



# The potential importance of the built-environment microbiome and its impact on human health

Thomas C. G. Bosch<sup>a,b,1</sup> , Mark Wigley<sup>c</sup> , Beatriz Colomina<sup>d</sup> , Brendan Bohannon<sup>e</sup>, Forrest Meggers<sup>f</sup> , Katherine R. Amato<sup>b,g</sup> , Meghan B. Azad<sup>b,h,i</sup> , Martin J. Blaser<sup>b,j,k</sup> , Kate Brown<sup>b,l</sup>, Maria Gloria Dominguez-Bello<sup>b,m,n</sup> , Stanislav Dusko Ehrlich<sup>b,o</sup>, Eran Elinav<sup>b,p,q</sup> , B. Brett Finlay<sup>b,r</sup> , Kate Geddie<sup>b,s</sup> , Naama Geva-Zatorsky<sup>b,t,u</sup> , Tamara Giles-Vernick<sup>b,w</sup> , Philippe Gros<sup>b,x</sup> , Karen Guillemin<sup>b,x</sup> , Louis-Patrick Haraoui<sup>b,y</sup> , Elizabeth Johnson<sup>b,z</sup> , Frédéric Keck<sup>b,aa</sup> , Jamie Lorimer<sup>b,bb</sup> , Margaret J. McFall-Ngai<sup>b,cc</sup> , Mark Nichter<sup>b,dd</sup> , Sven Pettersson<sup>b,ee</sup> , Hendrik Poinar<sup>b,ff</sup> , Tobias Rees<sup>b,gg</sup> , Carolina Tropini<sup>b,hh</sup> , Eduardo A. Undurraga<sup>b,ii</sup> , Liping Zhao<sup>b,m</sup>, and Melissa K. Melby<sup>b,jj,1</sup>

Edited by W. Doolittle, Dalhousie University, Halifax, NS, Canada; received October 12, 2023; accepted March 26, 2024

There is increasing evidence that interactions between microbes and their hosts not only play a role in determining health and disease but also in emotions, thought, and behavior. Built environments greatly influence microbiome exposures because of their built-in highly specific microbiomes coproduced with myriad metaorganisms including humans, pets, plants, rodents, and insects. Seemingly static built structures host complex ecologies of microorganisms that are only starting to be mapped. These microbial ecologies of built environments are directly and interdependently affected by social, spatial, and technological norms. Advances in technology have made these organisms visible and forced the scientific community and architects to rethink gene–environment and microbe interactions respectively. Thus, built environment design must consider the microbiome, and research involving host–microbiome interaction must consider the built-environment. This paradigm shift becomes increasingly important as evidence grows that contemporary built environments are steadily reducing the microbial diversity essential for human health, well-being, and resilience while accelerating the symptoms of human chronic diseases including environmental allergies, and other more life-altering diseases. New models of design are required to balance maximizing exposure to microbial diversity while minimizing exposure to human-associated diseases. Sustained trans-disciplinary research across time (evolutionary, historical, and generational) and space (cultural and geographical) is needed to develop experimental design protocols that address multigenerational multispecies health and health equity in built environments.

Anthropocene | evolution | microbiome | metaorganism | architectural design

Humans evolved in environments that continually exposed them to animal, water, soil, air, and plant microbes descended from the more than 3 billion years of microbial life that preceded the emergence of metaorganisms (1–4). As metaorganisms, humans therefore are nested ecosystems comprised of human cells interacting with a similar number of microbial cells (2, 4). For more than 10,000 y, our human environment has increasingly consisted of an anthropogenic “built” environment (BE) that is most evident in the physical shelter of buildings but extends through neighborhoods, cities, and infrastructural systems that cross vast territories—connecting and transforming diverse ecosystems (5–8). These trends will continue as two-thirds of the world is

expected to live in the built urban environment by 2050. Our current BE isolates us increasingly from the microbes of “natural” environments, among which there are very few human pathogens (<0.00001%) (9–14). Buildings are complex organic systems in their own right, in terms of the countless mutually interdependent microbial communities they host, that effectively affect the human metaorganism's health. Yet, they also pose a threat to well-being and survival (11, 13, 15, 16). Numerous studies have reinforced the contention that

