

Acute endurance exercise induces widespread transcriptional changes across tissues



Nicole Gay
Stanford University
Workshop 2: MoTrPAC



Stanford
MEDICINE

Disclaimers

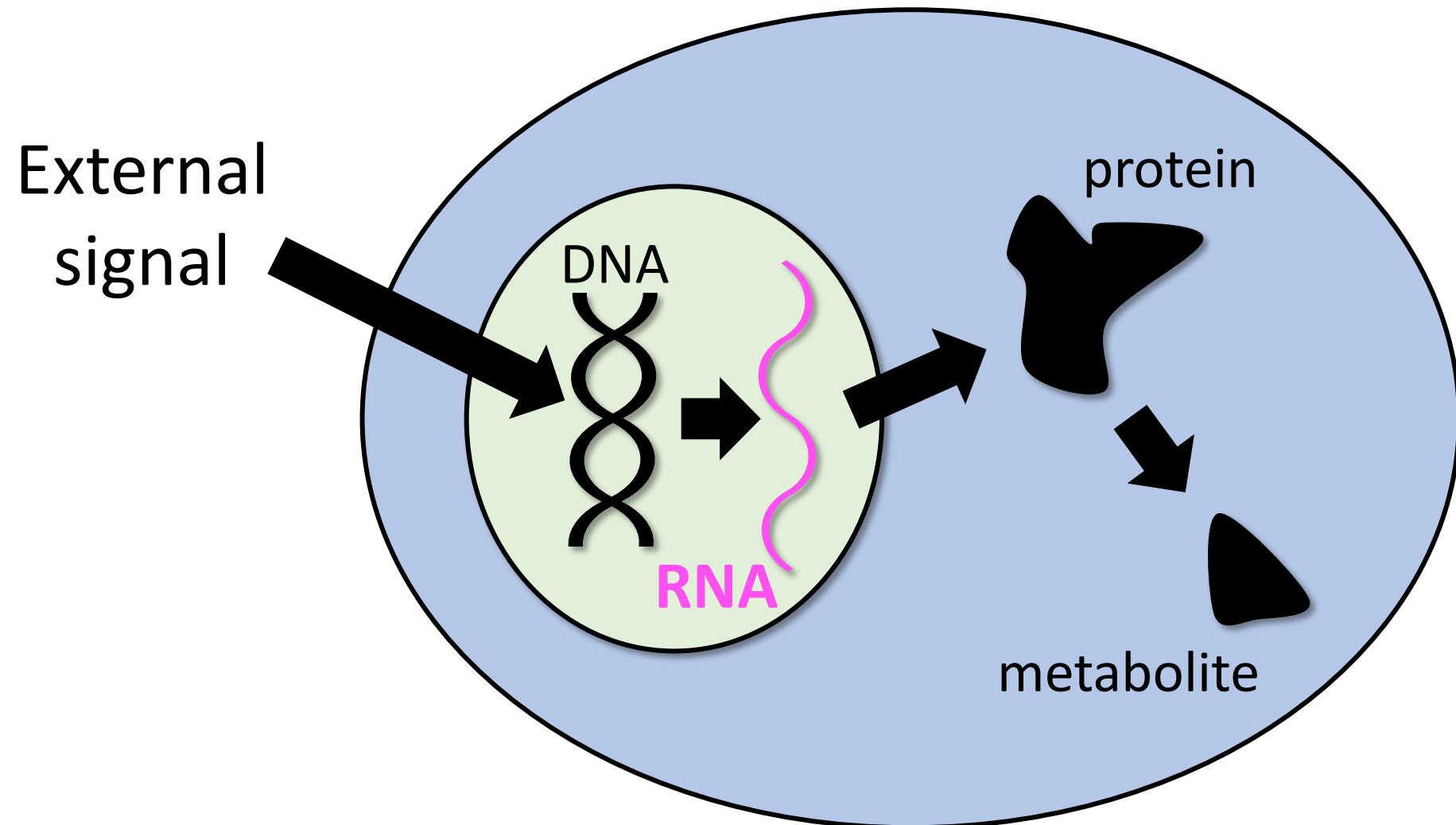
MoTrPAC-generated data have undergone preliminary analysis by the authors of this work; **results presented here do not represent the final consensus analysis by MoTrPAC.**

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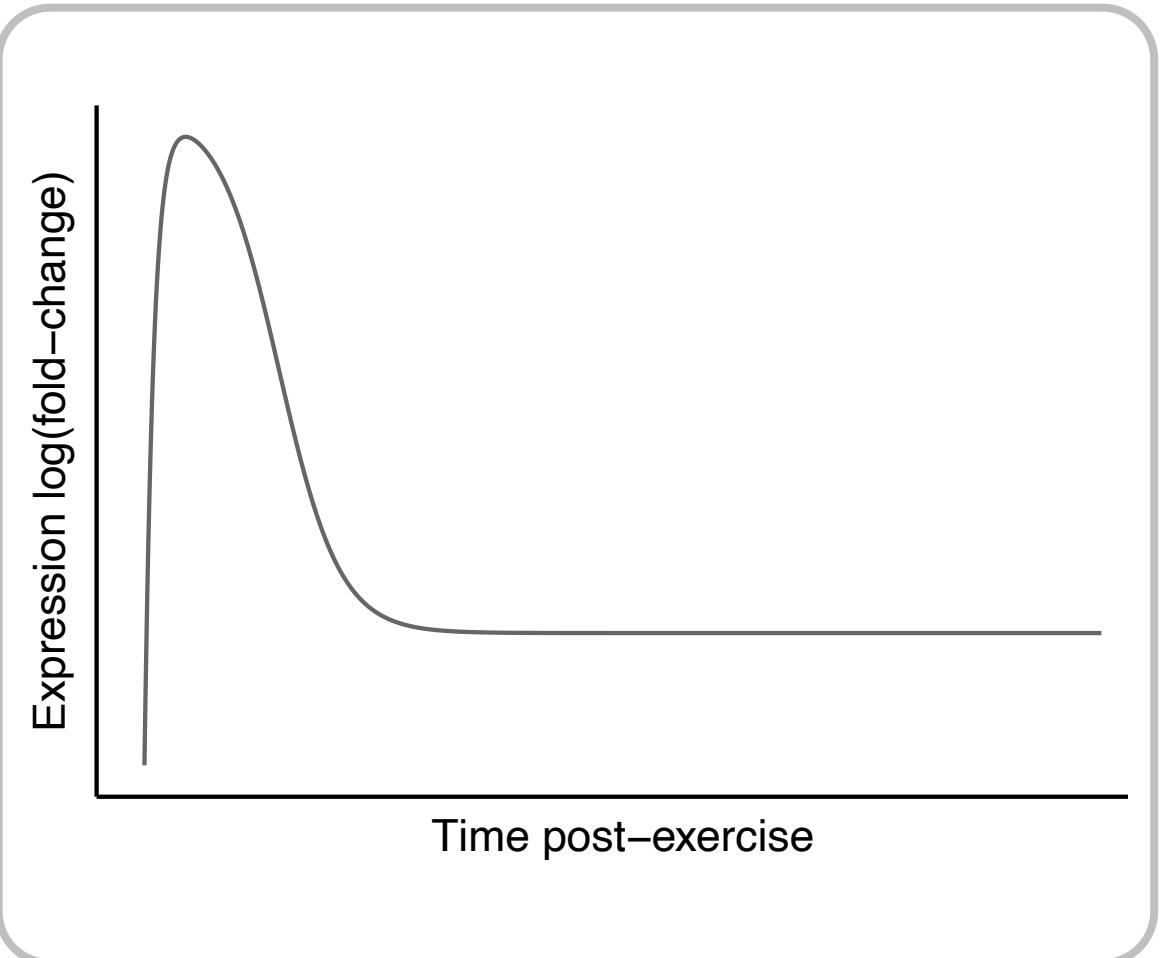
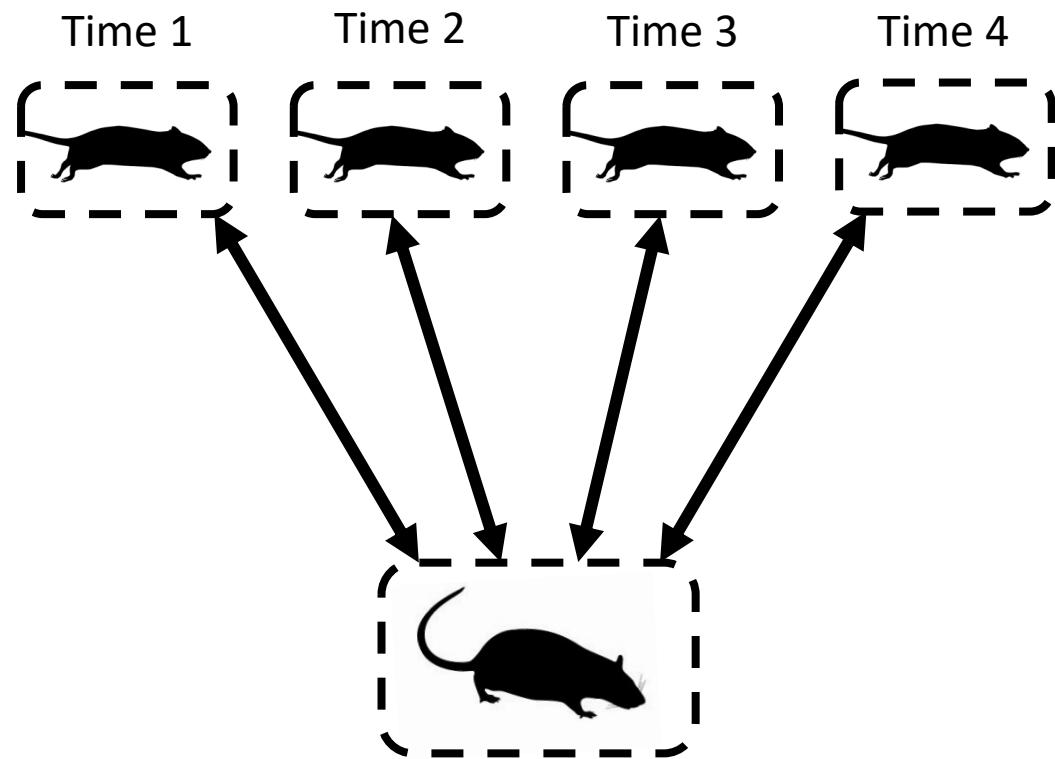
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The currently available animal dataset (Release 1.0) is not final. Specifically, data from more tissues will be added; and the current control dataset is limited in its coverage of fasting times and sacrifice time of day, which can confound the results when comparing to the exercised rats. Additional data will be made available in future releases.

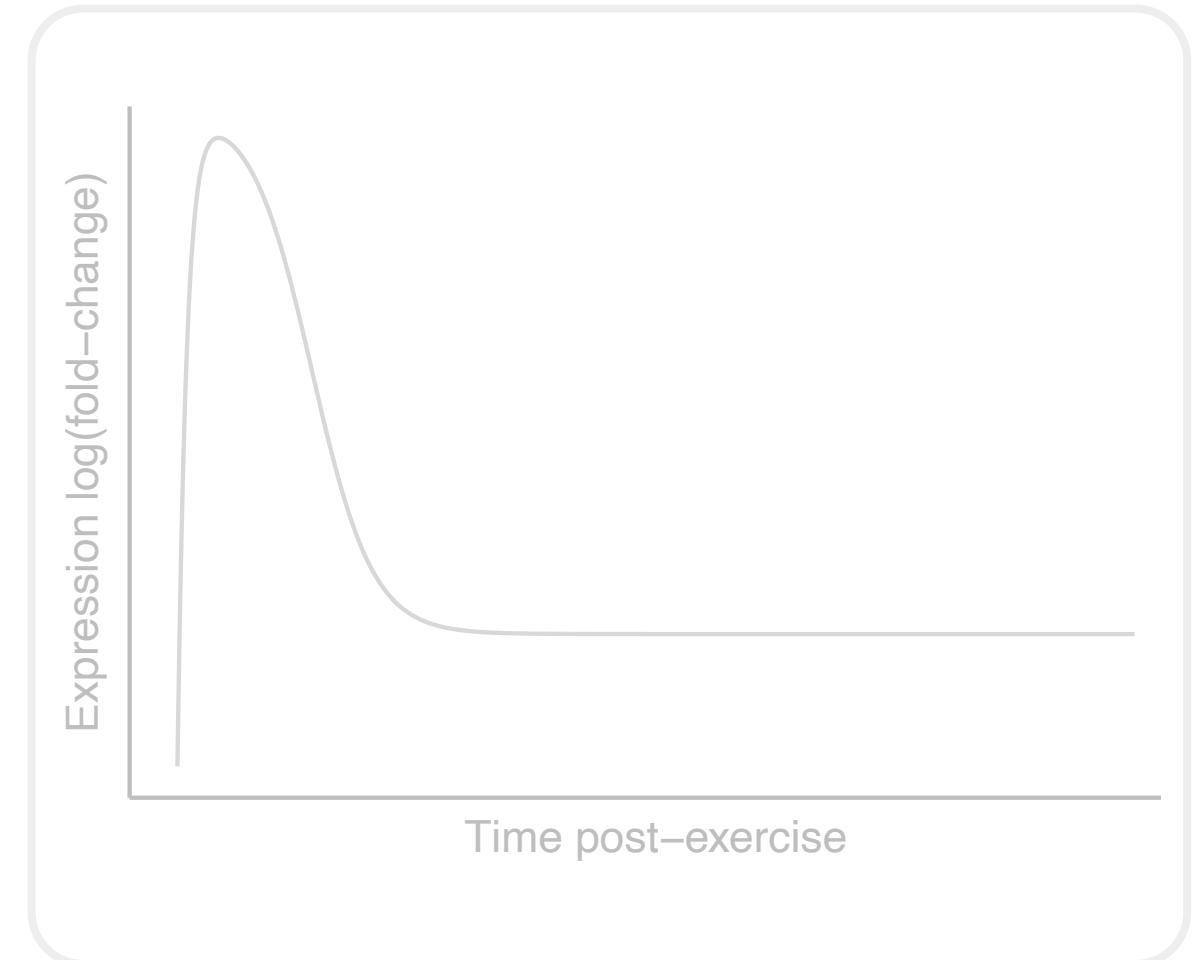
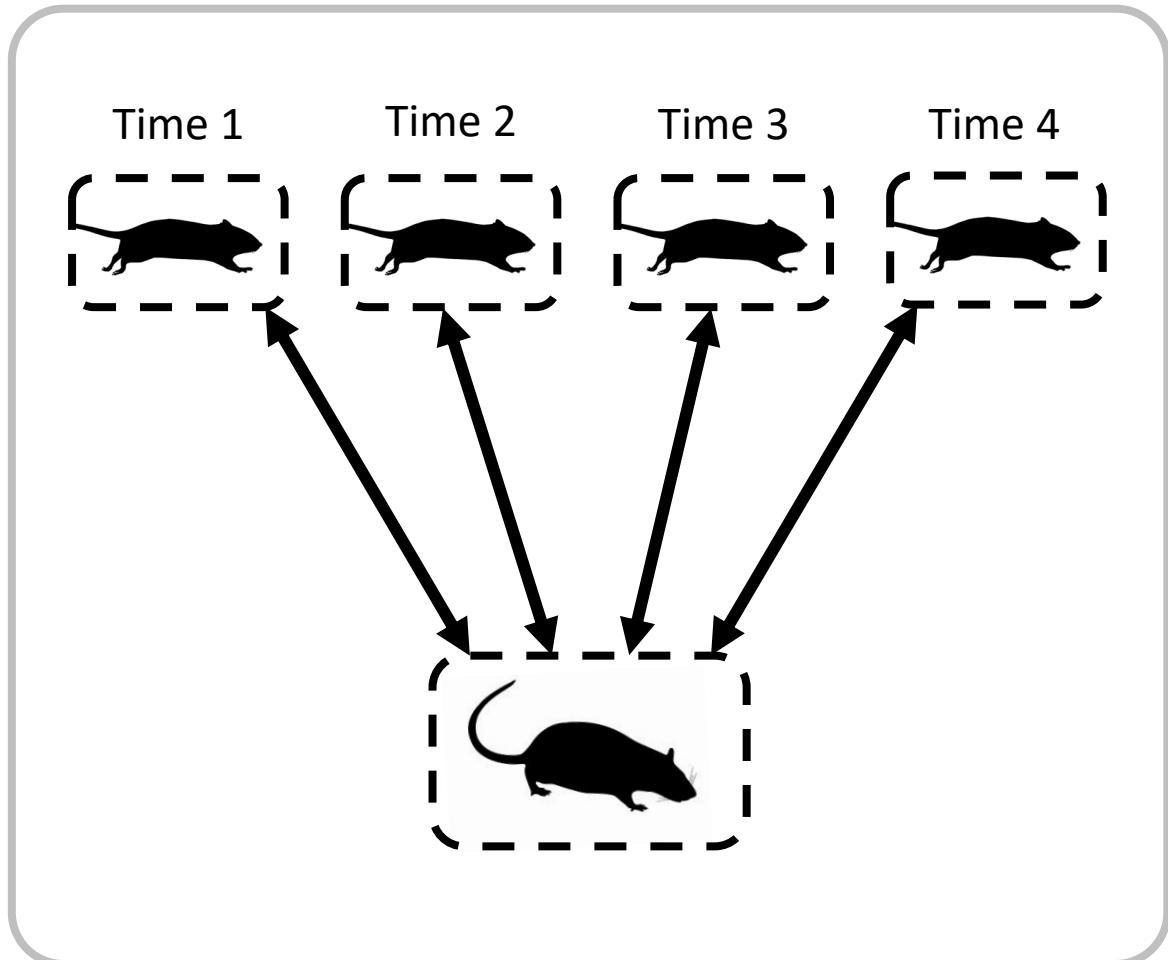
Transcriptomics is a key measurement of upstream molecular activity



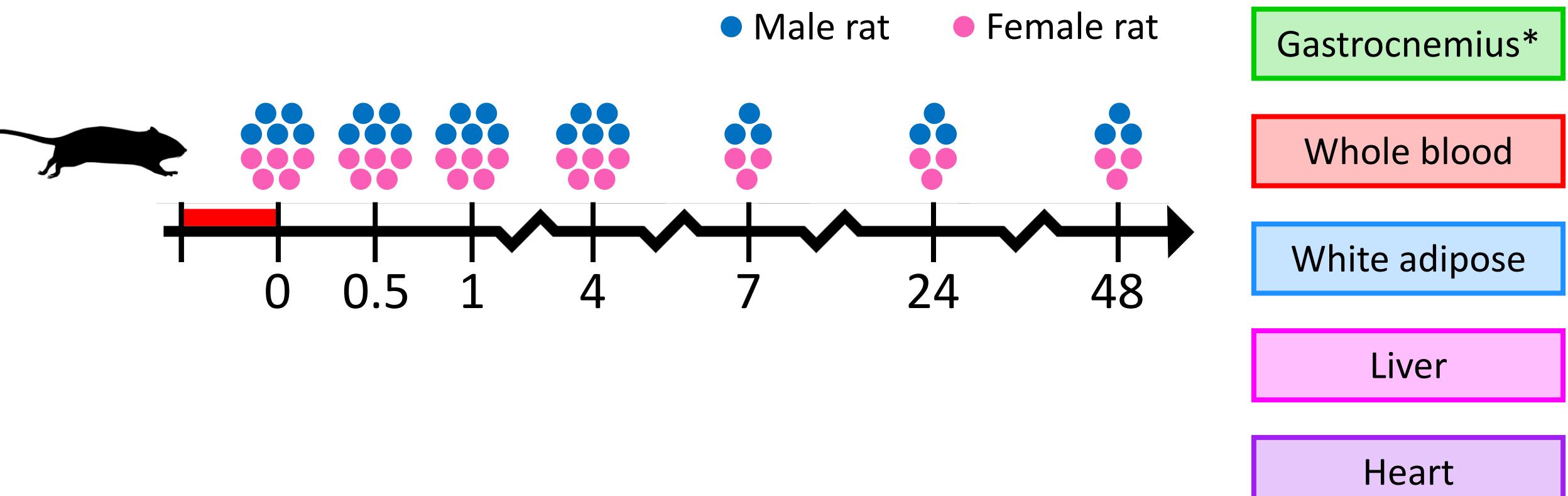
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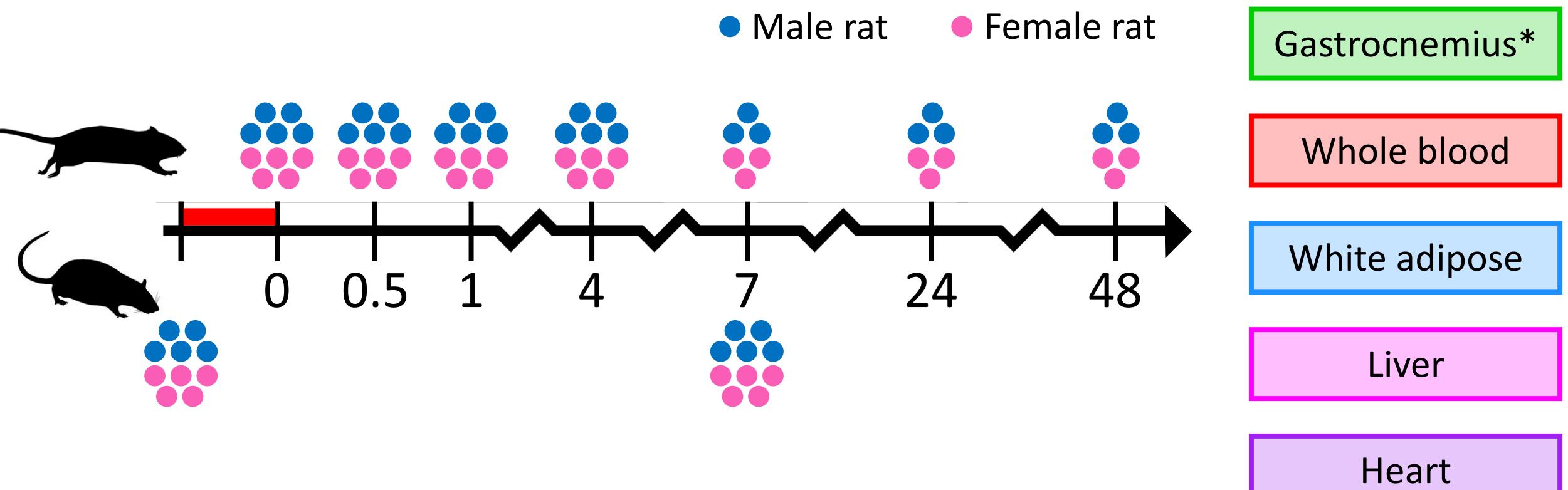
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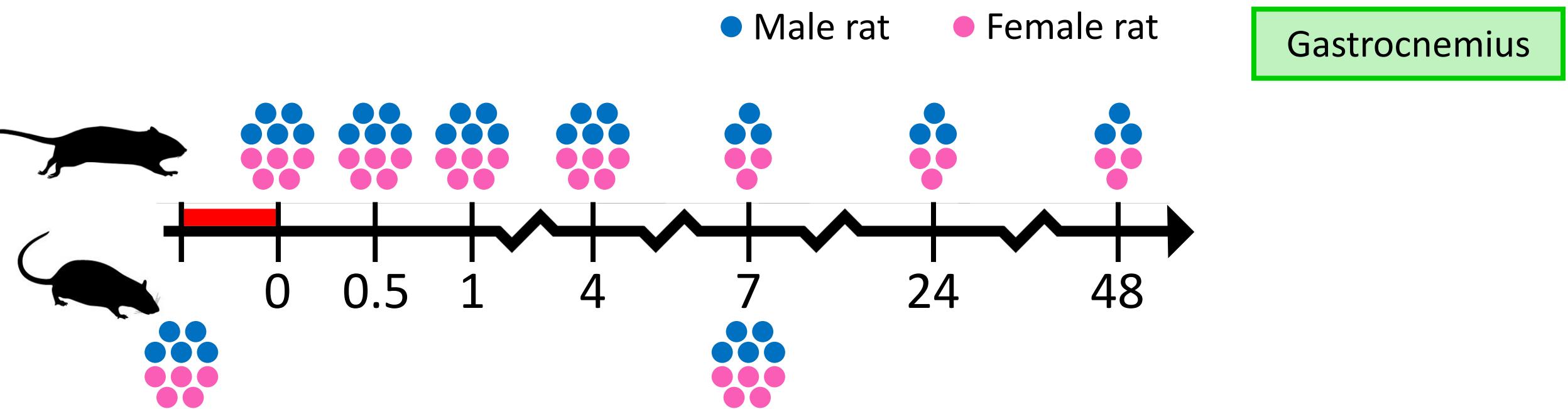
Publicly available MoTrPAC RNA-seq data from 5 rat tissues



