



HAL
open science

Simka: fast kmer-based method for estimating the similarity between numerous metagenomic datasets

Gaëtan Benoit, Pierre Peterlongo, Dominique Lavenier, Claire Lemaitre

► **To cite this version:**

Gaëtan Benoit, Pierre Peterlongo, Dominique Lavenier, Claire Lemaitre. Simka: fast kmer-based method for estimating the similarity between numerous metagenomic datasets. JOBIM 2015, Jul 2015, Clermont-Ferrand, France. , 10.1093/Bioinforma-cs/btu406 . hal-01180603

HAL Id: hal-01180603

<https://inria.hal.science/hal-01180603v1>

Submitted on 27 Jul 2015

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Metagenomic

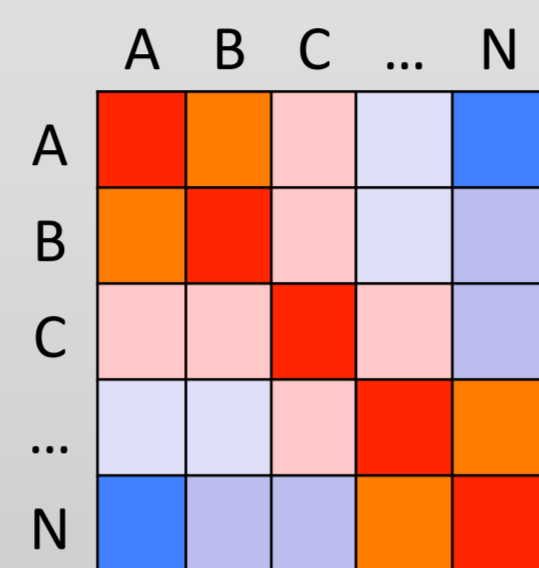


- A liter of sea water:**
- Hundred of millions of species
 - > 90% unknown species

Comparative metagenomics



N metagenomic samples
N > 1000 in Tara Oceans project



Similarity heatmap N² with hierarchical clustering

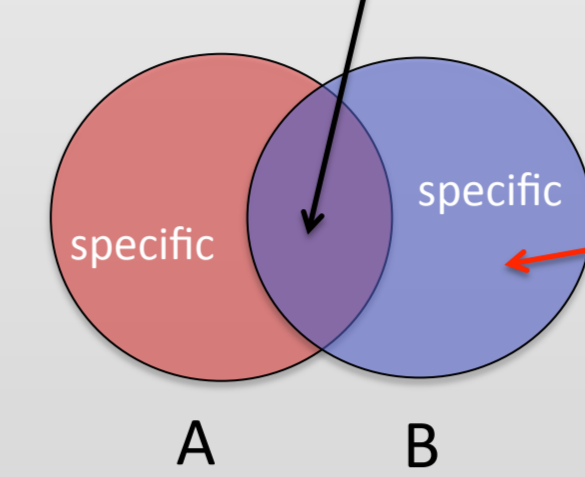


N read-sets
Usually >100M reads per dataset

Similarity between 2 read-sets

Idea: similarity is given by the size of the intersection

Intersection = number of similar reads



Similar: their alignment score > 90%

100M reads

✗ Blast-like approach required months of computation for a single intersection

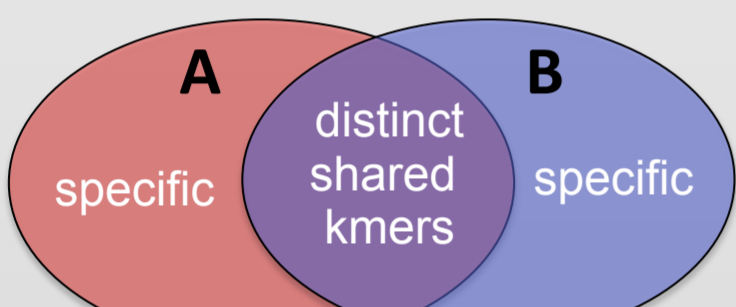
Commet [1] (state of the art)