Author affiliations: <sup>a</sup>Zoological Institute, University of Kiel, Kiel 24118, Germany; <sup>b</sup>Humans and the Microbiome Program, Canadian Institute for Advanced Research, Toronto, ON M5G 1M1, Canada; <sup>c</sup>Graduate School of Architecture, Planning and Preservation, Columbia University, New York, NY 10027; <sup>d</sup>School of Architecture, Princeton University, Princeton, NJ 08544; <sup>e</sup>The Institute of Ecology and Evolution, University of Oregon, Eugene, OR 97403-5289; <sup>f</sup>Princeton University School of Architecture & Andlinger Center for Energy and the Environment, Princeton, NJ 08540; <sup>g</sup>Department of Anthropology, Northwestern University, Evanston, IL 60208; <sup>h</sup>Department of Pediatrics and Child Health, University of Manitoba, Winnipeg, MB R3E 0Z3, Canada; <sup>i</sup>Department of Community Health Sciences, University of Manitoba, Winnipeg, MB R3E 3P5, Canada; <sup>j</sup>Children's Hospital Research Institute of Manitoba, Winnipeg, MB R3E 3P4, Canada; <sup>k</sup>Center for Advanced Biotechnology and Medicine at Rutgers Biomedical and Health Sciences, Rutgers University, Piscataway, NJ 08854-8021; <sup>l</sup>Program in Science, Technology and Society, Massachusetts Institute of Technology, Cambridge, MA 02139; <sup>m</sup>Department of Biochemistry and Microbiology, Rutgers University, New Brunswick, NJ 08901; <sup>n</sup>Department of Anthropology, Rutgers University, New Brunswick, NJ 08901; <sup>o</sup>Institute of Neurology, University College London, London WC1N 3RX, United Kingdom; <sup>p</sup>Systems Immunology Department, Weizmann Institute of Science, Rehovot 761000, Israel; <sup>q</sup>Division of Microbiome & Cancer, Deutsches Krebsforschungszentrum, 69120 Heidelberg, Germany; <sup>r</sup>Michael Smith Laboratories, University of British Columbia, Vancouver, BC V6T 1Z4, Canada; <sup>s</sup>Medical and Related Sciences Centre, The Canadian Institute for Advanced Research, Toronto, ON M5G 1L7, Canada; <sup>t</sup>Technion Integrated Cancer Center, Technion-Israel Institute of Technology, Haifa 3525433, Israel; <sup>u</sup>Department of Cell Biology and Cancer Science, Technion-Israel Institute of Technology, Haifa 3525433, Israel; <sup>v</sup>Anthropology & Ecology of Disease Emergence, Institut Pasteur, Université Paris Cité, Paris 75015, France; <sup>w</sup>Department of Biochemistry, McGill University, Montreal, QC H3G 1Y6, Canada; <sup>x</sup>Institute of Molecular Biology, University of Oregon, Eugene, OR 97403; <sup>y</sup>Department of Microbiology and Infectious Diseases, Université de Sherbrooke, Canada J1E 4K8; <sup>z</sup>College of Human Ecology, Cornell University, Ithaca NY 14853; <sup>aa</sup>Laboratoire d'Anthropologie Sociale, Collège de France, Paris 75005, France; <sup>bb</sup>School of Geography and the Environment, University of Oxford, OX1 3QY, United Kingdom; <sup>cc</sup>Division of Biology and Biological Engineering, Caltech, Pasadena, CA 91125; <sup>dd</sup>School of Anthropology, University of Arizona, Tucson, AZ 85721; <sup>ee</sup>Nanyang Technological University, Singapore 637715, Singapore; <sup>ff</sup>Department of Anthropology, McMaster University, Hamilton, ON L8S 4M4, Canada; <sup>gg</sup>LIMN, Berkeley, CA 94708; <sup>hh</sup>Department of Microbiology and Immunology and School of Biomedical Engineering, University of British Columbia, Vancouver, BC V6T 1Z3, Canada; <sup>ii</sup>Escuela de Gobierno, Pontificia Universidad Católica de Chile, Santiago 7820436, Chile; and <sup>jj</sup>Department of Anthropology, University of Delaware, Newark, DE 19716

Author contributions: T.C.G.B., M.W., B.C., B.B., F.M., K.R.A., M.B.A., M.J.B., K.B., M.G.D.-B., S.D.E., E.E., B.B.F., K. Geddie, N.G.-Z., T.G.-V., P.G., K. Guillemin, L.-P.H., E.J., F.K., J.L., M.J.M.-N., M.N., S.P., H.P., T.R., C.T., E.A.U., L.Z., and M.K.M. analyzed data; and wrote the paper.