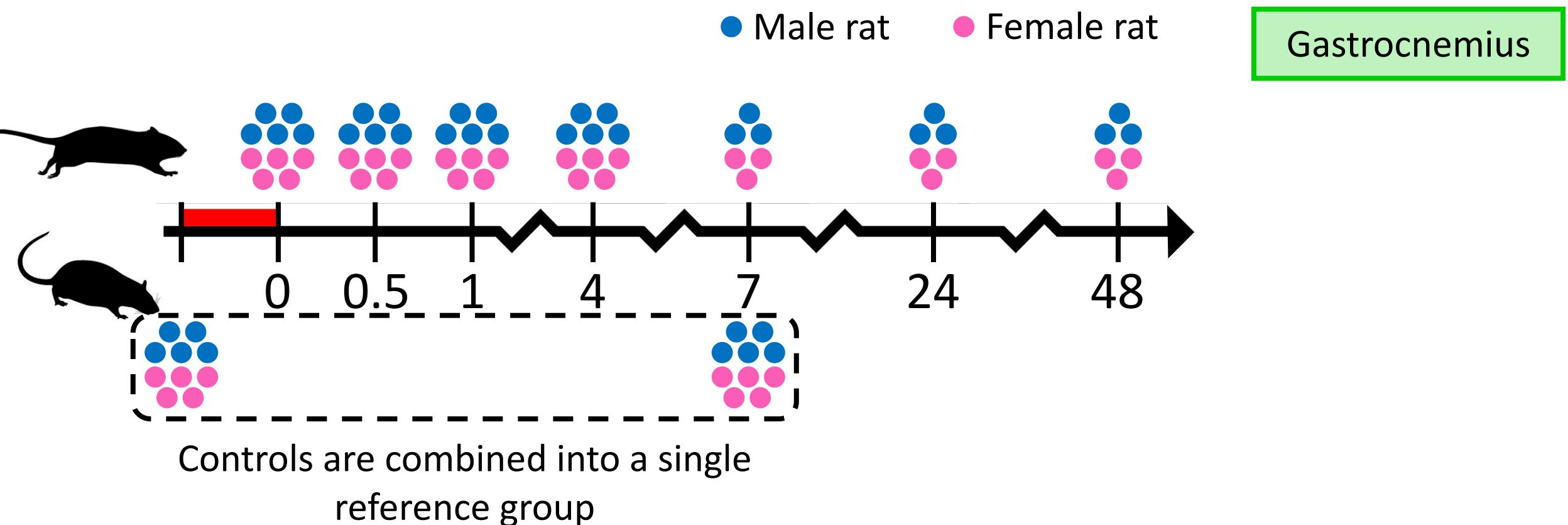
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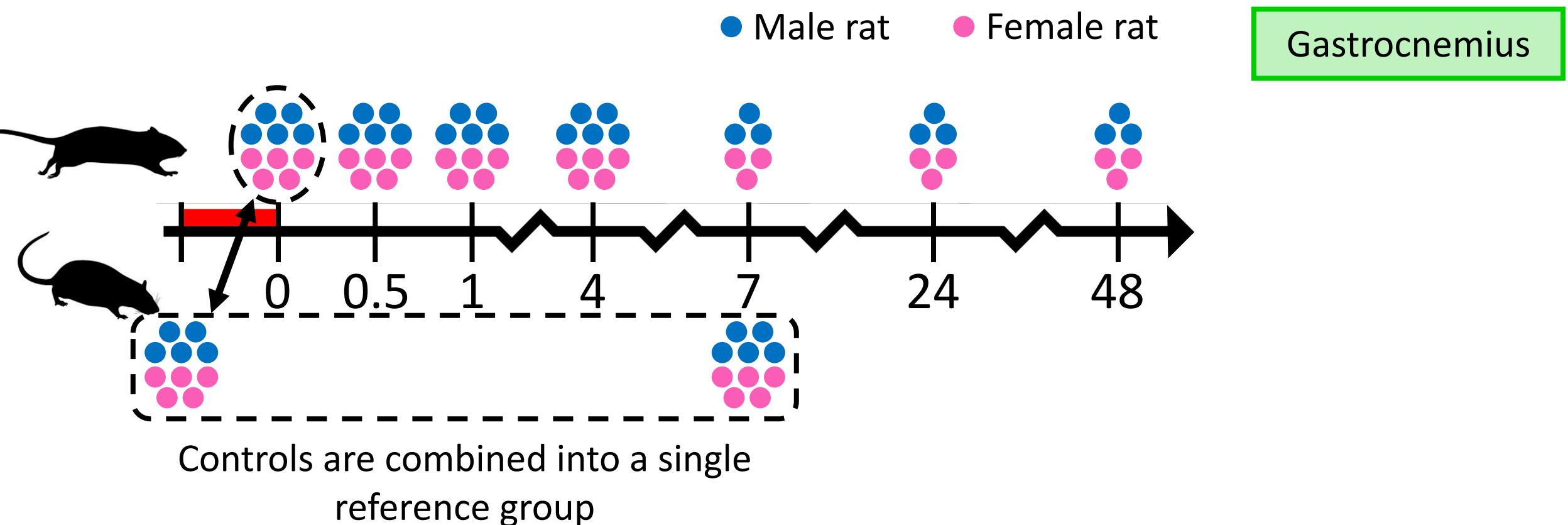
Differential expression analysis was performed independently in each tissue



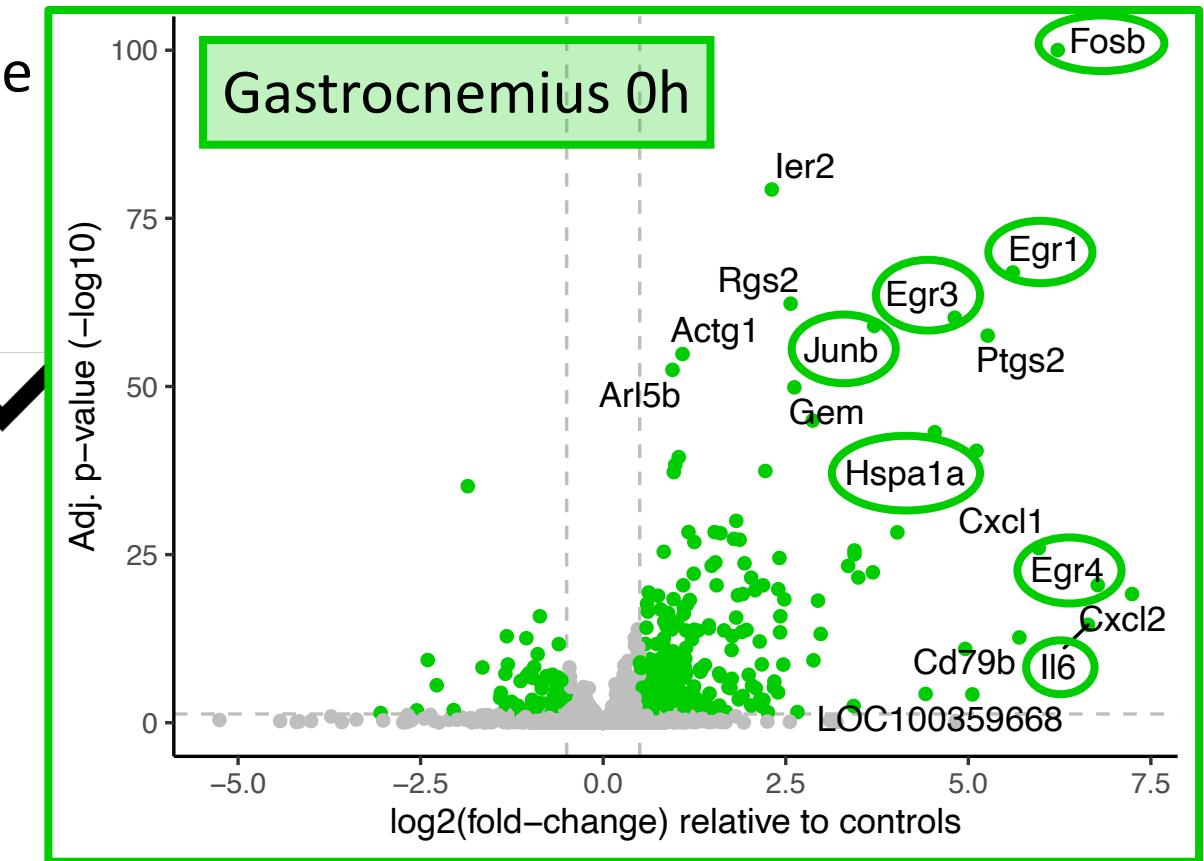
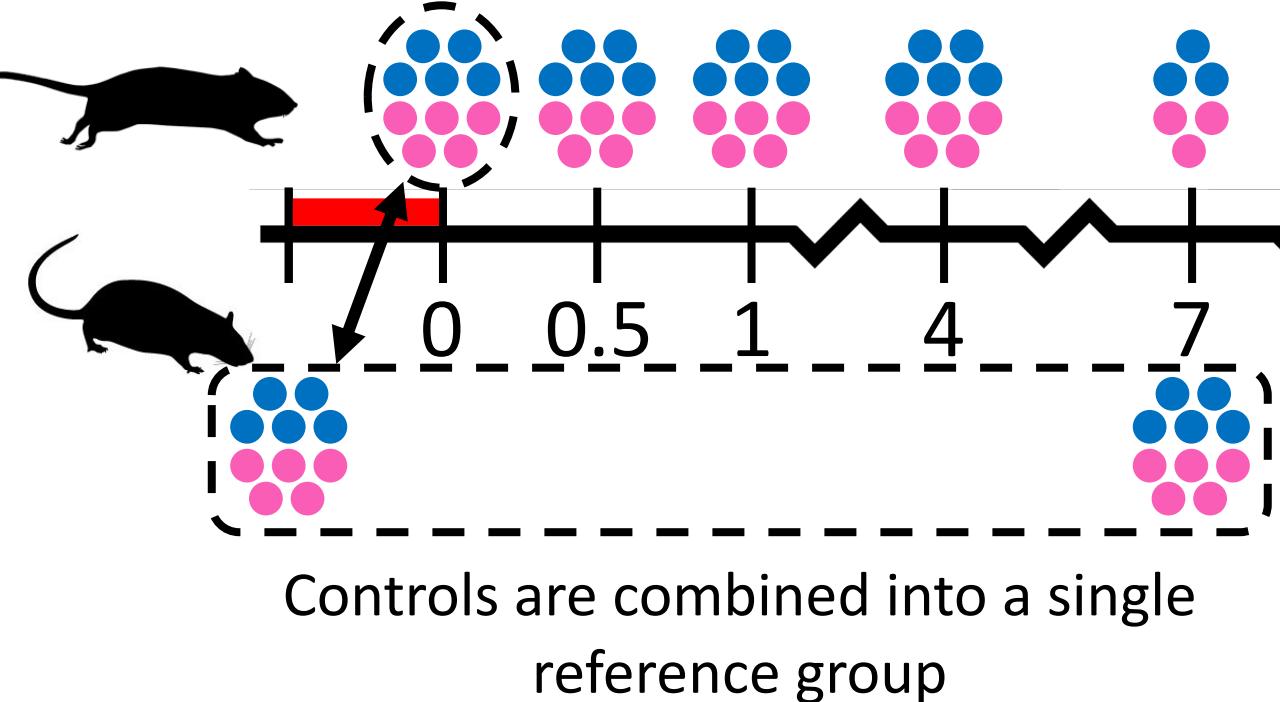
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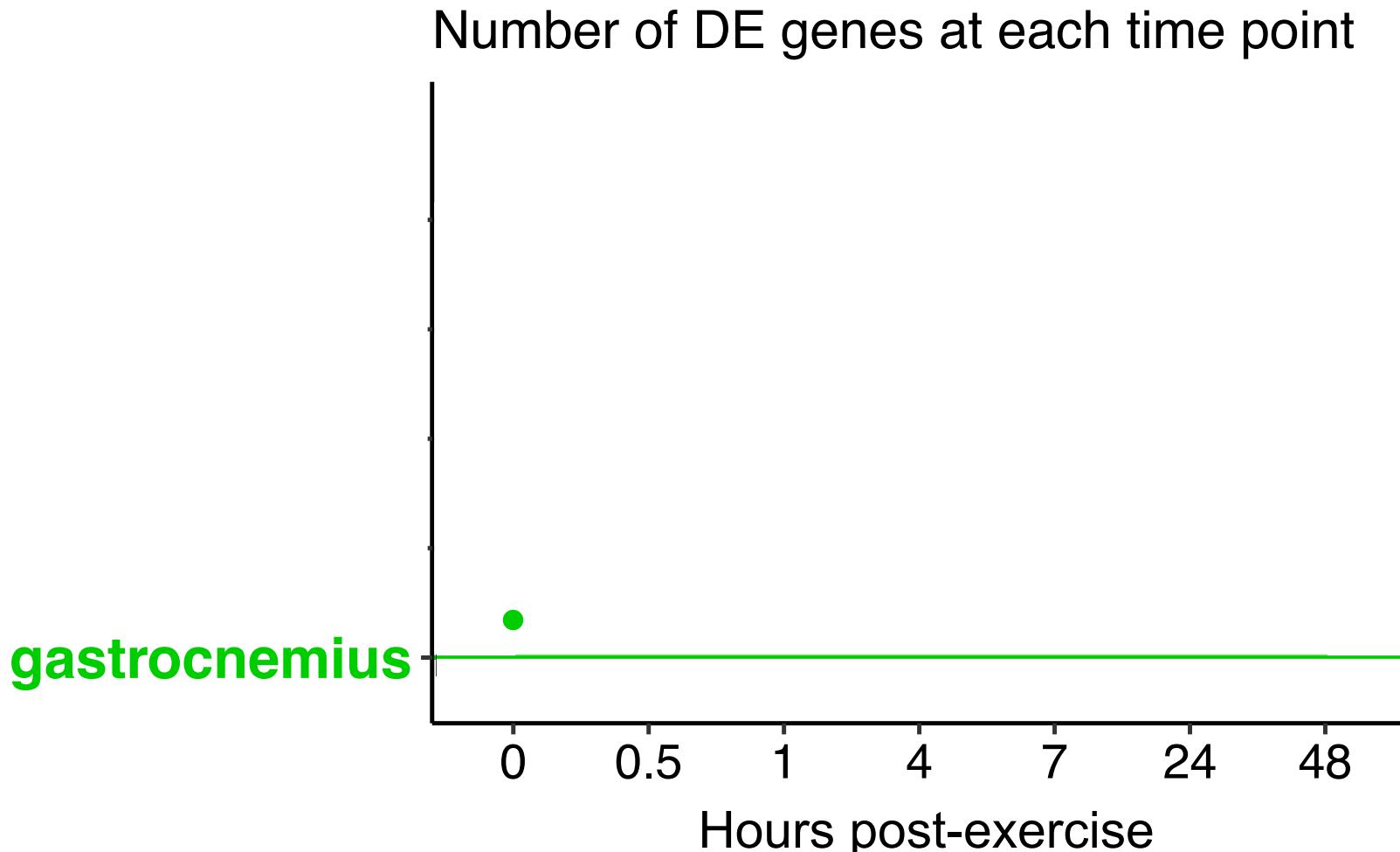
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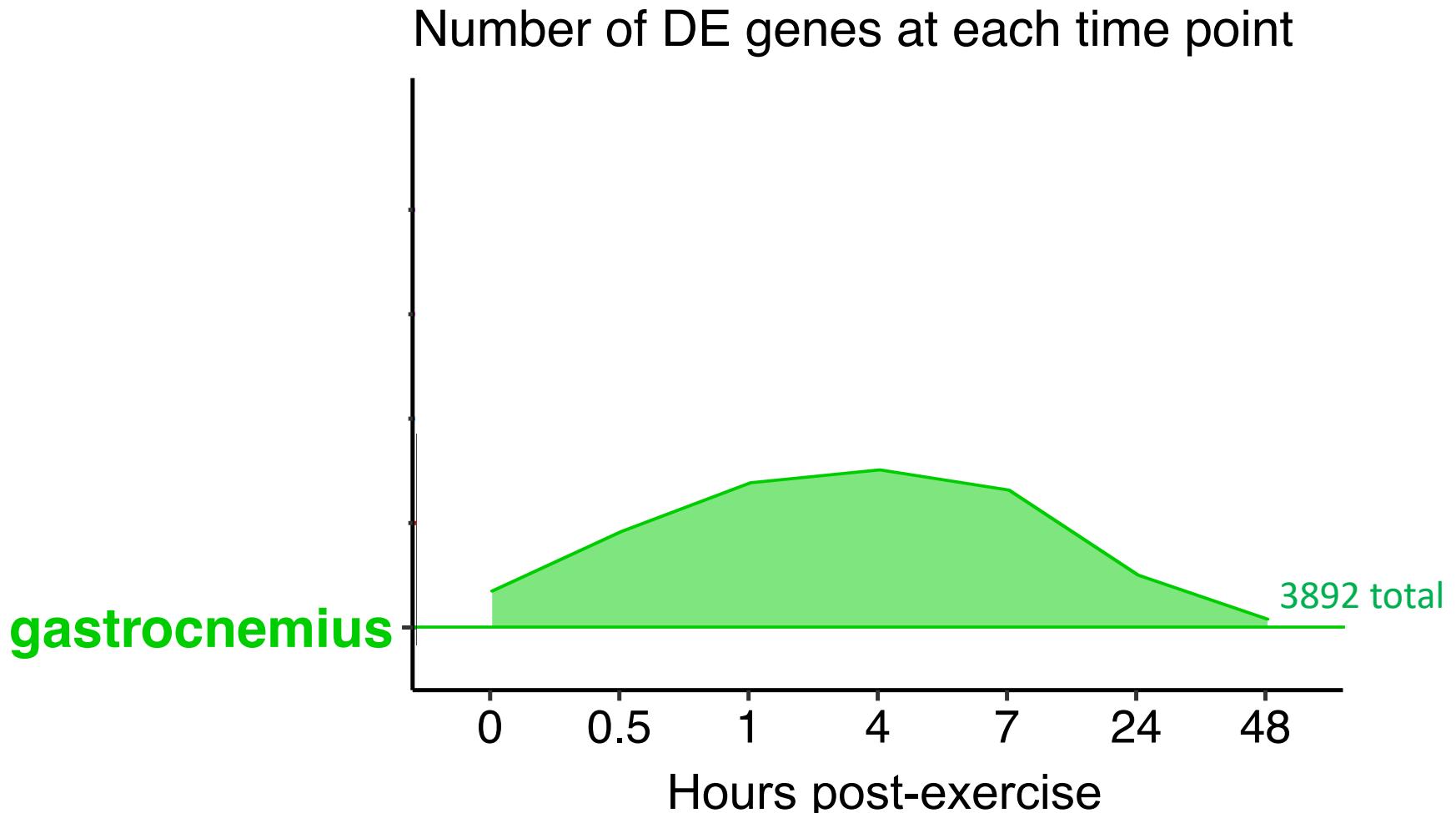
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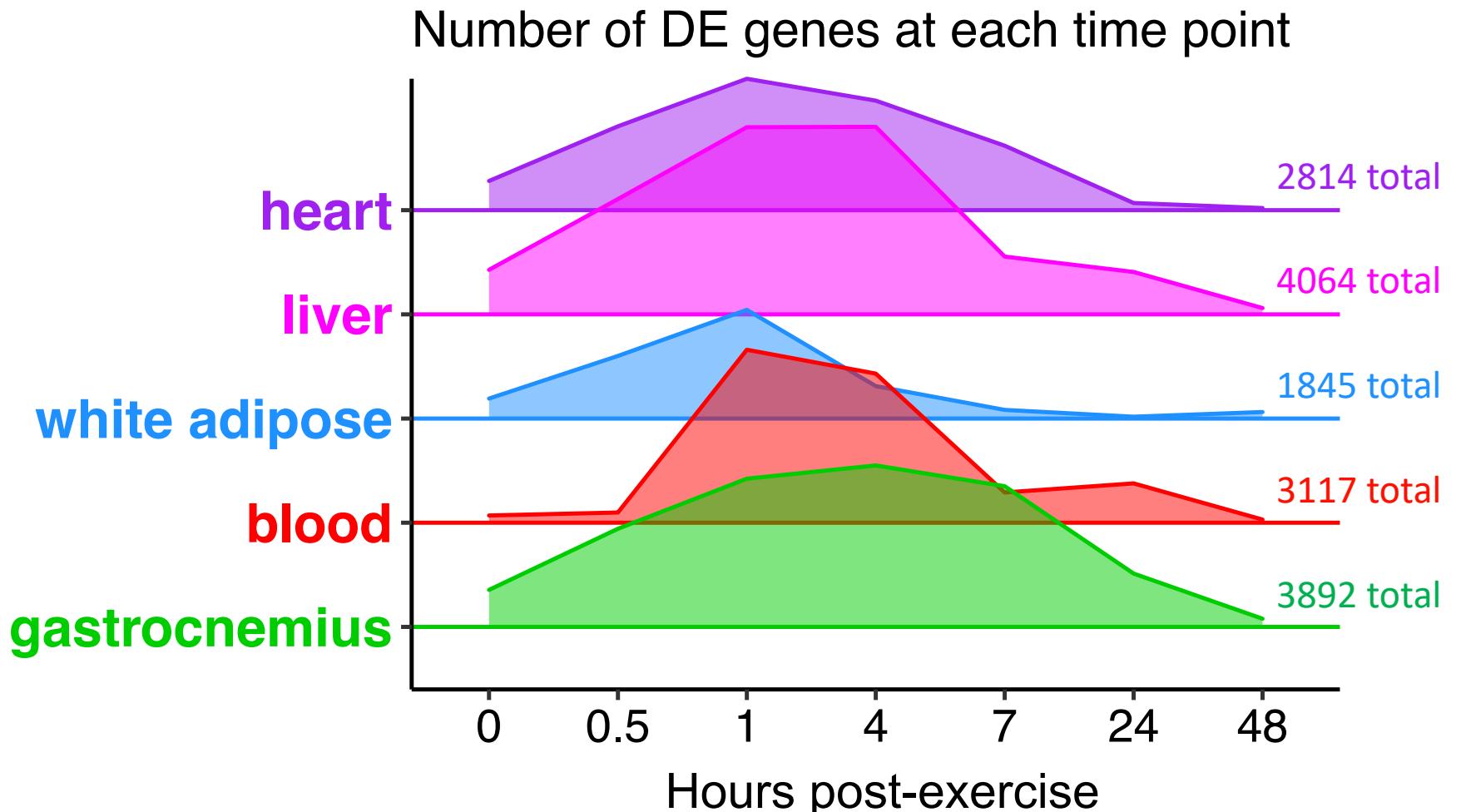
Thousands of genes are differentially expressed (DE) due to acute endurance exercise across tissues



