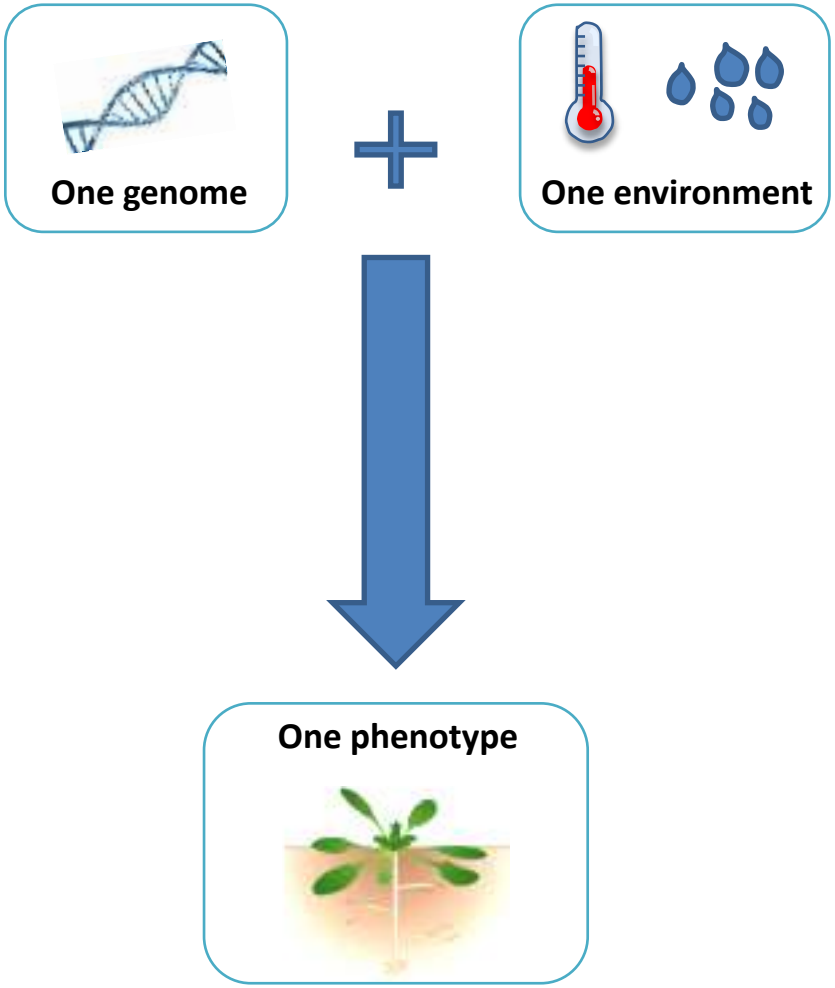
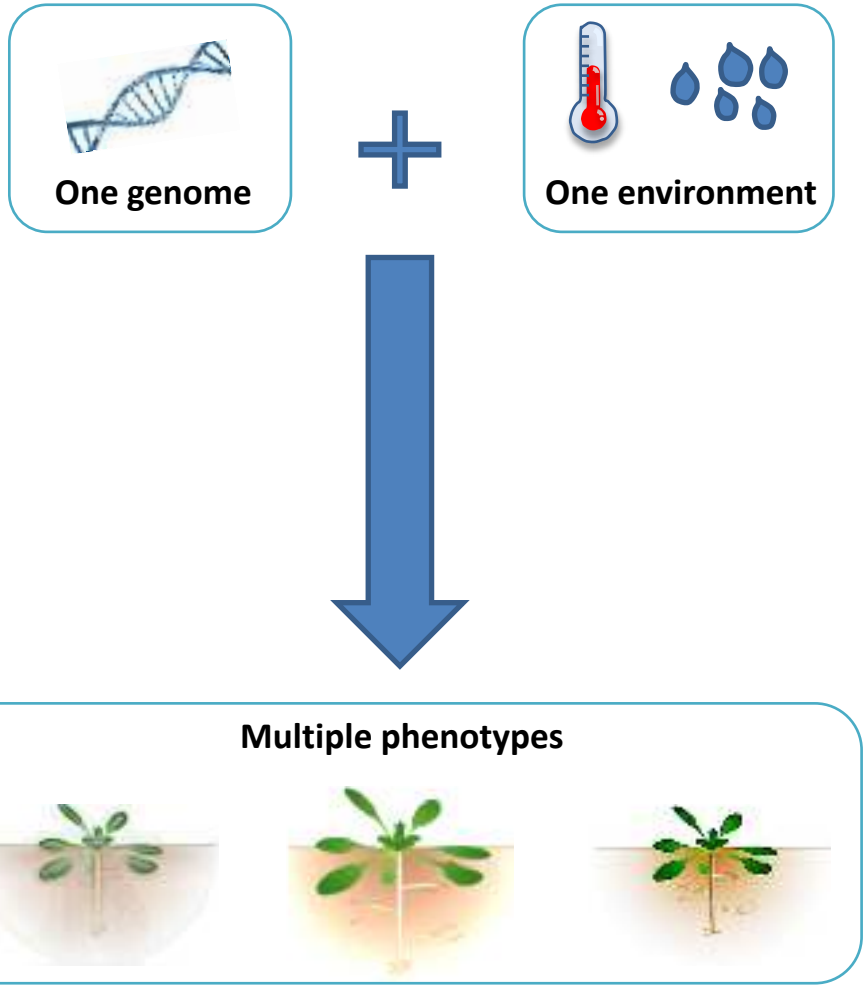
The same, yet different – Variability between genetically identical plants

Sandra Cortijo
Antoine Martin's group, BPMP (Montpellier)

Netbio– 20/09/2020


One genome
One environment
One phenotype

Phenotypic variability between genetically identical plants



What is transcriptional and phenotypic variability?

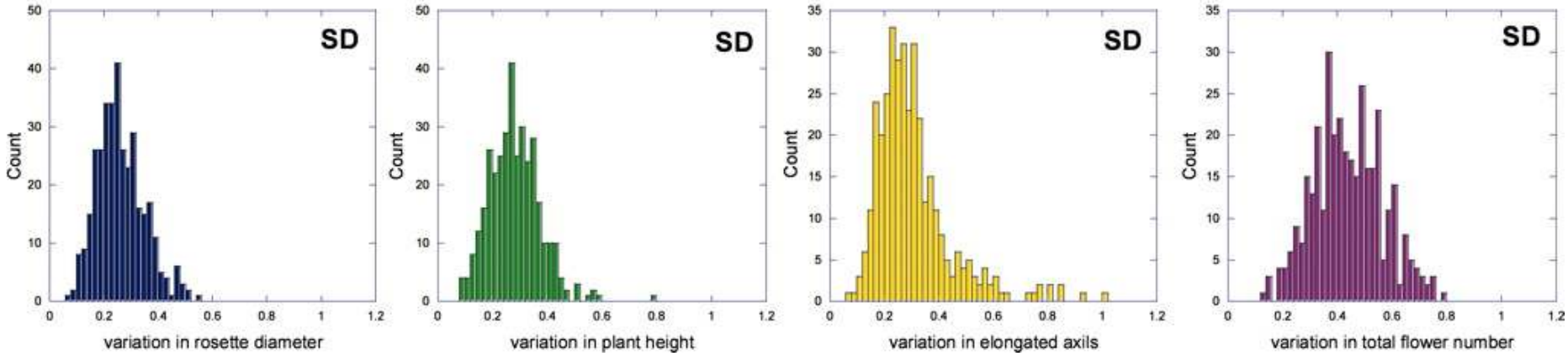
-> Differences between **genetically identical plants** that are in **the same environment**

NOT THE SAME AS:
Plasticity = Response to environmental changes
Genetic variation = Differences between ecotypes or in a mutant

Phenotypic variability between genetically identical plants

Genetics of microenvironmental canalization in *Arabidopsis thaliana*

Megan C. Hall, Ian Dworkin, Mark C. Ungerer, and Michael Purugganan



Phenotypic variability between genetically identical plants

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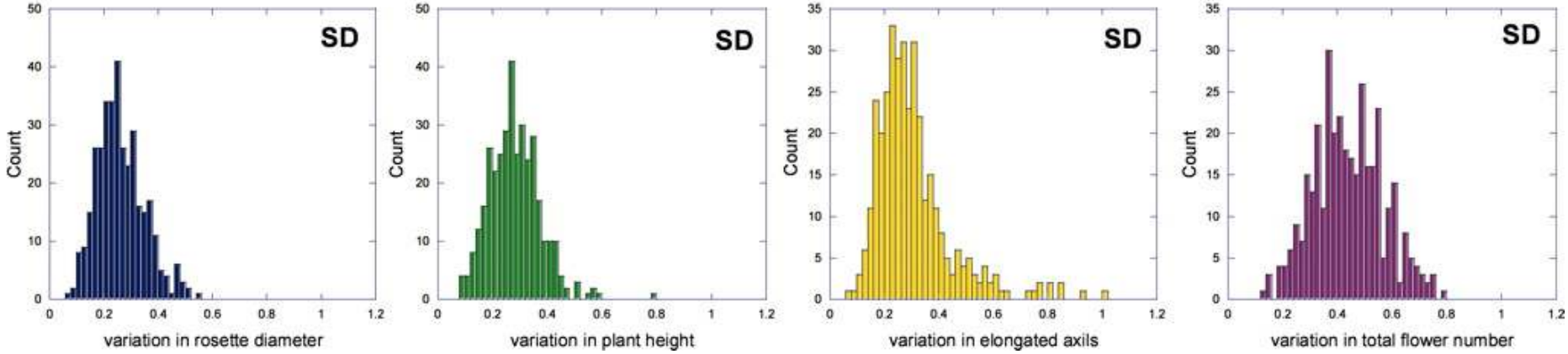
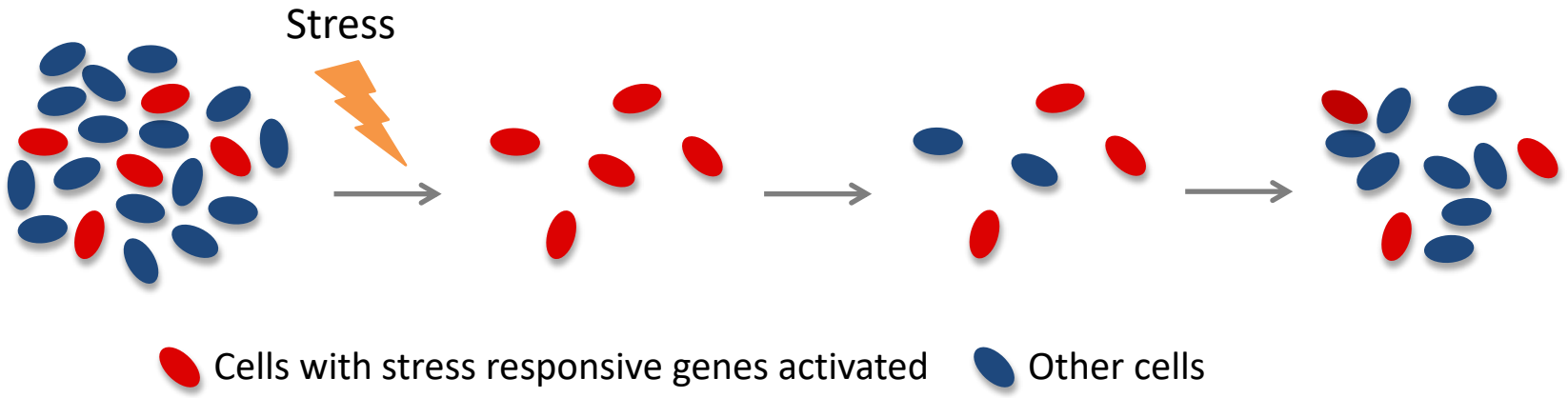


+ successfull GWAS and QTL studies :
shows **phenotypic variability is at least partly genetically controlled**

Variability between genetically identical plants could allow survival to unpredictable stress

In unicellular organisms:



Variability between genetically identical plants could allow survival to unpredictable stress

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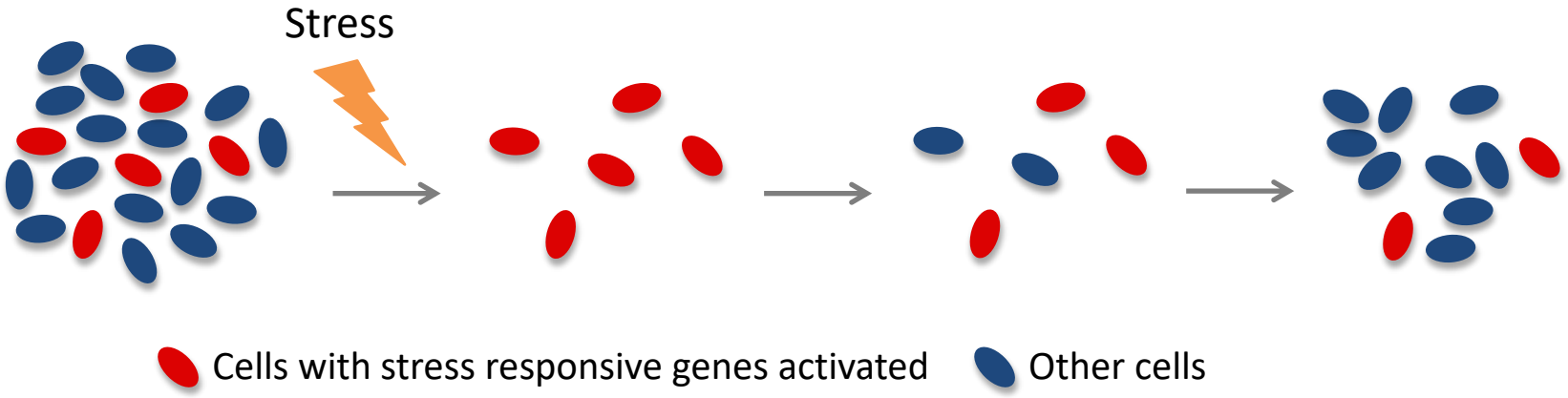
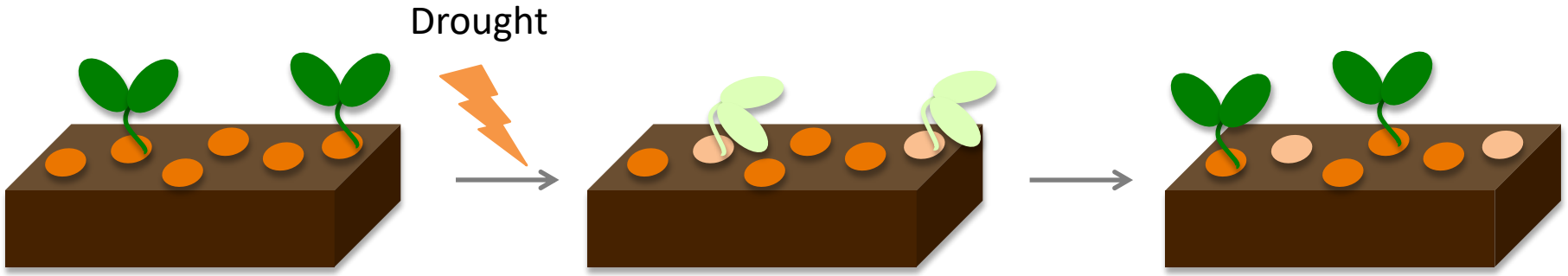
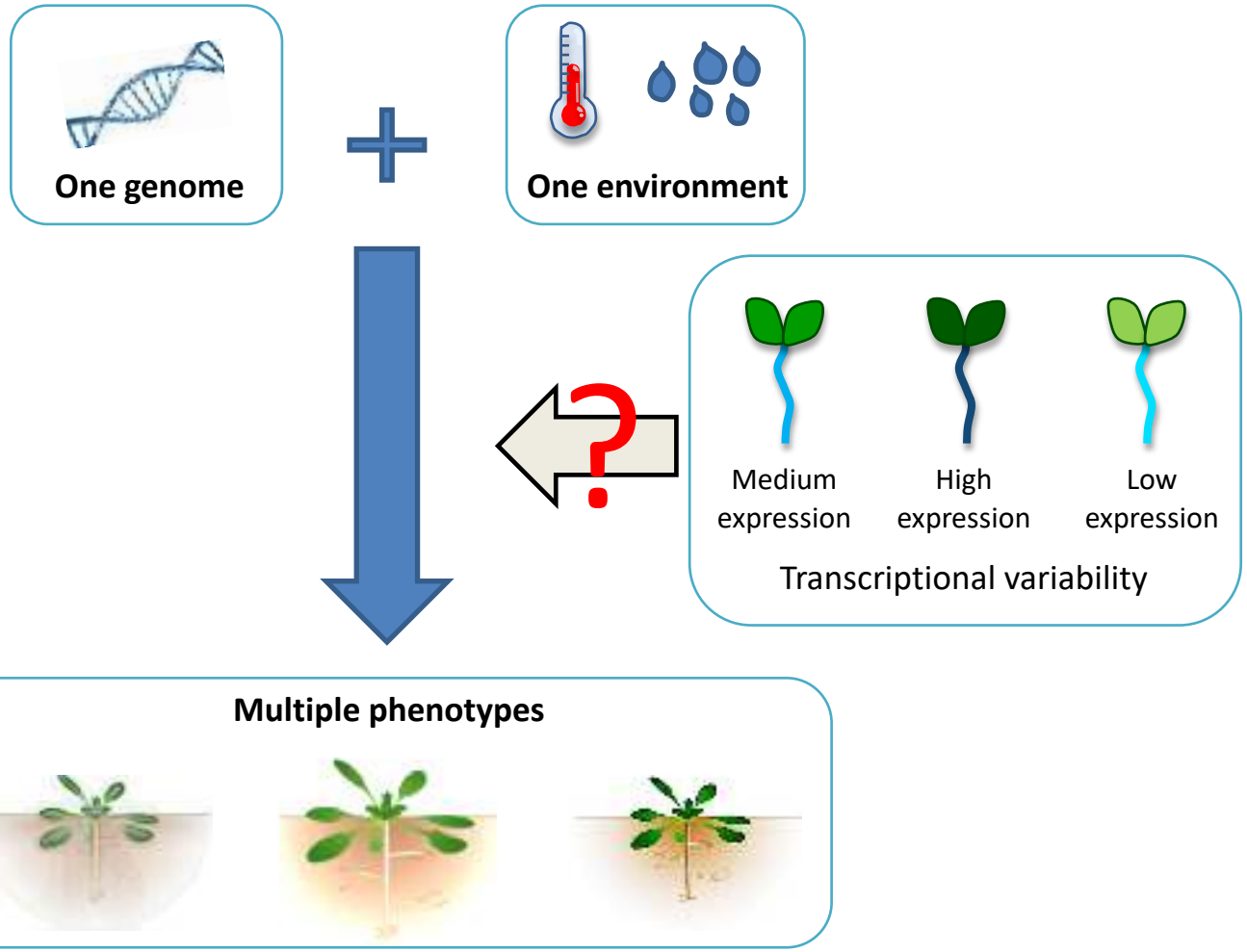


