UNIVERSITAT POLITÈCNICA DE VALÈNCIA

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GOBIERNO DE ESPAÑA
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UNIÓN DE ENTIDADES ESPAÑOLAS DE CIENCIA ANIMAL

GENERALITAT VALENCIANA

Correlated responses to selection for IMF on microbial genomes in rabbits (using compositional data analysis techniques)

Martínez-Álvaro M., Zubiri-Gaitán A., Hernández P. and Blasco A.

ICTA, Universitat Politècnica de València

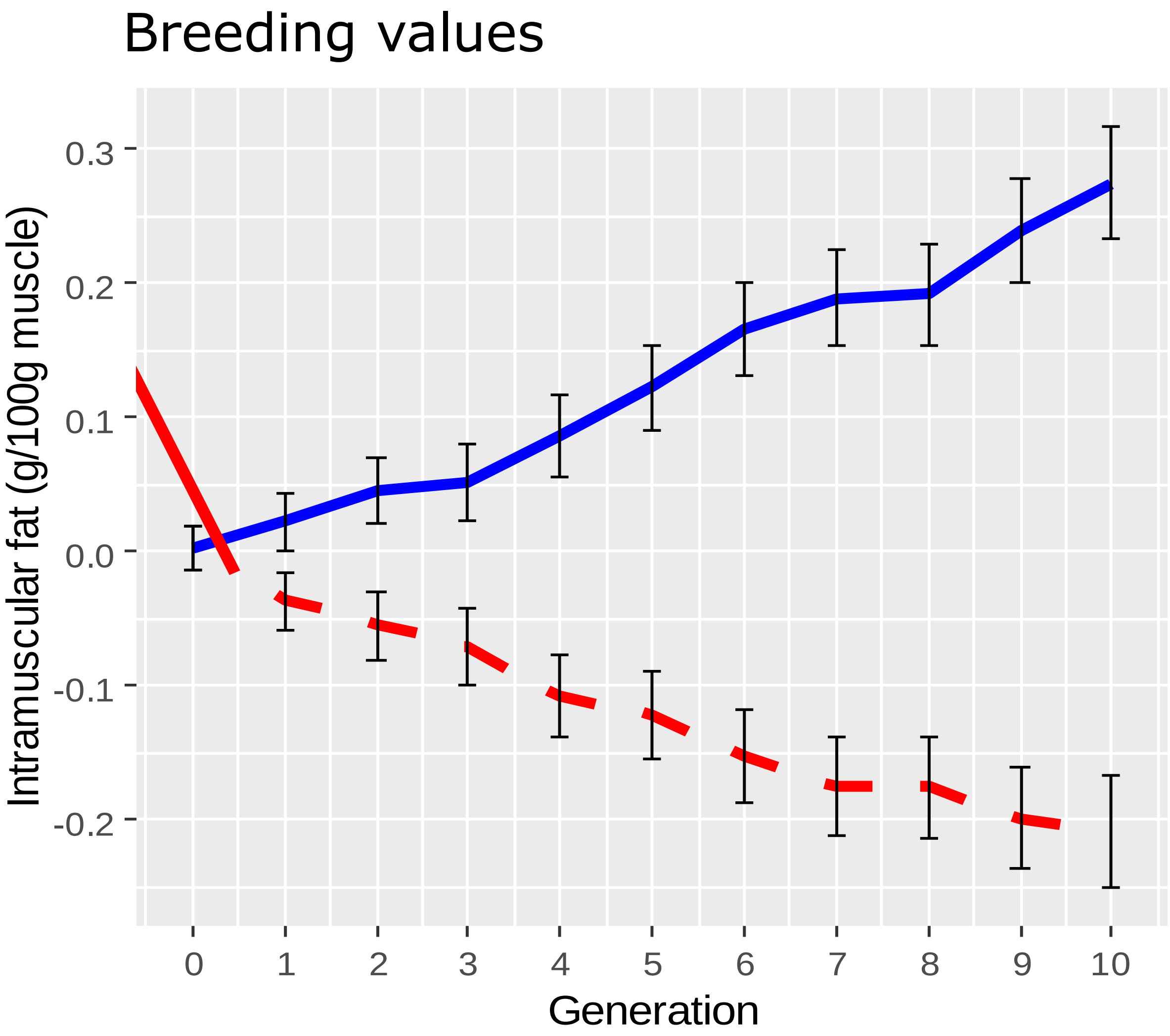
70th Annual Meeting of EAAP
27th August 2019, Ghent

WHY INTRAMUSCULAR FAT?

WHY IN RABBITS?

Divergent selection for IMF

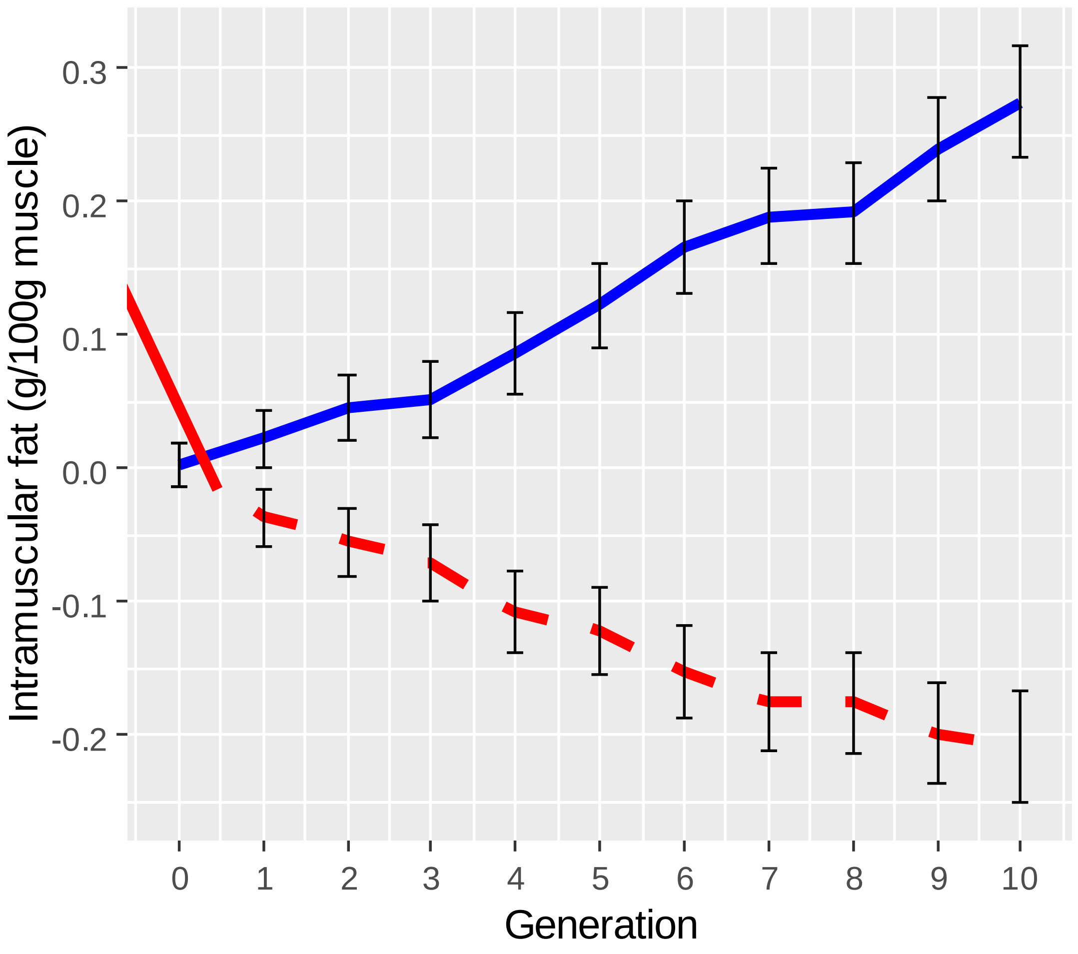
Response to selection for IMF



0.5 SD per gen

Divergent selection for IMF

SAME ENVIRONMENT!!

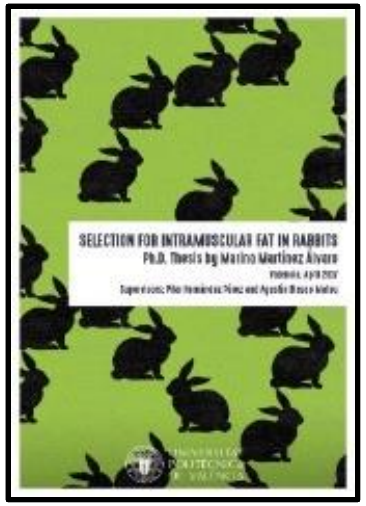


CORRELATED RESPONSES TO SELECTION FOR IMF IN OTHER TRAITS

PHENOTYPIC DIFFERENCES HIGH LINE – LOW LINE

Divergent selection for IMF

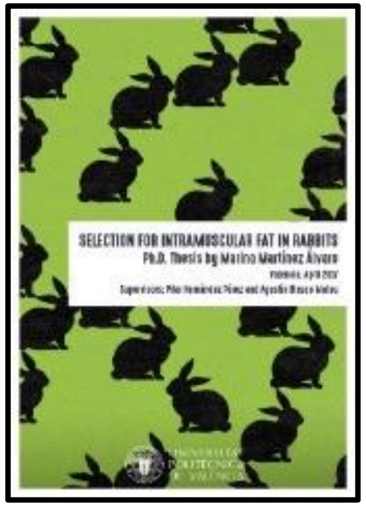
CORRELATED RESPONSES IN MEAT QUALITY TRAITS