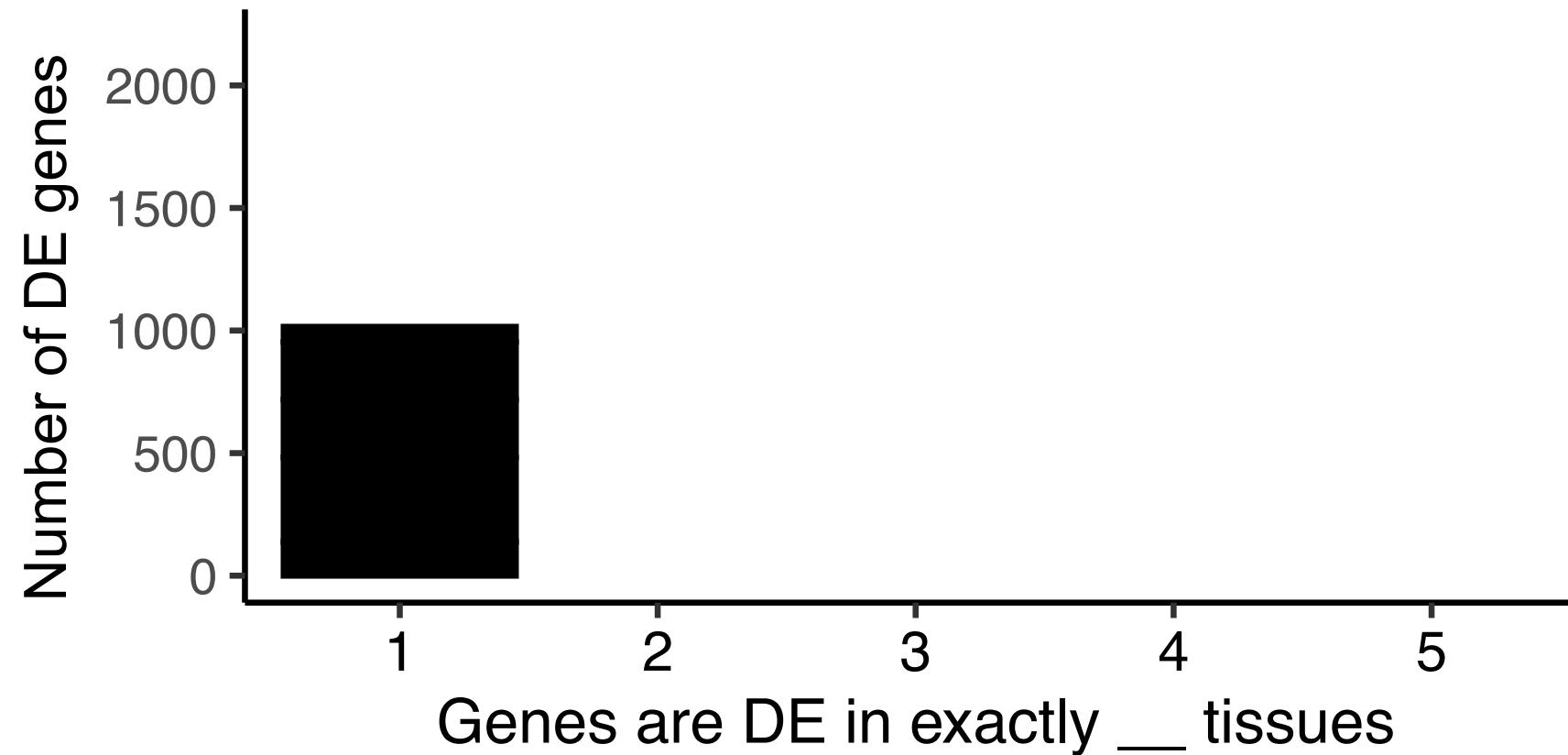
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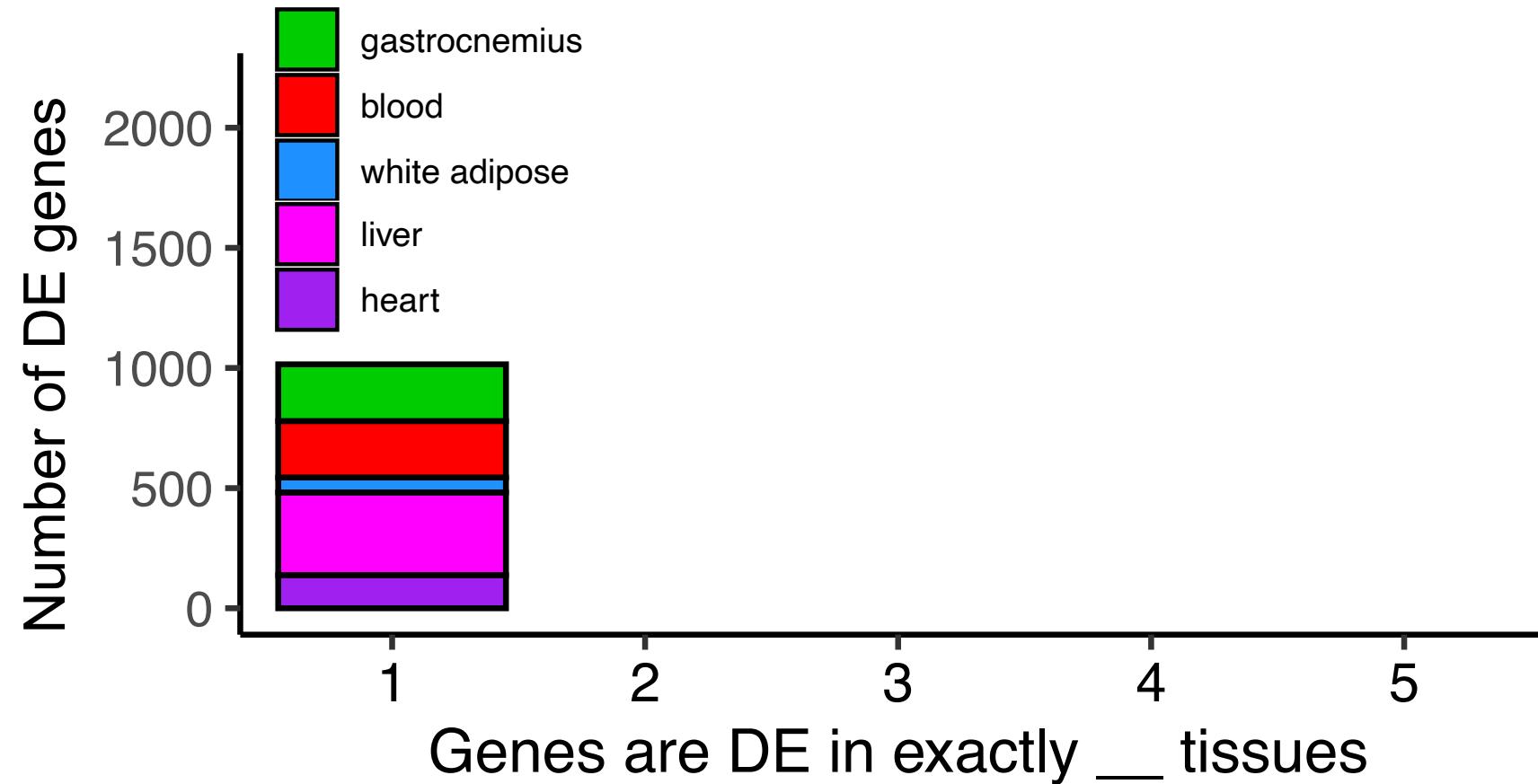
A large fraction of DE genes are shared across tissues



DE cutoffs:

- adjusted p-value < 0.05
- $\text{abs}(\log(\text{fold-change})) > 0.5$

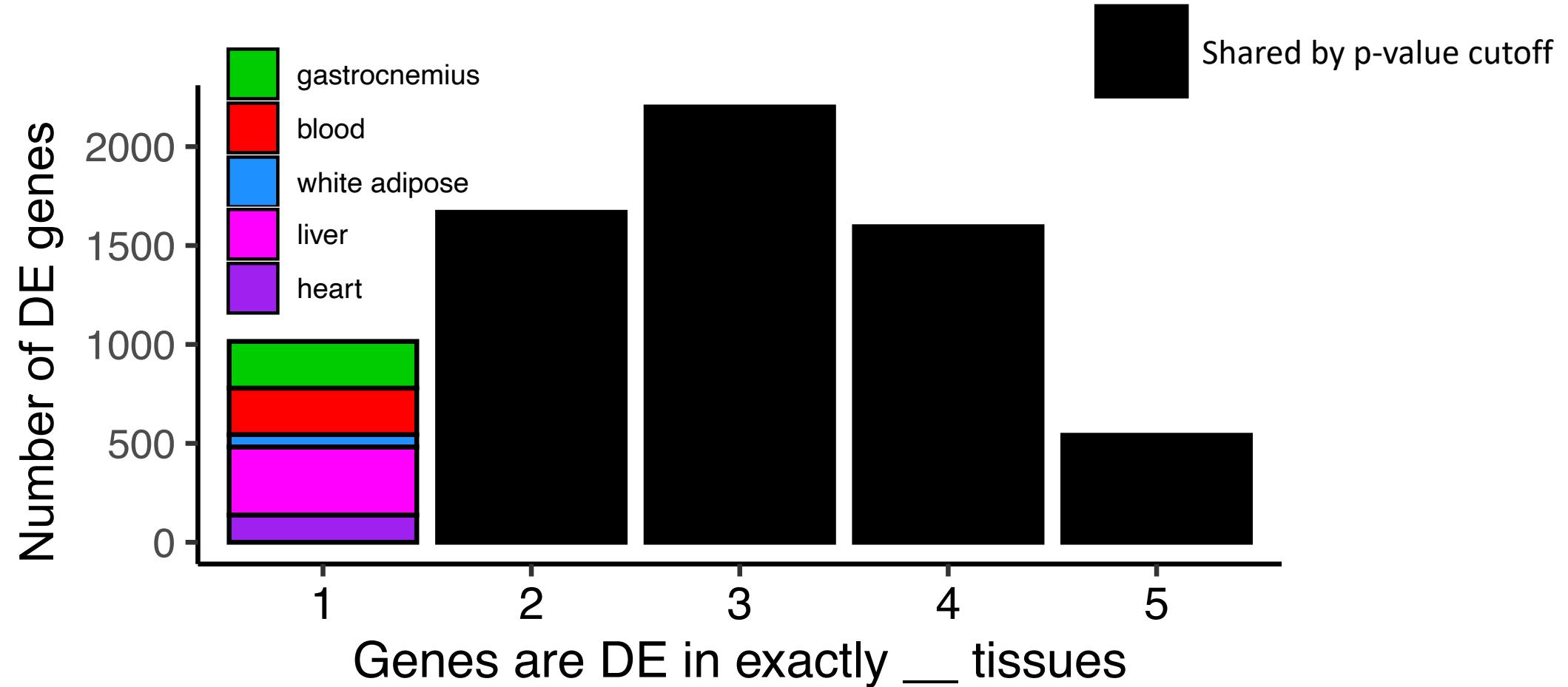
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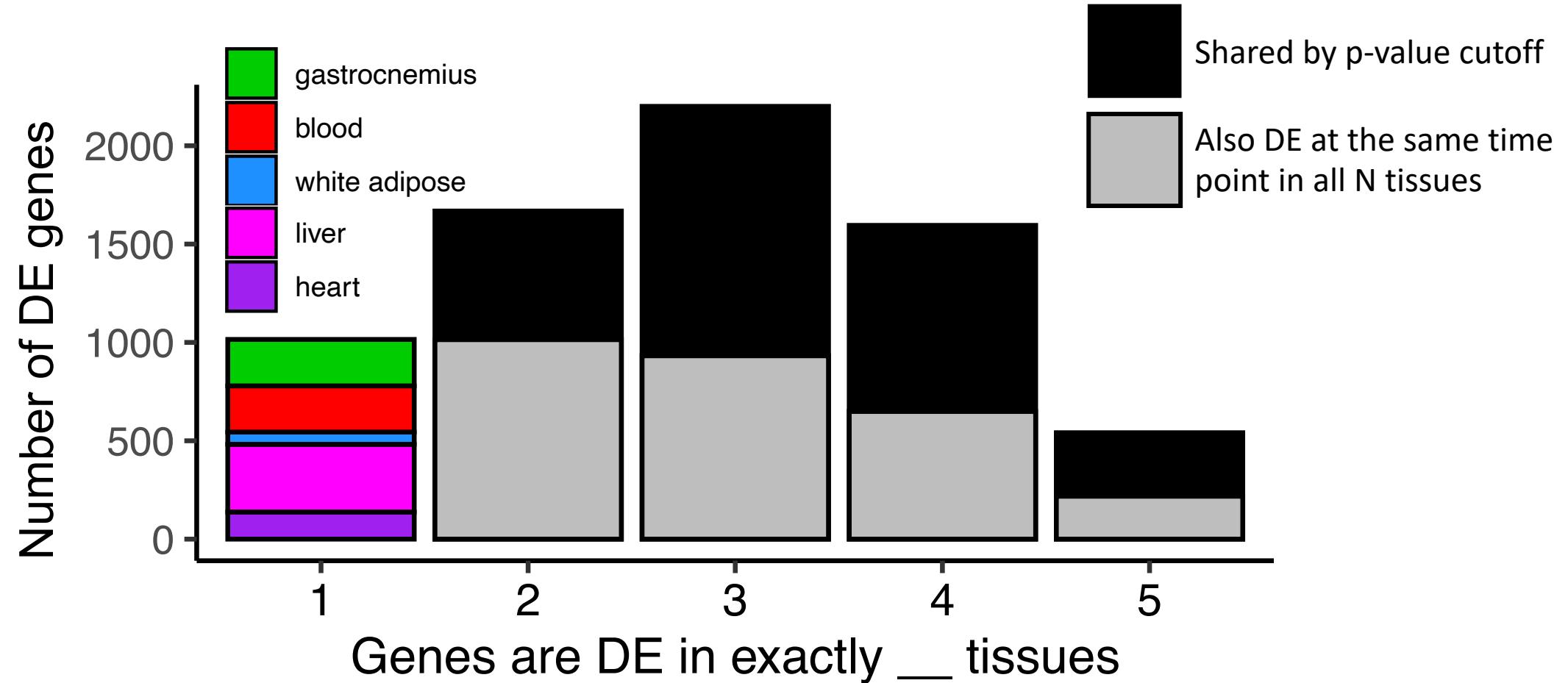
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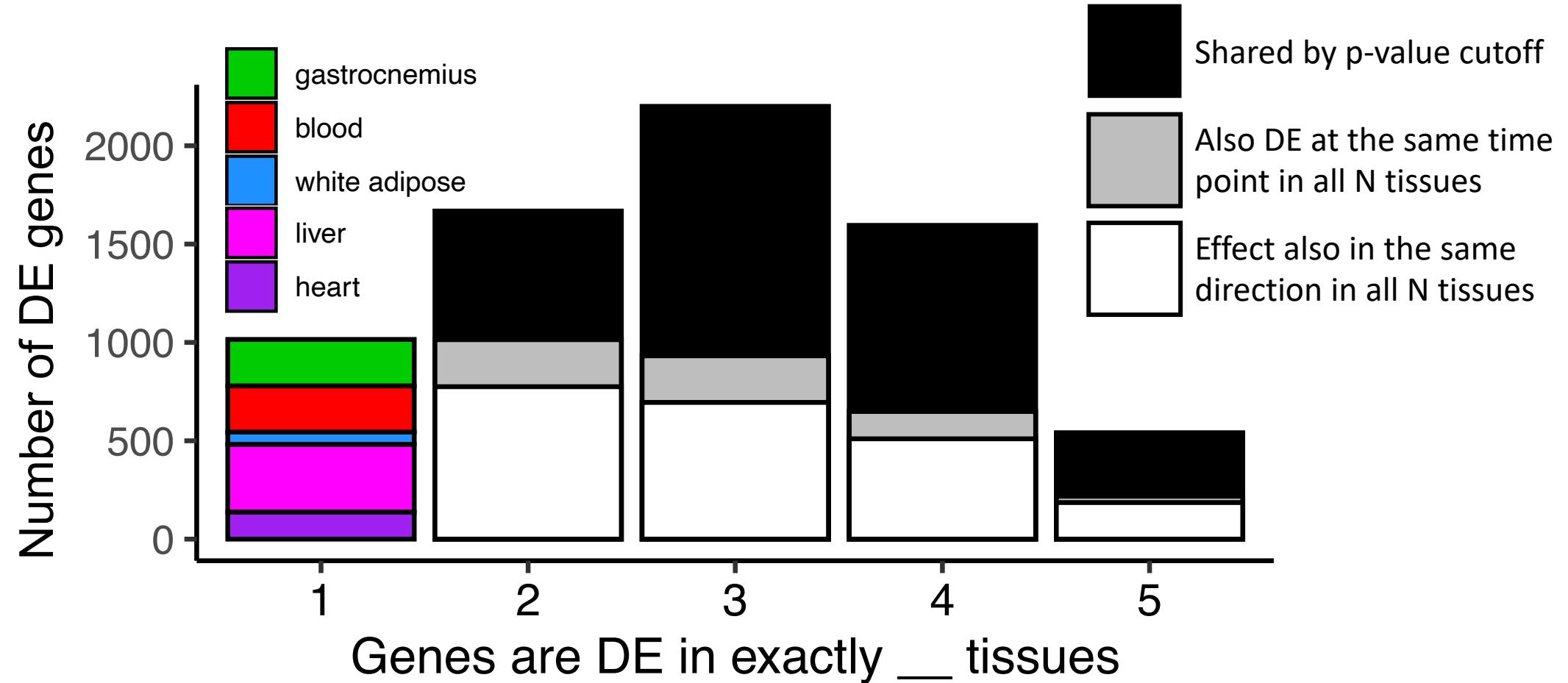
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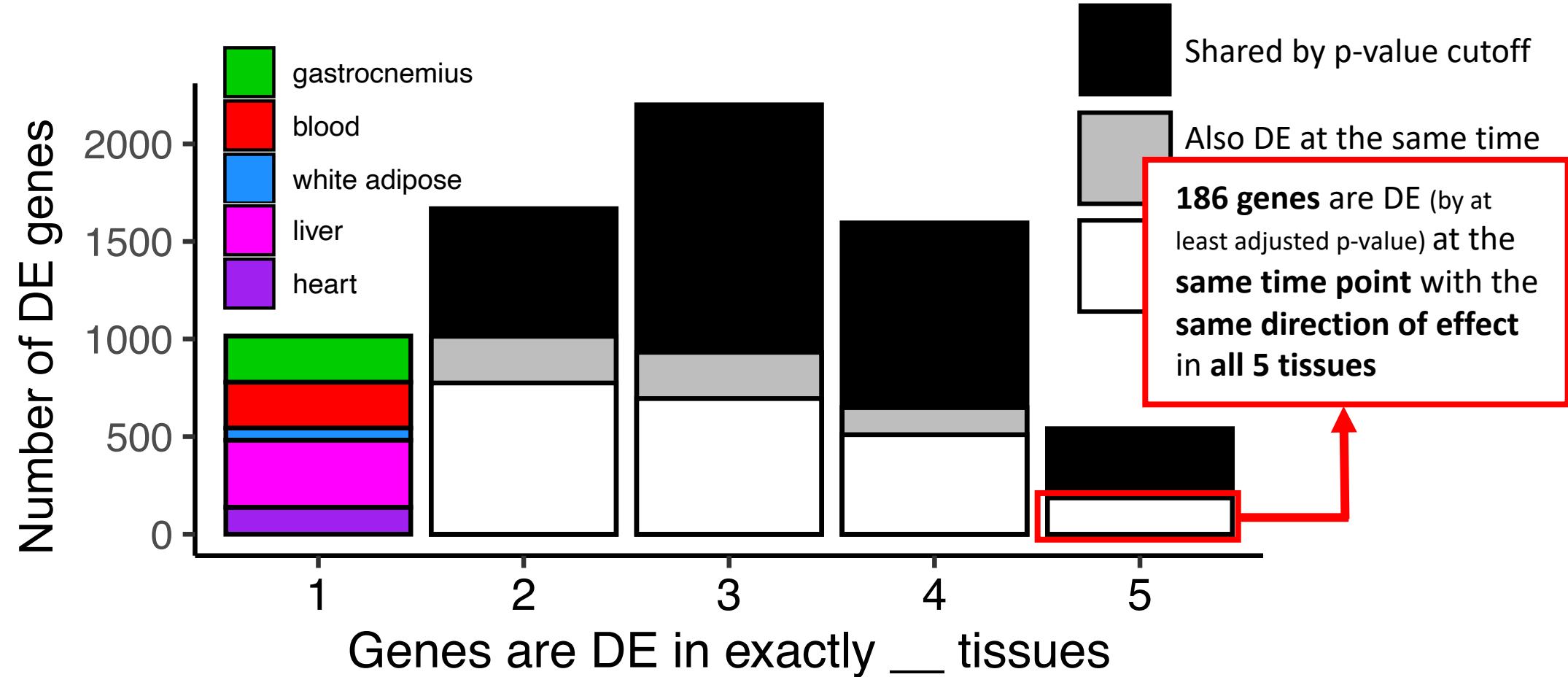
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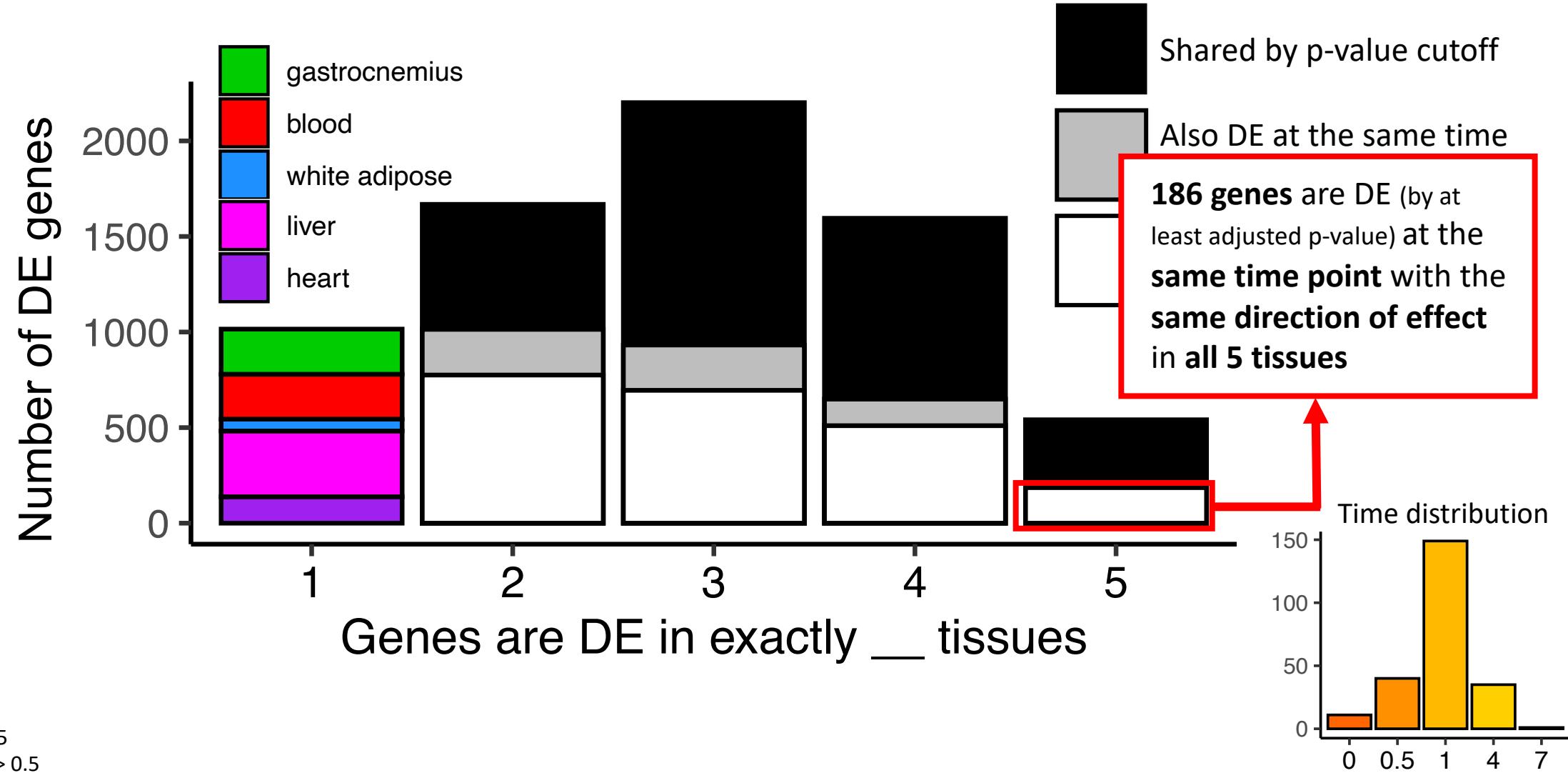
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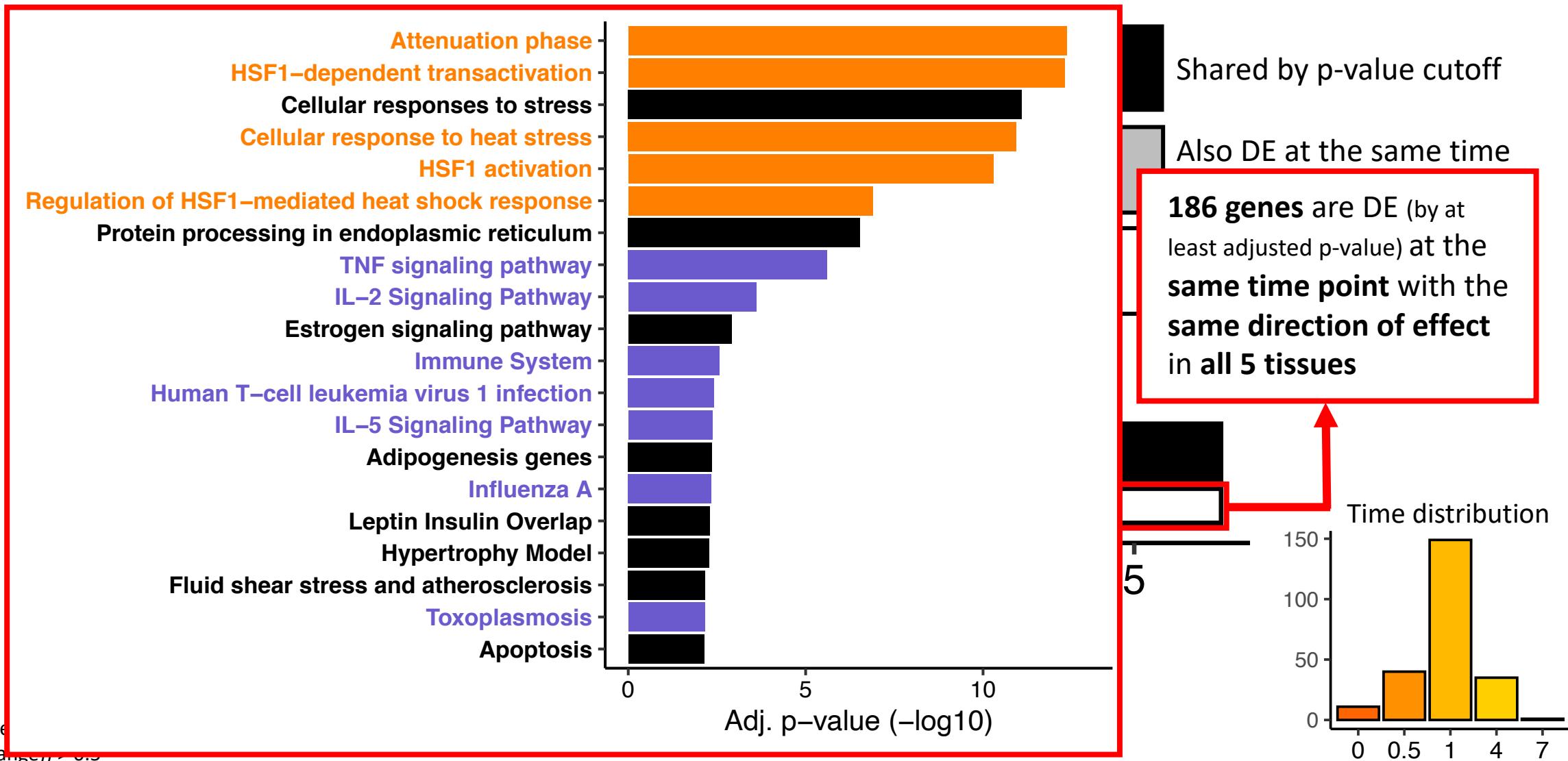
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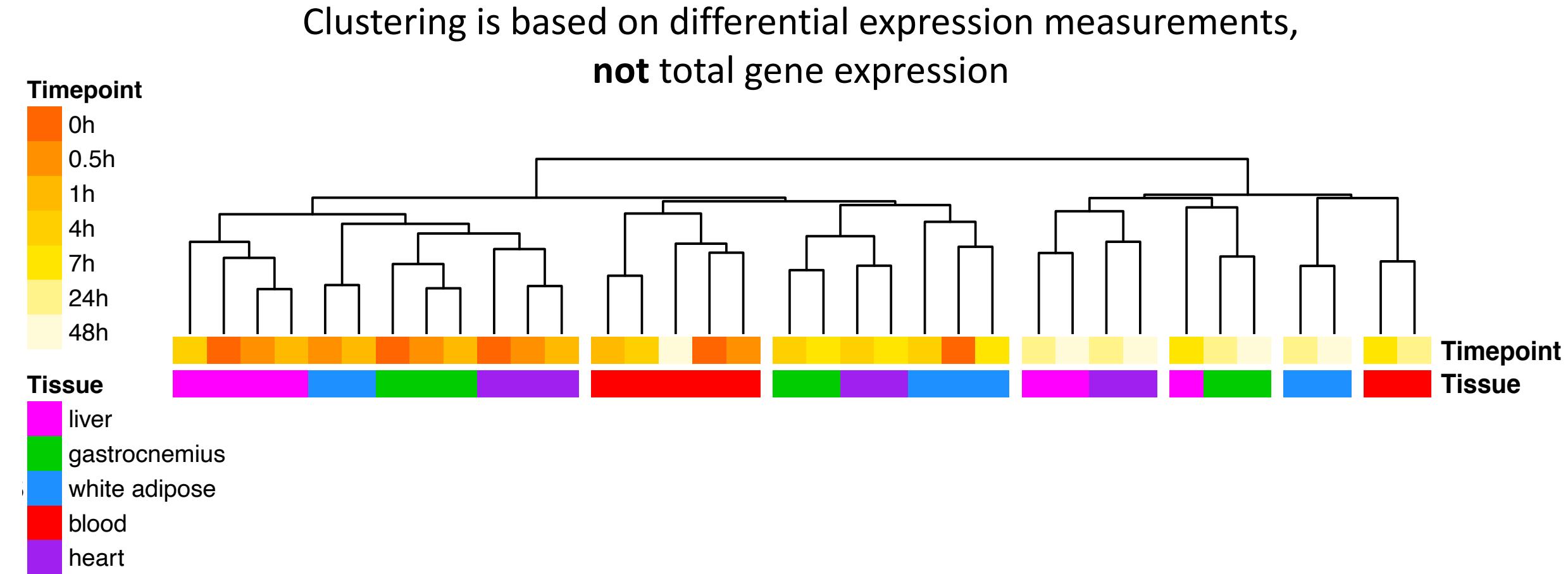