In plants:



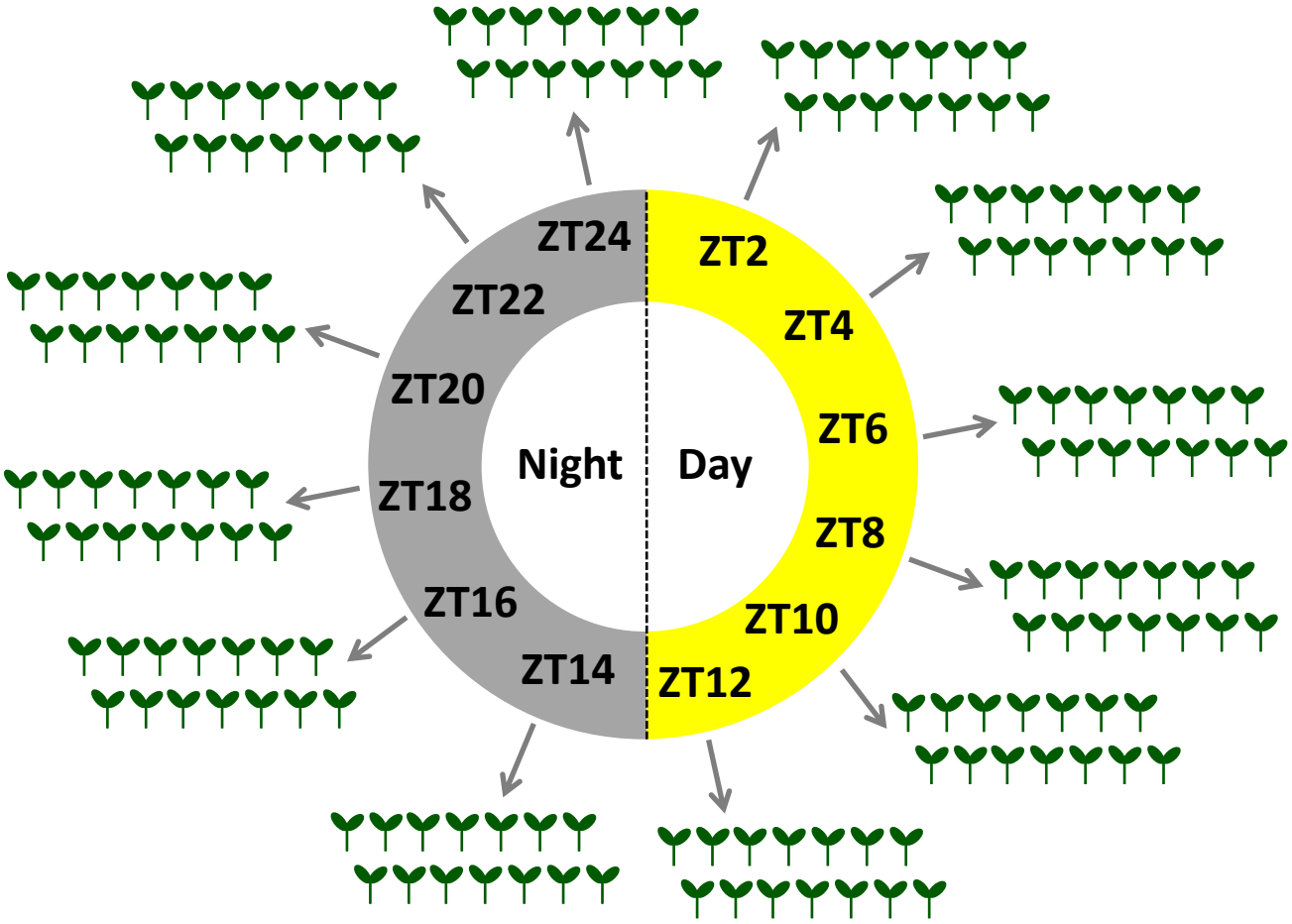
Phenotypic variability between genetically identical plants



Can we identify transcriptional variability between plants?

Is variability of gene expression changing during a day/night cycle?

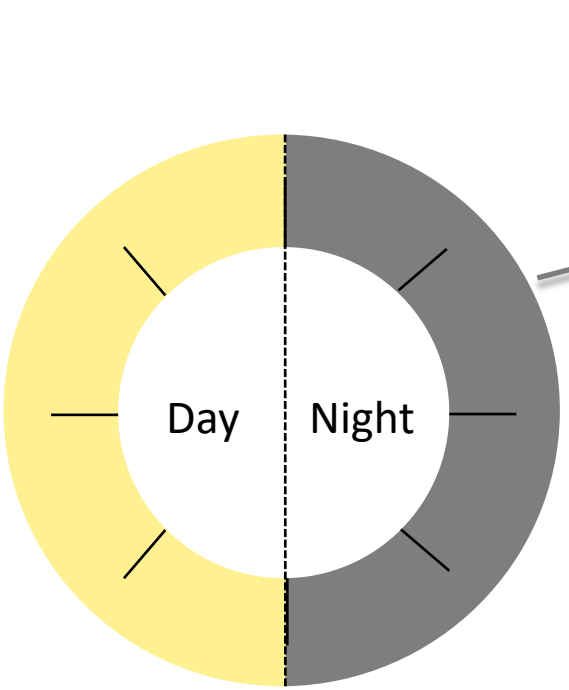
Transcriptional variability during a 24hrs cycle



RNA-seq on single seedlings

(14 seedlings per time point)

Transcriptional variability during a 24hrs cycle



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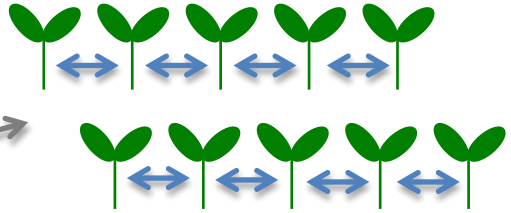
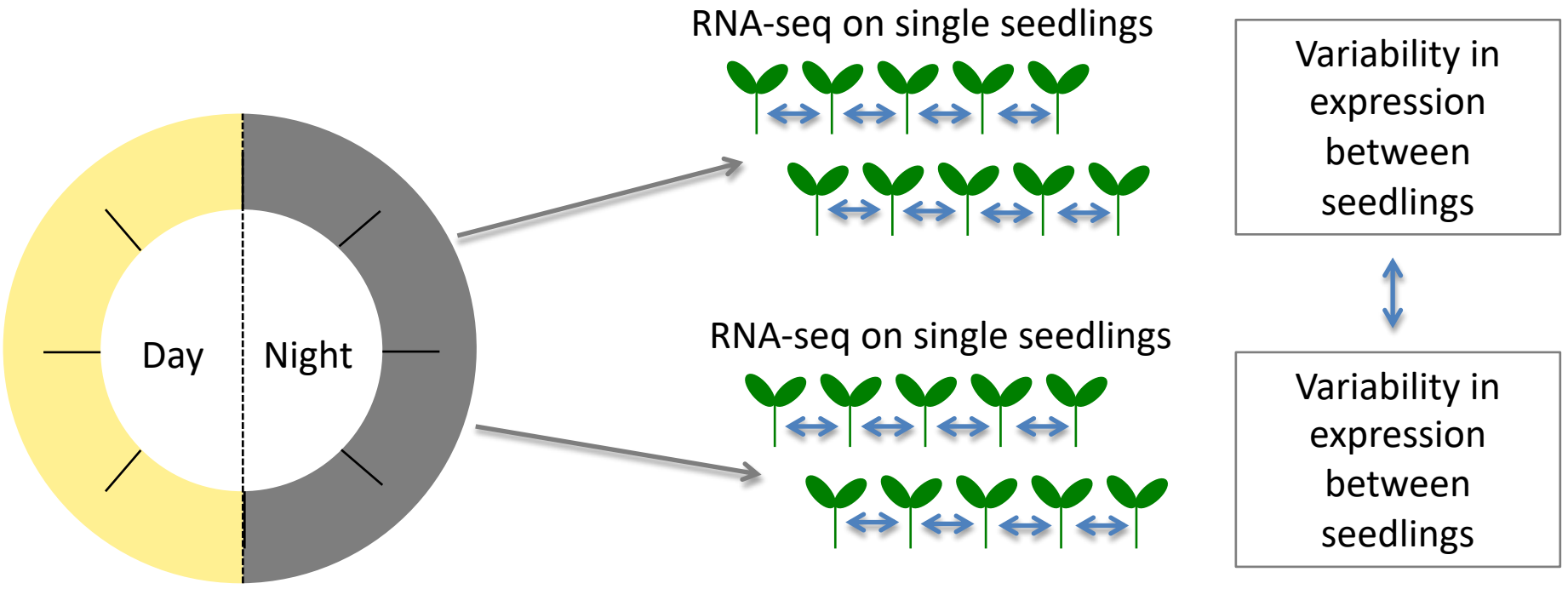
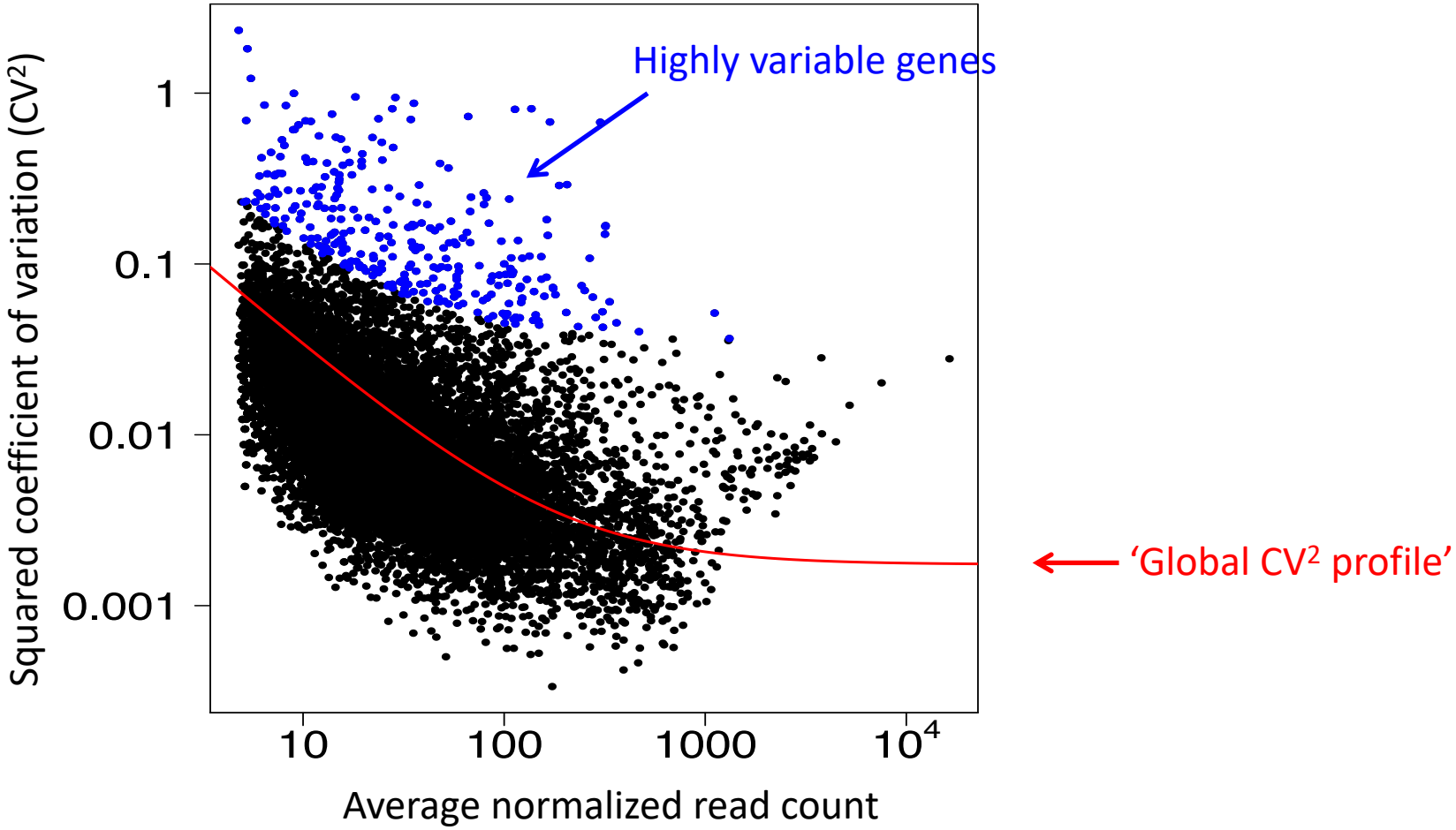


Variability in expression between seedlings

Transcriptional variability during a 24hrs cycle

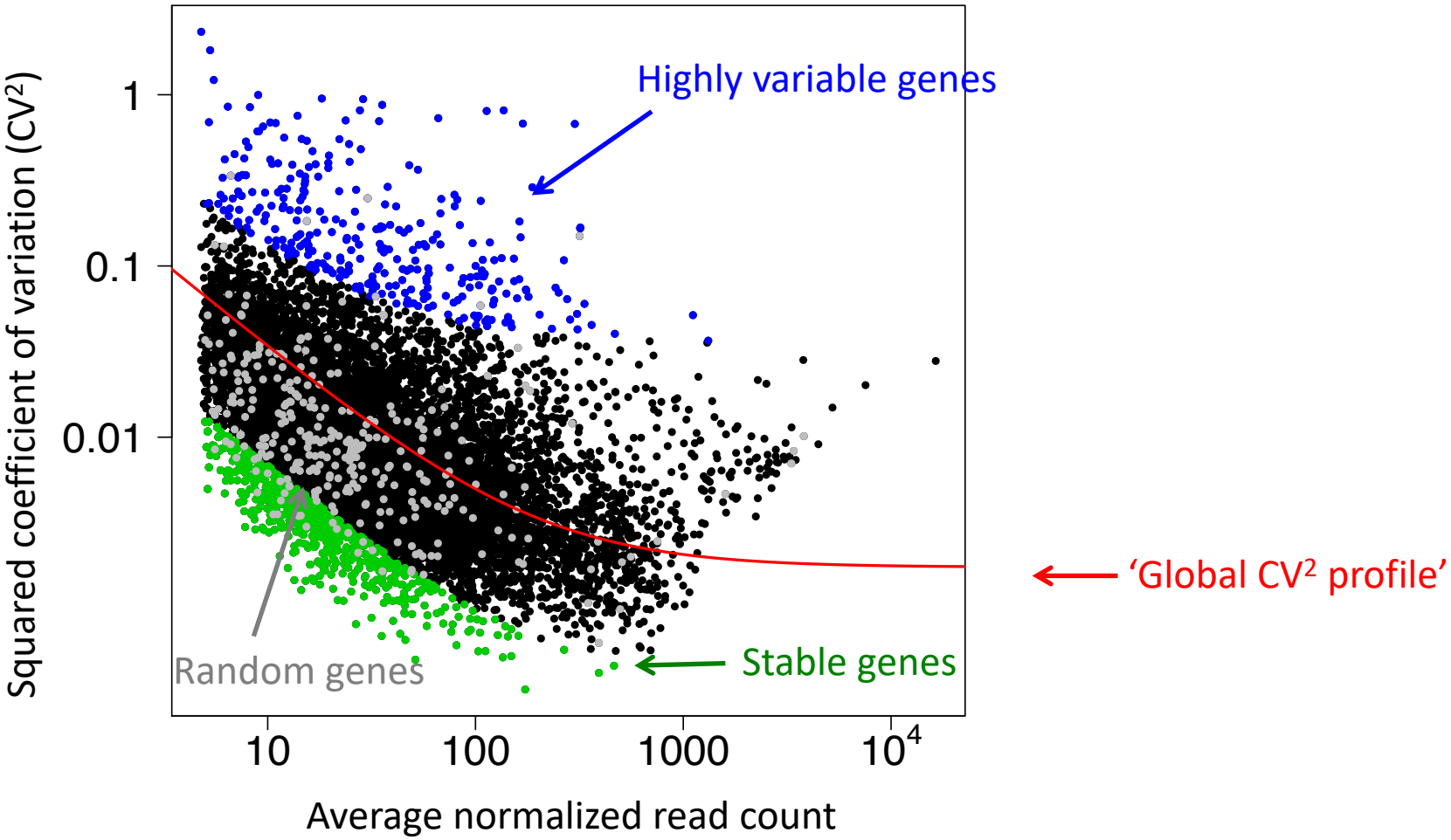


How to measure transcriptional variability?



CV^2 = variance/(average^2)

How to measure transcriptional variability?