Carcass fat

Divergent selection for IMF

CORRELATED RESPONSES IN MEAT QUALITY TRAITS



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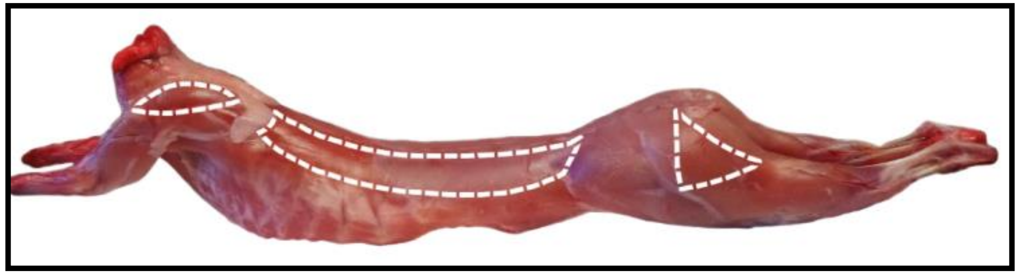
IMF in other muscles



Divergent selection for IMF

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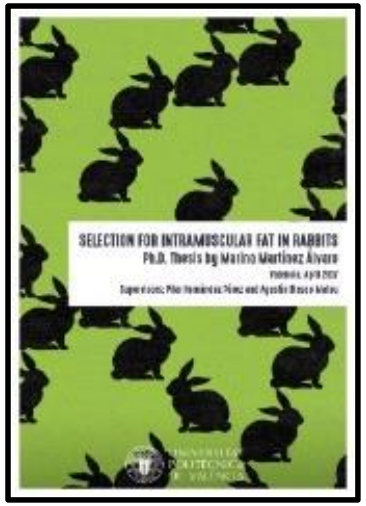

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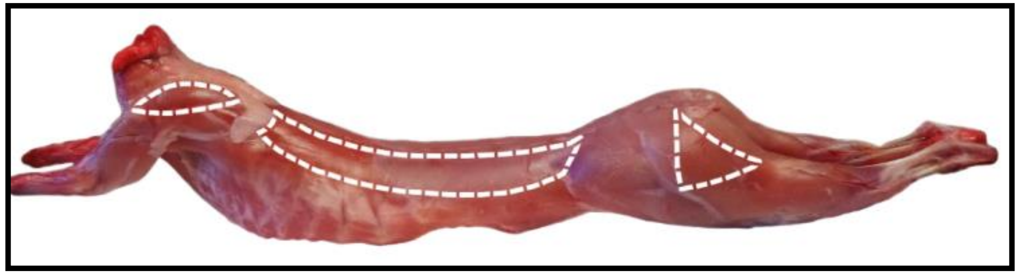
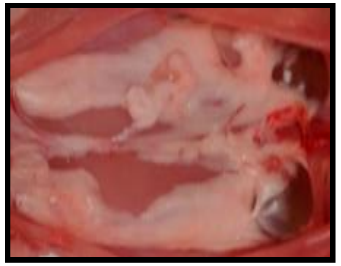
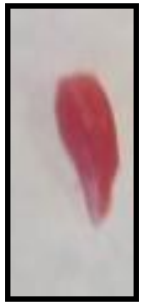


Lipogenic activity

G6PDH





Divergent selection for IMF

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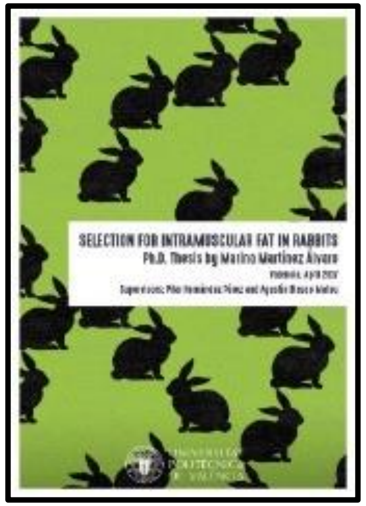

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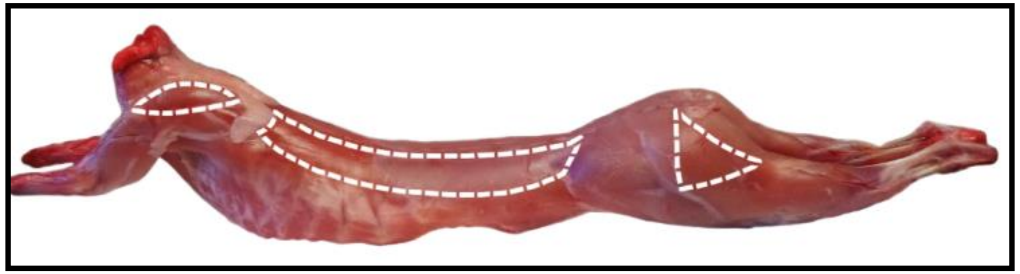

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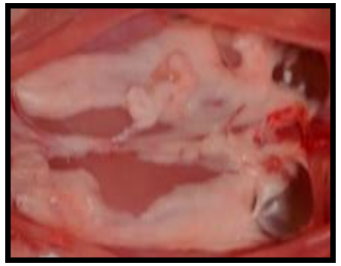

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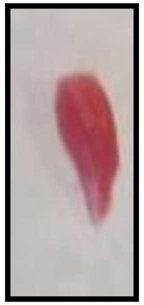
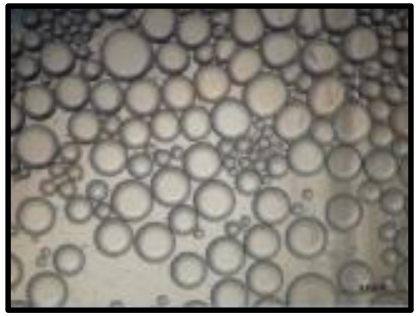
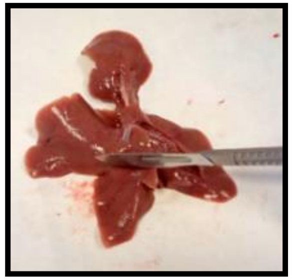


Adipocytes size



Liver size



Divergent selection for IMF

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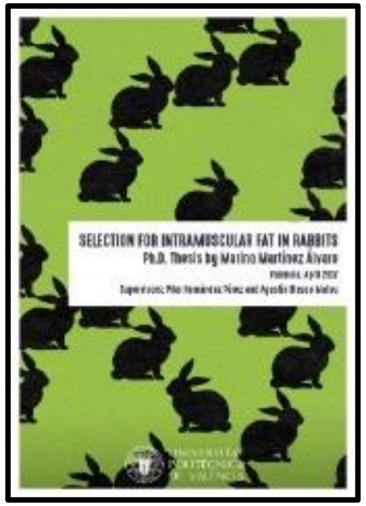

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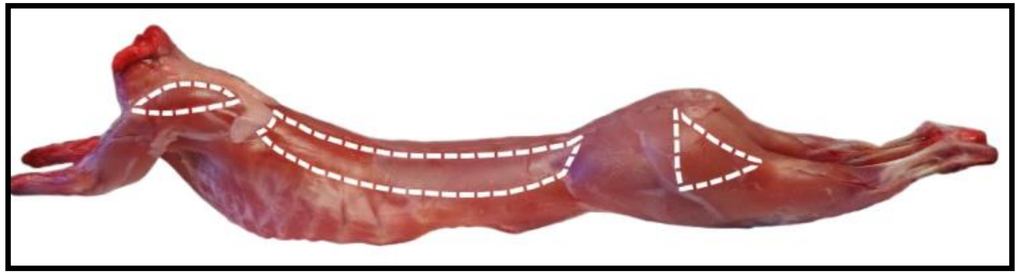

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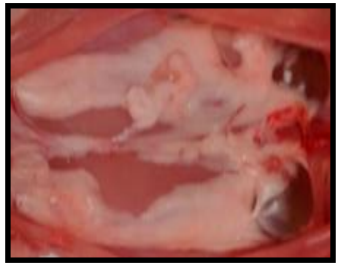

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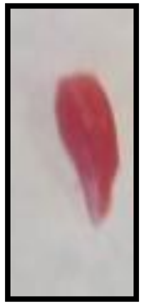

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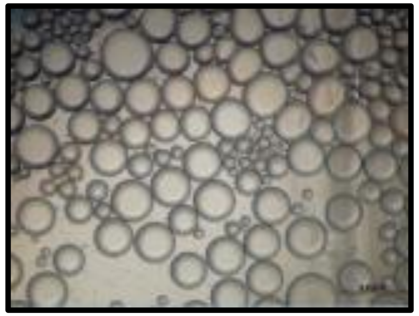

