

Microbes inhabit almost every part of the human body, living for example in gut, on the eye and skin in the total number of dozens of trillions of cells. Estimates suggest there are more than ten thousand bacterial species living in the human body, forming a complex community called the microbiome. This number is constantly being refined as researchers discover new species. On the other site, the total number of bacterial species living on Earth is estimated to be over 1 trillion. However, only about 660,000 species have their genome determined i.e. 99.99993% bacterial species remain undiscovered.

The microbiome, particularly the gut microbiome, plays a surprisingly vast role in our overall health. The gut microbiome helps break down food, allowing us to absorb nutrients effectively; helps regulate the immune system, fighting off harmful bacteria and prevents inflammation. Emerging research suggests the gut microbiome might influence brain function and mental health through a complex gut-brain connection. On the other site, An imbalance in the gut microbiome has been linked to various health conditions, including obesity, heart disease, diabetes, and even certain cancers. The relationship between the microbiome and obesity is complex. Obese individuals tend to have a different gut microbiome makeup compared to lean people. This often includes lower bacterial diversity and a shift in the ratio of certain types of bacteria. Moreover, the gut microbiome plays a role in regulating how our body extracts energy from food. Some gut bacteria are more efficient at extracting calories. While the exact cause-and-effect relationship with obesity is being explored, understanding this connection paves the way for potential future interventions.

We plan to develop a powerful new tool that can examine each individual bacterium in a community, like the gut microbiome. This tool would look at both the bacteria's DNA (its blueprint) and its active genes (like the instructions being used). We're developing this tool by combining cutting-edge techniques in chemistry, physics, and genetics. Here's how it works: We can analyze hundreds of thousands of bacteria at once, like taking a giant fingerprint of their DNA and genes. We use special labels to track each bacterium and sequence its entire genetic code, along with which genes are turned on. This allows us to see not only what kind of bacteria are present (species level) but also what each individual bacterium is doing (cell state level). This technology will be a game changer for understanding the microbiome. It's like creating detailed maps of healthy and diseased microbiomes, revealing not only the composition of the microbiome but also which biological or to be more specific metabolic pathways are affected in disease conditions. This knowledge could lead to new treatments.

Before we unleash this new methodology on real gut microbiomes, we need to make sure it works! We'll start by testing it on bacteria we already understand well. We will compare the results our method gives us with existing information from other studies that looked at single bacteria RNA molecules or how well we are in reconstructing known bacterial genomes. Once we're confident our tool is accurate, we will use it to study the gut microbiome. We're particularly interested in how these bacteria changes in shifts of Western diet. Currently, there is a worldwide rise in the popularity of the so-called Western diet, which is a high-fat diet high in saturated fatty acids of animal origin, simple sugars and salt. The consequence of consuming a Western-type diet is a sharp increase in obesity and its consequences known as metabolic syndrome. The goal of the project is to demonstrate that changing dietary habits by partially replacing animal fats with various vegetable oils in a Western-type diet can be beneficiary for maintaining the healthy microbiome and to understand the microbiome dynamics at longitudinal studies.

In addition, we will develop a new computational workflow for preprocessing and analysis of raw data generated in the project. The focus will be put on annotation, reconstruction, identification of the genome and characterization of cell states for each bacterial species. In addition, we will leverage a deep learning approach a powerful artificial intelligence technique to analyze the complex interactions between the products of bacteria's genes. This will help us understand the biological pathways active within each single cell, essentially figuring out what overall processes are happening inside each bacterium. The method will be validated extensively in multiple experiments on model bacteria.

Overall, this new proposed approach promises a revolutionary understanding of the complex world of microbiomes.