Metagenomic Binning Pipelines - the State of the Art

3 Outline

Abstract

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- \bullet Background/Introduction
- Binning problem definition (recover biological entities from metagenomic sequencing)
- problem relevance (Explosion in metagenomics, reduction in sequencing cost, increased computer capacity)
- Review objectives (Brief summary on popular tools, innovations overview of recent tools)
- Popular/Previous Binning software
- Proposed solutions (bin contings into bins(MAG if good quality) based on their kmer composition and abundance/coabundance)
 - Tools available (Cite recent benchmark)
- Overview of recent metagenomic binning tools
 - Innovations in binning tools
 - * Innovations in proposed solutions/strategy innovations Read binning gene-abundance binning (CAG, MGS, MSPi) Integrate new experimental data
 - * Software/algorithms innovations machine-learning/deep-learning implementation
- Innovations in specific biological questions Viral genomes and viral strains; Endosymbionts
- Choosing a binning algorithm
- Identify start point variables

- * Sample origin (Host contamination, diversity)
- * Number of samples (some tools require many samples to perform well)
- * Sequencing technology (Most tools employ illumina, LongReads are increasing)
- * Computational resources available
- Identify endpoint
 - * organism of interest viral(ref viral catalogue), bacteria, all
- Tools are complementary MSP/Metabat
 - Conclusions
- Current limitations and future directions Do not perform well on multiple strains, on the same sample
- Figure. Binning software historical citations barplot Figure. Decision tree, overview of metagenomic binning Table. List of binning software since 2017

35 Abstract

- 36 New generations of sequencing platforms coupled with numerous bioinformatics tools have led to
- rapid technological progress in metagenomics to investigate complex microorganism communities.
- 38 Nevertheless, a combination of different bioinformatic tools remains necessary to draw conclusions
- 39 out of microbiota studies. As sequencing costs have dropped at a rate above 'Moore's law', a
- 40 greater number of large data sets are being produced than ever before. Newer algorithms that
- take advantage of the size of these datasets are continually being developed. Binning algorithms
- 42 are defined as the grouping of assembled metagenomic contigs by their genome of origin. Selecting
- 43 the most appropriate binning algorithm can be a daunting task and is influenced by many factors.
- This review serves as a guide to direct the researcher to the binning algorithm that best suits their
- 45 needs.

46 Background

- 47 The explosion in popularity and success in the field of metagenomics over the last 25 years can
- 48 be largely attributed to the advances in computing technologies. An example of the outcomes of
- this can be found in the Human Microbiome Project; a project that has been greatly improved

the understanding of the microbila flora involved in human health and disease. These advances
have brought with them greater demands for storage, CPU time, and consequently more efficient
algorithms. The main function of binning tools is to reconstruct species/biological entities from
metagenomic samples. Compared to amplicon, shotgun metagenome can provide functional gene
profiles directly and reach a much higher resolution of taxonomic annotation. However, due to the
high demands on computational resources, cost, and expertise necessary to perform this analysis,
researchers have historically been limited in their capacity to collect and analyse sequencing data.
As the cost of sequencing is rapidly falling, this burden has been significantly lessened. At the
time of writing, shotgun metagenomic sequencing costs on average three times as much as 16S
sequencing in comparison. The objectives of this review is for the reader to be better informed
about the latest algorithms (since 2017) for binning metagenomic samples. The second part of
this review is for the reader to be informed about distinguishing factors between the methods.
The last part is for the reader to make an informed decision based on those factors for their needs.
This review will be broken down into the following sections:

Recent methods for metagenomic binning

A metagenomic sample is comprised of many organisms and the standard procedure is to retrieve the sequences from the mixture of organisms. The final goal of binning is to reconstruct the sequences from each organism present in the original sample. Among the binning tools developed in recent years we can distinguish a subset dedicated to cluster reads (read-binning) (MetaBBC-LR, BioBloom Tools, CLAME, LVQ-KKN, Meta VW, HirBin, MEGAN-LR). The main purpose of read-binning tools is to pre-process reads into clusters for a posterior targeted assembly, here we find reference-free and non-reference-free tools, and tools designed for short-read or long-read sequencing technologies. The majority of binning tools we can find are oriented toward clustering contigs (contig-binning) into bins, which may represent the genome from a single biological entity/organism. Contig-binning tools normally rely on coverage information and sequence composition. Progress in contig-binning algorithms can be seen in the proposals to integrate new sources of information (for example, from scaffold-graphs(Binnacle), paired-end reads(COCACOLA), or 3D contact information(MetaTOR)) and state of the art algorithms in machine learning (CoCoNet, Variational Autoencoders for Metagenomic Binning (VAMB)).

