

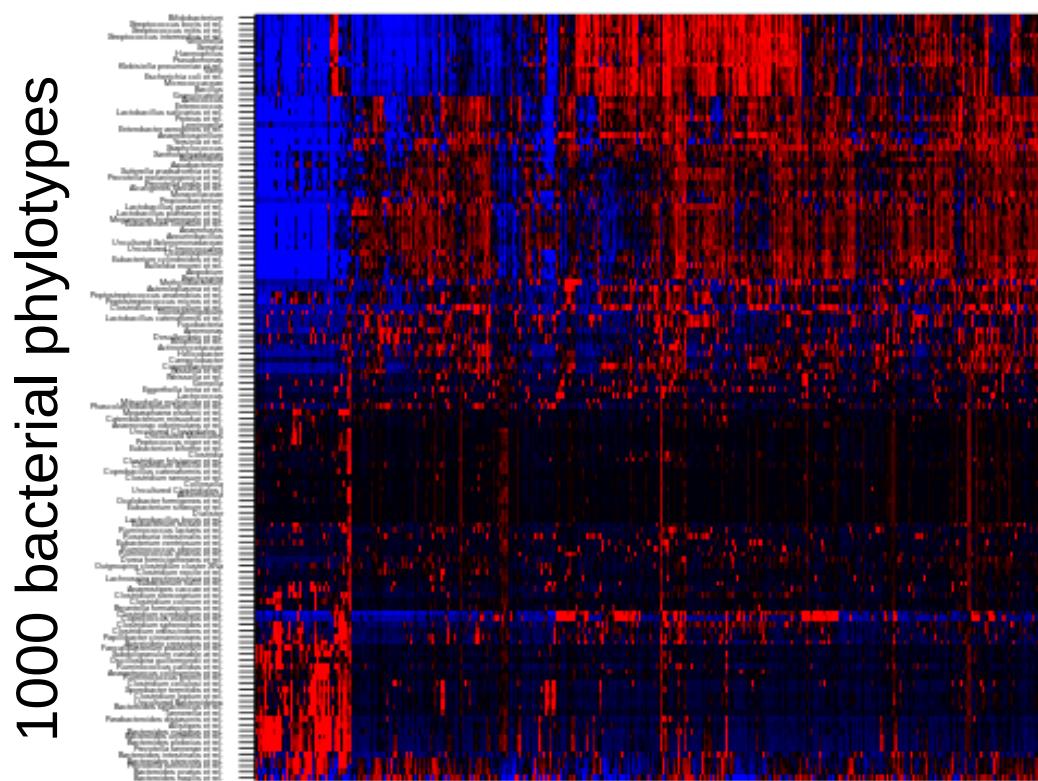
Opportunities and challenges in large-scale microbiome profiling studies

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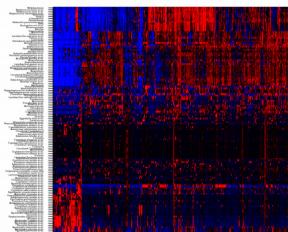


N ~ 10,000+ samples

Data availability: large & standardized cross-sectional cohorts

HITChip Atlas (microarrays):

- > 10,000 samples
- > 5,000 subjects
- > 1,000 phylotypes (~0.1%)
- versatile geography
- highly reproducible (>98%)
- long follow-ups (10+ y)
- Lahti et al. 2014



Flemish Gut Flora (NGS):

- > 5,000 samples
- > 1,000 subjects
- > 7,000 OTUs
- normal Flemish adults
- longitudinal follow-up
- Falony et al. 2016



Challenges for data availability:

- Standardization: protocols & metadata
- Collection of longitudinal & functional data
- Custom tools & workflows
- Ethical considerations

analysis tools: <http://microbiome.github.io>

Other collections: MetaHIT, Human Microbiome Project, American Gut...

Dedicated target sequence databases can significantly improve the analyses

- Dedicated HITdb for gut 16S rRNA outperforms generic target databases (Silva, Greengenes)
- Improved sensitivity and coverage for gut microbiota profiling
- Other body sites to be done
- Also in light-weight OTU clustering pipeline Lotus:
<http://psbweb05.psb.ugent.be/lotus/>



RESEARCH ARTICLE

Improved taxonomic assignment of human intestinal 16S rRNA sequences by a dedicated reference database

Jarmo Ritari^{1*}, Jarkko Salojärvi¹, Leo Lahti^{1,2} and Willem M. de Vos^{1,2,3}