- Heuristic: Two read are similar if they share some kmers
- Computes one intersection in few hours
- Still does not scale on large metagenomic projects
- N(N-1) intersections to compute

Kmer-based similarity functions

- We have very fast methods for indexing and querying kmers
- A read-sets is now view as a set of its kmers
- We define new pairwise similarity measures based on shared kmers

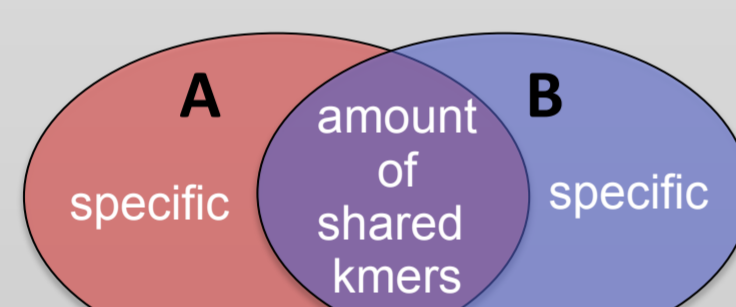
1) Presence / Absence of kmers



Similarity based on presence/absence of species

$$Jaccard(A, B) = \frac{DistinctKmers(A \cap B)}{DistinctKmers(A \cup B)}$$

2) Abundance of shared kmers

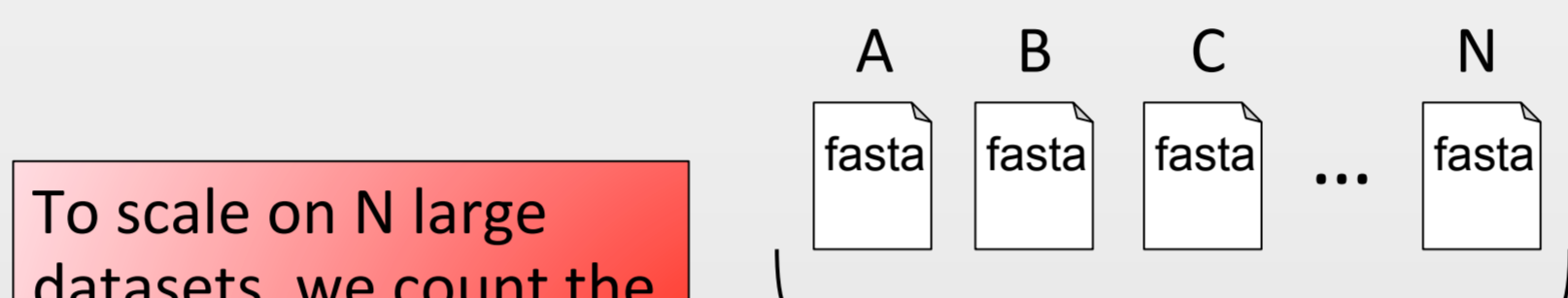


Similarity based on abundance of species

$$AbundanceJaccard(A, B) = \frac{\sum_{w \in A \cap B} N_A(w) + N_B(w)}{\sum_{w \in A \cup B} N_A(w) + N_B(w)}$$

w: kmer, Ni(w): abundance of w in read-set i

Method

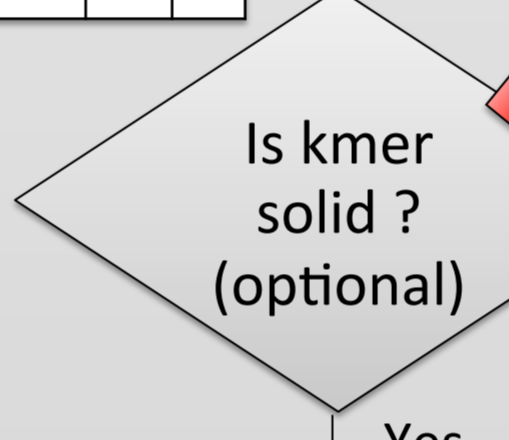


To scale on N large datasets, we count the kmers of N datasets simultaneously.

