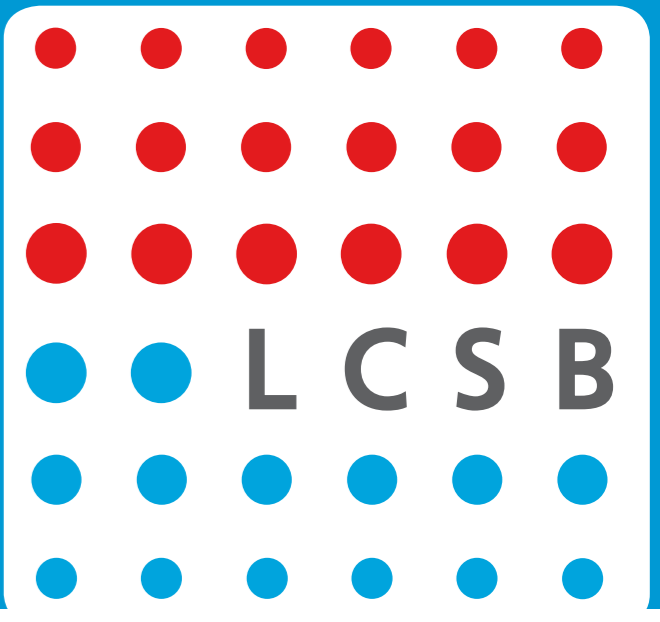


Temporal food restrictions lead to stronger mitochondrial gene regulation in mouse

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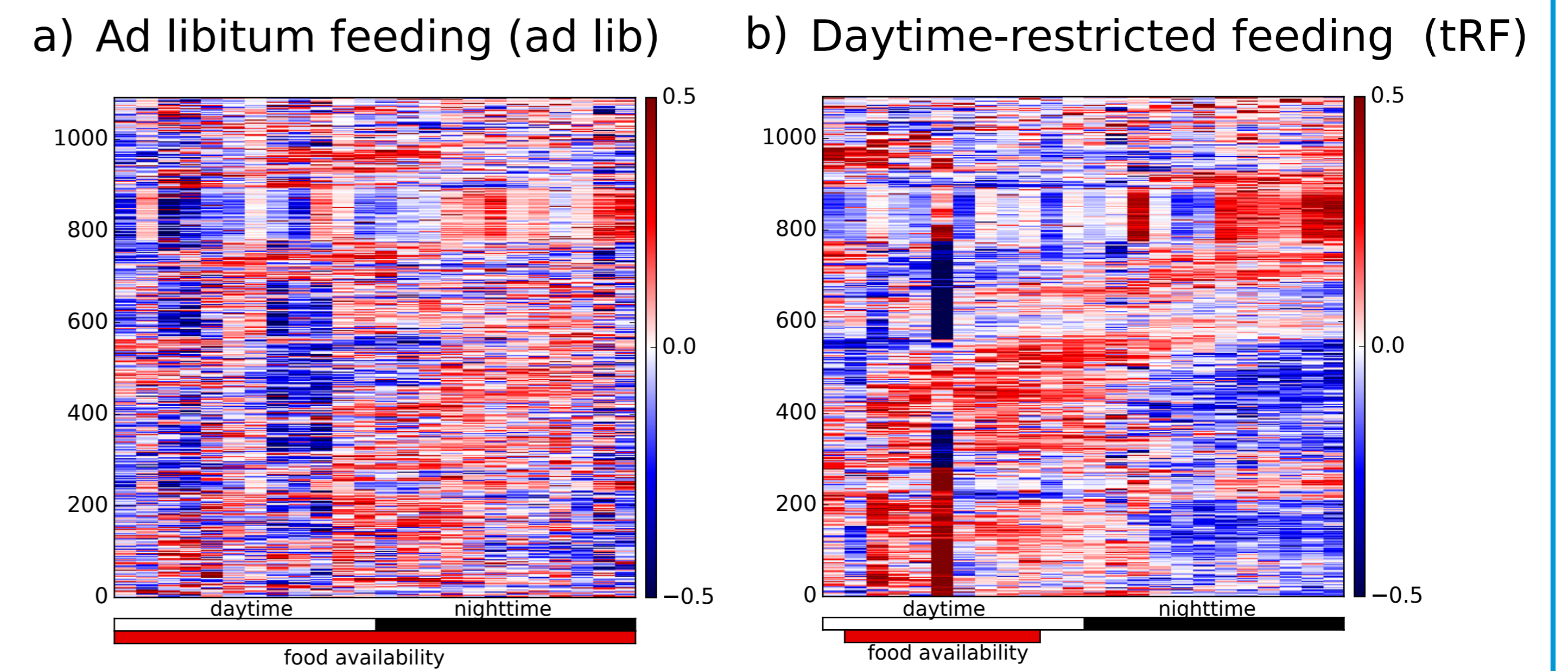