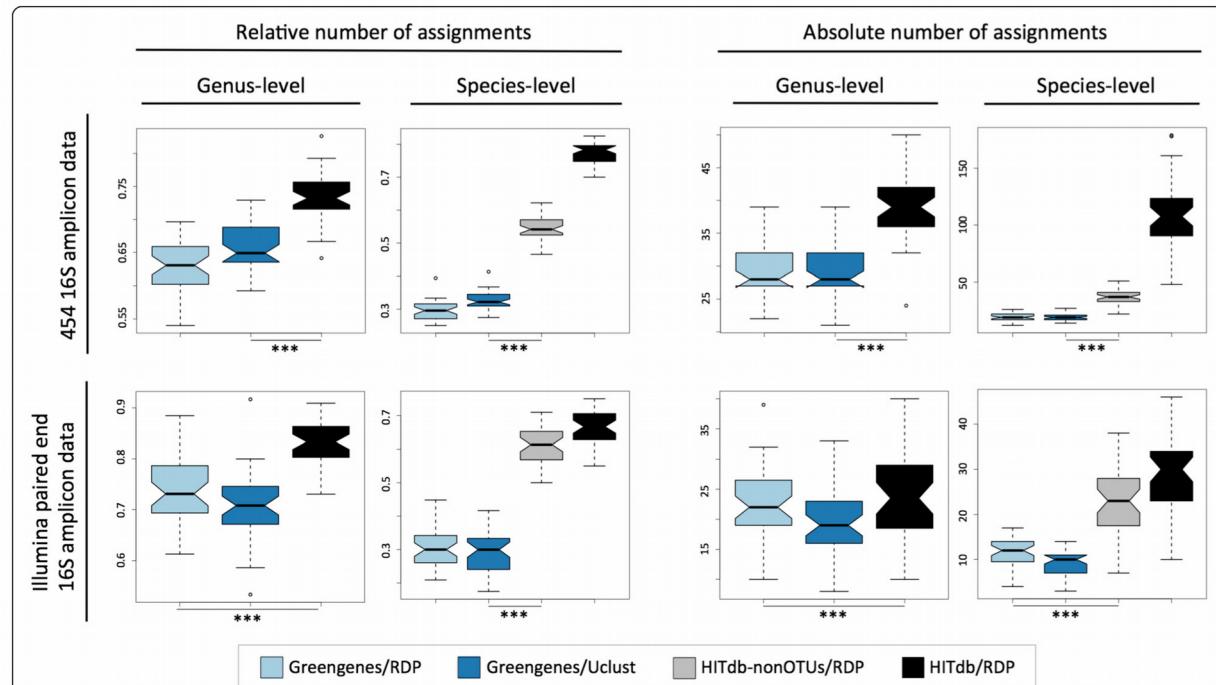
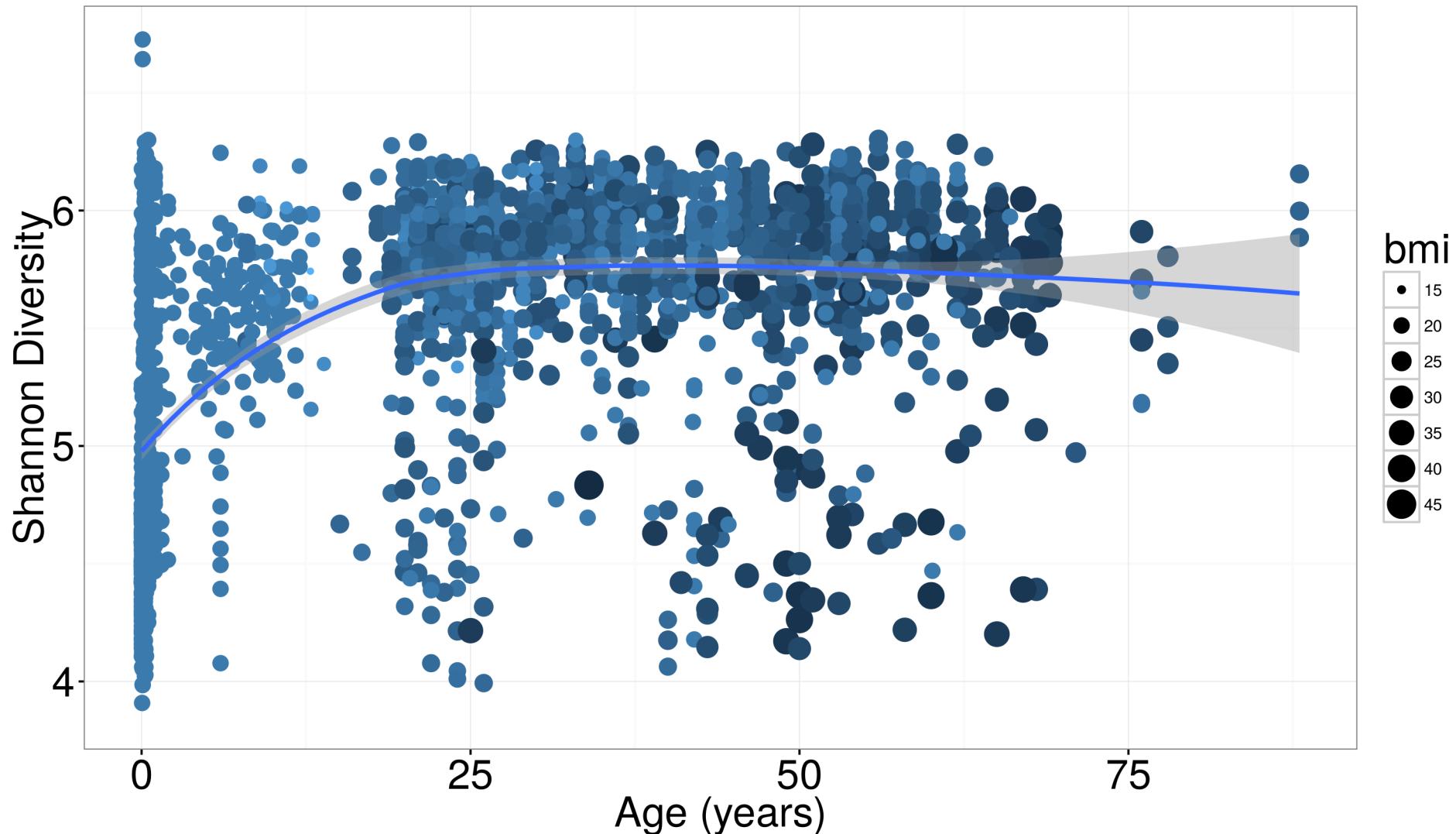