Strongly shared genes are enriched for terms related to heat shock and immune response

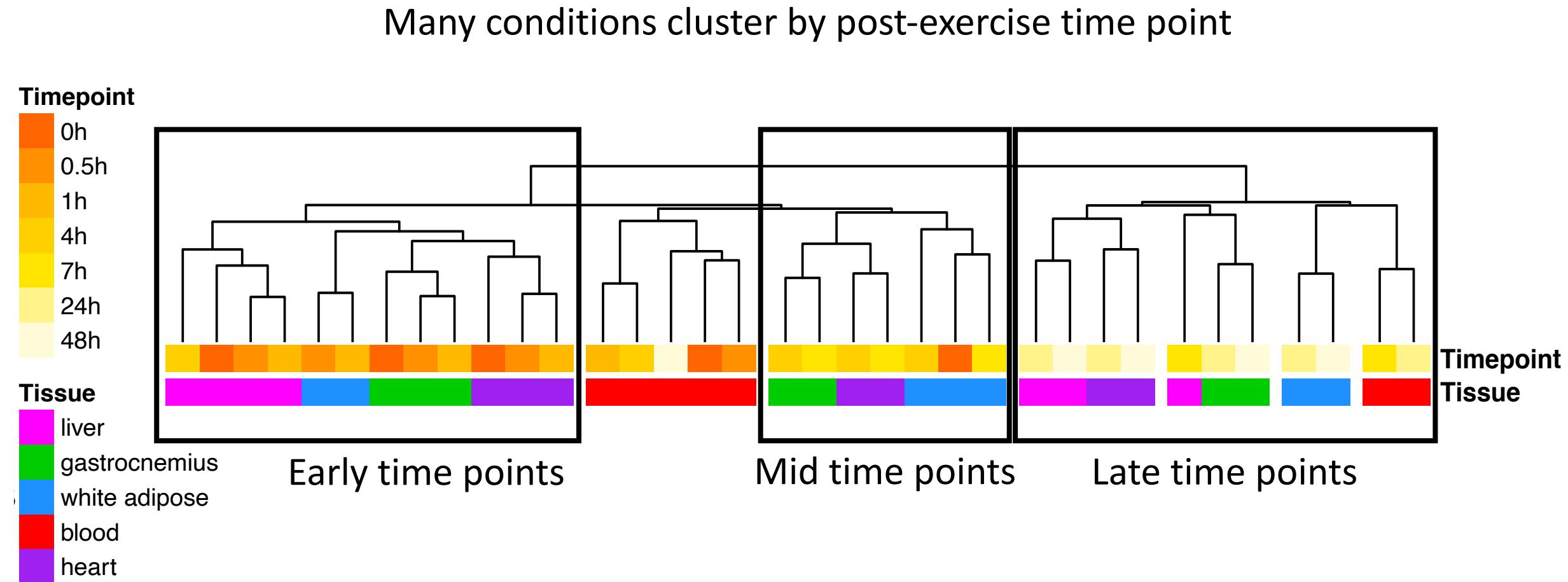


How do conditions (tissue and time point pairs) cluster in terms of transcriptional response to the exercise bout?

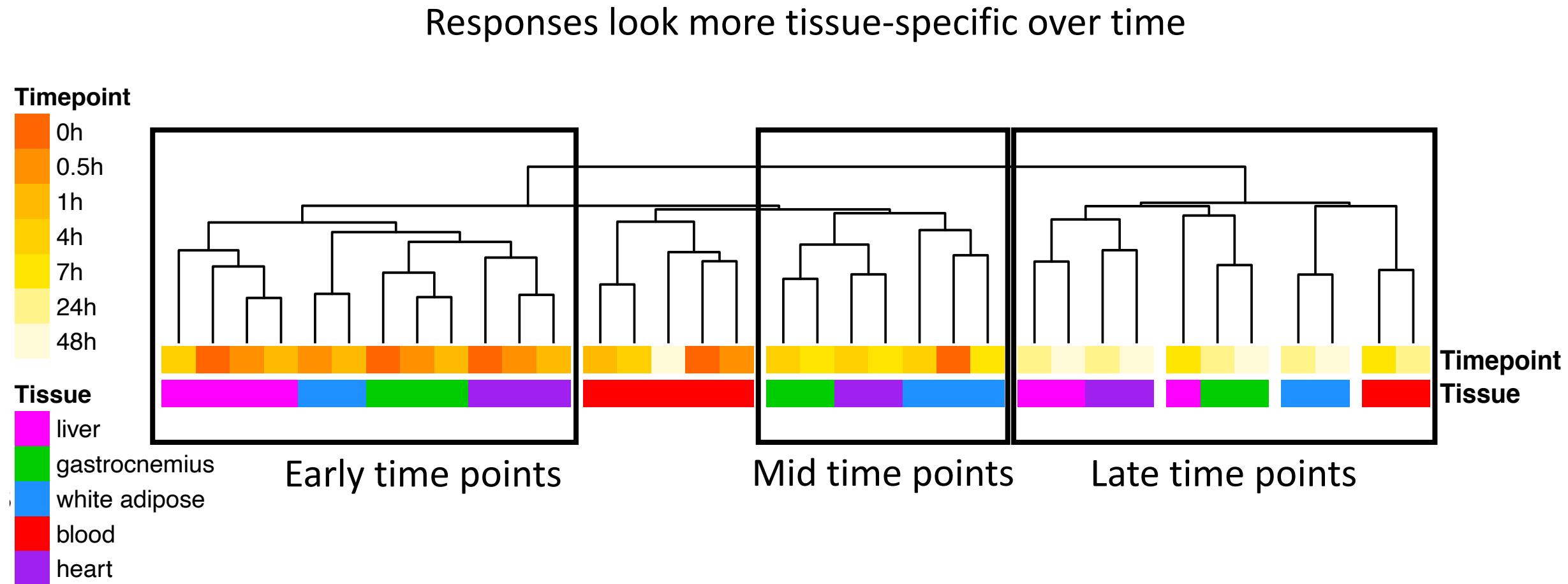
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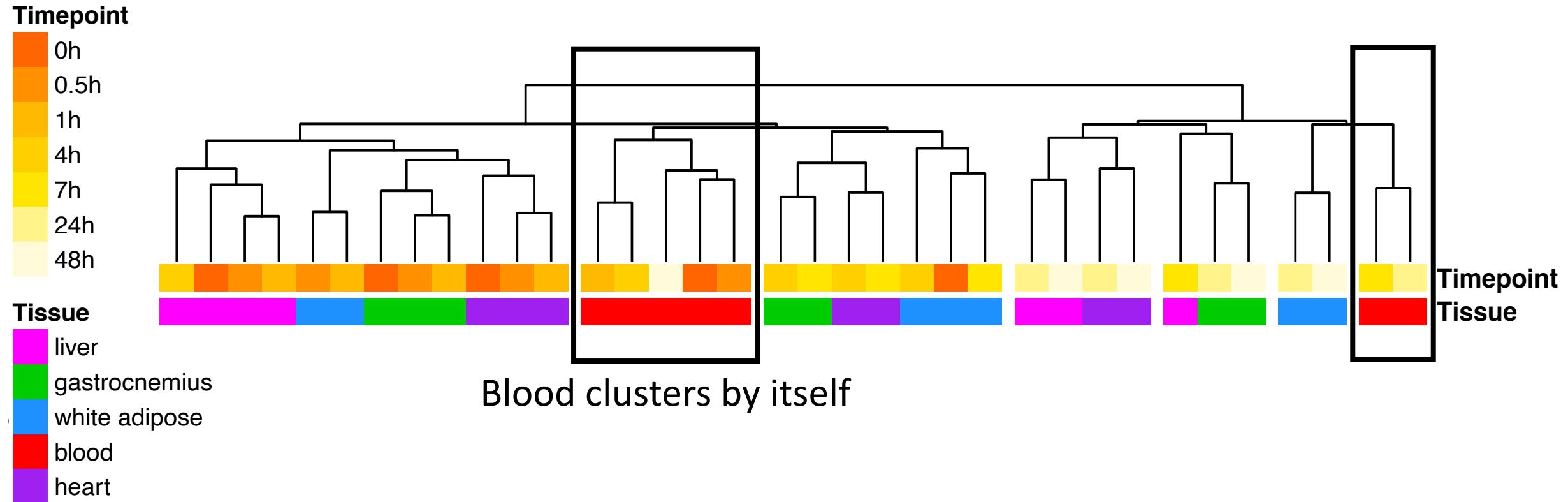
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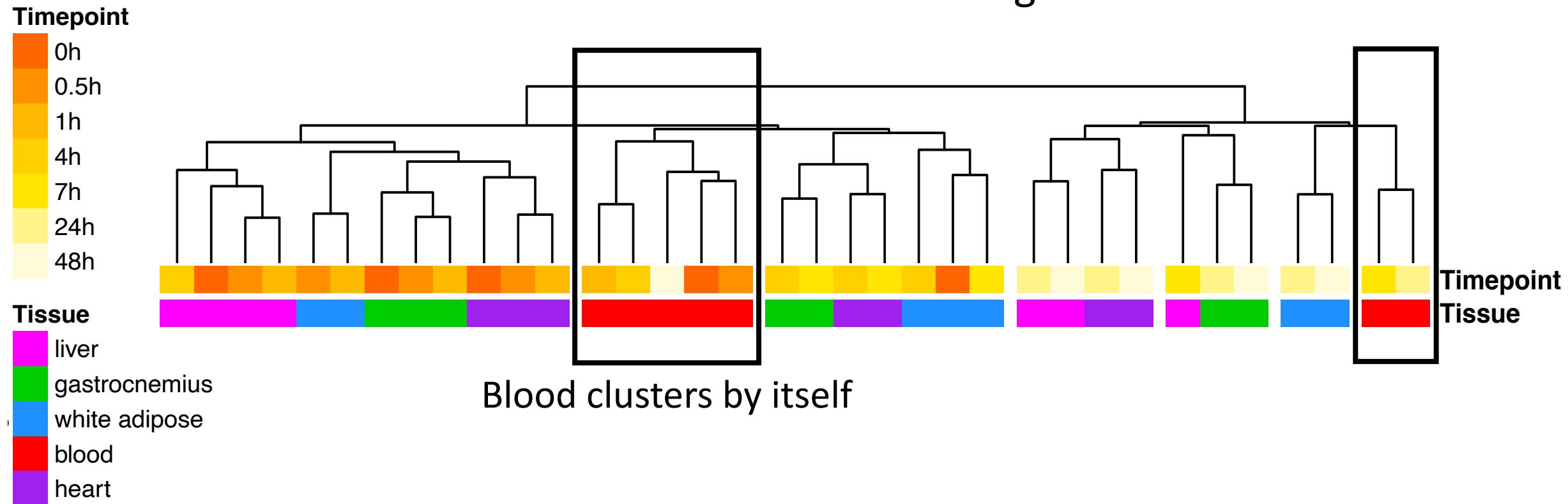


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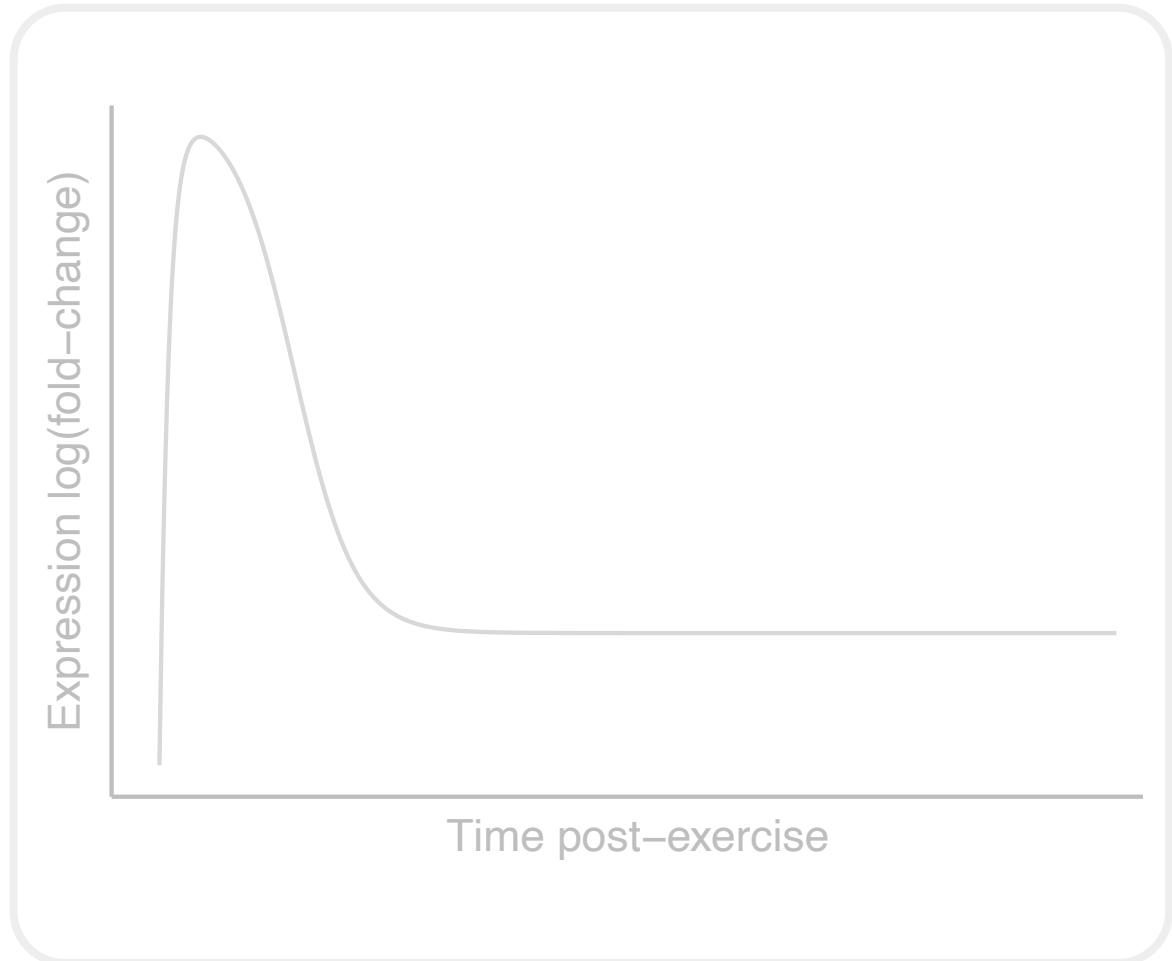
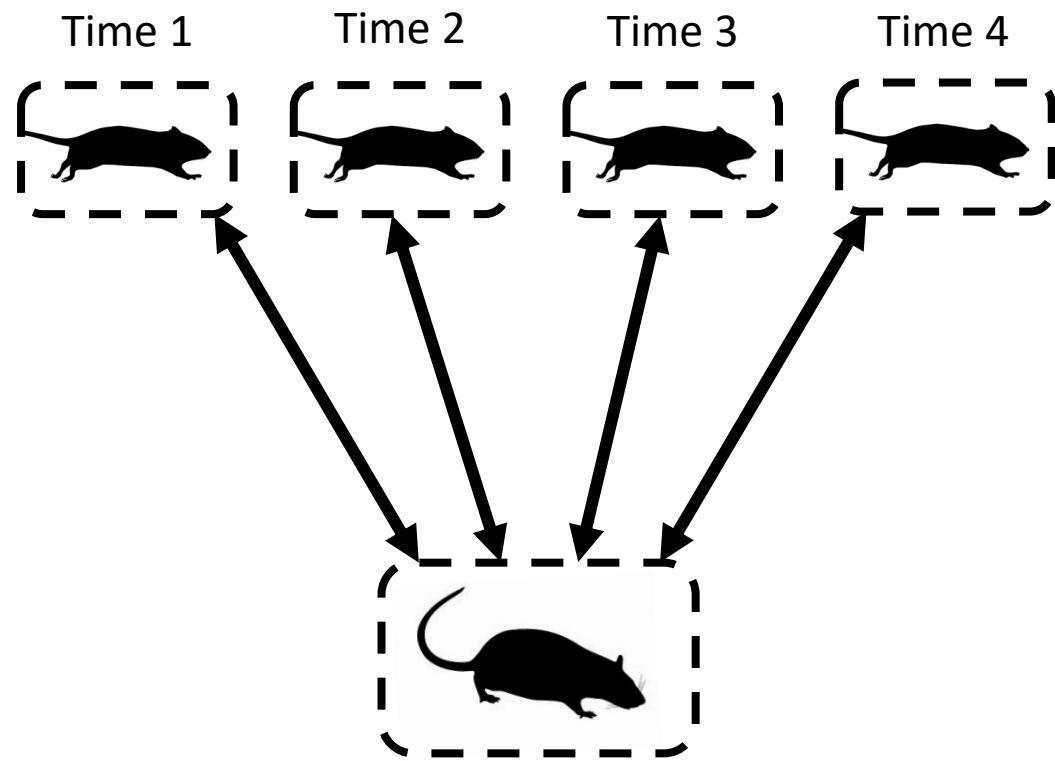