79 Metagenome Assembled Genomes

- 80 A Metagenome-Assembled Genome (MAG) is a single-taxon assembly based on one or more binned
- 81 metagenomes that has been asserted to be a close representation to an actual individual genome
- 82 (that could match an already existing isolate or represent a novel isolate).

Binning microbial genomes with deep learning

- ⁸⁴ The integration of deep learning techniques into the field of metagenomics has revolutionised
- ₈₅ the field of metagenomics. The VAMB pipeline was developed to take advantage of variational
- 86 autoencoders; a generative machine learning model that uses a deep variational autoencoders
- 87 (Nissen et al., n.d.)... COCONET (Arisdakessian, Nigro, Steward, Poisson, & Belcaid, 2021)...

Binning for viral genomes

- ⁸⁹ 2021 viral catalog (Nayfach et al., 2021)... New insights from uncultivated genomes of the global
- buman gut microbiome (Nayfach, Shi, Seshadri, Pollard, & Kyrpides, 2019)... Also mention
- 91 coconet suitability for viral genomes...

⁹² Choosing the most appropriate binning algorithm (Classifi-

s cation by output)

- ⁹⁴ A review on the benchmarking binning algorithms was done by Yue et al., 2020. Resource man-
- 95 agement is an important factor in the choice of binning algorithm. The tradeoff between number
- 96 of Central Processing Units (CPUs), memory, and time are important considerations. Newer ad-
- 97 vances in pipeline technologies have ameliorated these costs. An analysis pipeline is defined as
- 98 a program that combines several programs in a defined order to complete a complex analysis.
- ⁹⁹ Improperly developed, validated, and/or monitored pipelines may generate inaccurate results.

100 MSPs, binning co-abundant genes

Binning of co-abundant genes represents an alternative proposal to reconstruct species/biological

entities from a set of metagenomic samples. Co-abundant gene binning methods assume each gene

coming from a shared chromosome will display proportional abundances across samples, if you have

enough samples from a common environment you can identify the sets of genes from a common

