ATTRACTOR, a circadian clock transcriptional network based on ChIP-seq data unveils potential gene modules for crop improvement

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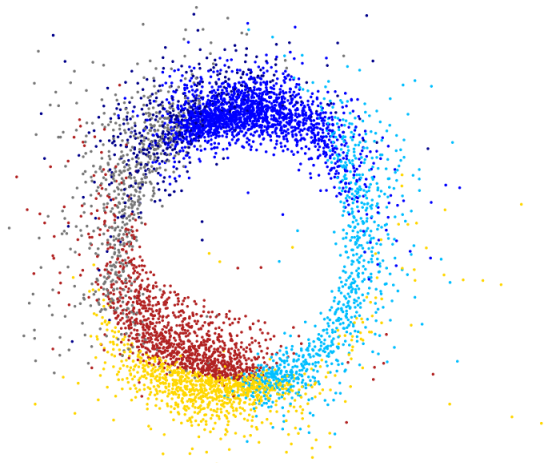
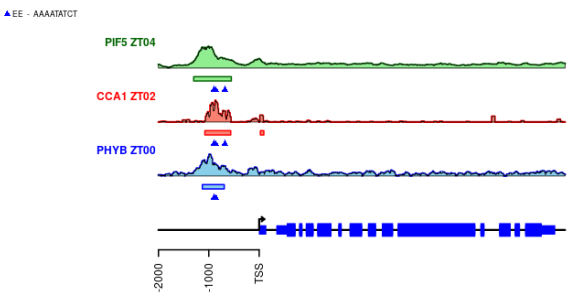
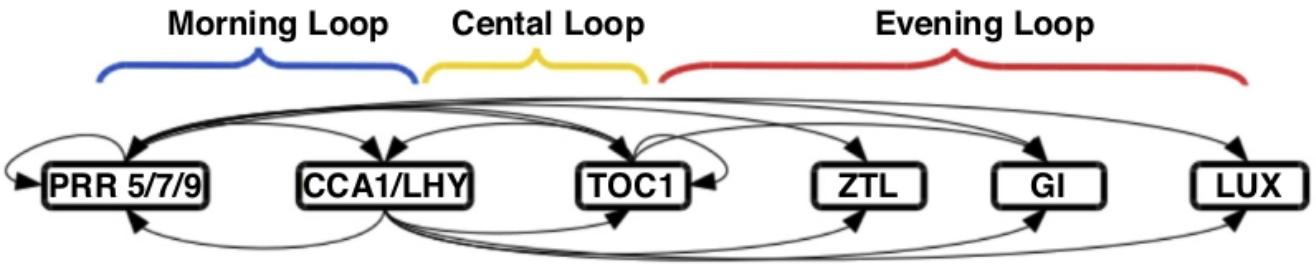




Circadian Clock is central to Plant Development and Physiology



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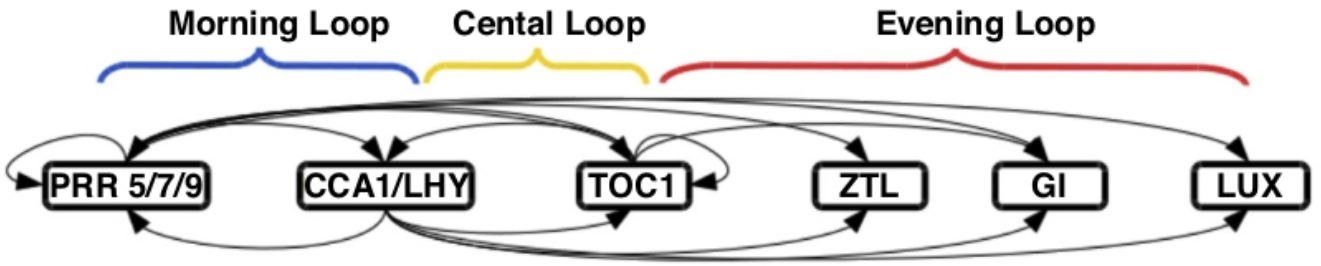
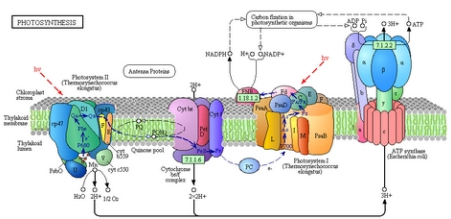
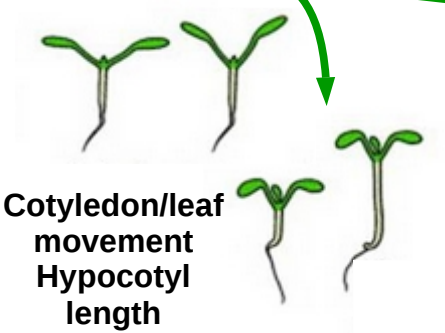


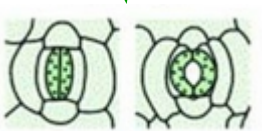


Photosynthesis

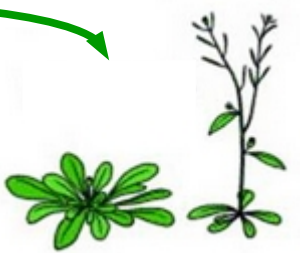
Starch/sugar metabolism



Cotyledon/leaf movement Hypocotyl length



Stoma opening/closing



Flowering transition

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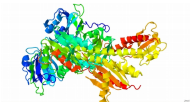
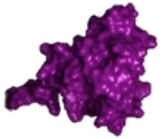
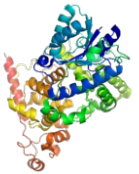


Phytochromes



Phytochrome Interacting Factors

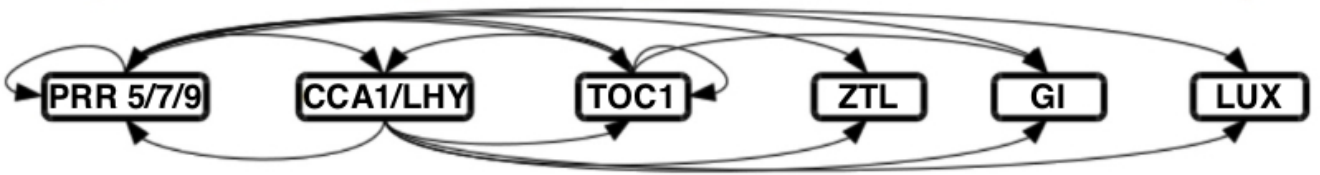


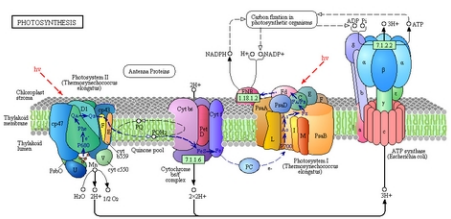
Cryptochromes

Morning Loop

Cental Loop

Evening Loop





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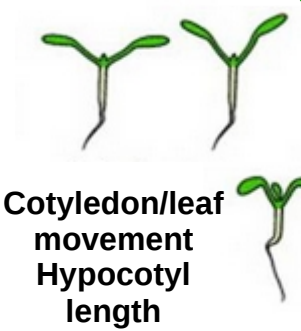

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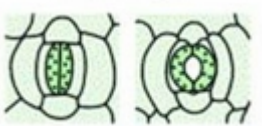

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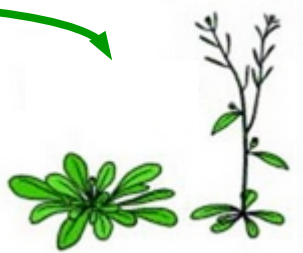

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Transcriptomics and Cistromics data accumulate in Data Bases for key regulators in the Circadian Clock

The Plant Cell, Vol. 17, 3257–3281, December 2005, www.plantcell.org © 2005 American Society of Plant Biologists

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+ See all authors and affiliations

Science 06 Apr 2012:
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DOI: 10.1126/science.1219075

Transcriptional repressor PRR5 directly regulates clock-output pathways

Norihito Nakamichi[a,b,c,d,1], Takatoshi Kiba[c], Mari Kamioka[b], Takamasa Suzuki[e,f], Takafumi Yamashino[b], Tetsuya Higashiyama[e,f], Hitoshi Sakakibara[c], and Takeshi Mizuno[b]

The Plant Cell, Vol. 28: 696–711, March 2016, www.plantcell.org © 2016 American Society of Plant Biologists. All rights reserved.

Direct Repression of Evening Genes by CIRCADIAN CLOCK-ASSOCIATED1 in the Arabidopsis Circadian Clock OPEN

Mari Kamioka,[a] Saori Takao,[b] Takamasa Suzuki,[c,d,e] Kyomi Taki,[e] Tetsuya Higashiyama,[b,c,e] Toshinori Kinoshita,[b,e] and Norihito Nakamichi[b,e,1]

Cryptochromes Interact Directly with PIFs to Control Plant Growth in Limiting Blue Light

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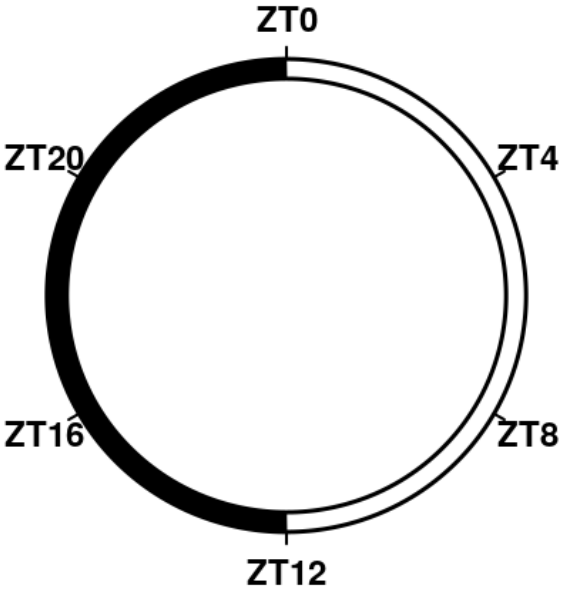

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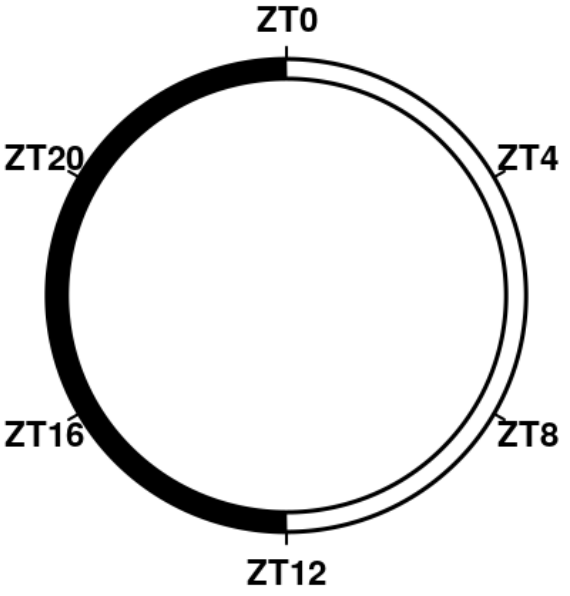

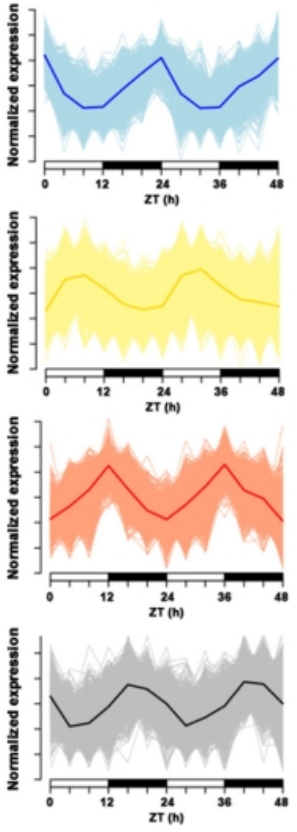

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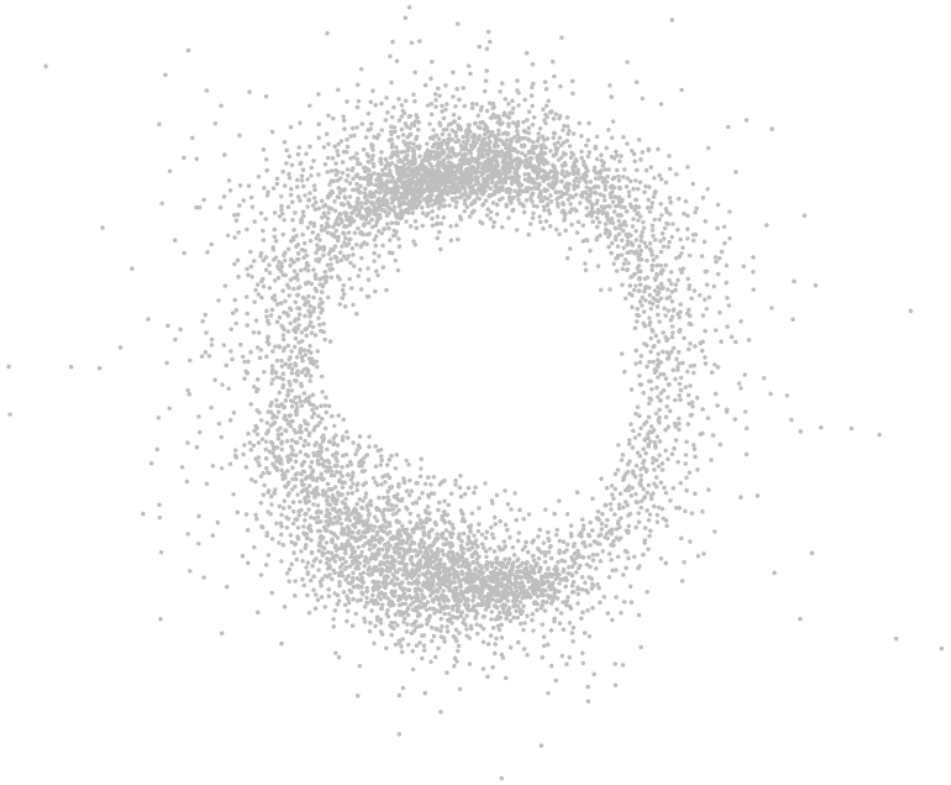

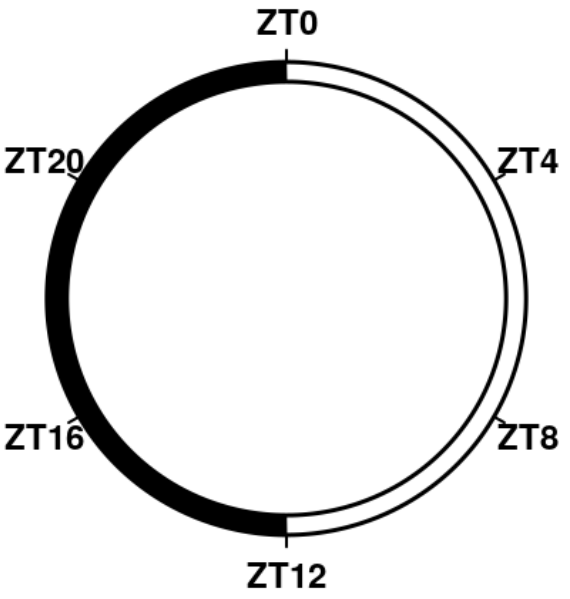

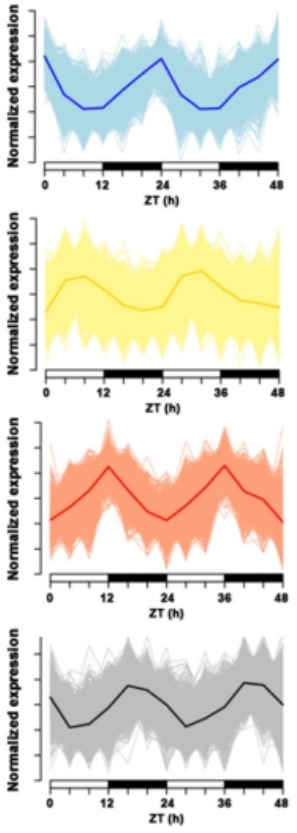

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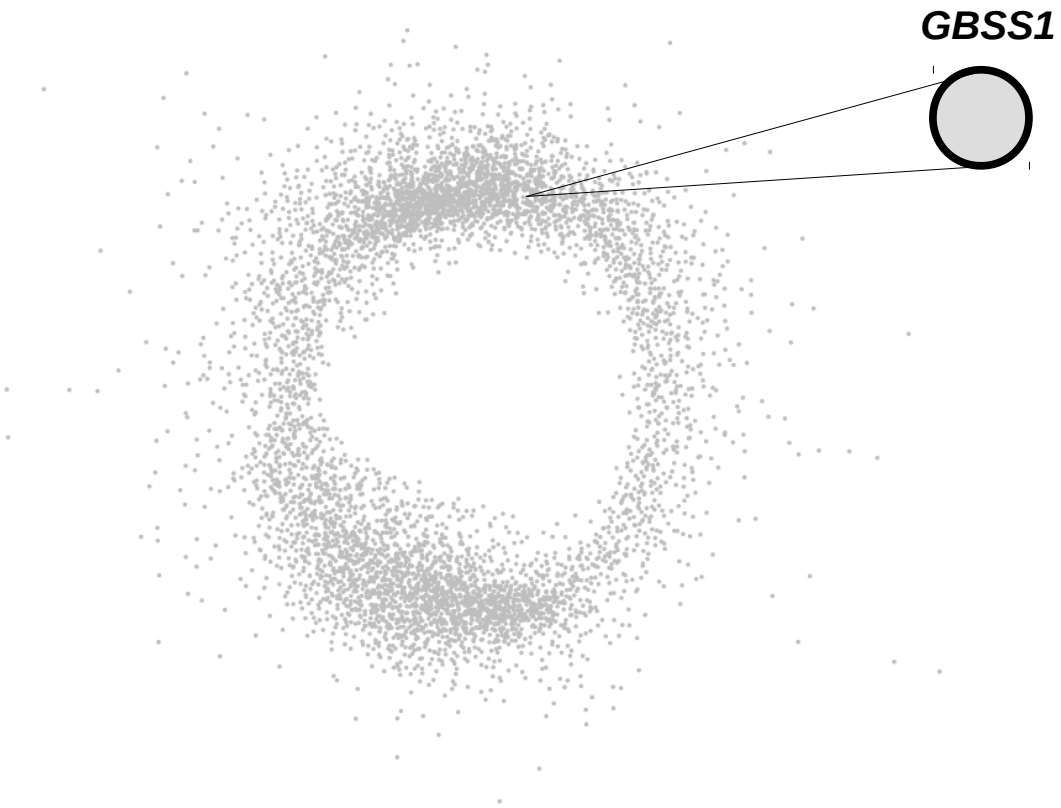

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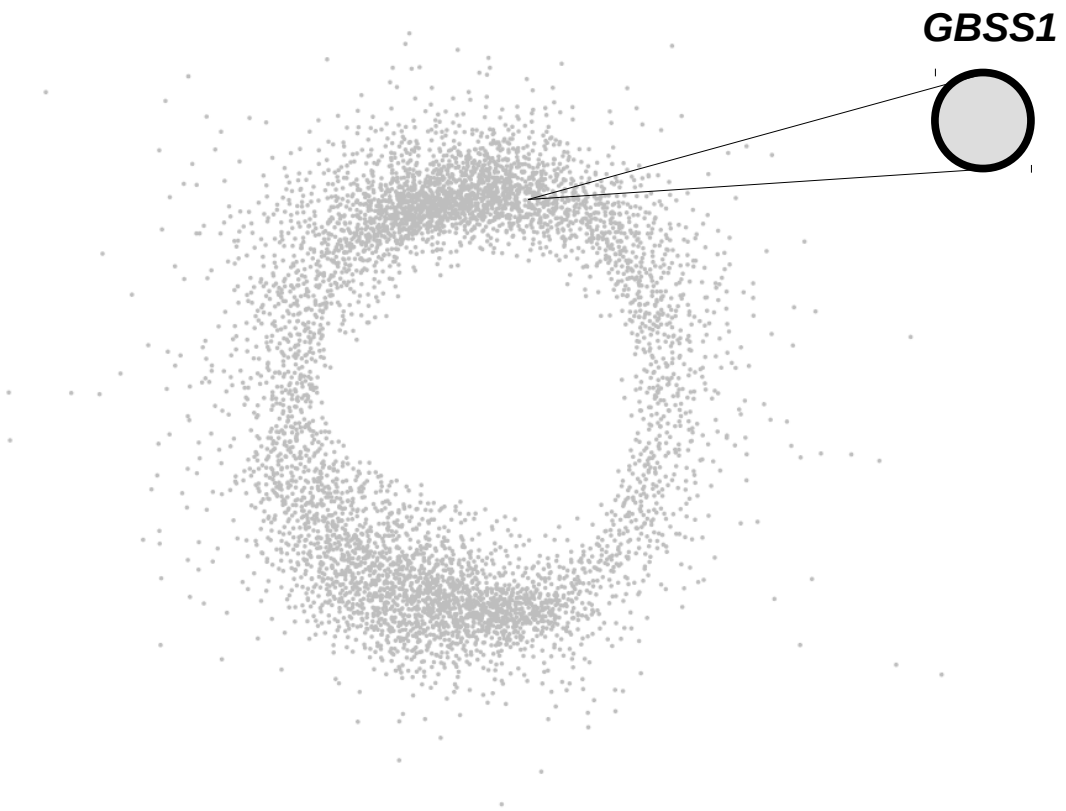

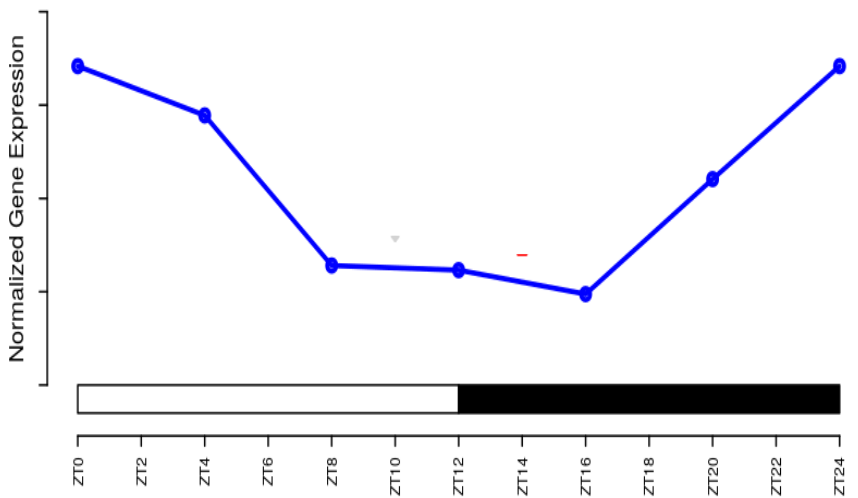

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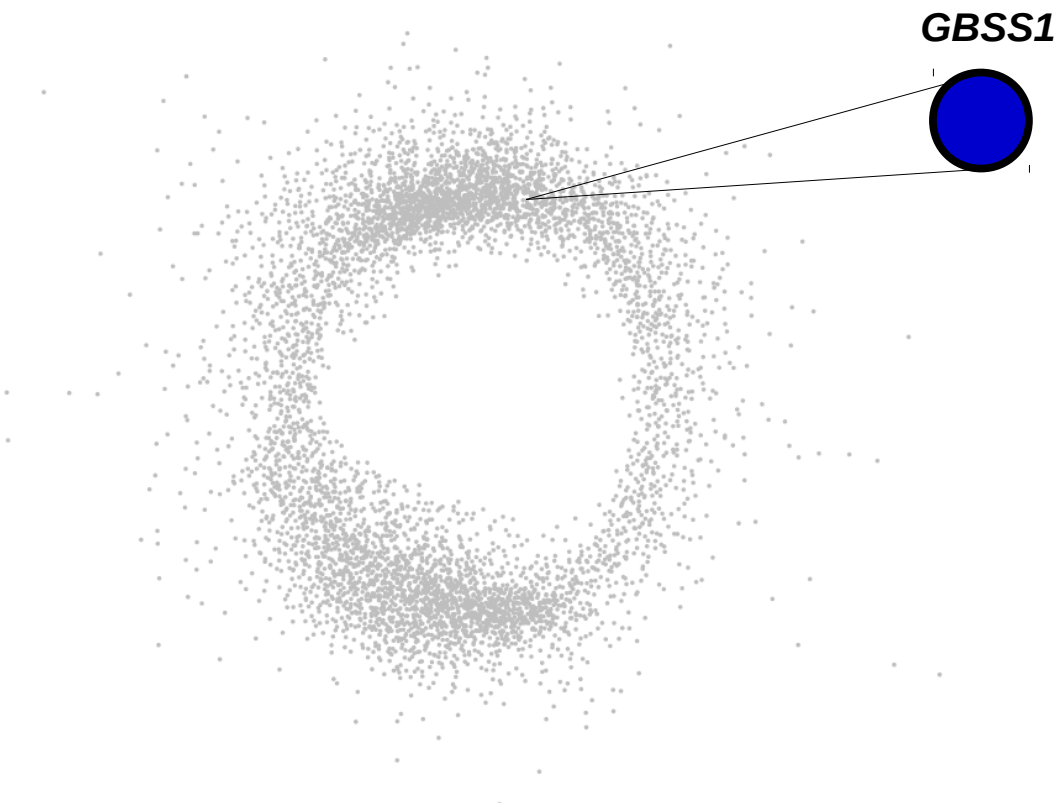