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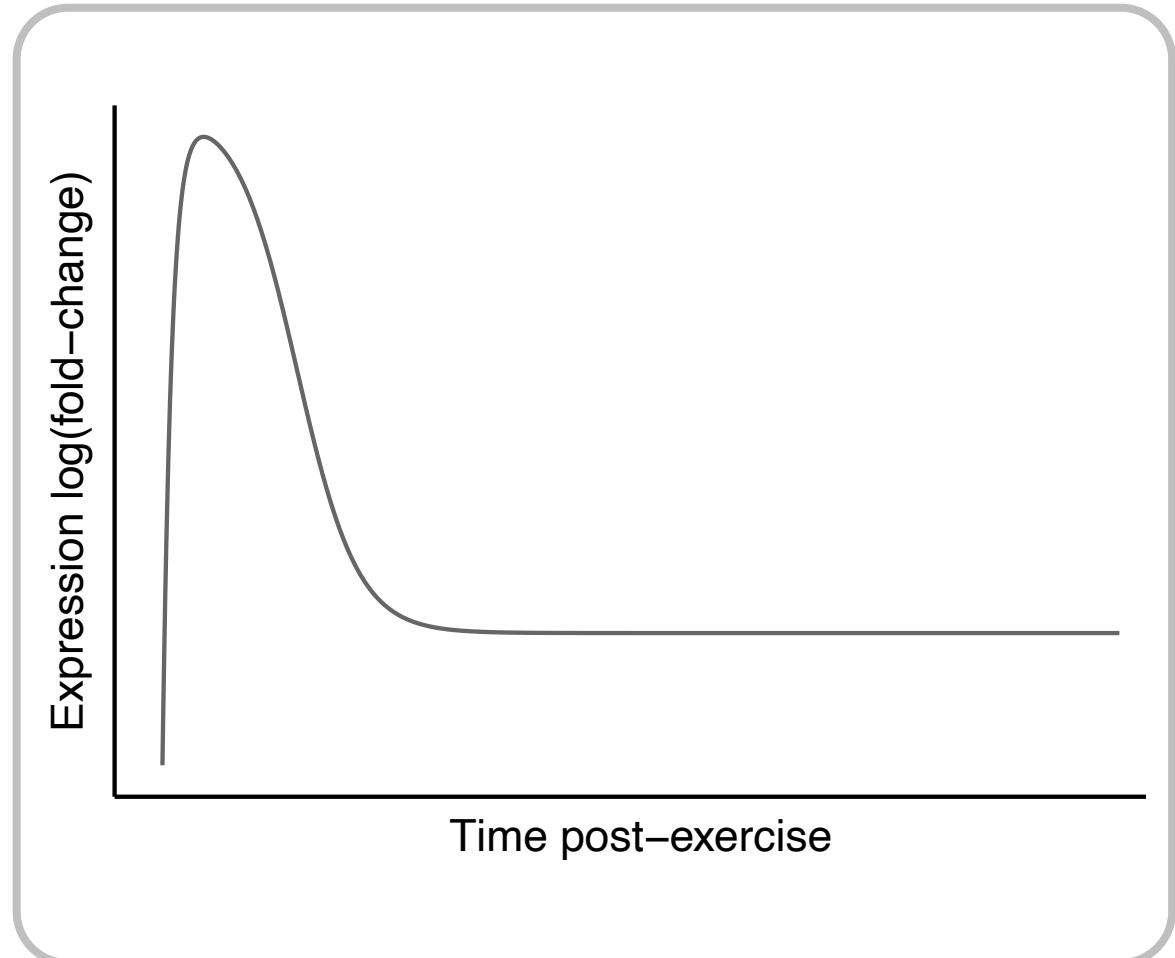
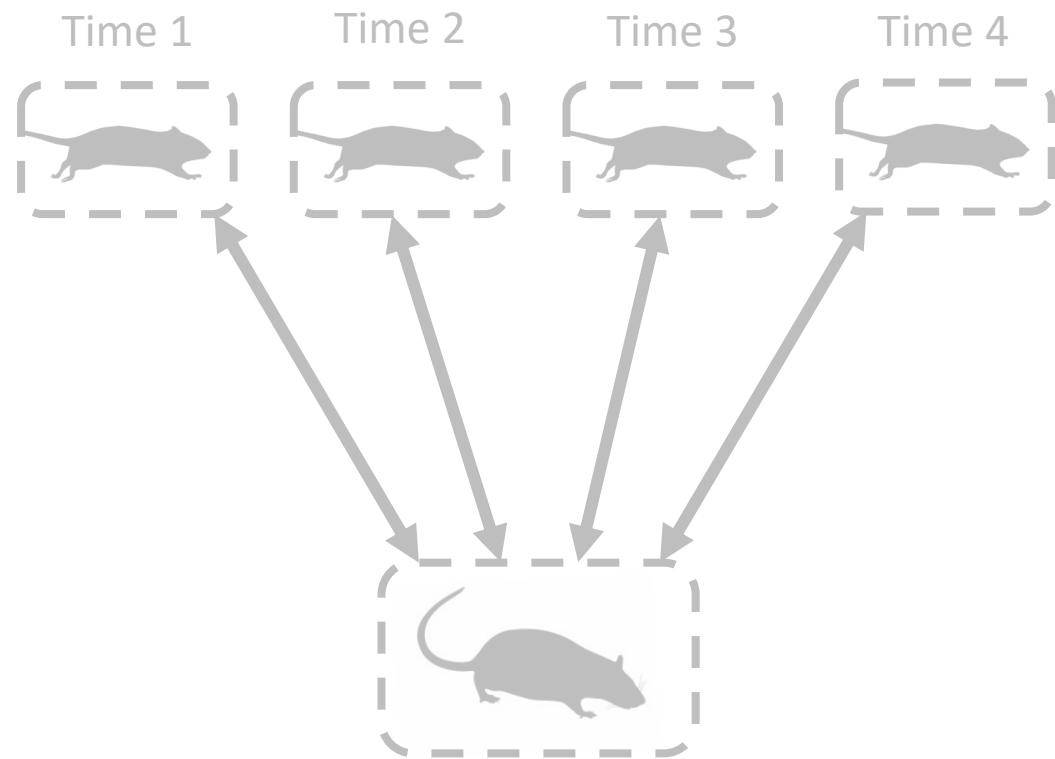
The dynamic changes occurring in blood
do not reflect changes in other tissues



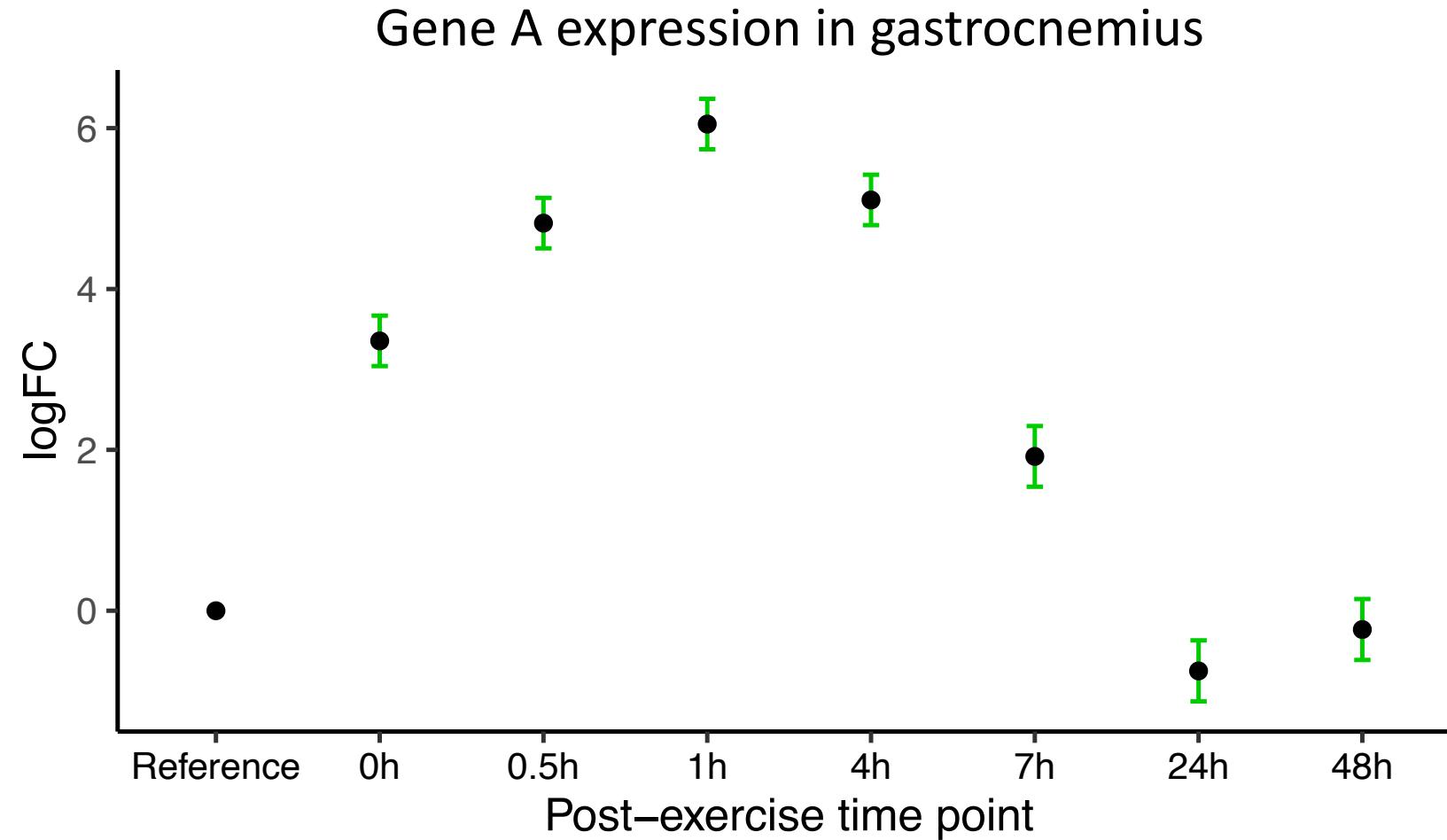
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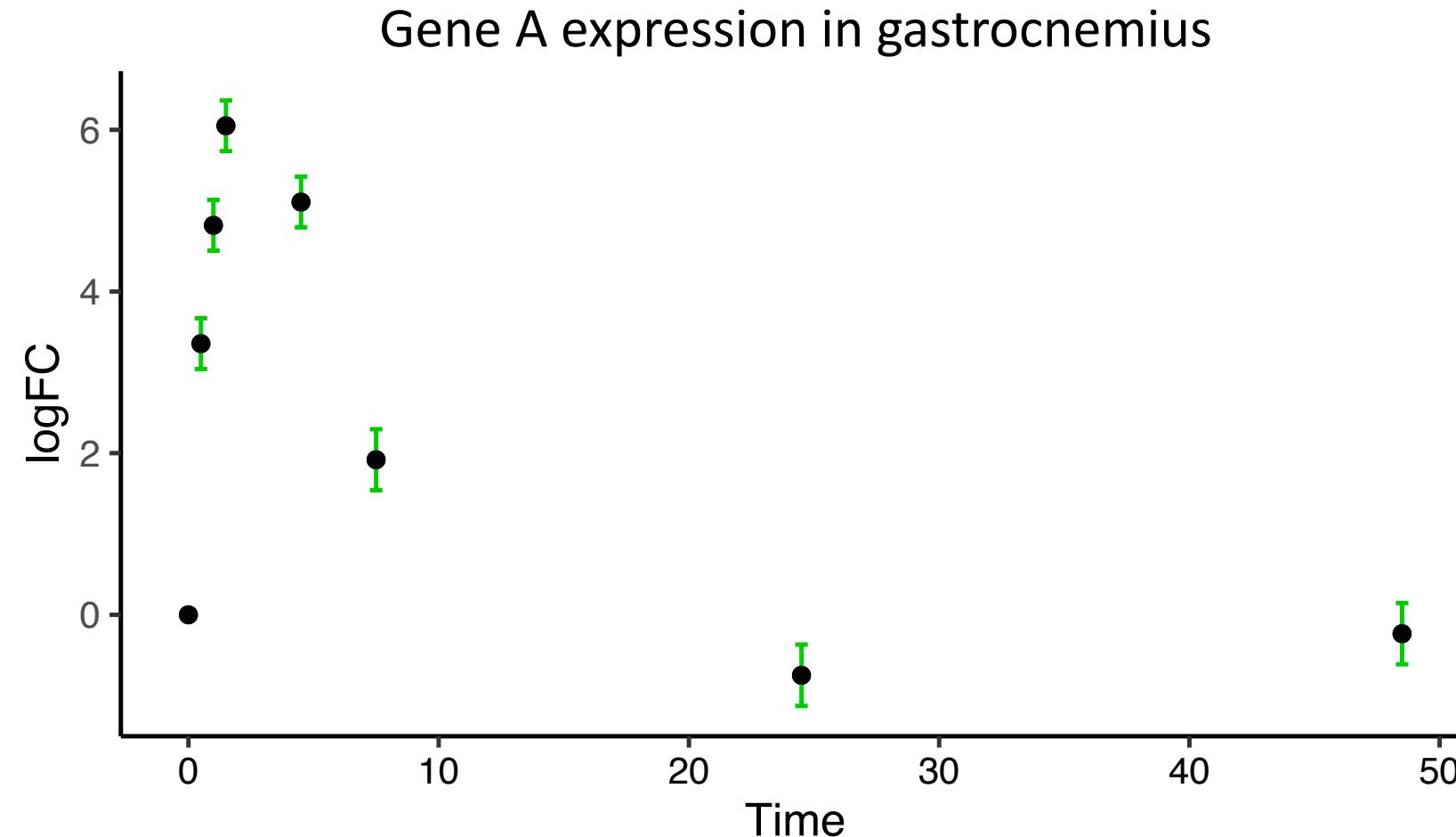
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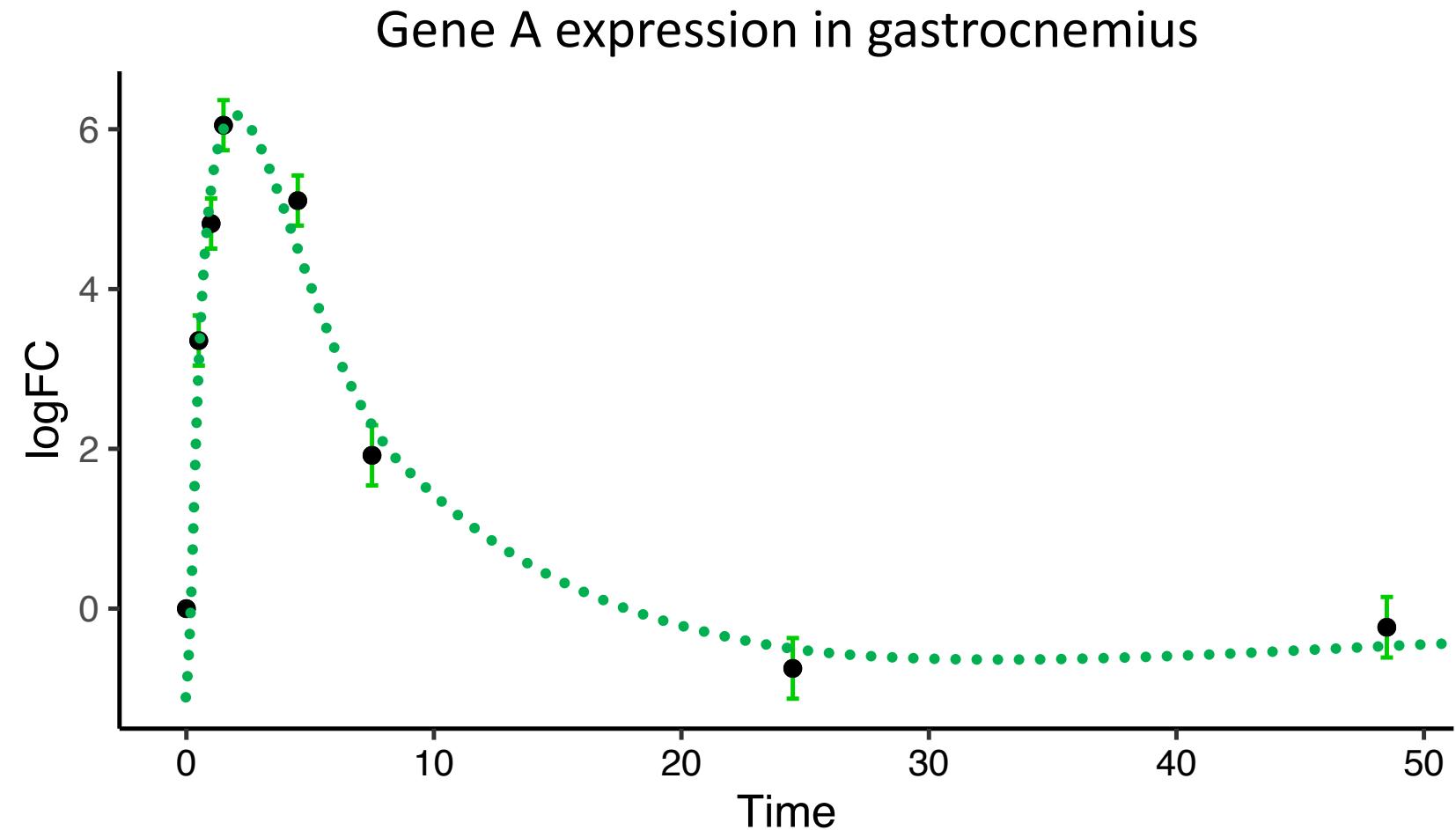
How can we take advantage of the longitudinal aspect of these gene expression profiles?



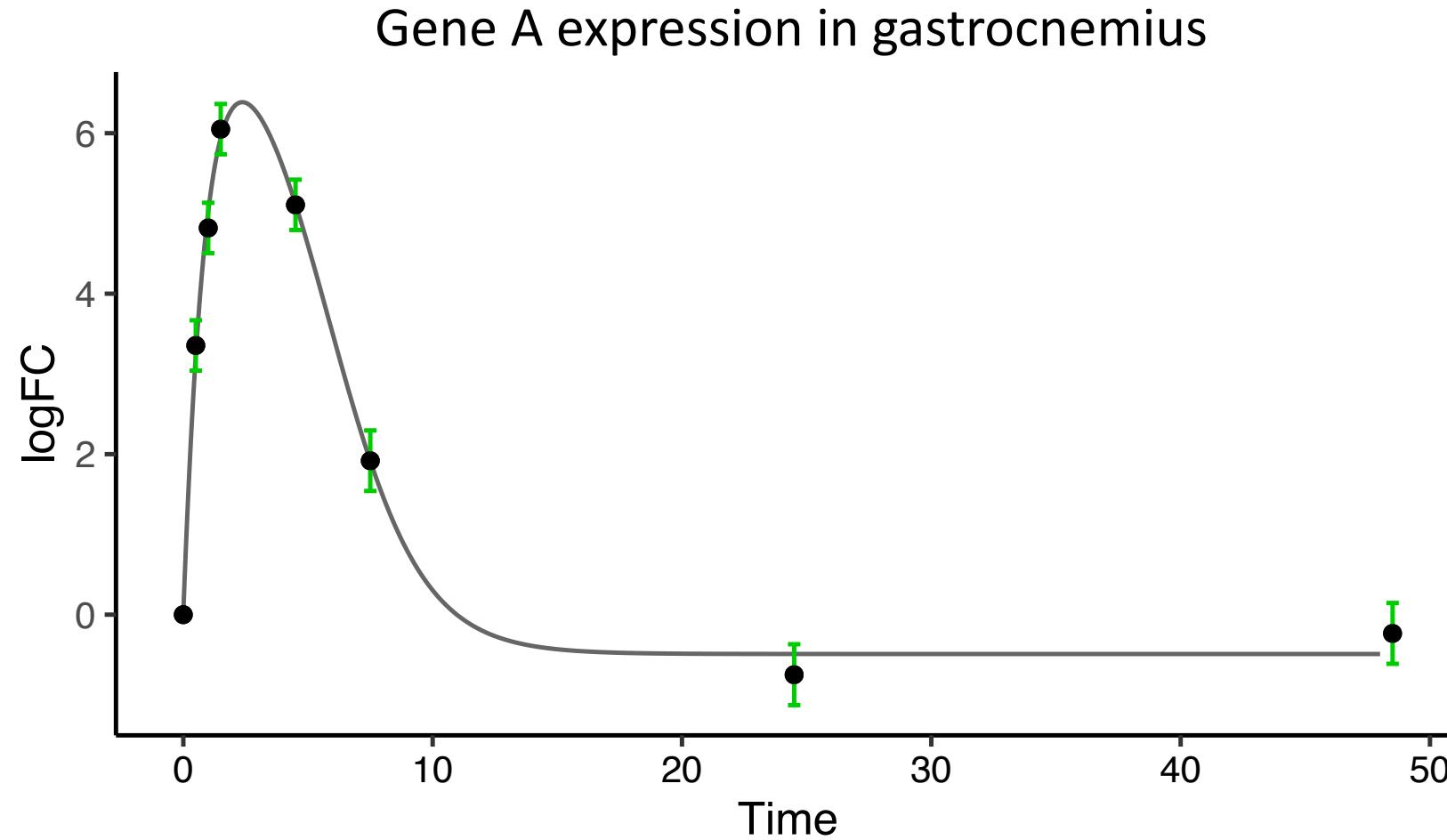
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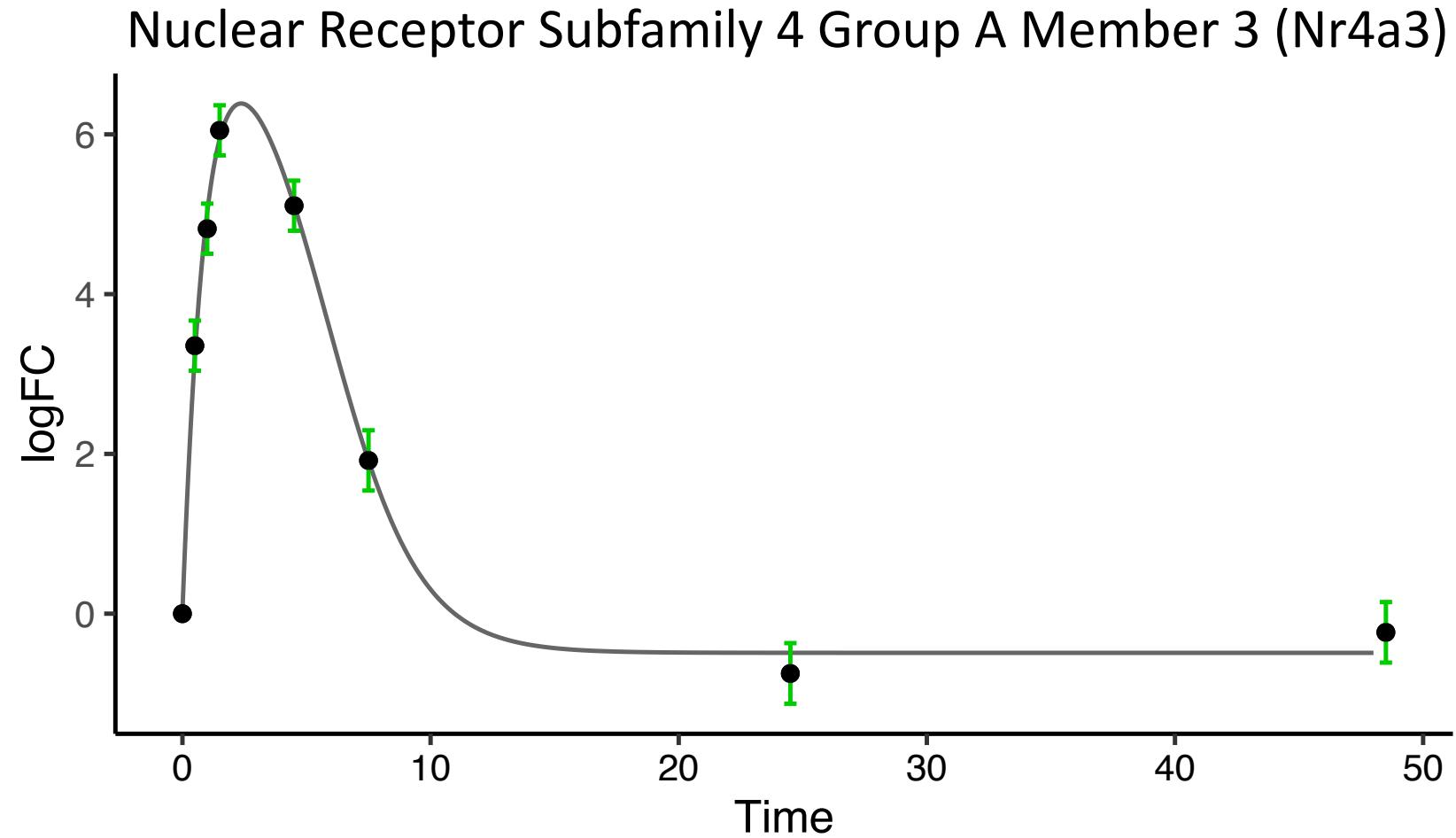


