OptiFit: a fast method for fitting amplicon sequences to existing OTUs

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2020-11-30

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Abstract

Assigning amplicon sequences to Operational Taxonomic Units (OTUs) is an important step in characterizing the composition of microbial communities across large datasets. OptiClust, a *de novo* OTU clustering method in the mothur program, has been shown to produce higher quality OTU assignments than other methods and at comparable or faster speeds (1, 2). A notable difference between *de novo* clustering and database-dependent methods is that OTU assignments clustered with *de novo* methods are not stable when new sequences are added to a dataset (3). However, in some cases one may wish to incorporate new samples into a previously clustered dataset without performing clustering again on all sequences, such as when deploying a machine learning model where OTUs are features (4). To provide an efficient and robust method to fit amplicon sequence data to existing OTUs, we developed the OptiFit algorithm as a new component of the mothur program. To benchmark the OptiFit algorithm against *de novo* clustering with the OptiClust algorithm, we used four published datasets isolated from soil (5), marine (6), mouse (7), and human (8) samples. For each dataset, a subset of sequences was randomly selected and clustered into OTUs with OptiClust, then the remaining sequences were fit to the existing OTUs using the OptiFit algorithm. This was repeated with subsets of varying sizes ranging from 10 to 90% of sequences in order to evaluate the bounds of the dataset size required for OptiFit. Separately, all sequences were clustered with OptiClust to provide a baseline of OTU assignment quality and runtime performance. Each of these routines was repeated 10 times with different random seeds to produce results that are robust to random variation. OTU quality was evaluated using the Matthews Correlation Coefficient (MCC) with a sequence similarity threshold of 97% as described previously (3, 9). On average, fitting sequences into existing OTUs with OptiFit performed 10 times faster than *de novo* clustering with OptiClust, while the average MCC scores produced were nearly indistinguishable across each dataset. The OptiFit results across subset sizes ranging from 10 to 90% of sequences were also very similar, with slightly higher MCC scores for

larger subset sizes. Thus, OptiFit is an efficient way to fit new sequences to existing OTUs yet without sacrificing the quality of OTU assignments.

Importance

Introduction

Results

Discussion

Materials and Methods

Acknowledgements

KLS received support from the NIH Training Program in Bioinformatics (T32 GM070449).

The funders had no role in study design, data collection and interpretation, or the decision to submit the work for publication.

References

1. **Westcott SL**, **Schloss PD**. 2017. OptiClust, an Improved Method for Assigning Amplicon-Based Sequence Data to Operational Taxonomic Units. mSphere **2**:e00073–17. doi:10.1128/mSphereDirect.00073-17.

2. **Schloss PD**, **Westcott SL**, **Ryabin T**, **Hall JR**, **Hartmann M**, **Hollister EB**, **Lesniewski RA**, **Oakley BB**, **Parks DH**, **Robinson CJ**, **Sahl JW**, **Stres B**, **Thallinger GG**, **Van Horn DJ**, **Weber CF**. 2009. Introducing mothur: Open-source, platform-independent, community-supported software for describing and comparing microbial communities. Applied and Environmental Microbiology **75**:7537–7541. doi:10.1128/AEM.01541-09.

3. **Westcott SL**, **Schloss PD**. 2015. De novo clustering methods outperform reference-based methods for assigning 16S rRNA gene sequences to operational taxonomic units. PeerJ **3**:e1487. doi:10.7717/peerj.1487.

4. **Topçuoğlu BD**, **Lesniak NA**, **Ruffin MT**, **Wiens J**, **Schloss PD**. 2020. A Framework

for Effective Application of Machine Learning to Microbiome-Based Classification Problems. mBio **11**. doi:10.1128/mBio.00434-20.

5. **Johnston ER**, **Rodriguez-R LM**, **Luo C**, **Yuan MM**, **Wu L**, **He Z**, **Schuur EAG**, **Luo Y**, **Tiedje JM**, **Zhou J**, **Konstantinidis KT**. 2016. Metagenomics Reveals Pervasive Bacterial Populations and Reduced Community Diversity across the Alaska Tundra Ecosystem. Front Microbiol **7**. doi:10.3389/fmicb.2016.00579.

6. **Henson MW**, **Pitre DM**, **Weckhorst JL**, **Lanclos VC**, **Webber AT**, **Thrash JC**. 2016. Artificial Seawater Media Facilitate Cultivating Members of the Microbial Majority from the Gulf of Mexico. mSphere **1**. doi:10.1128/mSphere.00028-16.

7. **Schloss PD**, **Schubert AM**, **Zackular JP**, **Iverson KD**, **Young VB**, **Petrosino JF**. 2012. Stabilization of the murine gut microbiome following weaning. Gut Microbes **3**:383–393. doi:10.4161/gmic.21008.

8. **Baxter NT**, **Ruffin MT**, **Rogers MAM**, **Schloss PD**. 2016. Microbiota-based model improves the sensitivity of fecal immunochemical test for detecting colonic lesions. Genome Med **8**:37. doi:10.1186/s13073-016-0290-3.

9. **Schloss PD**. 2016. Application of a Database-Independent Approach To Assess the Quality of Operational Taxonomic Unit Picking Methods. mSystems **1**:e00027–16. doi:10.1128/mSystems.00027-16.