Fig. 4 Comparison between Greengenes and HITdb using data from biological samples. The used data set is indicated in rows, and relative and absolute numbers of assignments at genus and species levels in columns. At species level, the results for HITdb additionally show the biological species only (i.e. without OTUs) for easier comparison with Greengenes. *** $p < 0.001$. n = 119 and n = 40 samples for 454 and Illumina data sets, respectively

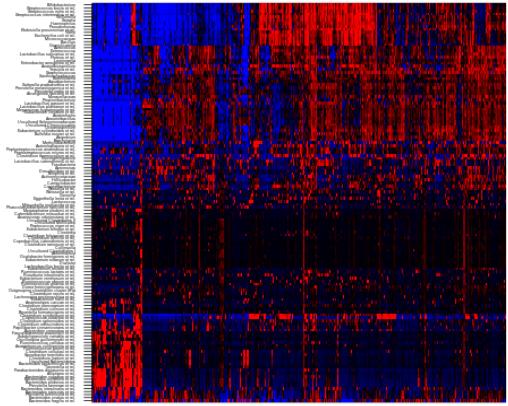
Gut microbiota diversity, ageing and overweight (healthy & normal obese subjects)

N = 2363

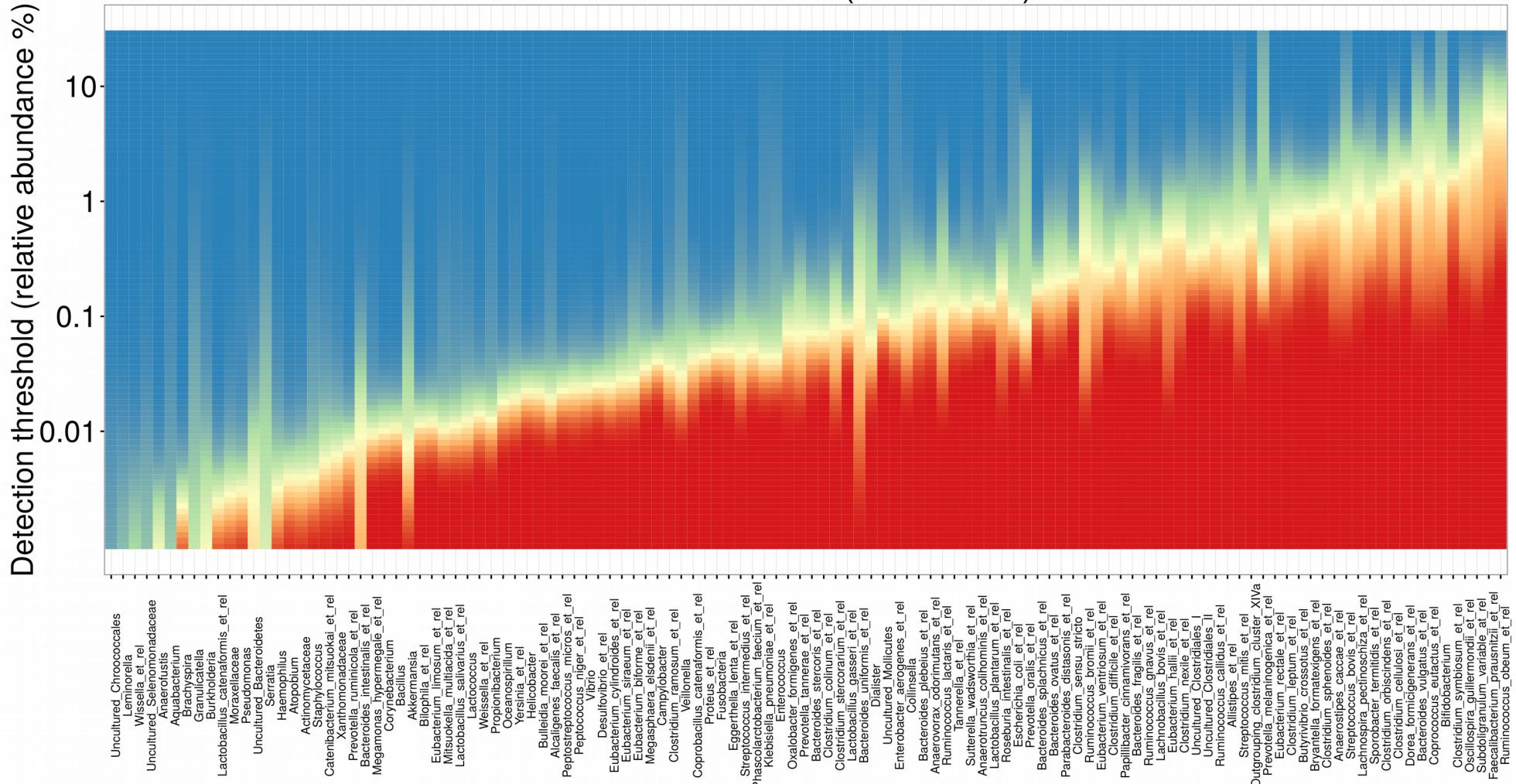


Core microbiota

only few species are prevalent (shared)
in population at a high abundance



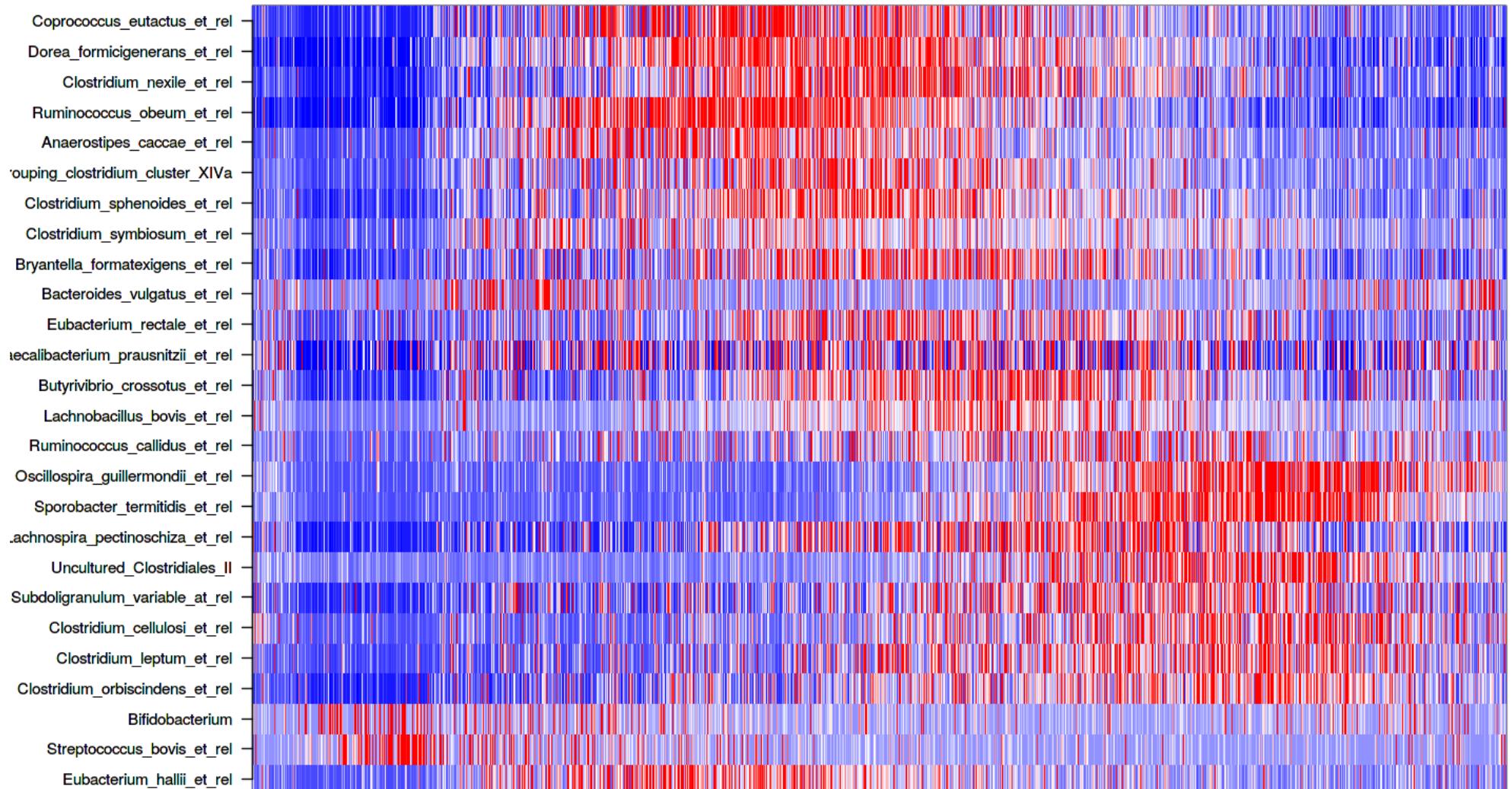
Core microbiota (N = 10763)