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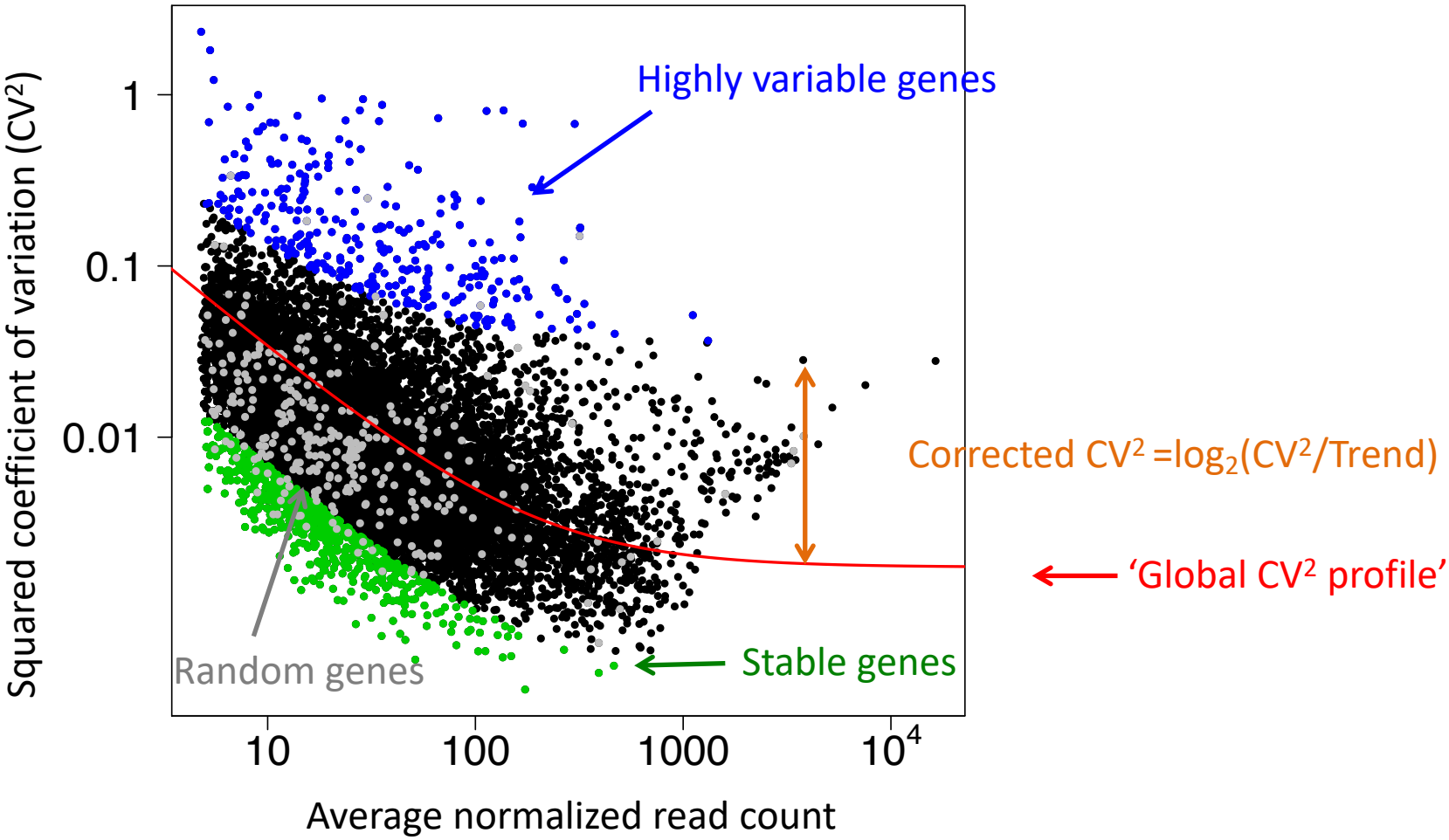
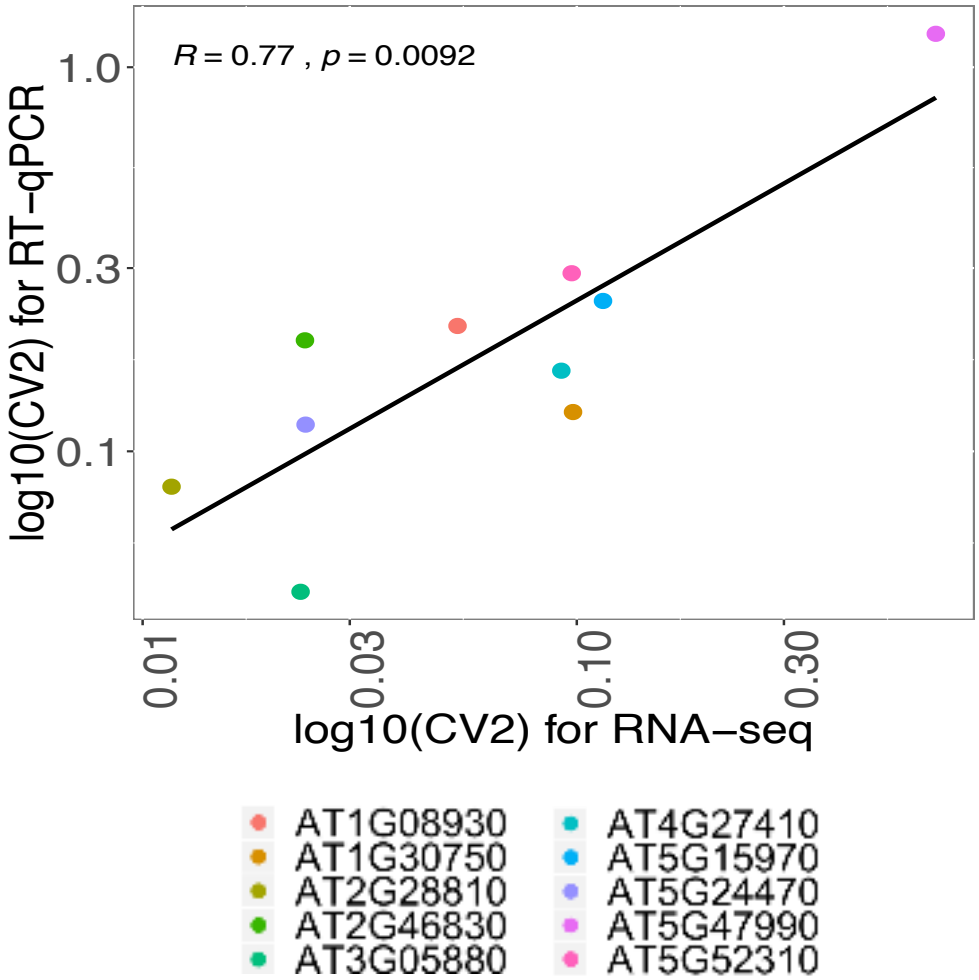
How to measure transcriptional variability?



CV^2 = variance/(average^2)

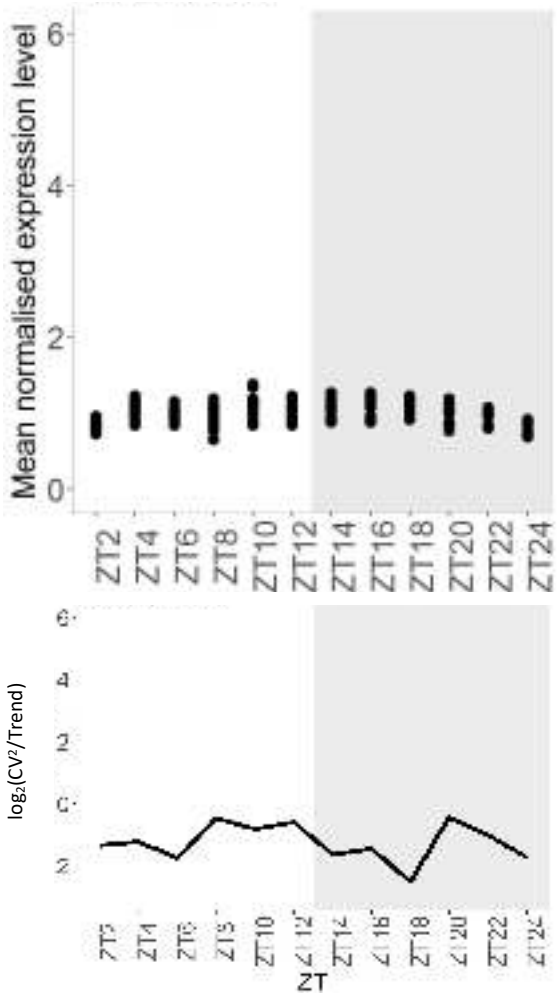
Confirming the results by RT-qPCR



Zeynep Aydin

Variability profiles during the time course

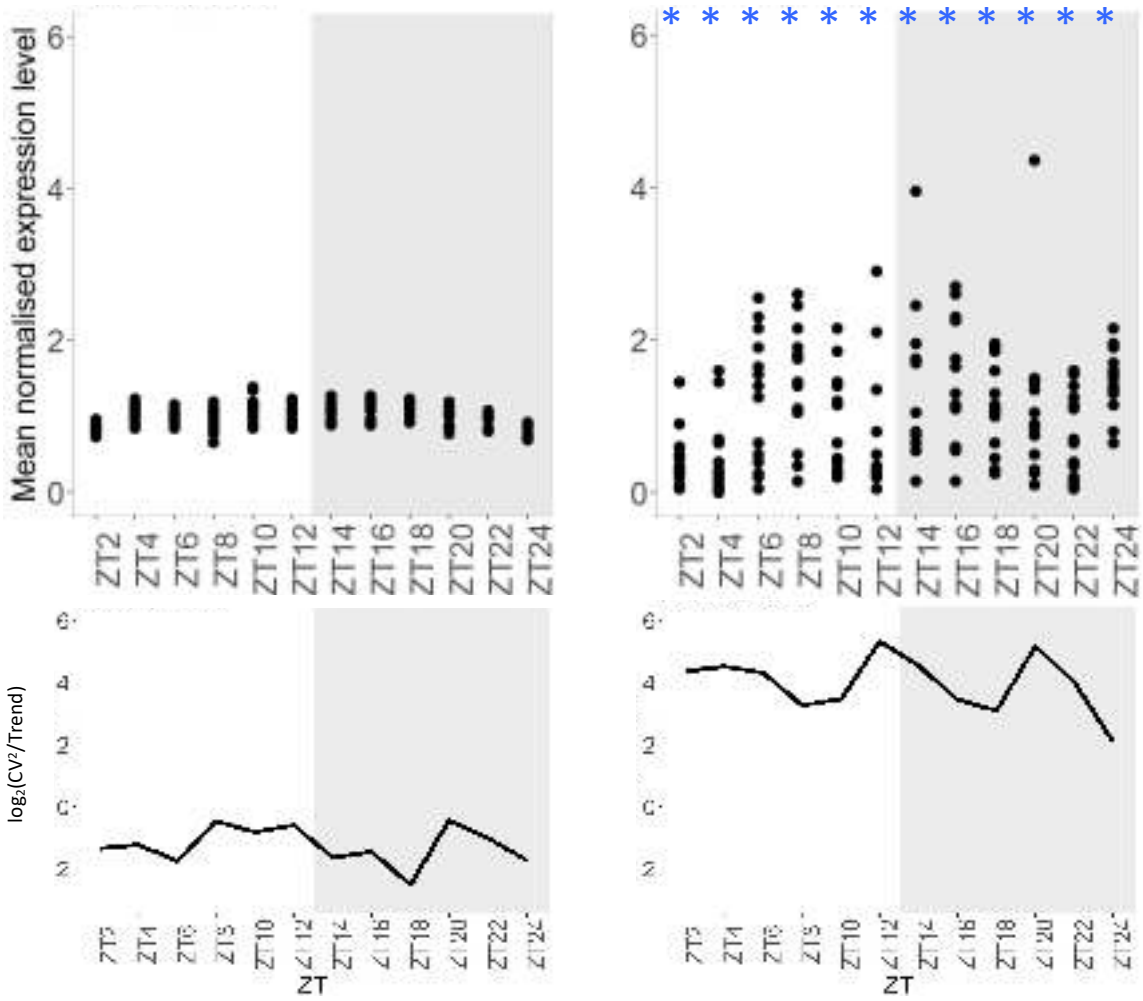
AT2G28810 (not HVG)



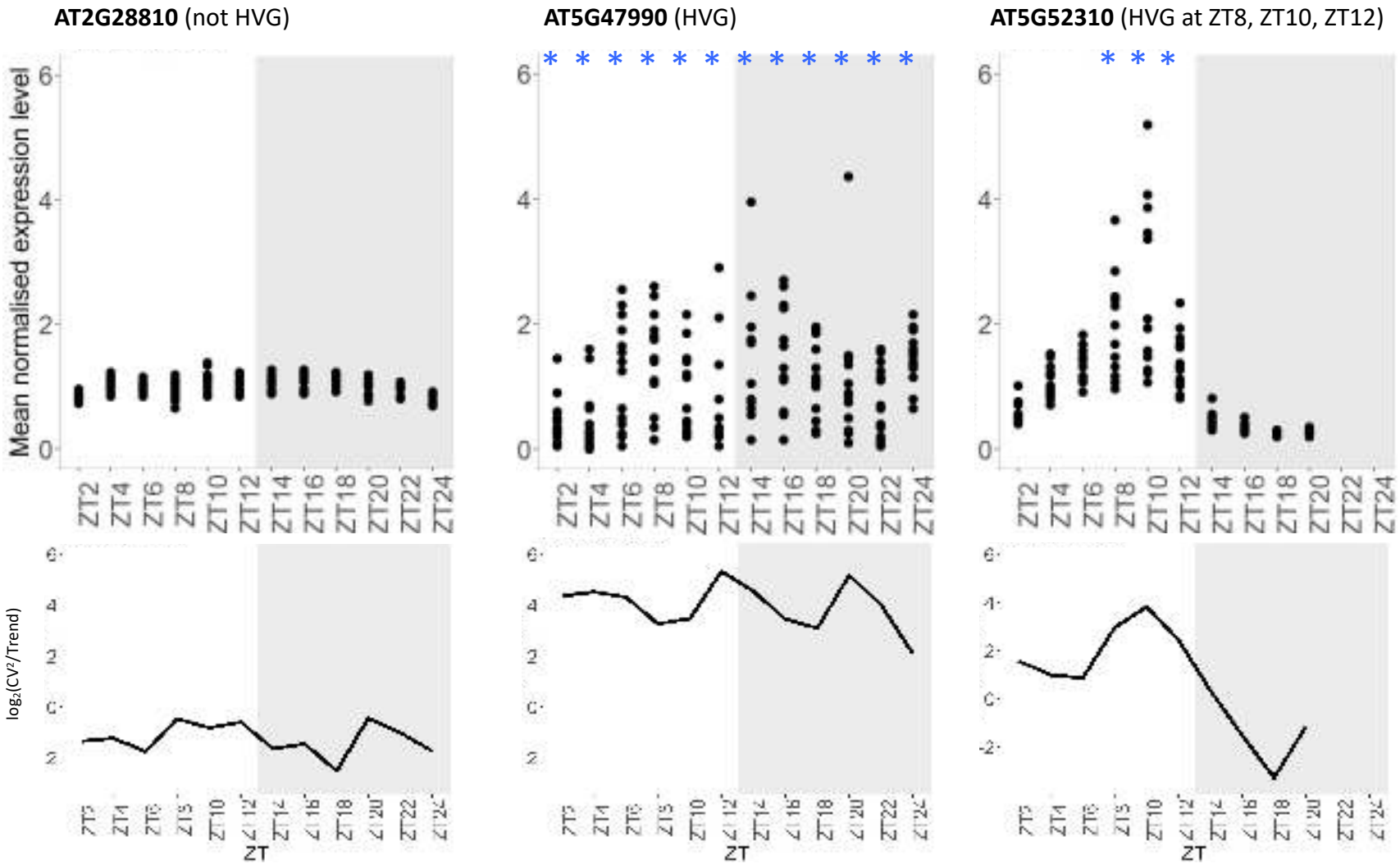
Variability profiles during the time course

AT2G28810 (not HVG)

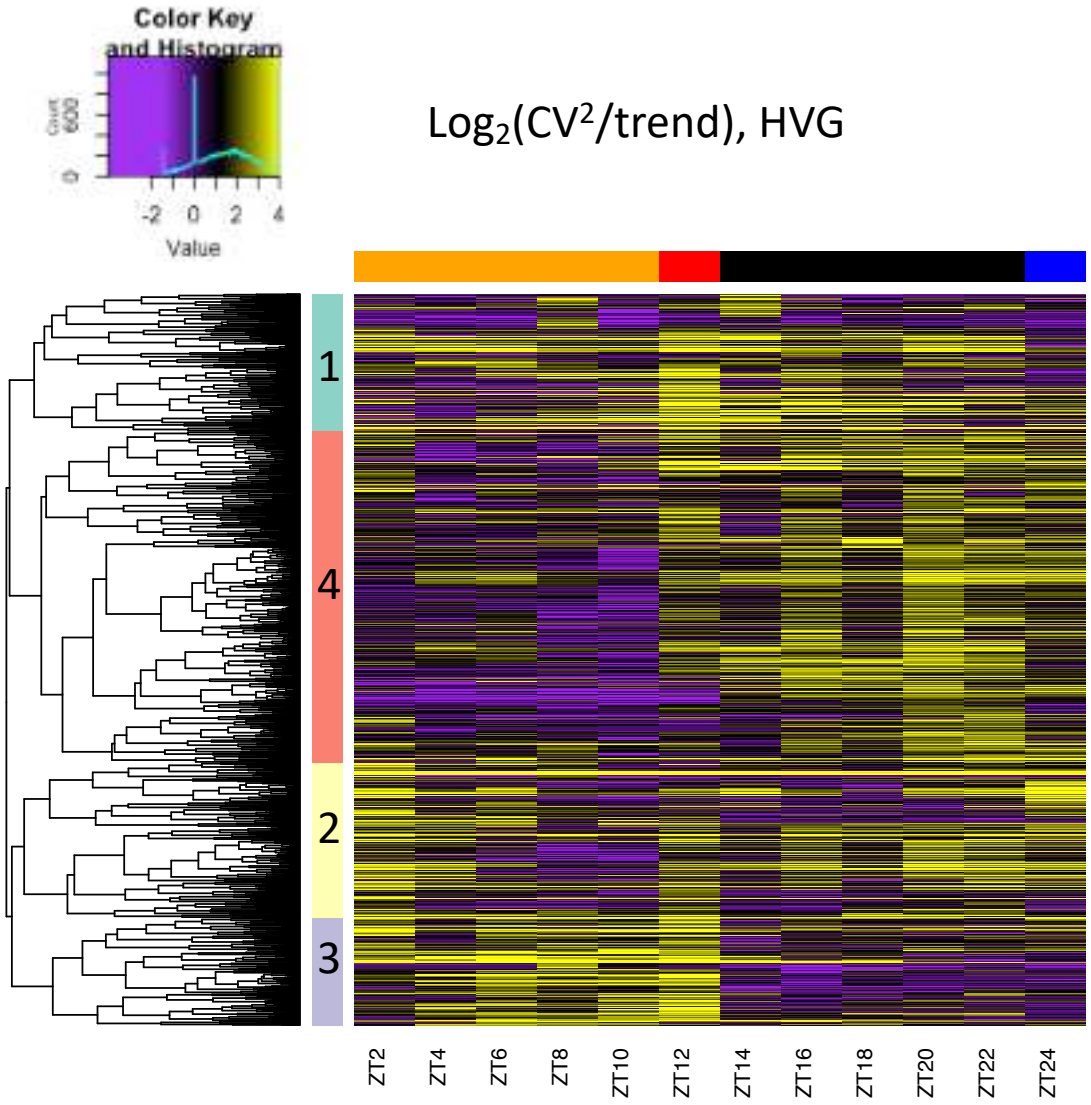
AT5G47990 (HVG)