Introduction

Large extends of the transcriptome of the hypothalamic suprachiasmatic nucleus (SCN) and liver exhibit daily rhythms in a tissue specific way [1]. While the SCN is quiet insensitive to perturbations of the feeding pattern, the rhythms in the liver are determined by the interplay of the cell-autonomous molecular clock and the feeding pattern [2]. Thus, metabolism is believed to be temporally coordinated to maintain metabolic homeostasis [3]. To understand in detail how the temporal organization of metabolism is achieved, we analyzed patterns of gene expression for mitochondrial proteins [4] under ad libitum and time restricted feeding conditions. We analyzed co-expression networks of these genes, and use hierarchical clustering algorithms to group genes with similar co-expression dynamics. We found distinct temporal patterns of expression for many genes under different feeding patterns, where genes exhibited the tendency of stronger co-regulations under time restricted feeding conditions.

1. Expression dynamics of mito genes

Hepatic gene expression of mice under different feeding conditions:



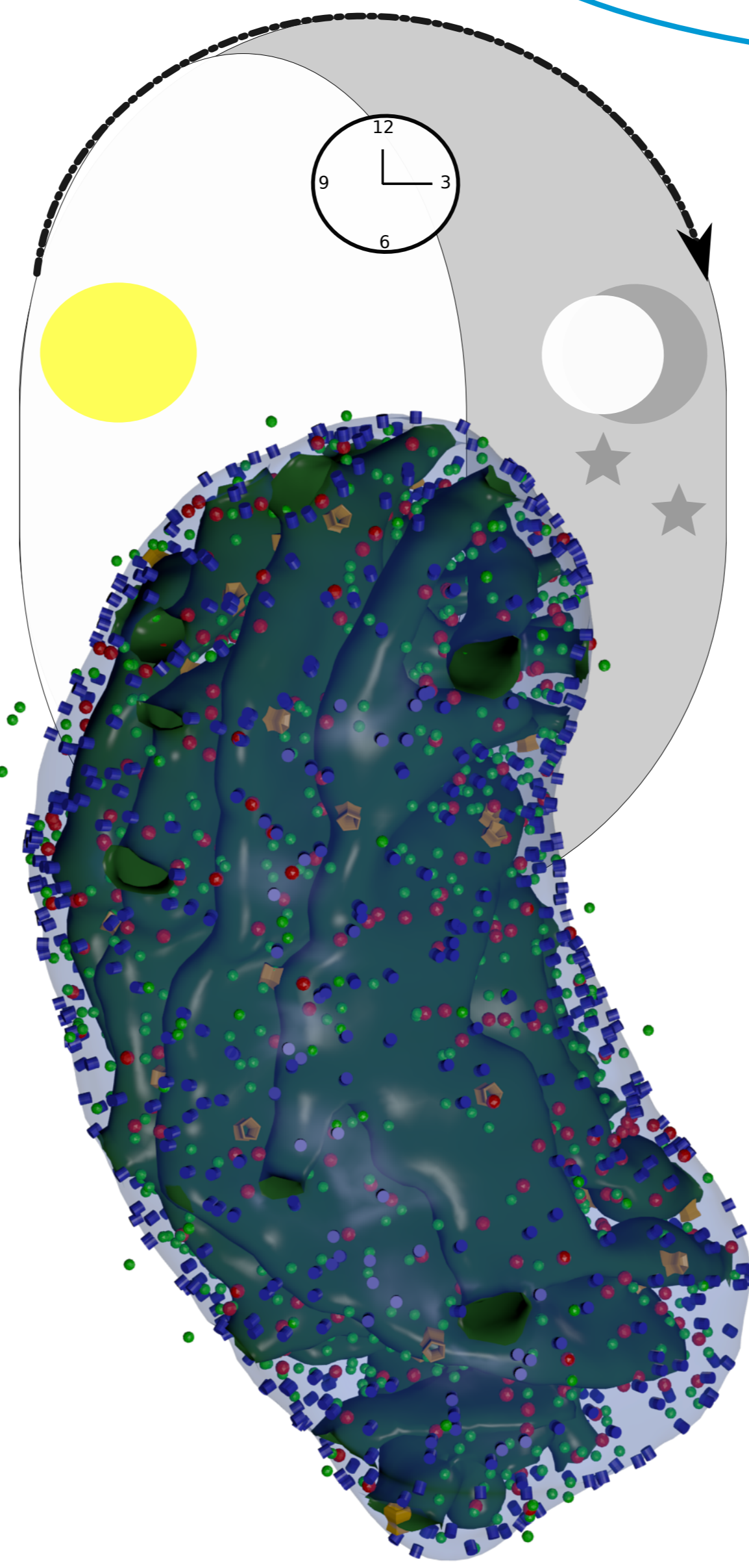
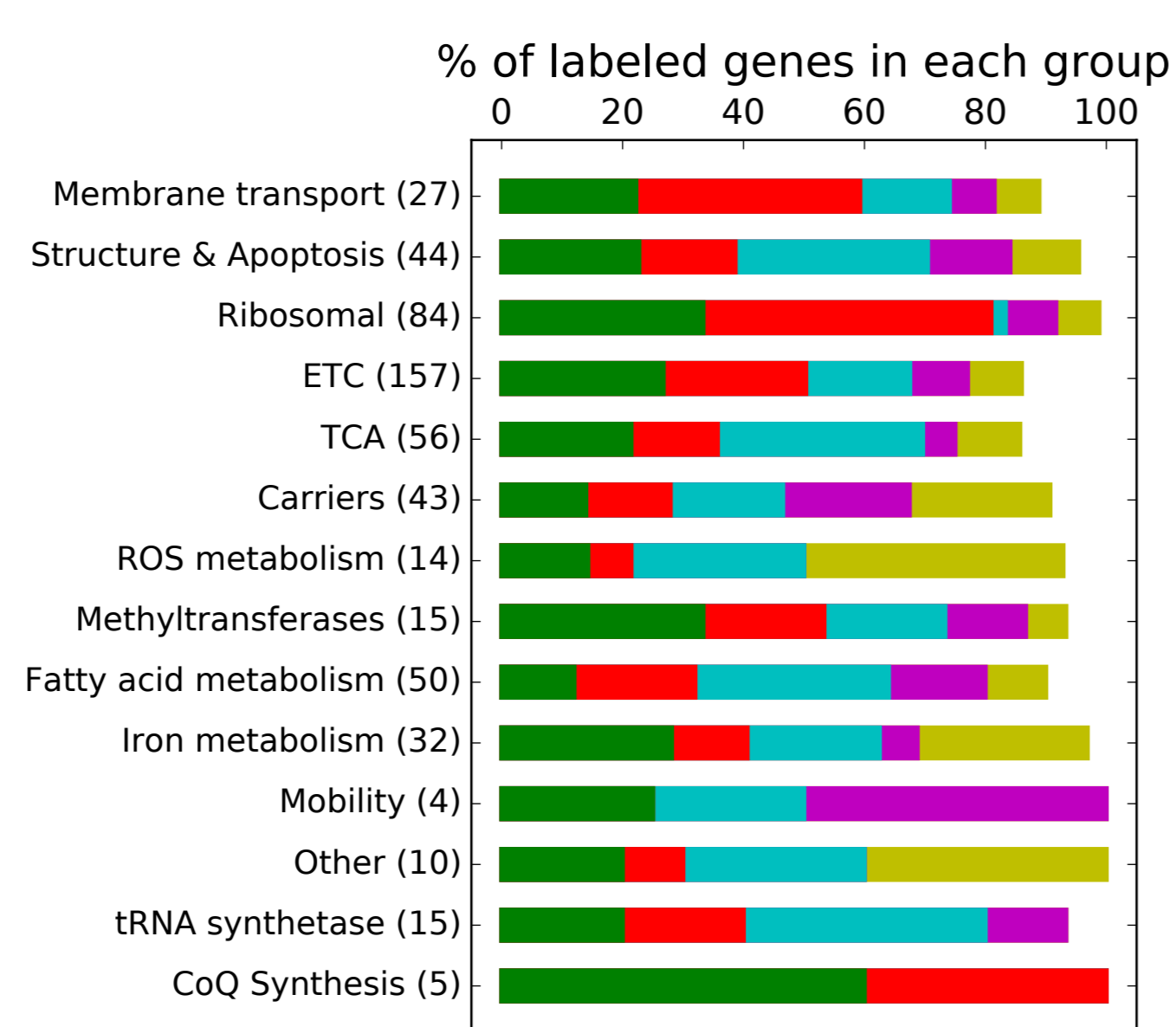
Expression over time, white bars indicate daytime, black bars indicate nighttime, and red bars indicate food availability.