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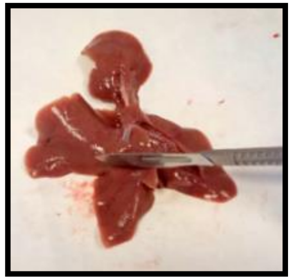
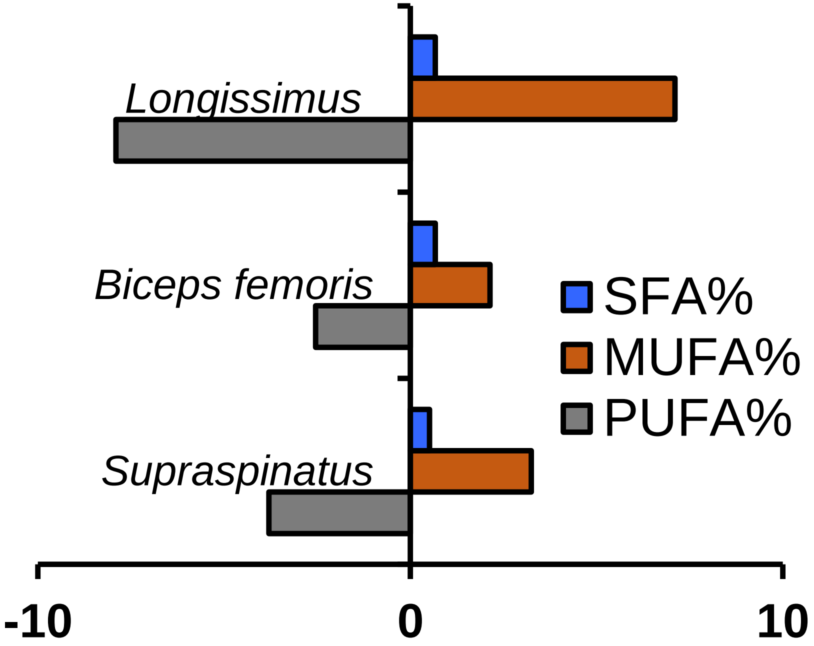


Meat Fatty Acid profile



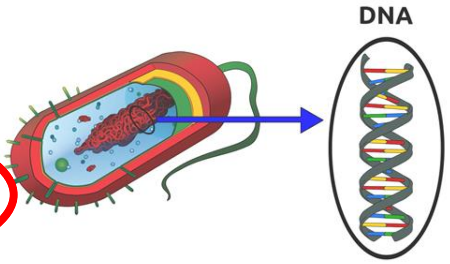
OBJECTIVE

CORRELATED RESPONSES IN MICROBIALS GENOME

GENOME

LINK

METAGENOME & MICROBIOME

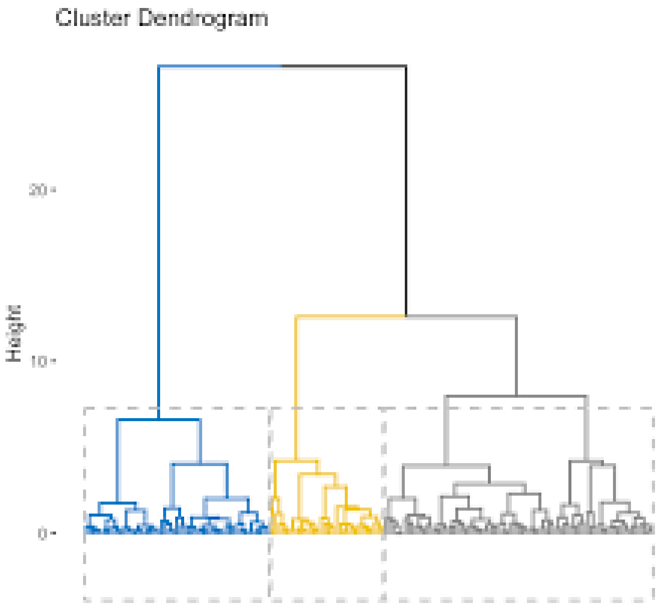


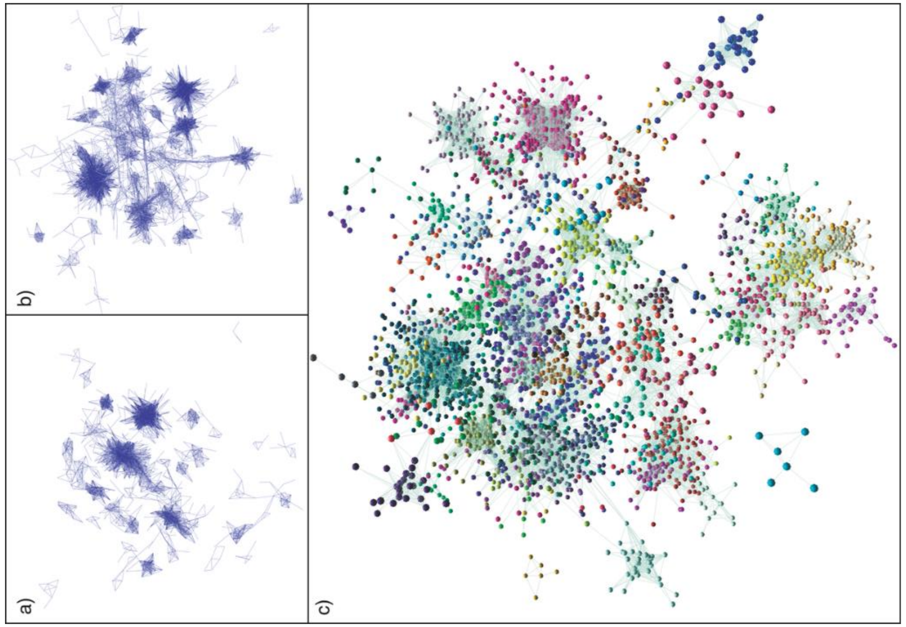
SOME IDEAS ABOUT COMPOSITIONAL DATA ANALYSIS…

STATISTICAL ANALYSIS OF METAGENOMIC DATA

MULTIVARIATE ANALYSIS DATA
BASED ON COV OR CORRELATIONS

PLS, Clusters, Correlation networks, Multiple regression, etc





STATISTICAL ANALYSIS OF METAGENOMIC DATA

INTERPRETATION PROBLEM

ABSOLUTE VALUES

IMF (g/100 g)	1	2	5
Microbial gene A	1	10	40
Microbial gene B	4	6	8

↑ IMF ↑ Microbial Genes A & B

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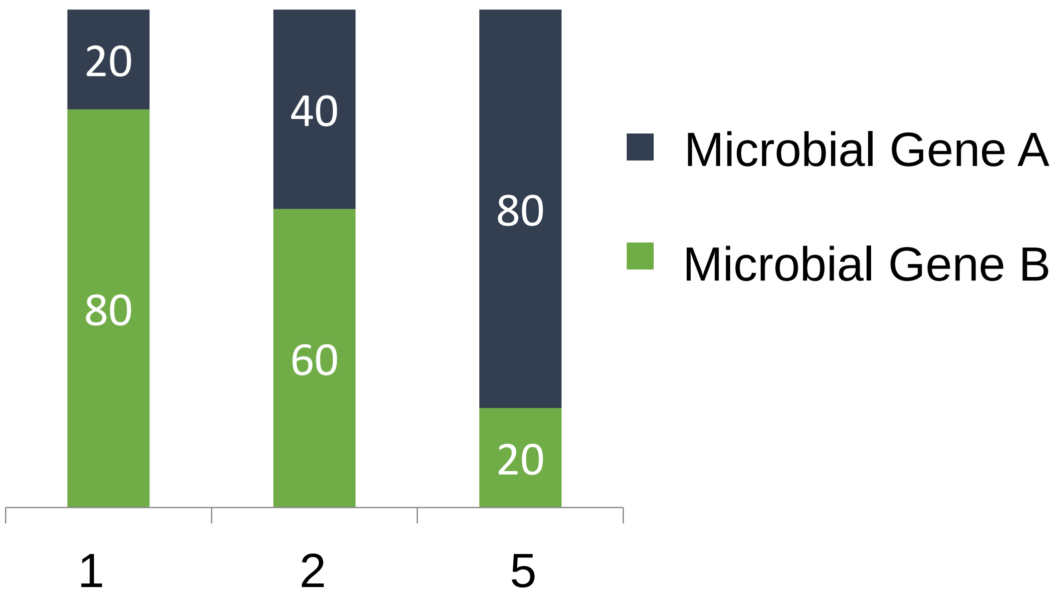

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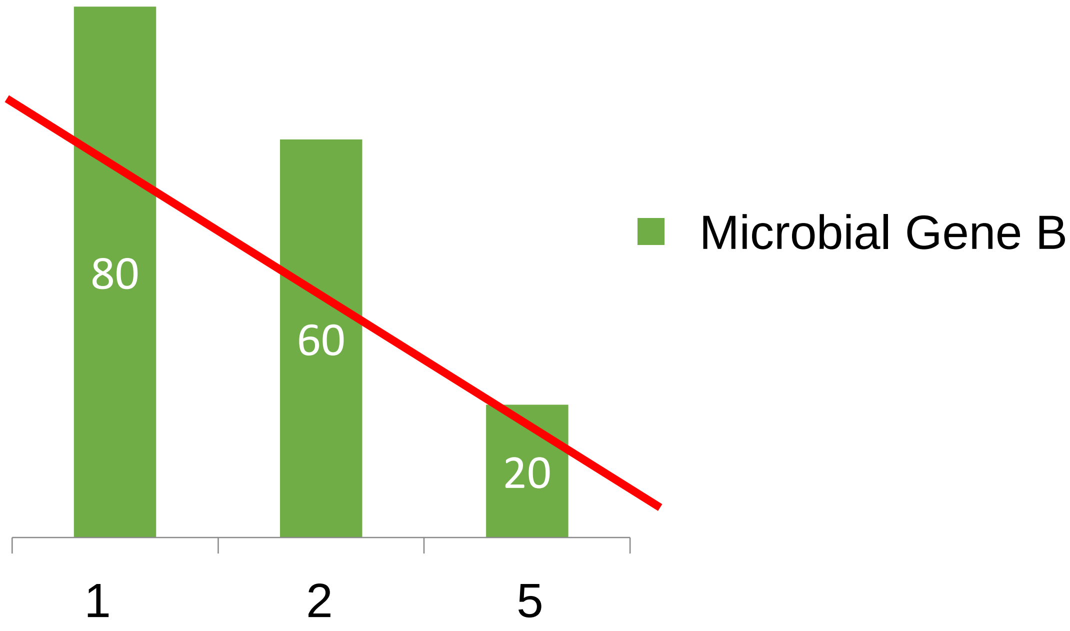