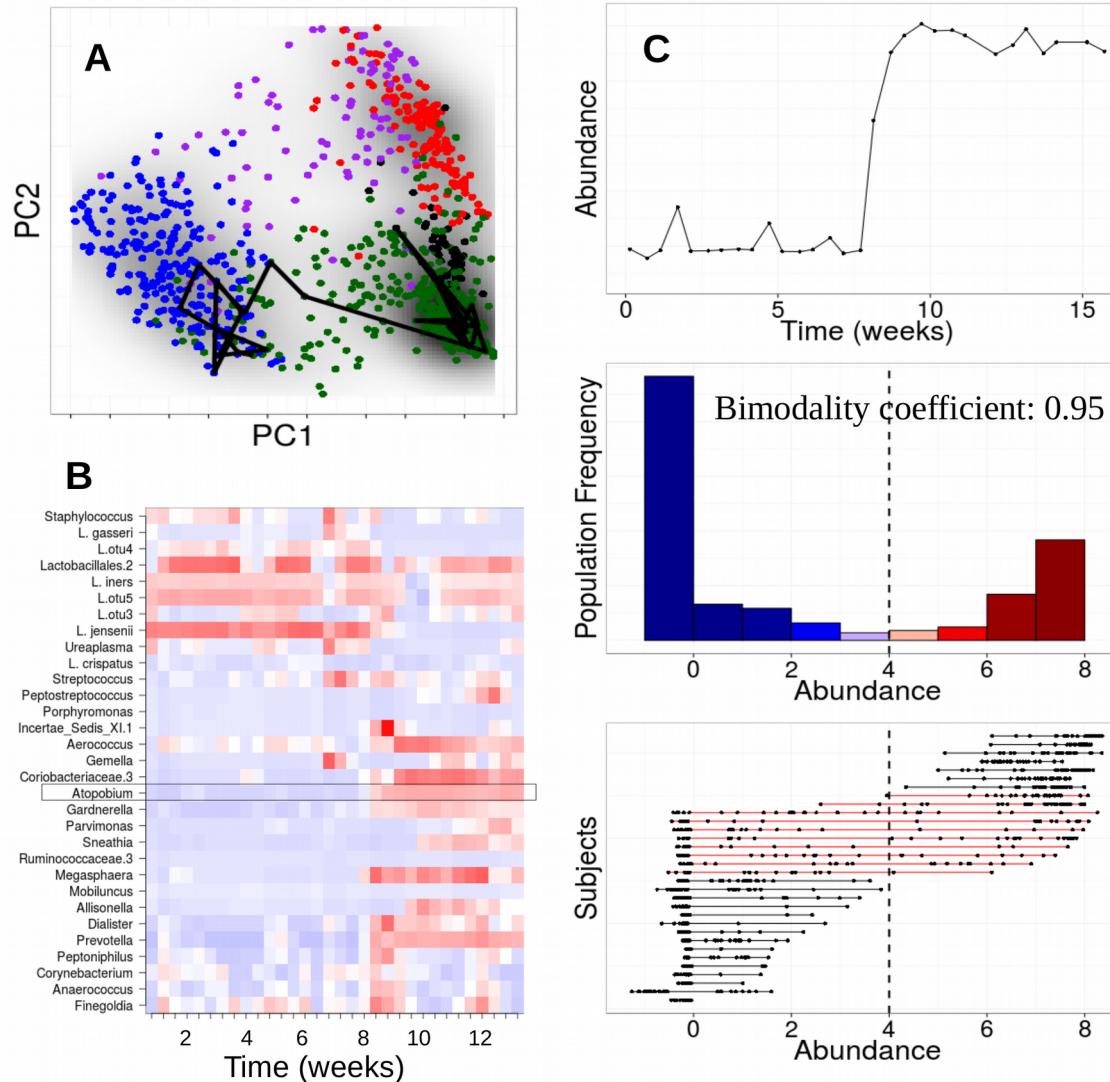
Data: HITChip Atlas

Core microbiota variation (N = 5005)

Z-score across subjects: red – high abundance & blue – low abundance
Core microbiota shows remarkable variation across population.



Cross-sectional vs. longitudinal analyses: community-level dynamics in vaginal microbiota is supported by pooling limited longitudinal data from multiple individuals