Kmer's abundances v

	A	B	C	...	N
ACGTAT	0	4	52	...	0

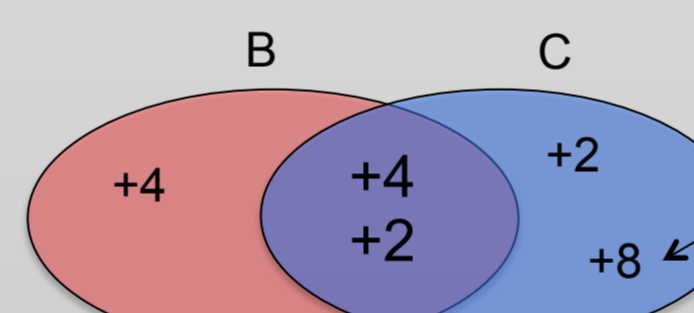
For each kmer, we get a vector of its abundances in N datasets



Update intersections

Kmer shared by B and C

	A	B	C
ACC	0	4	2



Kmer specific to C

	A	B	C
TGC	0	0	8

Estimating similarity is now a problem of counting kmers

Execution time repartition:

- Counting kmers O(N): 75%
- Updating intersections O(N²): 25%

Filtering sequencing errors

Kmer solid:

A kmer that contains no sequencing errors

Statistics:

80% of distinct kmers appear only one time and only in a single dataset

Noisy data:

It is hard to distinguish erroneous kmers from unique genomic kmers

We defined a solidity definition that can saved some unique kmers:

Given a solidity threshold t (t=2), a kmer w is solid if:

abundance(w) in at least one dataset >= t

Examples on 4 datasets:

A	B	C	D
2	0	1	0

A	B	C	D
52	0	1	1

A	B	C	D
0	1	1	0

Statistics on solid 31-mers from 21 Tara Oceans samples:

- Distinct: 18G (15% of all distinct kmers)
- Abundance: 106G (49% of all kmers)



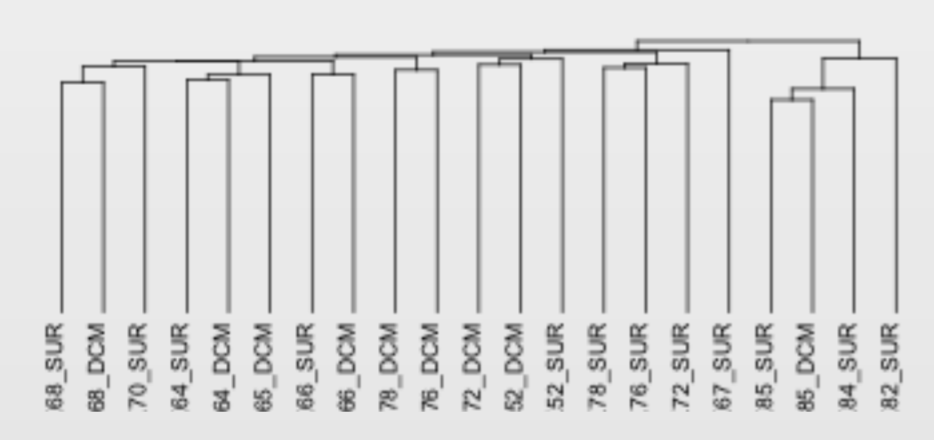
Datasets

- Simka was tested and compared to Commet[1] (state of the art) on 21 Tara Oceans samples:
- 3G reads
 - 400 GB of data
 - 219G 31-mers
 - 123G distinct 31-mers