Impulse curves are a suitable model for transcriptional responses to acute stimuli



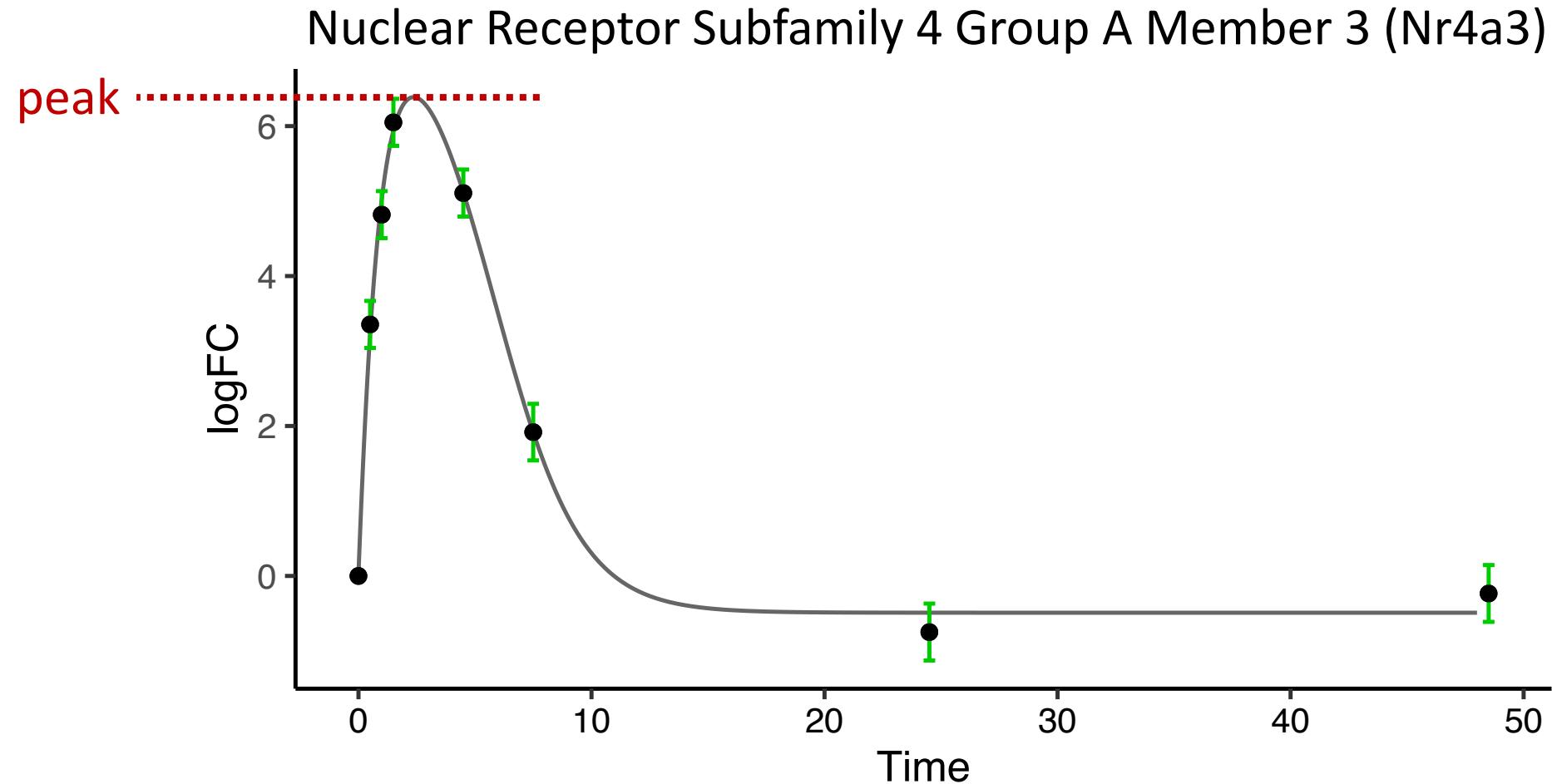
Chechik and Koller, J Comp Bio (2009)
Sara Mostafavi et al., Cell (2016)

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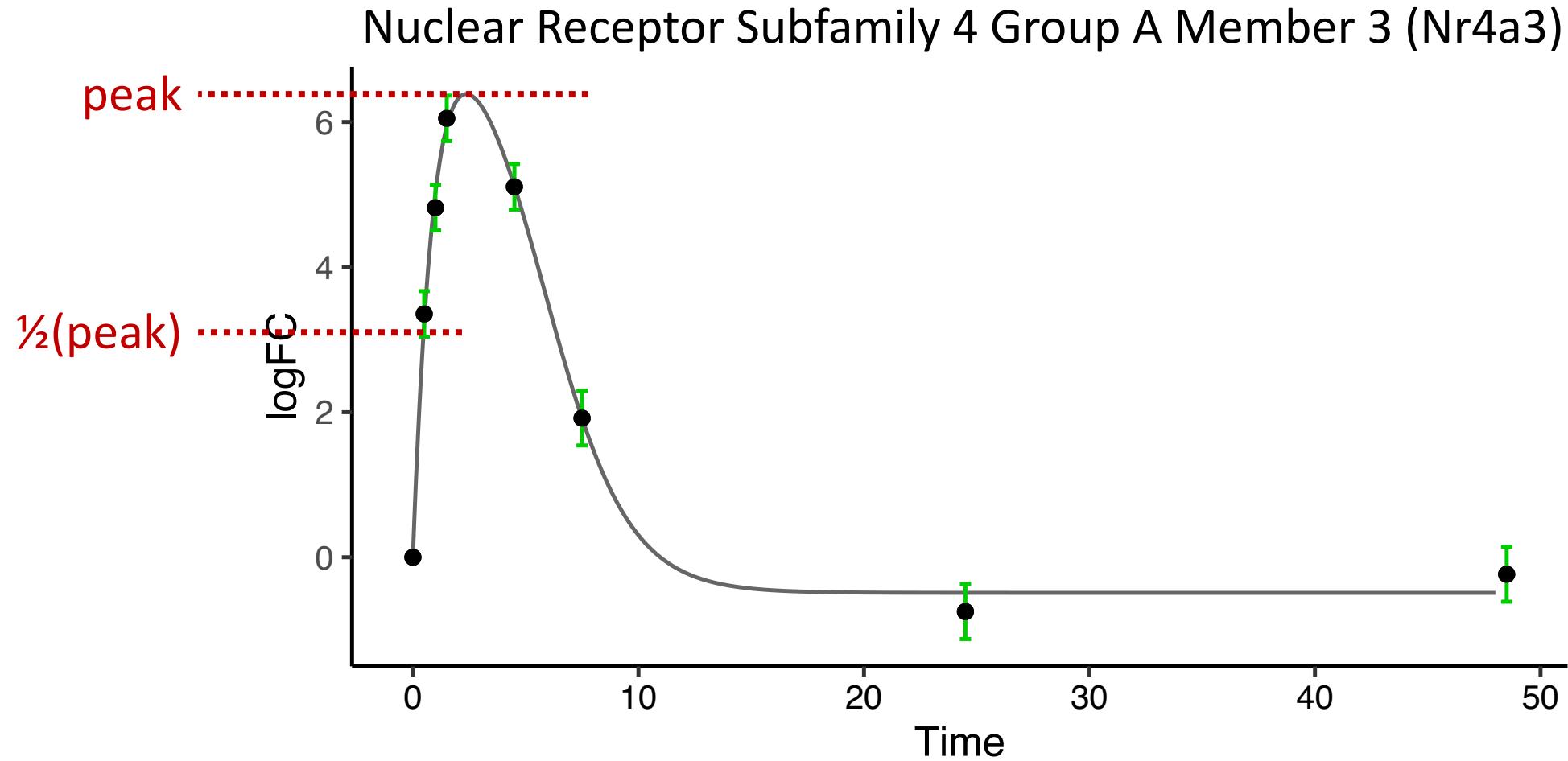
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Impulse curves have biologically meaningful and interpretable characteristics



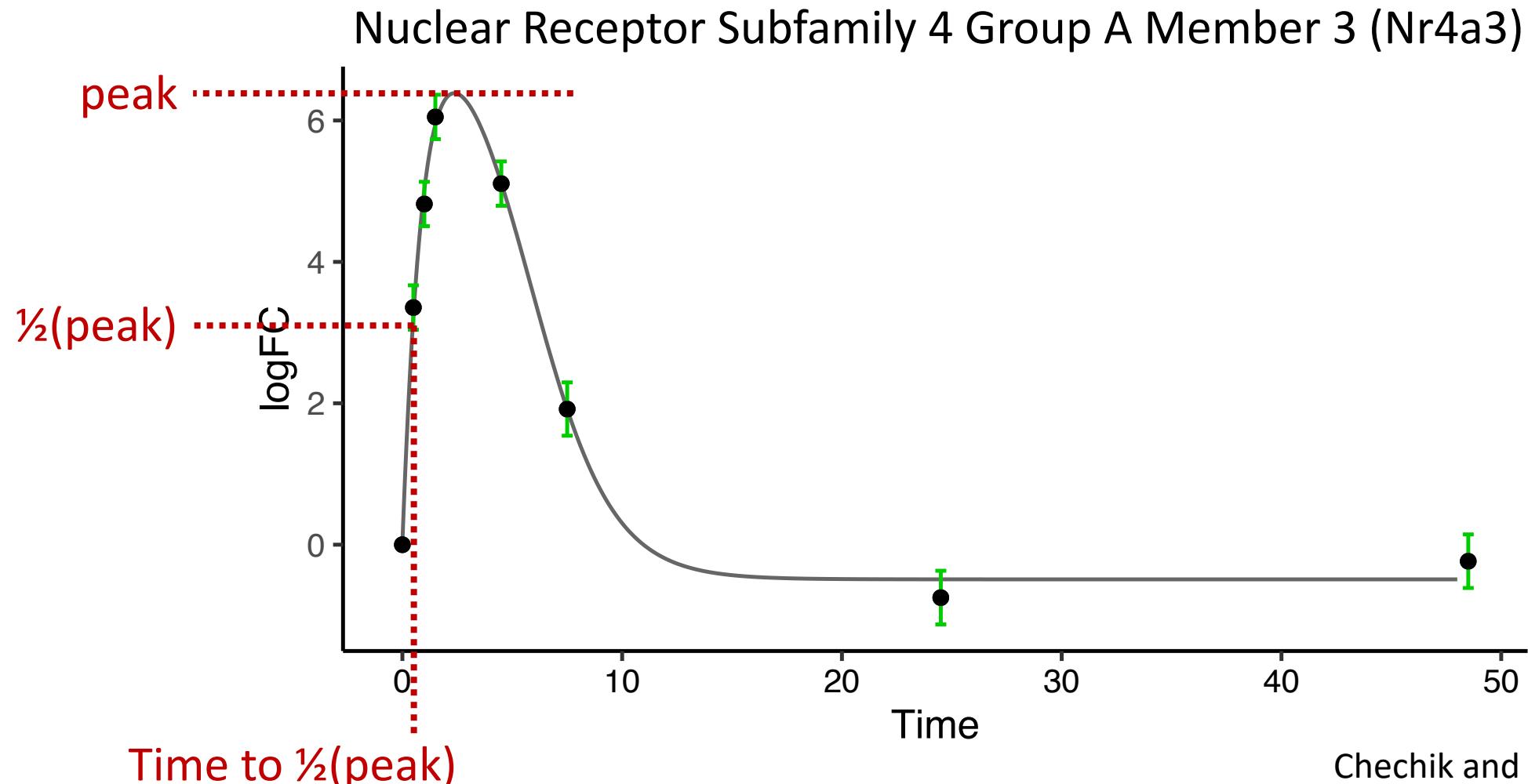
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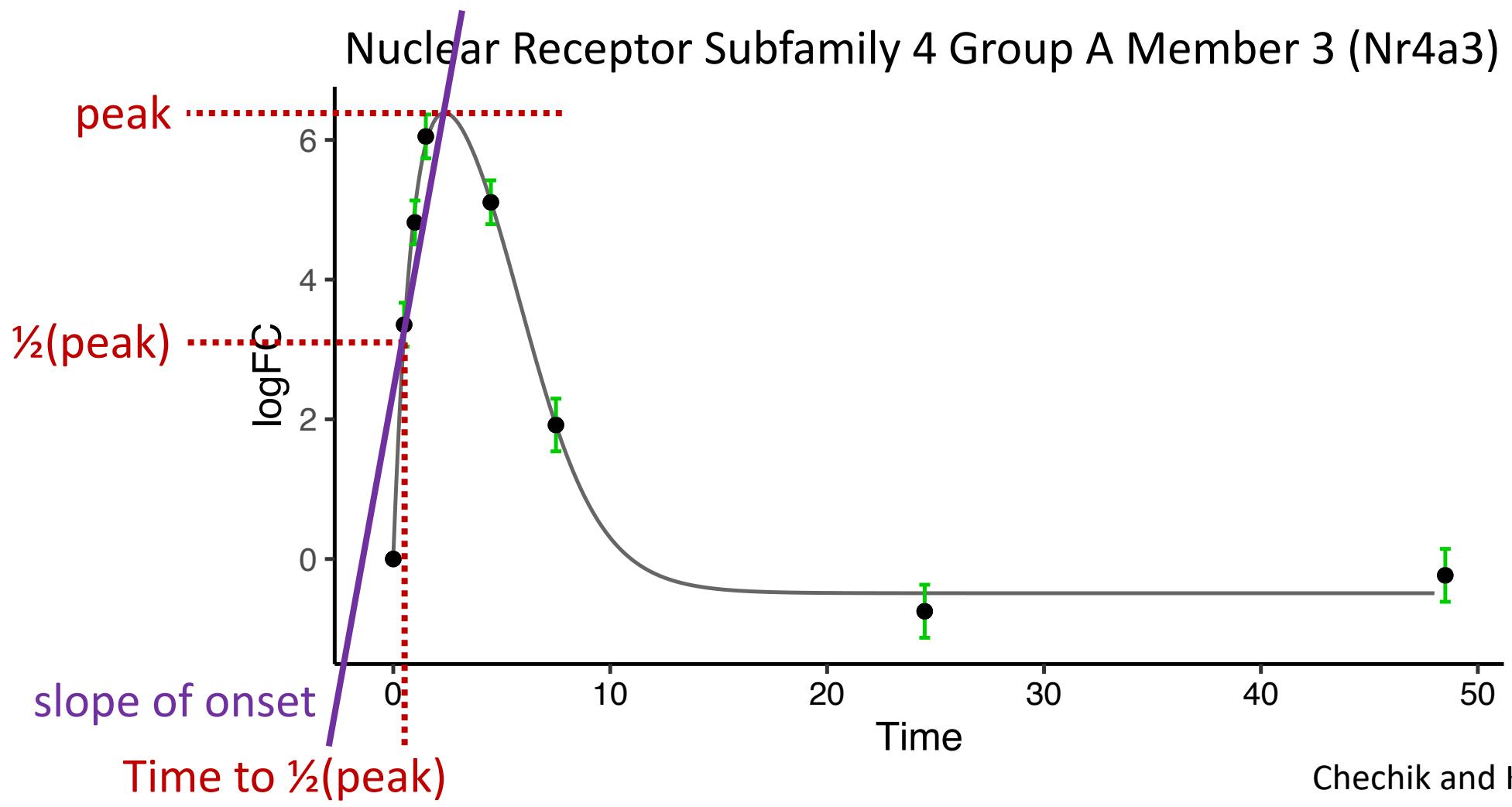
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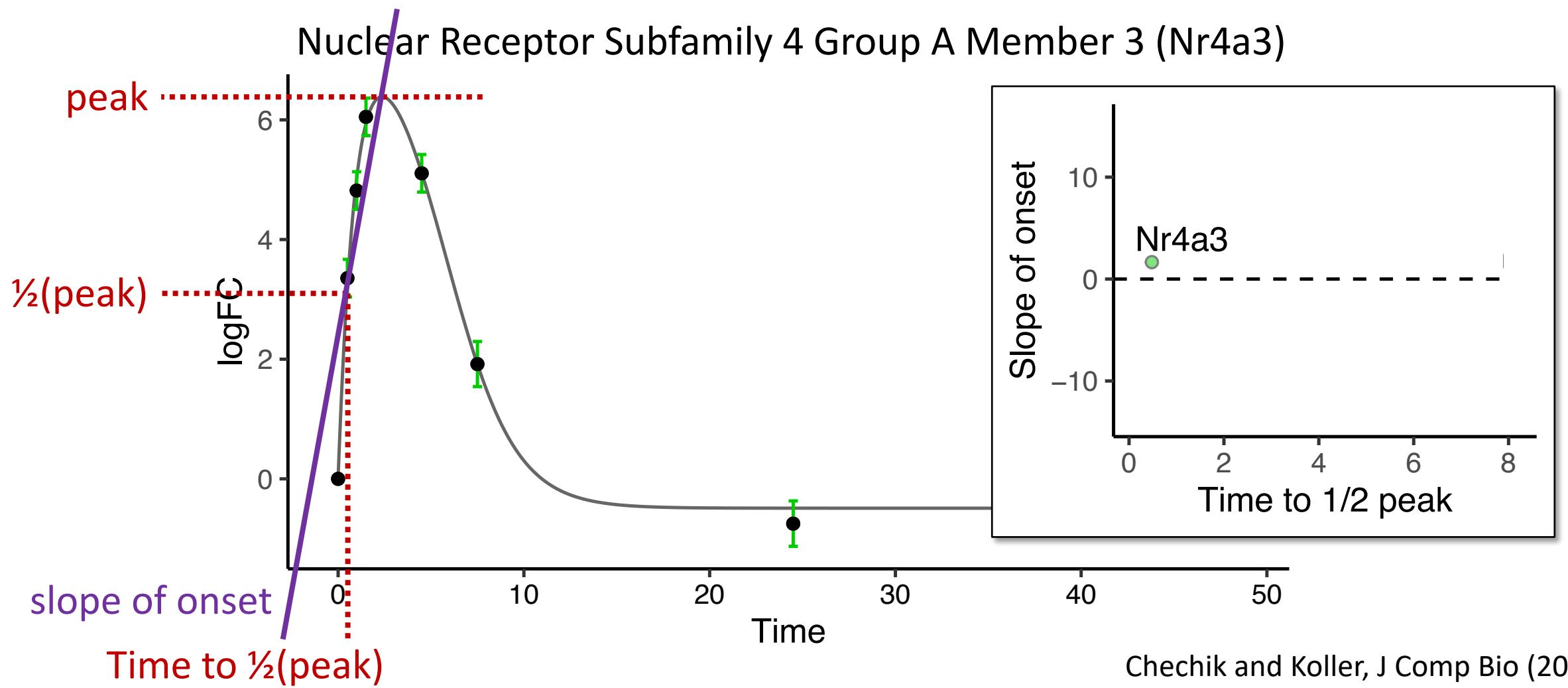
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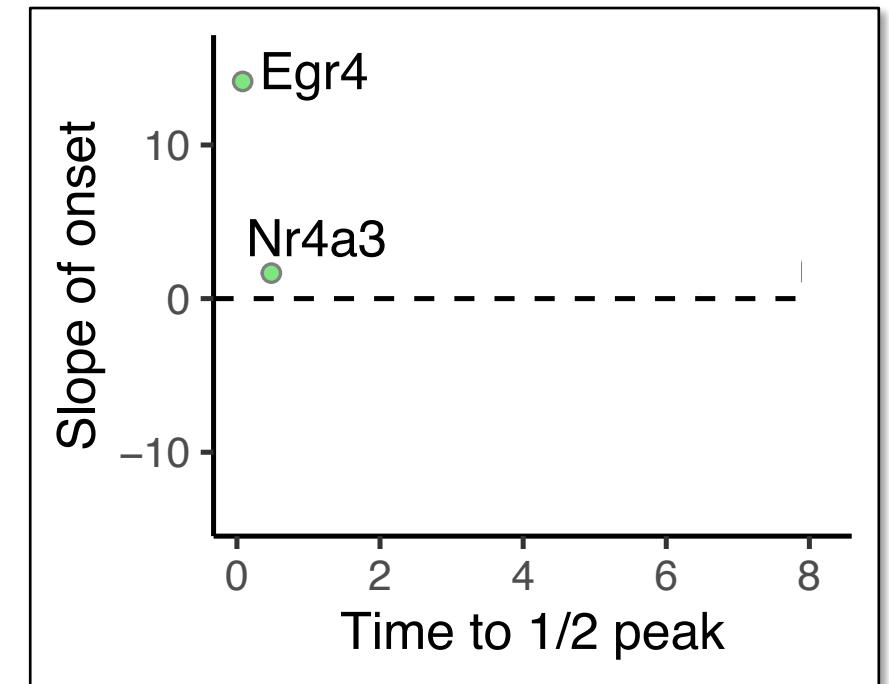
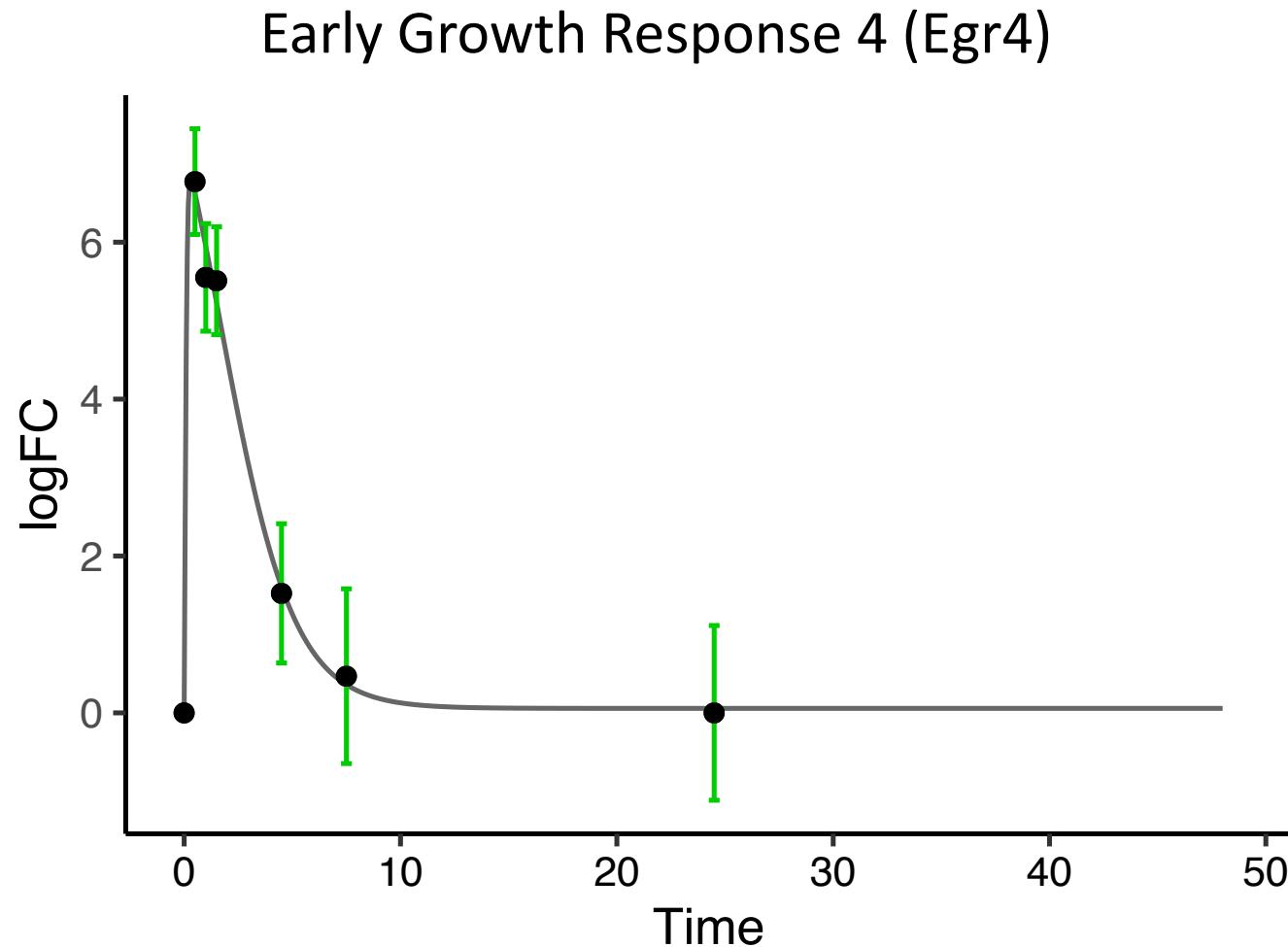