6. References

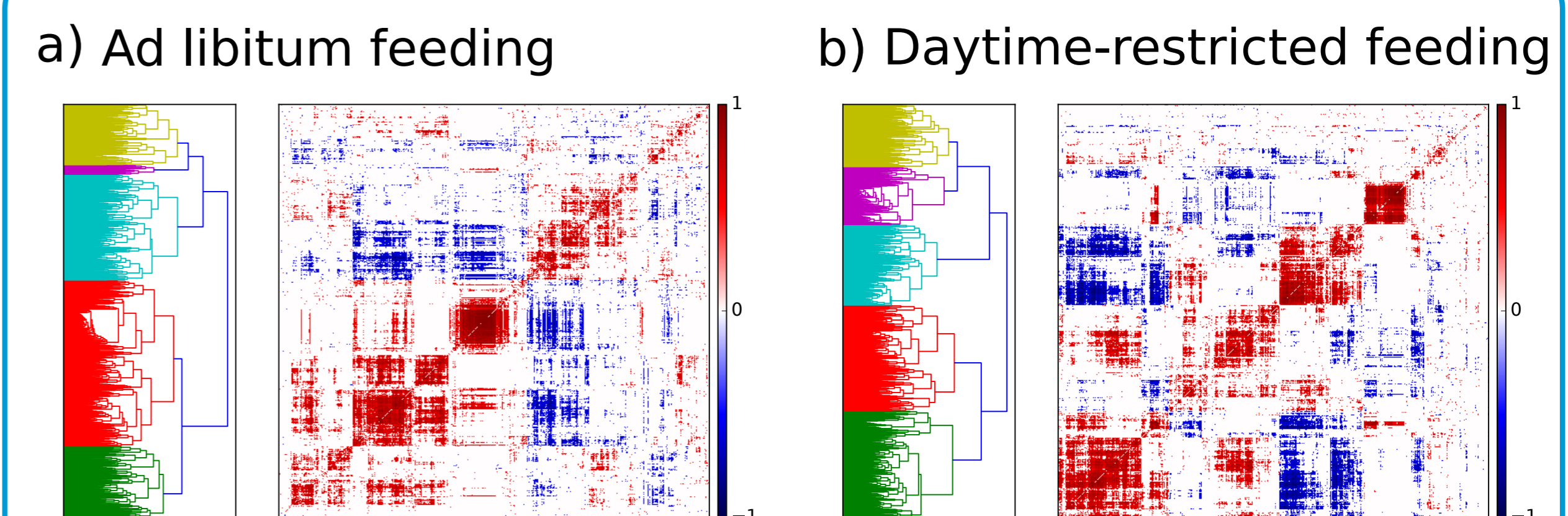
- [1] Panda, S., Antoch, M.P., Miller, B.H., Su, A.I., School, A.B., Straume, M., Schultz, P.G., Kay, S.A., Takahashi, J.S. and Hogenesch, J.B., 2002. Coordinated transcription of key pathways in the mouse by the circadian clock. *Cell*, 109(3), pp.307-320.
- [2] Vollmers, C., Gill, S., DiTacchio, L., Pulivarthy, S.R., Le, H.D. and Panda, S., 2009. Time of feeding and the intrinsic circadian clock drive rhythms in hepatic gene expression. *Proceedings of the National Academy of Sciences*, 106(50), pp.21453-21458.
- [3] Zarrinpar, A., Chaix, A. and Panda, S., 2016. Daily eating patterns and their impact on health and disease. *Trends in Endocrinology & Metabolism*, 27(2), pp.69-83.
- [4] Calvo, S.E., Clauser, K.R. and Mootha, V.K., 2015. MitoCarta2.0: an updated inventory of mammalian mitochondrial proteins. *Nucleic acids research*, 44(D1), pp.D1251-D1257.