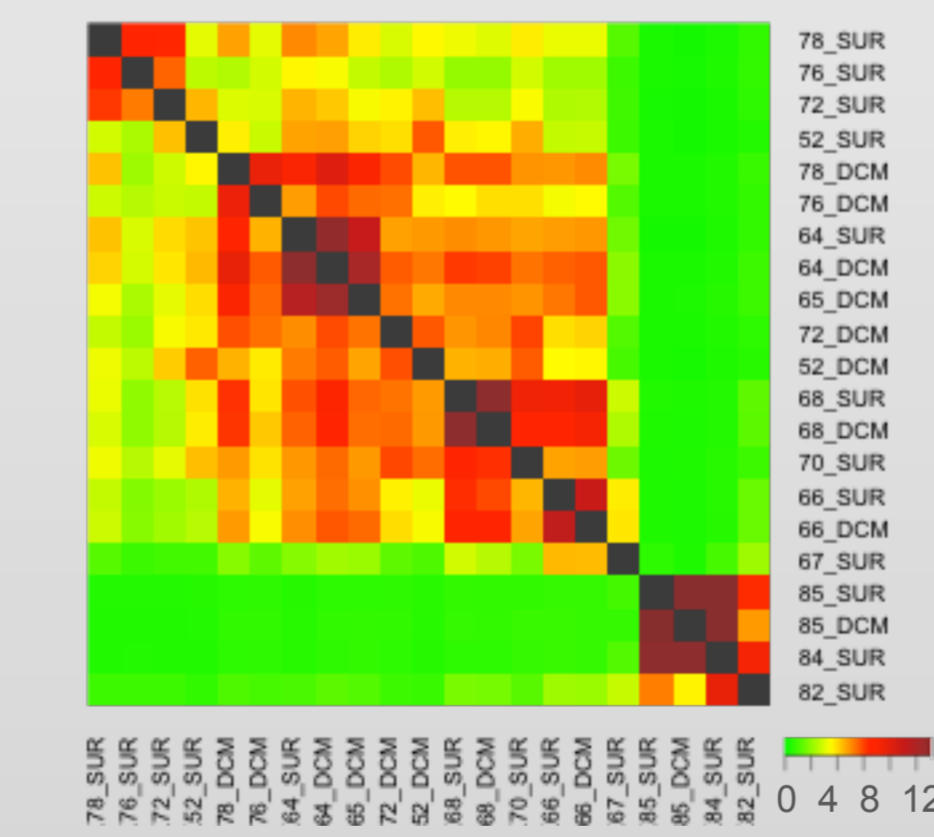


Presence / Absence of kmers

Relative similarity:



Absolute Similarity:

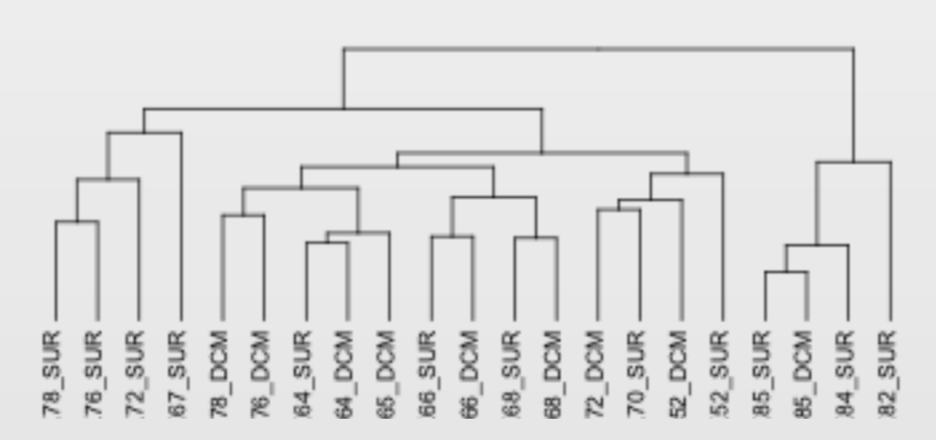


5 Hours

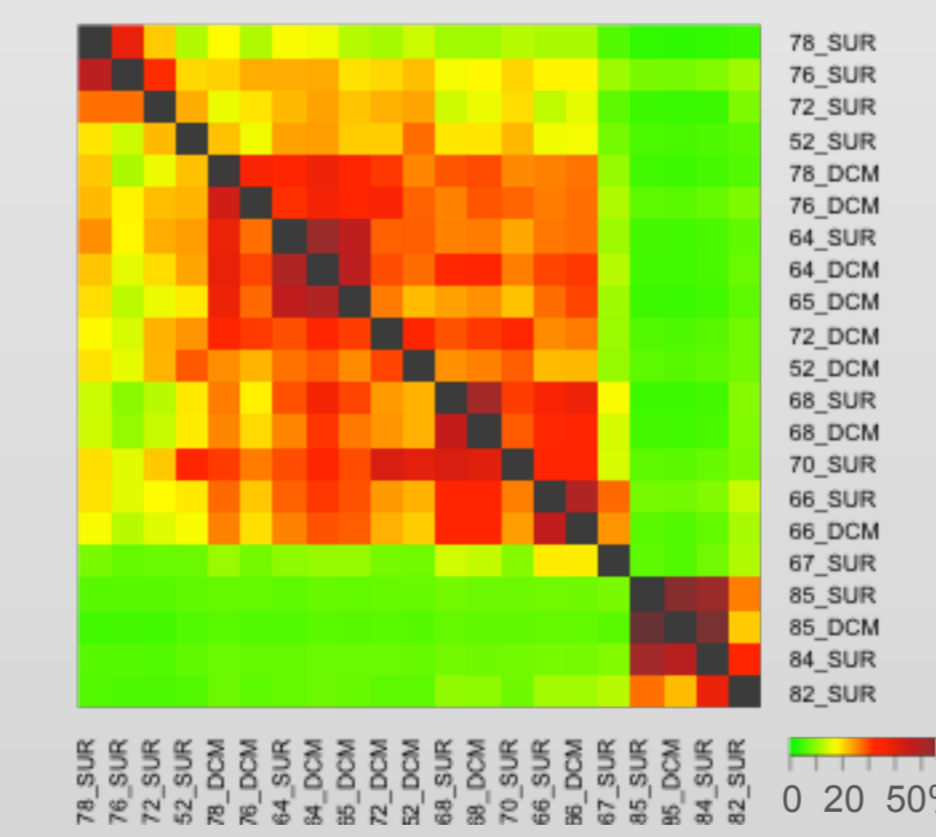
- ✗ Can differs from Commet because not based on species's abundance
- ✓ Simka is the first method to provide quickly information about presence and absence of species

Abundance with error filter

Relative similarity:



Absolute Similarity:

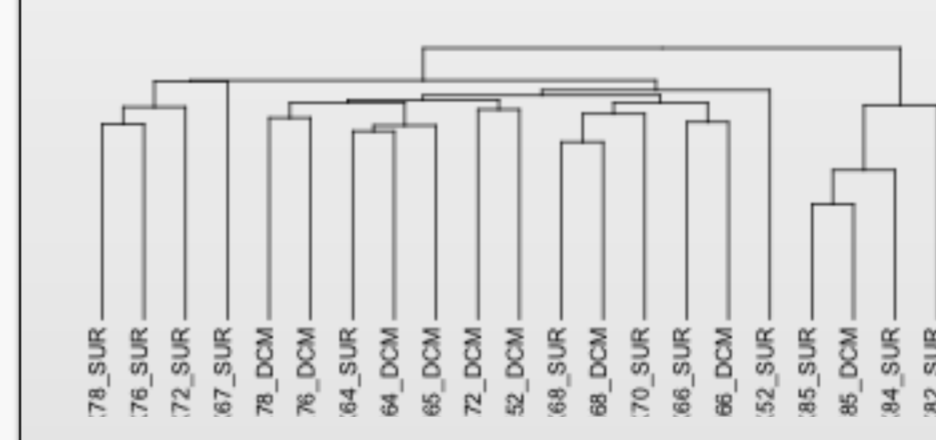


5 Hours

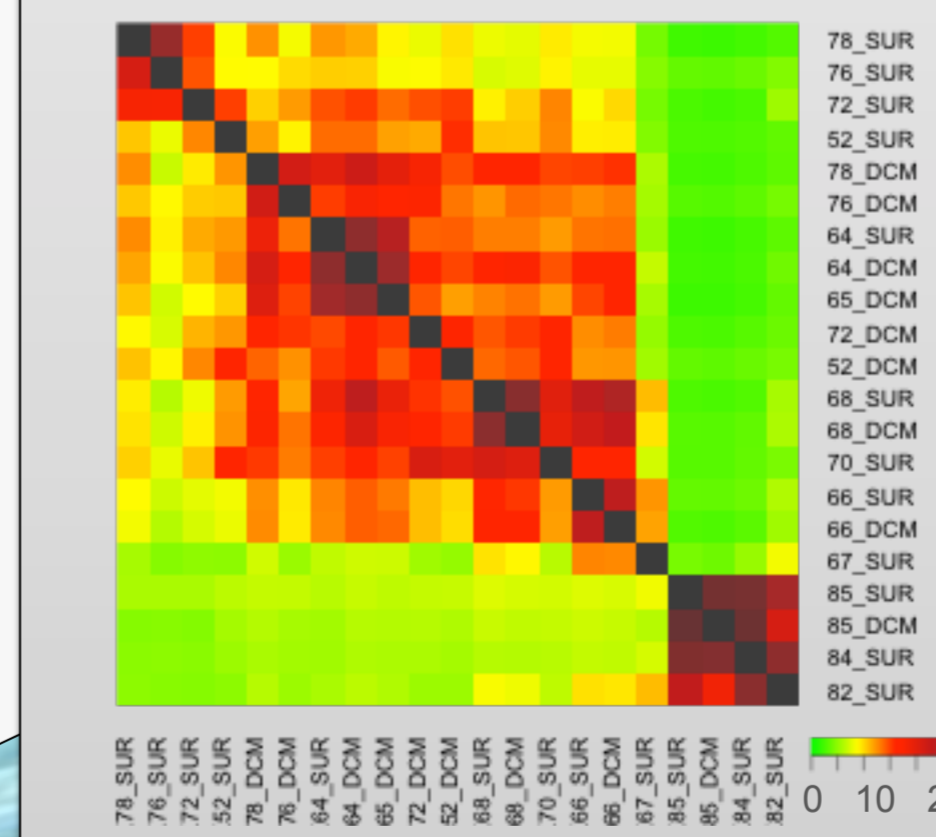
- ✓ Clustering less noisy and more readable
- ✓ Close to Commet while using only 18% of distinct kmers (half of the datasets)

Abundance of shared kmers

Relative similarity:



Absolute Similarity:

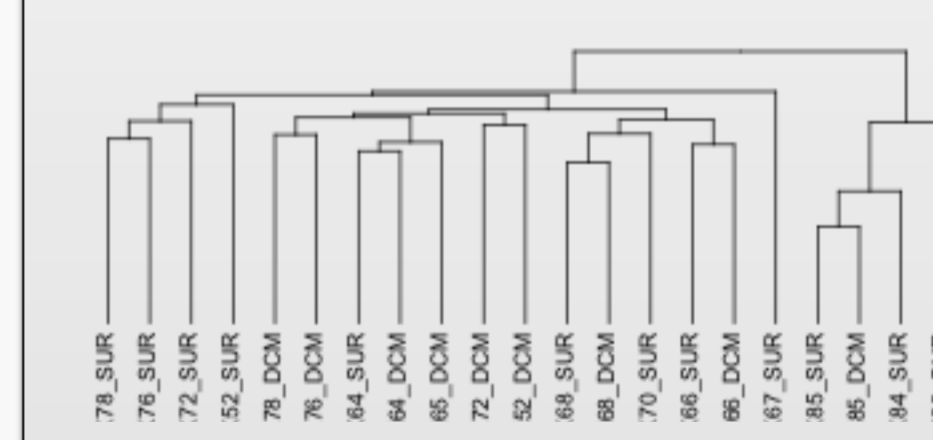


5 Hours

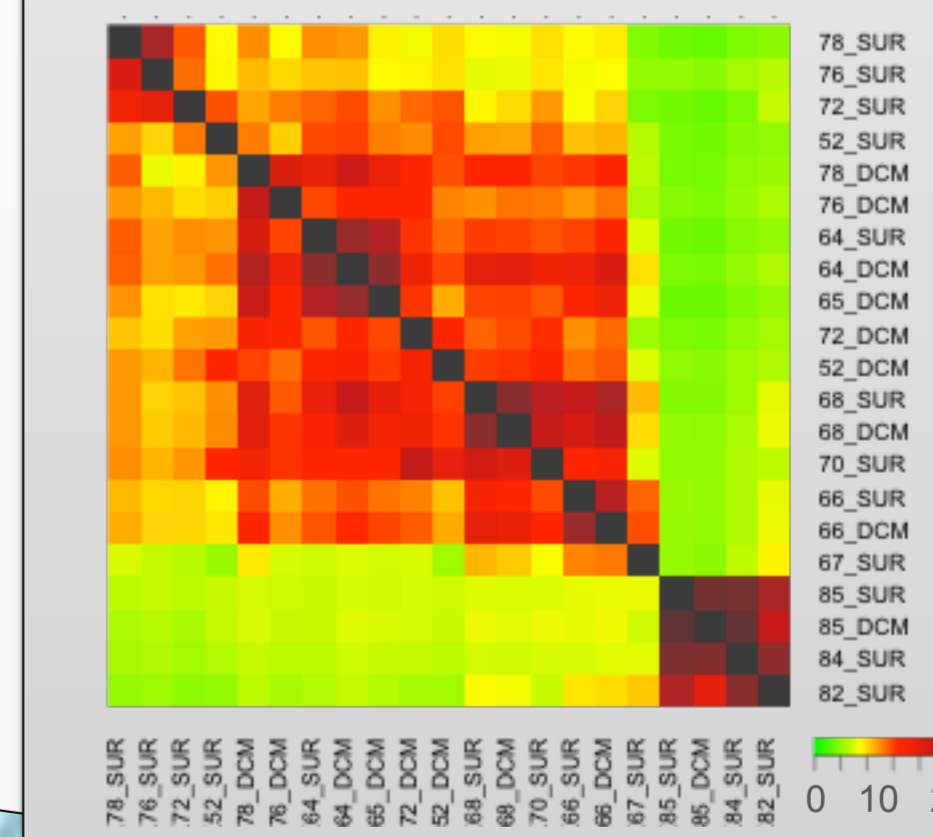
- ✓ Similarity and clustering close to read-based methods

Commet (state of the art)

Relative similarity:



Absolute Similarity:



Weeks

- ✓ Read-based
- ✗ Too slow on large metagenomic projects

Alignment based methods

Years

Perspectives

- Filtering input reads
- Provide similarity confidence intervals with bootstrap
- Selecting discriminative kmers

Simka

- ★ New similarity functions based on shared kmers
- ★ Based on abundance and presence/absence of species
- ★ Results close to read-based methods
- ★ Fast and low memory thanks to the GATB library [2]

References

- [1] COMMET: comparing and combining multiple metagenomic datasets
N. Maillet, G. Collet, T. Vannier, D. Lavenier, P. Peterlongo
IEEE BIBM, 2014
- [2] GATB: Genome Assembly & Analysis Tool Box
E. Drezon, G. Rizk, R. Chikhi, C. Delteil, C. Lemaitre, P. Peterlongo, D. Lavenier
10.1093/Bioinformatics/btu406, 2014
<https://gatb.inria.fr/>

Funding: ANR Hydrogen, ANR-14-CE23-0001