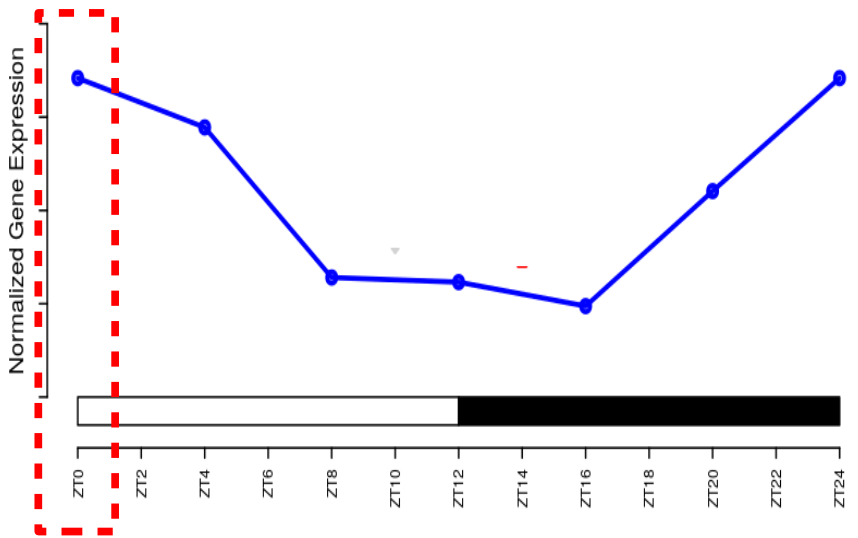

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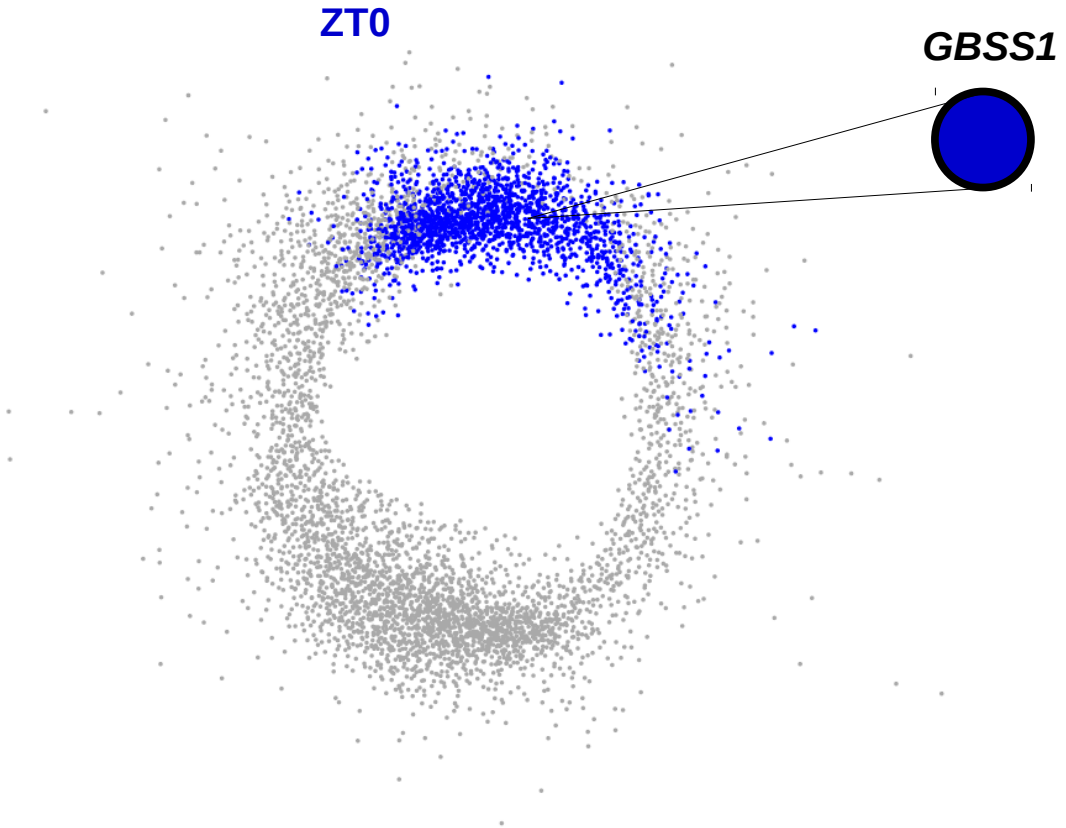

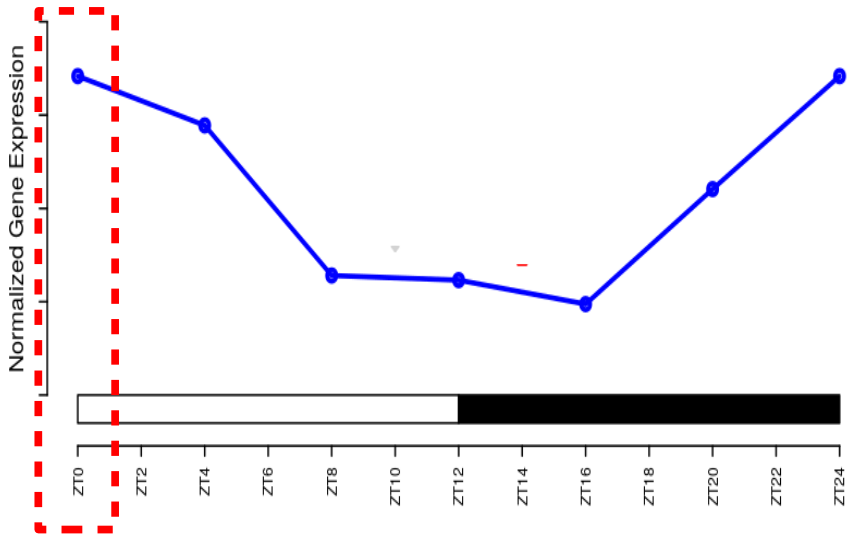

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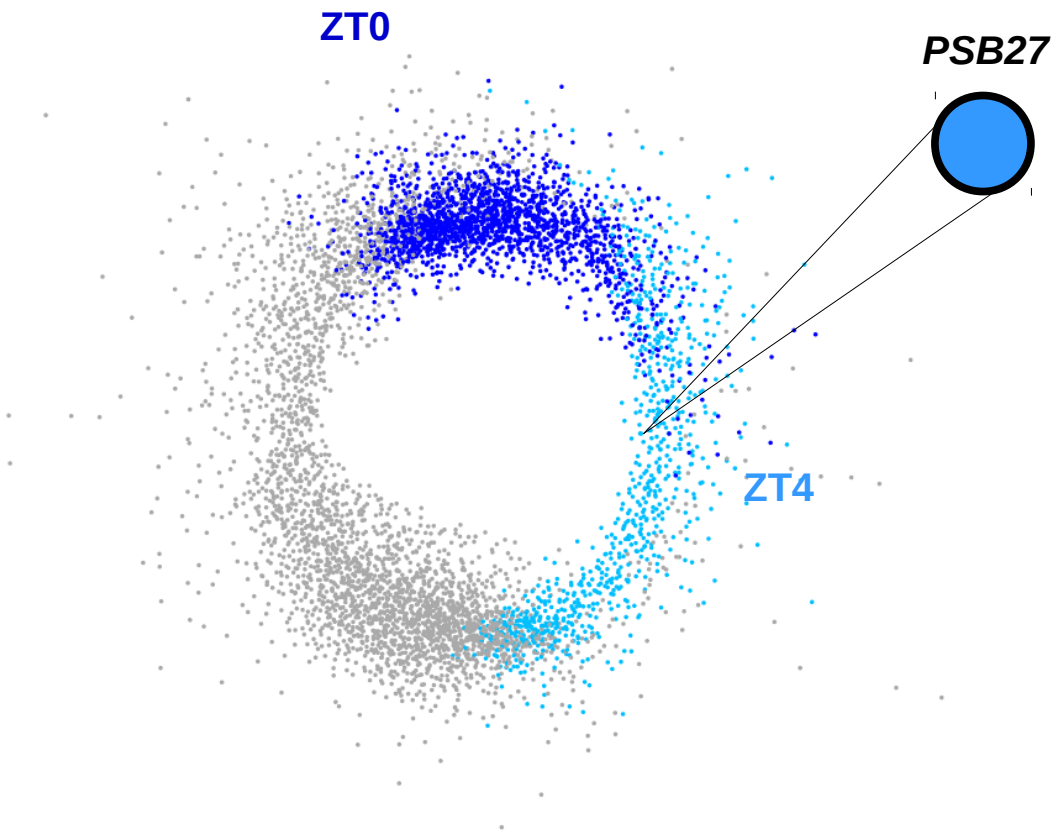

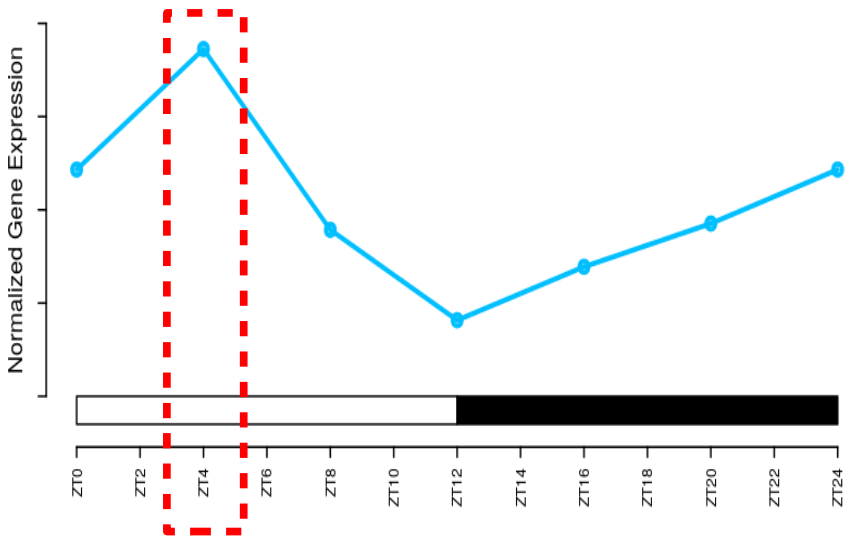

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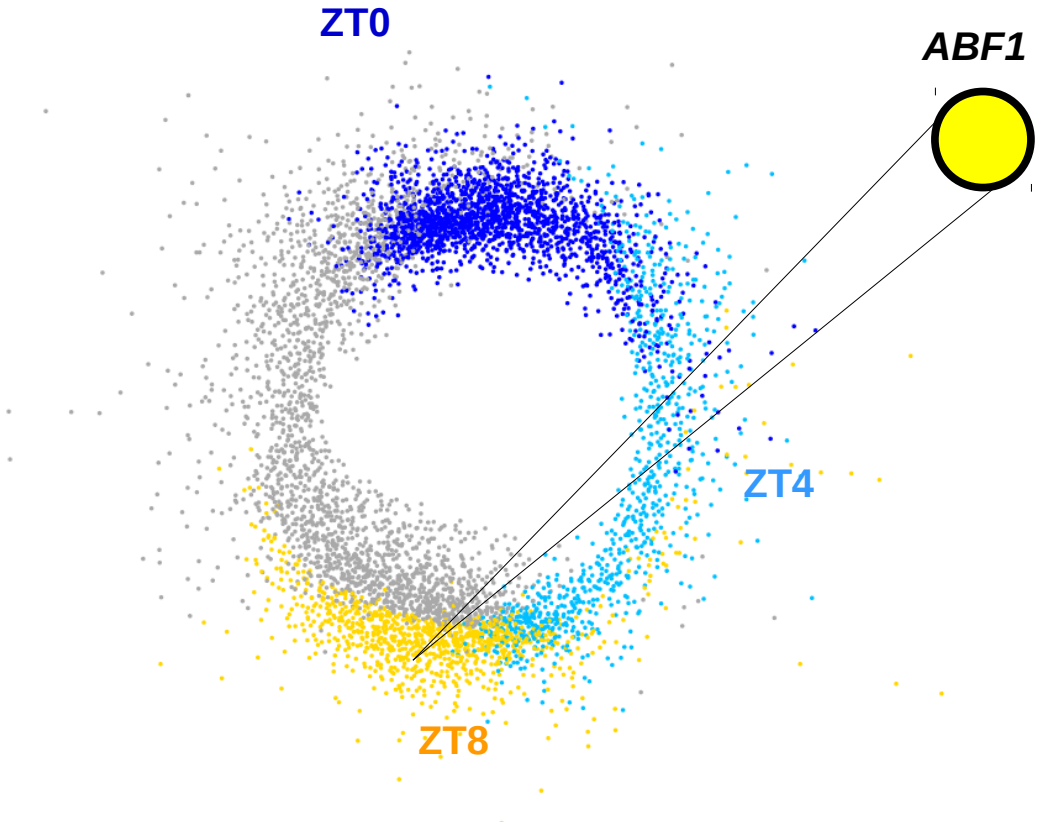

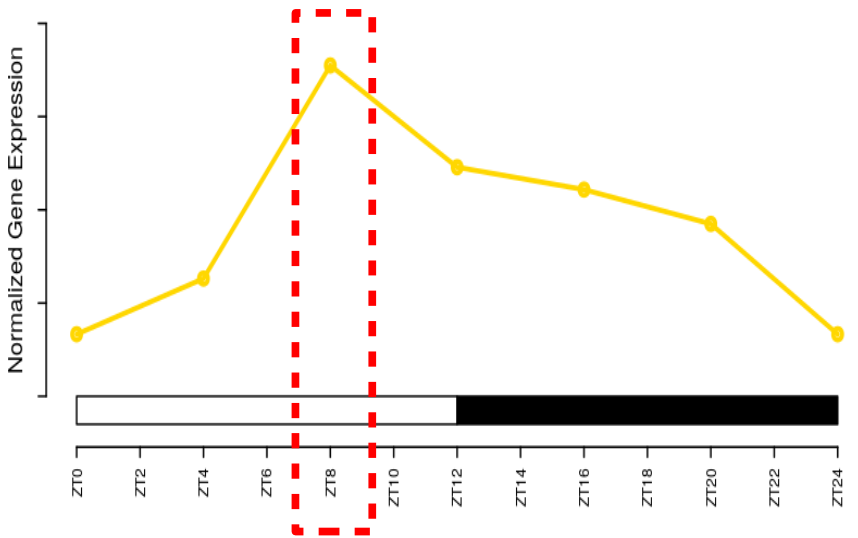

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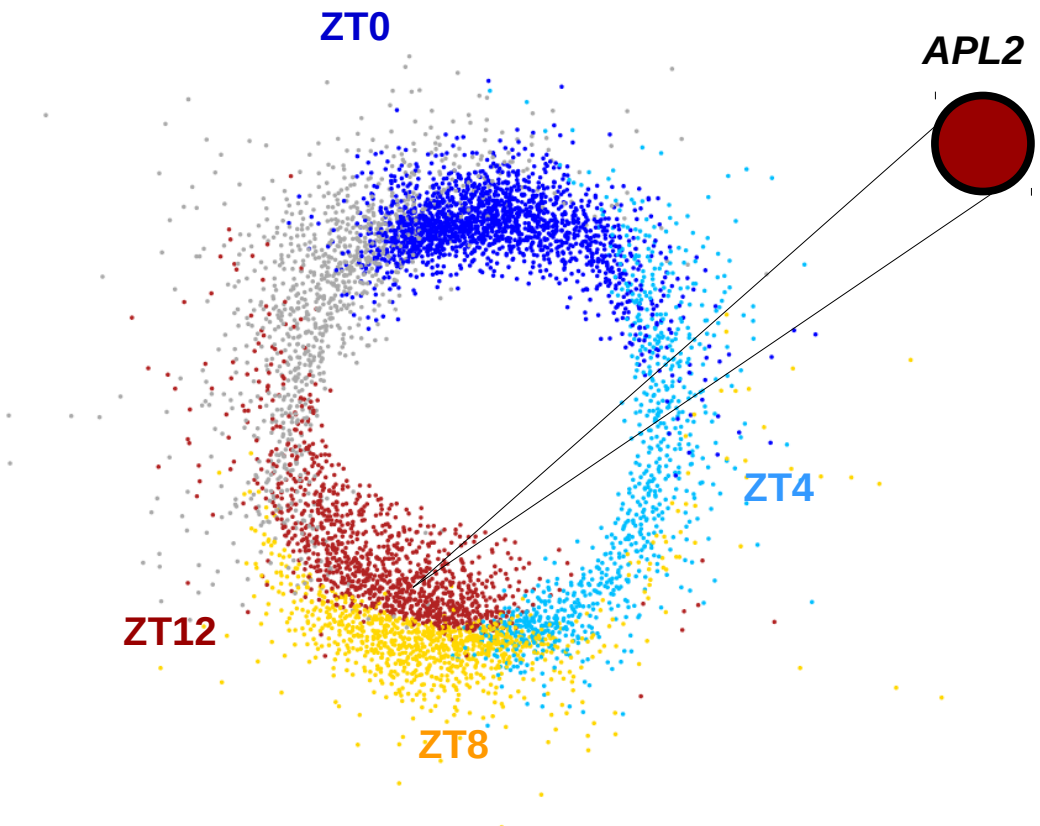

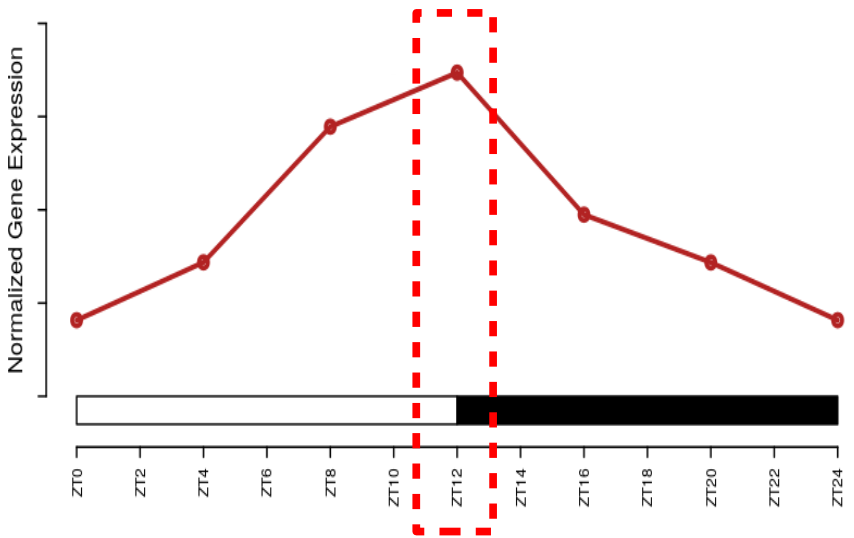

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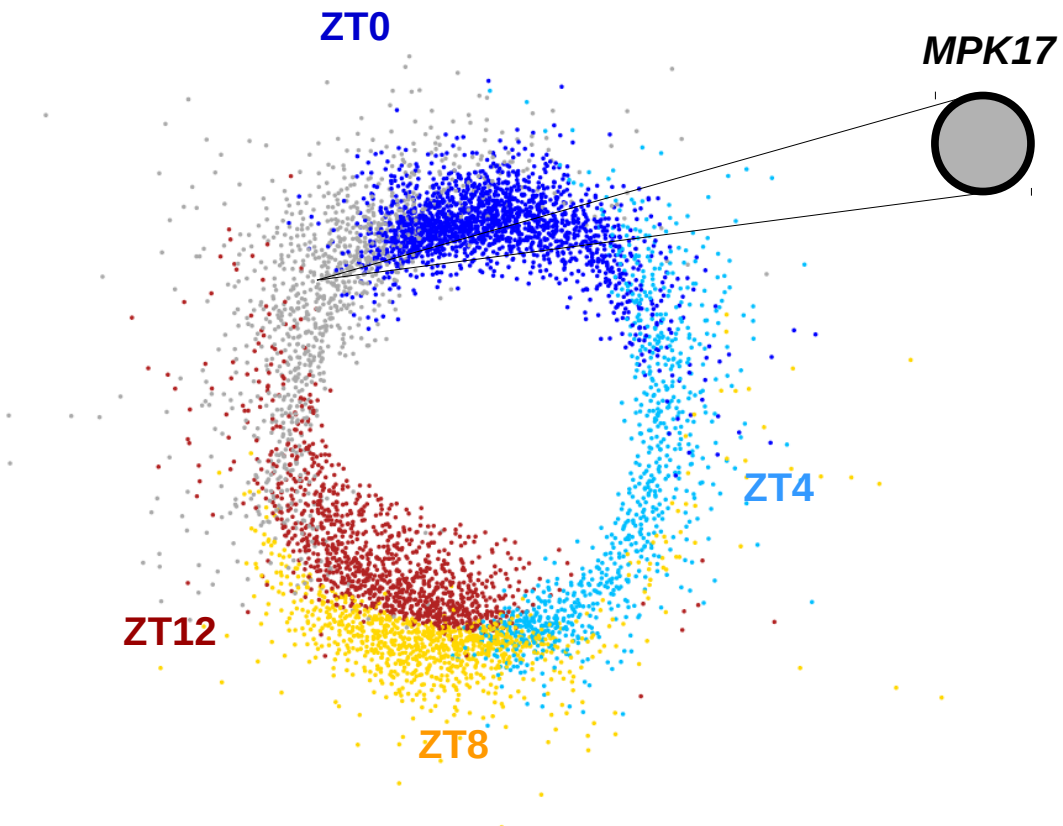

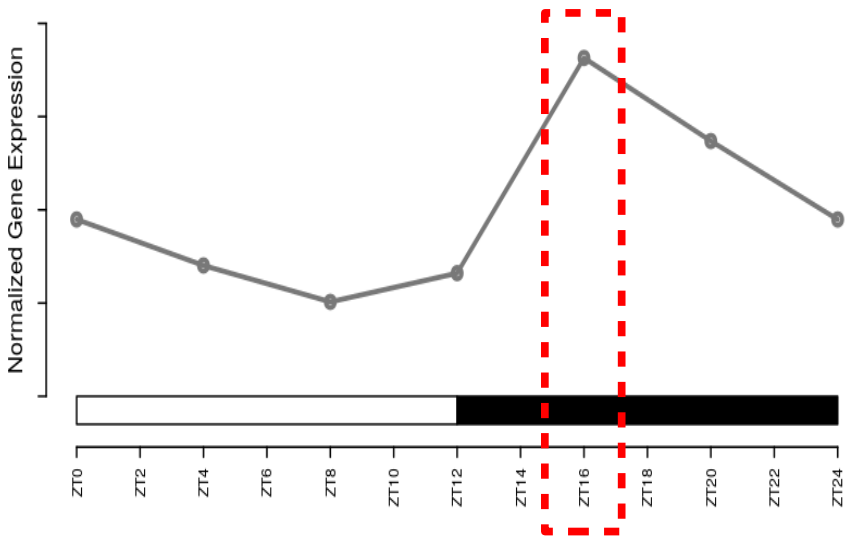

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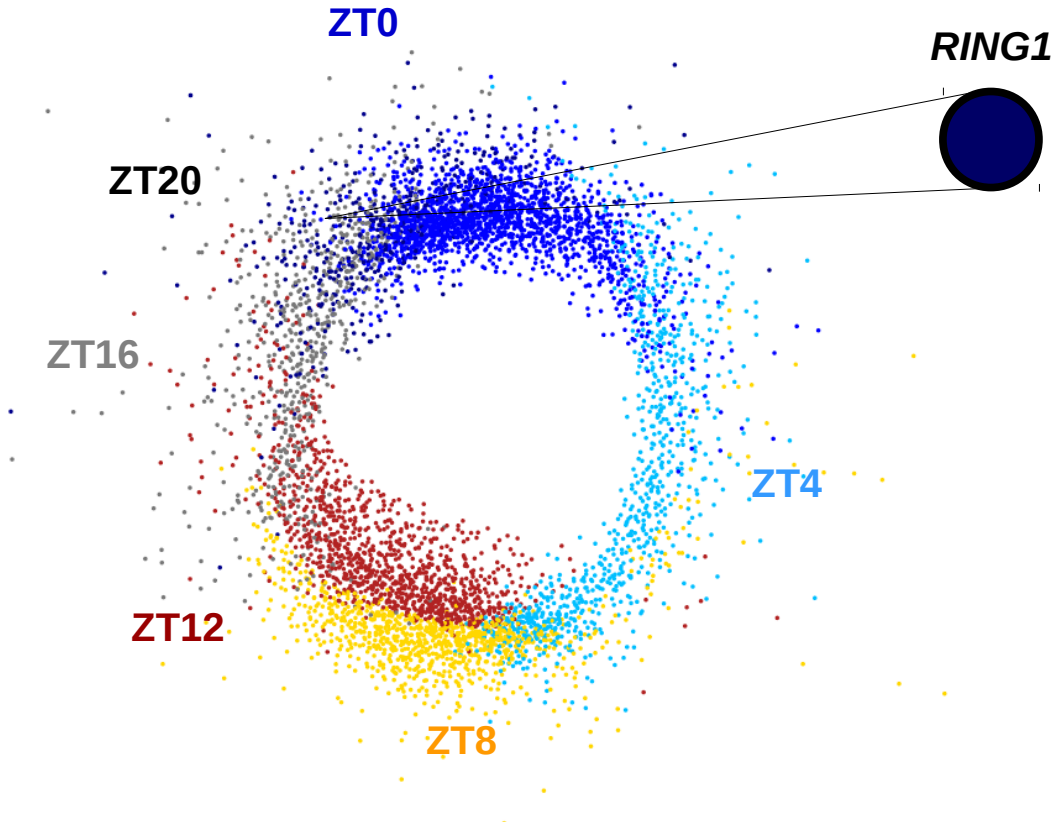
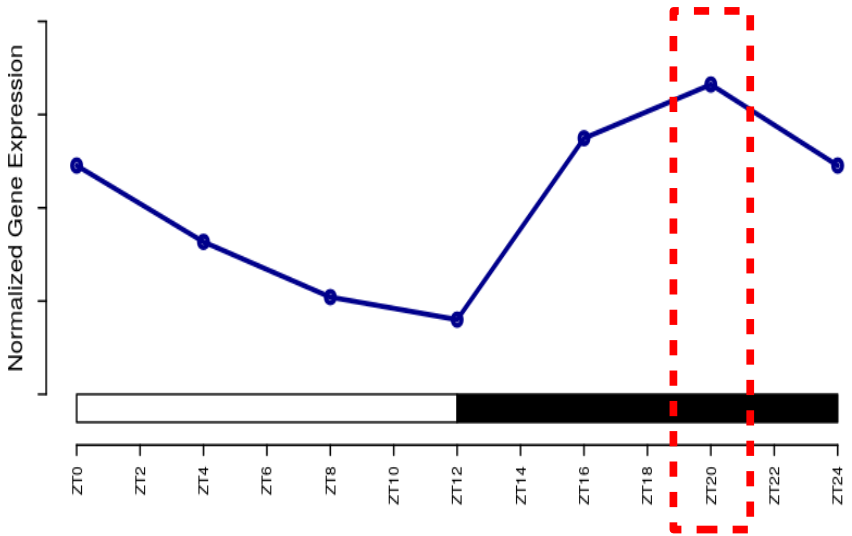




de los Reyes, Romero-Campero, et al (2017) Frontiers in Plant Science

Transcriptomics and Cistromics data accumulate in Data Bases for key regulators in the Circadian Clock