5. Future Perspectives

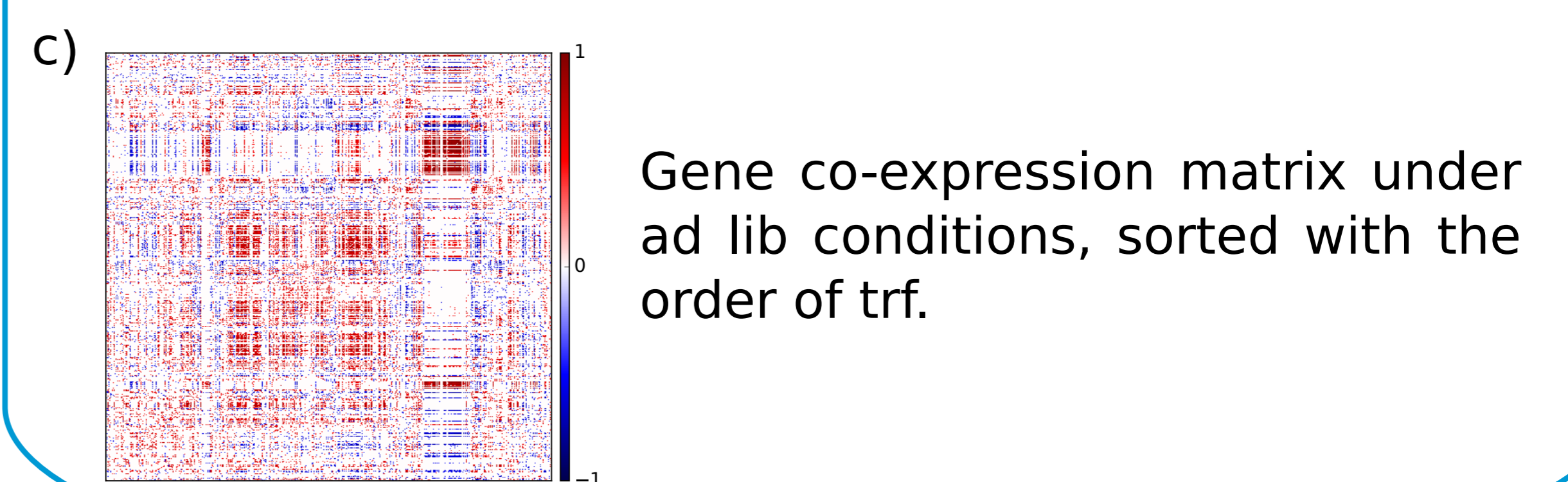
Preliminary analysis indicates some functional relation to temporal organization