Table 1: Comparison of binning algorithms

Software / Algorithm Year Description/propose Common/Highlight Dos CoCoNet 202 Despitation/propose 10.1009/Abusinformatics/Phab213 10.1009/Abusinformatics/Phab213 VANIE 202 Metagenome Banning and Alexa sentiation and and an analysis of Metagenome banning and Metagenome Contige and Metagenome Continuing Deptagenome Continuing Deptagenome Continuing Deptagenome Continuing Deptagenome Continuing Deptagenome Continuing Deptagenome Continuing Continuing Deptagenome Continuing Deptagenome Continuing Deptagenome Continuing Deptagenome Continuing Continuing Deptagenome Continuing Continuing Deptagenome Continuing Continuing Continuing Continuing Continuing Continuing Continuing Continuing Continuin						
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222 Using scaffolds to improve Mategagnome Binning Reconstructs varied at the processing Activities and MAG assembly alterated and Machagagnome Binning using deep variational autoc 222 Metagenomic binning study of Congress and Mategagnome Congress assembly and MAG assembly. Surface assembly, alterated and Mategagnomic congress assembly and MAG assembly alterated assembly alterated binning of mateganomic congress assembly and mateganomic attains and mateganomic congress assembly and mateganomic attains and mateganomic congress assembly and mateganomic attains and mateganomic congress assembly and and annotation. 2011 Improvement binning and mateganome binning and annotation. 2012 Metagenomic binning and mateganome complets and annotation. 2013 Metagenomic binning and association of plantane and annotation. 2014 Metagenomic binning and association of plantane and annotation. 2015 Improve decembly and association of plantane and annotation. 2016 Improved contains agreegation and annotation. 2017 Intercruce-free learning sequence classific 2018 Interpret of Metagenome Binners and annotation. 2019 Interpret of Metagenome Binners and annotation and annotat	7	000			5 5 6 6 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7	
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2020 SRINA profiling and MAG assembly 2020 Metagenomic binning for Long-Reads 2020 Metagenomic binning for Long-Reads 2020 Refined binning for targeted assembly, alignment. 2020 Simulating metagenomic contigs using assembly graphs information 2020 Simulating metagenomic contigs using extended contigs 2020 Simulating metagenomic contigs using content in the properation for large scale metage. 2020 Simulating metagenomic contigs using content in mixed s. 2020 Simulating metagenomic contigs using content in mixed s. 2020 Simulating metagenomic state in an analysis of MACs 2021 Grant manualian gits using from mixed s. 2021 Grant manualian gits using from mixed s. 2022 Simulating metagenomic scale metagenome in dividual. 2023 Grant metagenome binning disputed description of mirrobal parameter through the properties of population for genome reconstruction of mirrobal parameter description of mirrobal parameter description of mirrobal parameter comp. 2023 Grant mirrobal mining disputed description of mirrobal parameter description of mirrobal parameter comp. 2024 Simulation metagenomic binning disputed description of mirrobal parameter description of	VAMB	2021	Metagenome binning using deep variational autoe	Autoencoder algorithm, fast processing	10.1038/s41587-020-00777-4	33398153
2020 Reads binning for totageted assembly, alignment 2020 Reads binning for totageted assembly, alignment 2020 Reads binning for totageted assembly, alignment 2020 Reads binning for targeted assembly, alignment 2020 Reads binning of netagenomic contage using as 2020 Simulating metagenomic stable isotope probligs and analysis of MAGs 2020 Binning viral haplotypes from assembled contage. 2020 The proportion and analysis of MAGs 2020 Enone separation of Endosymbionts from mixed s 2021 Ashaptative binning algorithm for large scale mear 2021 Ashaptative binning algorithm for large scale mear 2022 Alignment based algorithm individual 2023 Alignment based algorithm individual 2024 Alignment based algorithm individual 2025 Alignment based constitution of mitrobial parases and aspectation of mitrobial general algorithm of metagenomic sequence classific 2026 Angegonemic binning trough low description of mitrobial parases mention of mitrobial parases mention of mitrobial parases and aspectation of mitrobial parases and parases and aspectation of mitrobial parases a	phyloFlash	2020	ssrRNA profiling and MAG assembly	incorporates ssrRNA profiling info into MAG ass	10.1128/mSystems.00920-20	33109753
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2020 Refined binning of netagenomic contigs as: 2020 Simulating metagenomic stable isotope probing a content binning viral haplotypes from assembled contigs 2020 Simulating metagenomic stable isotope probing a pipeline and search of Endosymbions from mixed s 2021 Genome separation of Endosymbions from mixed s 2022 Applicative binning algorithm for genome recons 2023 Adugment black of partitioning polypic did up genomes b 2024 Mignant based algorithm allowed description of microbial genomes from individual 2025 Anguant based and content free met 2026 Anguant based angorithm allowed description of microbial genome from individual 2027 Alignment based angorithm allowed description of microbial genome resolved metagenome sequence chagners 2028 Anguant based angorithm allowed description of microbial genome econstitution of differential 2017 Metagenomic binning and acoring strategy and contractive visualisation tool for verification. Single sample, microbial genome propriation genome binning using fuzzy C-Means Method of mining using fuzzy C-Means Method of contractive visualisation tool	BioBloom Tools	2020	Reads binning for targeted assembly, alignment	Data preparation for targeted assembly, using s	10.1073/pnas.1903436117	32641514
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Pinning viral haplotypes from analysis of MAGs	MetaCon	2019	Unsupervised binning k-mers and coverage, focus	Focus different lengths contigs	10.1186/s12859-019-2904-4	31757198
Pramework for Production and analysis of MA Gss	VirBin	2019	Binning viral haplotypes from assembled contigs	Viral haplotypes MAGs	10.1186/s12859-019-3138-1	31684876
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Scalable binning algorithm for large scale meta Soluble binning and grithm for large scale meta Method for partitioning polyploid sup genomes b Method for partitioning polyploid supprevois Method for partitioning with semi-supervis Soluble pineling processing method for alignment free met Method for partitioning with semi-supervis Migment based algorithm allowed description of Alignent based favorithm allowed description of Alignent based algorithm allowed binning using Puzzy C-Means Method Alignent of long sequence classific Alignent of long sequence sequences Alignent based for highly allowed binning using Puzzy C-Means Method Add codon usage information of differential Plasmid control for verification of differential Alignent based for highly allowed binning using Puzzy C-Means Method Add sequence endesigned content or competition, or	MetaBAT 2	2019	Adatptative binning algorithm for genome recons	Eliminates manual parameter tuning from previou	10.7717/peerj.7359	31388474
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	GroopM (2)	2014	Tool for automatic recovery of population genom	Adds differential coverage to complement compos	10.7717/peerj.603	25289188

