

A pluralistic approach to thinking about the human microbiome

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In "The Conceptual Ecology of the Human Microbiome," published in the June 2019 issue of *The Quarterly Review of Biology*, Nicolae Morar and Brendan J. M. Bohannan examine in detail the different metaphors scientists use to describe the human microbiome. Because it appears that each view has both advantages and disadvantages, the authors suggest the pragmatic approach of considering all metaphors when exploring therapies for diseases and disorders.

The human [microbiome](#) is the complex system of microorganisms on and in the [human body](#) that is crucial to many metabolic and immunity functions. Morar and Bohannan chose five of the most common ways scientists think of the human microbiome, examining the benefits that each [conceptual framework](#) offers in designing therapeutics, as well as the limitations of each.

"Each of the common conceptual frameworks we describe here captures important truths—and misses crucial aspects—of our human-microbe selves." Morar and Bohannan write. "Although there is no evidence (yet) that one conceptual framework is more accurate or more useful or somehow 'better' than another, insights emerge as we consider these metaphors together as a whole."

The "organ" framework views the function of our microbiome as that of an organ of human body. From this perspective, some very specific therapies emerge, in which the infections of the microbiome are viewed as "organ failure" that can be remedied with a transplant. For example,

in treating the infection of the gut by the bacterium *Clostridium difficile*, one study found that a treatment of antibiotics and subsequent transplant of a donor's feces produced a much higher cure rate than those treated with antibiotics alone.

But while the organ framework captures the important functional contributions that microbes make to human physiology, it misrepresents the fact that the composition is not static, but rather, is ever-changing. The authors write that "[o]rgans tend not to change substantially over time...However, there is ample evidence that changes of the microbiota over time can be associated with [significant changes](#) in organism function."

The "immune system" framework views the human microbiome as a component of the immune system, emphasizing the importance of how the microbiome is acquired early in life and the role that the acquisition may play in the development of the immune system, both by stimulating the development of the immune system and by training it. This view is important when considering the implications, for instance, of vaginal canal birth versus cesarean section. It has been observed that babies delivered through the birth canal have a more diverse microbiome, which could lead to a more robust immune system. Therapies wherein a mother's vaginal canal is swabbed and transferred to a newborn's mouth and skin is one such therapy arising from this framework.

Ultimately, the [immune system](#) view of the human microbiome is incomplete, because it does not take into account all of the metabolic services we receive from our microbiome, nor does it consider the complexity of host-microbe interactions.

The "superorganism" framework focuses on the coevolved, cooperative mechanisms at play in the human-microbe system. Under this framework, it is assumed that there is a health risk in allowing niches

that were formerly occupied by bacterium remain vacant, and emphasis is put on the idea that restoring the ancestral human microbiome will help treat many disorders. This is relevant, for instance, in the potential link between antibiotics and some metabolic diseases, with some researchers even proposing that the rise of modern allergies, asthma, and metabolic diseases such as type 2 diabetes are due to the breakdown of the ancestral microbiome, Morar and Bohannan write.

The framework runs into problems, however, in its assumption that variation in group fitness is genetically heritable. This is not what has been observed, the authors write, citing a 2018 study that estimated fewer than 2% of the microbial taxa in the human microbiome show significant heritability. The framework also downplays the many possible instances where competition occurs among the individuals in a superorganism, since one of the tenants of the framework is that all members are equal in fitness. Although a truly mutualistic situation is plausible, it is most likely rarer than this framework implies.

The "holobiont" framework views humans and their microbes as entities that coevolved together to maximize the fitness of their combined genome. Like the superorganism view, this framework regards humans and their microbes as a tightly-knit product of coevolution, but takes into greater account the dynamism and porosity between host and microbes. One therapy that emerges from this view is probiotic therapy, wherein specific microbes are introduced as a means to promote health. Like the superorganism view, this framework relies on the assumption that [human microbiome](#) as a whole has significant heritability, which is not something that scientists have found.

The "ecosystem" framework emphasizes the ongoing movement of microbes entering and leaving the human-microbe system. Heritability is downplayed in this view, with emphasis instead on local factors, as well as even an element of randomness, affecting the movement of microbes

and composition of our microbiomes. This framework runs into problems, however, in its failure to recognize the strength of some of the connections between host and microbe, which do have the ability to coevolve. Moreover, this view might present difficulties in developing therapies.

"It has been argued that it is especially difficult to assign causality in complex systems with fluid boundaries...which could make it very difficult to use this metaphor to develop clinical applications," Morar and Bohannan write. "Thus, the ecosystem metaphor may result in a view of human-microbe systems that is too complex to be helpful."

The authors suggest that researchers keep all viewpoints in mind when developing therapies, writing that there is not, at present, a clear view of which framework is more "correct" than others. More than likely, each framework is probably very useful in some scenarios and not very useful in others.

Morar and Bohannan write "...that some aspects of our microbial selves can be transplanted successfully (with subsequent transfer of function), while others must be restored gradually and carefully managed over time, and still other aspects may be highly sensitive to their initial development (and may be very difficult to subsequently change)."

The authors also say that "[t]he ultimate goal then is not to avoid using various concepts and metaphors to describe the human-microbe system, nor to choose the 'best' conceptual [framework](#), but rather to use all of these concepts to guide the exploration of our complexity as chimeric beings, and ultimately to fully understand the multitude of ways in which we are human."

More information: Nicolae Morar et al, The Conceptual Ecology of the Human Microbiome, *The Quarterly Review of Biology* (2019). [DOI:](#)

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