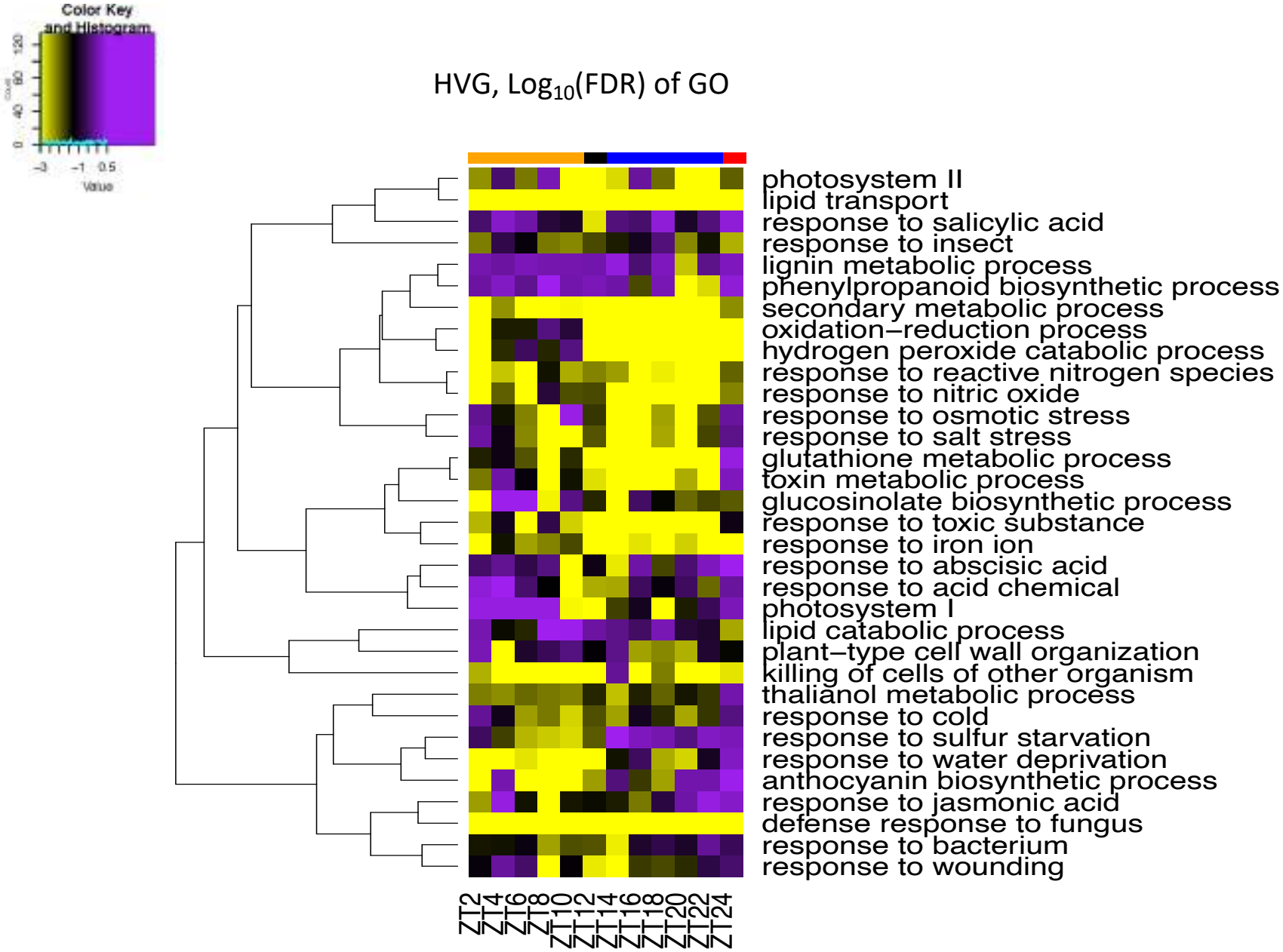
Variability profiles during the time course

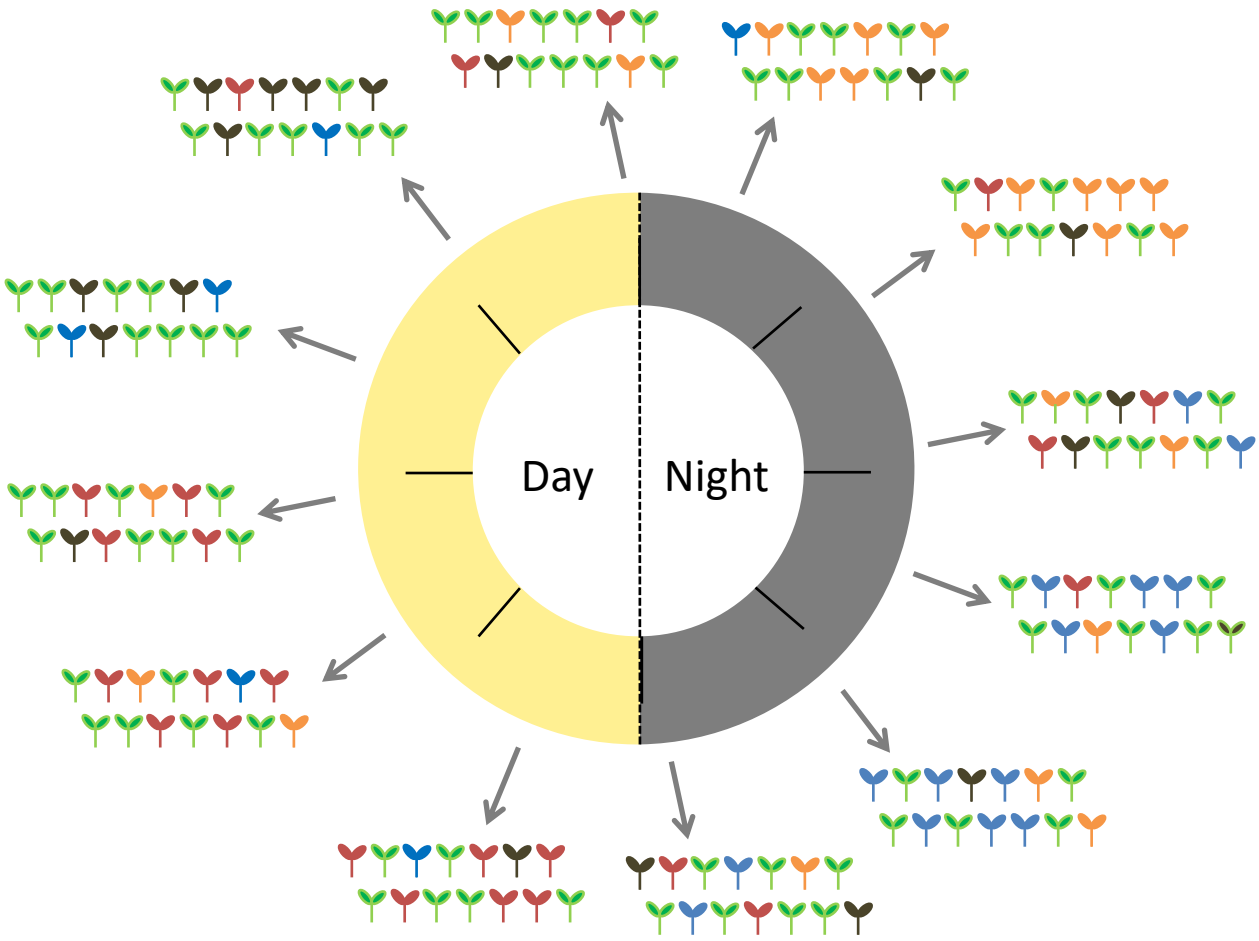


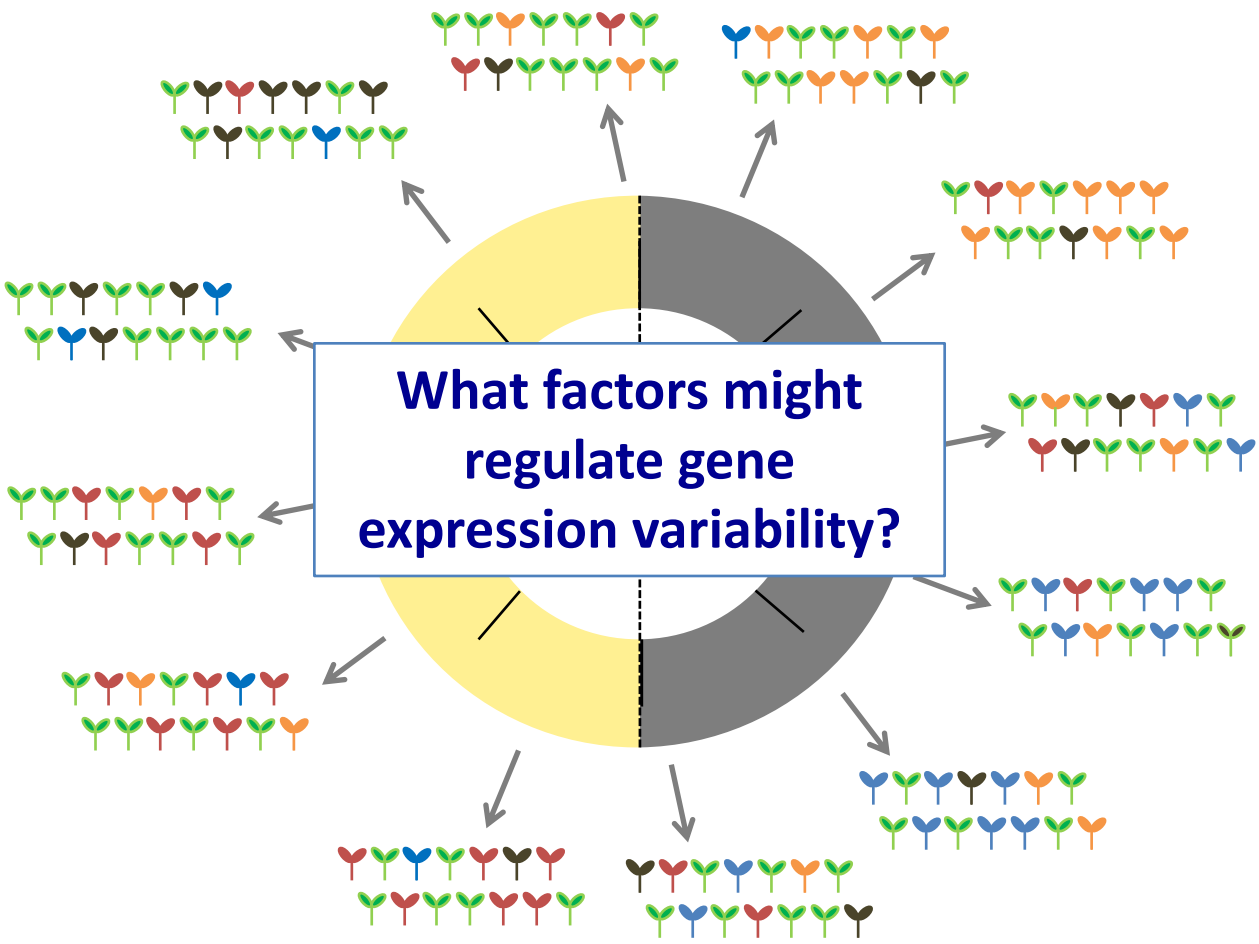
Variability profiles during the time course



HVGs are enriched for environmentally responsive genes

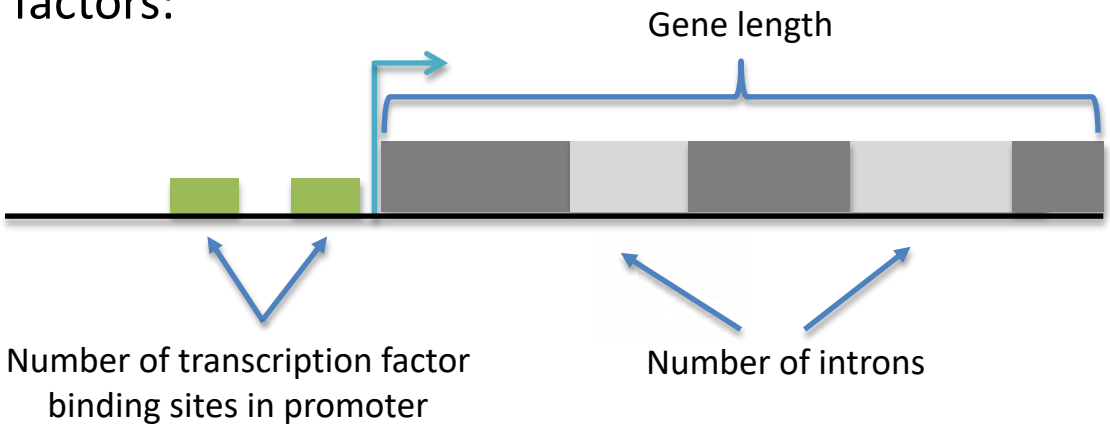



Day
Night


What factors might regulate gene expression variability?

Genomic and epigenomic factors we analysed

- Genomic factors:



Genomic and epigenomic factors we analysed

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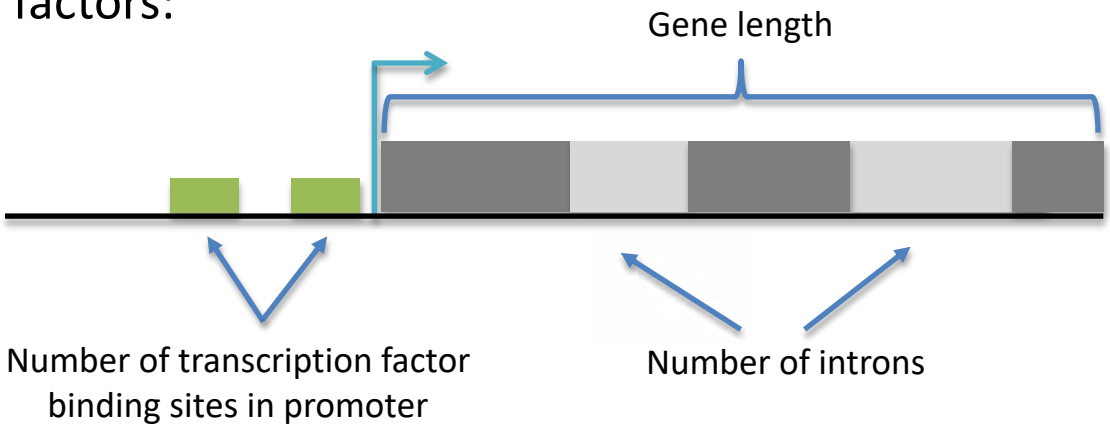
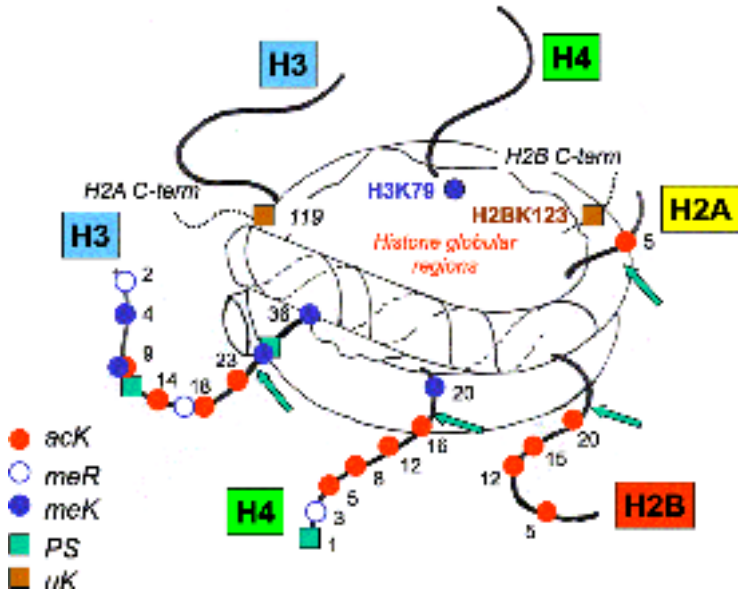
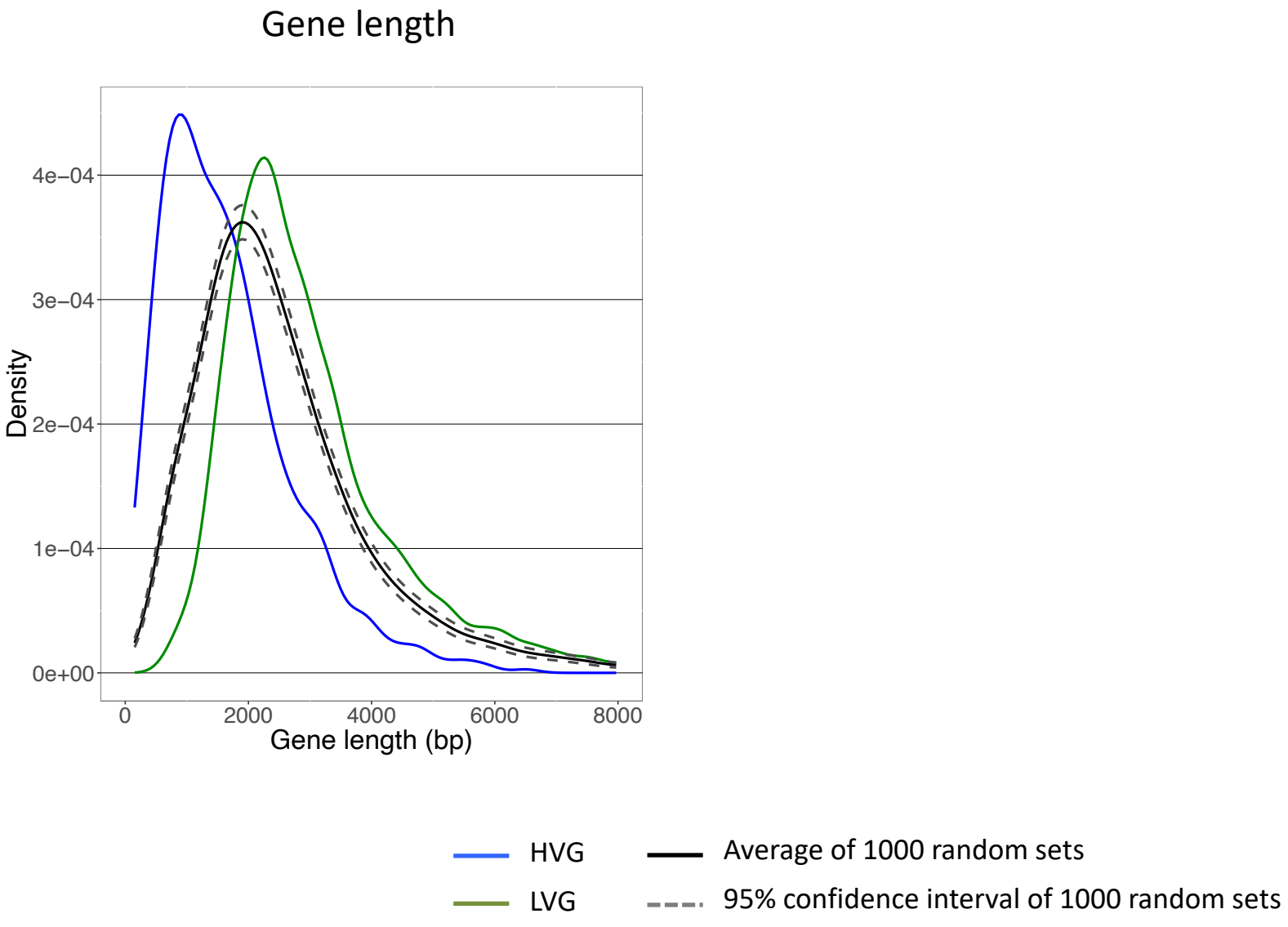


