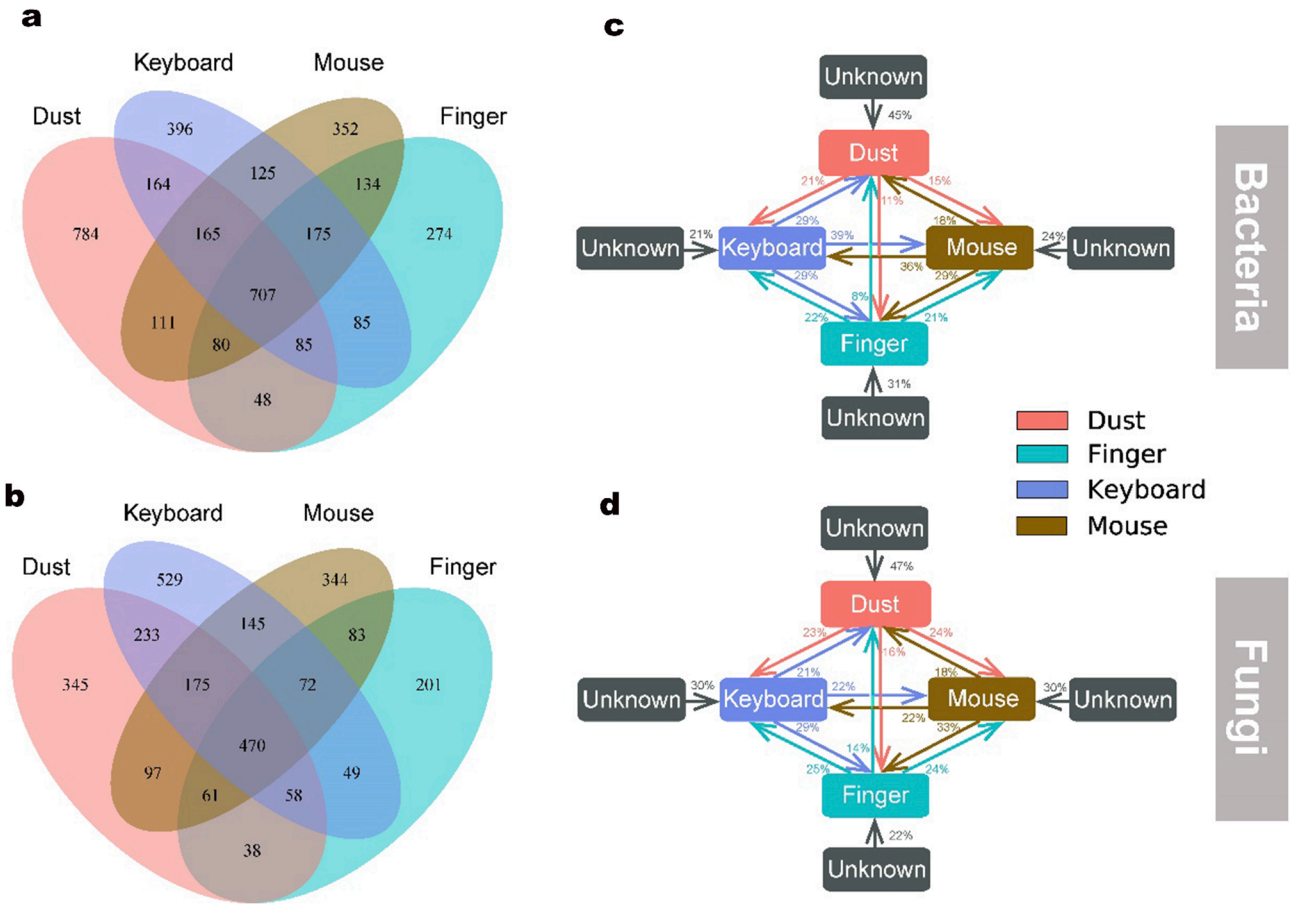

Fig. 4. Venn diagram at microbial ASV level from dust, finger, keyboard, and mouse samples (a) and (b). Fast expectation- maximization microbial source tracking (FEAST) analysis for dust, finger, keyboard and mouse samples based on microbial ASV level (c) and (d). Direction of the arrows represents the source-sink relationships, and percentages represent the contribution of sources to sink.

Main sources of microbial communities for each surface type differed (Fig. 4c). The predominant source (45 %) of the dust microbiome was external to the studied system, whereas both the keyboard and mouse were the main sources for the bacterial community of each other, 39 % and 36 %, respectively. The bacterial community associated with finger samples had an equal contribution (29 %) from both keyboard and mouse. With regard to fungal communities, though the percentage contributions were slightly different, the same source pattern occurred for dust and finger samples (Fig. 4d). However, for keyboard and mouse samples, instead of a single main source all other sources contributed approximately equally to the fungal community (Fig. 4d).