2. Temporal organization



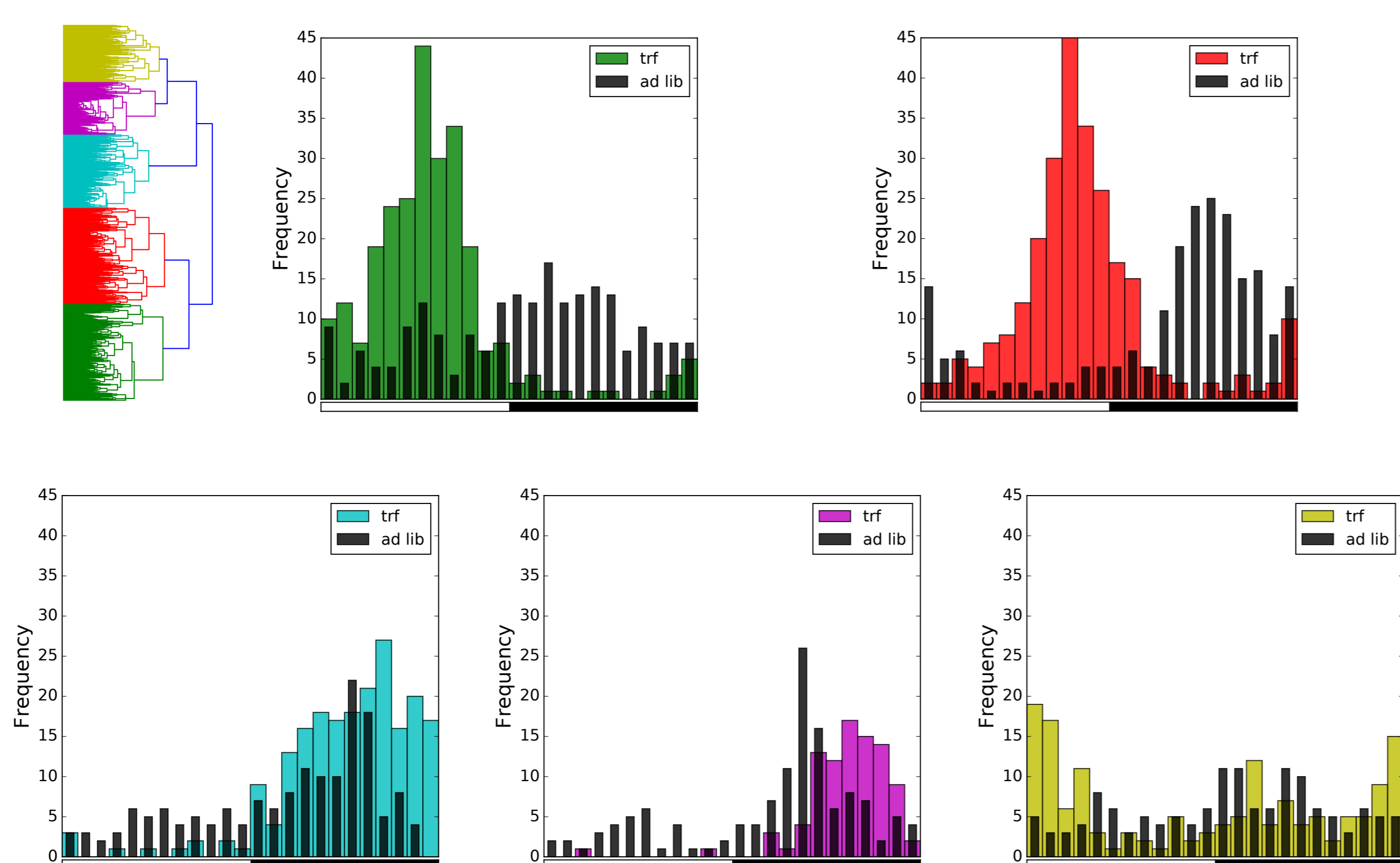
Thresholded gene-gene correlation matrices. The order is different in each network, obtained using hierarchical clustering of the corresponding matrices.



Gene co-expression matrix under ad lib conditions, sorted with the order of trf.

