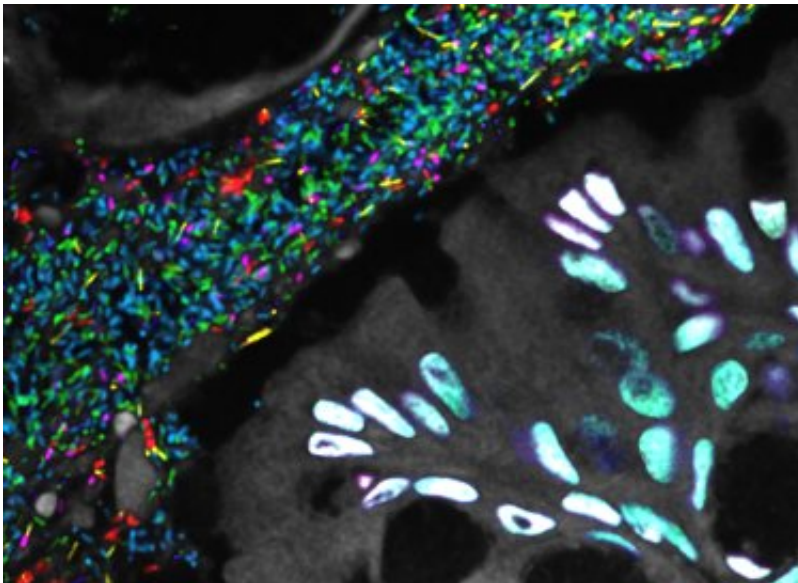


# Researchers create map of the gut's microbial landscape

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Credit: Forsyth Institute

A collaborative effort by a team of researchers from three institutions including the Marine Biological Laboratory (MBL) in Woods Hole, the Forsyth Institute in Cambridge and Washington University in St. Louis provided an early glimpse of how microbial communities in the gut - known collectively as the gut microbiome - are spatially organized, uncovering a surprising degree of mixing among different bacterial members.

The study, which will appear in the October 13 issue of *The Proceedings*

*of the National Academy of Sciences (PNAS)*, is the first to examine the three-dimensional structure of a diverse array of [gut microbes](#) and uncovers some stark differences between the microbial landscape of the gut and those of other body sites, such as the mouth.

"No one has looked at a complex microbial community in the gut this way before," said senior author Gary Borisy, a senior research investigator at the Forsyth Institute. "If we truly want to understand the role of the [microbiome](#), it is not enough to know just which microbes are present. We must also learn what they are doing, who they are talking to and why. Part of the answer to that problem is to figure out who is next to who and who is next to what."

That is precisely what Borisy and his colleagues, including first author Jessica Mark Welch of the Marine Biological Laboratory and colleagues in the Gordon laboratory at Washington University in St. Louis, set out to do. The research team introduced 15 different bacterial species into germ-free mice, creating a humanized model of the gut microbiome. Although it is only a partial representation of the full suite of microbes typically found in the [human gut](#), this simplified microbial community provided a key opportunity to explore how microbes assemble into distinct neighborhoods.

"We used probes that lit up each of the bacterial species with a different color, so that we could see exactly how the bacteria were arranged relative to each other and relative to landmarks like food and host tissue," said Jessica Mark Welch, associate scientist with the Marine Biological Laboratory.

Based on previous studies of the gut microbiome as well as their own research on the oral microbiome (specifically the plaque that forms on teeth), the research team expected to see a significant amount of structure.

"At the sites we've examined so far in the mouth, we see highly ordered microbial communities - so much so that you might imagine them as multicellular organs, like a liver or a thymus gland," explained Borisy. "They are made of bacterial cells, of course, but there are many different cell types organized in a highly structured way like a body organ."

But that is not what they found. In the gut, the researchers observed a high degree of mixing among microbes - not a completely homogeneous mixture, but still highly intermingled. "We liken it to a bioreactor, where things are stirred around and well mixed," added Borisy.

Even though this model gut microbiome lacked highly organized structure, the researchers did identify some "micro"-habitats, where bacterial cells tend to congregate. These sites include the tissue lining the interior surface of the gut (the "epithelium"), which is typically coated with a layer of mucus. They also include the central space (the "lumen"), where food as well as mucus are collected. While the microbial populations at these locations varied somewhat in their overall makeup - that is, the relative proportions of the different bacteria may fluctuate - the researchers did not observe any stark differences, such as a [bacterial species](#) found exclusively at one site and not another.

"We think the host is homogenizing the microbial community, using muscle contractions to mix the contents of the gut and push them up against the gut wall, and sloughing mucus and epithelial cells from the wall into the lumen," added Mark Welch. "It may be that this mixing is what enables a stable relationship between the host and the microbes."

The researchers' ability to resolve this intricate microbial picture flows from an experimental strategy in which Borisy and his colleagues combine sophisticated technologies and methods. These include chemical techniques that make it possible to label 15 different microbes; advanced imaging methods that can detect and resolve these labels;

cutting-edge microscopy that can slice through tissues optically (rather than physically) to visualize complex, three-dimensional specimens; and software that facilitates the analysis and reconstruction of hundreds of biological images. This innovative approach was first applied to studies of the plaque microbiome, published by Borisy and his colleagues in 2016, and more recently to the gut microbiome, as described in their new PNAS study.

Although the [gut microbiome](#) may seem disconnected from those found in other parts of the body, there are crucial lessons that may emerge from studying them in a holistic way. Most of the Forsyth Institute's work is on the oral microbiome with a driving goal to better understand microbial communities. In addition to better understanding what the rules are for governing one particular microbiome by studying a variety of sites in the body, it is also possible that [microbial communities](#) - while physically separate - can interact in ways that influence health.

Borisy emphasized that this type of microbiome research is in its infancy. Nevertheless, it is essential for developing a deep understanding of microbial function. "Imagine that you come into Boston and someone hands you a telephone directory of everyone who lives there. That's great - now you have a list of who is there. But tell me, how much have you learned about Boston as a city?"

**More information:** Mark Welch JL, Hasegawa Y, McNulty NP, Gordon JJ, Borisy GG. "Spatial organization of a model 15-member human gut microbiota established in gnotobiotic mice." *Proceedings of the National Academy of Sciences* [DOI: 10.1073/pnas.171596114](https://doi.org/10.1073/pnas.171596114)

Provided by Forsyth Institute

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