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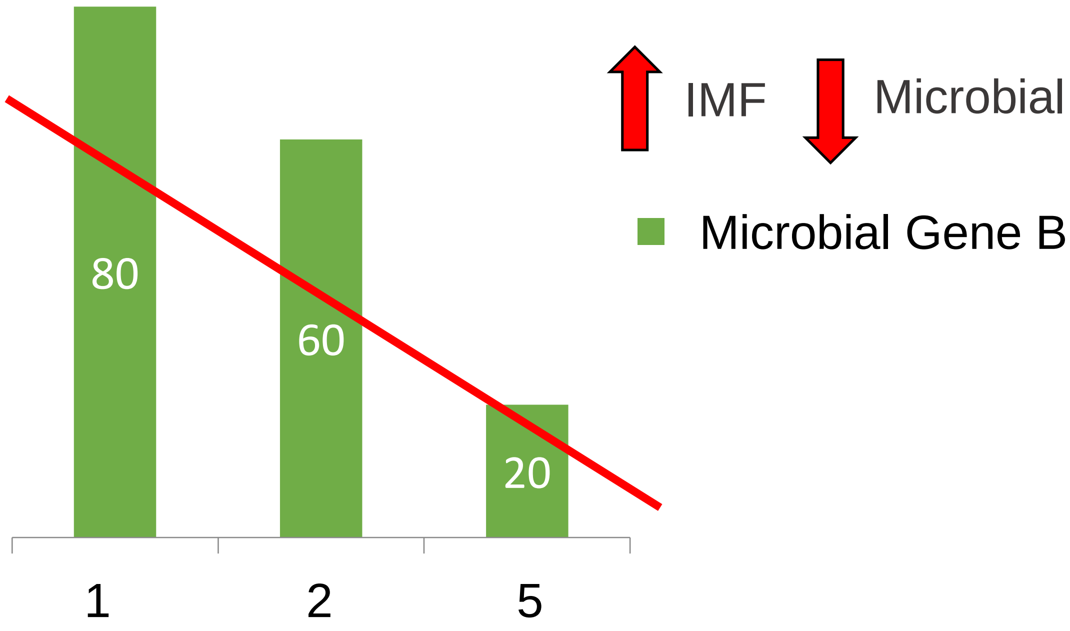


↑ IMF ↓ Microbial Gene B

CONFUSION

COMPOSITIONAL DATA

SIMPLEX restricted space	Aitchison geometry (not real)

STATISTICAL ANALYSIS OF METAGENOMIC DATA

COMPOSITIONAL DATA

SIMPLEX
restricted space

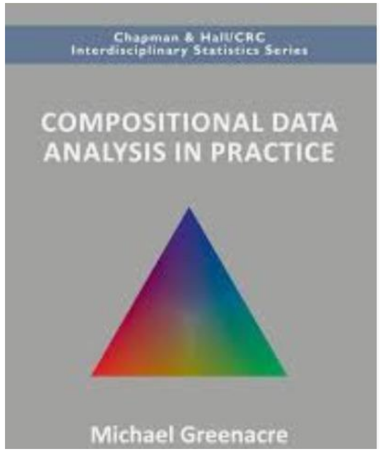
Aitchison geometry
(not real)

TransformaTions
Log ratio

Clr
Alr
Ilr

From Simplex to Real Space

Metrics in Euclidean geometry of real space



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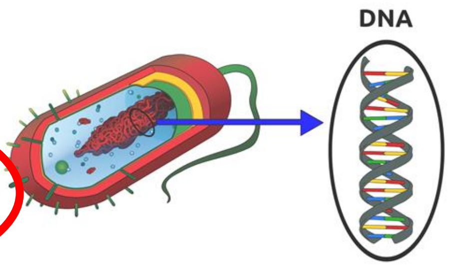
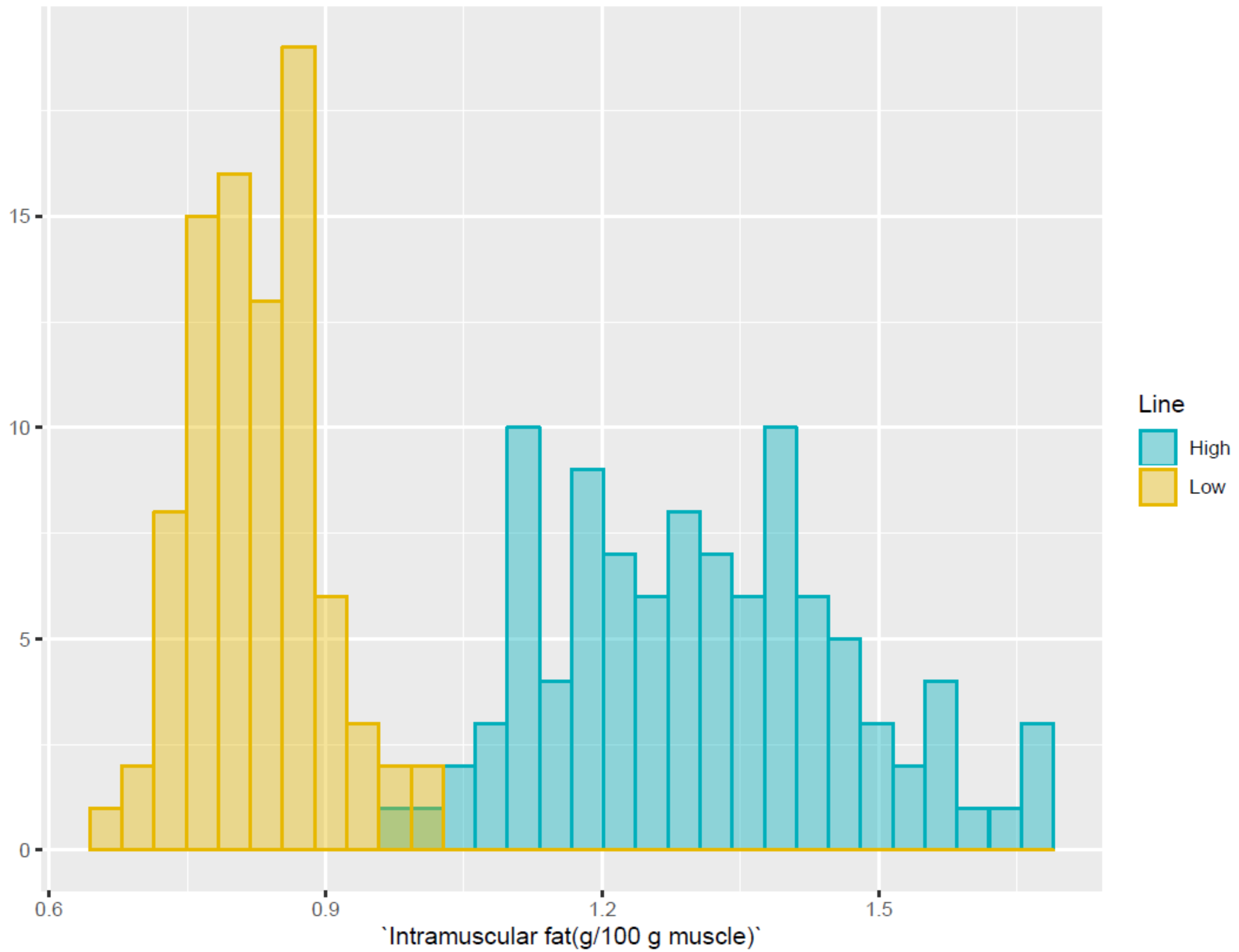


