MetaCHIP

Community-level horizontal gene transfer (HGT) identification through the combination of best-match and explicit phylogenetic tree approaches

Centre for Marine Bio-Innovation, University of New South Wales

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songwz03@gmail.com

Introduction

MetaCHIP is implemented in Python, a list of dependencies needs to be installed before running. Details of these dependencies can be found at: https://github.com/songweizhi/MetaCHIP.

To install MetaCHIP simply download the package and run the programs from the command line interface. **Full path to a list of dependencies needs to be specified in the config.txt file if they are not in environment variables**; otherwise, keep the config.txt file as it is.

MetaCHIP's input is the sequence file of a set of genome bins derived from metagenomic data.

The MetaCHIP pipeline contains three scripts: Get_clusters.py, Best-match.py and Phylogenetic.py.

1. **Get_clusters.py** clusters input genome bins into sub-groups according to their phylogenetic relationships.
2. **Best-match.py** performs the best-match approach.
3. **Phylogenetic.py** performs the phylogenetic approach.

Get_clusters.py

```
-i          input genome folder
-x          file extension
-p          output prefix
-dc         distance cutoff
-fs         leaf name font size
```

Get_clusters.py will cluster input genome bins into sub-groups based on the phylogenetic tree derived from the protein sequences of 43 universal single-copy genes (SCG) used by CheckM [1].

Clustering profile generated in this step **should be manually curated** by comparing it with the SCG tree or taxonomic classifications of the input genomes (if available) prior to the HGT identification step. You can do this by changing the group assignment of input genome bins specified in the first column of [prefix]_grouping_g[num].txt file. Or, you can modify clustering sensitivity by re-run this step with a customized `distance cutoff` (`-dc`) after had a look at the [prefix]_grouping_g[num].png file.

Output files:

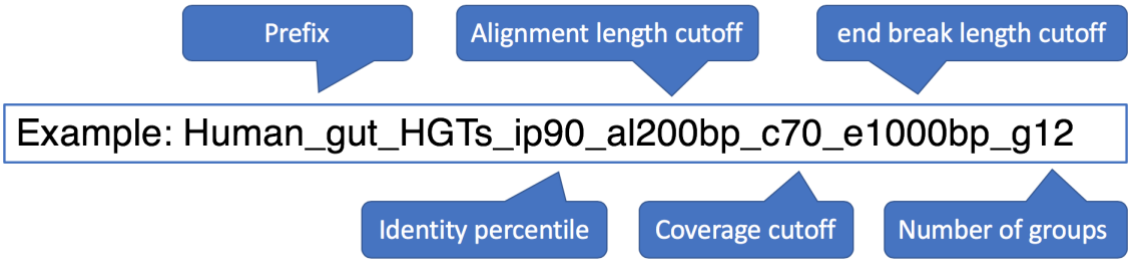
1. Clustering results were exported to [prefix]_grouping_g[num].txt.
2. SCG trees ([prefix]_grouping_g[num]_tree.jpg) of the input genome bins.
3. A dendrogram ([prefix]_grouping_g[num].png) showing the hierarchical clustering of input genome bins.

The **[prefix]_grouping_g[num].txt** file will be used as input for running Best-match.py and Phylogenetic.py.

Best-match.py

```
-p                output prefix
-g                grouping file
-blastall         all vs all blast results
-cov              coverage cutoff
-al               alignment length cutoff
-flk              the length of flanking sequences to plot
-ip               identity percentile cutoff
-eb               minimal length to be considered as end break
-tmp              keep temporary files
-num_threads      number of threads for running blastn
```

HGT candidates predicted by the best-match approach, as well as the plots of their flanking regions are exported to a folder with name in the following format:



A list of HGT candidates identified by best-match approach are exported to **HGT_candidates_BM.txt**. Their nucleotide and amino acid sequences are exported to HGT_candidates_BM_nc.fasta and HGT_candidates_BM_aa.fasta.

Phylogenetic.py

```
-p          output prefix
-g          grouping file
-cov        coverage cutoff
-al         alignment length cutoff
-ip         identity percentile
-eb         the minimal length to be considered as end break
-a          Prokka output
-o          orthologs folder
```

All protein orthologs within the input genomes need to be obtained for the phylogenetic approach, you can get it with GET_HOMOLOGUES [2]. The input is a bunch of annotation files for input genome bins in Genbank format, which have been generated by Get_clusters.py (**[prefix]_gbk_files**). Here is an example command:

```
get_homologues.pl -f 70 -t 3 -S 70 -E 1e-05 -C 70 -G -n 16 -d human_gut_gbk_files
```

Output files:

HGT candidates validated by phylogenetic approach are exported to the same folder as best-match approach.

1. **HGT_candidates_PG.txt**: Best-match approach predicted HGTs, with additional information provided by phylogenetic approach.
2. **HGT_candidates_PG_validated.txt**: Only phylogenetic approach validated HGTs.
3. **HGT_candidates_PG_aa.fasta**: Nucleotide sequences of phylogenetic approach validated HGTs.
4. **HGT_candidates_PG_nc.fasta**: Amino acid sequences of phylogenetic approach validated HGTs.

References

1. Parks DH, Imelfort M, Skennerton CT, Hugenholtz P, Tyson GW: CheckM: assessing the quality of microbial genomes recovered from isolates, single cells, and metagenomes. Genome research 2015, 25:1043-1055.
2. Contreras-Moreira B, Vinuesa P: GET_HOMOLOGUES, a versatile software package for scalable and robust microbial pangenome analysis. Applied & Environmental Microbiology 2013, 79:7696-7701.