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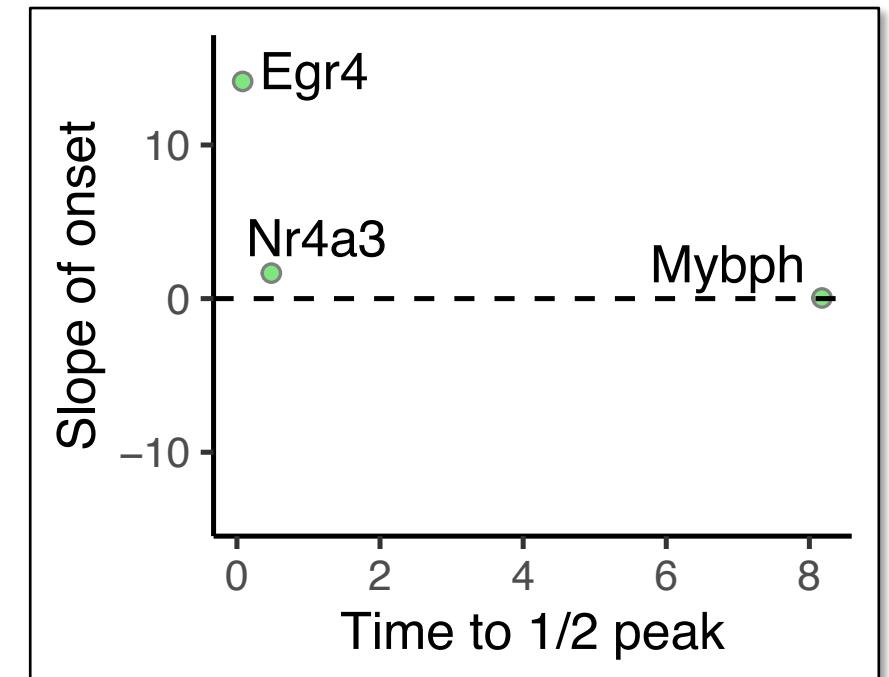
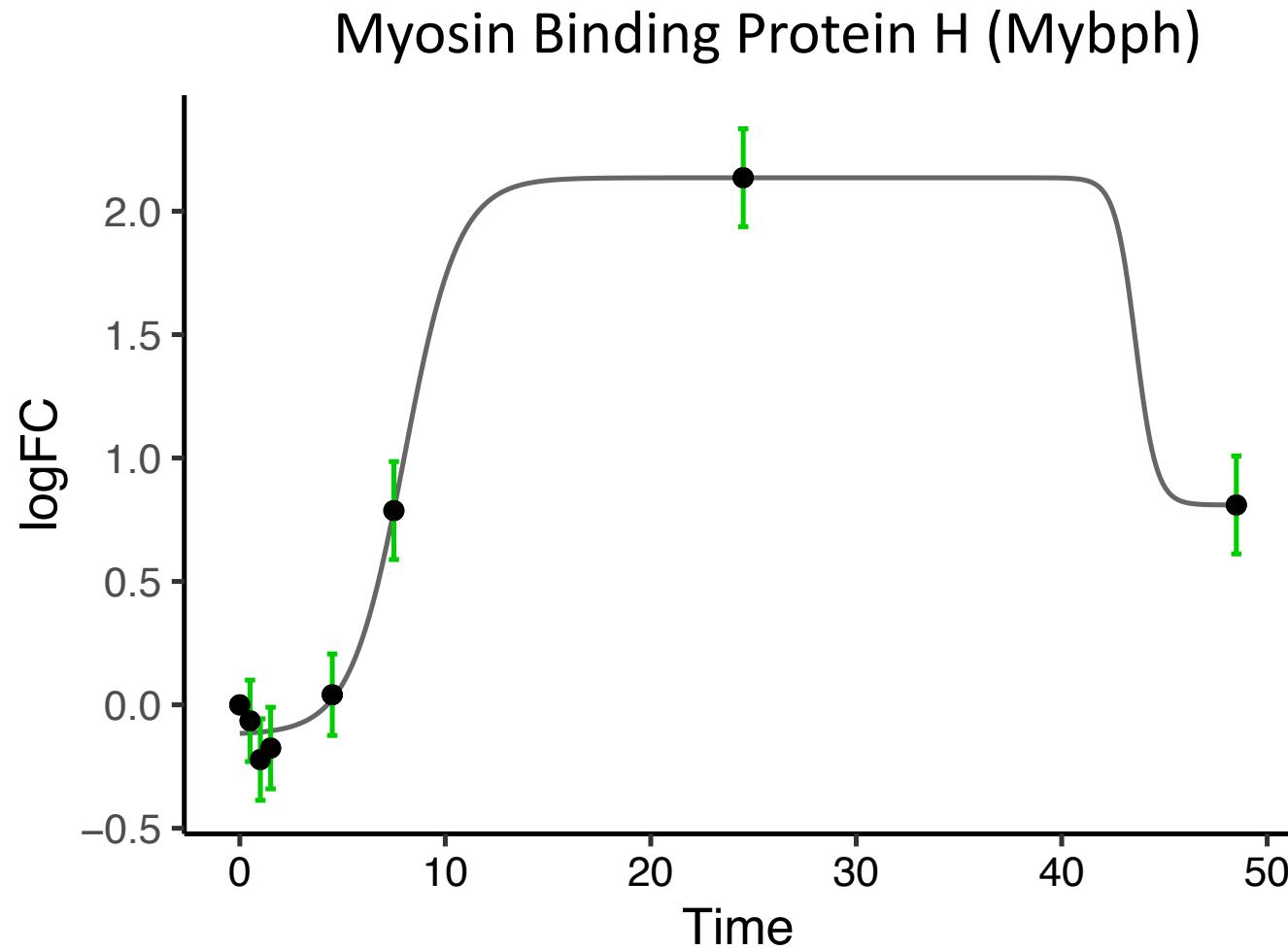


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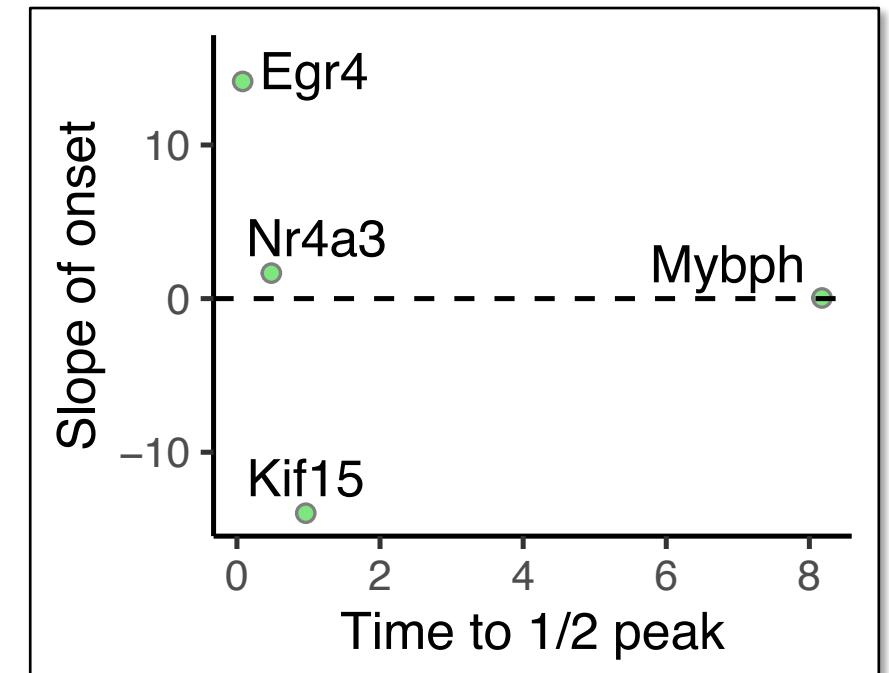
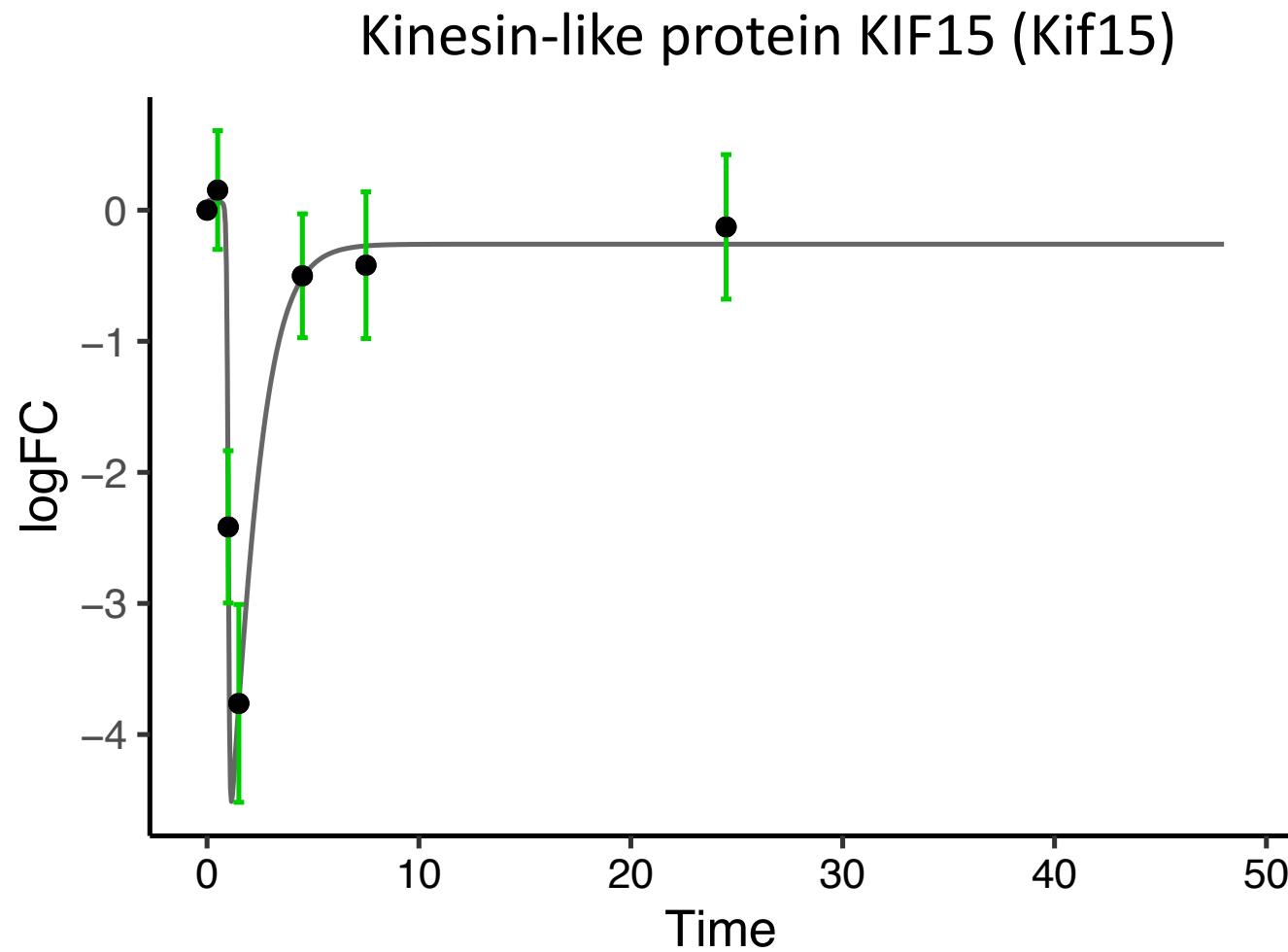
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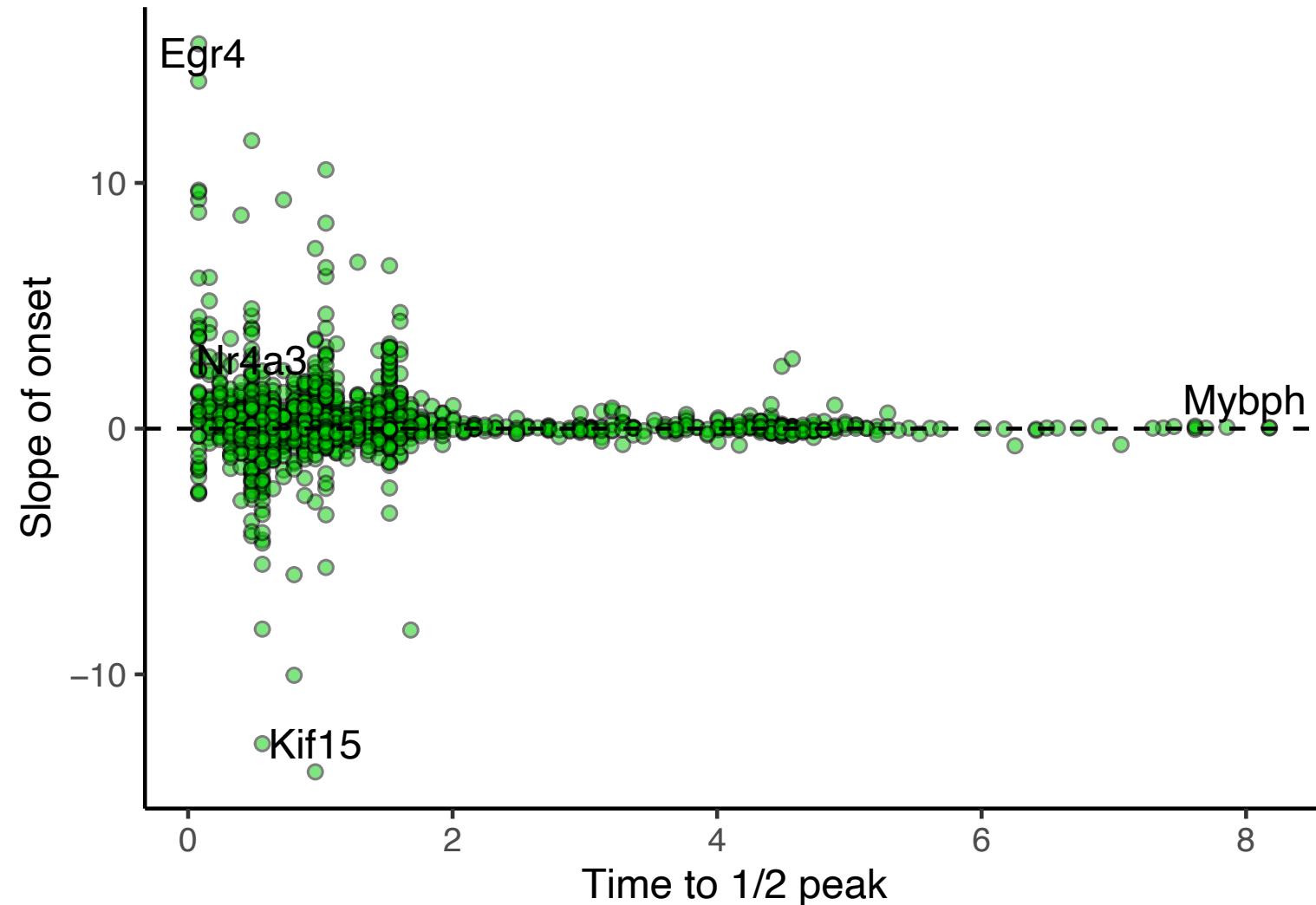
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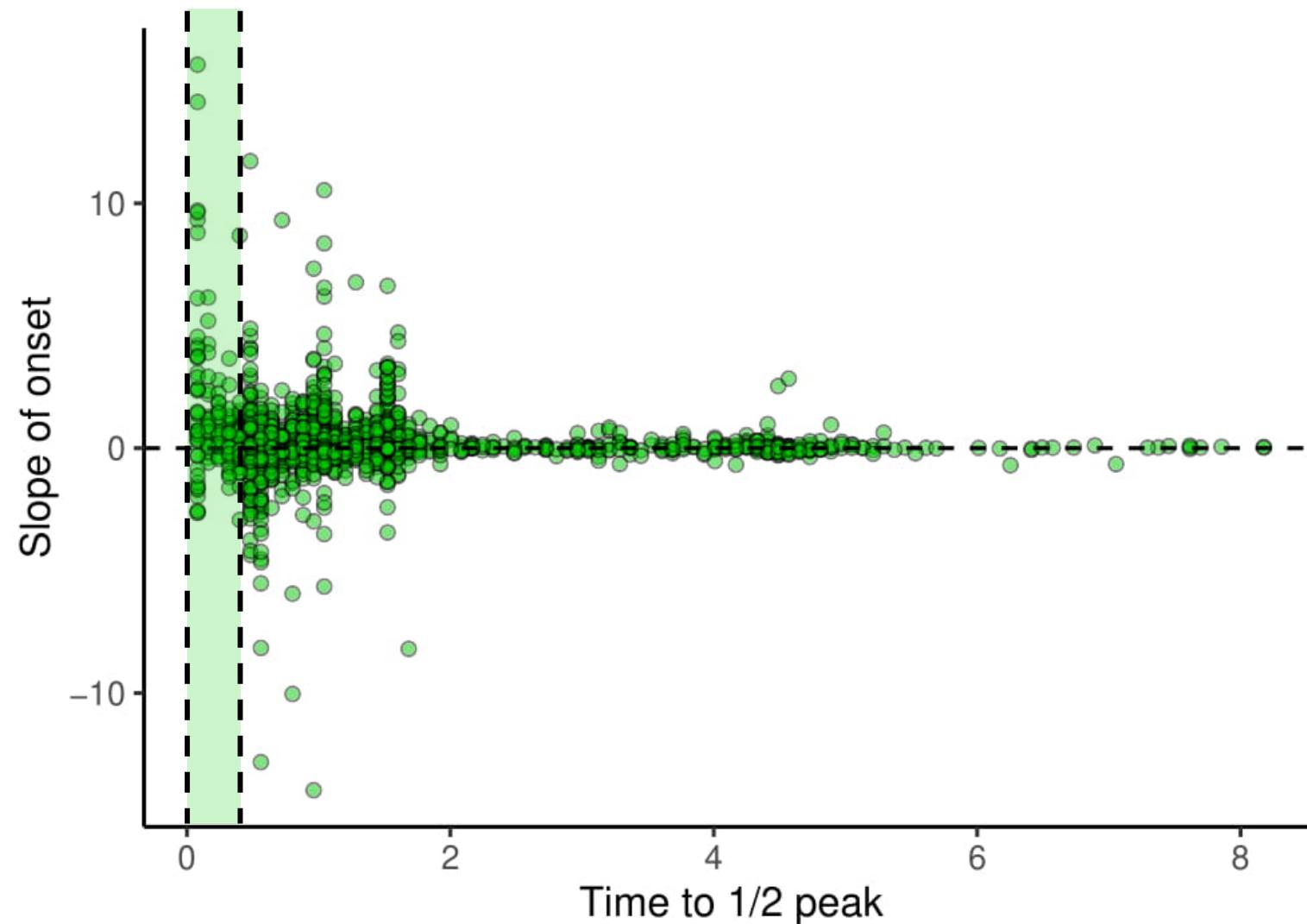