M & M

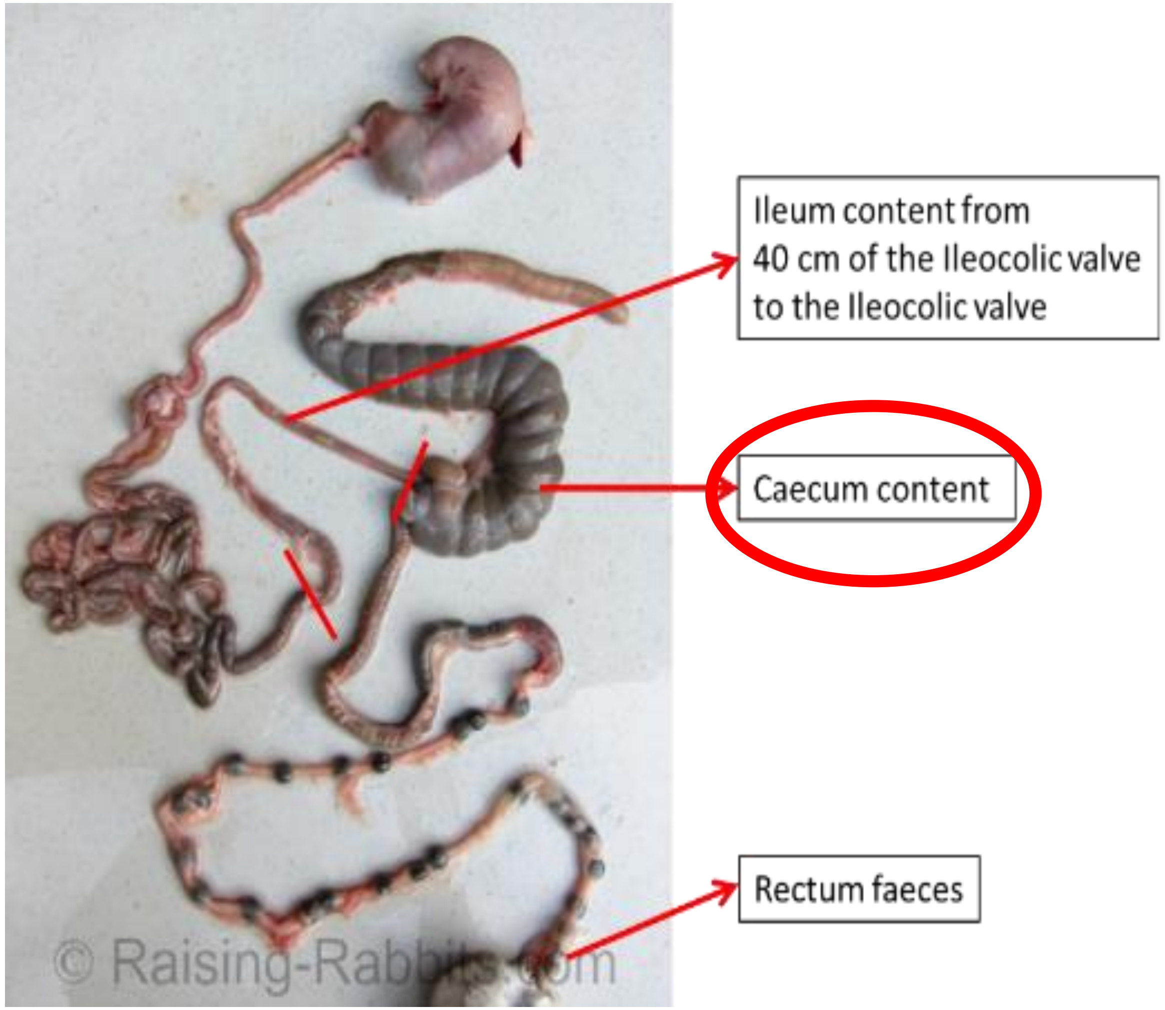
ANIMALS

Distribution of IMF fat data in the 10th generation



M & M

METAGENOMIC MEASURMENTS



N = 33 (16 H & 17 L)

- Illumina NextSeq
  - Reads (2 x 150 bp)
- KEGG database

STATISTICAL PIPELINE

1. “0s” study and replacement (zCompositions R)

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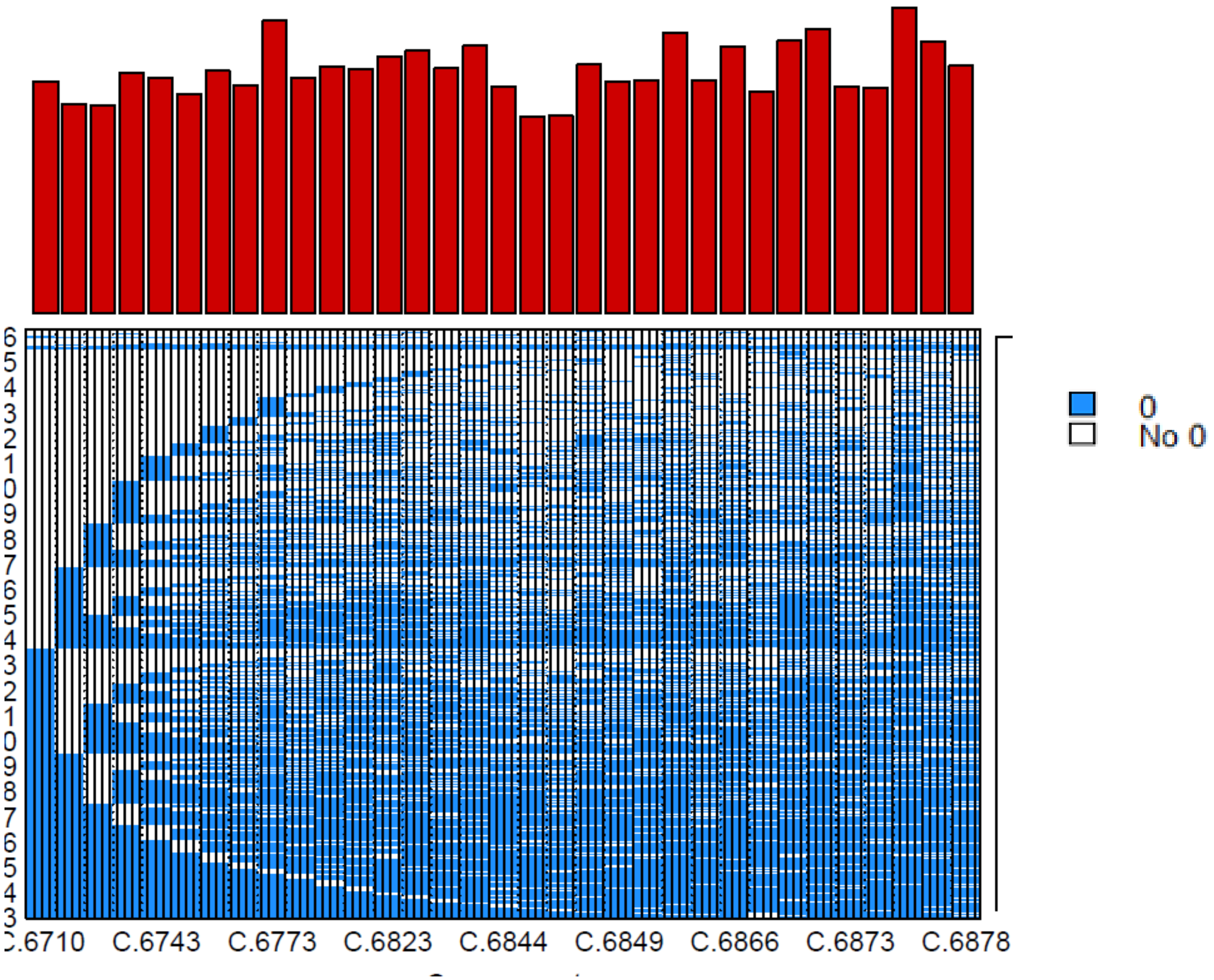
16 % of 0s