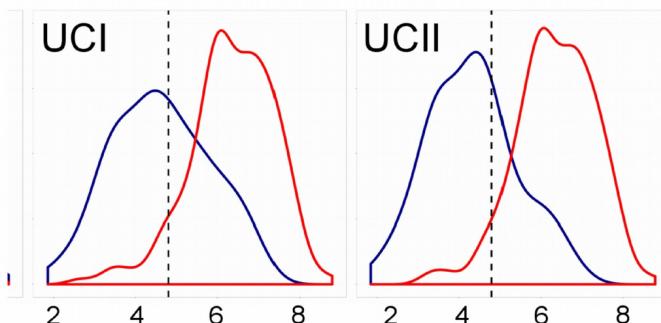


Effect on the overall ecosystem

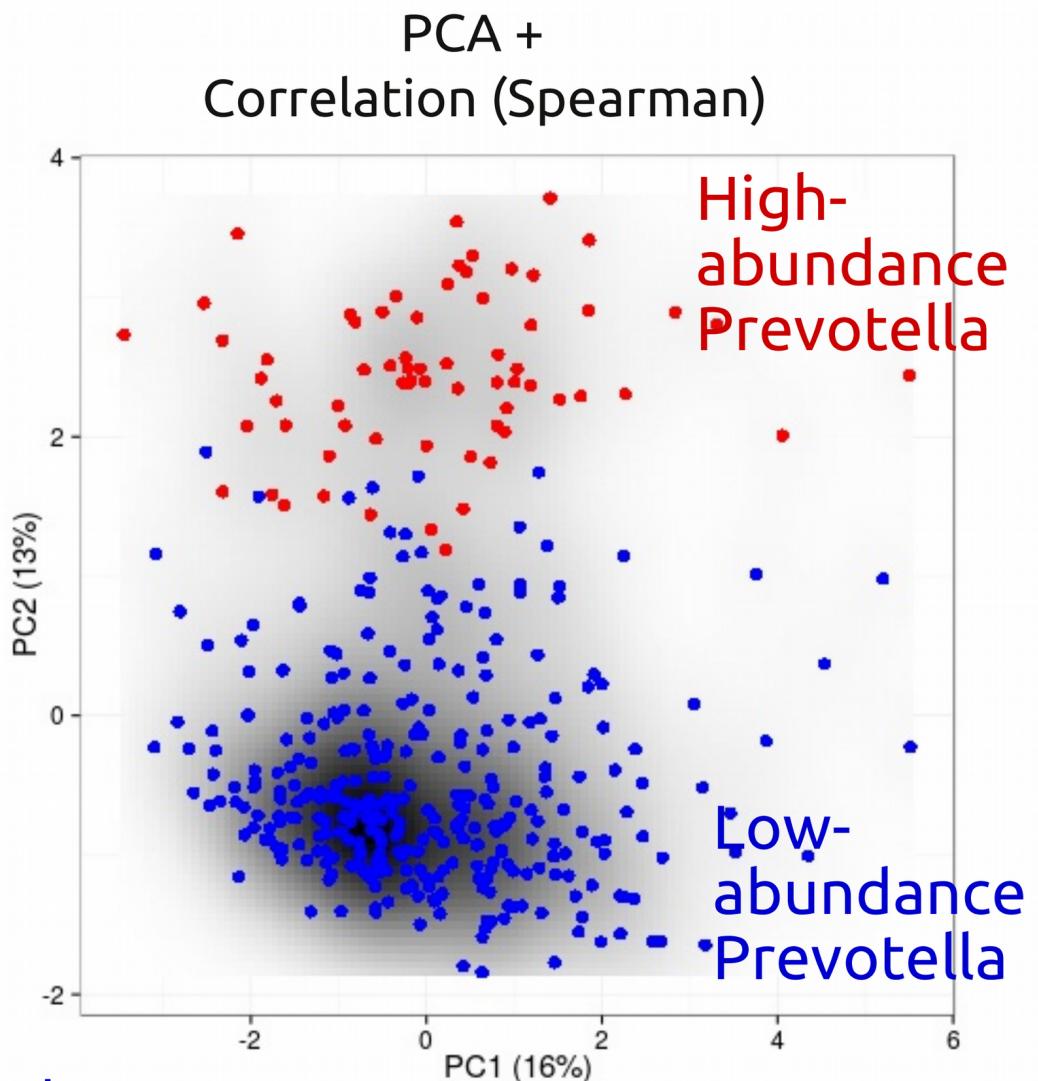
Prevotella states seen at ecosystem level

High ~10% relative abundance !

Other bi-stable taxa:
<2% relative abundance,
no ecosystem-level switches are visible