- Epigenomic factors:



HVGs tend to be smaller and targeted with more TFs



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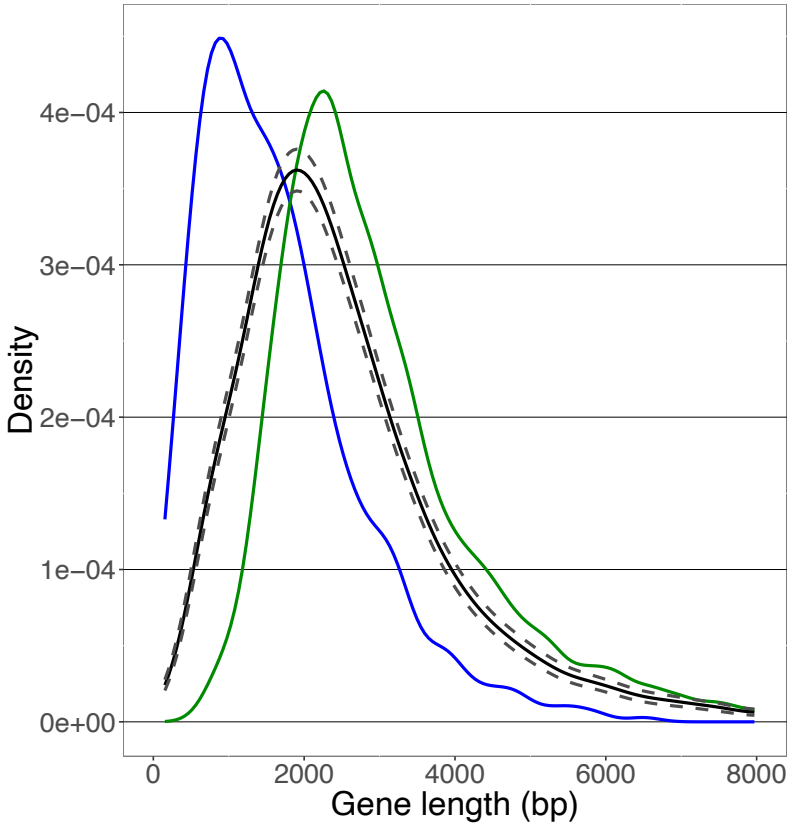
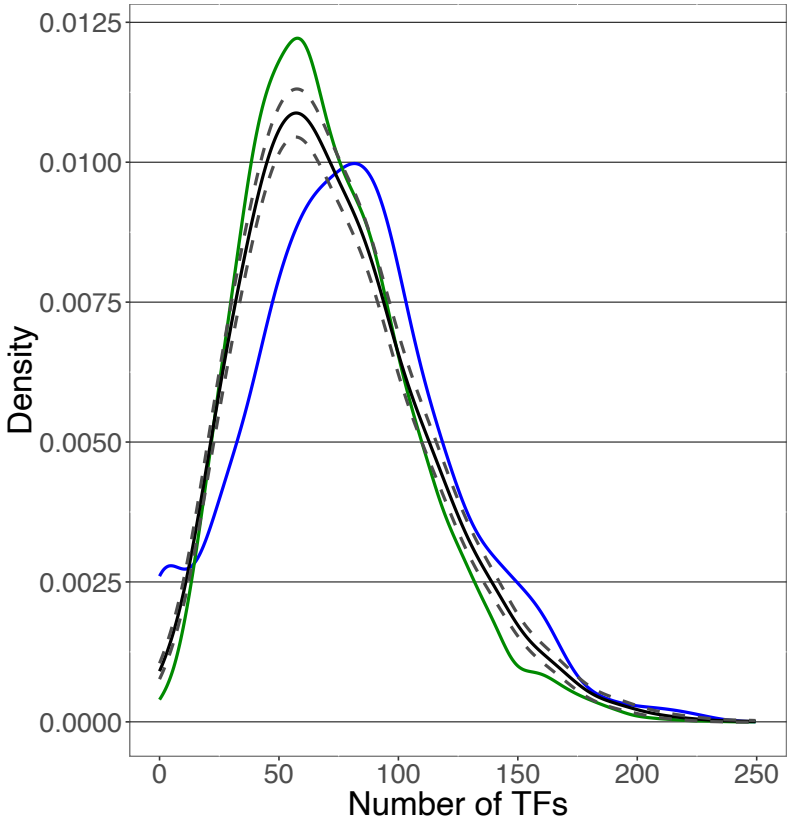
Gene length



Number of TFs binding to the promoter of the gene



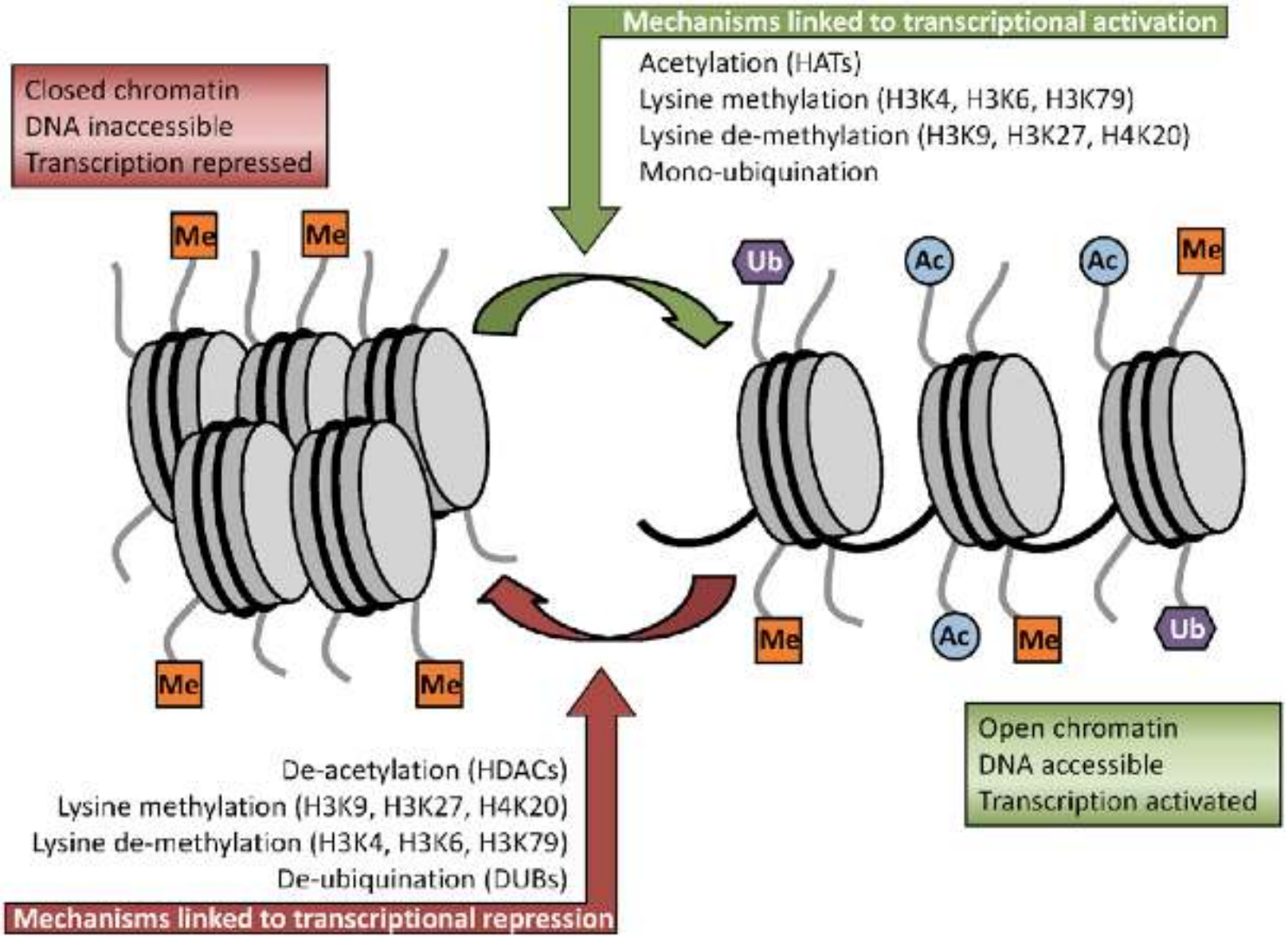
HVG

LVG

Average of 1000 random sets

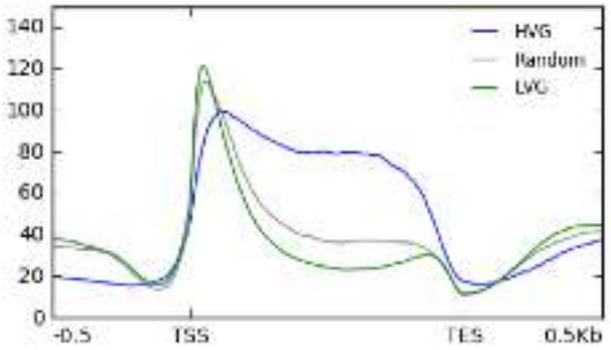
95% confidence interval of 1000 random sets

Chromatin environment of HVGs

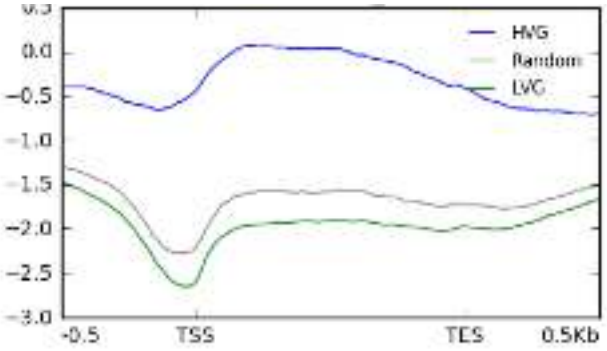


HVGs tend to be characterized by a ‘closed’ chromatin environment

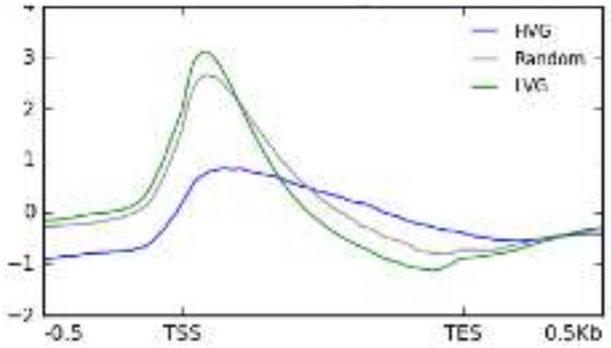
H2A.Z



H3K27me3



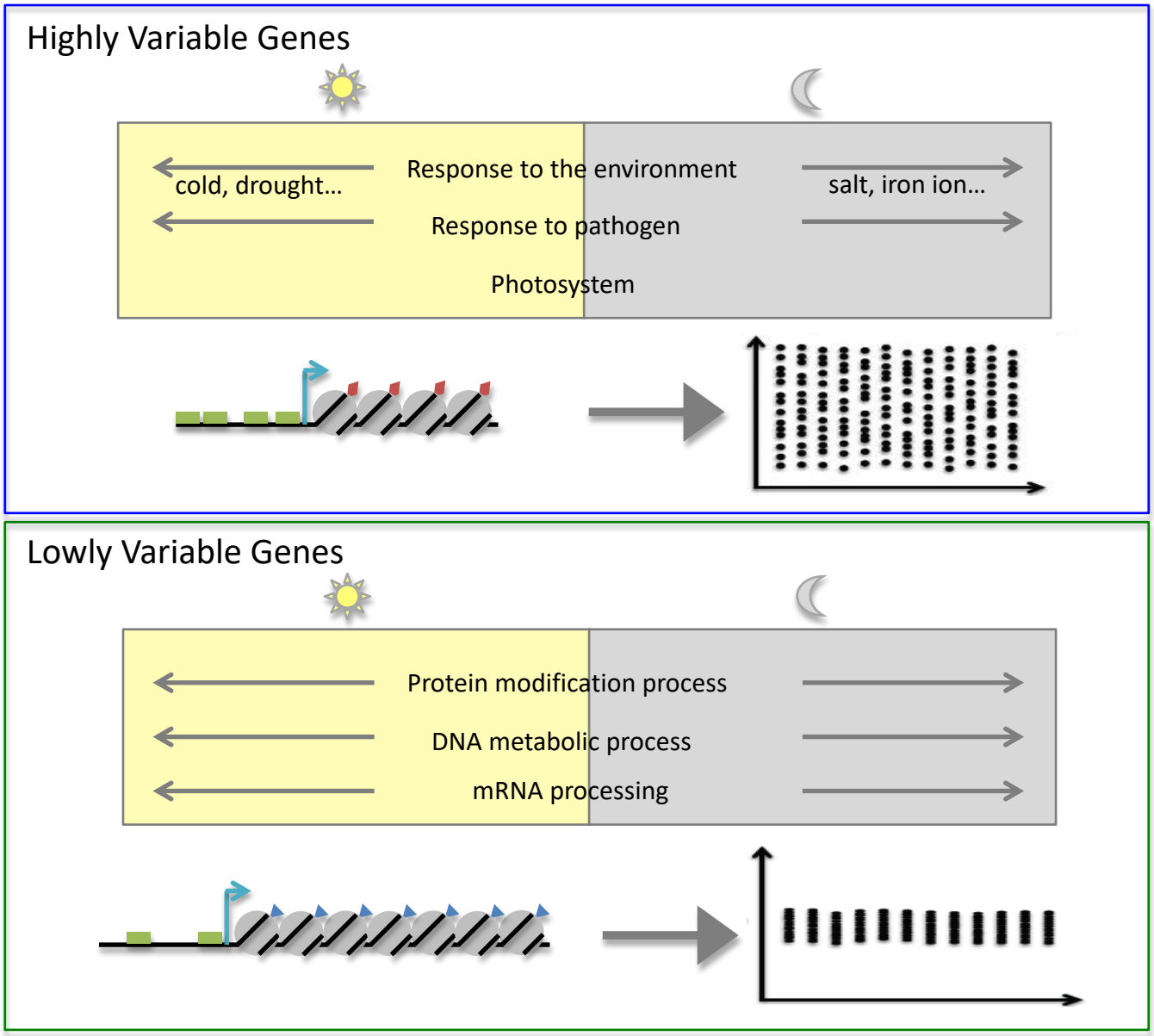
H3K4me3



Gene distance (Kb)

variable stable random

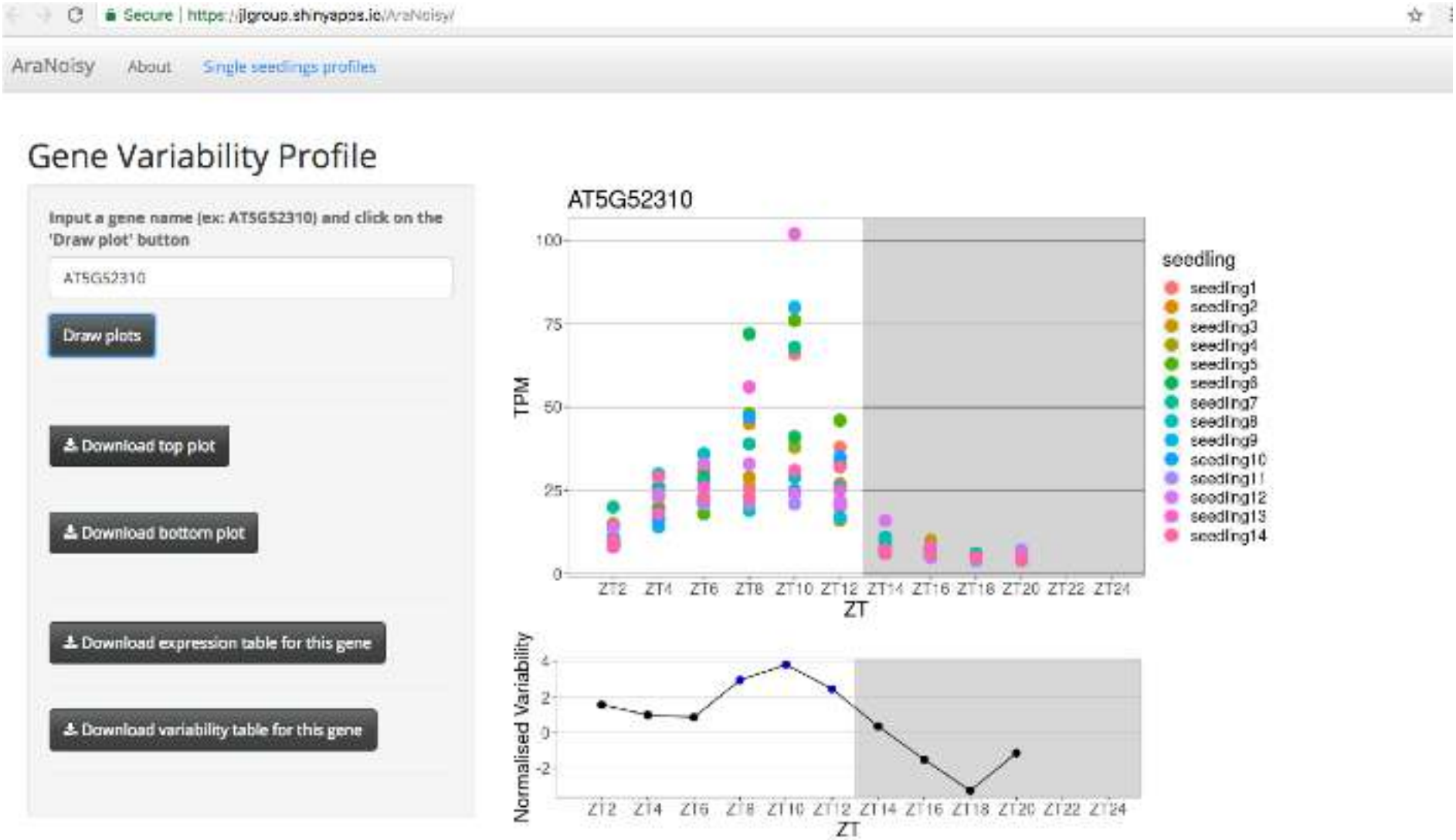
Summary



Cortijo et al, Mol Sys Biol 2019

AraNoisy, a webApp to explore gene expression variability for your gene of interest:

https://jlgroup.shinyapps.io/AraNoisy/



Can we harness inter-individual gene expression variability to better understand gene expression regulation?