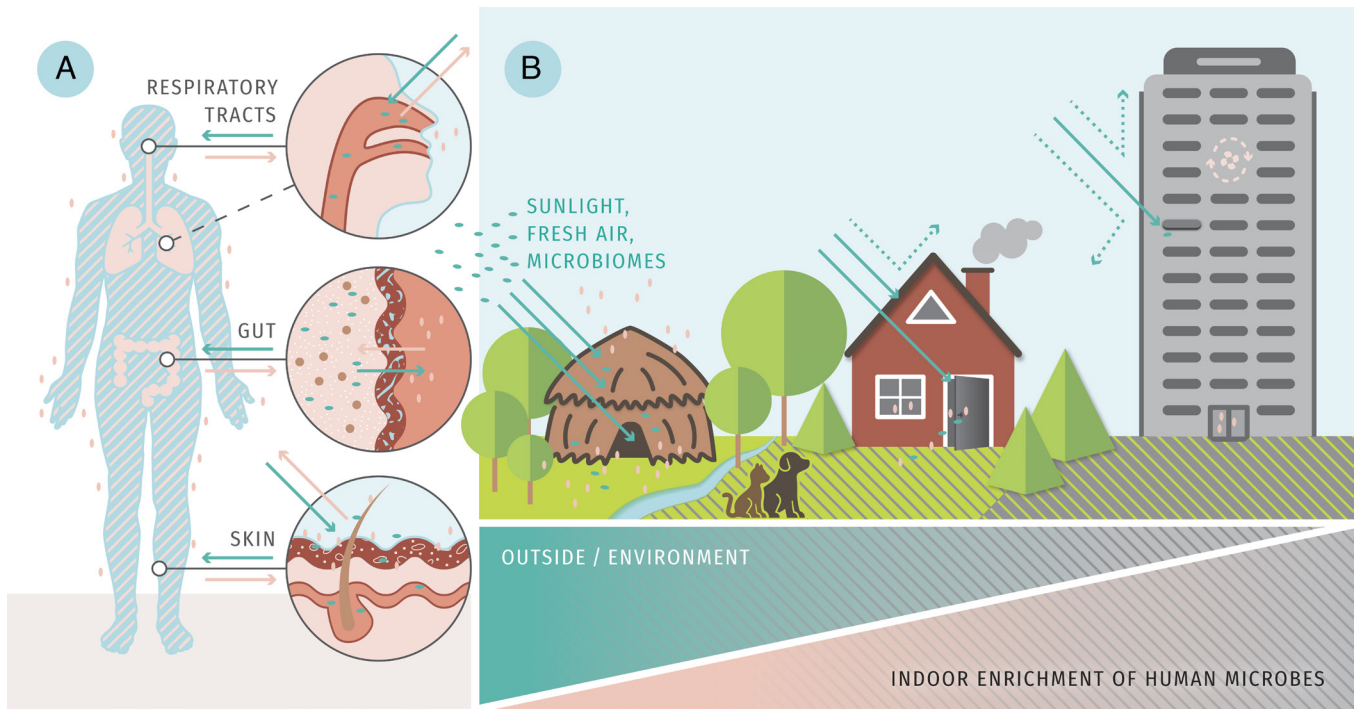
The authors declare no competing interest.

This article is a PNAS Direct Submission.

Copyright © 2024 the Author(s). Published by PNAS. This open access article is distributed under [Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 \(CC BY-NC-ND\)](https://creativecommons.org/licenses/by-nc-nd/4.0/).

<sup>1</sup>To whom correspondence may be addressed. Email: [tbosch@zoologie.uni-kiel.de](mailto:tbosch@zoologie.uni-kiel.de) or [mmelby@udel.edu](mailto:mmelby@udel.edu).

Published April 25, 2024.



**Fig. 1.** Healthy porosity. (A) The human body is constantly exposed to its microbial environment. (B) Traditional lifestyle buildings that are open to nature allow human exposures to natural microbes and other elements. As humans urbanize, dwellings are placed in settings where natural elements are highly reduced compared to the environment we have evolved in (e.g., there is less dirt, fewer trees) and architectural design encloses buildings. In these enclosed, almost impermeable urban buildings humans become the main source of microbes, thus impairing human exposure to nature and its elements. Image credit: Katja Duwe-Schrinner.

increasing separation from “nature” has had a substantial impact on physical and mental well-being. If health correlates with increased microbiome diversity (17, 18), then much of the contemporary built environment (its form, materials, systems, construction, maintenance, and modes of occupation) reduces diversity and thus could lead to poorer health. In this context, therefore, our understanding of health is primarily about securing human health which includes the whole interactive ecology (19, 20). The invention of the BE has increased our life expectancy, but at the same time has also given rise to conditions for disease by creating new niches for disease hosts and vectors, concentrating waste and toxic materials, and decreasing ventilation and sunlight, thereby changing circuits of microbial exchange within the communities of humans and newly domesticated animals, plants, and their larger environments (8, 21–26).

The BE may influence the human microbiome by 1) acting as an evolutionarily unique reservoir of human-adapted commensal and harmful microbes (e.g., biofilms on plastic surfaces that comprise increasing amounts of the BE that could potentially colonize humans); 2) decreasing the exposure of individuals to beneficial microbes by increasing disconnection from the natural biodiversity by acting as a barrier between humans and the wider environmental microbiome (e.g., the rich ecosystem of soil microbes); 3) altering human behavior and interactions thereby affecting microbial exposure and transmission (e.g., by increasing indoor social interactions and promoting the transmission of respiratory diseases such as Covid-19, TB, or influenza) and 4) reducing diversity, thereby likely accelerating symptoms of chronic diseases such as metabolic syndrome, type 2 diabetes, and

chronic obstructive lung diseases (27). In this paper, we advocate and present an expanded view of the human metaorganism that includes its multiple links to the BE. Exploring the parallels between the BE and the immune system as gatekeepers of boundaries between inside and outside may hold promise for promoting health equity in environments throughout the world.