M & M

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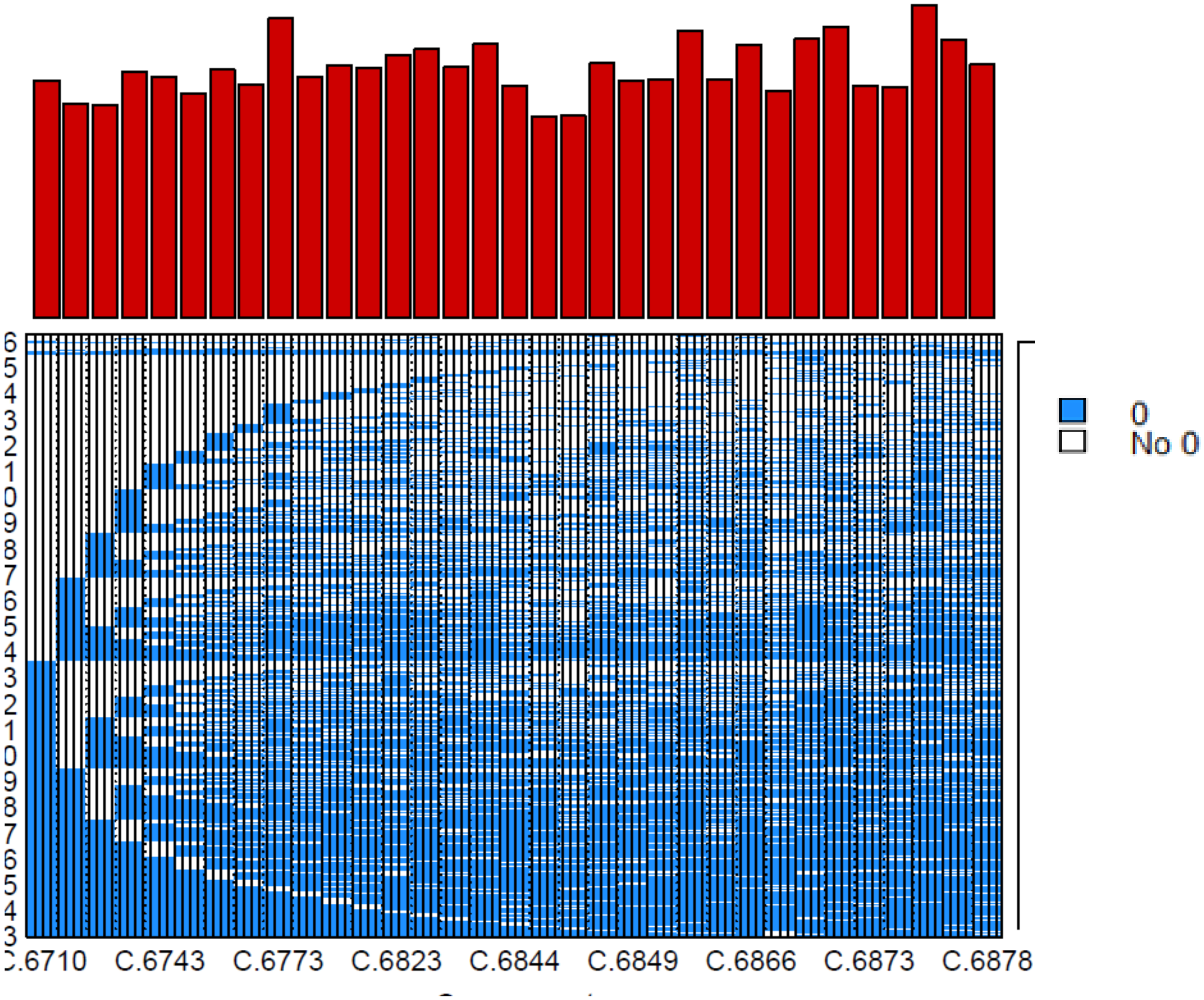
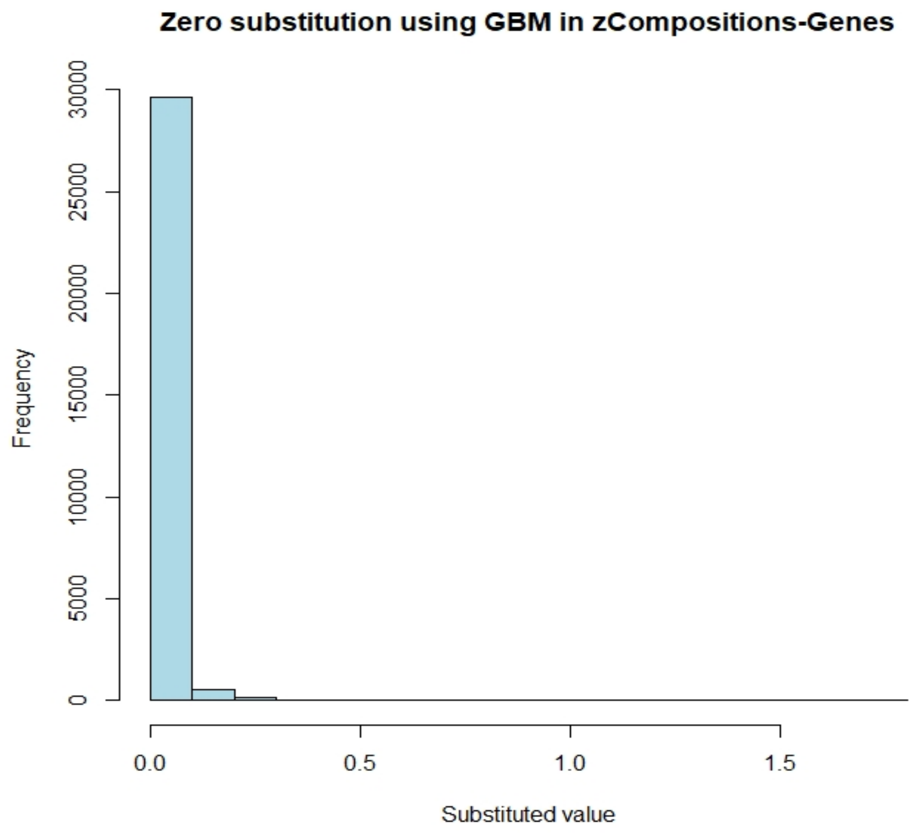


Bayesian-multiplicative replacement

Martín-Fdez et al. 2104



STATISTICAL PIPELINE

1. “0s” study and replacement (zCompositions R)
2. Estimation of relative abundances

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2. Estimation of relative abundances
3. **Weighed** centered log ratio transformation

$$\mathrm{clr}(x_i) = \log\frac{x_i}{G} = \log x_i - \frac{1}{n}\sum_{1}^{n}\log(x_i)$$

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$$\mathrm{clr}(x_i) = \log\frac{x_i}{G} = \log x_i - \boxed{\cancel{\frac{1}{n}}\sum_{1}^{n}\log(x_i)}$$

Weighed mean

1/n → Mean relative abundance

STATISTICAL PIPELINE

1. "0s" study and replacement (zCompositions R)
2. Estimation of relative abundances
3. **Weighed** centered log ratio transformation
4. Selection of discriminant microbial genes with DA - PLS
   - VIP
   - Regression coefficients

RESULTS

DISCRIMINATING MICROBIAL GENES
DA-PLS

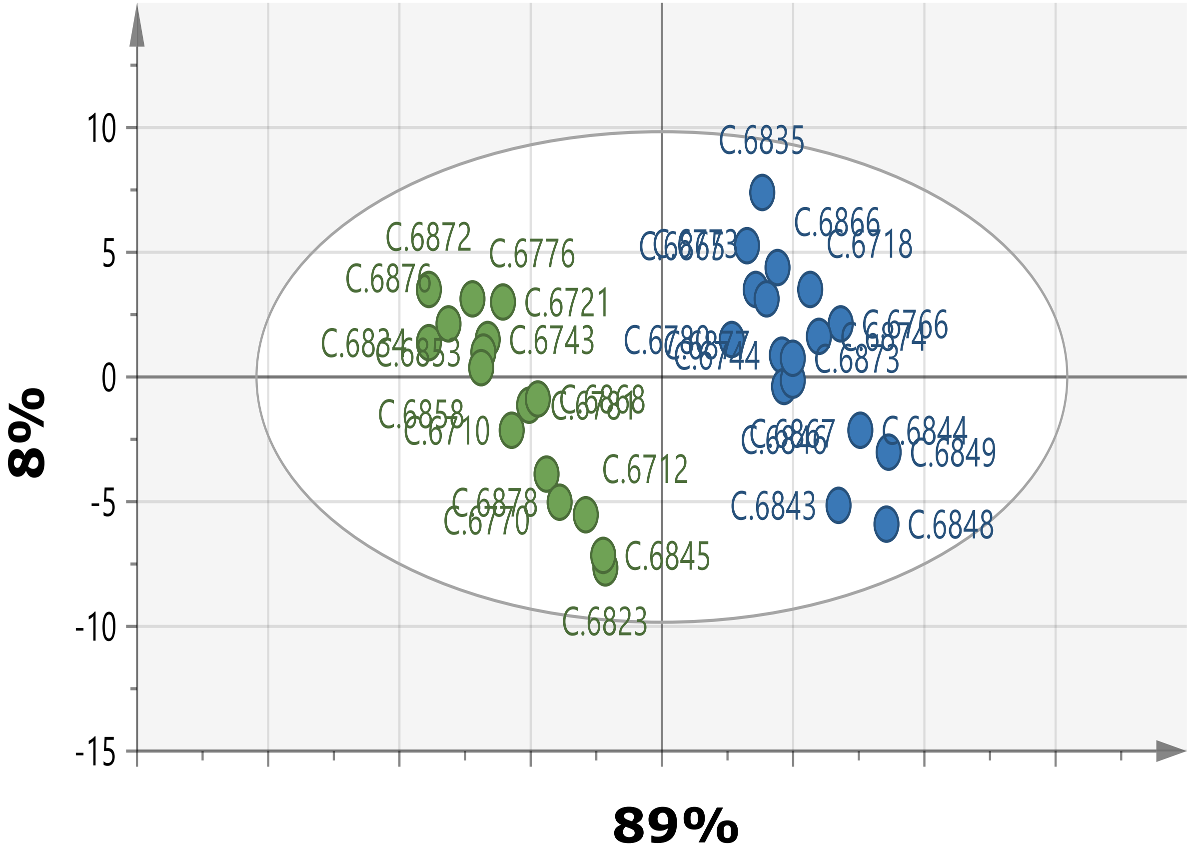
PC	R^2	Q^2
1	0.89	0.84
2	0.97	0.91
3	0.99	0.92

251 GENES INCLUDED IN THE MODEL

SELECTION FOR IMF MODIFIED THE MICROBIAL GENOME OF THE LINES!!!