The Plant Cell, Vol. 17, 3257–3281, December 2005, www.plantcell.org © 2005 American Society of Plant Biologists

Gene Expression Omnibus

Sugars and Circadian Regulation Make Major Contributions to the Global Regulation of Diurnal Gene Expression in *Arabidopsis*

Oliver E. Bläsing,[a,1] Yves Gibon,[a] Manuela Günther,[a] Melanie Höhne,[a] Rosa Morcuende,[b] Daniel Osuna,[a] Oliver Thimm,[a] Björn Usadel,[a] Wolf-Rüdiger Scheible,[a] and Mark Stitt[a]

LNK genes integrate light and clock signaling networks at the core of the *Arabidopsis* oscillator

Matias L. Rugnone, Ana Faigón Soverna, Sabrina E. Sanchez, Ruben Gustavo Schlaen, Carlos Esteban Hernando, Danelle K. Seymour, Estefanía Mancini, Ariel Chernomoretz, Detlef Weigel, Paloma Más, and Marcelo J. Yanovsky

PNAS July 16, 2013 110 (29) 12120-12125; https://doi.org/10.1073/pnas.1302170110

RNA-seq / Microarray Data

NCBI SRA

Mapping the Core of the *Arabidopsis* Circadian Clock Defines the Network Structure of the Oscillator

W. Huang[1], P. Pérez-García[1], A. Pokhilko[2], A. J. Millar[2,3], I. Antoshechkin[4], J. L. Riechmann[1,4,5], P. Mas[1,*]
+ See all authors and affiliations

Science 06 Apr 2012:
Vol. 336, Issue 6077, pp. 75-79
DOI: 10.1126/science.1219075

Transcriptional repressor PRR5 directly regulates clock-output pathways

Norihito Nakamichi[a,b,c,d,1], Takatoshi Kiba[c], Mari Kamioka[b], Takamasa Suzuki[e,f], Takafumi Yamashino[b], Tetsuya Higashiyama[e,f], Hitoshi Sakakibara[c], and Takeshi Mizuno[b]

The Evening Complex coordinates environmental and endogenous signals in *Arabidopsis*

Daphne Ezer[1], Jae-Hoon Jung[1], Hui Lan[1], Surojit Biswas[1,†], Laura Gregoire[2], Mathew S. Box[1], Varodom Charoensawan[1,3], Sandra Cortijo[1], Xuelei Lai[1,2], Dorothee Stöckle[1], Chloe Zubieta[1], Katja E. Jaeger[1], and Philip A. Wigge[1]

The Plant Cell, Vol. 28: 696–711, March 2016, www.plantcell.org © 2016 American Society of Plant Biologists. All rights reserved.

Direct Repression of Evening Genes by CIRCADIAN CLOCK-ASSOCIATED1 in the Arabidopsis Circadian Clock[OPEN]

Mari Kamioka,[a] Saori Takao,[b] Takamasa Suzuki,[c,d,e] Kyomi Taki,[e] Tetsuya Higashiyama,[b,c,e] Toshinori Kinoshita,[b,e] and Norihito Nakamichi[b,e,1]

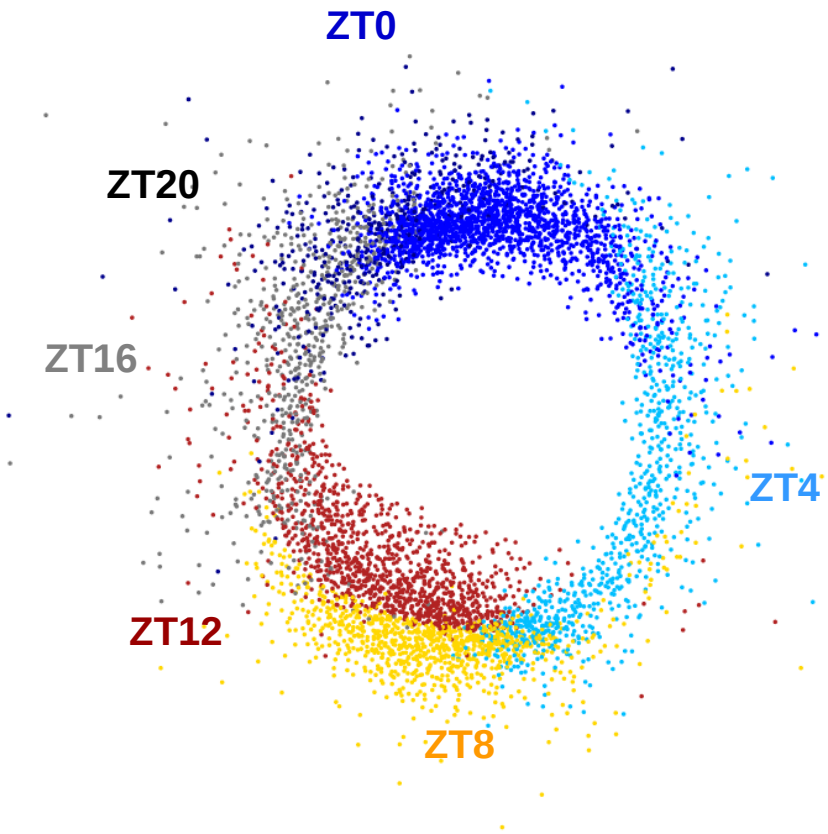
Cryptochromes Interact Directly with PIFs to Control Plant Growth in Limiting Blue Light

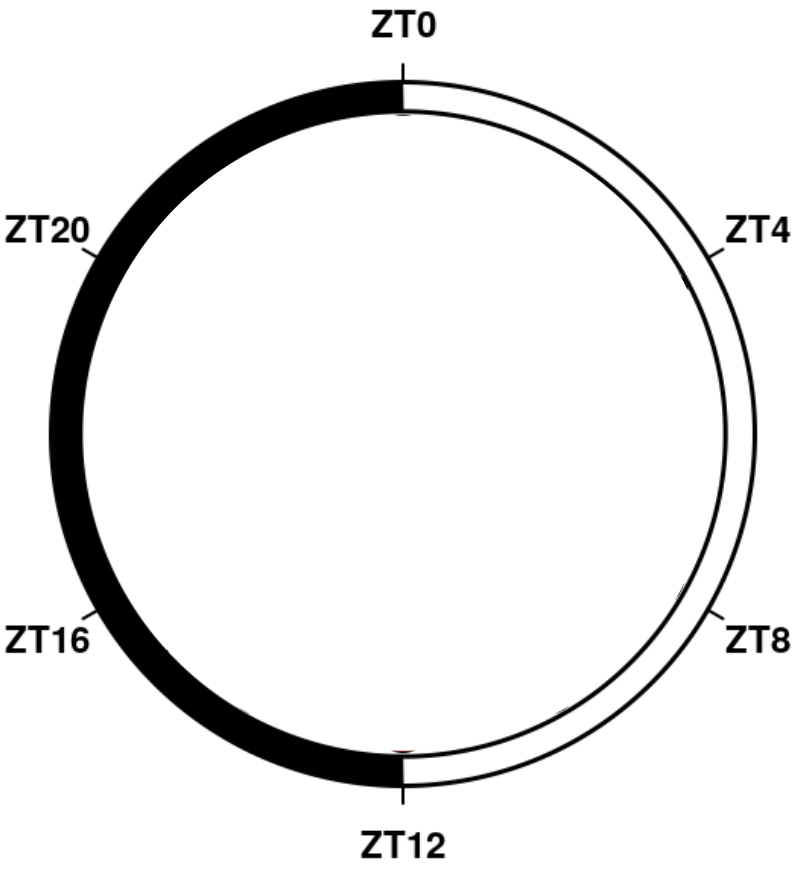
Ullas V. Pedmale,[1,2,*] Shao-shan Carol Huang,[2,3] Mark Zander,[2] Benjamin J. Cole,[2,4,8] Jonathan Hetzel,[2,4] Karin Ljung,[5] Pedro A.B. Reis,[2,6] Priya Sridevi,[7] Kazumasa Nito,[2] Joseph R. Nery,[3] Joseph R. Ecker,[1,2,3] and Joanne Chory[1,2,*]

... ...

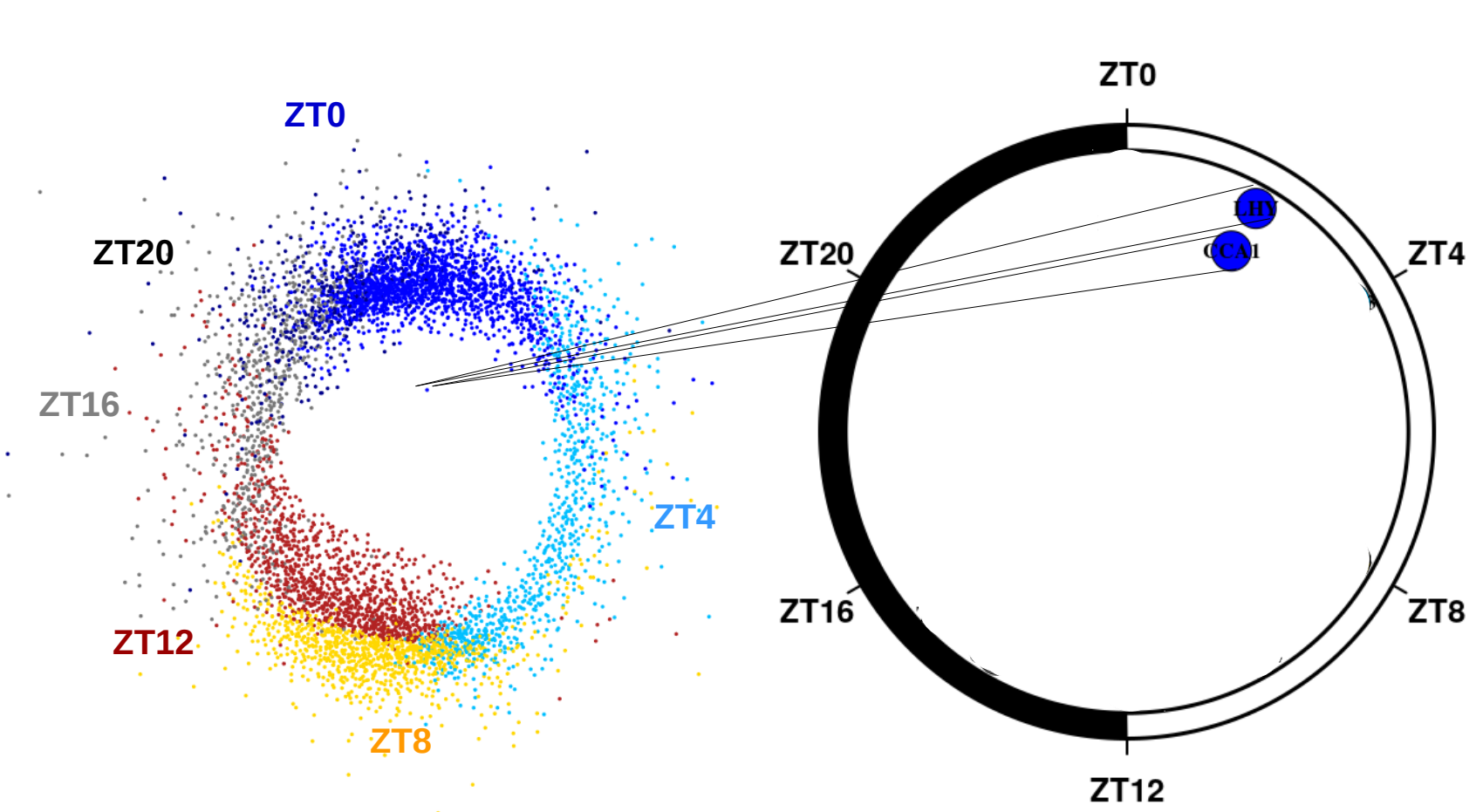
ChIP-seq Data

ATTRACTOR, a Transcriptional Network integrating key Circadian Regulators and Light Signaling

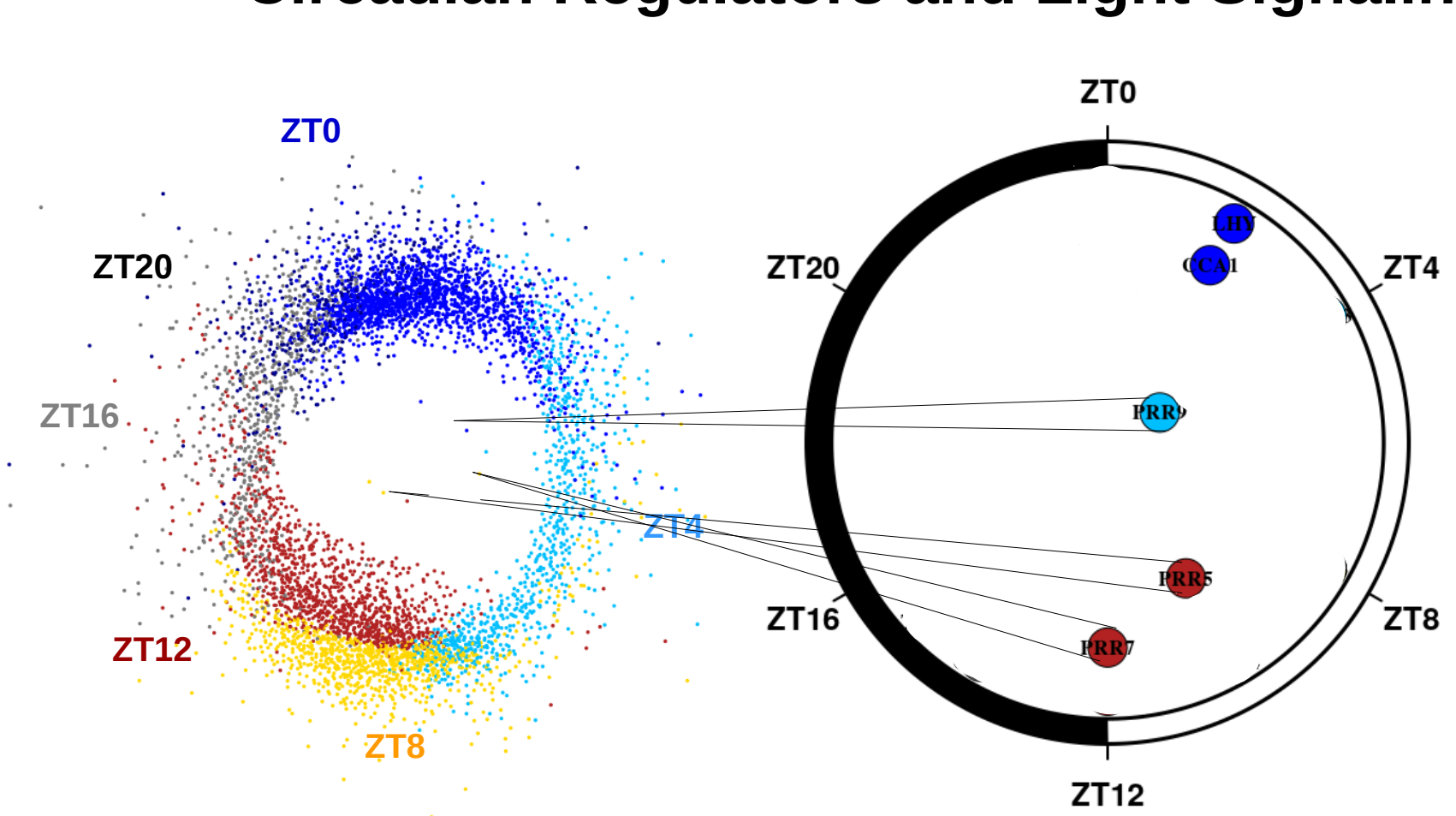




ATTRACTOR, a Transcriptional Network integrating key Circadian Regulators and Light Signaling

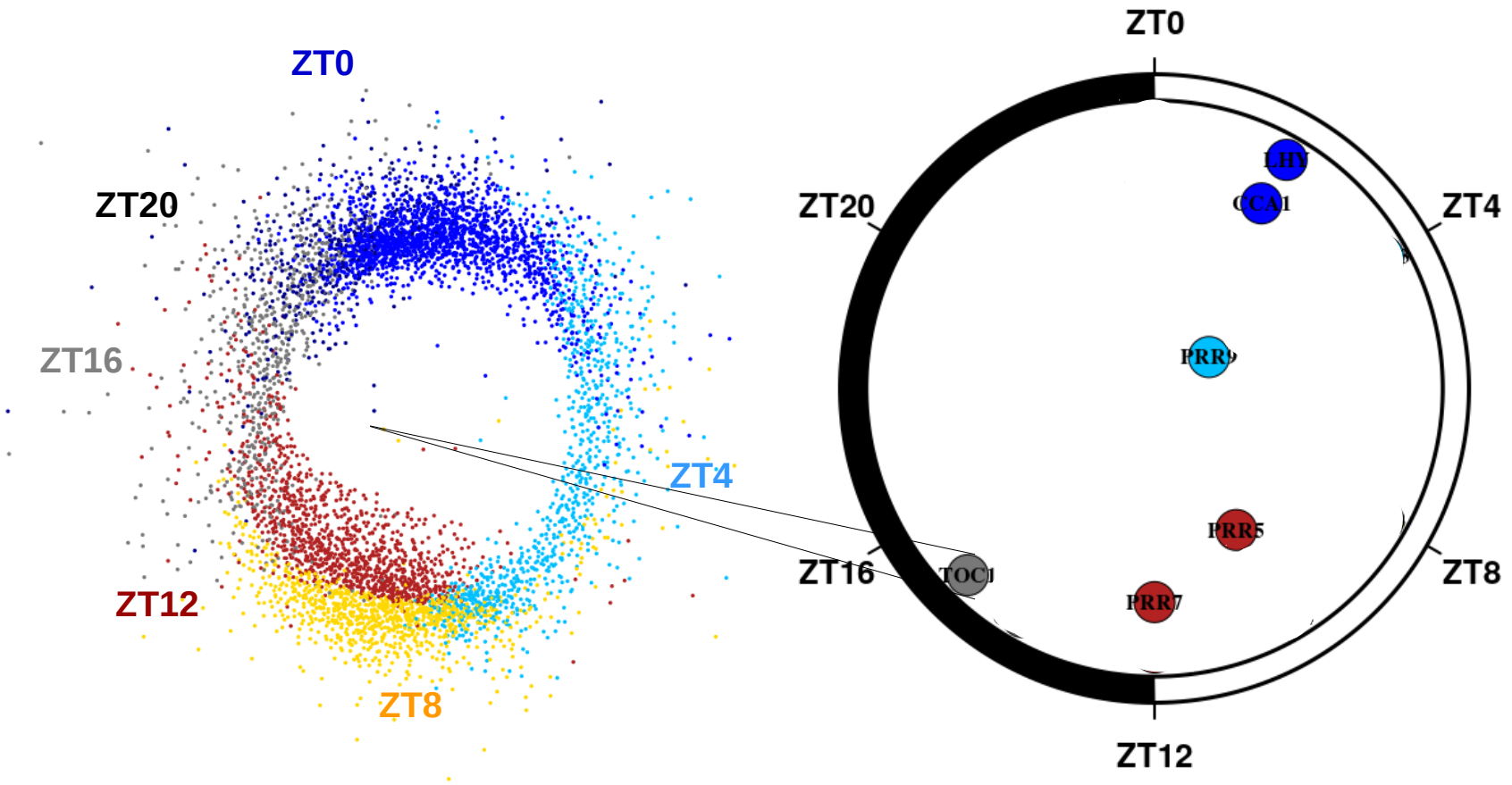


ATTRACTOR, a Transcriptional Network integrating key Circadian Regulators and Light Signaling



CCA1
LHY
PRR9
PRR7
PRR5
Morning Loop

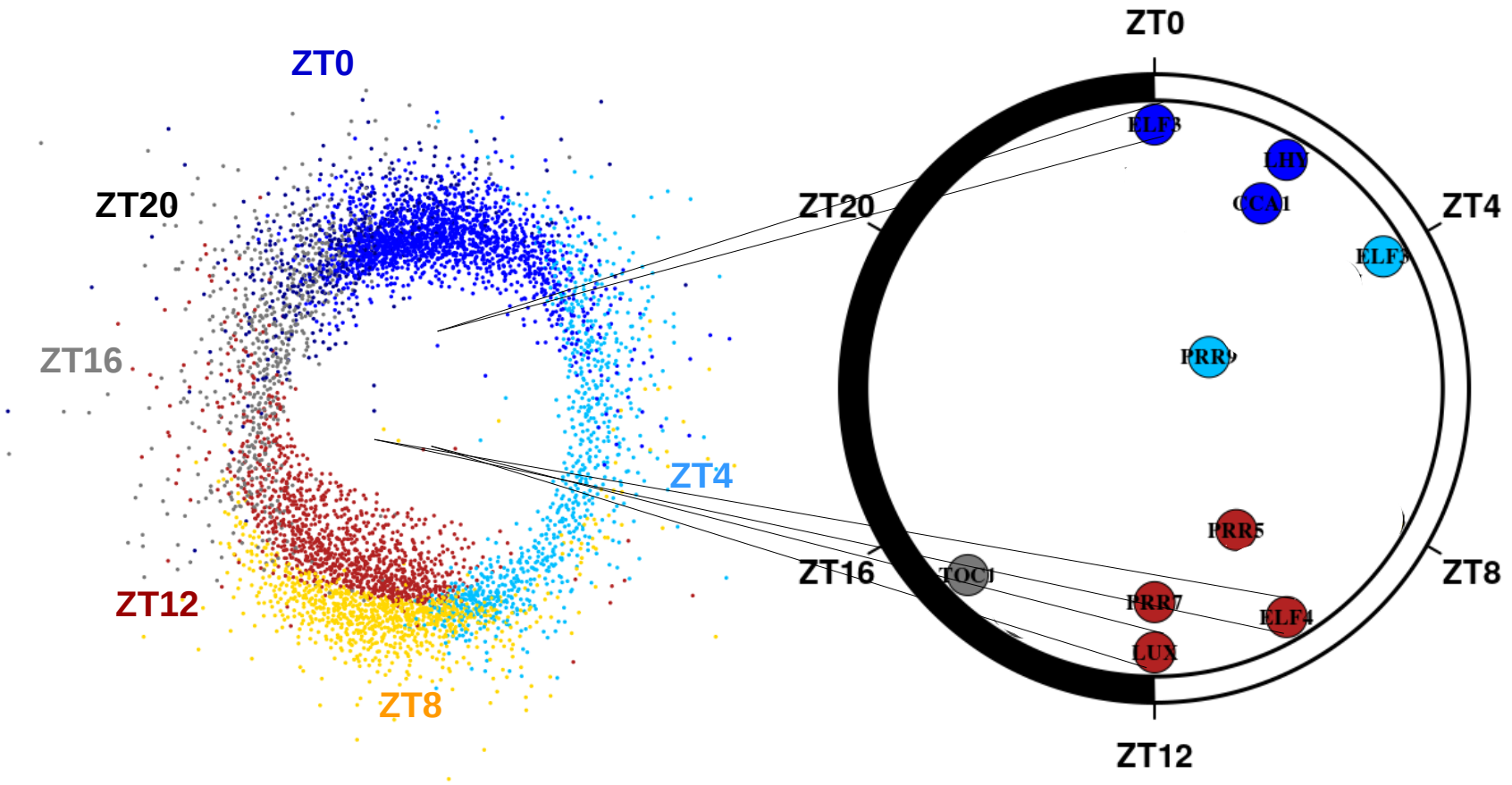
ATTRACTOR, a Transcriptional Network integrating key Circadian Regulators and Light Signaling