### Healthy Porosity

BE are interactional spaces shaped by multiple barriers and filters at different scales from buildings to neighborhoods to cities to landscapes. BEs allow climate control and enable humans to live in otherwise inhospitable sites. Architectural design often reduces natural elements such as soil and trees, and there is a reduction of environmental microbes from nature entering the building. It is estimated that 90% of contemporary human life in “developed” economies is now spent “indoors” (28). Like living organisms, buildings are formed by folding the exterior world into an interior (29). They become part of the organisms that inhabit them by acting as a second skin that modulates environmental conditions such as temperature into a narrow range and fosters internal symbiotic exchanges among the resident communities. However, shared pockets of space are partially sealed off from what is now treated as the “outside.” Increasing building porosity does not necessarily make for a healthier indoor environment. There are plenty of toxic microbiomes in the agricultural countryside, and there are pockets of healthy microbial environments in areas of cities. Here, we are advocating for a recalibration of porosity to permit desired circulations and

exposures, with the caveat that we are not yet sure what the ideal microbiome looks like.

As buildings become increasingly sealed, humans become the main source of microbes for the BE (9–11). But what kinds of microbiomes? Nineteenth century sanitary reform called for buildings to be reopened to fresh air, sunlight, and plants in response to the ravages of infectious disease (notably typhus, cholera, and tuberculosis) (30). However, building design has increasingly responded to energy constraints with ever more tightly enclosed buildings, often situated in settings that are themselves isolated from natural environments. Multiple BE systems (impervious materials, seals, filters, gaskets, layers, chemicals, air conditioning, nonoperable windows, etc.) create barriers between inside and outside and restrict diversity of environmental conditions and organisms. However, boundaries in the human metaorganism are not as strict (31). The human body and its resident microbes can communicate directly or indirectly—as in the gut where microbes or their metabolites can cross through intestinal membranes and communicate with the host immune and nervous system (Fig. 1A) (32–35). The interfaces between environment and organism (such as the gut and skin) are occupied by the microbiome (36). They are not solid lines but porous zones of communication and exchange between inner and outer. A more porous BE is likely to be healthier for all the metaorganisms that inhabit it (pollutants notwithstanding) for many reasons including that a more porous BE can increase exposure to outside microbes (which tend to contain very few human pathogens [ $<0.00001\%$ ; (9–13)] and dilute exposure to human-adapted microbes (which includes human pathogens).

## Buildings and the Immune Systems

Insights from immunology offer a way to think differently about the BE. The immune system may be understood as maintaining specific mixtures of microbes rather than simply defending inside commensals from outside pathogens (37–39). Is it possible to think about the built environment as an extension of the immune system, particularly considering that the brain and culture, which actively manage human-microbial interactions, are components of this system? The BE is somewhat similar to the immune system in terms of its ability to discriminate between desired and undesired exposures. Perhaps health is not simply microbial diversity but rather a dynamic maintenance of diversity (40). Does the BE become unhealthy because of exposure to its unhealthy components, or because it leads to the loss of exposure to healthier nonbuilt environments? Or both? Buildings may need to curate microbial diversity better to promote health, requiring us to rethink what “boundaries” we should be striving for. Extending the logic of the immune system (37), the BE does not consist simply of fixed physical limits but interactional spaces characterized by movement and exchange. These interactions change as space/place boundaries are crossed or not, with sociospatial inequities existing across various time and space scales. For example, children interact with the BE in ways that adults do not (licking, slobbering, ingesting things from the floor), and differences in exposures likely differ considerably throughout the world. We must inquire how we should map/layer microbiome studies along these

mobility networks, interaction networks, ages/life stages, and other intersectional demographic variables like “class”, income-levels, gender, and race/ethnicity.

Architecturally, variation in relationships between outside and inside is influenced by culture, climate, and available technological and environmental resources (Fig. 1B). In Japan, for example, sliding doors in traditional homes can be appreciated in microbiological terms as they allow more diverse microbial flows. Such nonwestern or indigenous structures may offer models of healthy BE because they often foster more fluid sets of relationships between inside and outside and emphasize transactional spaces that are neither inside nor outside (e.g., ref. 41). It is not yet clear how such structures alter the human microbiome, but we can hypothesize that a stronger connection to microbiomes outside of BEs results in greater overall microbial diversity “inside” BEs, which in turn increases the diversity of human microbiomes in ways associated with increased human health. This hypothesis should be tested across time (evolutionary, generational, and historical) and space (culturally and geographically).

## Rewilding the Interior

To rethink the BE in terms of curated exposure rather than prophylactic shelter is to argue that, in a deeper sense, genuine shelter to the human species is paradoxically offered by exposure. Furthermore, to promote health, we may need to optimize our BE by taking into consideration the existing microbial communities, treating them as fellow collaborative inhabitants (42). We may also initiate research on small scales to explore the conditions and composition of materials that favor the establishment of BEs that promote human health. The resolutely antimicrobial philosophy governing the design and occupation of contemporary spaces might give way to a probiotic one. We may need to “naturalize” the BE, e.g., by reintroducing soil and plants, using less toxic building materials, and less prophylactic assemblages. Is it worth experimenting with the idea of rewilding the interior (43, 44)?