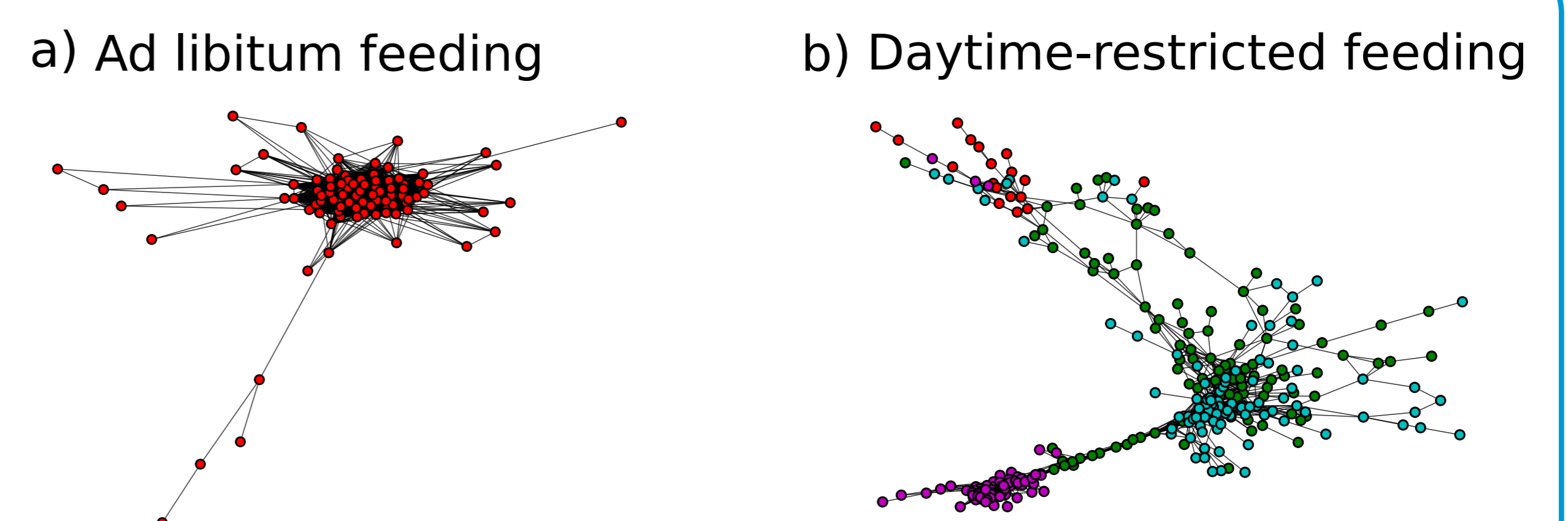
4. Phase distributions

Phase distributions of gene groups (see Panel 2, fig b)

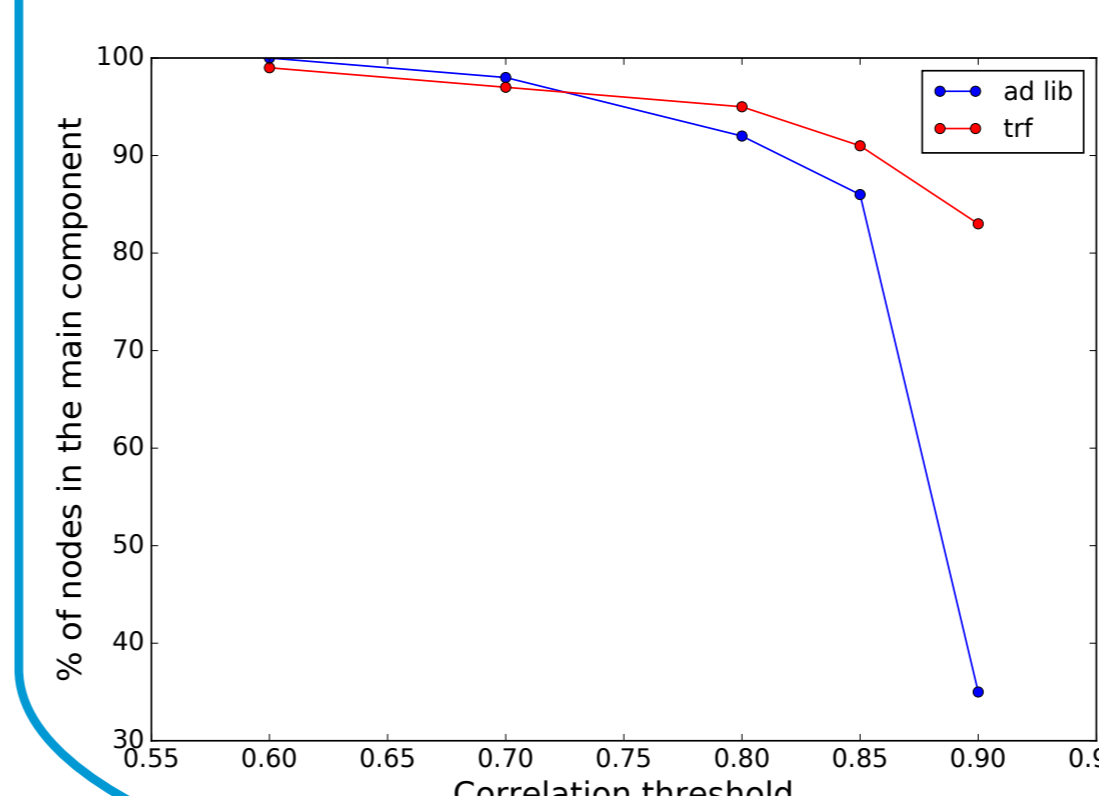


Food has a significant impact on the phase of some genes, shifting the phase of several transcripts (upper panels) or leaving them unaltered (lower panels).

3. Network analysis



From the correlation matrices we built networks, where the genes are nodes and links correspond to correlations, in this case greater than 0.9. Above we plot the main connected component.



Temporal feeding restrictions lead to stronger temporal organization