CCA1
LHY
PRR9
PRR7
PRR5
TOC1

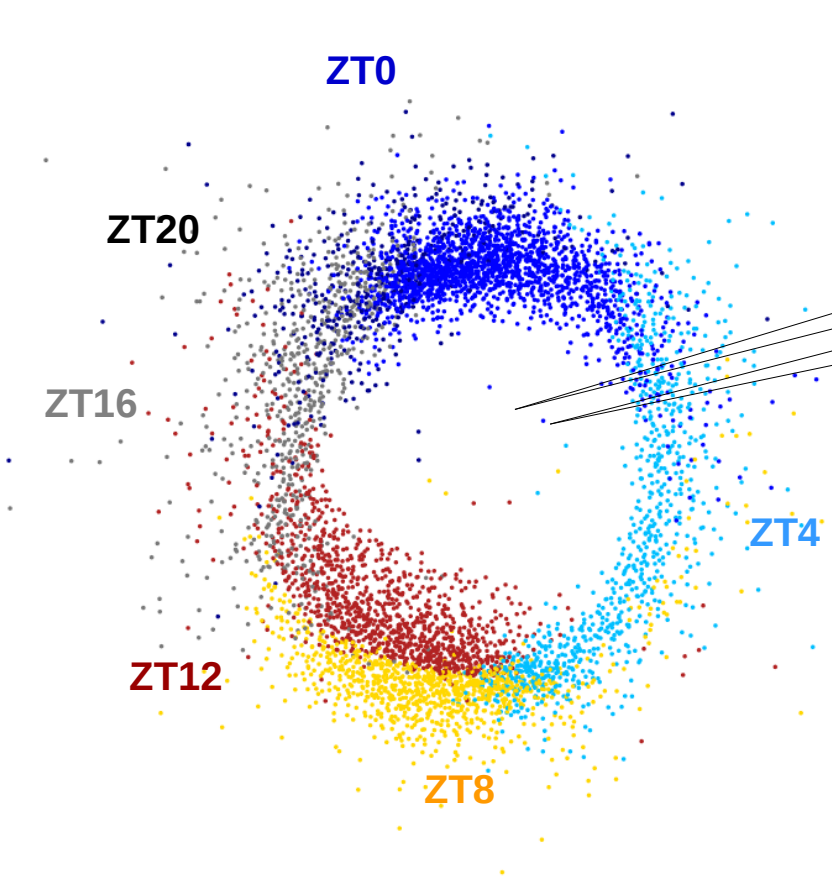
Morning Loop

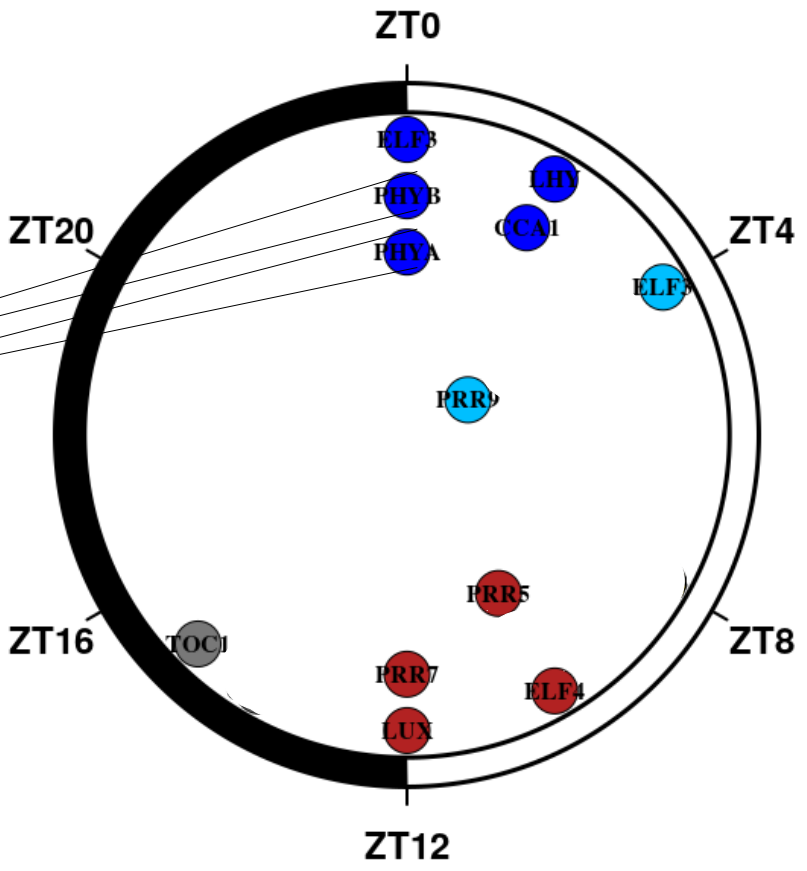
ATTRACTOR, a Transcriptional Network integrating key Circadian Regulators and Light Signaling



CCA1
LHY
PRR9
PRR7
PRR5
Morning Loop
TOC1
LUX
ELF3
ELF4
Evening Loop

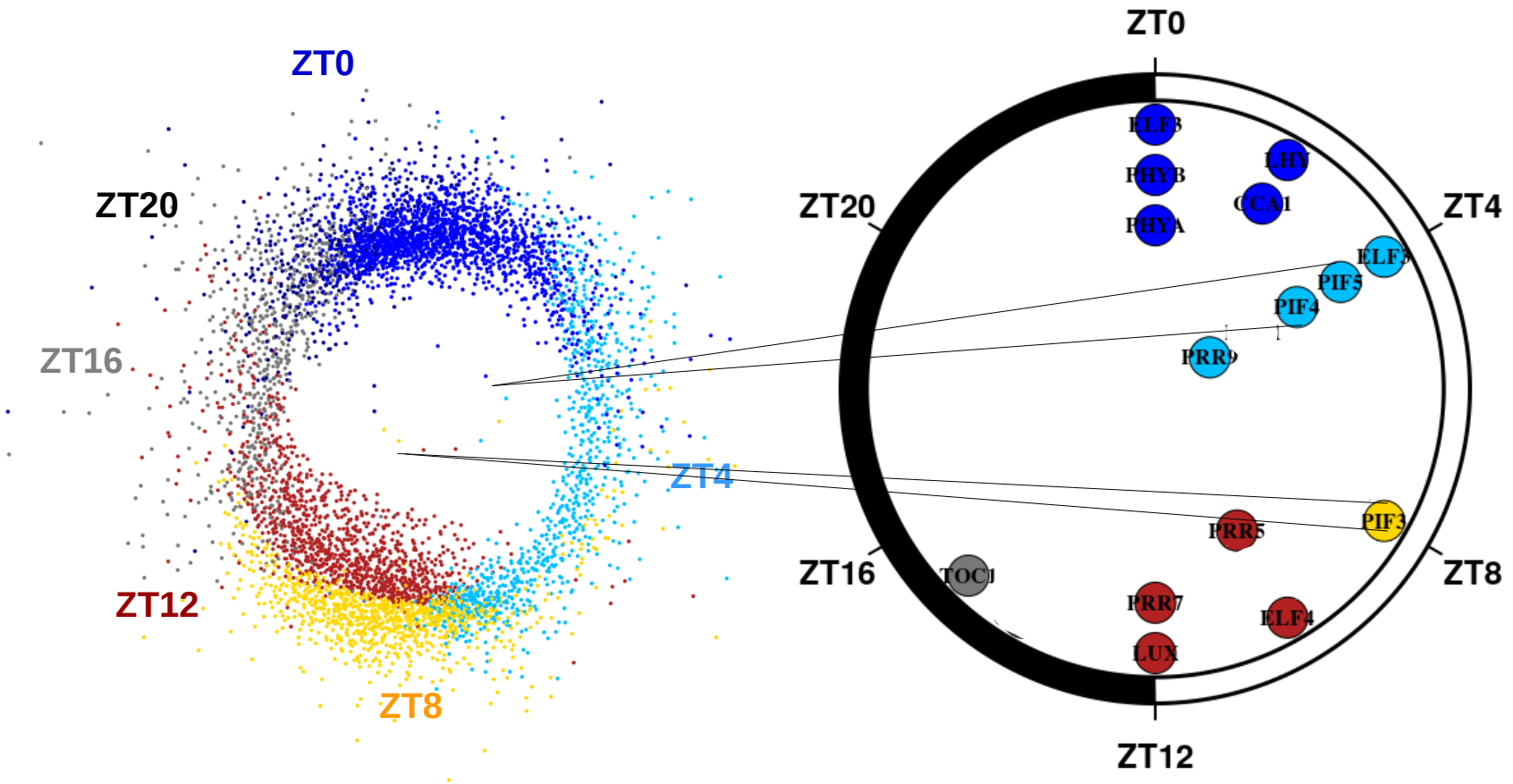
ATTRACTOR, a Transcriptional Network integrating key Circadian Regulators and Light Signaling





CCA1
LHY
PRR9
PRR7
PRR5
Morning Loop
TOC1
LUX
ELF3
ELF4
Evening Loop
PHYA
PHYB

ATTRACTOR, a Transcriptional Network integrating key Circadian Regulators and Light Signaling



CCA1
LHY
PRR9
PRR7
PRR5

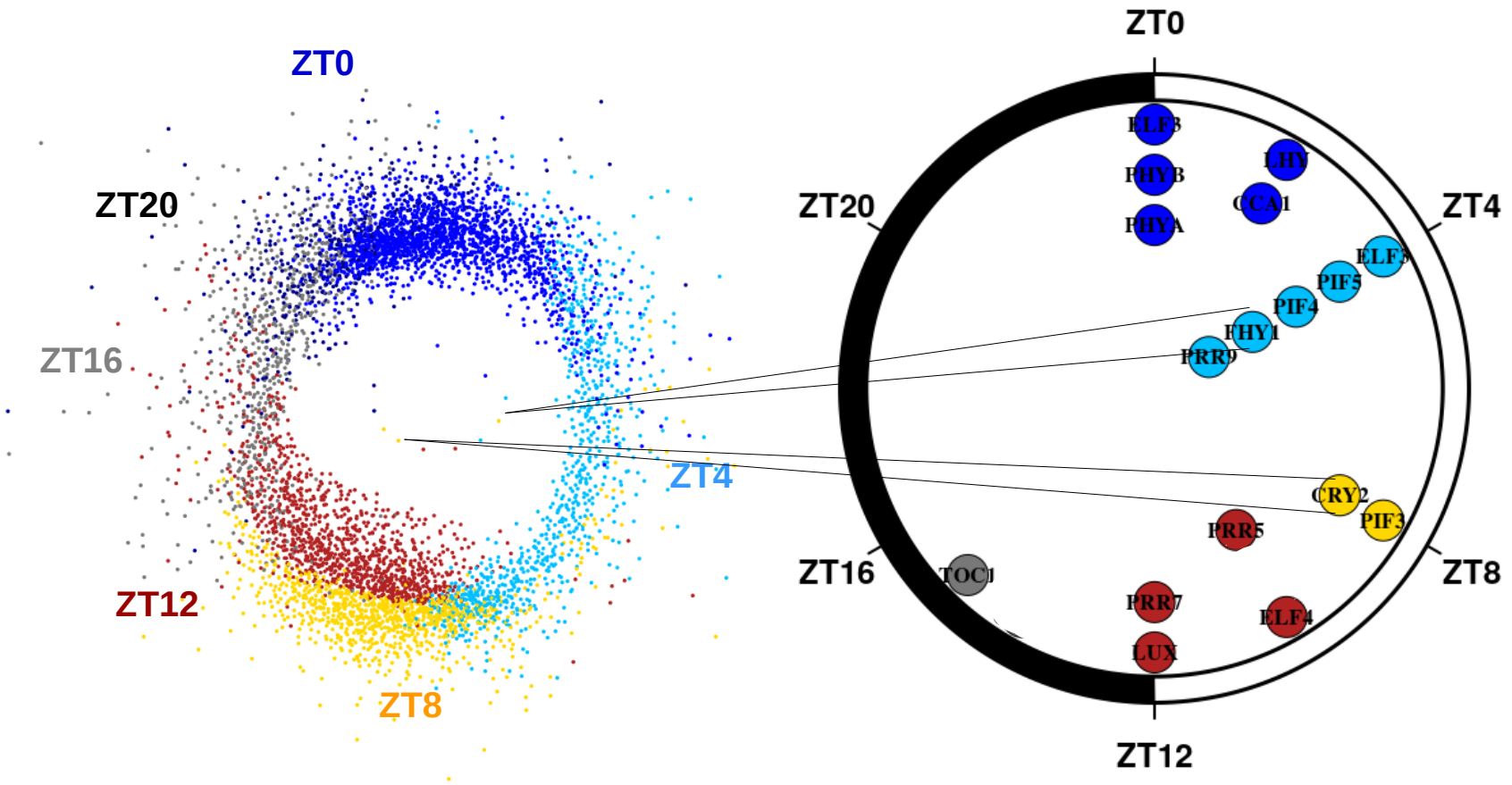
Morning Loop

TOC1
LUX
ELF3
ELF4

Evening Loop

PHYA
PHYB
PIF3
PIF4
PIF5

ATTRACTOR, a Transcriptional Network integrating key Circadian Regulators and Light Signaling

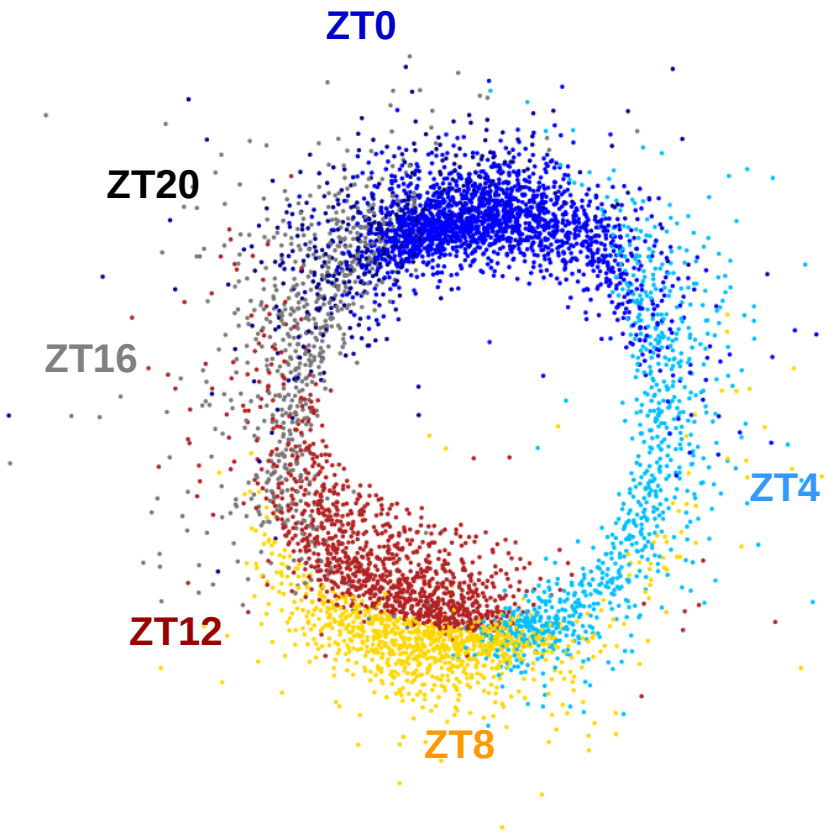


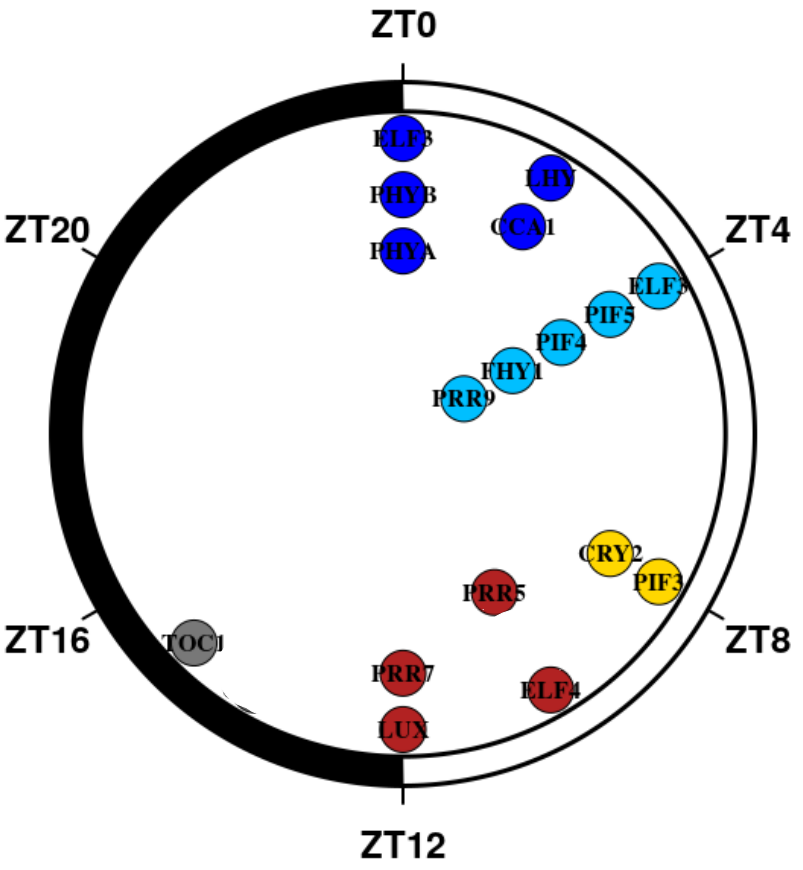
CCA1
LHY
PRR9
PRR7
PRR5
Morning Loop

TOC1
LUX
ELF3
ELF4
Evening Loop

PHYA
PHYB
PIF3
PIF4
PIF5
CRY2
FHY1
Light Signalling

ATTRACTOR, a Transcriptional Network integrating key Circadian Regulators and Light Signaling





CCA1
LHY

PRR9
PRR7
PRR5

Morning Loop

TOC1

LUX
ELF3
ELF4

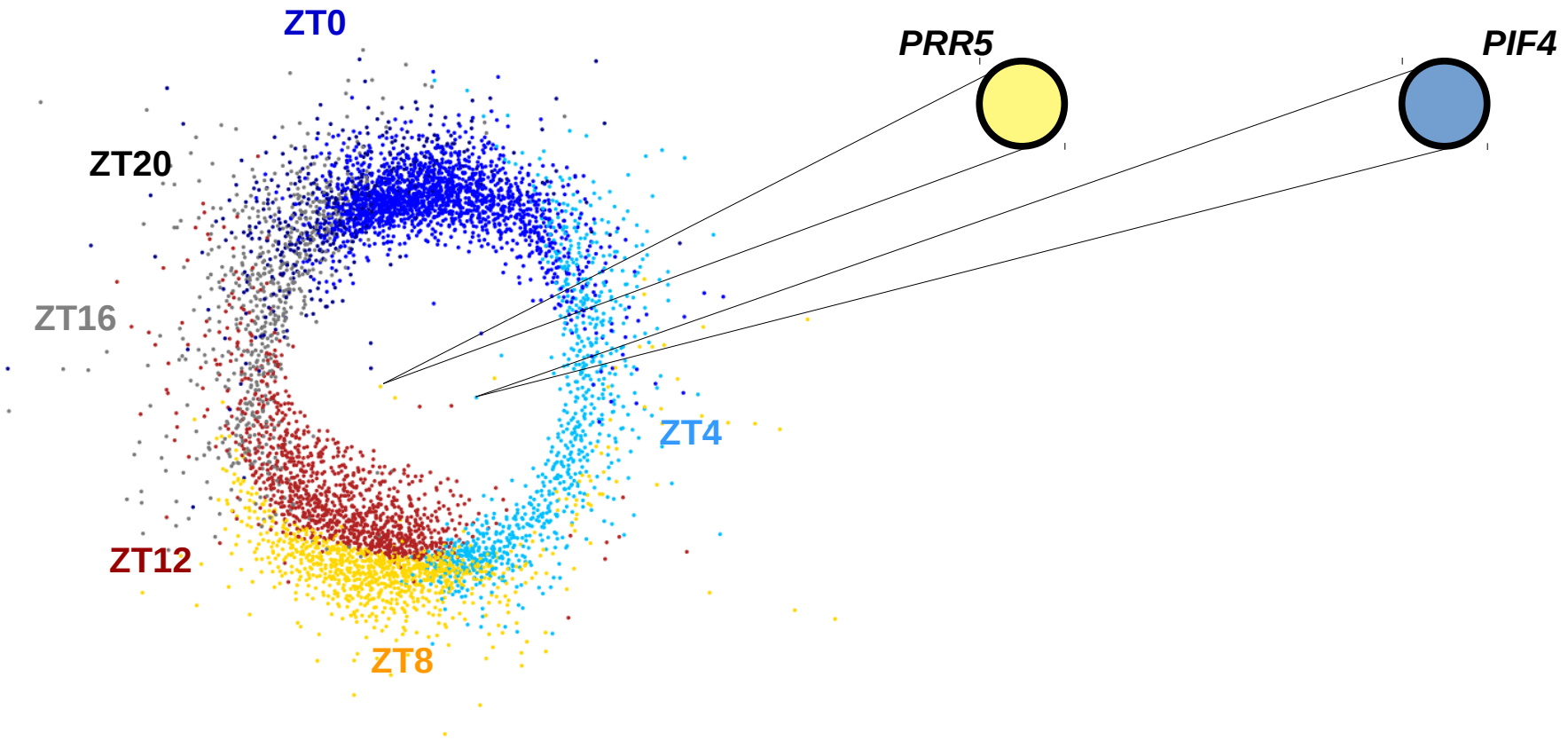
Evening Loop

PHYA
PHYB
PIF3
PIF4
PIF5

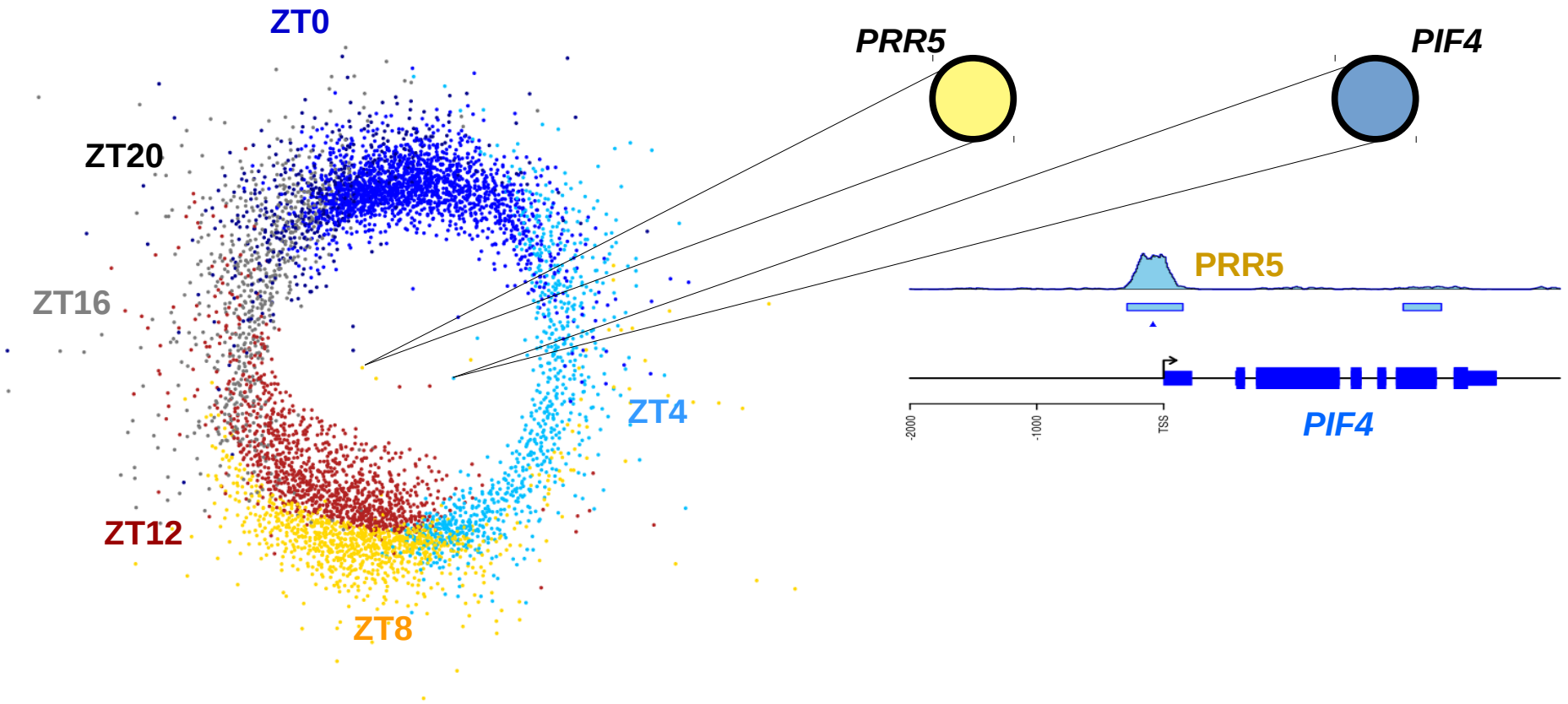
CRY2
FHY1

Light Signaling

Transcriptional regulations are assigned a positive/negative/neutral effect depending on the target expression profile



Transcriptional regulations are assigned a positive/negative/neutral effect depending on the target expression profile



