## Metagenome Binning

# What information do we want from metagenomes?

- Identity of the genes
- Abundance of the genes
- Evolution history
- Taxonomy of known and unknown organisms

Complex Samples

## he most out of your data

ID, Abundance, Function

16S rRNA amplicon sequencing

#### Pros:

1) Commonly used approach

Assembly based

2) Deep characterization

#### Cons:

- 1) Limited knowledge
- 2) Resolution remains low

Shotgun sequencing

#### Pros:

- 1) Massive data
- Identity and abundance answered simultaneously
- 3) Look at all data\*\*

#### Pros:

- Large contigs
- 2) Positional Information
- Most direct method to identify novel orgs/genes

#### Cons:

- 1) Computational resource intensive
- Assembling difficulties
  - Sequencing error
  - genomic redundancy chimeras

Read-based / Mapping Methods

#### Cons:

- Massive data (short + with errors)
- Lack of specificity due to FPs from genomic redundancy
- 3) Difficult to detect novel genomes must infer

- Fragmented
- Difficult to produce full-length genomes

### **Patrick Chain**

# How can we differentiate gene fragments from different genomes?

- Sequence identity
- G+C content
- Direct identification

## Metagenome binning

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## Classification of metagenomic sequences: methods and challenges

Sharmila S. Mande, Monzoorul Haque Mohammed and Tarini Shankar Ghosh

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 Binning, a process conceptually similar/ analogous to established machine learning techniques, involves classifying and/or clustering reads into specific bins. Binning is ...

Clustering & Classification

## General binning approaches

- Reference based approach
  - aka. supervised approach

Unsupervised approach

REVIEW Open Access



## Recovering complete and draft population genomes from metagenome datasets

Naseer Sangwan<sup>1,4\*</sup>, Fangfang Xia<sup>2</sup> and Jack A. Gilbert<sup>1,3,4,5</sup>

### **Abstract**

Assembly of metagenomic sequence data into microbial genomes is of fundamental value to improving our understanding of microbial ecology and metabolism by elucidating the functional potential of hard-to-culture microorganisms. Here, we provide a synthesis of available methods to bin metagenomic contigs into species-level groups and highlight how genetic diversity, sequencing depth, and coverage influence binning success. Despite the computational cost on application to deeply sequenced complex metagenomes (e.g., soil), covarying patterns of contig coverage across multiple datasets significantly improves the binning process. We also discuss and compare current genome validation methods and reveal how these methods tackle the problem of chimeric genome bins i.e., sequences from multiple species. Finally, we explore how population genome assembly can be used to uncover biogeographic trends and to characterize the effect of in situ functional constraints on the genome-wide evolution.

Keywords: Metagenomics, Genotype, Assembly, Binning, Curation



# MetaBAT, an efficient tool for accurately reconstructing single genomes from complex microbial communities

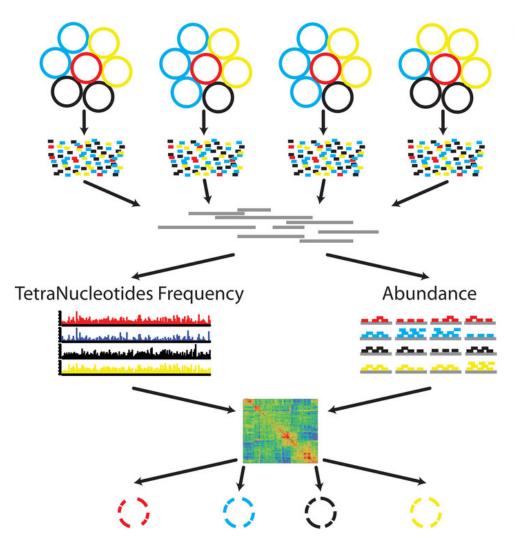
Dongwan D. Kang<sup>1,2</sup>, Jeff Froula<sup>1,2</sup>, Rob Egan<sup>1,2</sup> and Zhong Wang<sup>1,2,3</sup>

- <sup>1</sup> Department of Energy Joint Genome Institute, Walnut Creek, CA, USA
- <sup>2</sup> Genomics Division, Lawrence Berkeley National Laboratory, Berkeley, CA, USA
- <sup>3</sup> School of Natural Sciences, University of California at Merced, Merced, CA, USA

## **ABSTRACT**

Grouping large genomic fragments assembled from shotgun metagenomic sequences to deconvolute complex microbial communities, or metagenome binning, enables the study of individual organisms and their interactions. Because of the complex nature of these communities, existing metagenome binning methods often miss a large number of microbial species. In addition, most of the tools are not scalable to large datasets. Here we introduce automated software called MetaBAT that integrates empirical probabilistic distances of genome abundance and tetranucleotide frequency for accurate metagenome binning. MetaBAT outperforms alternative methods in accuracy and computational efficiency on both synthetic and real metagenome datasets. It automatically forms hundreds of high quality genome bins on a very large assembly consisting millions of contigs in a matter of hours on a single node. MetaBAT is open source software and available at <a href="https://bitbucket.org/berkeleylab/metabat">https://bitbucket.org/berkeleylab/metabat</a>.

## MetaBAT process



## **Preprocessing**

- Samples from multiple sites or times
- Metagenome libraries
- Initial de-novo assembly using the combined library

#### **MetaBAT**

- Calculate TNF for each contig
- Calculate Abundance per library for each contig
- Calculate the pairwise distance matrix using pre-trained probabilistic models
- Forming genome bins iteratively

## MetaBAT methodology

- Requires pre-trained models
  - Tetra nucleotide patterns
  - Genome abundance profile
  - Multiple samples
- Binning algorithm
  - Modified k-medoids
  - Heuristic
- Input
  - Assembled contigs (fasta file)
    - >2.5 kb worked the best
  - Mapped reads (sorted bam file)

## Reproducible benchmarking

https://bitbucket.org/berkeleylab/metabat/wiki/Home

Wiki

MetaBAT / Home

View History

## Benchmark of Automated Metagenome Binning Software in Complex Metagenomes

For a realistic benchmark of metagenome binning software, we constructed a dataset from 264 MetaHIT human gut metagenome data (Accession #: ERP000108). We took Canopy, CONCOCT, GroopM, and MaxBin as the alternative software to compare with MetaBAT. These tools are easy to use and identify genome bins automatically. Canopy is scaleable clustering algorithm used in Nielsen et. al, 2014; here we used it as a contigs binning tool. GroopM has manual refinement step, which may improve binning significantly. MaxBin was selected as one of non co-abundance binning tools, which utilize one abundance; it may be fair comparison for MaxBin if only one sample is used; however, we assumed the availability of many samples.

# Other tools use oligonucleotide frequency and coverage for binning

- CONCOCT
- GroupM
- MaxBin
- Databionic ESOM tools