SETTING NEW STANDARDS IN METAGENOMICS AND MICROBIOME SEQUENCING

HIGH-RESOLUTION SEQUENCING TO RESOLVE AND CHARACTERIZE COMPLEX MICROBIAL COMMUNITIES

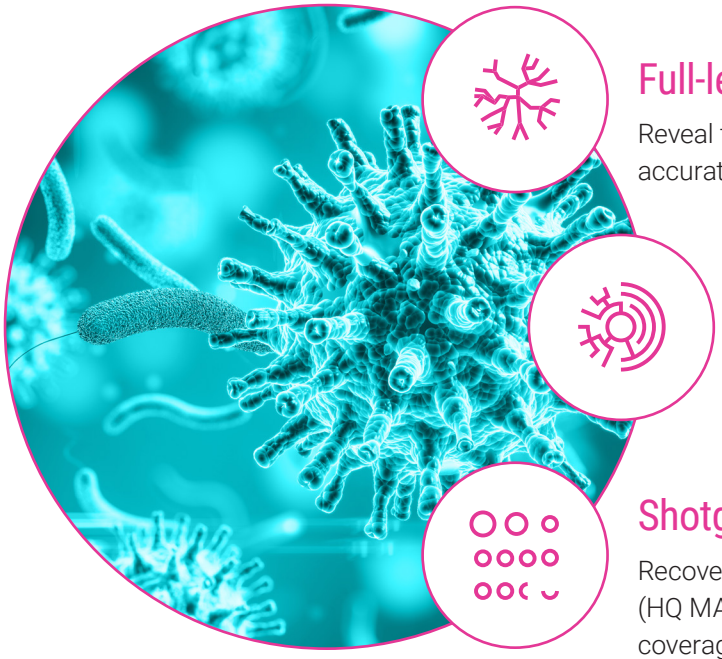
The microbiome is the collection of trillions of microbes, including bacteria, fungi, and viruses, that live in, on, and around us and the systems we depend on.[1] Characterizing the composition of microbial communities and exploring how these microbes interact with each other in the human gut, in animals, on built environments, and in natural ecosystems is central to understanding their role in human, animal, and environmental health. Accurate and flexible HiFi solutions for metagenomics and microbiome sequencing allow researchers to study microbes and microbial communities in high resolution without the need for culturing.

The outstanding accuracy and long read lengths of HiFi sequencing gives scientists the flexibility and high resolution they need to:

- Comprehensively dissect entire microbial communities to strain-level resolution without the need to culture
- Characterize complex microbial communities to understand their role in human, animal, and environmental health
- Identify and fully characterize novel species and better assemble new genomes

*"With [PacBio], we can now **sequence complete genomes** of nearly all abundant bacteria in a microbiome. Short-read studies rarely provided complete sequences of even a single microbe."*[2]

— Mikhail Kolmogorov, National Cancer Institute



Full-length 16S

Reveal the true diversity of complex microbiomes with highly accurate, species- and strain-level resolution

Shotgun metagenome profiling

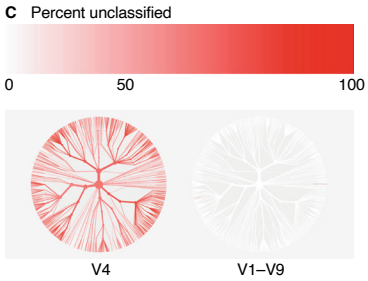
Achieve taxonomic profiles with high precision and recall and obtain rich functional information

Shotgun metagenome assembly

Recover far more high-quality metagenome assembled genomes (HQ MAGs) and more circular, single-contig MAGs, even at lower coverage

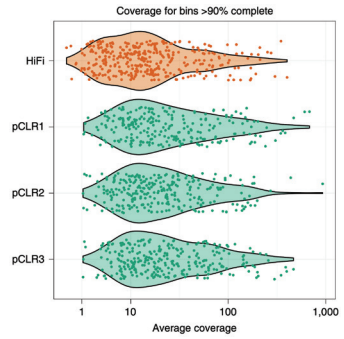
"HiFi reads allows us to generate a nearly complete picture of the metagenome**, not just a fragmented assembly. Like complete genomics, which is already being applied to rare disease diagnostics, **complete metagenomics may soon make its way into medicine and many other disciplines."[2]

— Pavel A. Pevzner, University of California San Diego



Full-length 16S is the only way to resolve all clades in the human gut, without bias[3]

- The proportion of 16S sequences from each bacterial genus that cannot be identified at the species level varies significantly depending on which variable region is used
- Since the human gut can harbor a broad diversity of bacterial clades, only full-length sequences (V1–V9) can provide unbiased resolution of all the species present

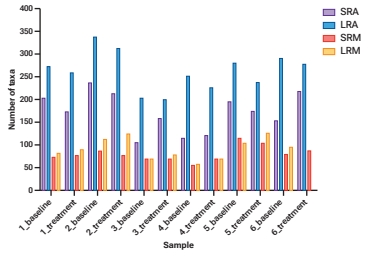


HiFi data yields more high-quality MAGs than noisy long-read data, especially at low coverage[4]

- HiFi assembled complete MAGs for low relative abundant species and high-quality bins revealed a substantial number of HiFi bins below 10× coverage compared to the noisy long-read (pCLR) datasets
- In >90% complete bins, the average coverage of the HiFi bins is lower than pCLR, and several HiFi bins have <1× average coverage as opposed to pCLR with none

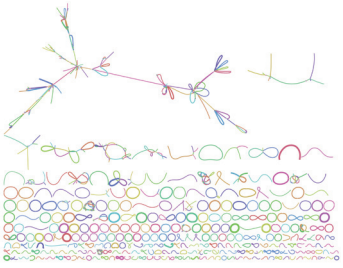
*"Such **high-quality metagenome assemblies may fundamentally change the practice in metagenome analysis** and shed light on the biological and biomedical implications of microbial communities."*[5]

— Xiaowen Feng, Dana-Farber Cancer Institute, Harvard Medical School



Obtain more taxa with high precision from HiFi data for both amplicon and shotgun approaches[6]

- After filtering out noise from short-read shotgun metagenomics (SRM), amplicon approaches detected more unique taxa than shotgun metagenomics
- Long-read amplicon (LRA) and shotgun metagenomics (LRM) detected more taxa than both with short reads



With highly accurate HiFi reads, hifiasm-meta moves metagenome assembly even further with more MAGs[5]

- When evaluated on seven empirical datasets, hifiasm-meta reconstructed tens to hundreds of single-contig circular bacterial genomes per dataset
- hifiasm-meta outperforms other metagenome assemblers with more complete circular single-contig MAGs

Learn more about our applications: pacb.com/metagenomics

1. https://www.niehs.nih.gov/health/topics/science/microbiome/index.cfm
2. Baxt, J. (2022). Long-reads and powerful algorithms identify "invisible" microbes
3. Johnson, J. S., et al. (2019) Evaluation of 16S rRNA gene sequencing for species and strain-level microbiome analysis. *Nature Communications.* 10(1), 5029
4. Bickhart, D. M., et al. (2022) Generating lineage-resolved, complete metagenome-assembled genomes from complex microbial communities. *Nature biotechnology*. 0.1038/s41587-021-01130-z
5. Feng, X., et al. (2022) Metagenome assembly of high-fidelity long reads with hifiasm-meta. *Nature methods.* 10.1038/s41592-022-01478-3
6. Gehrig, J., et al. (2022) Finding the right fit: evaluation of short-read and long-read sequencing approaches to maximize the utility of clinical microbiome data. *Microbial Genomics*, 8(3), 10.1099/mgen.0.000794

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