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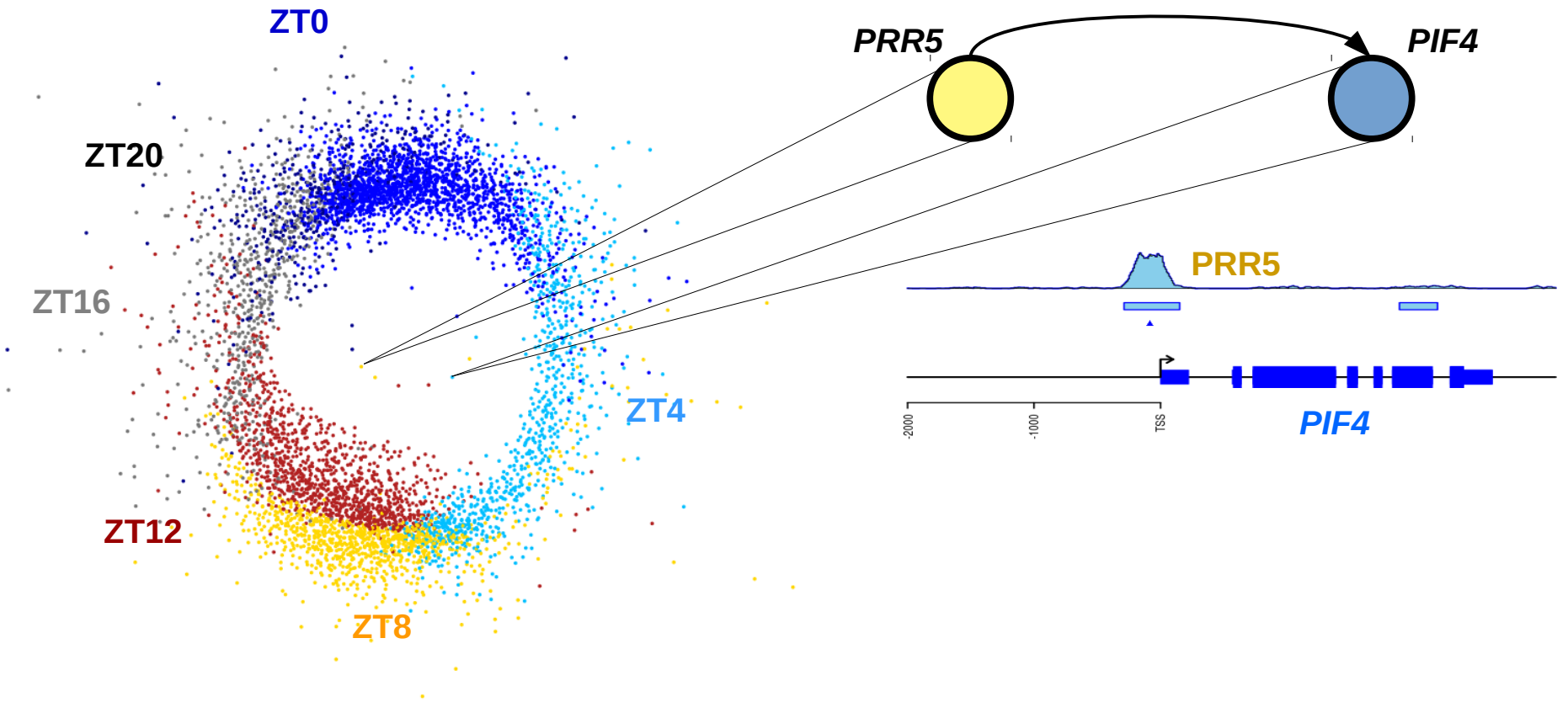

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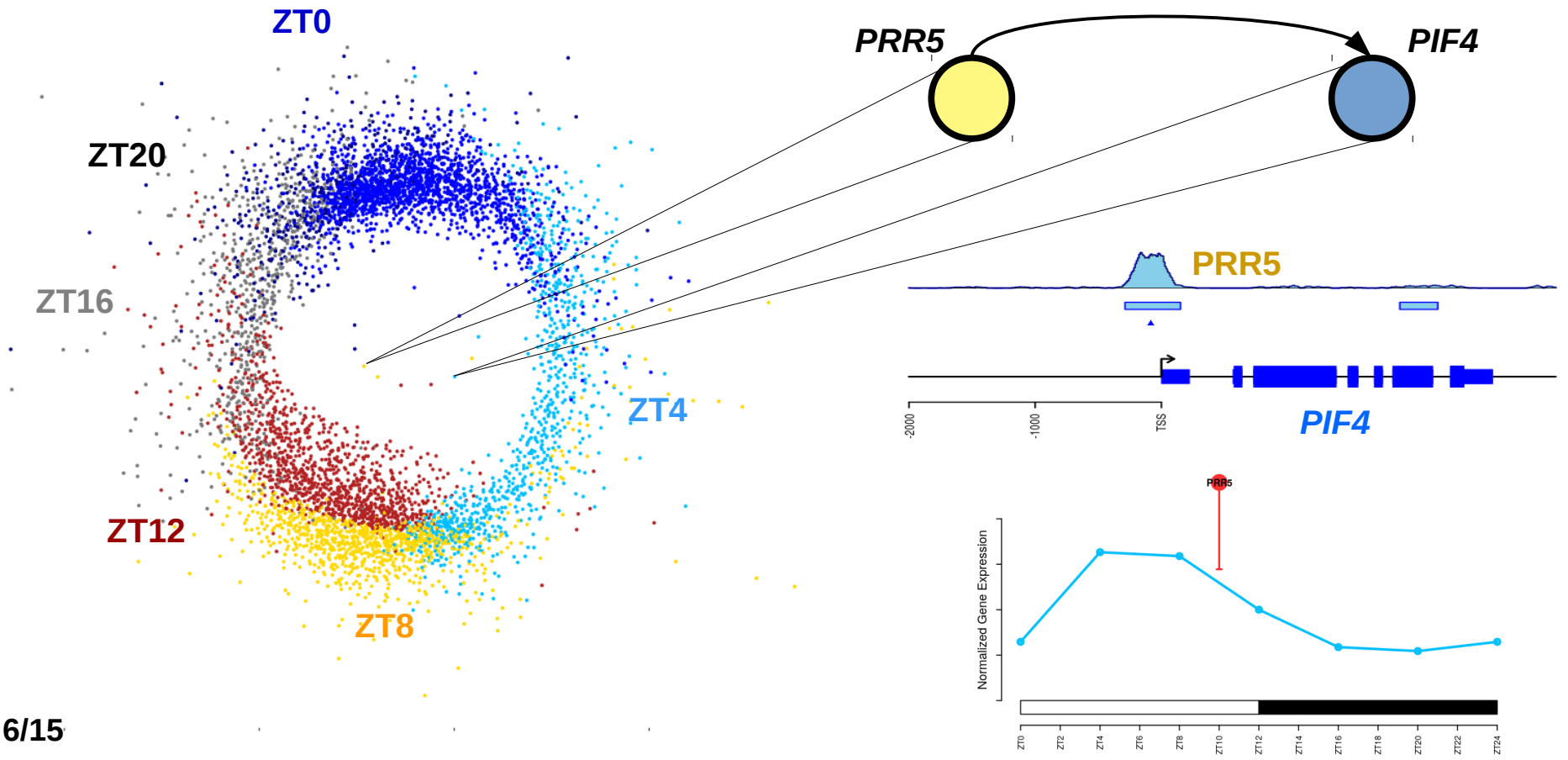
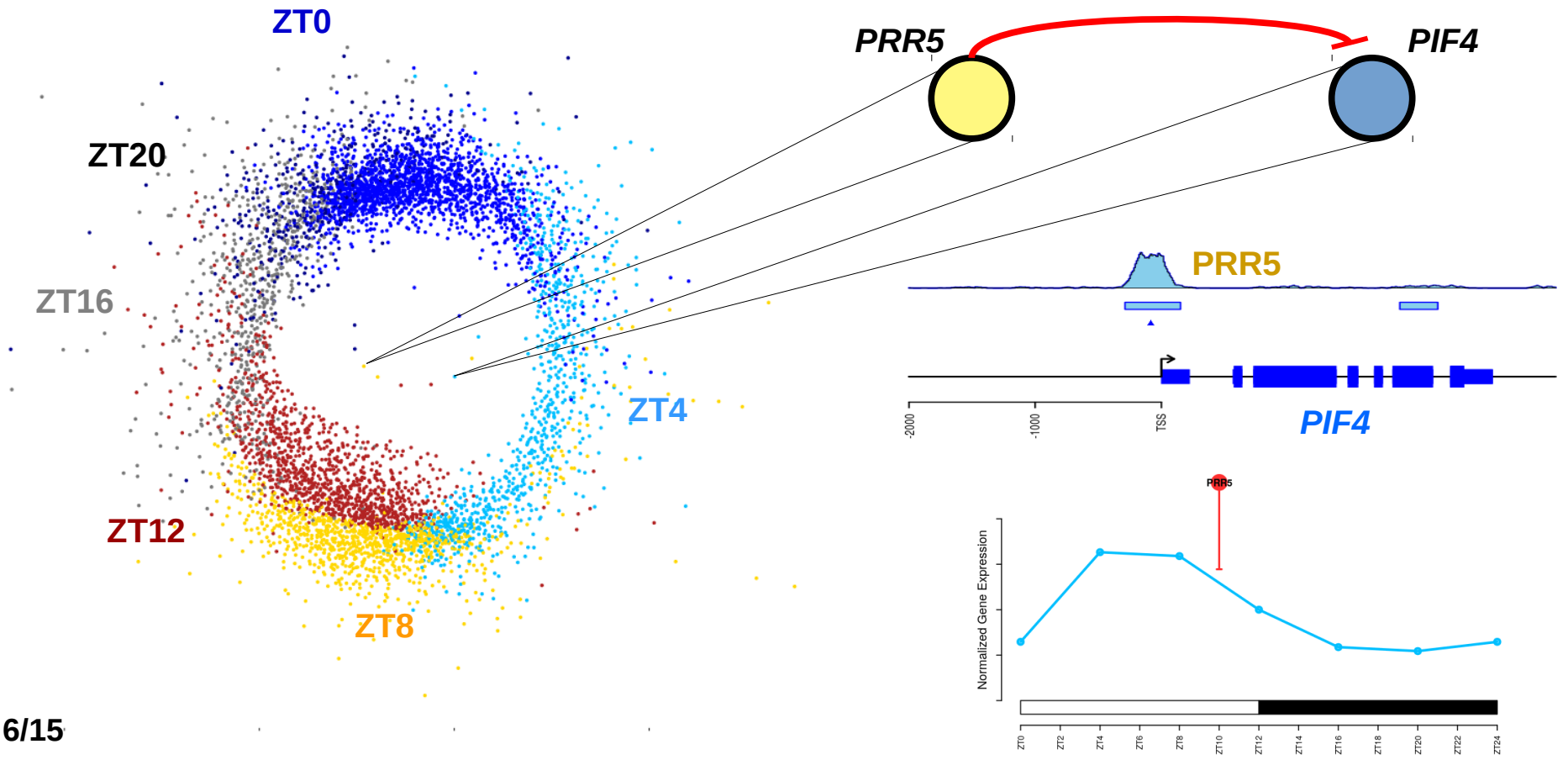
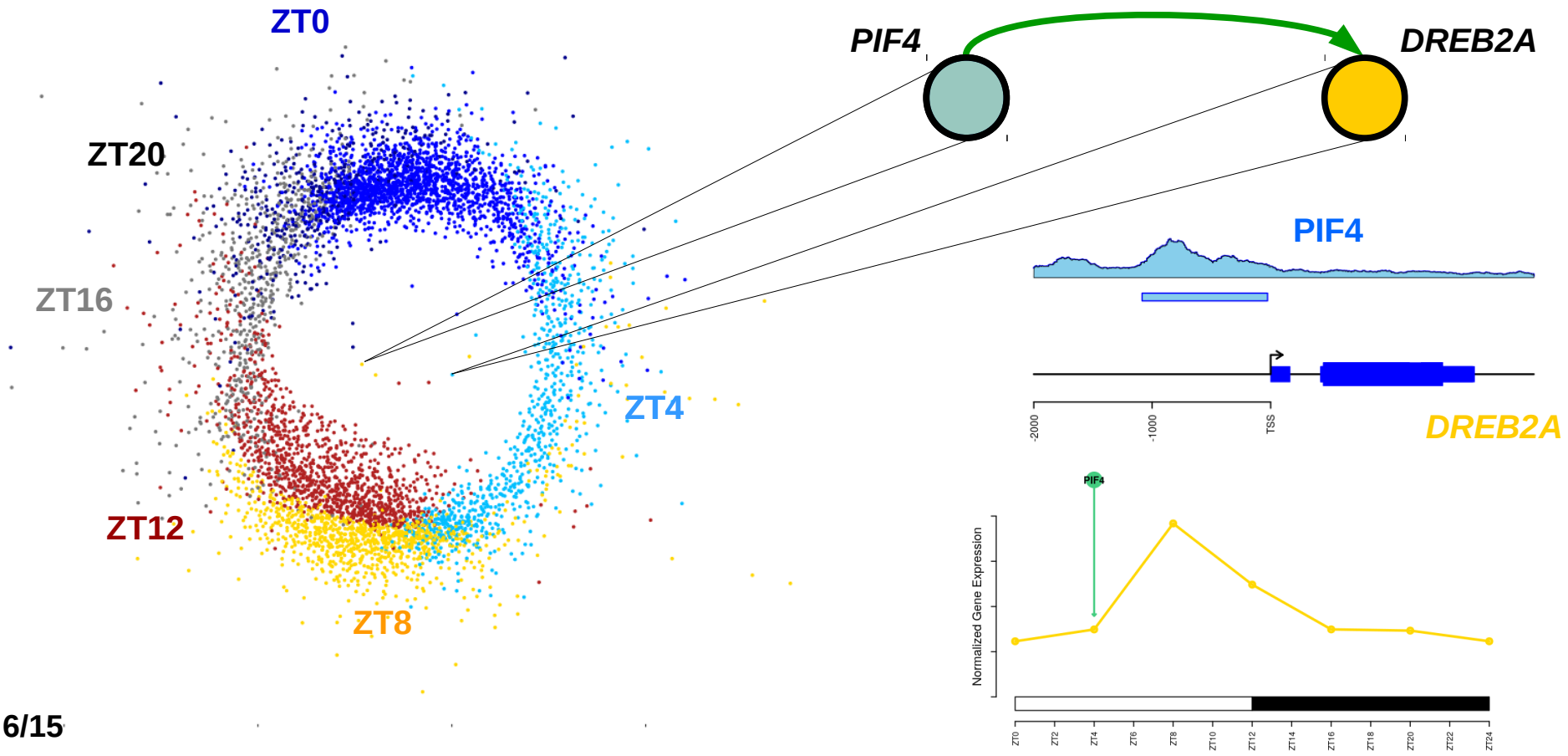


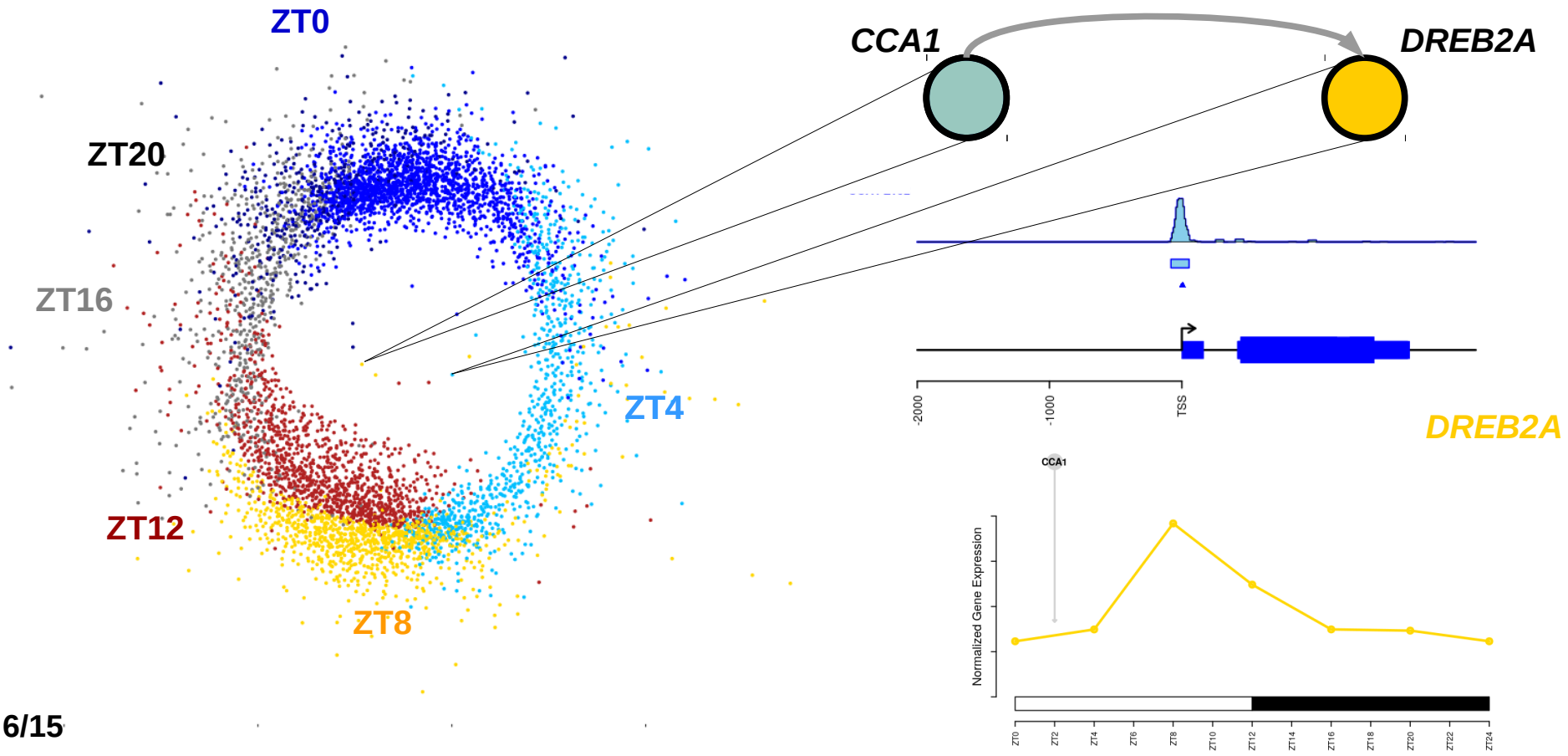
Transcriptional regulations are assigned a positive/negative/neutral effect depending on the target expression profile



Transcriptional regulations are assigned a positive/negative/neutral effect depending on the target expression profile



Transcriptional regulations are assigned a positive/negative/neutral effect depending on the target expression profile



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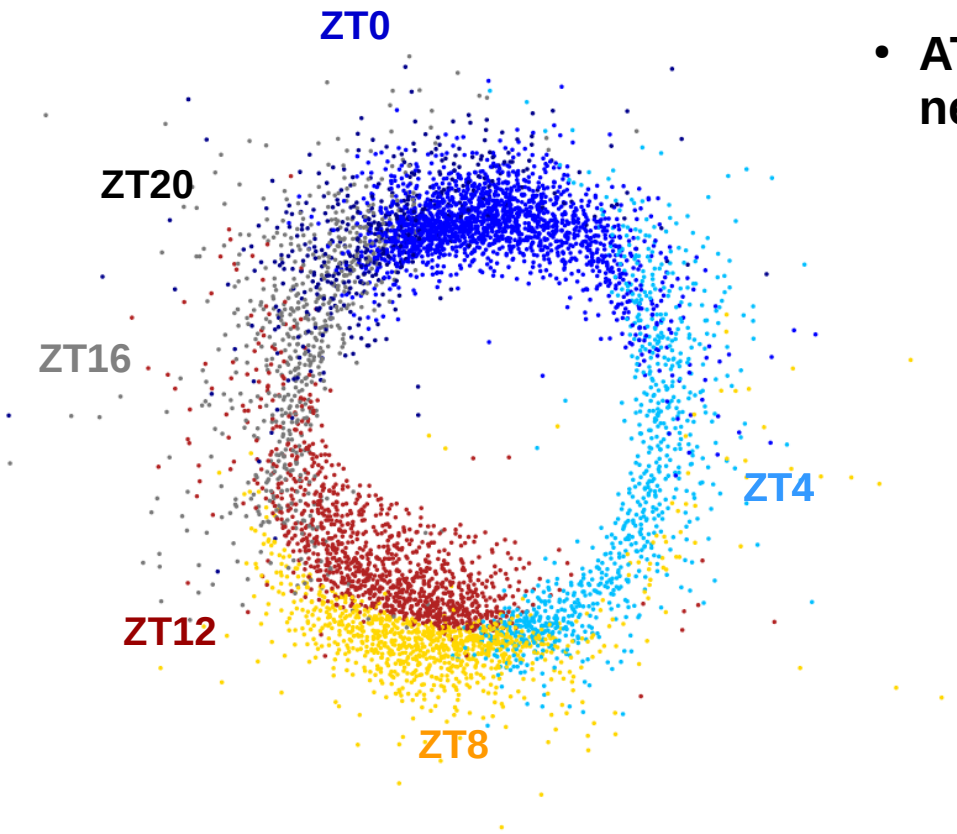
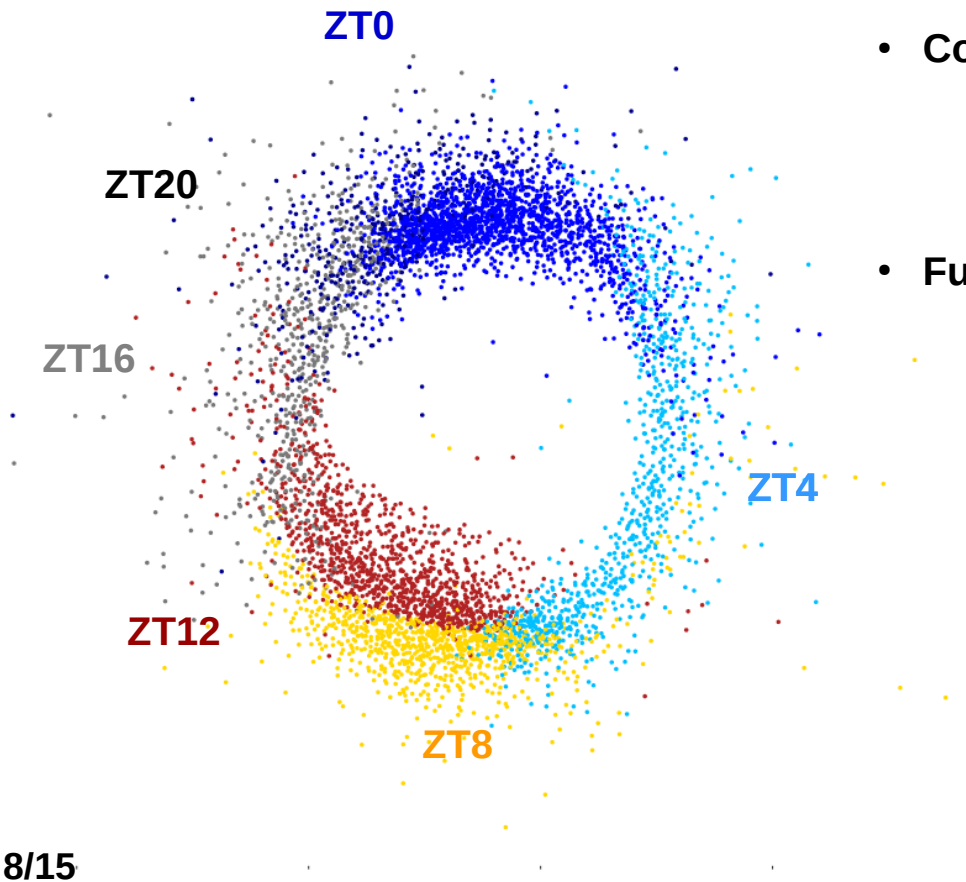


- **ATTRACTOR is a gene transcriptional network comprising:**

  - 5778 nodes or genes with rythmic expression profiles

  - 14529 edges or transcriptional regulations

ATTRACTOR, a web based tool for the exploration of a transcriptional network integrating key regulators of the circadian clock and light signalling



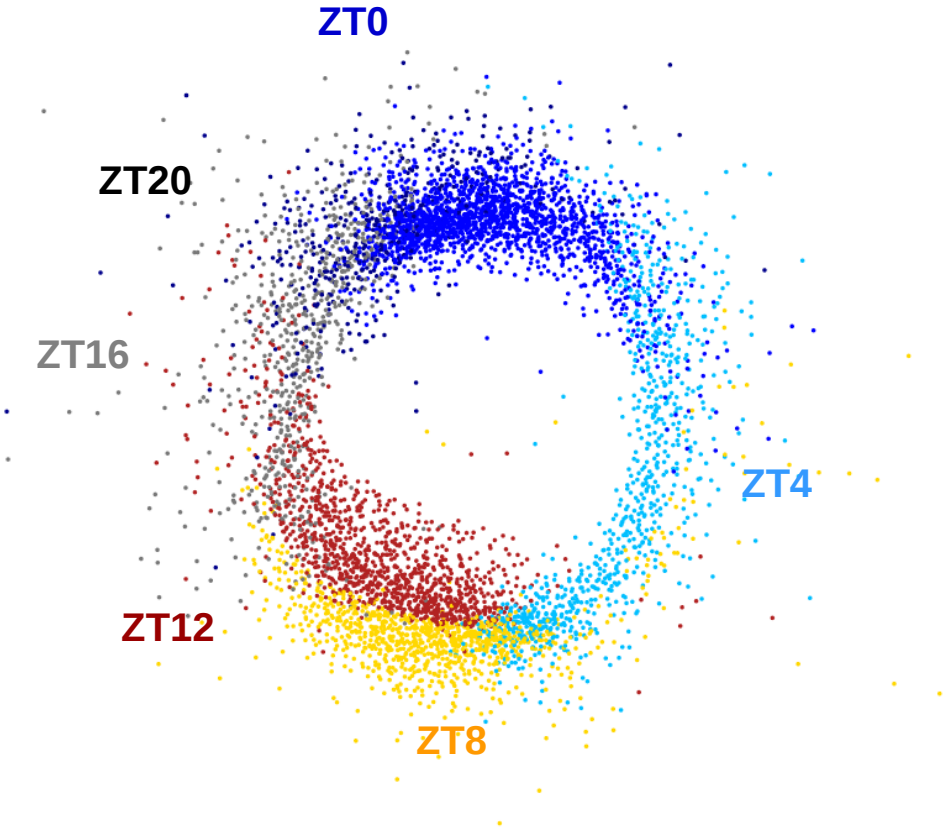
- Completely developed using R packages.