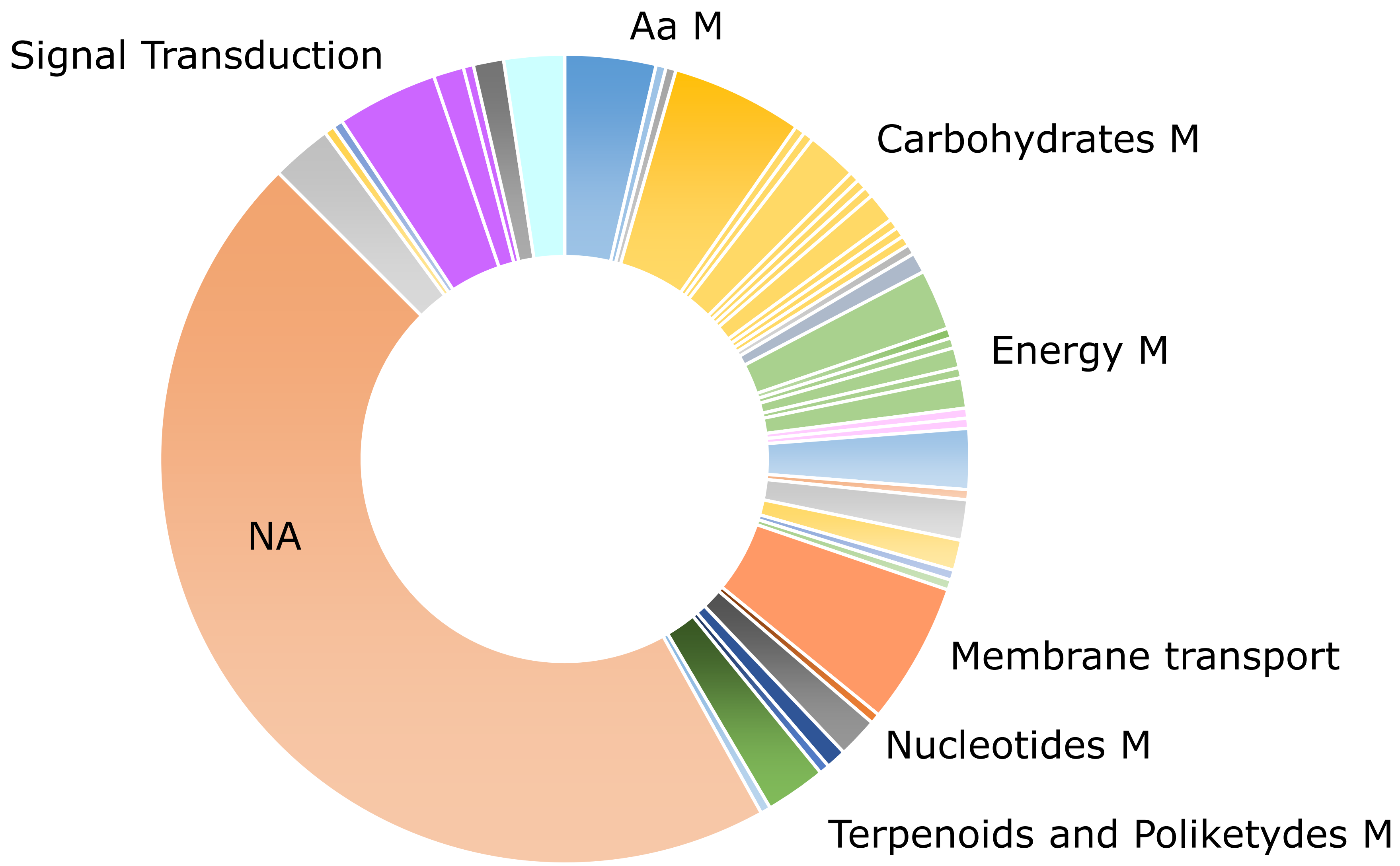
LINK
HOST GENOME-METAGENOME

SCORE PLOT



RESULTS

WHICH 251 MICROBIAL GENES?



RESULTS

LOG TRANSFORMATION EFFECTS IN PRACTISE

ANALYSIS WITHOUT wclr TRANSFORMATION

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ANALYSIS WITHOUT wclr TRANSFORMATION

PREDICTION ABILITY OF DA-PLS MODEL

	PC	R^2	Q^2	Number of genes
Rel. abundances	3	0.987	0.917	227

RESULTS

LOG TRANSFORMATION EFFECTS IN PRACTISE

ANALYSIS WITHOUT wclr TRANSFORMATION

PREDICTION ABILITY OF DA-PLS MODEL

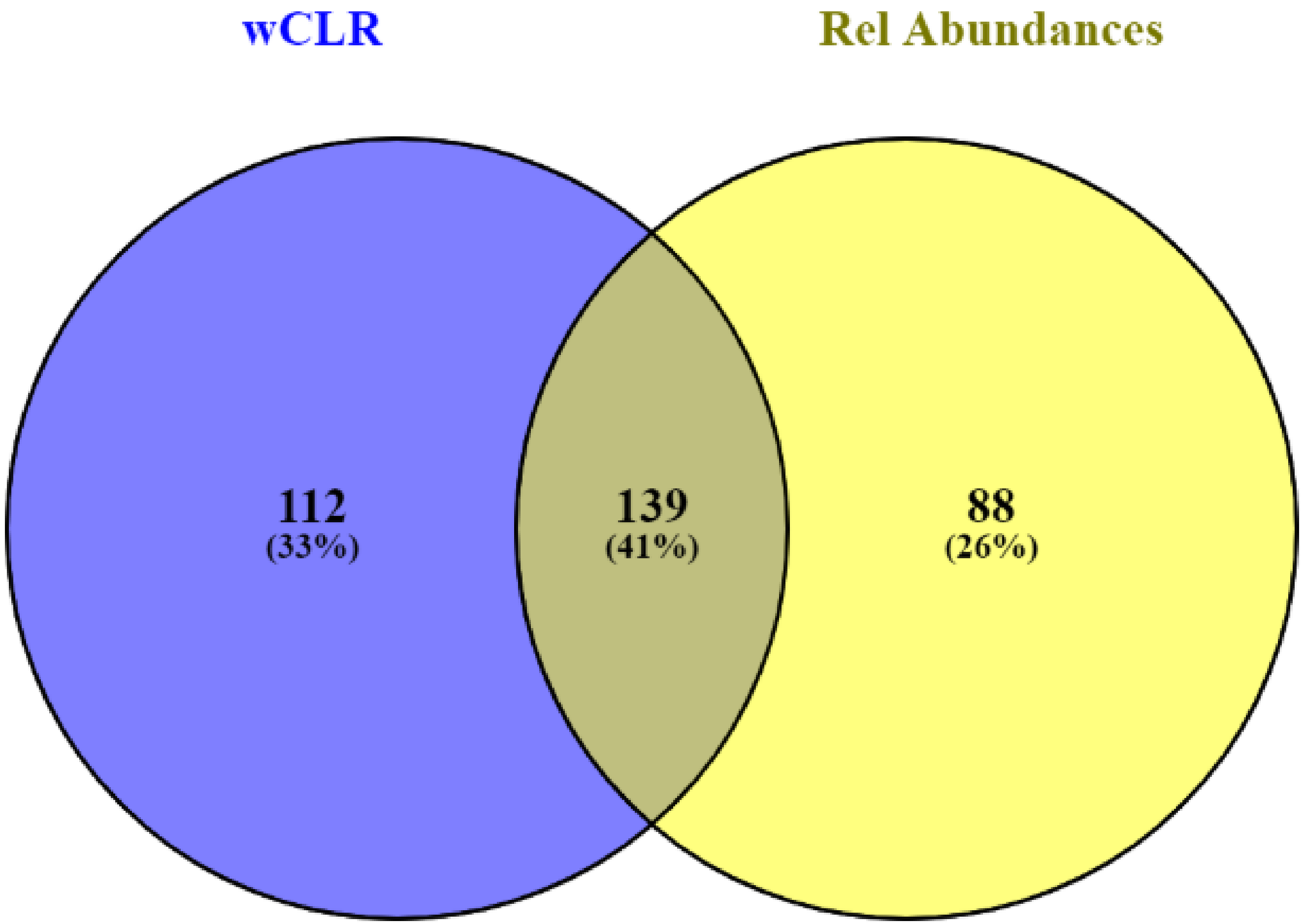
	PC	R^2Y	Q^2	Number of genes
Rel. abundances	3	0.987	0.917	227
wClr	3	0.987	0.922	251