In collaboration with Sebastian Ahnert
(University of Cambridge, UK)

Why Gene Co-expression Networks are useful

Help to identify genes that are co-regulated. It suggests the genes can:

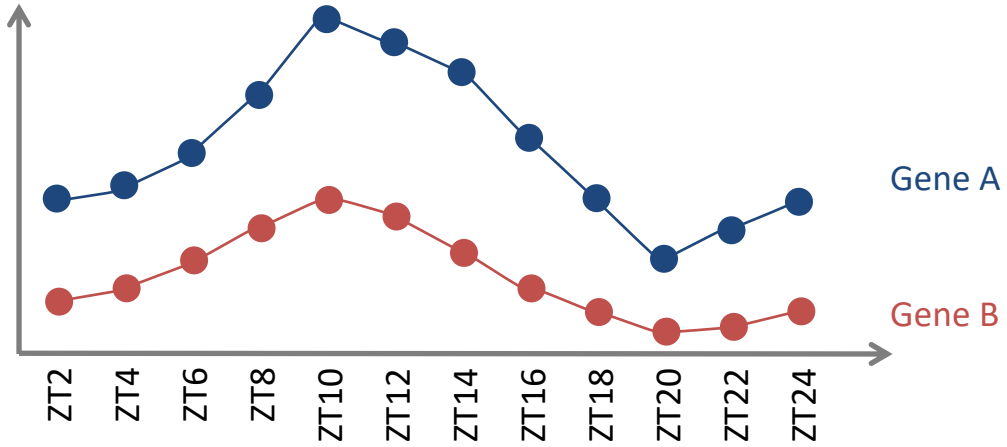
- Have a similar function
- Be involves in a common biological process
- Be controlled by the same transcriptional regulatory program

This can be used to :

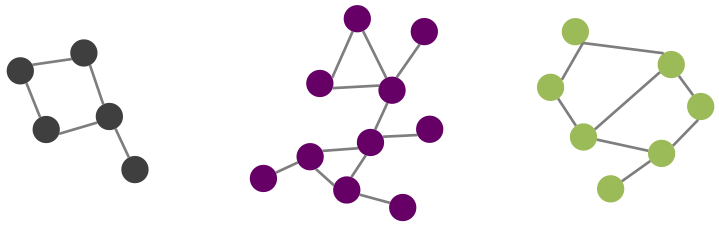
- Identify new genes in a pathway
- Identify new functions of a gene
- Identify potential regulators

What are Gene Co-expression Networks

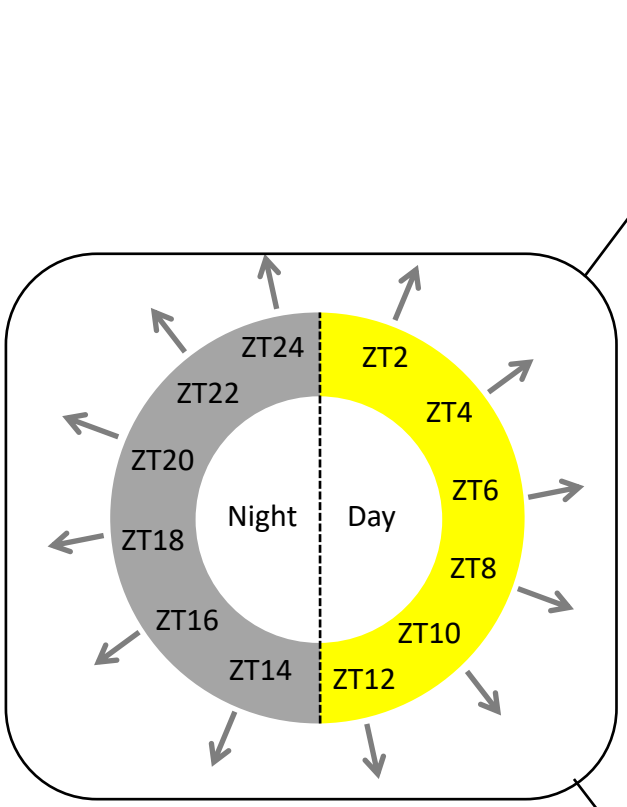
- Gene co-expression network can be constructed by looking for pairs of genes which show a similar expression pattern across samples



- Modules are cluster of genes that are more connected in the co-expression network

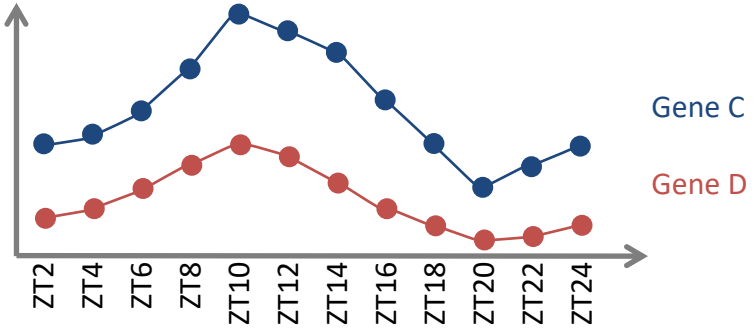


Gene Co-expression Networks: The usual approach uses perturbations

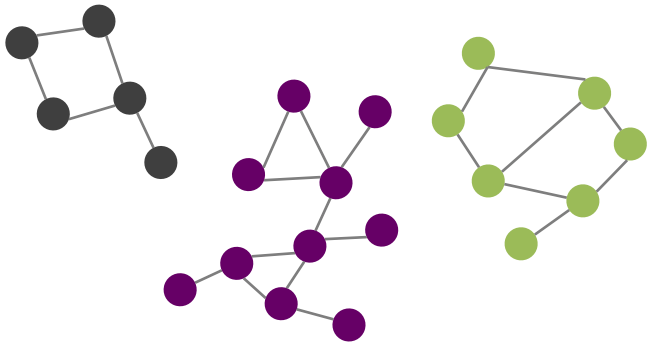


Time course co-expression network

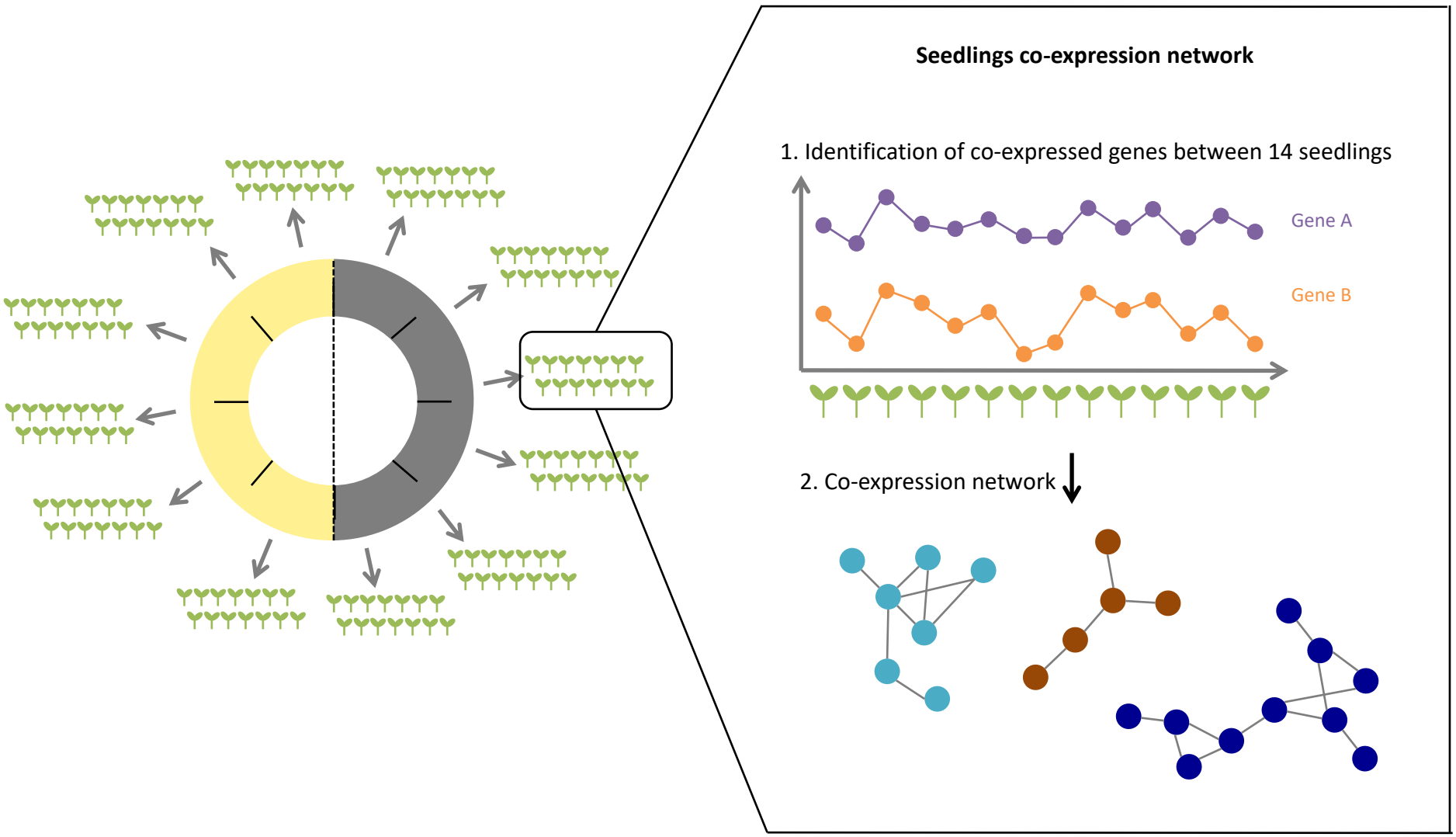
1. Identification of co-expressed genes between time point using the average expression level of all 14 seedlings in each time point



2. Co-expression network



Gene Co-expression Networks
Using inter-individual gene expression variability



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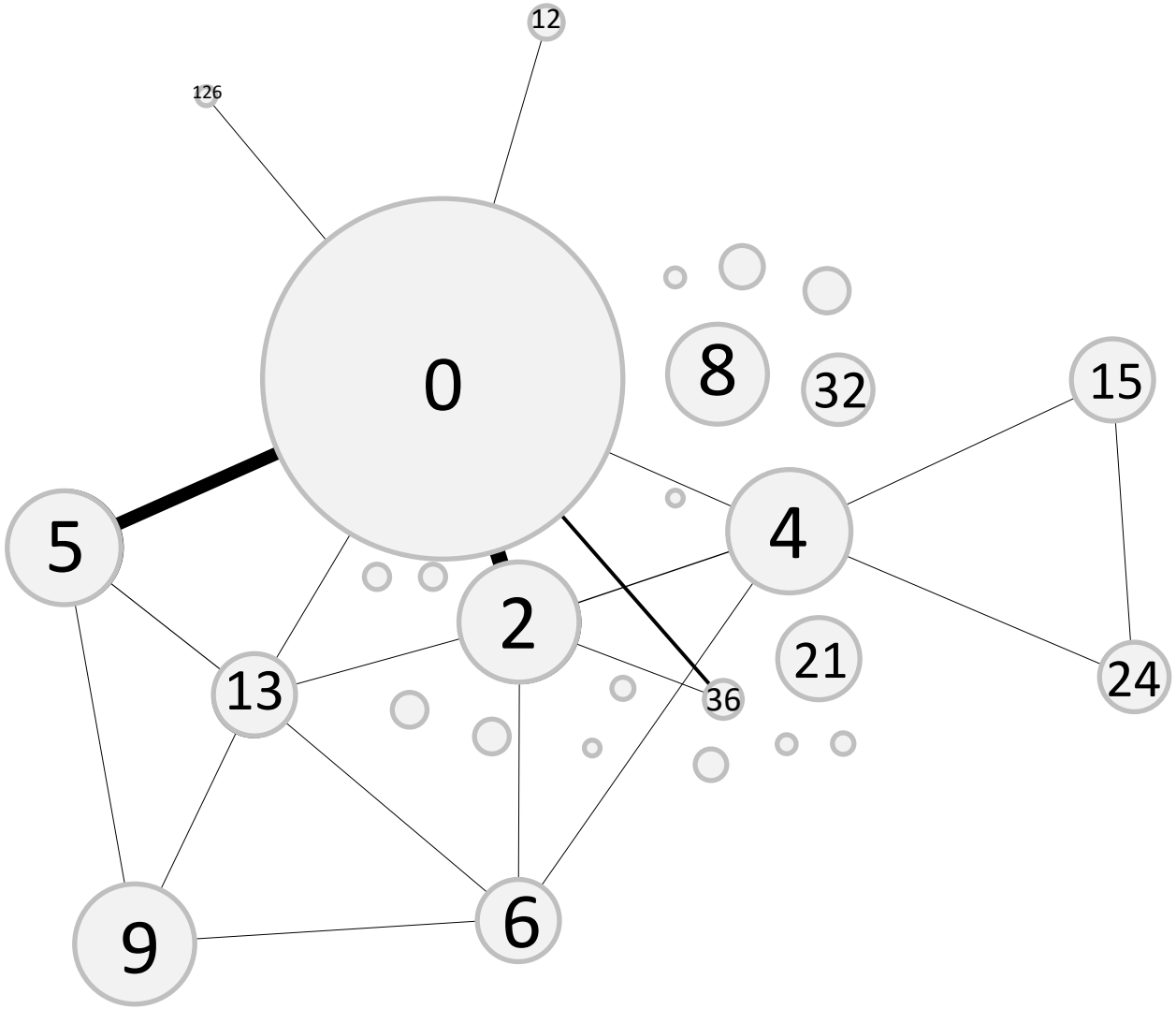
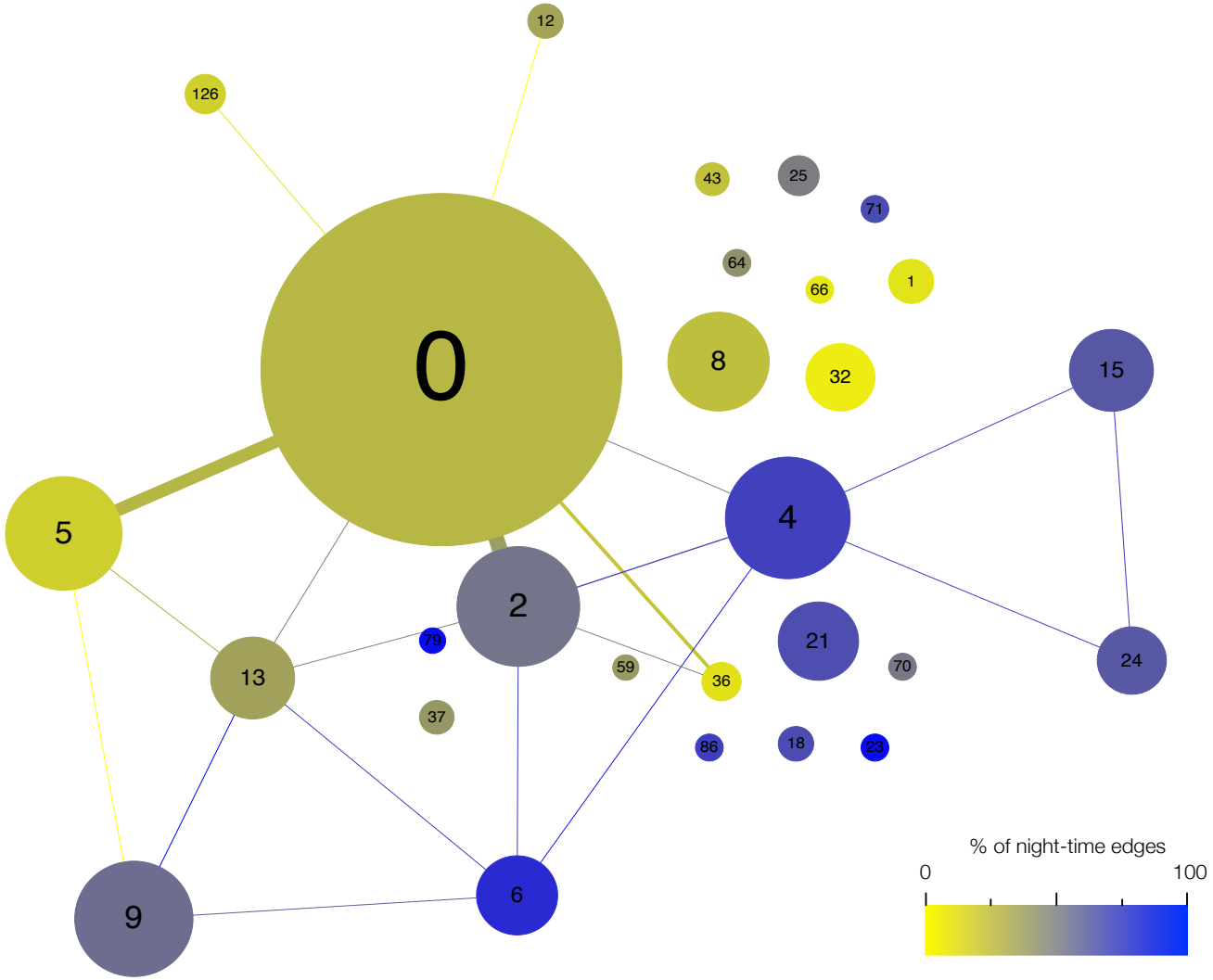
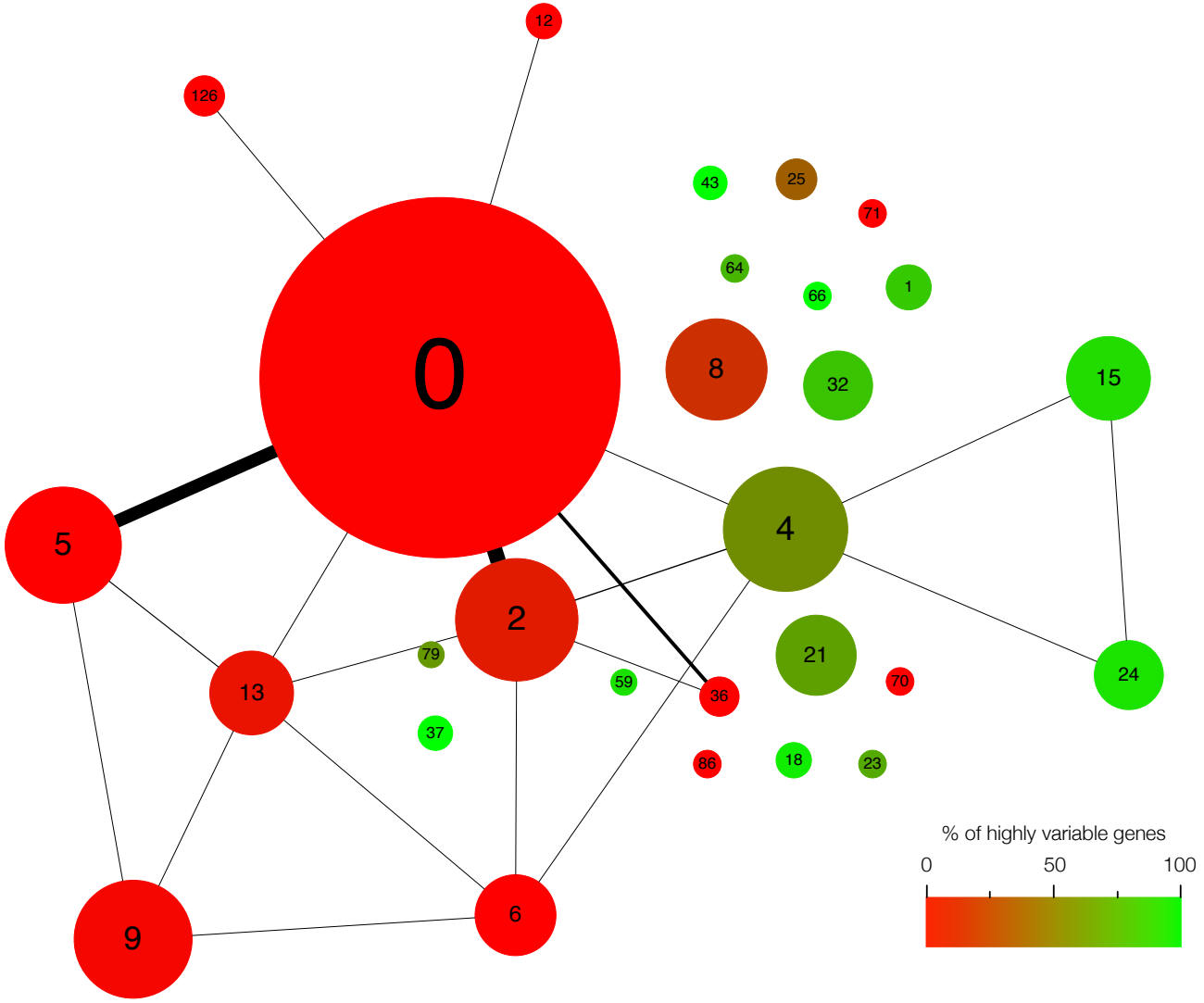