3.3. Recognition of potential pathogens

LEfSe analysis identified potential bacterial and fungal biomarkers for all sample types (Fig. 5a and b) as follows: mouse, *Lachnoclostridium* (bacteria) and *Thielavia* (fungi); keyboard, *Sporosarcina* (bacteria) and *Malassezia* (fungi); finger, *Staphylococcus* (bacteria) and *Candida* (fungi); and dust, *Rhizobiaceae* (bacteria) and *Fimetariella* (fungi).

A total of 125 potential pathogens (human and plant) were identified from samples, of which 13 had a relative abundance > 1 % and were shared across all sample types (Fig. 5c). In contrast, *Gardnerella vaingalis* and *Streptococcus sanguinis* were unique to finger samples (Fig. 5c). The relative abundance of *S. epidermidis* was greatest in finger samples, while *Bacillus cereus* was greatest in dust samples (Fig. 5d).

4. Discussion

The composition of the bacterial community from workstation dust differed from the other tested surfaces. This concurs with our *a priori* assumption and previously published studies (Zwa et al., 2020) that bacterial communities associated with workstation dust would likely originate from external sources such as aerosol deposition. This was supported by FEAST analysis which identified that 45 % of the bacteria detected was from external sources and included *Rhizobiaceae*, a bacterial family typical of soil (Rintala et al., 2008). One potential source of soil-derived bacteria, was the building facade external to the studied office which was planted with climbing plants and is a known source of transferable microbiota (Zhou et al., 2021d). In addition, airborne PM 2.5 or PM 10 could also have transferred microorganisms to the indoor environment (Zhou et al., 2021a) via open windows and once entered, circulated throughout the office area via the air conditioning system.

As would be expected, microbial communities of surfaces in most frequent contact with humans, in this study, computer keyboards and mice had the least contribution (c. 25 %) from dust sources to their respective community composition. A two-way contribution to both bacterial and fungal communities existed between skin and computer devices with approximately 20–30 % of the community derived from each source. Furthermore, reconstructed bacterial networks of computer keyboards and mice had higher modularity and lower average clustering coefficients (avgCC), suggesting more complex and robust network relationships associated with skin (finger) contact (Deng et al., 2012). This is likely through several potential scenarios including migration and subsequent colonization (Gibbons, 2016), and natural sweating that provides a nutrient resource for micro-organisms (Hayashi et al., 2021). In addition, introduced microbes through skin contact may impact the intrinsic surface microbial community, disrupting the original microbial network structure and making it more complex (Yuan et al., 2021).