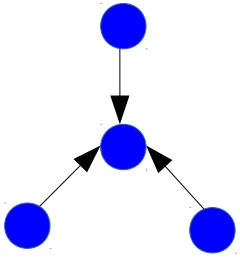
Shiny from RStudio · Bioconductor OPEN SOURCE SOFTWARE FOR BIOINFORMATICS · GitHub

- Functionalities:
  - Global properties analysis and visualization
  - Analysis of the regulation of individual genes
  - Analysis of coordinated regulation over set of genes including:
    - Significance enrichment in specific expression patterns
    - GO enrichment and TFBS overrepresentation
    - Significance of binding sites overlaps between different transcription factors

de los Reyes, Romero-Losada, in preparation

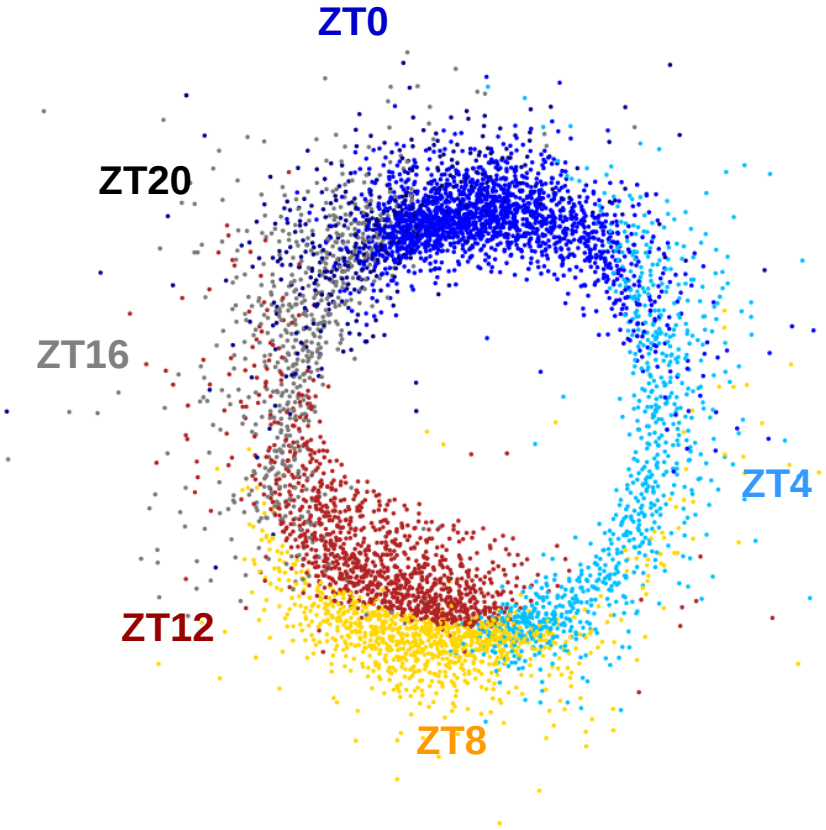
ATTRACTOR suggests that the Circadian Clock Transcriptional Program is simultaneously robust to random perturbations and sensitive to directed tuning

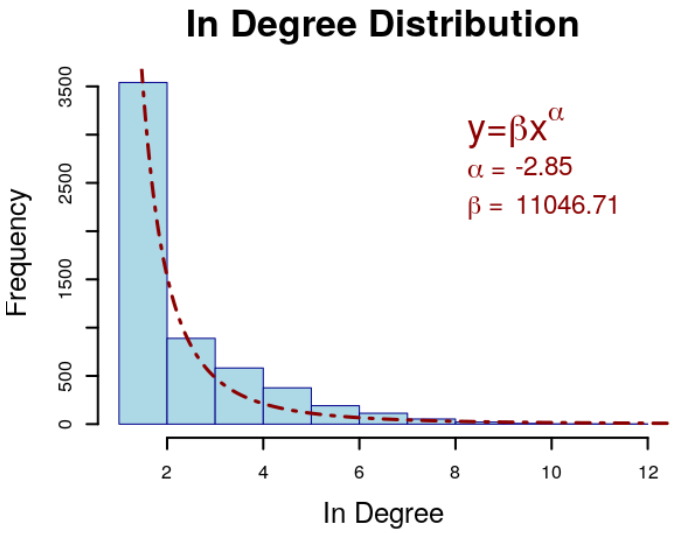


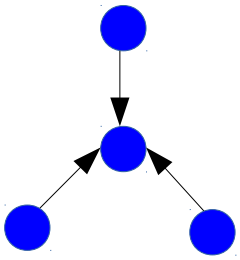


In degree 3
Number of regulators

ATTRACTOR suggests that the Circadian Clock Transcriptional Program is simultaneously robust to random perturbations and sensitive to directed tuning







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Number of regulators

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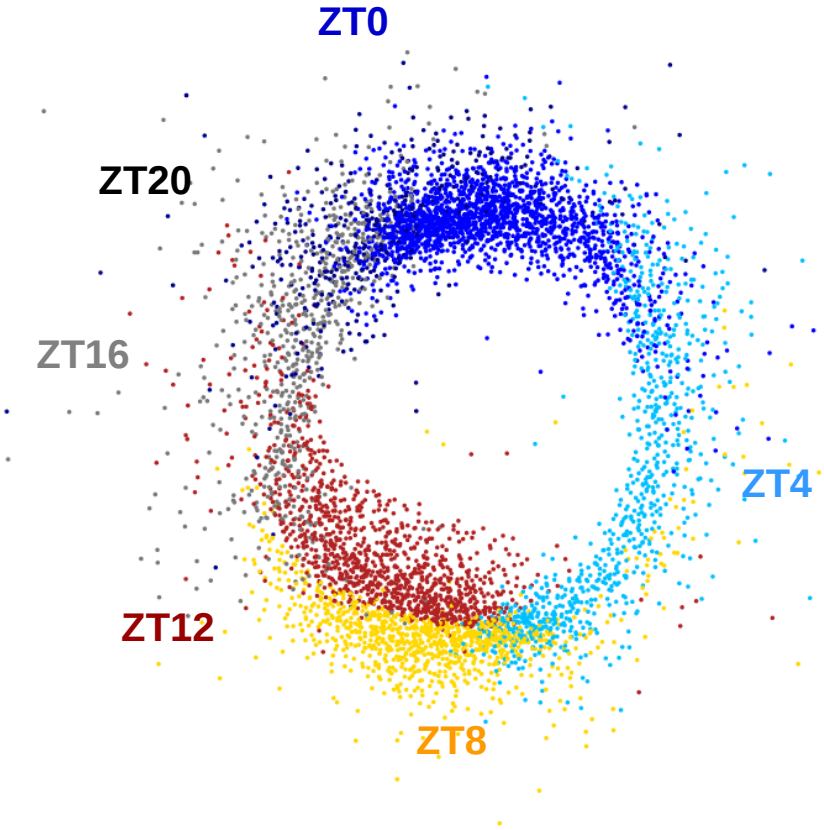

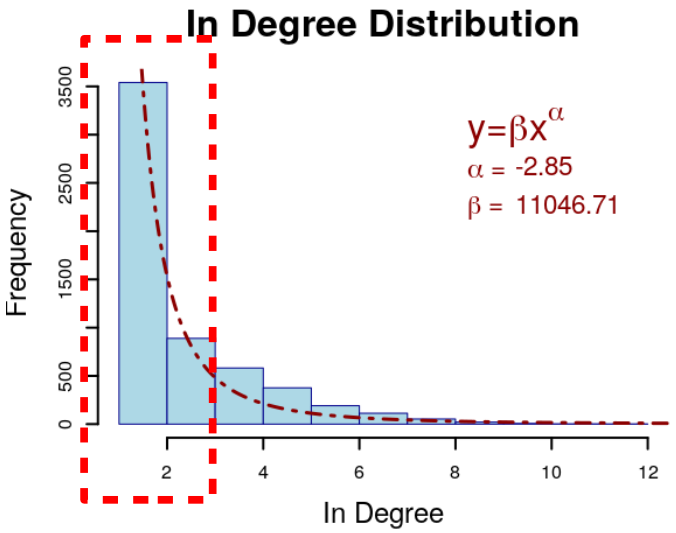

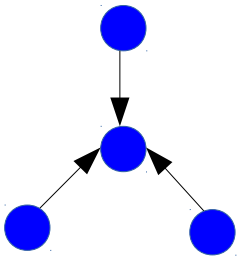

In degree 3
Number of regulators

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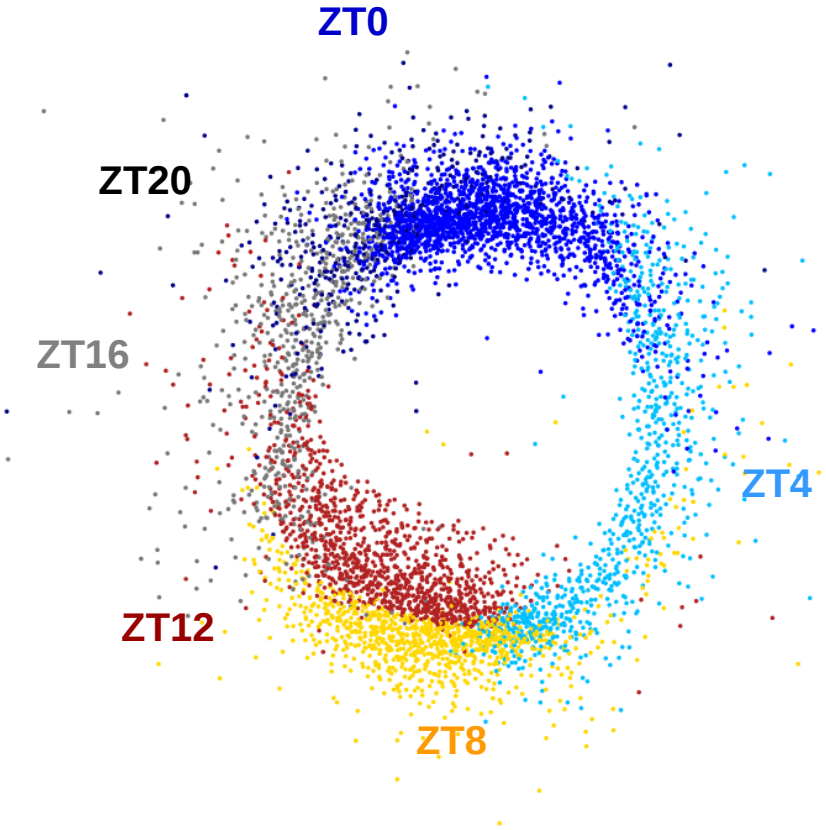

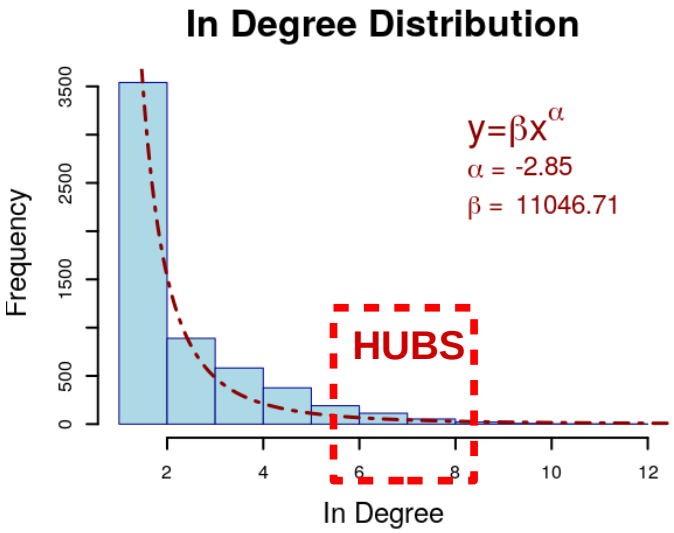

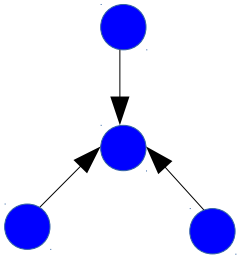

In degree 3
Number of regulators

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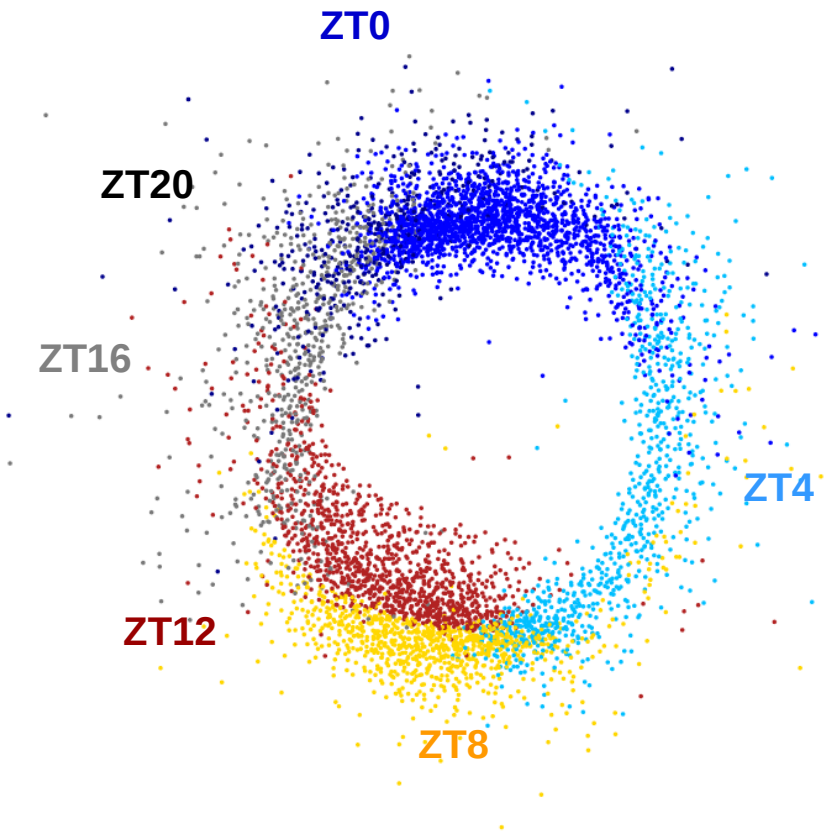
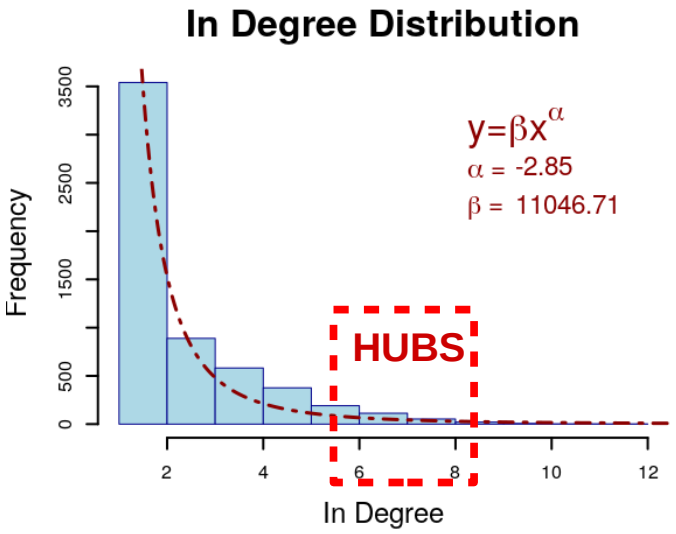
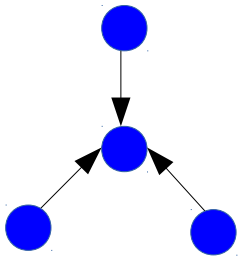
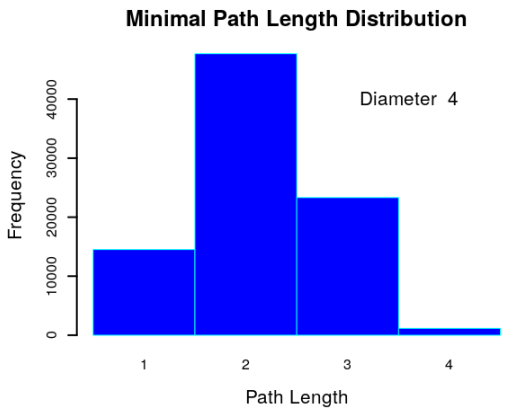




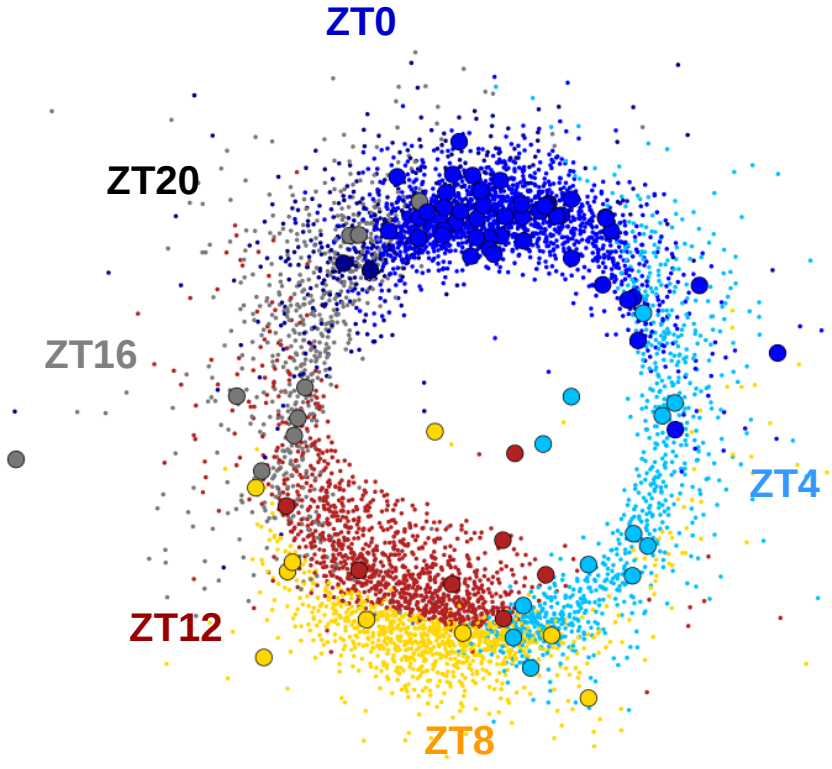
An ultra-small world network

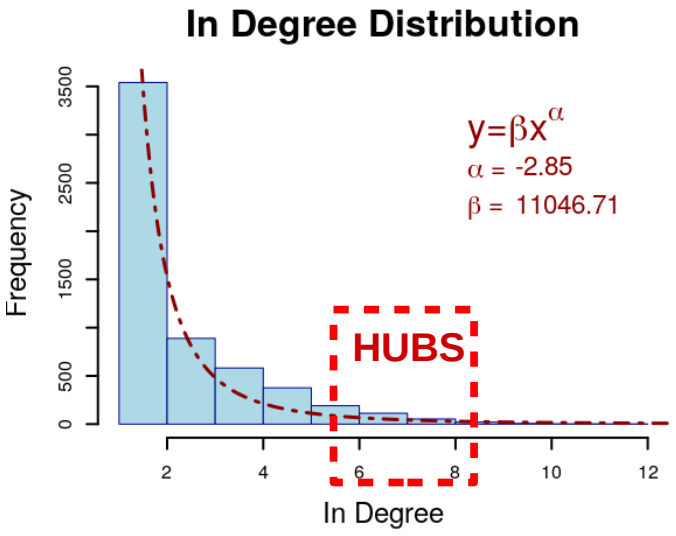


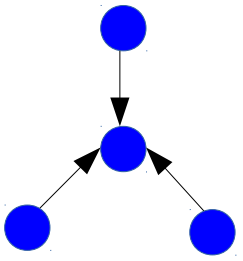
In degree 3
Number of regulators



ATTRACTOR suggests that the Circadian Clock Transcriptional Program is simultaneously robust to random perturbations and sensitive to directed tuning

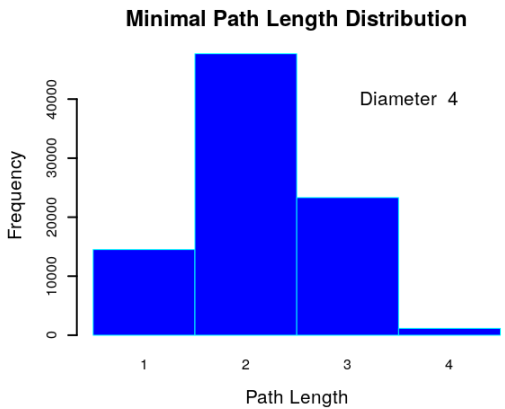






In degree 3
Number of regulators

An ultra-small world network



Hubs genes significantly enriched in genes peaking at the dark/light transition (p-value = 1.16×10^{-8})

ATTRACTOR enables researchers to explore the expression profile, potential regulators and their binding sites of individual genes

Target gene

AT1G22770 - GI

Select Transcription Factors:

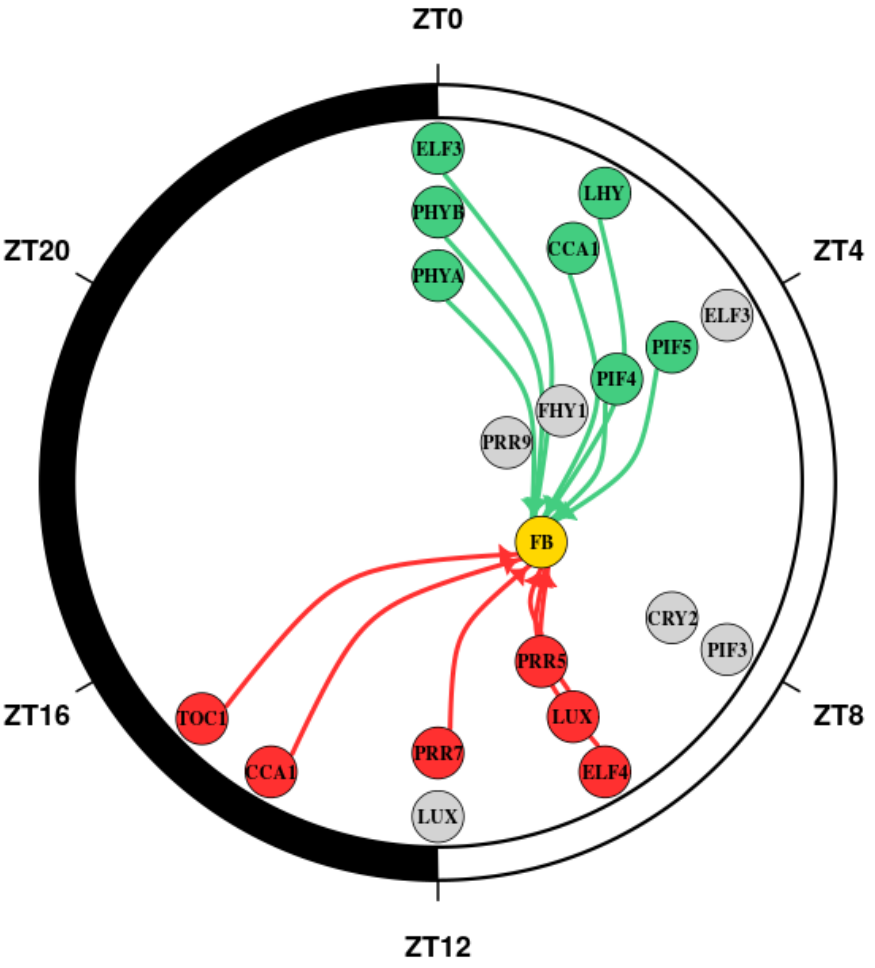
- [ ] CCA1
- [ ] LHY
- [ ] TOC1
- [ ] PRR5
- [ ] PRR7
- [ ] PRR9
- [ ] PHYA
- [ ] PHYB
- [ ] CRY2
- [ ] FHY1
- [ ] LUX
- [ ] PIF3
- [ ] PIF4
- [ ] PIF5
- [ ] ELF4
- [ ] ELF3

- [x] Select All

Show interactions between TFs?

No

GO



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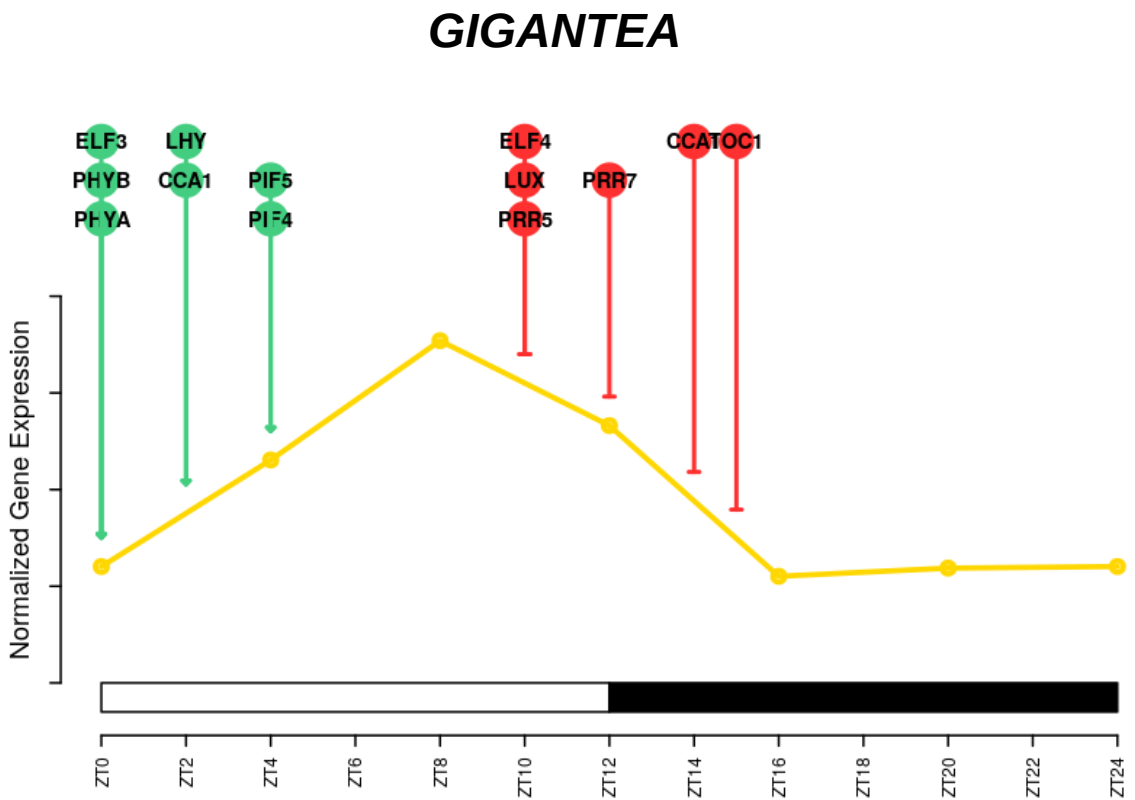
- [ ] LUX
- [ ] PIF3
- [ ] PIF4
- [ ] PIF5
- [ ] ELF4
- [ ] ELF3

- [x] Select All

Show interactions between TFs?