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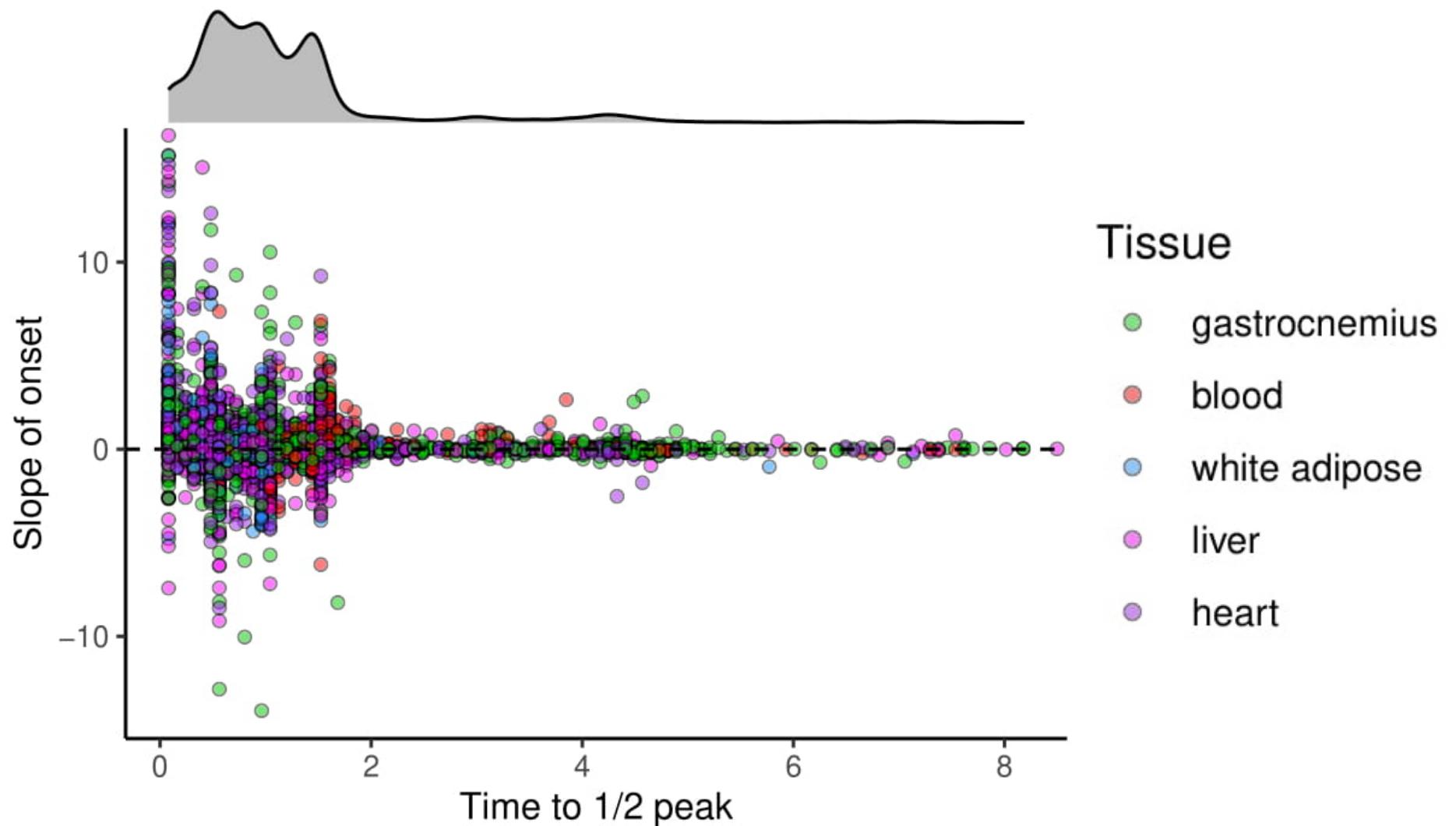
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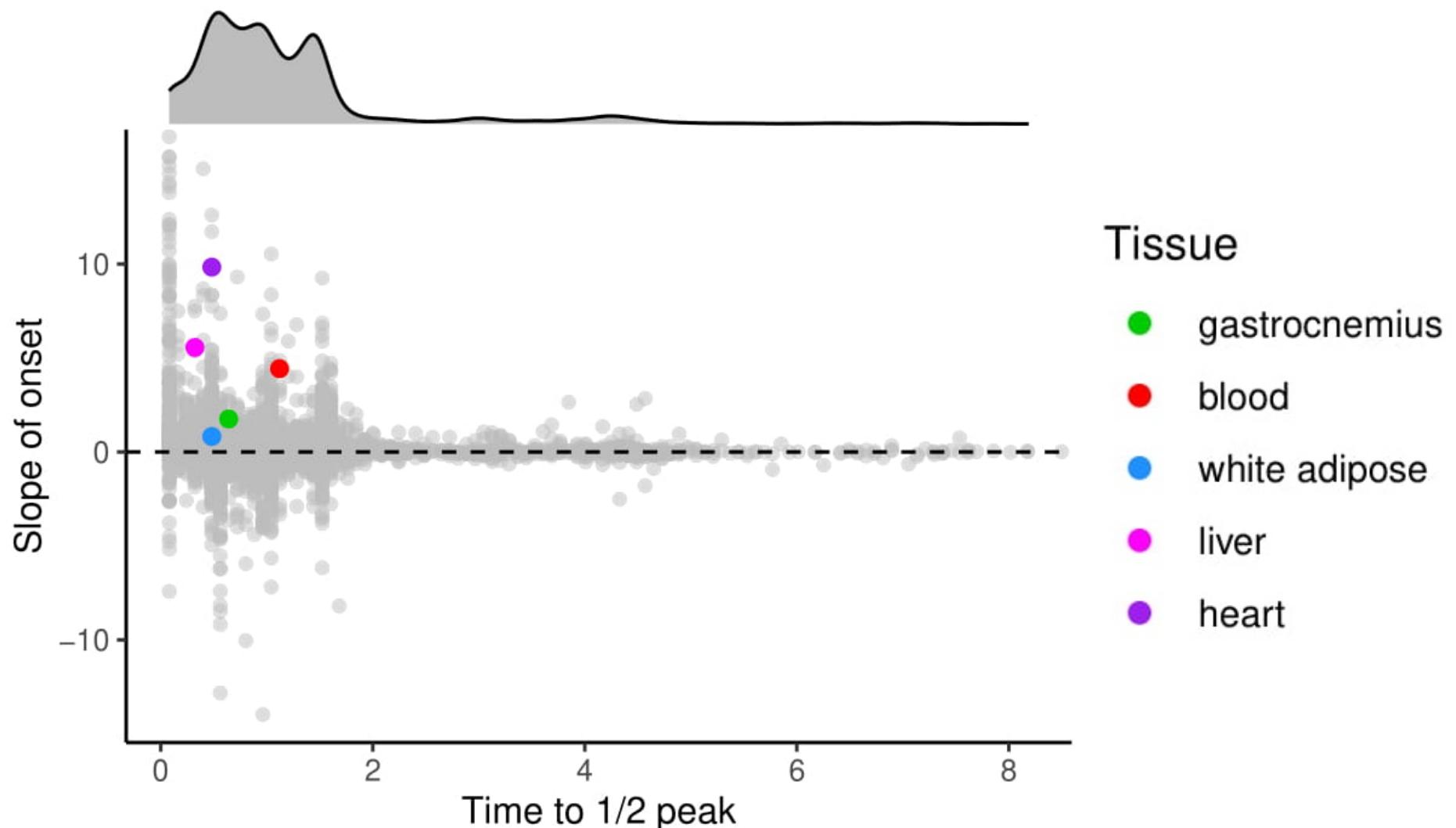
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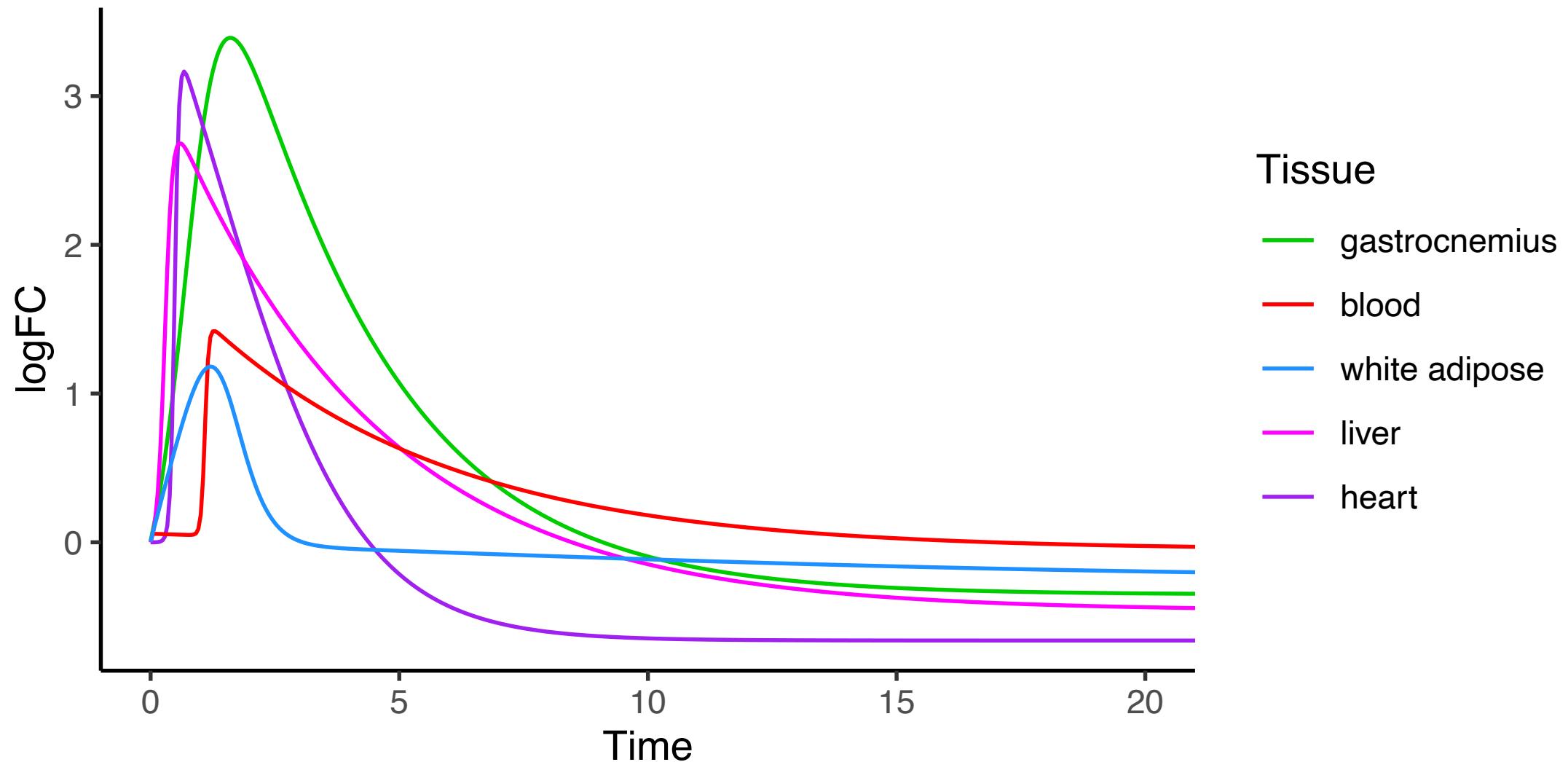
Similar analyses can be done with results across all tissues



Now it becomes easier to look at phase shifts across tissues
Example: Insulin Receptor Substrate 2 (Irs2)

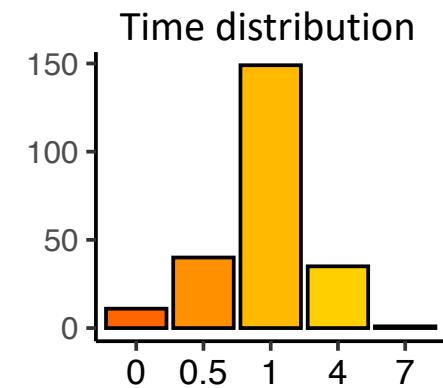


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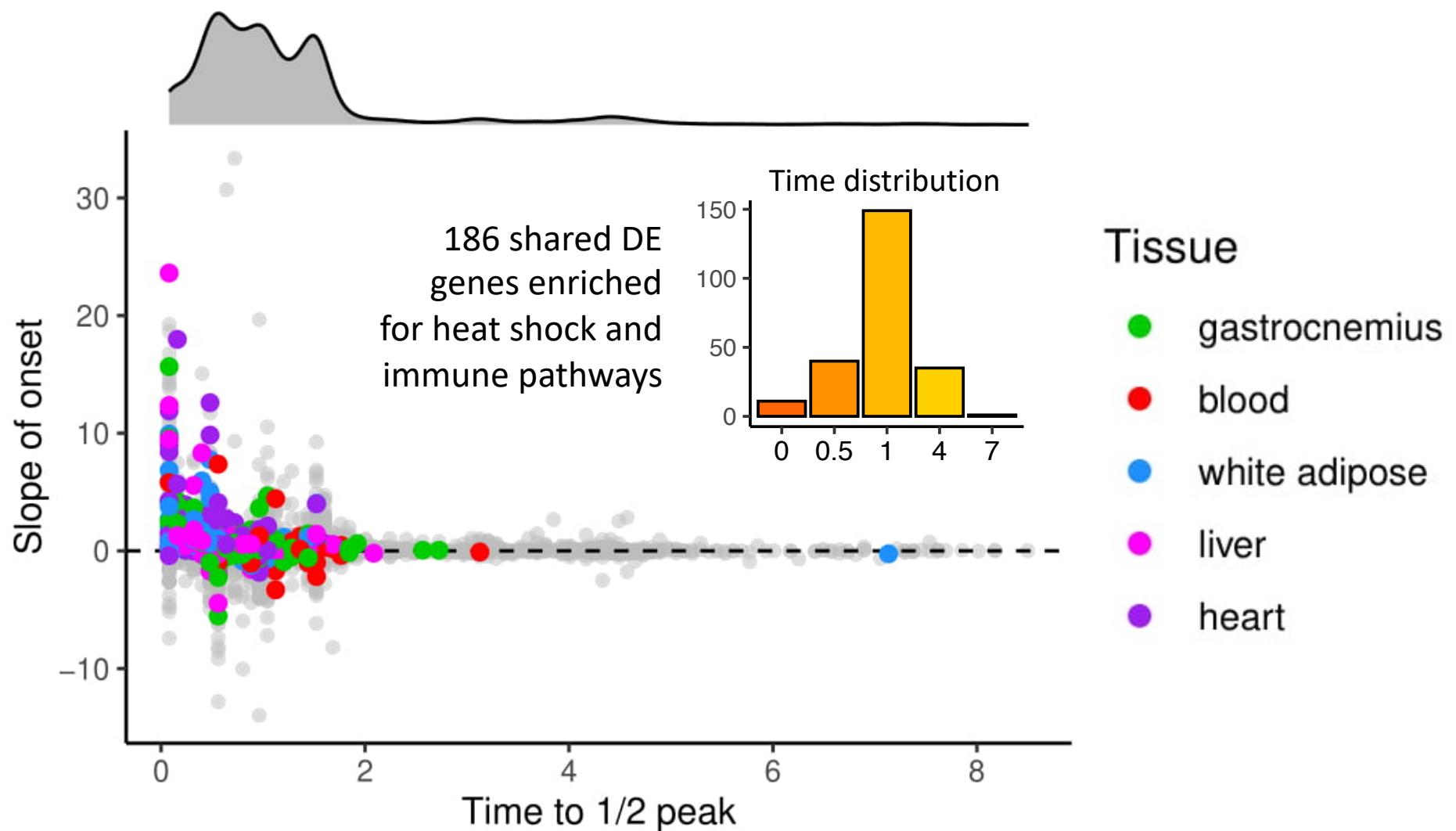


This temporal resolution is much finer than the pair-wise differential expression at each time point

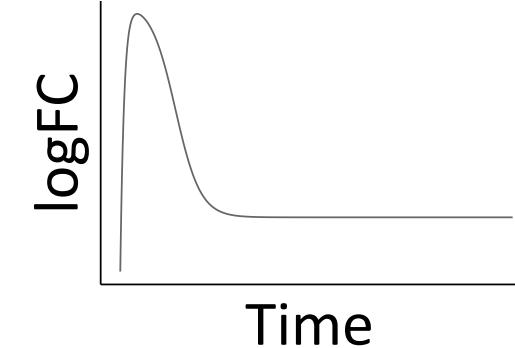
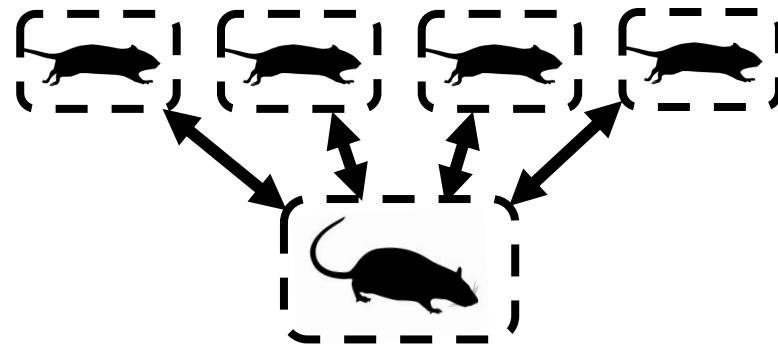
186 shared DE genes enriched for heat shock and immune pathways



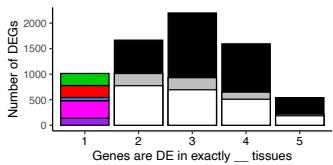
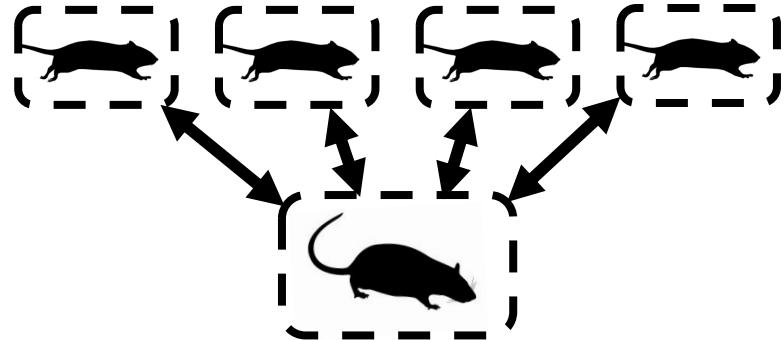
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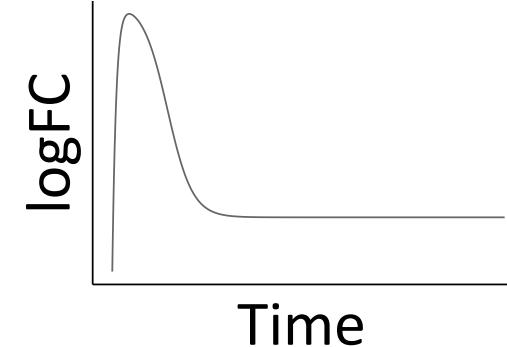
Conclusions



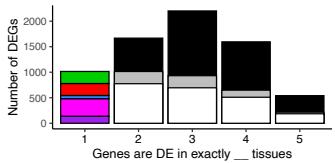
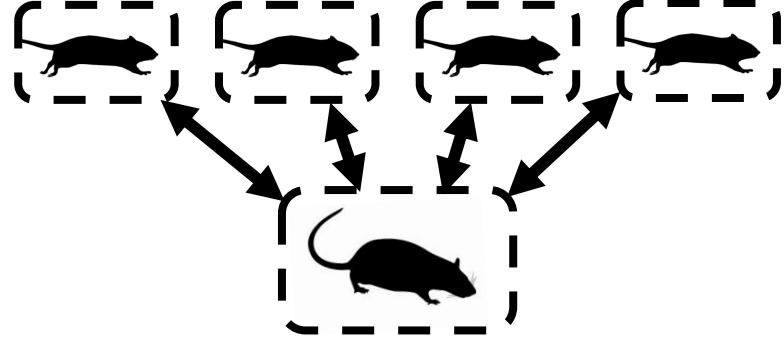
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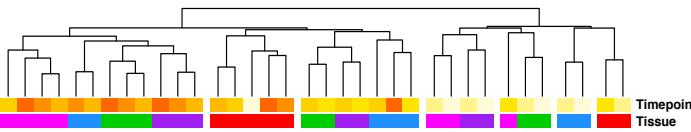
- Thousands of genes are differentially expressed due to acute endurance exercise
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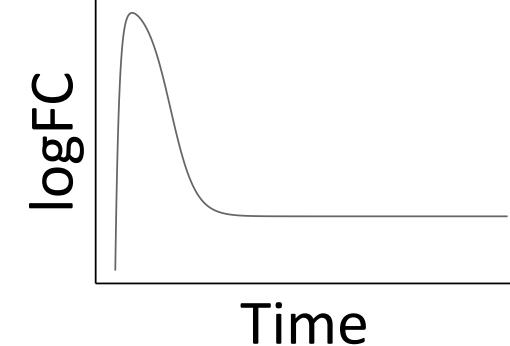
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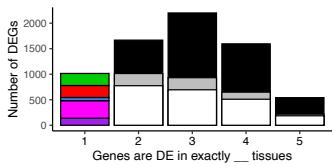
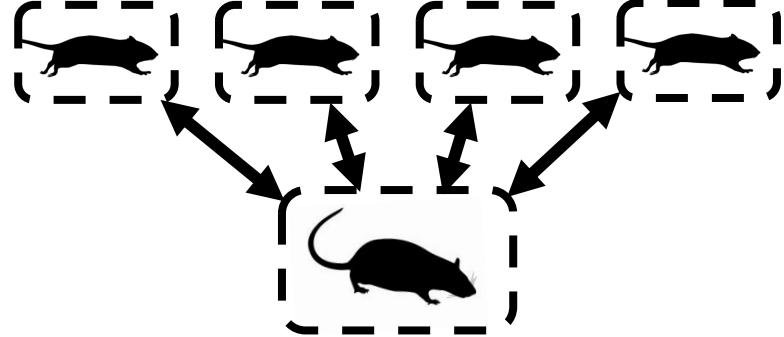
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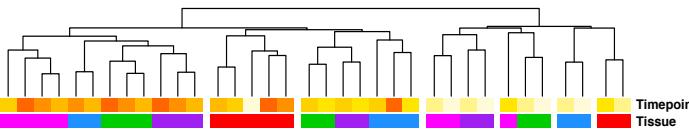
- Differential expression profiles become more tissue-specific over time
- Blood clusters away from solid tissues



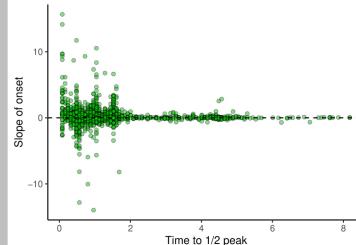
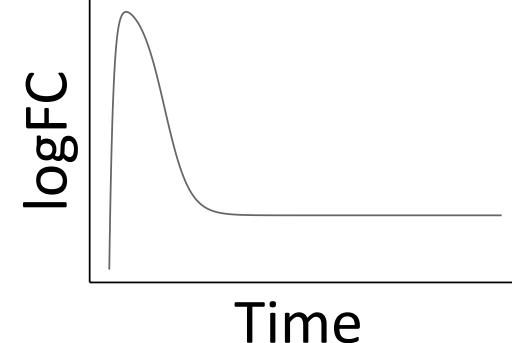
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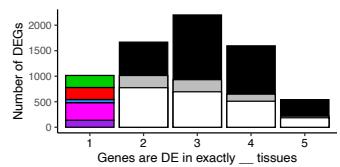


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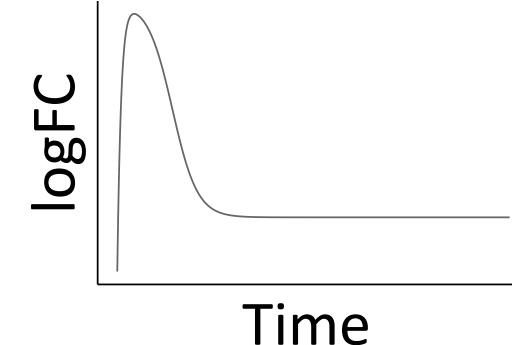
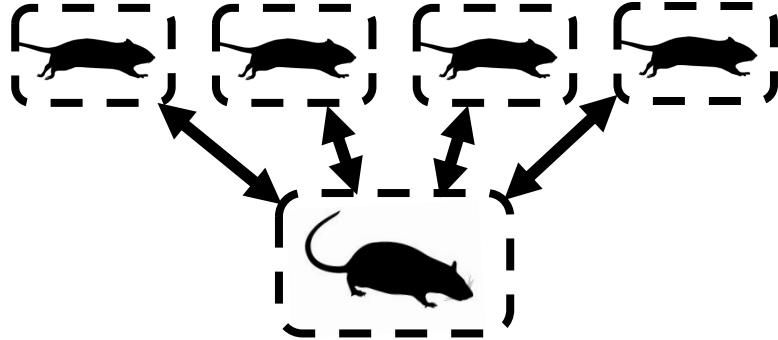


- Impulse model provides biologically meaningful and interpretable parameters for individual gene expression profiles

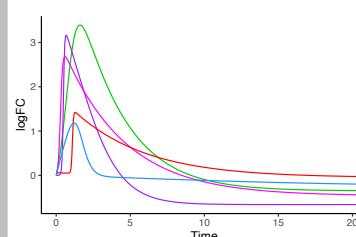
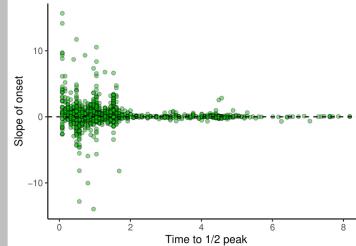
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Time



- Impulse model provides biologically meaningful and interpretable parameters for individual gene expression profiles
- Impulse model provides much finer temporal resolution than the pairwise DE analysis alone

Acknowledgements

Genomics, Epigenomics, and Transcriptomics



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*Stuart Sealfon

*Martin Walsh

Yongchao Ge

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Yifei Sun

Elena Zaslavsky



*Michael P. Snyder
*Stephen Montgomery
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Laure Frésard
Chia Jiu Hung
Kevin Smith
Navid Zebarjadi
Bingqing Zhao

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*Matthew Wheeler Jimmy Zhen

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Karen Dalton Archana Raja

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*Mike Miller Cindy Stowe

Delilah R. Cook

*=PI

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Olivia de Goede
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Matt Durrant
Tiffany Eulalio
Nicole Ferraro
Mike Gloudemans
Pagé Goddard

Emily Greenwald
Daniel Nachun
Abhiram Rao
Kameron Rodrigues
Craig Smail
Nikki Teran
Rachel Ungar



GRFP



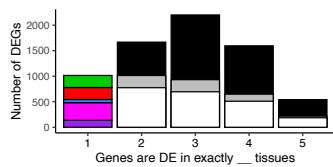
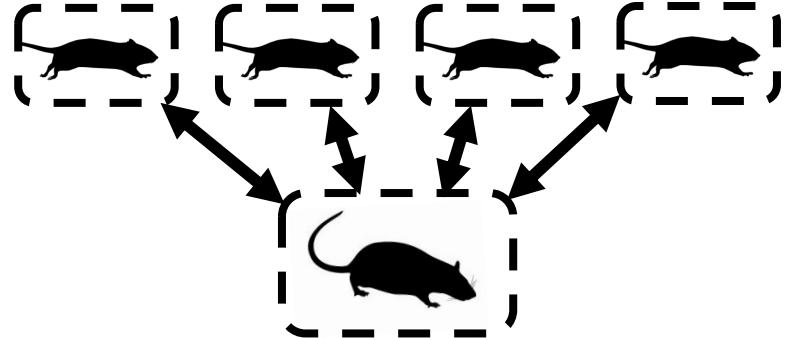
NHGRI

KEYSTONE SYMPOSIA

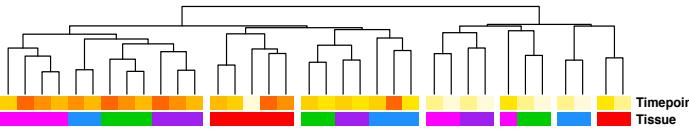
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Conclusions

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- Thousands of genes are differentially expressed due to acute endurance exercise
- Strongly shared genes are enriched for heat shock and immune pathways



- Differential expression profiles become more tissue-specific over time
- Blood clusters away from solid tissues