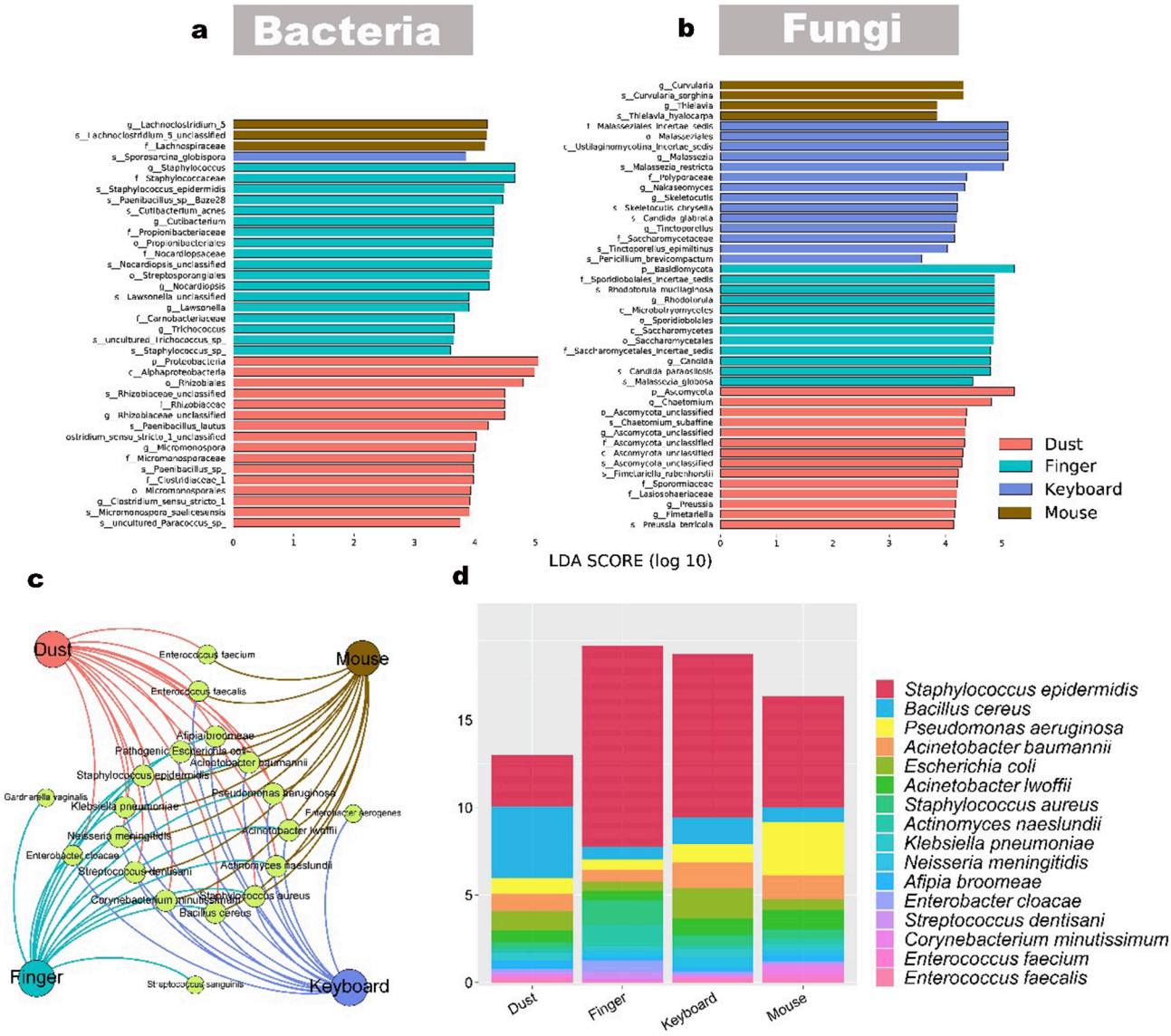

Fig. 5. LDA Effect Size (LEfSe) analysis highlights the bacterial and fungal biomarkers associated with dust, finger, keyboard and mouse samples ($\alpha > 0.01$, LDA score > 3.6) (a) and (b). Shared network and relative abundance of potential pathogens (>1%) among dust, finger, keyboard, and mouse (c) and (d).

As perhaps could be anticipated, all communities from the different sample types were determined by deterministic processes, with keyboard and mouse samples having higher NST values than dust. This contrasts with a recent study which found indoor expiratory bacteria and fungi were determined by stochastic processes (Zhang et al., 2022), possibly due to differences in habitat and nutrient availability resulting in microbial communities being driven by different processes (Adams et al., 2015). Both NCM and NST analysis further confirmed that bacterial communities had higher migration rates than fungi, perhaps due to differences in body size (bacteria vs fungi) (De Bie et al., 2012).

Through LEfSe analysis, bacterial and fungal biomarkers indicative of each sample type were identified. *Staphylococci*, in line with other studies (O'flaherty et al., 2005; Tong et al., 2015), were prevalent in skin samples. However, *Lachnoclostridium* and *Sporosarcina,* usually found in the human gut (Liang et al., 2020; Priyodip and Balaji, 2019), were identified as biomarkers for computer mice and keyboards, respectively, suggesting anthropogenic mediated colonization of microbes. Although in comparatively low abundance, several pathogens were present in the sample types tested including human pathogens, for example, *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Escherichia coli*, which were reported previously from domestic residences (Ijaz et al., 2016; Rosas et al., 1997; Whitby and Rampling, 1972). Furthermore, our data suggests that potential pathogens such as *Staphylococcus epidermidis*, once introduced to and established in the office environment, can increase in abundance through human interaction with computer keyboards and mice. This concurs with a previous study, that found *Staphylococcus epidermidis* with antibiotic resistance associated with computer touch screens (Gerba et al., 2016).

Overall, this study has demonstrated that distinct microbial communities are associated with several components of a typical office environment, including opportunistic pathogens. The formation of microbial communities at the office interface is mediated by the hand. Fingers drive the migration of microbial communities in all sectors. To minimize potential negative consequences of pathogens being present in an office environment, mitigation strategies such as personal hygiene is essential (Two et al., 2016); as is effective cleaning of office surfaces (Gerba et al., 2016); and maintaining room ventilation (Hobday and Dancer, 2013).

CRediT authorship contribution statement

Hu Li: Conceptualization, Data curation, Formal analysis,

Investigation, Methodology, Software, Visualization, Funding acquisition, Writing – review & editing. **Shu-Yi-Dan Zhou:** Data curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. **Roy Neilson:** Funding acquisition, Writing – review & editing. **Xin-Li An:** Funding acquisition, Resources, Writing – review & editing. **Jian-Qiang Su:** Conceptualization, Resources, Project administration, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2022.107493.

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