Uncultured Clostridiales associated with overall metagenomic richness

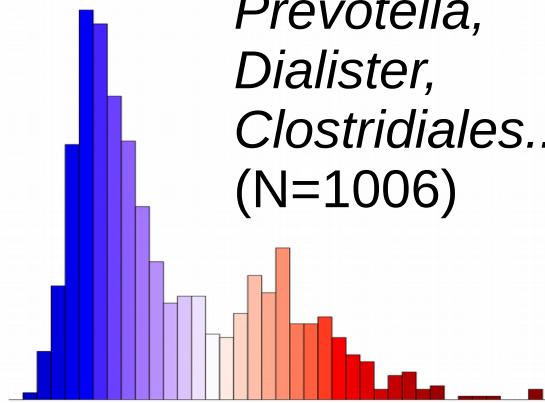


N = 401 western adults

Lahti et al. Nat. Comm. 5:4344, 2014

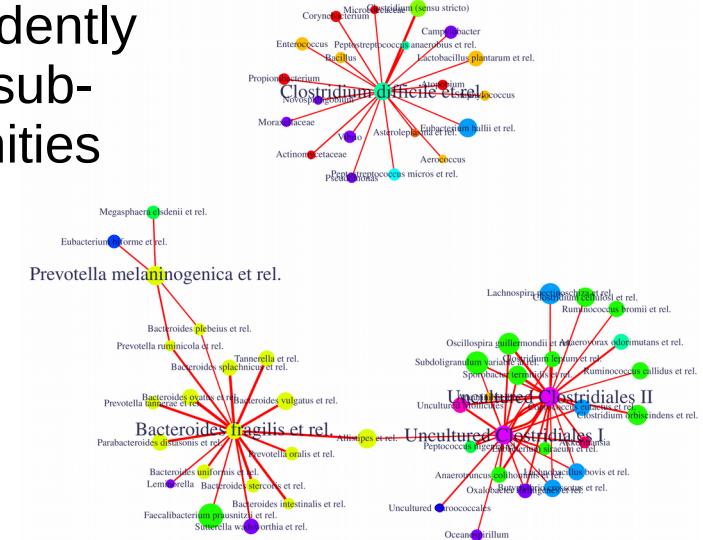
Subject stratification into community types can reduce complexity

Bistable groups:
Prevotella,
Dialister,
Clostridiales..
(N=1006)

