Quantifying the impact of tree choice in metagenomics differential abundance studies with R

Antoine Bichat[1,2], Mahendra Mariadassou[3], Jonathan Plassais[2] and Christophe Ambroise[1]

1. LaMME - Université d'Évry-Val-d'Essonne; 2. Enterome; 3. MaIAGE - INRA

Microbiota

- **Ecological community of microorganisms that resides in an environmental niche**
- 10^{14} bacteria in the gut among 1 500 species
- Associations with:
  - metabolism (diet, obesity, drug absorption, …)
  - diseases (IBD, allergies, diabete…)
  - behavior (smokers, antibiotics, C-section…)
  - environment (pet, water…)

Objectives

- Find which bacteria are differentially abundant between two or more groups
- Use a FDR multiple testing correction to prevent false positives (one test per bacteria)
- Incorporate hierarchical information to increase power
- Which tree?

Hierarchical False Discovery Rate

The z-scores $\mathbf{z} = \Phi^{-1}(\mathbf{p})$ are smoothed using the following hierarchical model:

$$\mathbf{z}|\mu \sim \mathcal{N}_n\left(\mu, \sigma^2\mathbf{I}_n\right) \qquad \mu \sim \mathcal{N}_m\left(\gamma\mathbf{1}, \tau^2\mathbf{C}_\rho\right)$$

where $\mathbf{C}_\rho = \left(\exp(-2\rho\mathbf{D}_{i,j})\right)$ with $\mathbf{D}$ the patristic distance matrix between taxa from the tree. By applying Bayes's formula:

$$\mathbf{z} \sim \mathcal{N}_m\left(\gamma\mathbf{1}, \tau^2\mathbf{C}_\rho + \sigma^2\mathbf{I}_m\right)$$

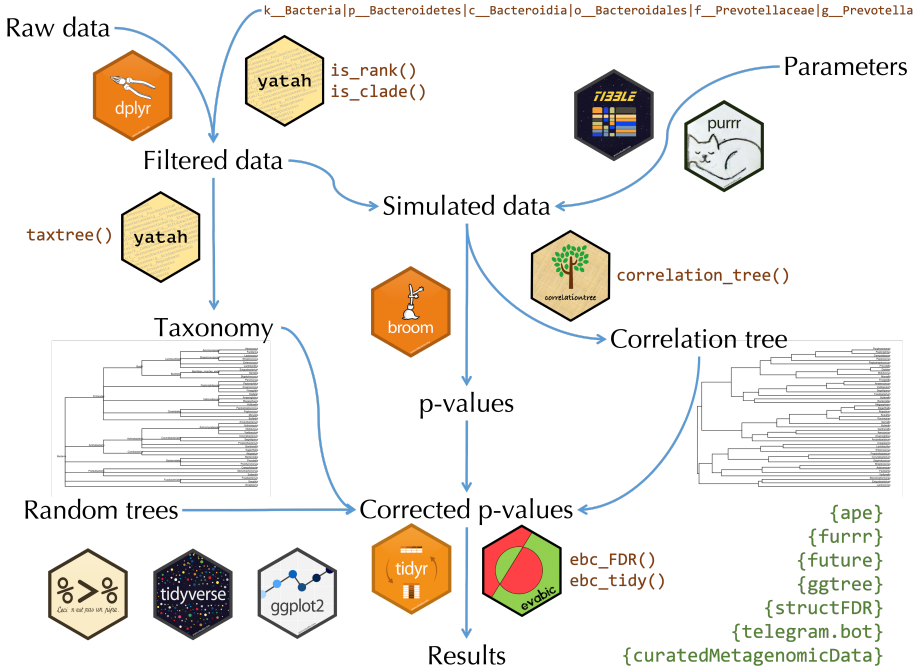
$$\mu^* = \left(\mathbf{I}_m + \frac{\sigma_0^2}{\tau_0^2}\mathbf{C}_{\rho_0}^{-1}\right)^{-1}\left(\frac{\sigma_0^2}{\tau_0^2}\mathbf{C}_{\rho_0}^{-1}\gamma_0\mathbf{1} + \mathbf{z}\right)$$

Finally, a permutation-based FDR control is applied on μ^*

Data: taxonomy and abundance

Phylum	Class	Order	Family	Genus	S001	S002	S003	S004	S005	…
Actinobacteria	Coriobacteriia	Coriobacteriales	Atopobiaceae	Atopobium	84	0	12	54	0	…
Actinobacteria	Coriobacteriia	Eggerthellales	Eggerthellaceae	Eggerthella	2	0	0	7	0	…
Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	525	7	134	753	0	…
Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	88	1770	1490	119	2136	…
Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	0	0	138	4	0	…
Firmicutes	Negativicutes	Veillonellales	Veillonellaceae	Dialister	152	4	2	192	0	…
Firmicutes	Negativicutes	Veillonellales	Veillonellaceae	Megasphaera	402	0	4	102	0	…
Fusobacteria	Fusobacteriia	Fusobacteriales	Leptotrichiaceae	Sneathia	302	0	35	272	0	…

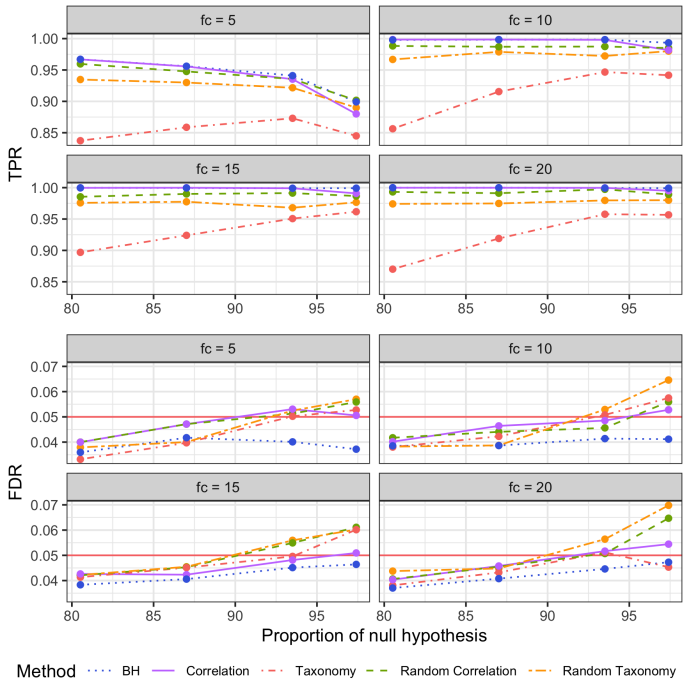
Workflow



Take-home message

- The tree choice has little impact on detection power
- Benjamini-Hochberg procedure is still the most powerful method and the only one which respects the FDR control
- The ease of creating R packages greatly increases the reproducibility of analysis
- **tidyverse** and especially list-columns allow to write elegant and efficient R code when manipulating non-standard structures (trees, statistical model outputs…)

Results



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Contact Information

abichat@enterome.com
abichat.github.io
antoinebichat
@_abichat
@abichat

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