There is a huge gap in knowledge about the importance of the BE for microbiomes. Throughout our evolutionary history, humans have manipulated, modified, and built their environments for survival, protection, convenience, social structure, aesthetics, and other reasons, usually with particular concepts of health in mind. New thinking about health is likely to foster new BEs (e.g., ref. 7). Changing microbial composition and diversity may constitute an emerging threat to global health, as BEs increasingly move toward less porous boundaries between interior and exterior. Hospitals provide important case studies for built environment-microbiome attention since they are BEs dedicated to the restoration of health. Recognition of hospitals as ecosystems themselves has led to the creation of a Hospital Microbiome Consortium (45). We are still far from an understanding of what an unhealthy (dysbiotic) microbiome is, apart from reduced diversity. In addition, completely sterile environments are not optimal for developmental programs and optimal organ function to sustain health and longevity (18, 46).

Buildings have had unintended health consequences since their invention, and while humans keep trying to make them healthier and safer, they often only induce more (and/or different) disease/health risks. In this sense, the “sick building

syndrome" (SBS) is as old as buildings (21). There are new toxicities today, in materials and systems, but the problem is ancient. Often societal attention on certain causes obscures others, as in the case of SBS where the focus on labor accidents in the workplace made people blind to potential building-related causes of illness. The fact that there are gender-specific differences in SBS prevalence, with a higher susceptibility in women (47), suggests that to understand this complex syndrome, understanding historical and social factors, among others, is necessary (21, 48). Such examples also challenge culturally and historically specific associations of inside-outside, home-work, and individual-communal distinctions. Cross-cultural studies may provide insights into the fluidity of boundaries and risks of the BE.

### Need for Experimental Model Systems

Future research must uncover causal relationships and go beyond correlative associations. Causality must, however, be sought in all directions and cannot be restricted to a simple separation between BE, BE microbiome, and human microbiome. To fully understand the interaction between the BE microbiome and the health of its inhabitants, we therefore crucially need experimental model systems that allow us to manipulate this interaction. However, all laboratory animal models are also BE models (since they are maintained in experimentally tractable BEs), but historically they have not been recognized as such, and consequently have been underutilized to address questions about BEs and metaorganism health and functioning. Such experimental BE models often exhibit phenomena similar to those of human BEs; for example, plastics used in laboratory BEs contain many synthetic chemicals, including endocrine disruptors which may impact the development and behavior of their residents, as well as health outcomes related to the microbiome (49–51). In addition to experimental models, there are many "natural models" of BE microbiome–human interactions. Many animals construct and manage BEs such as nests (52), burrows, tunnels, honeycombs made of plants, earth, sand, clay, paper, wood, wax, stones, slime, and silk (53), which are models of efficient ecological building and sustainability. Such BEs have long been considered important components of an animal's "extended phenotype," and as such are both a product and a driver of its evolution (54, 55). Such an intimate association between humans and their BEs is seldom considered. Comparative studies of human and animal interactions with their respective BE microbiomes (56) could bring an explicitly evolutionary perspective to BE research that currently is lacking.

### Realistic Engineering Considerations for Rethinking the Built Environment

Previous work has shown that microbial diversity in our bodies is crucial for health (9, 10, 18, 43, 49) and that all aspects of building design may influence human health outcomes. The way indoor spaces are conditioned conflict with promoting microbiome diversity. For example, the contemporary standards in place that define how "air conditioning" systems operate aim to create thermostasis by setting boundaries on the conditions inside (57). While many recognize problems

with thermal monotony of these systems, these mainly address the perception and psychology of unchanging climate conditions. New standards and concepts such as WELL standard, biophilic design, and Living Building Standard are starting to address these (58). However, the vast majority of our standard HVAC (heating ventilation and air conditioning) systems limit the evolution of interior ecosystem diversity and sometimes limit it to pathogens that have also evolved to enjoy humans' preferred climates (59). Alternative heating and cooling methods that depend on alternative heat transfer mechanisms such as radiant heat transfer can enable passive natural ventilation (60). At the core of this solution is the simple idea of opening windows, but the real innovation and challenge is recognizing and accepting that a sensation of hot or cold can be achieved independent of air temperature, and thermal comfort can be maintained at temperatures ranging from 10 to 34 °C (61), way outside standard thermostat controls, which have propagated the myth that indoor air temperature is the factor that determines one's comfort. It does certainly determine the types of bacteria that will be most common. By breaking conventional paradigms and expectations for our built environment to be at a constant temperature, we can open the door, literally and figuratively to a more dynamic thermal experience and microbiome. On a conceptual level, such considerations make it clear that the question of microbial diversity and climate change are not rival priorities but deeply interrelated.