Network of 1729 genes, with 153 modules of 2 to 334 gènes.

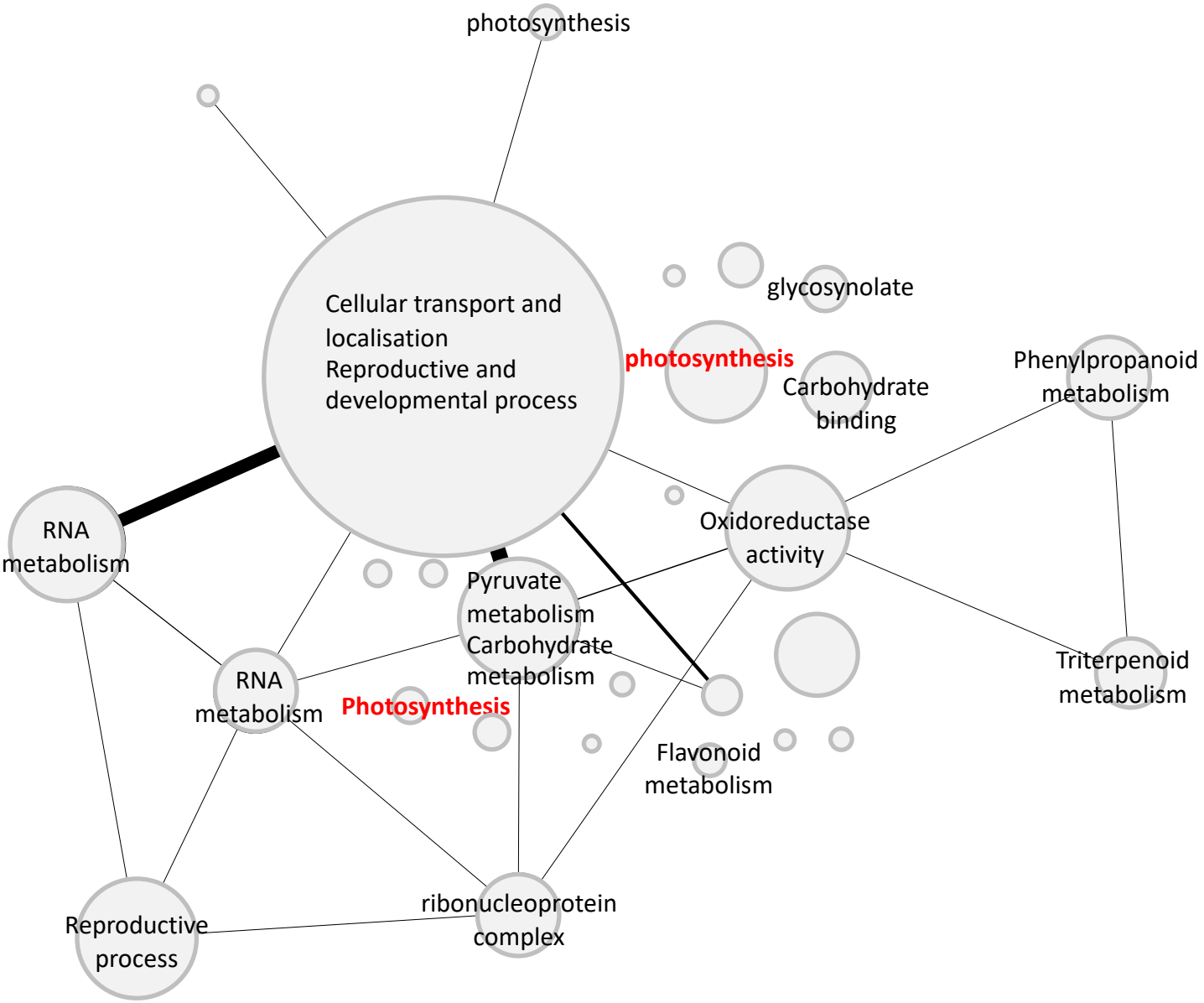
Modules structure



Modules structure



Functional characterisation of modules



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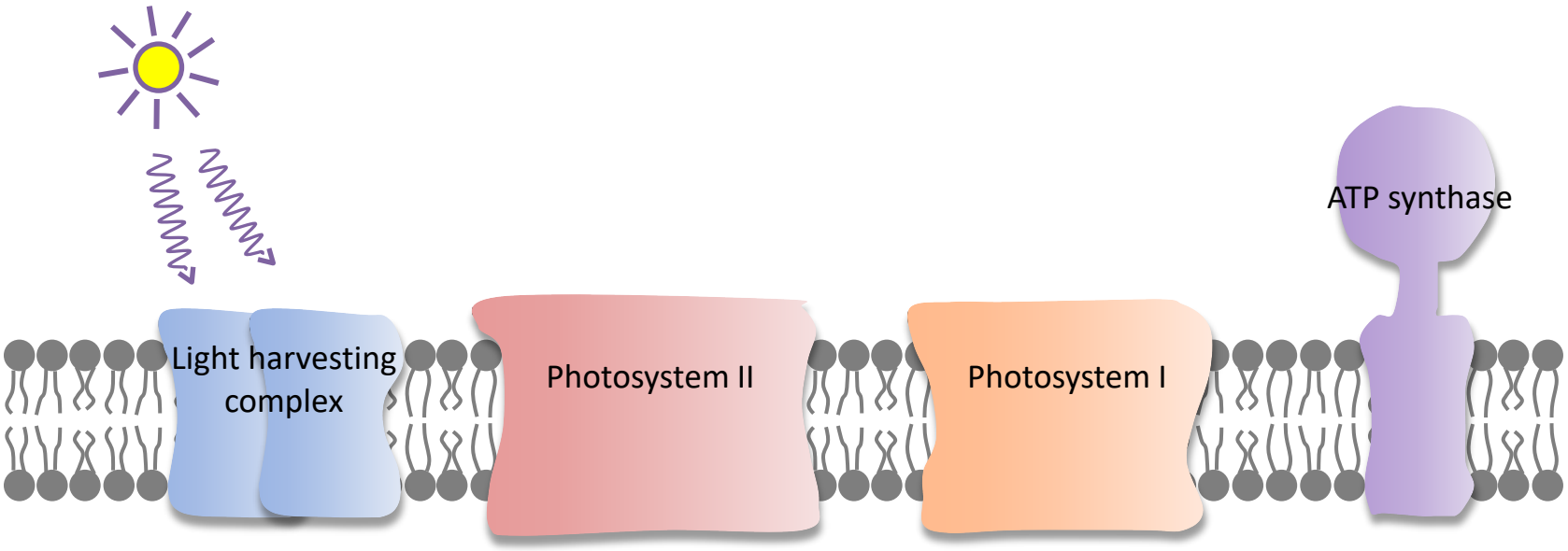
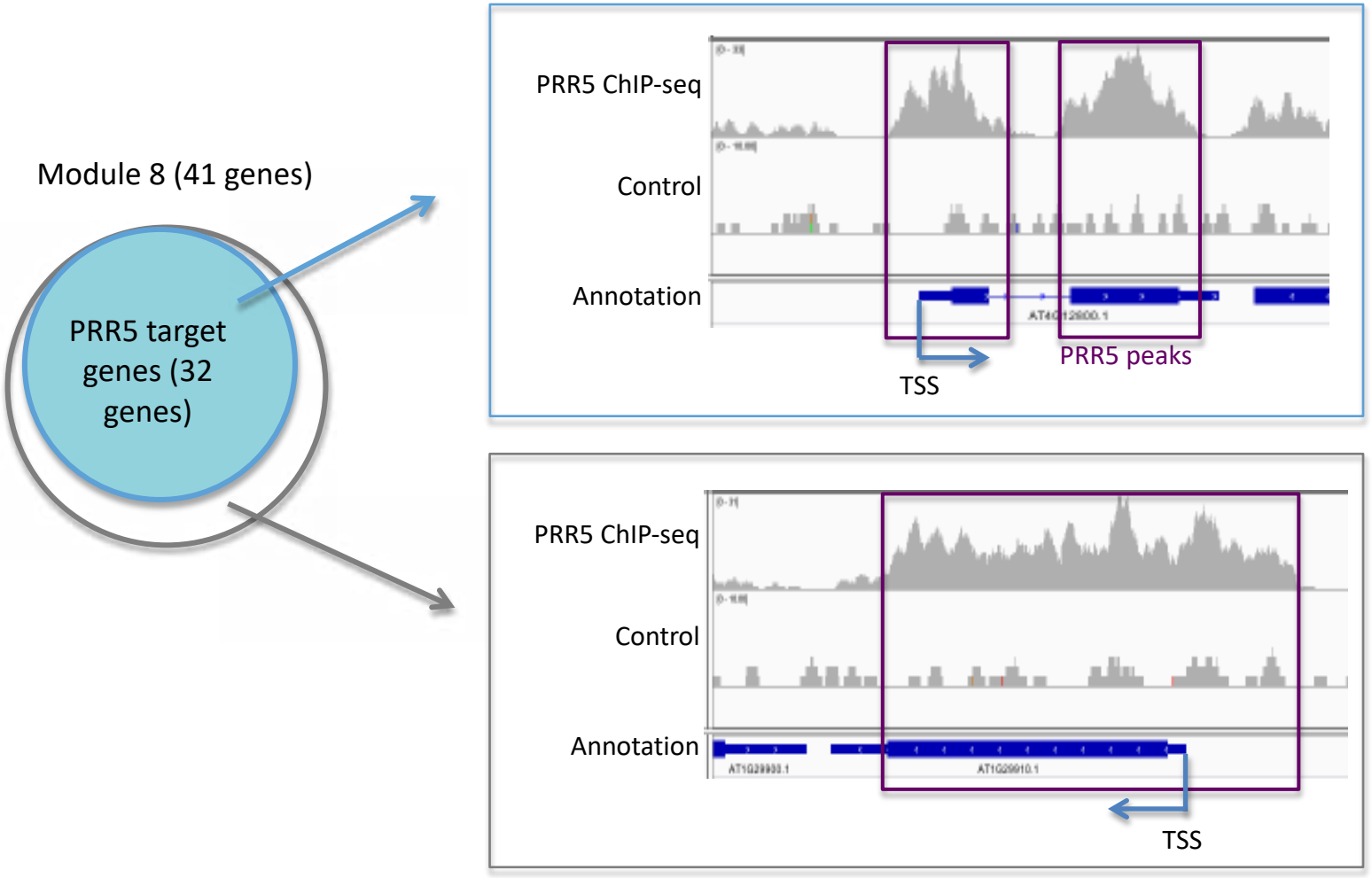


Module 8: 33/41 genes involved in photosynthesis
Module 37: 9/12 are chloroplast genes

Identification of new TF targets in modules



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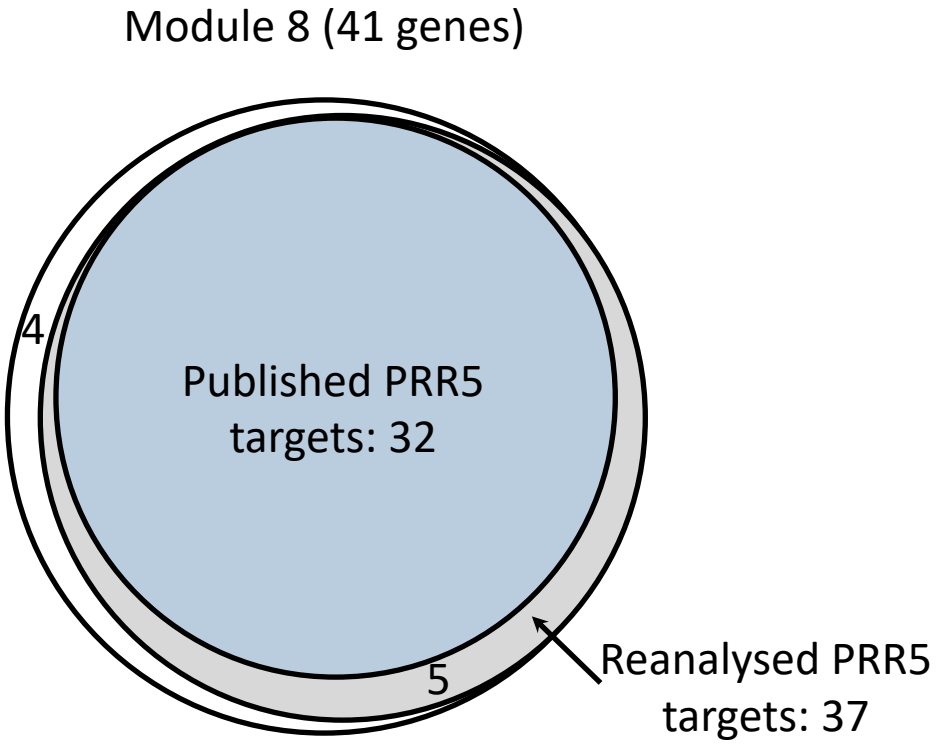


Summary

- Highly variable genes have specific features

- Gene expression variability between seedlings can be used to infer gene co-expression networks

- These networks can be used to detect new gene pathways or functions: PRR5 regulation of a not yet identified target

Website: https://jlgroup.shinyapps.io/VariabilityNetwork/

Current work

One genome

+

One environment

Medium expression

High expression

Low expression

Transcriptional variability

?