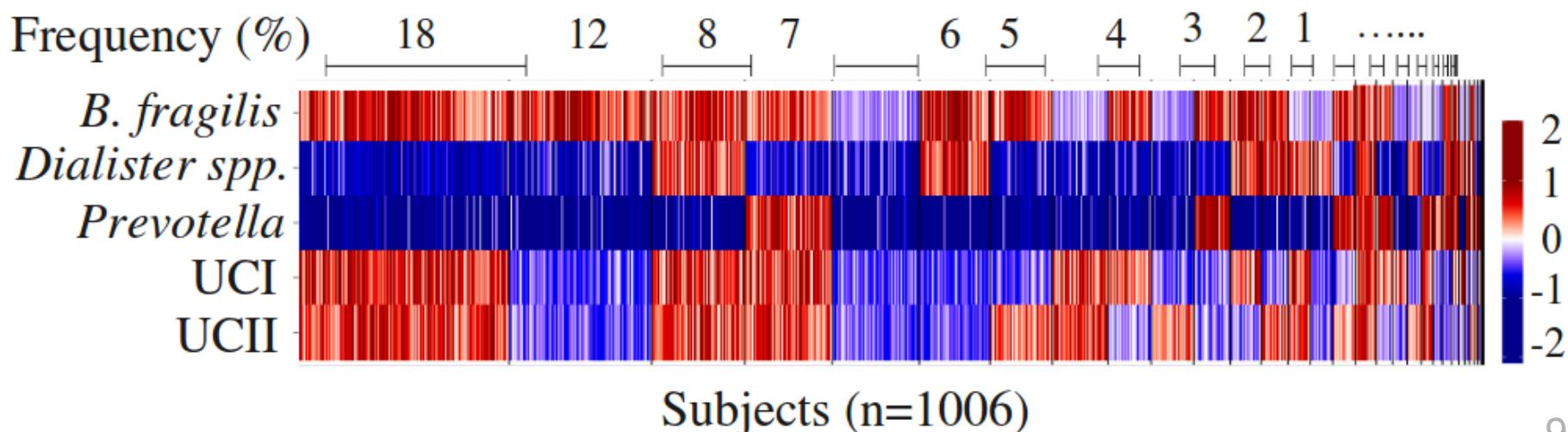


Lahti et al. Nat. Comm. 5:4344, 2014

Independently varying sub- communities

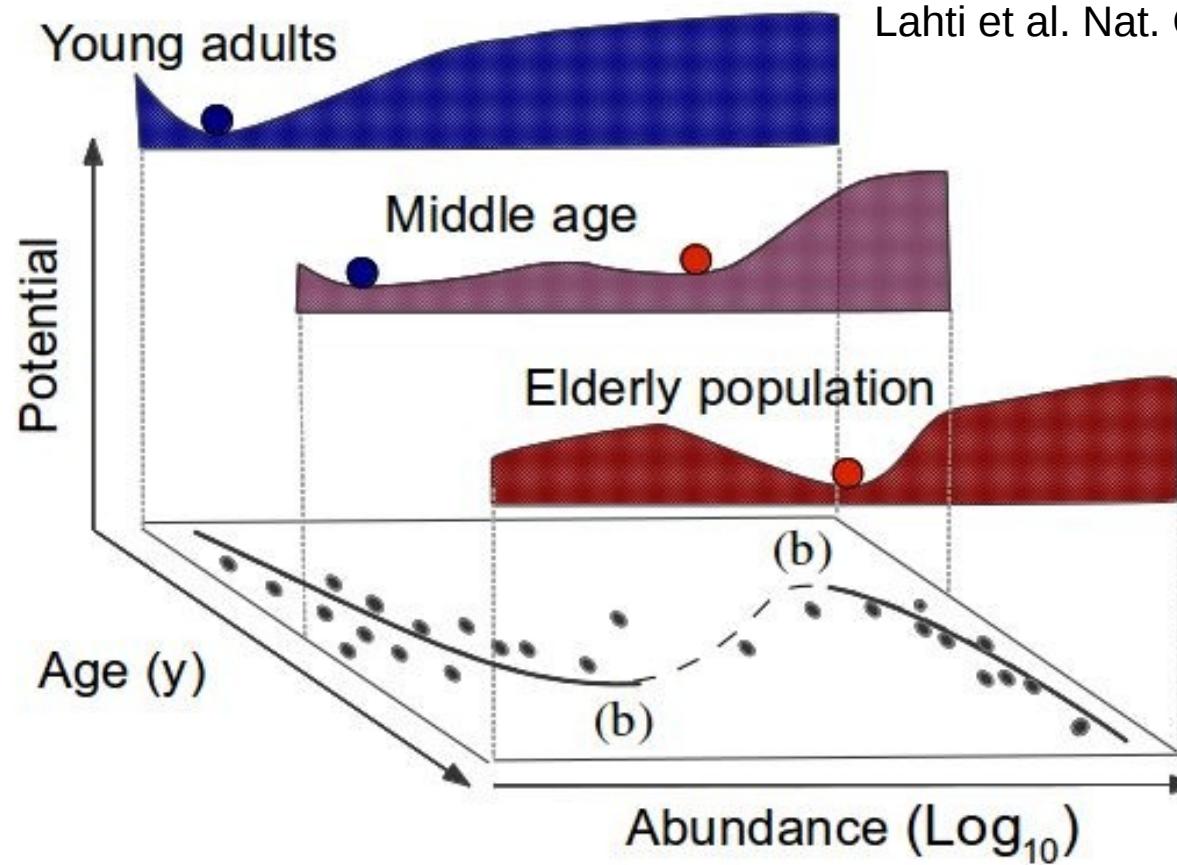


Ecosystem states are rich combinations of independent
tipping elements of the intestinal ecosystem



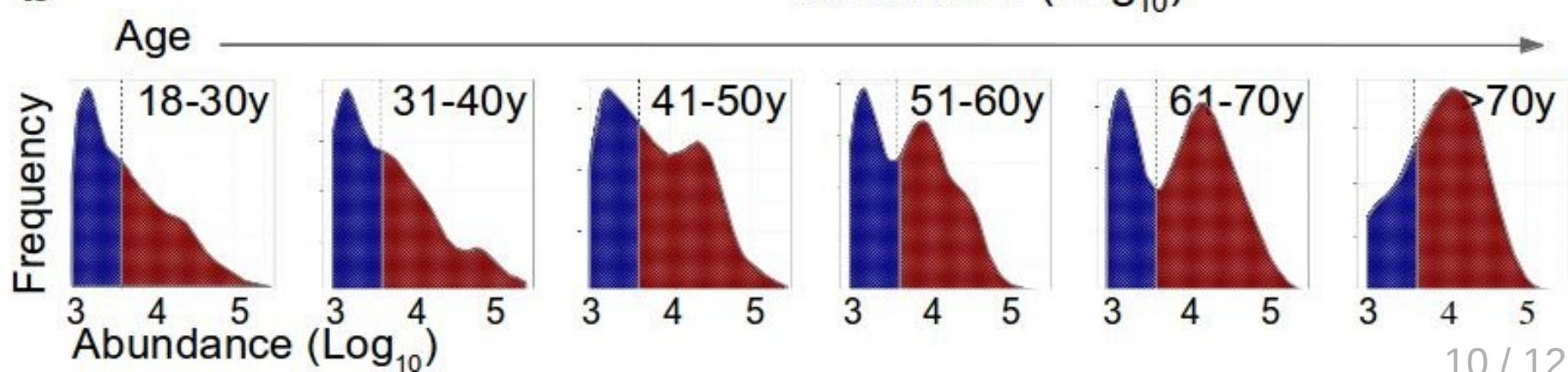
Cross-sectional analysis suggests a hidden lifetime trend in a less abundant group: state shift in Uncultured Clostridiales

a



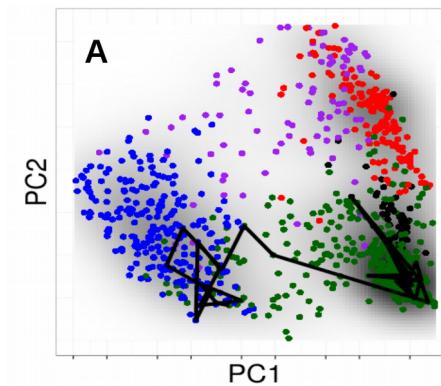
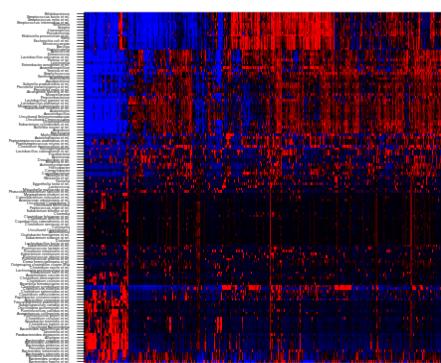
Lahti et al. Nat. Comm. 5:4344. 2014

b



Summary

- Individuality and temporal dynamics better understood in the context of larger populations
- Standardization, study design and confounder analysis remain essential yet easily overlooked
- Sharing of data & algorithms is essential



Thank You !

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<http://microbiome.github.io>



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