No

GO



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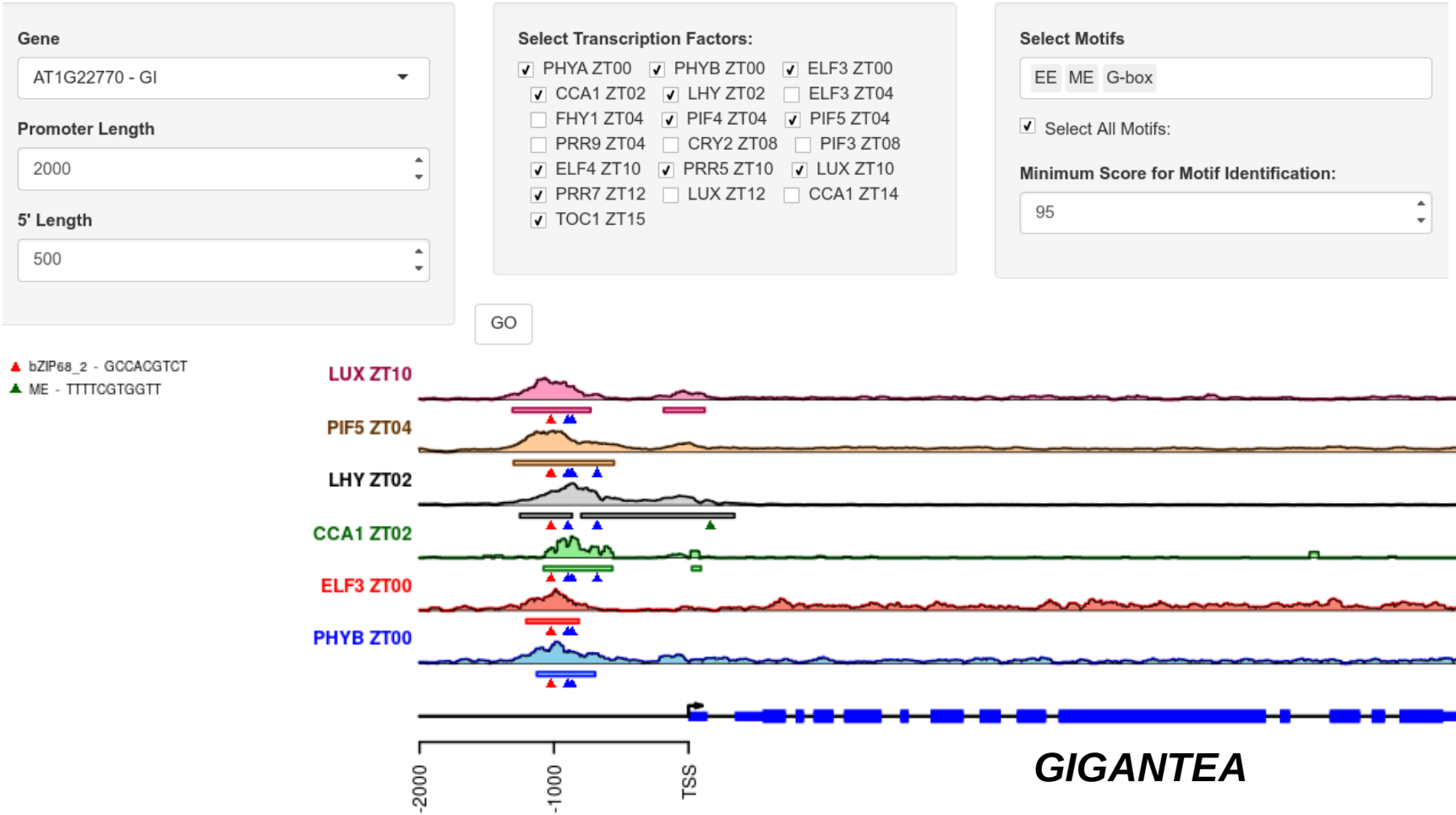
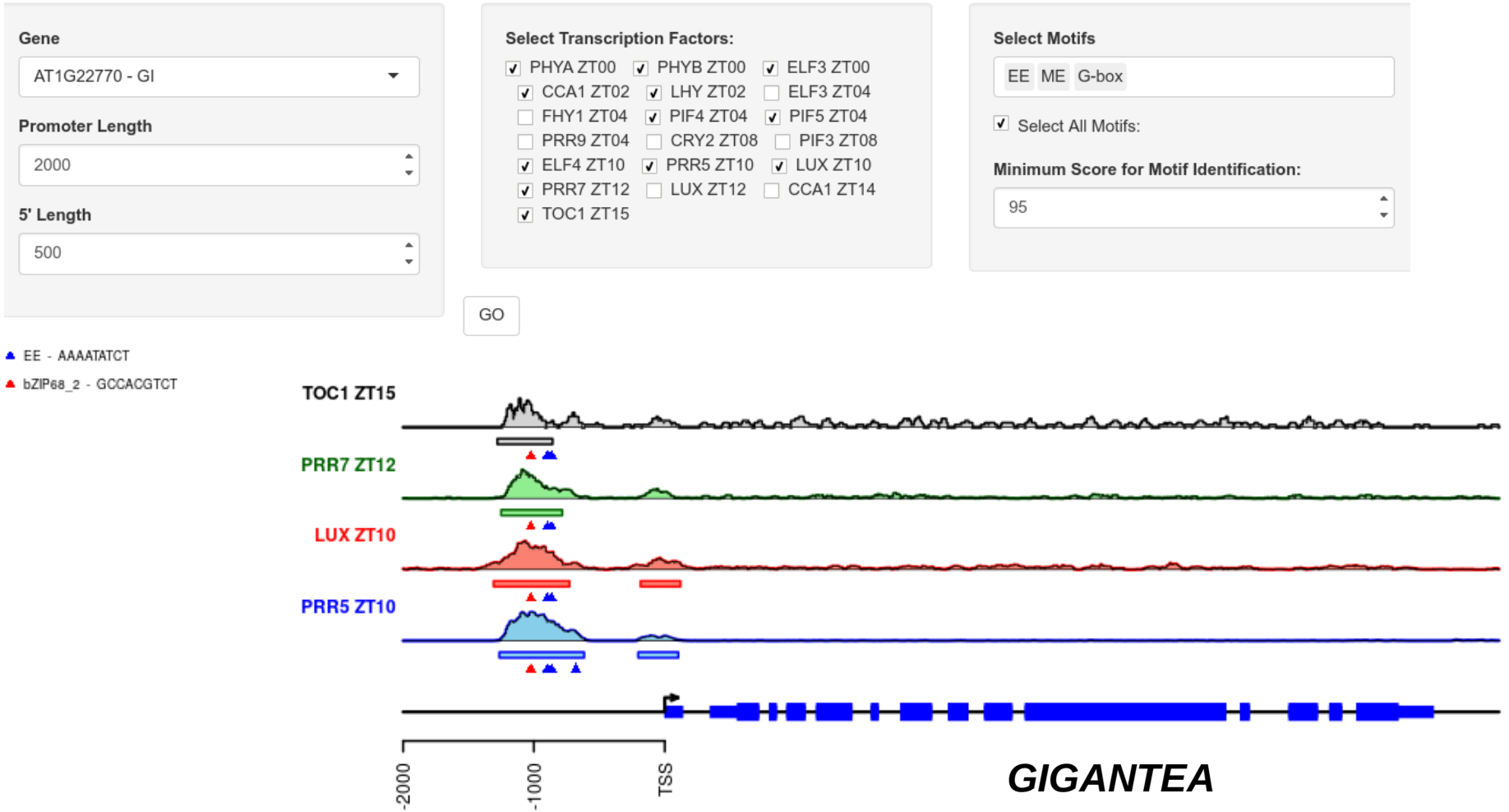
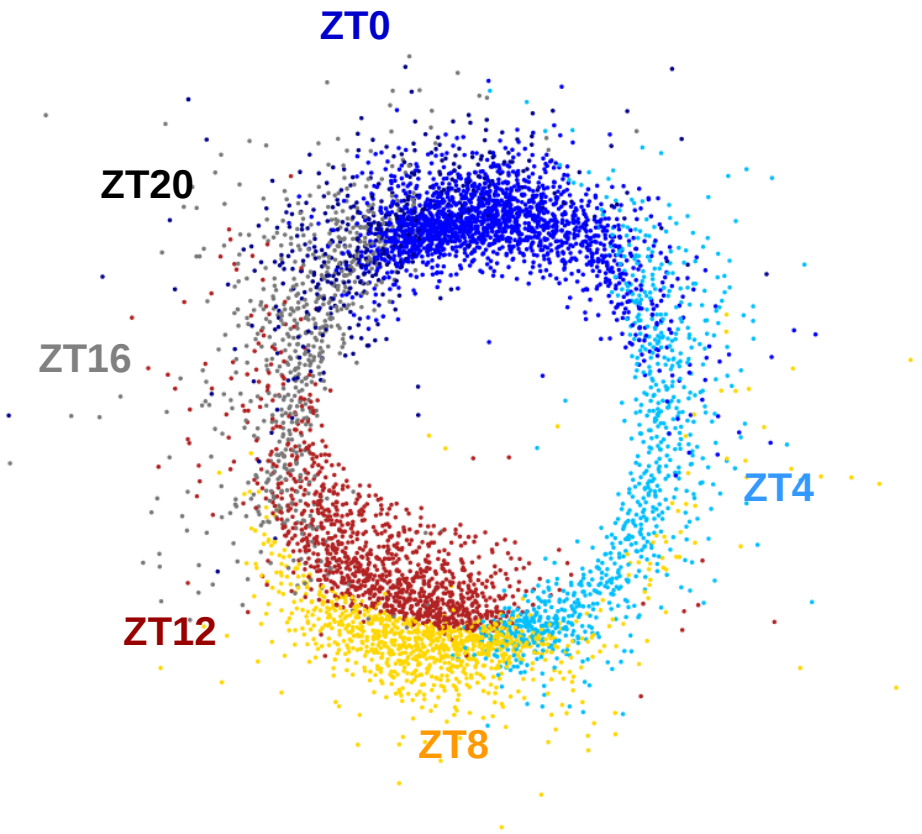
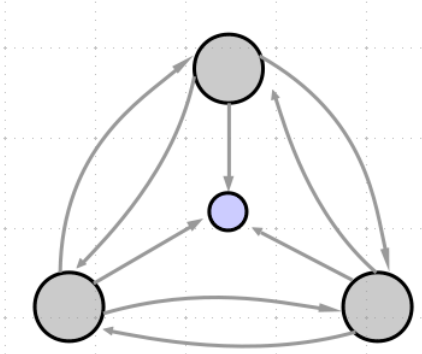


ATTRACTOR enables researchers to explore the expression profile, potential regulators and their binding sites of individual genes



ATTRACTOR is constituted by non-random subgraphs called network motives





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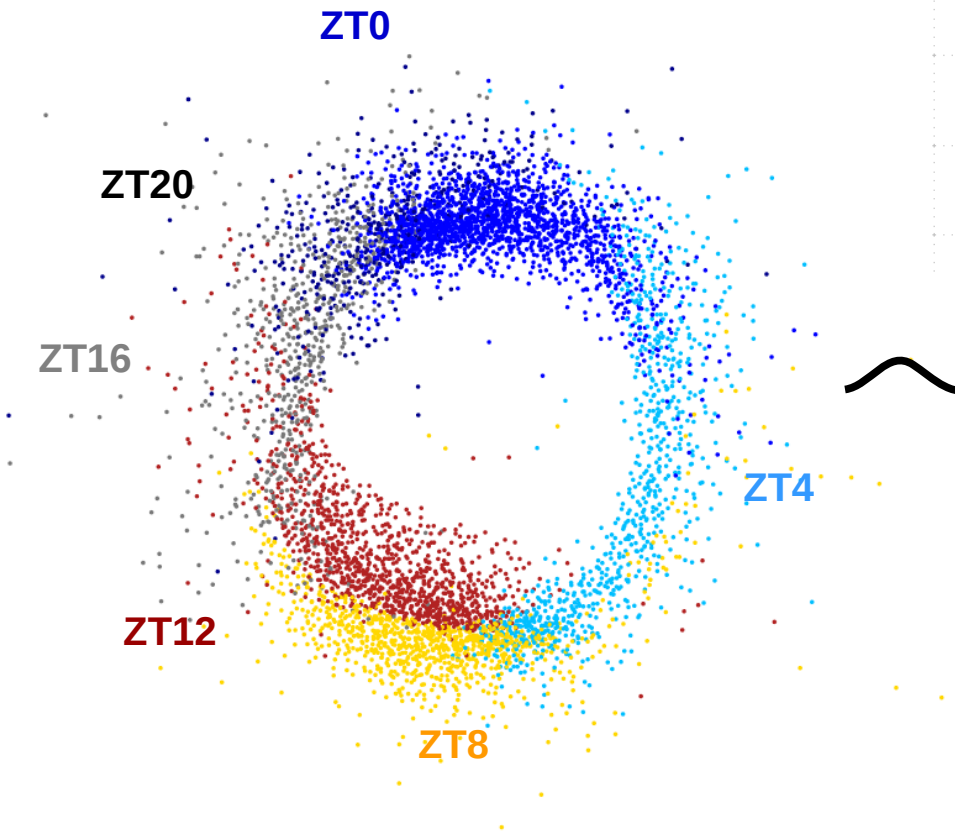

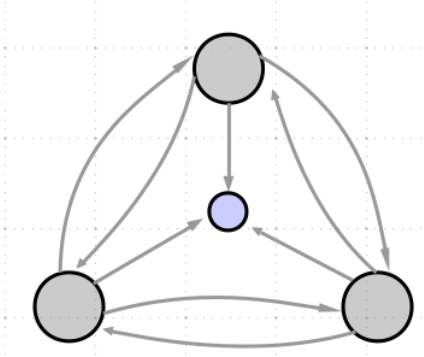

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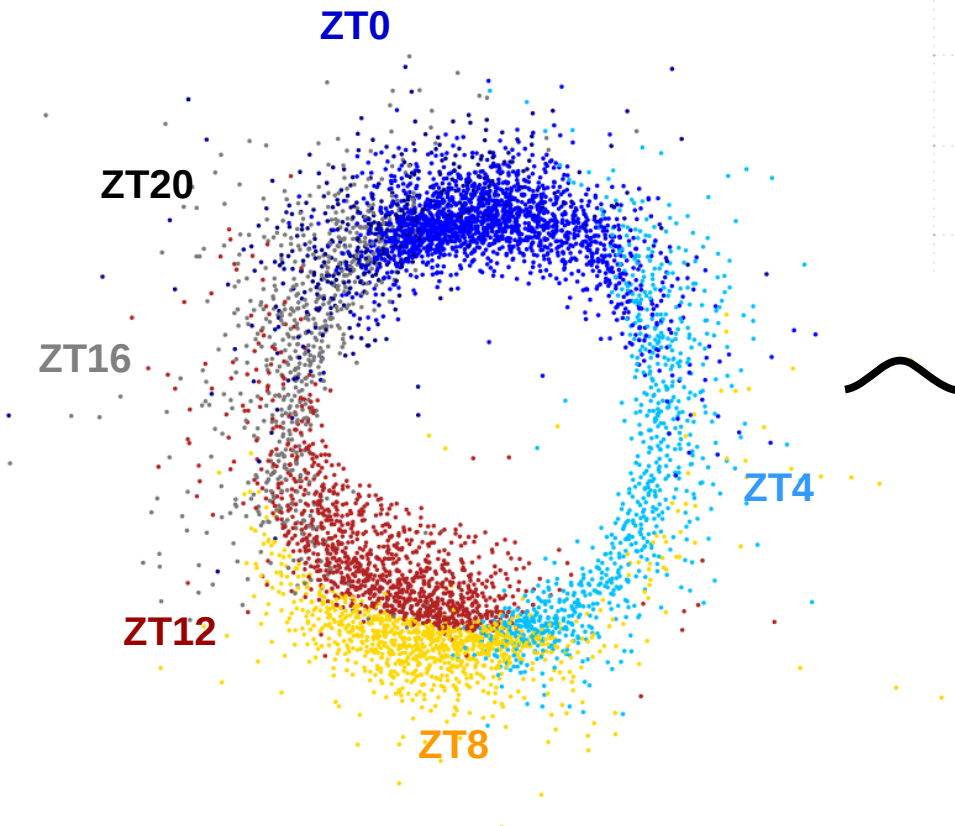

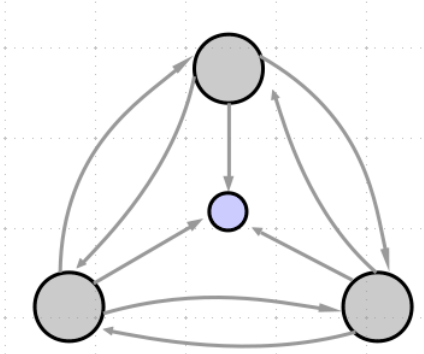

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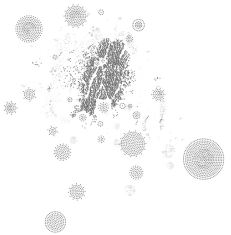

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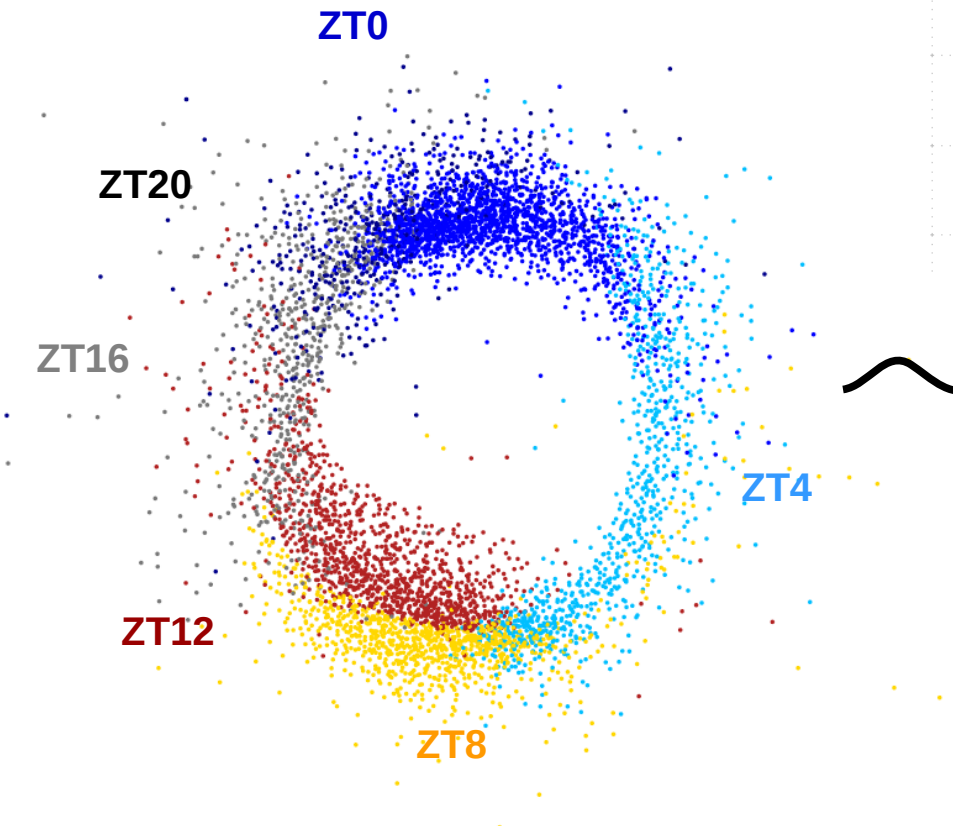

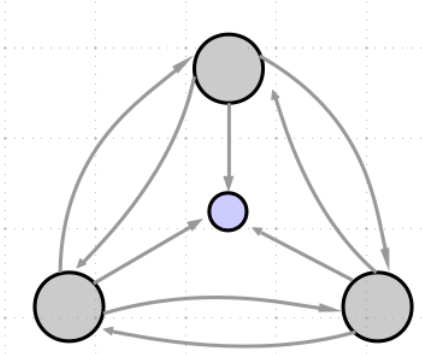

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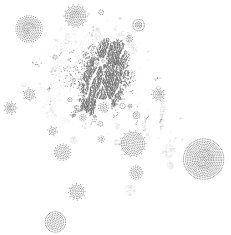

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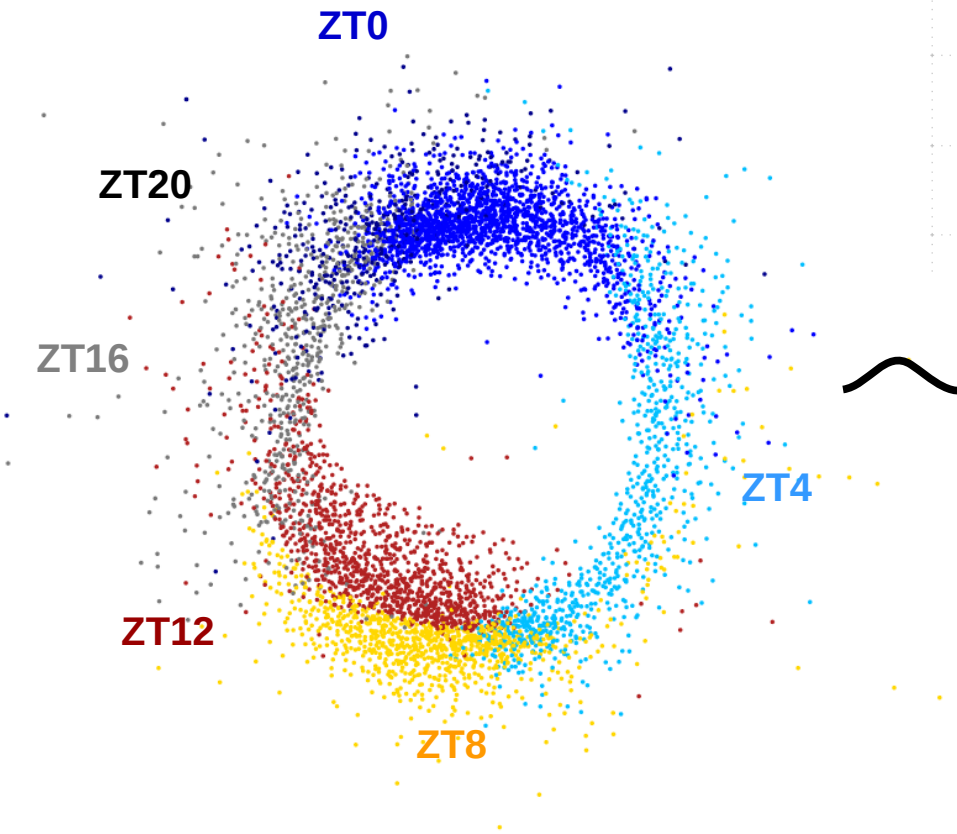

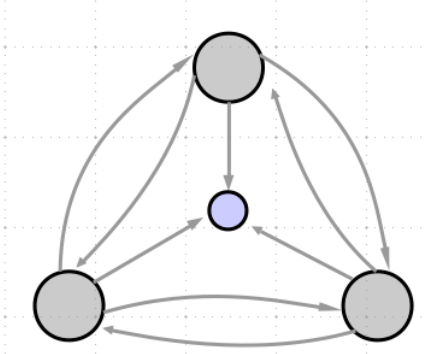

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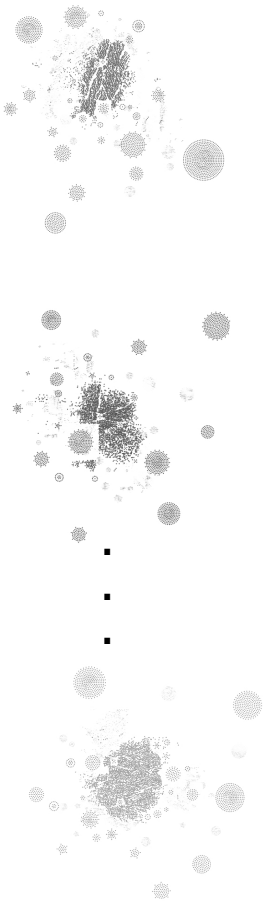

