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To cite this version:
Clémence Frioux, Arnaud Belcour, Méziane Aite, Anthony Bretaudeau, Falk Hildebrand, et al.. Assessment of metabolic complementarity in large-scale microbiotas for the identification of key species. IHMC 2021 - 8th International Human Microbiome Consortium Congress, Jun 2021, Barcelone, Spain. pp.1. hal-03438983

HAL Id: hal-03438983
https://hal.science/hal-03438983
Submitted on 22 Nov 2021

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Assessment of metabolic complementarity in large-scale microbiotas for the identification of key species

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Context

- Microbiota analyses through metagenomic sequencing lead to huge resources of data in order to determine the organisation of microbial communities.
- Understanding the interactions within communities entails the identification of functions carried out by microbes as well as the redundancy of and complementarity between these functions.
- Genome-scale metabolic network (GSMN) reconstruction is validated method to model and simulate organisms’ functions.

How to efficiently screen the metabolic functions and metabolic complementarity in hundreds or thousands of species?

How to identify key species and minimal communities associated to functions of interest?

Met2ge2metabo (M2M)

A flexible software resource [1] for:
- Metabolic network reconstruction
- Modelling of individual and collective metabolic capabilities
- Identification of the cooperation potential within a community
- Community reduction and identification of key species with respect to a metabolic objective

Application to 1,520 reference genomes of the gut microbiota

- 1,520 reference genomes from cultivable bacteria of the human gut microbiota [3]
- 1,520 GSMNs to be compared and analysed.
- Identification of key species (KS) within the 1,520 GSMNs for groups of metabolic end-products (lipids, carbohydrates...)
- Enumeration of minimal communities associated to these metabolites.
- Analysis of associations between KS within reduced communities: identifications of bacterial groups with equivalent roles in the community with respect to the metabolic end-products.

Suitability of metabolic modelling to MAGs

- 913 Metagenome Assembled Genomes (MAGs) of the cow rumen microbiota [2] were randomly degraded: removal of 2% of genes, 5% of genes in 80% or 100% of MAGs, removal of 10% of genes in 70% of genomes.
- GSMNs characteristics are comparable to those of GSMMs obtained with reference sequences.
- M2M analyses on metabolic potential of associated GSMNs, cooperation potential, community reduction and key species show a stability of the predictions to moderate degradations of genomes.

Discussion

- Modelling is qualitative, using the network expansion algorithm [4]; robustness to data imprecision despite a loss in quantitative predictions.
- M2M pinpoints mutualistic metabolic interactions within large communities of bacteria.
- Application to metagenomic samples: 1 sample = 1 community. Illustrated on the MetaHIT dataset [5] in [1].
- M2M can help identifying cornerstone taxa in microbiomes.

Table 1. Community reduction analysis of the metabolite categories in the gut. All minimal communities were enumerated, starting from the set of 1,520 GSMNs with respect to sets of target metabolites. KS: key species, ES: essential symbionts, AS: alternative symbionts. Pmm: Firmicutes, Bact: Bacteroidetes, Act: Actinobacteria, Prot: Proteobacteria, Fus: Fusobacteria

Fig 1: M2M pipeline and main functionalities.

Fig 2: Definition of key species (KS). Reducing the complexity of a large community can help understand the mechanisms and interactions associated to functions. Yet, up to millions of equivalent minimal communities exist for a given metabolic objective. KS consist in all species occurring in at least one minimal community. They can be further distinguished in essential symbols (occurring in all minimal communities) and alternative symbols.

Fig 3: Comparison of the outputs of M2M for various degradations of MAGs in a set of 913 rumen MAGs from [2].

References