RESULTS

LOG TRANSFORMATION EFFECTS IN PRACTISE

ANALYSIS WITHOUT wclr TRANSFORMATION

OVERLAPPING BETWEEN MICROBIAL GENES SELECTED BY DA-PLS



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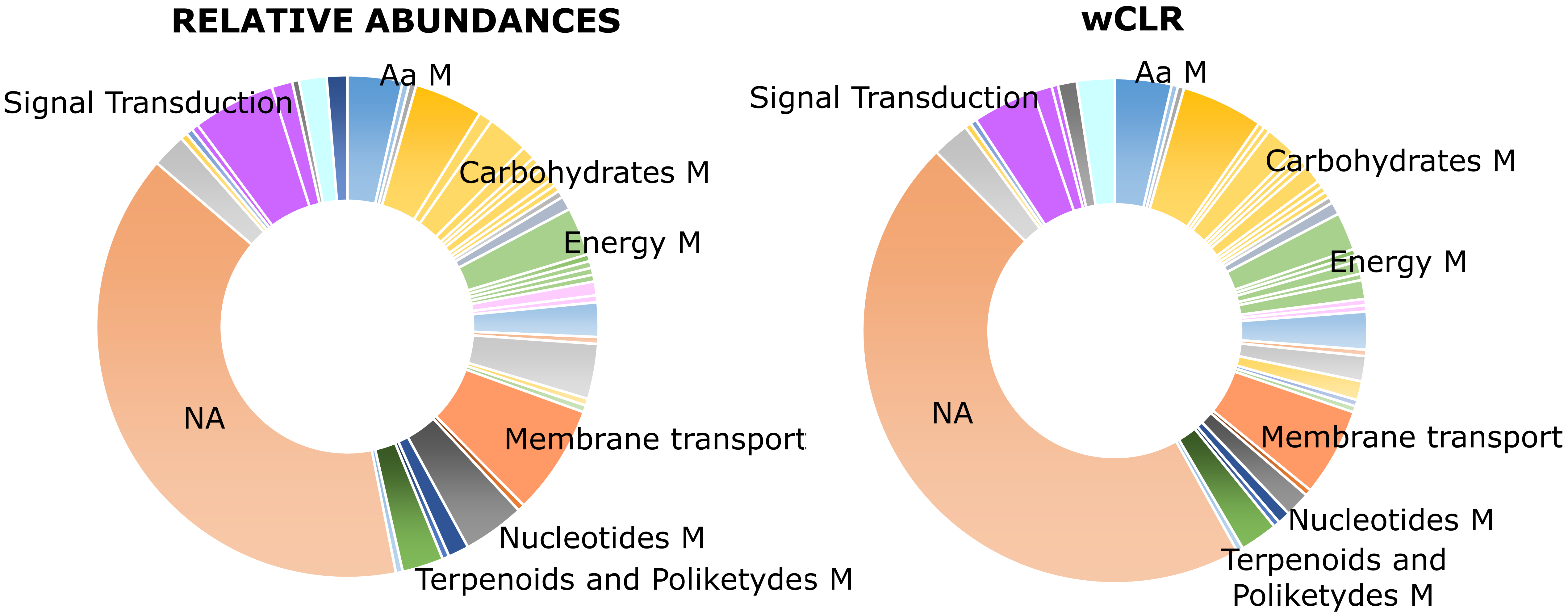
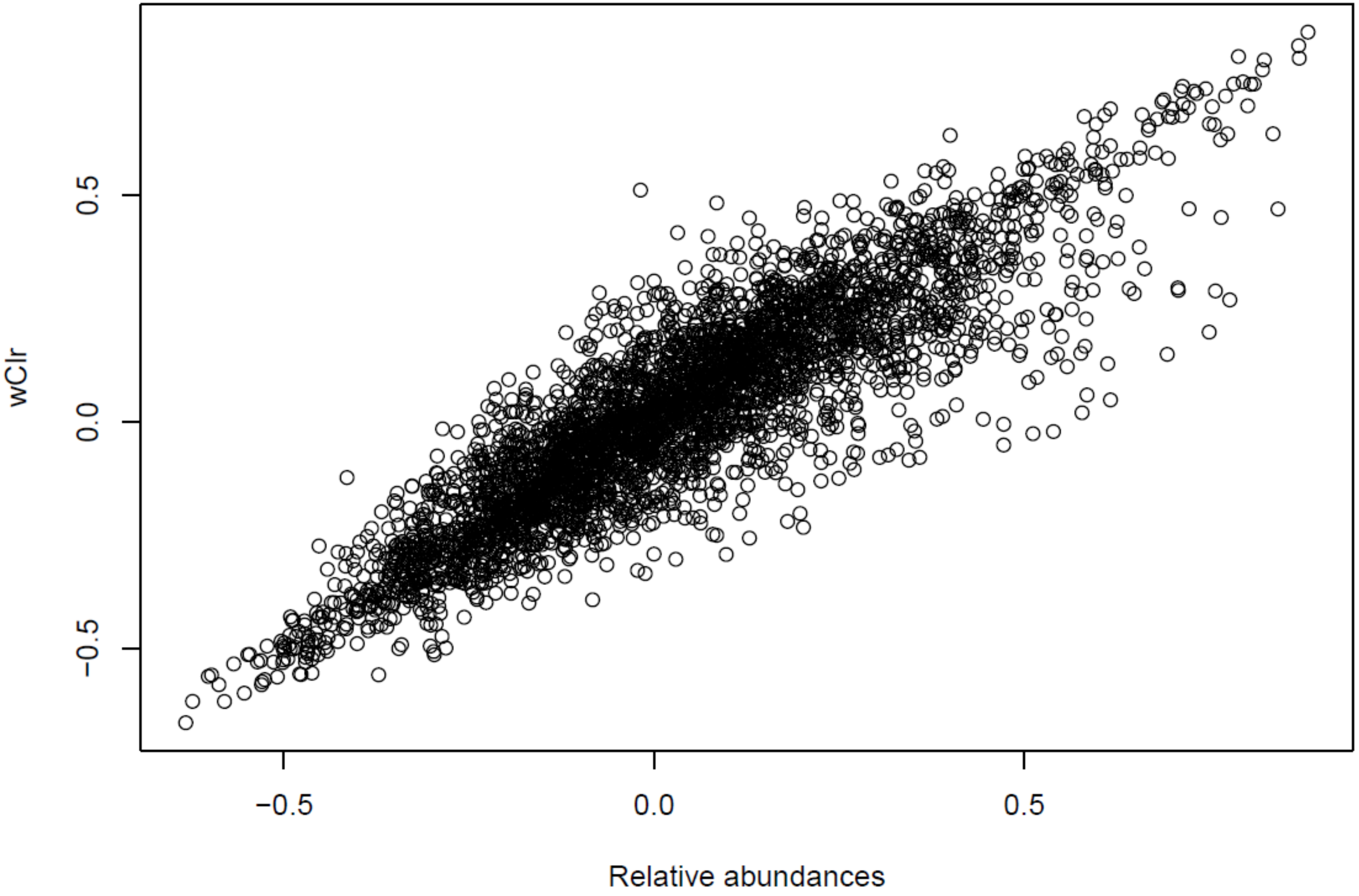


LOG TRANSFORMATION EFFECTS IN PRACTISE

CORRELATIONS BETWEEN MICROBIAL GENES IN wCLR VS. REL. ABUNDANCES



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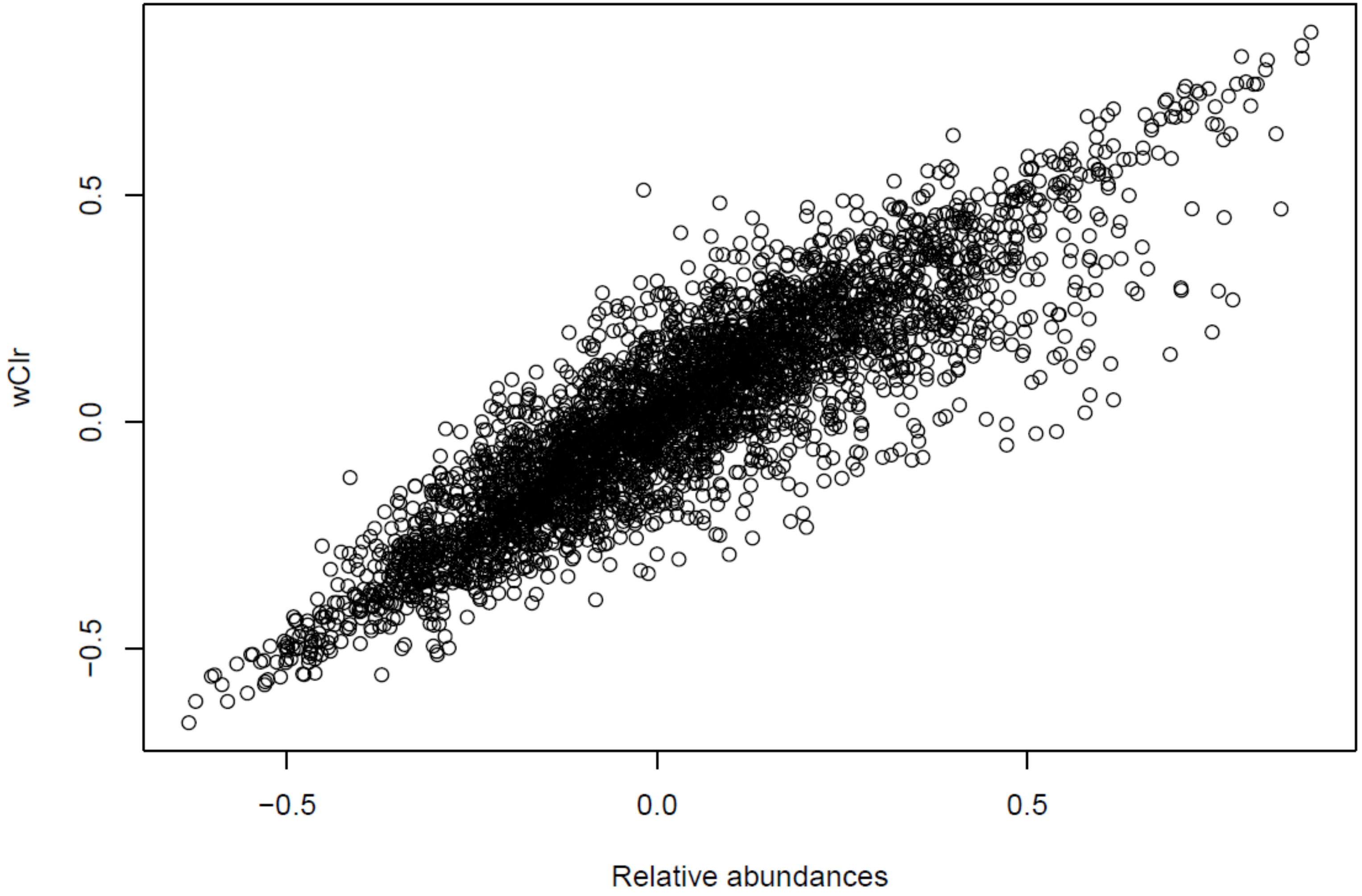

Rank of relative abundances
[1 x 10^{-6}, 1 x 10^{-1}]

MAY BE NOT LIKE THIS IN OTHER DATABASES

CONCLUSIONS

Selection for IMF modifies the microbials genome

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Link genome - metagenome

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Correlated responses in genes involved in several metabolic pathways, as carbohydrates and energy metabolism

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Correlated responses in genes involved in several metabolic pathways, as carbohydrates and energy metabolism

In our study, log transformations did not change results

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