The concept of the "healthy house" (both as prevention and as cure) is ancient. In addition, the idea to avoid sealed buildings unless there is an evidence-based reason to do so is old wisdom (from Florence Nightingale and before). However, although we now have a new perspective on why a connection to the outside environment is important, we have not yet understood the role of built environment design in maintaining a diverse microbiome and preventing disease simply because we have not addressed the question from a BE microbiome–human health perspective. Questions to be addressed in the future include the following: How do we define a healthy building? A healthy microbiome? How do we reconcile BE and nature? How can we transform BEs to maximize microbial diversity in all its forms—which allows for flexibility and resilience and, in turn, permits adaptation to changing forces and challenges? And for whom? How do we consider all animal and plant-life, and even the microbes themselves, as the residents of BE equally deserving care? Answering those questions (see also refs. 62 and 63) requires a radical rethinking of how buildings (and the expanded BE) are designed, made, lived, and maintained at the macro- and microscale. That is, BE microbiome and building material research are highly warranted and should be applied to consider regional climate variation, ecological variation, and cultural variation among human beings.

### Conclusion

Most of human evolution occurred in contact with nonhuman worlds, often through very porous "homes." Our contemporary way of life ignores the fact that over thousands of years the body has come to terms with its environment and its microbes in the best possible ways and that it is only fit and healthy as a metaorganism. Only by embracing this

multiorganismic complexity will we come to a deep understanding of health and thus to an understanding of common lifestyle diseases. The decisions we make about our BEs influence how we sustain and support microbial diversity. Constructing BEs with the microbiome in mind is a grand challenge for the 21st century, with opportunities for addressing social and environmental justice from a broad ecological and One Health perspective (20). Microbiome-aided design aims to ensure that the specific needs of certain microbial communities are incorporated into architectural designs for new buildings and urban spaces. This can only be reached in inter- and trans-disciplinary projects between architects, designers, anthropologists, and microbiologists integrating cross-space (cultural, geographical), cross-time

(historical, evolutionary), cross-scale, and cross-species perspectives. The potential of microbe-sensitive BEs is huge and has been relatively unexplored to date. This article highlights the need for novel experimental research where biologists and social scientists work closely with engineers to develop 21st-century buildings that support prolonged human and environmental health.

**Data, Materials, and Software Availability.** All study data are included in the main text.

**ACKNOWLEDGMENTS.** We acknowledge funding from the Canadian Institute for Advanced Research. T.C.G.B., M.W., and B.C. thank the Wissenschaftskolleg zu Berlin for generous support. We thank Katja Duwe-Schrinner for help with the figure.