organism of origin (MLGs Chameleon-clust 2012, CAGs and MGSs Canopy 2014, Markovclust-105 MGCs Karlsson 2013, MSPs MSPminner 2018). To the extent of our knowledge, in the past few years MSPminer is the only available Software exploiting this approach. MSPminer introduced a 107 robust proportionality measure detecting to abundant but no necessarily co-occurring. MSPminer introduced a robust proportionality measure detecting to abundant but no necessarily co-ocurring. 109 This tools groups co-abundant genes into Metagenomic Species Pan-genomes or Metagenomic 110 Species Pan-genomess (MSPs) and classify genes within an MSP as core, accessory and shared. 111 The factors that impact directly on MSP quality include the sample composition, the sequencing 112 depth, the previous bioinforamtic steps to build the reference gene dataset and to map the reads. 113 A high number of samples with varying phenotypes improve the quality of MSPs. MSPs can 114 be employed for taxonomic profiles of new samples from similar ecosystems, to compare strains 115 between samples building a presence/absence table of accessory genes and for biomarker discovery. 116 By binning contigs carrying genes from the same MSP it is also possible to build a MAG. Co-117 abundant gene binning methods perform better in large sample datasets. 118

119 Metagenomic Species Pan-genomes

Microbial pan-genomes are gene repertoires composed of core genes present in all strains and 120 accessory genes present in only some of them (Medini et al., 2005). In a shotgun metagenomic 121 sequencing context, we define as shared the genes detected in some samples where the species is 122 not present. A strain found in a sample is an instance of the species pan-genome: it is made of all 123 the species (shared) core genes and of a subset of (shared) accessory genes. Core genes are suitable 124 for taxonomic profiling at species-level while accessory genes can be used to compare strains across 125 samples. Genes tagged as shared should be used carefully as they contain false positives counts or are subject to horizontal transfer. Core genes are suitable for taxonomic profiling at species-127 level while accessory genes can be used to compare strains across samples. Genes tagged as shared should be used carefully as they contain false positives counts or are subject to horizontal transfer. 129

Weaknesses and future developments

Until now binning methods perform poorly in samples that contain similar strains...

32 Conclusion

- 133 New and open areas of research in which the application of metagenomic pipelines are relevant
- 134 The increased impact of machine learning in analysis Short section just for past-present-future
- completeness Future developments for metagenomic analysis

References

- Arisdakessian, C. G., Nigro, O. D., Steward, G. F., Poisson, G., & Belcaid, M. (2021). Coconet:

 an efficient deep learning tool for viral metagenome binning. *Bioinformatics*.
- ¹³⁹ Nayfach, S., Páez-Espino, D., Call, L., Low, S. J., Sberro, H., Ivanova, N. N., ... others (2021).
- Metagenomic compendium of 189,680 dna viruses from the human gut microbiome. *Nature Microbiology*, 1–11.
- Nayfach, S., Shi, Z. J., Seshadri, R., Pollard, K. S., & Kyrpides, N. C. (2019). New insights from uncultivated genomes of the global human gut microbiome. *Nature*, 568(7753), 505–510.
- Nissen, J. N., Johansen, J., Allesøe, R. L., Sønderby, C. K., Armenteros, J. J. A., Grønbech,
- C. H., ... others (n.d.). Improved metagenome binning and assembly using deep variational
- autoencoders. Nature Biotechnology, 1–6.
- Yue, Y., Huang, H., Qi, Z., Dou, H.-M., Liu, X.-Y., Han, T.-F., ... Tu, J. (2020). Evaluating
- metagenomics tools for genome binning with real metagenomic datasets and cami datasets.
- BMC bioinformatics, 21(1), 1–15.