Multiple phenotypes

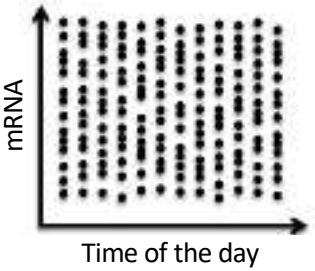
?

Environment

Genetic and epigenetic factors

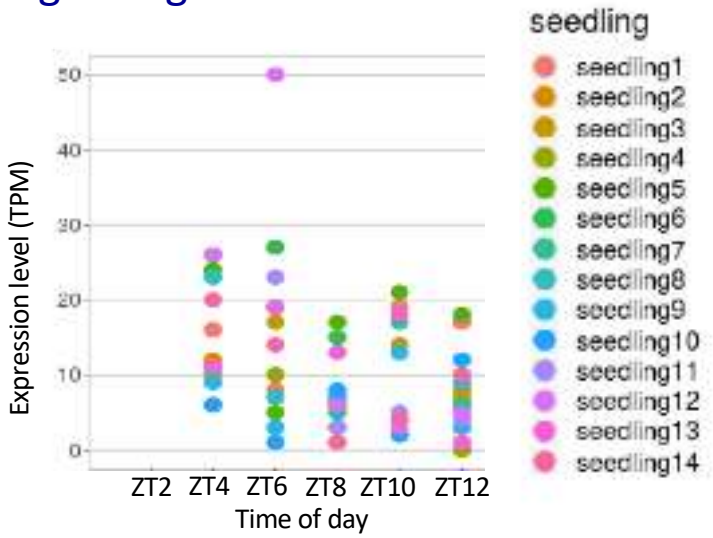
Highly variable genes are environmentally responsive

Highly Variable Genes

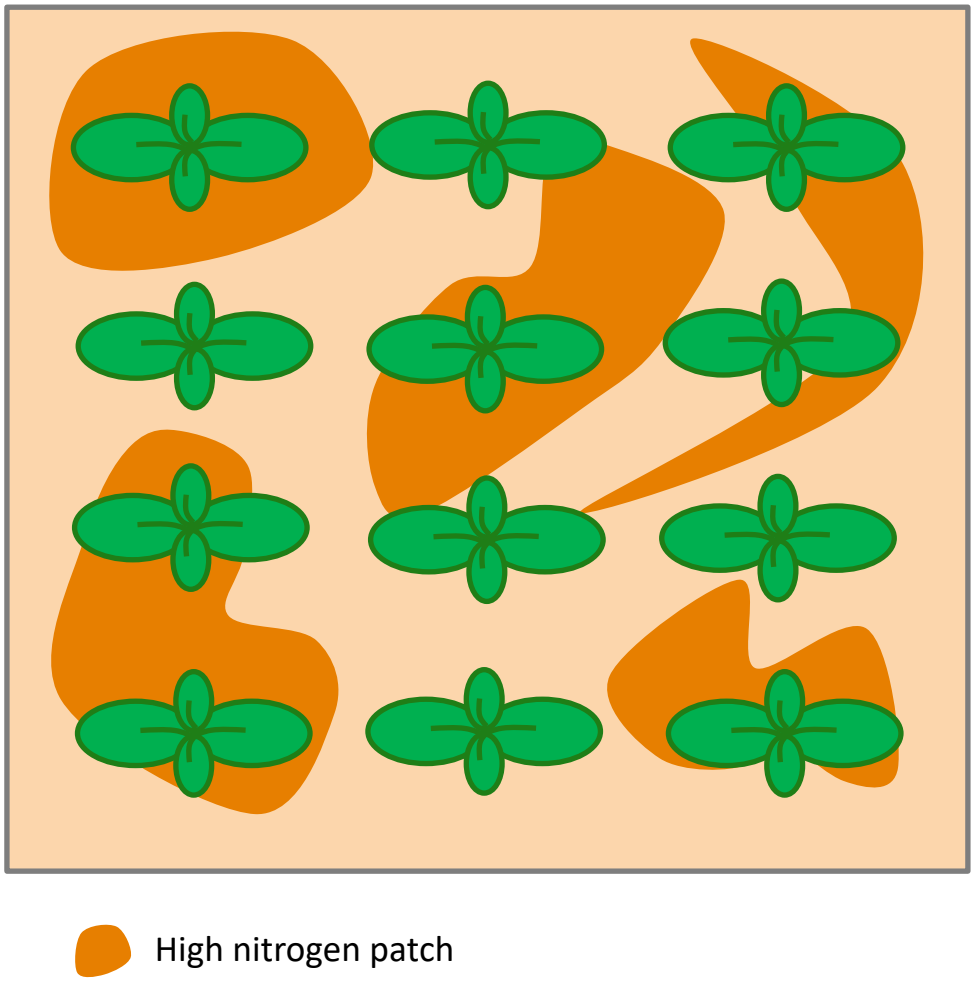


Response to the environment

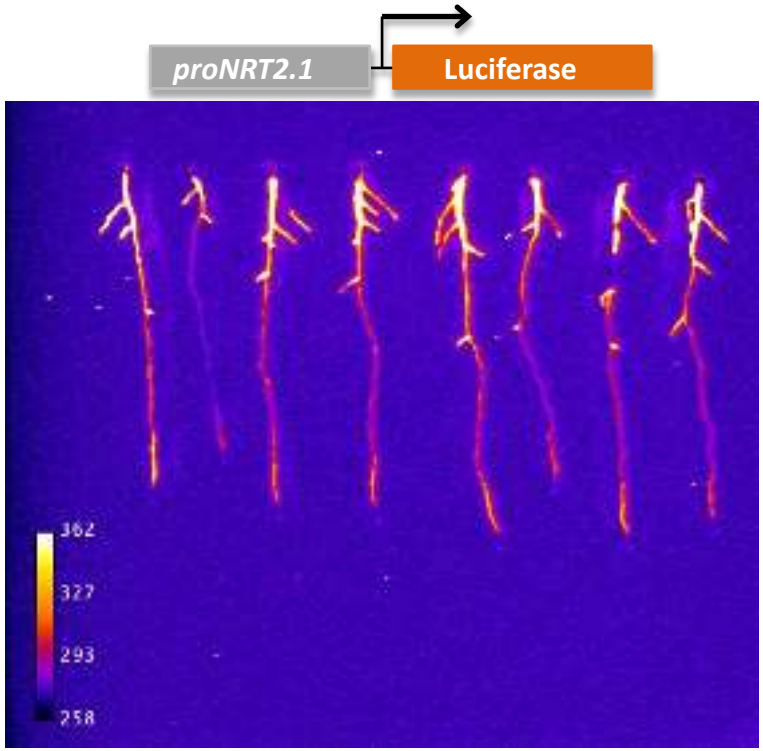
Including nitrogen nutrition



Nitrate in soil is fluctuating over time and space



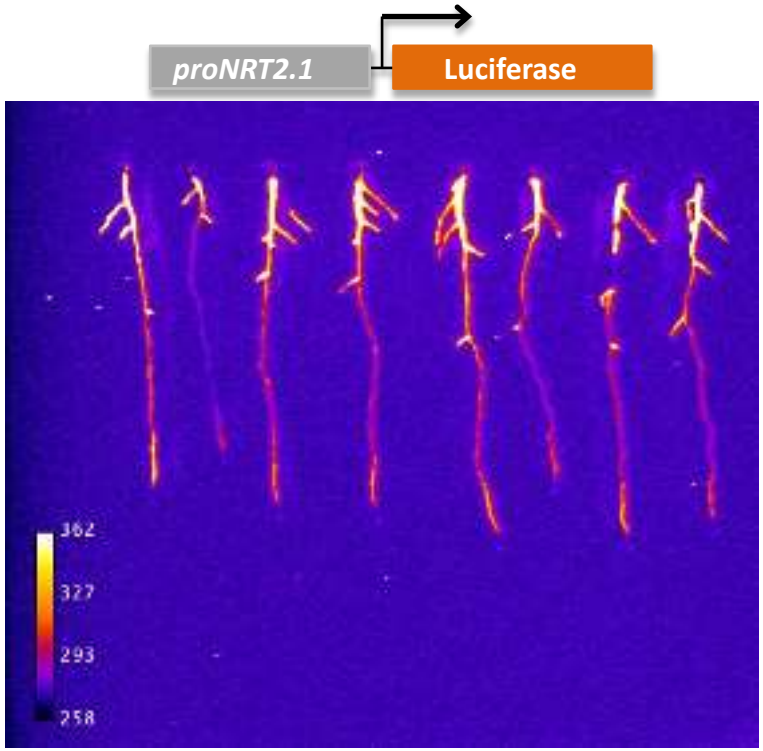
NRT2.1, a key nitrate transporter, is a highly variable gene



11 days old *pNRT2.1:LUC* plants on 1mM KNO_3

Tou Cheu Xiong (BPMP)

NRT2.1, a key nitrate transporter, is a highly variable gene



11 days old *pNRT2.1:LUC* plants on 1mM KNO_3

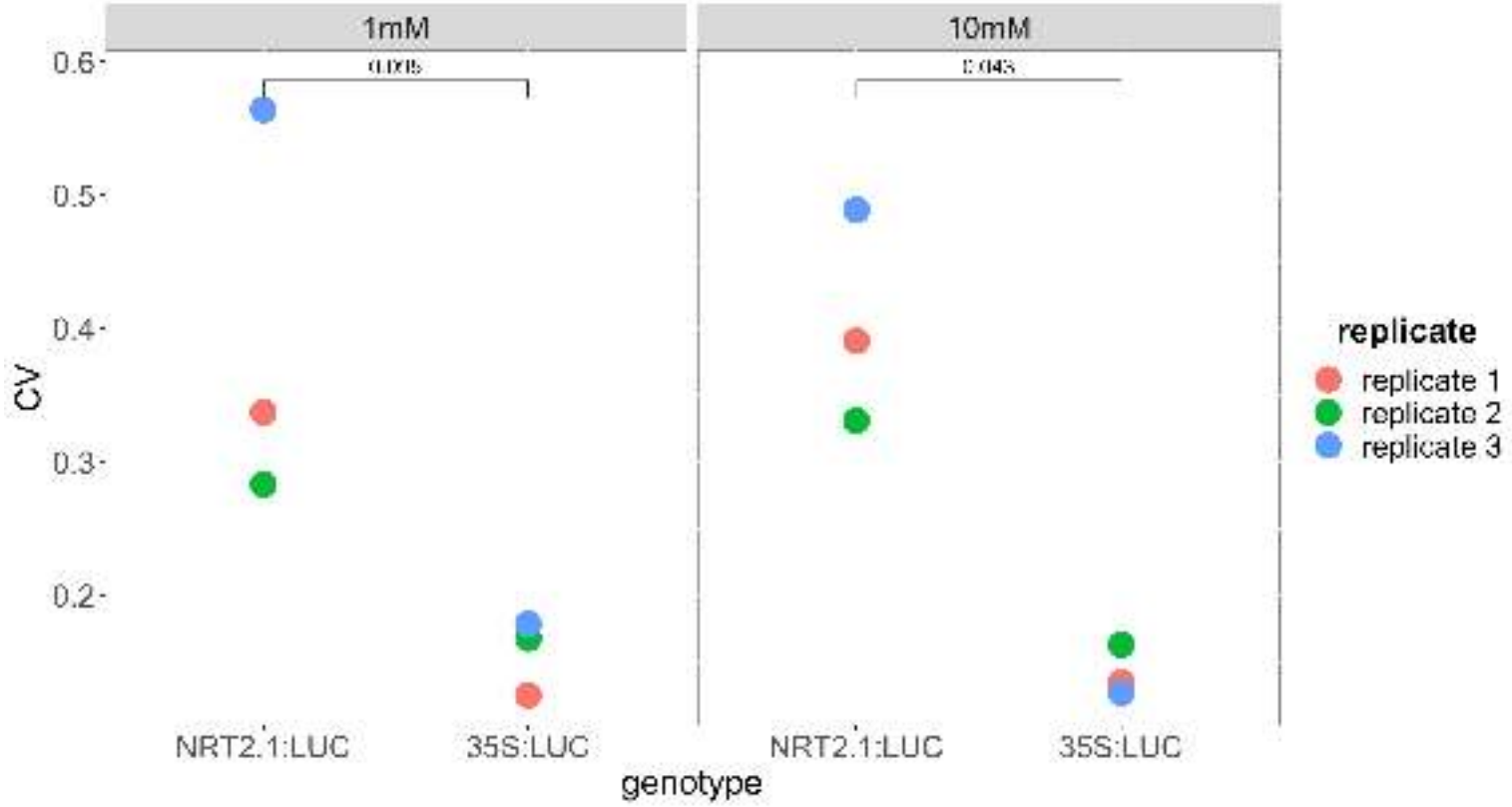
Tou Cheu Xiong (BPMP)

CV to measure the level of variability

CV= Standard deviation / average

(using ~30 plants)

NRT2.1, a key nitrate transporter, is a highly variable gene

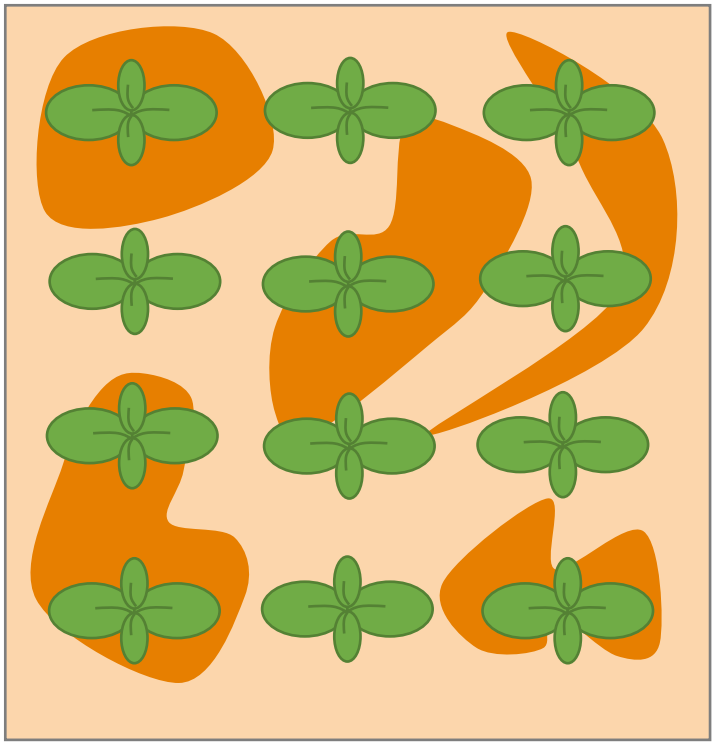


NRT2.1 is more variable than the constitutive 35S promoter

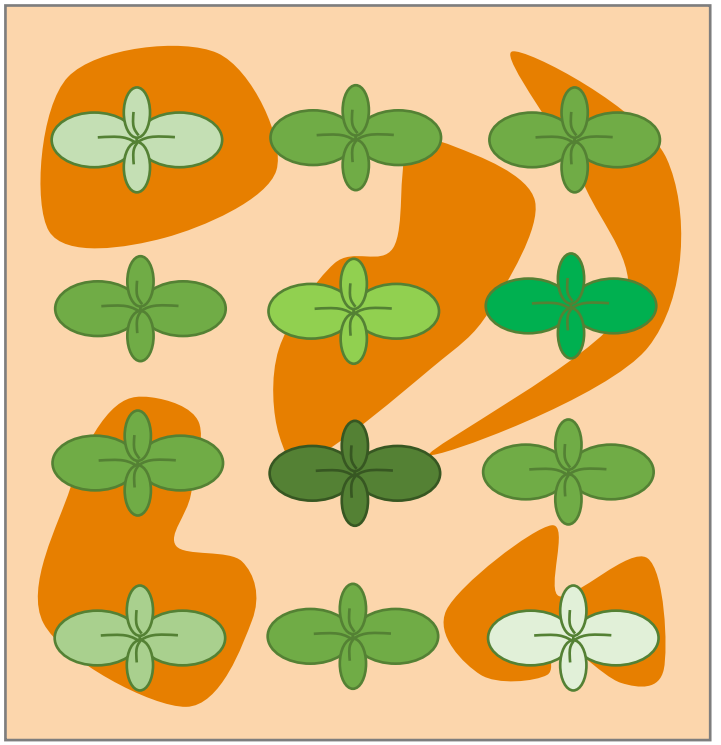
Variability can help populations of plants to survive

NRT2.1 is a highly variable gene

Nitrate in soil fluctuates temporally and spatially



Non variable population

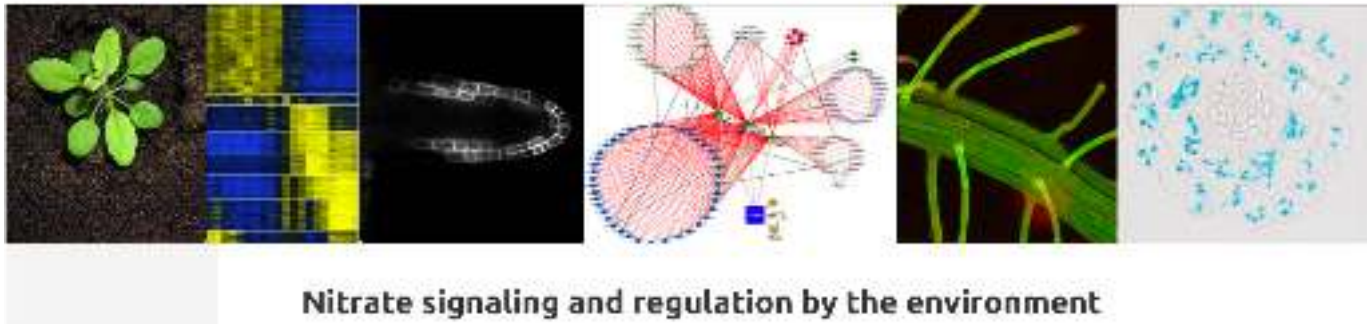


Variable population

Could variability in key genes in nitrate nutrition help plants to deal with unpredictible changes in nitrate concentration in soil?

Current work

Consequences and regulation of gene expression variability for nitrate nutrition in Arabidopsis



Nitrate signaling and regulation by the environment

Thanks!

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Antoine Martin's group (BPMP)
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Oscar Main

Tou Cheu Xiong (BPMP)