1. P. J. Turnbaugh *et al.*, The human microbiome project. *Nature* **449**, 804–810 (2007), 10.1038/nature06244.
2. M. McFall-Ngai *et al.*, Animals in a bacterial world, a new imperative for the life sciences. *Proc. Natl. Acad. Sci. U.S.A.* **110**, 3229–3236 (2013), 10.1073/pnas.1218525110.
3. R. Knight *et al.*, Best practices for analysing microbiomes. *Nat. Rev. Microbiol.* **16**, 410–422 (2018).
4. S. Runge, S. P. Rosshart, The mammalian metaorganism: A holistic view on how microbes of all kingdoms and niches shape local and systemic immunity. *Front. Immunol.* **12**, 702378 (2021), 10.3389/fimmu.2021.702378.
5. E. Turpin, *Architecture in the Anthropocene: Encounters Among Design, Deep Time, Science and Philosophy* (Open Humanities Press–Michigan Publishing, University of Michigan Library, Ann Arbor, MI, 2014).
6. S. Hagan, *Ecological Urbanism: The Nature of the City* (Routledge, 2014).
7. S. Hagan, *Revolution? Architecture and the Anthropocene* (Lund Humphries, 2022).
8. A. S. Wilkins, A molecular investigation of human self-domestication. *Trends Genet.* **36**, 227–228 (2022), 10.1016/j.tig.2020.01.002.
9. L. I. McCall *et al.*, Home chemical and microbial transitions across urbanization. *Nat. Microbiol.* **5**, 108–115 (2020), 10.1038/s41564-019-0593-4.
10. J. F. Ruiz-Calderon *et al.*, Walls talk: Microbial biogeography of homes spanning urbanization. *Sci Adv.* **2**, e1501061 (2016), 10.1126/sciadv.1501061.
11. J. A. Gilbert, B. Stephens, Microbiology of the built environment. *Nat. Rev. Microbiol.* **16**, 661–670 (2018), 10.1038/s41579-018-0065-5.
12. J. Chase *et al.*, Geography and location are the primary drivers of office microbiome composition. *mSystems* **1**, e00022-16 (2016).
13. D. Danko *et al.*, International MetaSUB Consortium, A global metagenomic map of urban microbiomes and antimicrobial resistance. *Cell* **184**, 3376–3393.e17 (2021), 10.1016/j.cell.2021.05.002.
14. L. J. Martin *et al.*, NESCent Working Group on the Evolutionary Biology of the Built Environment, Evolution of the indoor biome. *Trends Ecol. Evol.* **30**, 223–232 (2015), 10.1016/j.tree.2015.02.001.
15. A. J. Hoisington *et al.*, The microbiome of the built environment and mental health. *Microbiome* **3**, 60 (2015), 10.1186/s40168-015-0127-0.
16. J. Peccia, S. E. Kwan, Buildings, beneficial microbes, and health. *Trends Microbiol.* **24**, 595–597 (2016), 10.1016/j.tim.2016.04.007.
17. M. J. Claesson *et al.*, Gut microbiota composition correlates with diet and health in the elderly. *Nature* **488**, 178–184 (2012), 10.1038/nature11319.
18. B. B. Finlay *et al.*, The hygiene hypothesis, the COVID pandemic, and consequences for the human microbiome. *Proc. Natl. Acad. Sci. U.S.A.* **118**, e2010217118 (2021), 10.1073/pnas.2010217118. Erratum. In: *Proc. Natl. Acad. Sci. U.S.A.* **118**, PMID: 33472859; PMCID: PMC8017729.
19. S. A. Inkpen, Health, ecology and the microbiome. *eLife* **8**, e47626 (2019), 10.7554/eLife.47626.
20. J. S. Mackenzie, M. Jeggo, The one health approach—Why is it so important? *Trop. Med. Infect. Dis.* **4**, 88 (2019), 10.3390/tropicalmed4020088.
21. M. Murphy, *Sick Building Syndrome and the Problem of Uncertainty: Environmental Politics, Technoscience, and Women Workers* (Duke University Press, 2006).
22. S. W. Kembel *et al.*, Architectural design influences the diversity and structure of the built environment microbiome. *ISME J.* **6**, 1469–1479 (2012), 10.1038/ismej.2011.211.
23. S. W. Kembel *et al.*, Architectural design drives the biogeography of indoor bacterial communities. *PLoS ONE* **9**, e87093 (2014).
24. S. Lax *et al.*, Longitudinal analysis of microbial interaction between humans and the indoor environment. *Science* **345**, 1048–1052 (2014), 10.1126/science.1254529.
25. Y. Shan *et al.*, Modern urbanization has reshaped the bacterial microbiome profiles of house dust in domestic environments. *World Allergy Organ. J.* **13**, 100452 (2020), 10.1016/j.waojou.2020.100452.
26. P. F. Horve *et al.*, Building upon current knowledge and techniques of indoor microbiology to construct the next era of theory into microorganisms, health, and the built environment. *J. Expo. Sci. Environ. Epidemiol.* **30**, 219–235 (2020), 10.1038/s41370-019-0157-y.
27. G. Mitman, *Breathing Space: How Allergies Shape Our Lives and Landscapes* (Yale University Press, 2008).
28. N. Klepeis *et al.*, The National Human Activity Pattern Survey (NHAPS): A resource for assessing exposure to environmental pollutants. *J. Expo. Sci. Environ. Epidemiol.* **11**, 231–252 (2021), 10.1038/sj.sj.7500165.
29. M. Wigley, “The excremental interior” in *Edible: Or, The Architecture of Metabolism*, L. Kallipoliti, A. Markopoulou, Eds. (Tallin Architecture Biennale, 2022).
30. Institute of Medicine, *The Future of Public Health* (The National Academies Press, Washington, DC, 1988).
31. T. Rees, T. C. G. Bosch, A. E. Douglas, How the microbiome challenges our concept of self. *PLoS Biol.* **16**, e2005358 (2018), 10.1371/journal.pbio.2005358.
32. V. Neveu *et al.*, The human microbial exposome: Expanding the Exposome-Explorer database with gut microbial metabolites. *Sci. Rep.* **13**, 1946 (2023), 10.1038/s41598-022-26366-w.
33. M. Valles-Colomer *et al.*, Cardiometabolic health, diet and the gut microbiome: A meta-omics perspective. *Nat. Med.* **29**, 551–561 (2023), 10.1038/s41591-023-02260-4.
34. S. Miri *et al.*, Neuroimmunology, an emerging neuro-metabolic facet of the gut microbiome? *Front. Microbiol.* **14**, 1098412 (2023), 10.3389/fmicb.2023.1098412.
35. K. G. Jameson *et al.*, Toward understanding microbiome-neuronal signaling. *Mol. Cell.* **78**, 577–583 (2020), 10.1016/j.molcel.2020.03.006.
36. B. B. Finlay, CIFAR Humans, The Microbiome, Are noncommunicable diseases communicable? *Science* **367**, 250–251 (2020), 10.1126/science.aaz3834.
37. E. Martin, Toward an anthropology of immunology: The body as nation state. *Med. Anthropol. Q.* **4**, 410–426 (1990), <http://www.jstor.org/stable/649224>.
38. M. McFall-Ngai, Care for the community. *Nature* **445**, 153 (2007), 10.1038/445153a.
39. T. C. G. Bosch, Rethinking the role of immunity: Lessons from Hydra. *Trends Immunol.* **35**, 495–502 (2014), 10.1016/j.it.2014.07.008.
40. A. I. Tauber, *Immunity: The Evolution of an Idea* (Oxford Academic, New York, NY, 2017), 10.1093/acprof:oso/9780190651244.001.0001.
41. K. Stagaman *et al.*, Market integration predicts human gut microbiome attributes across a gradient of economic development. *mSystems* **3**, e00122-17 (2018).
42. B. Colomina, M. Wigley, The bacterial clients of modern architecture. *Docomomo J.* **62**, 6–17 (2020).
43. J. G. Mills *et al.*, Relating urban biodiversity to human health with the “holobiont” concept. *Front. Microbiol.* **10**, 550 (2019), 10.3389/fmicb.2019.00550.
44. C. Ramirez-Figueroa, R. Beckett, Living with buildings, living with microbes: Probiotics and architecture. *Archit. Res. Q.* **24**, 155–168 (2020), 10.1017/S1359135520000202.
45. D. Smith *et al.*, The Hospital Microbiome Project: Meeting Report for the 1st Hospital Microbiome Project Workshop on sampling design and building science measurements, Chicago, USA, June 7th–8th 2012. *Stand. Genom. Sci.* **8**, 112–117 (2013), 10.4056/sigs.3717348.
46. K. B. Hooks, M. A. O’Malley, Dysbiosis and its discontents. *mBio* **8**, e01492-17 (2017), 10.1128/mBio.01492-17.
47. S. Brasche *et al.*, Why do women suffer from sick building syndrome more often than men? Subjective higher sensitivity versus objective causes. *Indoor Air* **11**, 217–222 (2001), 10.1034/j.1600-0668.2001.110402.x.
48. I. L. Niza *et al.*, Sick building syndrome and its impacts on health, well-being and productivity: A systematic literature review. *Indoor Built. Environ.* **33**, 218–236 (2024), 10.1177/1420326X231191079.
49. S. P. Rosshart *et al.*, Wild mouse gut microbiota promotes host fitness and improves disease resistance. *Cell* **171**, 1015–1028.e13 (2017), 10.1016/j.cell.2017.09.016.
50. S. E. Hamilton *et al.*, New insights into the immune system using dirty mice. *J. Immunol.* **205**, 3–11 (2020), 10.4049/jimmunol.2000171.
51. H. K. Kwon, J. K. Seong, New insights into the microbiota of wild mice. *Mamm. Genome* **32**, 311–318 (2021), 10.1007/s00335-021-09887-z.
52. F. Campos-Cerda, B. J. M. Bohannan, The nidobiome: A framework for understanding microbiome assembly in neonates. *Trends Ecol. Evol.* **35**, 573–582 (2020), 10.1016/j.tree.2020.03.007.
53. M. L. Smith, N. Napp, K. H. Petersen, Imperfect comb construction reveals the architectural abilities of honeybees. *Proc. Natl. Acad. Sci. U.S.A.* **118**, e2103605118 (2021), 10.1073/pnas.2103605118.
54. R. Dawkins, *The Extended Phenotype: The Long Reach of the Gene*, C. Simonyi, Ed. (Oxford Landmark Science, Oxford University Press, Oxford, 1982).
55. P. Hunter, The revival of the extended phenotype: After more than 30 years, Dawkins’ extended phenotype hypothesis is enriching evolutionary biology and inspiring potential applications. *EMBO Rep.* **19**, e46477 (2018).
56. S. P. Rosshart *et al.*, Laboratory mice born to wild mice have natural microbiota and model human immune responses. *Science* **365**, eaaw4361 (2019), 10.1126/science.aaw4361.
57. ASHRAE Standard 55—Thermal environmental conditions for human occupancy. <https://www.ashrae.org/technical-resources/bookstore/standard-55-thermal-environmental-conditions-for-human-occupancy>. Accessed 8 April 2024.

