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Microbiology

Microbial life on our tongue

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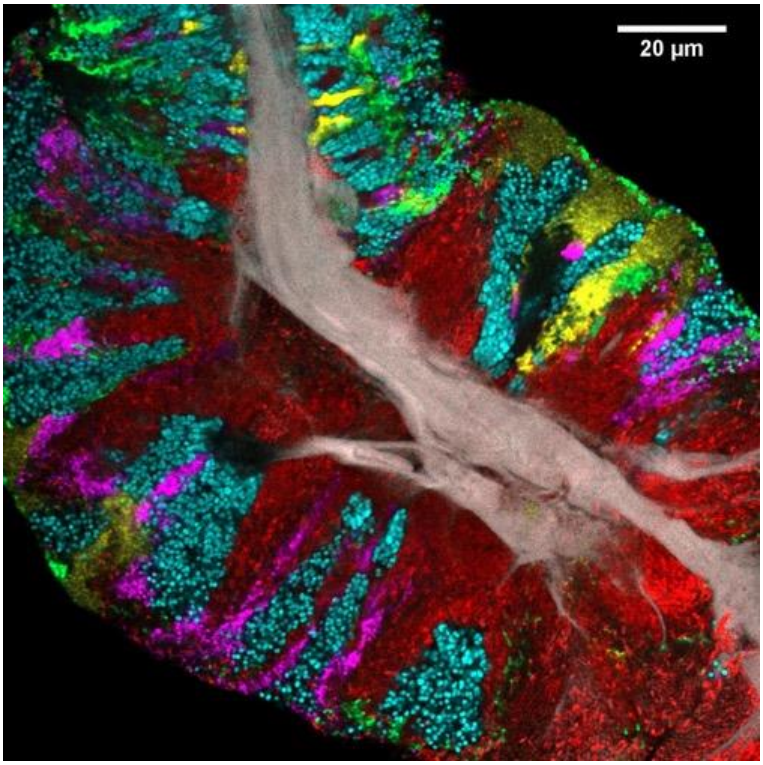
Our tongue is inhabited by billions of microbes. But are they beneficial for us? A new imaging technique reveals that these microbes build organized communities with a patchy mosaic structure, extending our understanding of how microbes live with us and contribute to our health.



Microscope picture of microbes on a human tongue. Each small dot shows a bacterial cell and the colors indicate different types of bacteria. The wide gray stripe at the core comes from human tongue cells.
Image credits: Steven Wilbert and Gary Borisy, The Forsyth Institute

Stick out your tongue! That's one of the first things you hear when you visit a doctor. The tongue has been used as an indicator of health or disease for thousands of years: from ancient Egypt and Chinese traditional medicine to today's modern medical practice worldwide. But what does the doctor hope to learn by looking at your tongue? The color, texture, and smell of the coating on the tongue are all clues to the body's health. We now know that our health is tightly connected with microbes that live in or on us. Amazingly, around 20 billion microbes live on our tongue.

The tongue's coating is the consequence of an 'evolutionary bargain' struck between the body and its microbes. We offer microbes a comfortable place to live: a warm and moist tongue surface bathed in saliva on which they can feed. In return, they protect us from invaders and help train our immune system, and astonishingly, some help us control blood

pressure. To see how this evolutionary bargain might work, we wanted to look at the structure of communities that microbes build on the tongue. Everywhere in biology, function is tied to structure. If we want to know how microbes interact with each other, we have to learn how their communities are organized on the scale on which they live – the microscopic scale.

To see the tongue microbial communities in all their complexity, we developed a new experimental strategy and combined it with advanced optical microscopy. The strategy was to label each kind of microbe with a different color. We took advantage of the fact that DNA – which carries the unique genetic information of every living thing – has differences that we could use to distinguish the different kinds of microbes. We designed a barcode molecule – a short piece of synthetic DNA that specifically recognizes the target microbe and reports the presence of the microbe by producing a color. We then collected tongue microbes and tongue surface cells by gently scraping the tongue of a volunteer. Not to worry! Although scraping dislodges some of the microbes, many remain and the full population grows back by the next day. Then we stained our samples with our multi-color set of DNA barcodes. To see the many colors at once, we used a microscope that could record the full range of colors from each pixel. Since the colors were too similar to distinguish by eye, we used a mathematical algorithm to separate them and distinctly visualize all the color-labeled microbes and their arrangement in space.

The results were stunning. The microbes built intricate and organized structures on the tongue. These microbial communities had a patchy, mosaic structure organized around a core of tongue surface cells. Different microbes took up different positions in the community: large patches near the core (shown as red in the cover image), stripes stretching from the core toward the surface (cyan or magenta), and a thin crust on the surface (green). While the images were only snapshots in time, they let us develop ideas about the dynamic growth of the microbial community. The shapes and locations of the patches, stripes, and crusts show us how fast the different microbes grow in different places on our tongue.

Why do microbes form these characteristic structures in our mouths? What do they get out of it? Is it beneficial to us? Some microbes use nitrate instead of oxygen to burn food and produce energy. In the process, they convert nitrate to nitrite. This benefits us because we use the nitrite to make nitric oxide, a key regulator of blood pressure. So, by eating vegetables that are rich in nitrate, we help the microbes live and they help us control our blood pressure. Our microscope pictures captured that these nitrate-consuming microbes formed patches on the tongue's surface, perhaps to make their use of nitrate more efficient. Our body has likely encouraged the growth of these microbes on the tongue as a way to process dietary nitrate. This is a striking example of the 'win-win' evolutionary bargain struck by the body with its oral microbes.

The patchy, mosaic pattern created by microbe communities is universal, but individuals may differ in the detailed structure of their tongue microbial communities. These differences may prove useful in the diagnosis of health and disease. Learning how to interpret the significance of such differences will require future research. Someday we might be able to use oral microbes as a therapeutic or a probiotic. There are still barriers to that dream: we don't know how to remove a particular type of microbe from the community or how to get a new one to thrive there. We believe that studying the microbial actors in their native landscape will give us the clues we need to get closer to that goal.