58. International WELL Building Institute. <https://www.wellcertified.com/>. Accessed 8 April 2024.
59. R. Leach, Ventilation and the risk of health care-associated infections. *Infect. Control Today* **27**, 7 (2023).
60. D. Aviv *et al.*, A fresh (air) look at ventilation for COVID-19: Estimating the global energy savings potential of coupling natural ventilation with novel radiant cooling strategies. *Appl. Energy* **292**, 116848 (2021), 10.1016/j.apenergy.2021.116848.
61. E. Teitelbaum *et al.*, Membrane-assisted radiant cooling for expanding thermal comfort zones globally without air conditioning. *Proc. Natl. Acad. Sci. U.S.A.* **117**, 21162–21169 (2020), 10.1073/pnas.2001678117.
62. R. I. Adams *et al.*, Ten questions concerning the microbiomes of buildings. *Build. Environ.* **109**, 224–234 (2016), 10.1016/j.buildenv.2016.09.001.
63. National Academies of Sciences, Engineering, and Medicine, National Academy of Engineering, Division on Engineering and Physical Sciences, Health and Medicine Division, Division on Earth and Life Studies, Board on Infrastructure and the Constructed Environment, Board on Environmental Studies and Toxicology, Board on Life Sciences, Committee on Microbiomes of the Built Environment: From Research to Application, *Microbiomes of the Built Environment: A Research Agenda for Indoor Microbiology, Human Health, and Buildings* (National Academies Press, Washington, DC, 2017).