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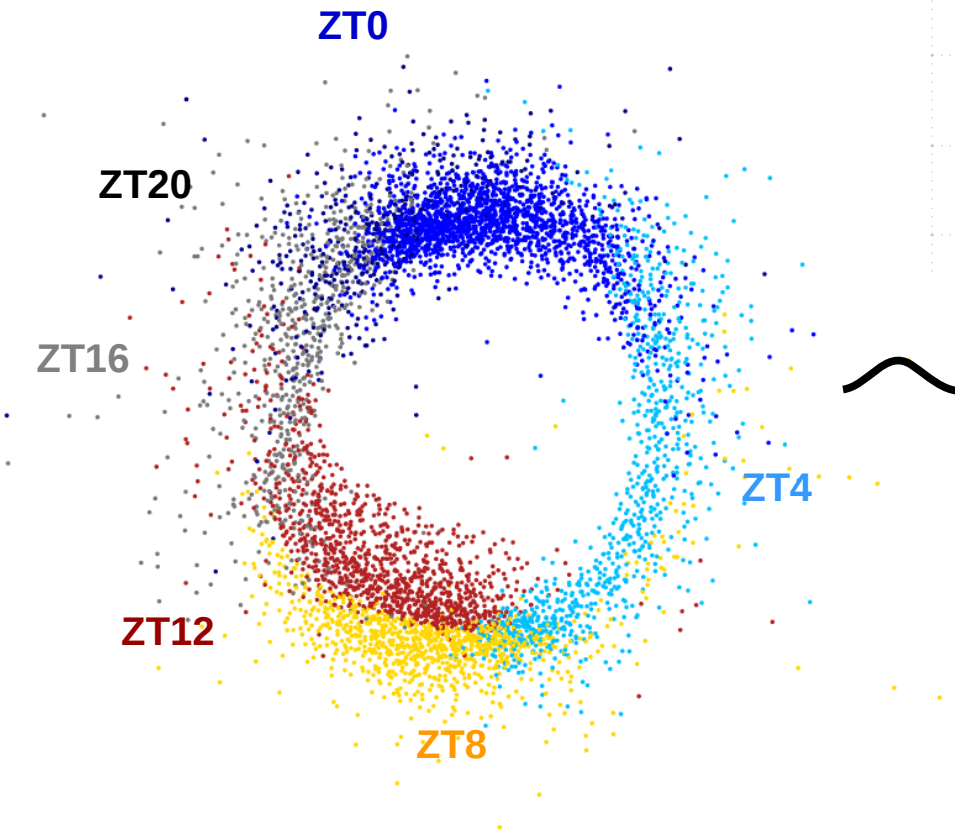

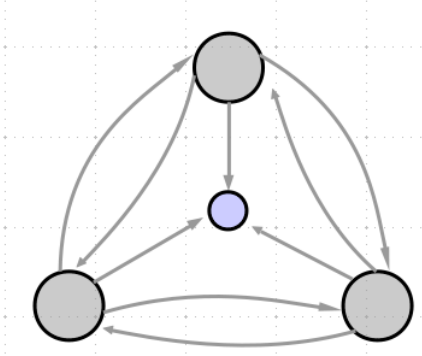

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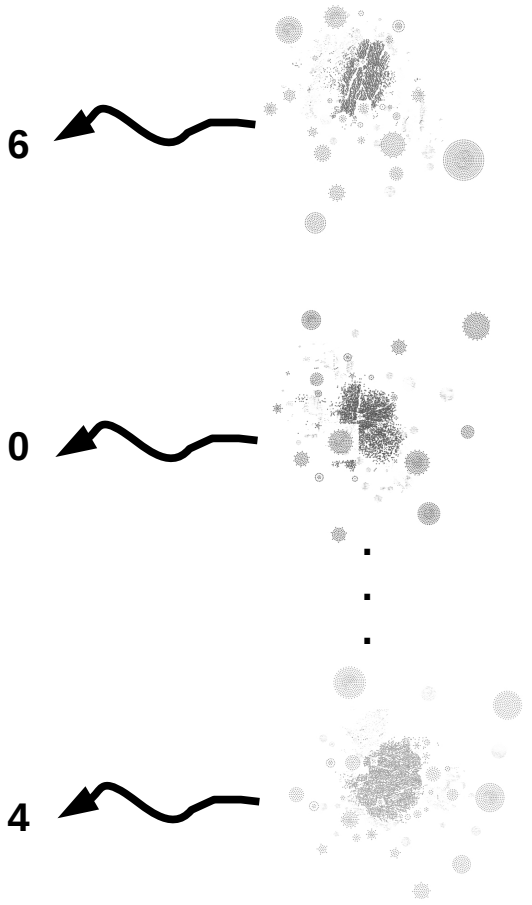

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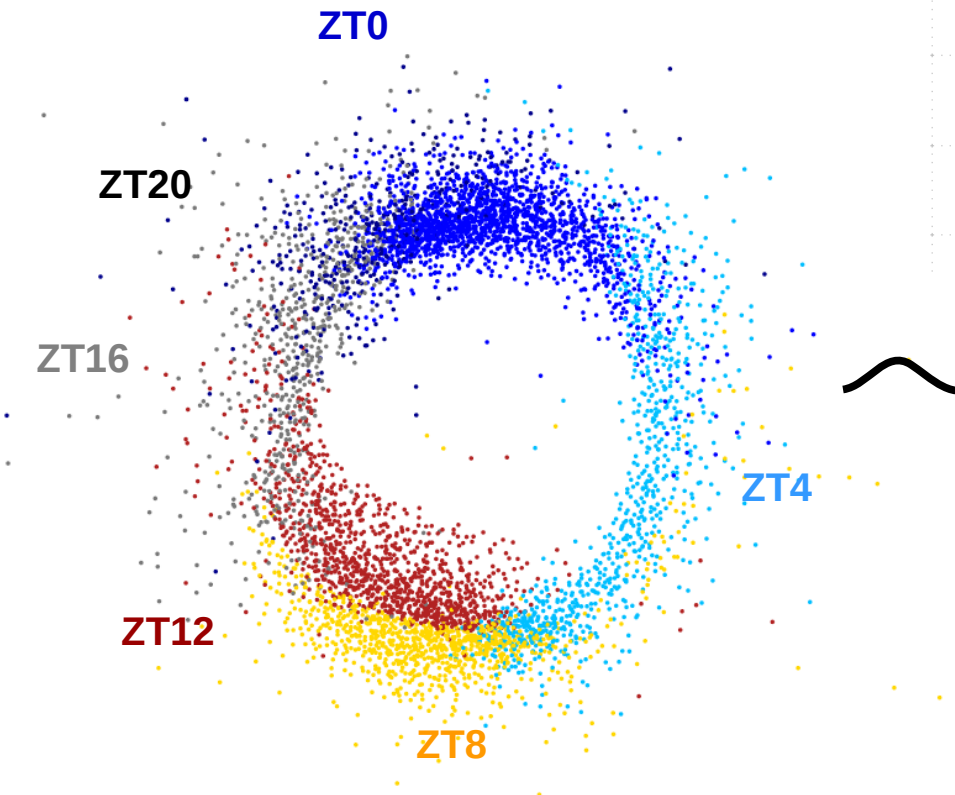

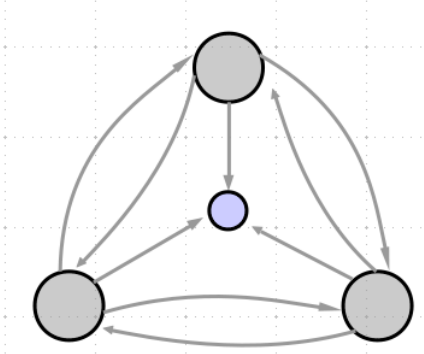

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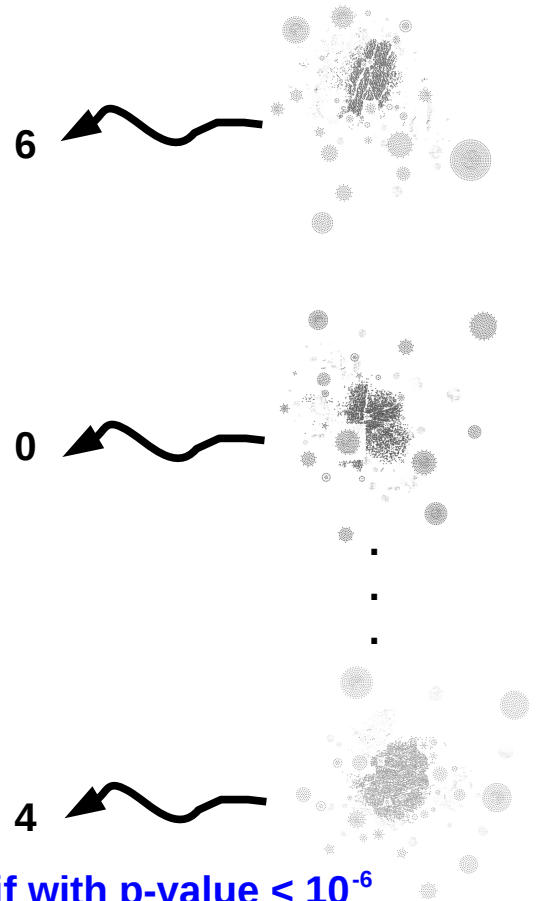
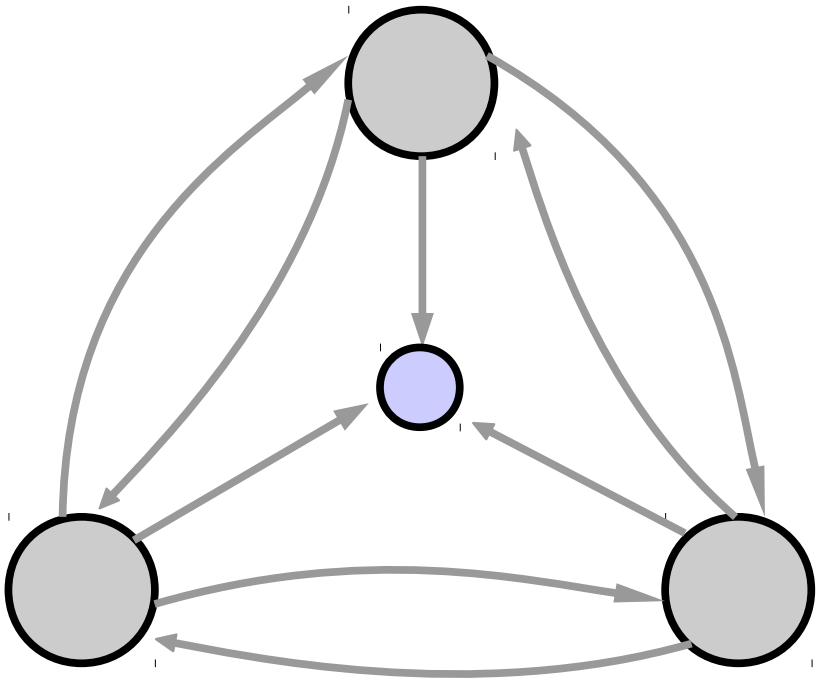


The triple linked feedback loops with multiple output is a network motif with p-value < 10^{-6}

PIFs establish multiple output linked feedback loops with PRRs and CCA1/LHY producing specific expression patterns involved in drought response



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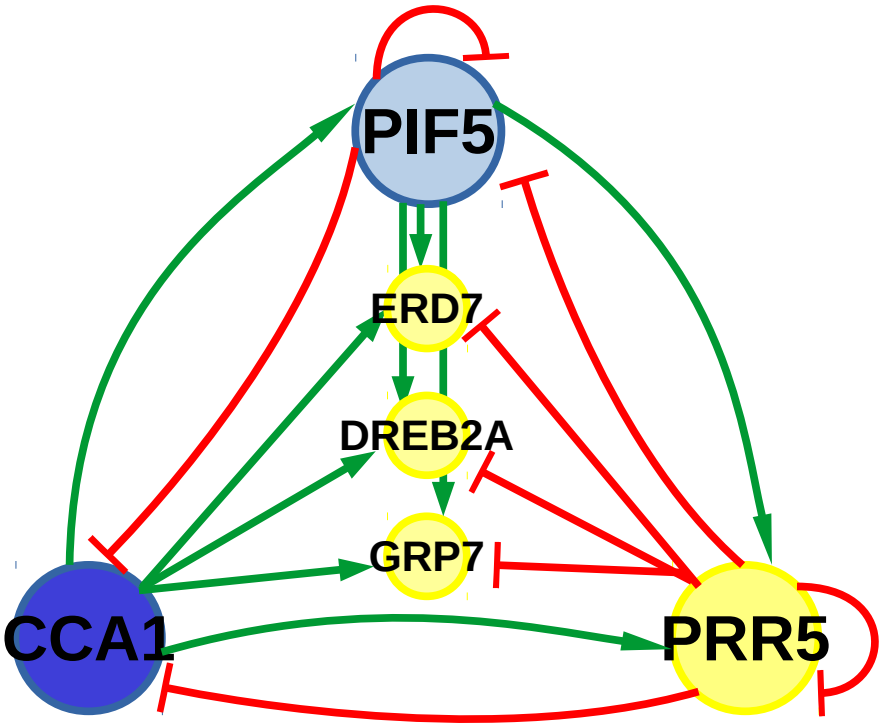

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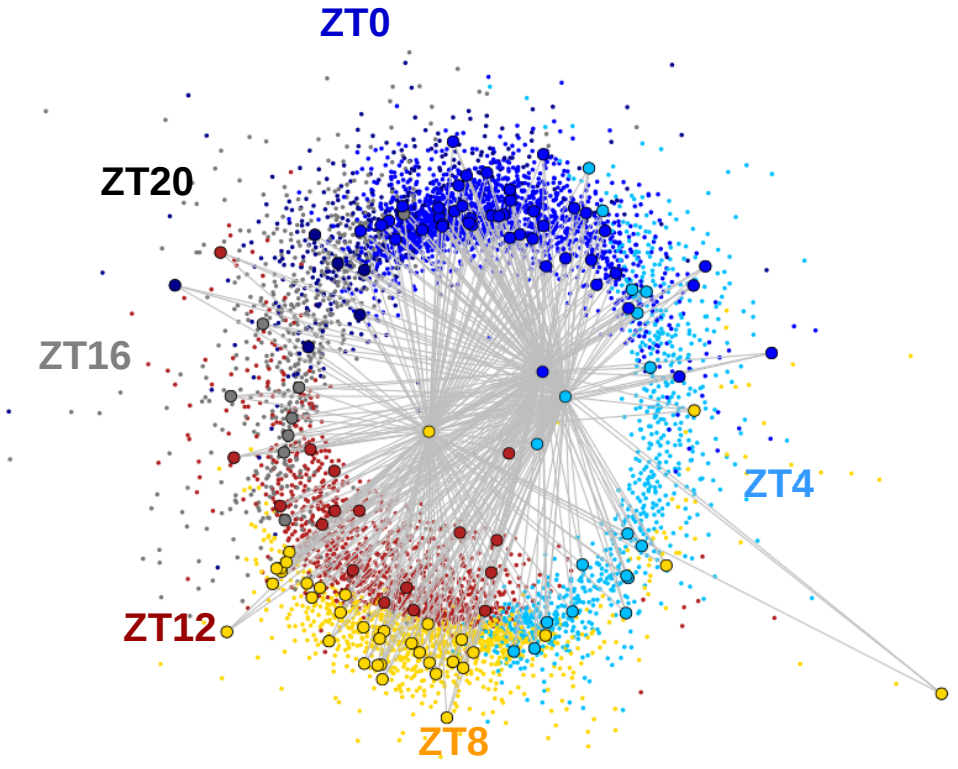
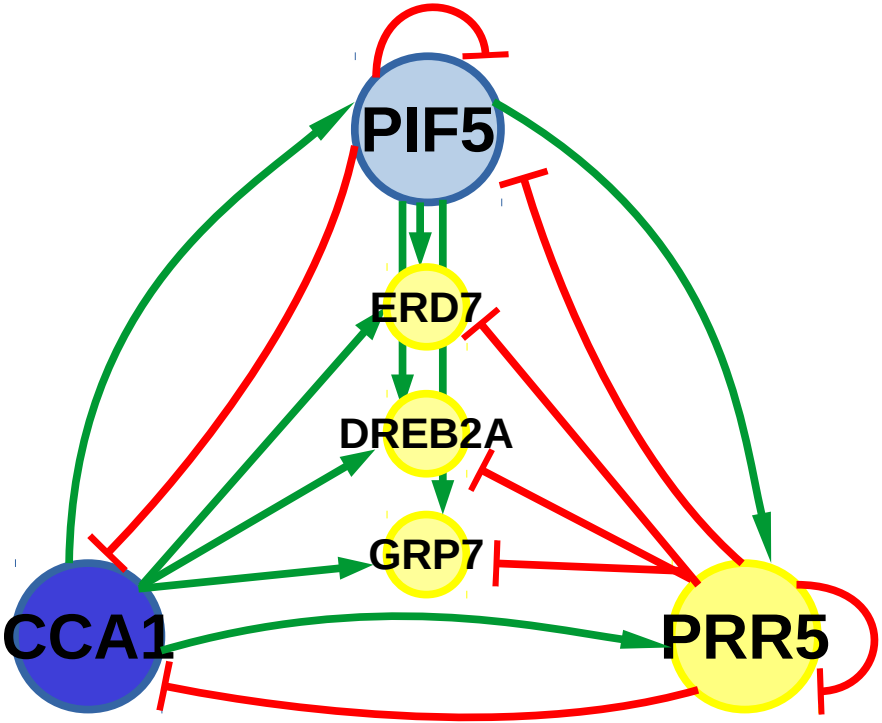
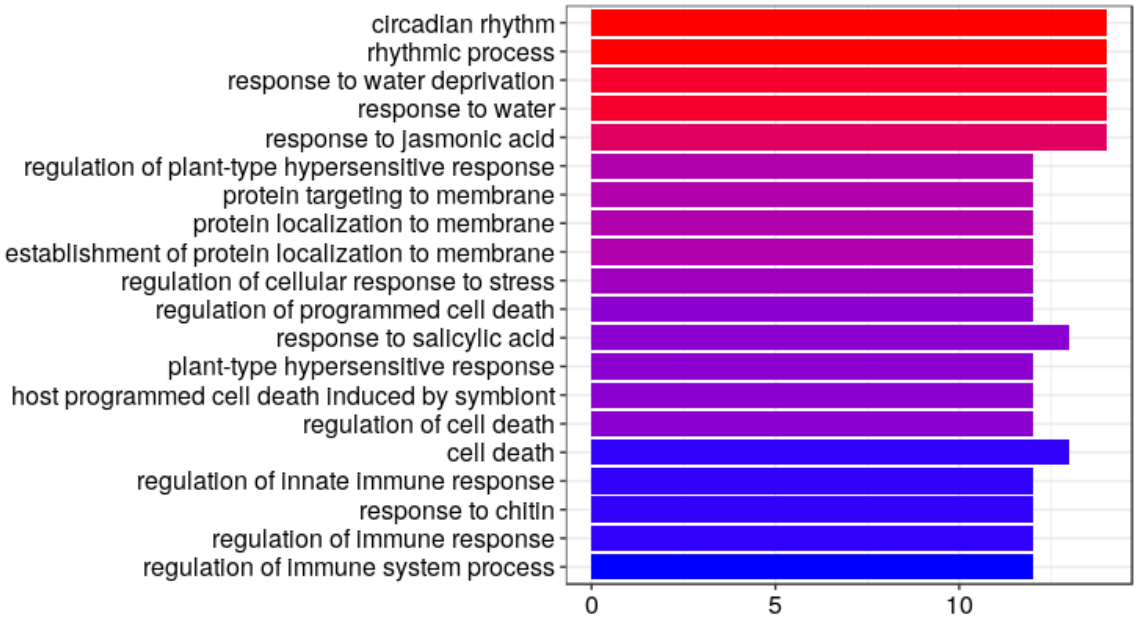
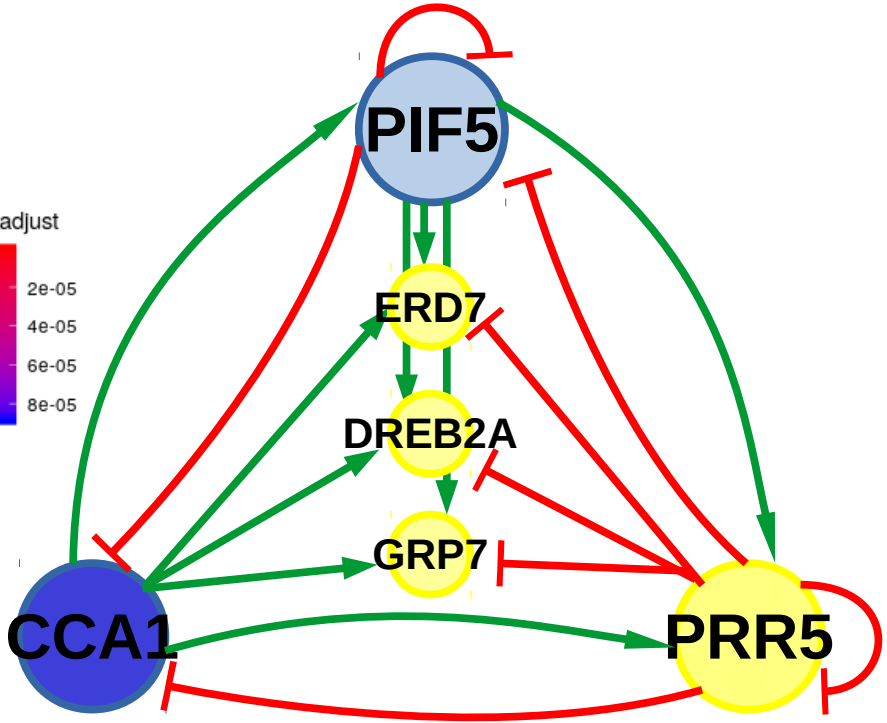




The common targets are not uniformly distributed but they are enriched in genes peaking at ZT8.

PIFs establish multiple output linked feedback loops with PRRs and CCA1/LHY producing specific expression patterns involved in drought response





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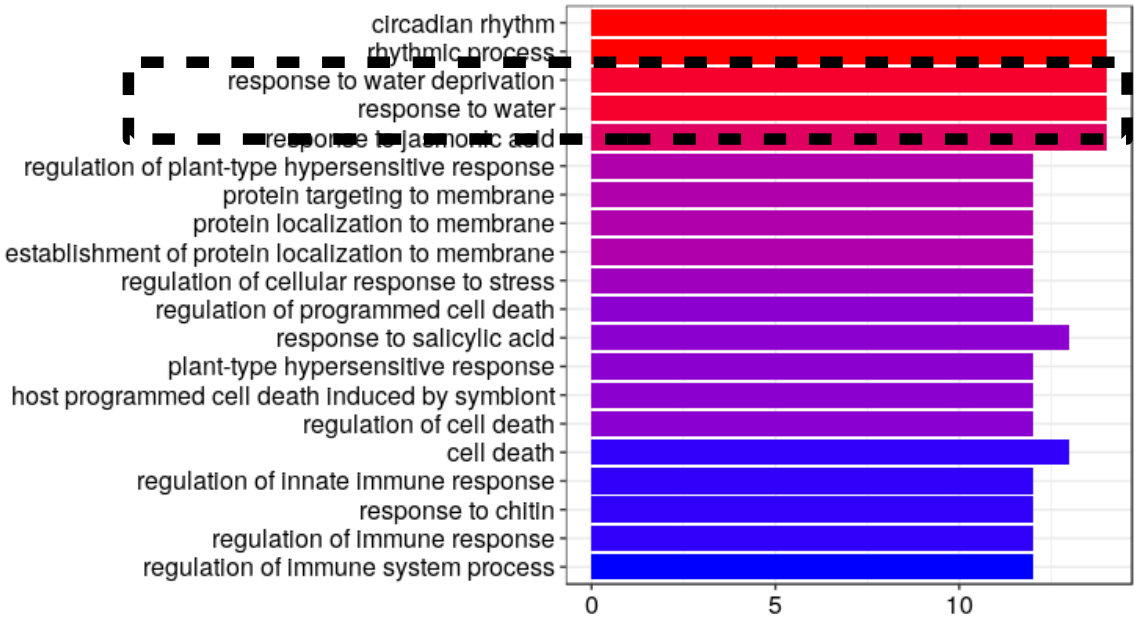

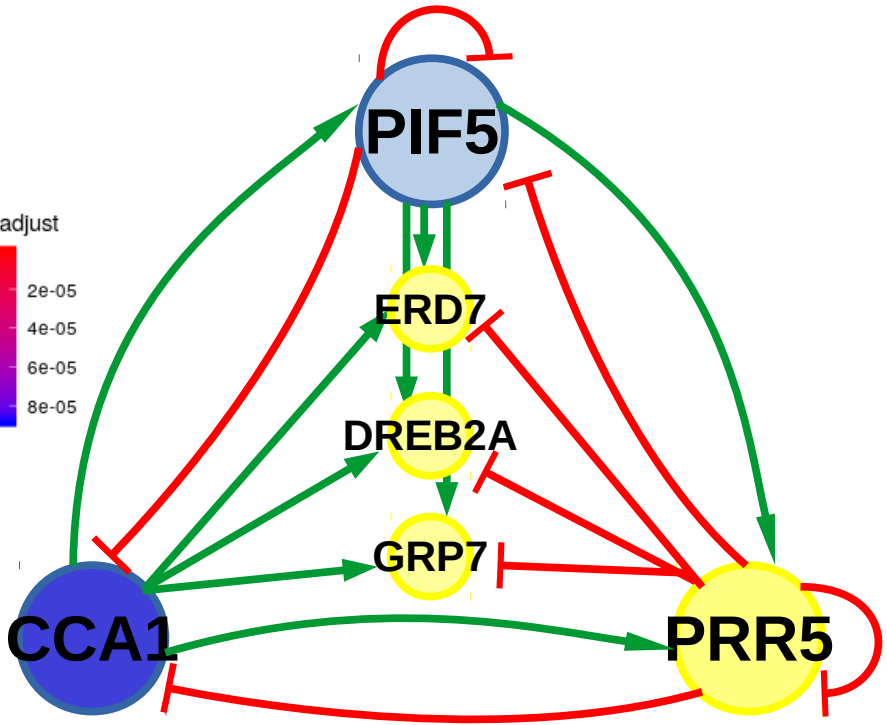

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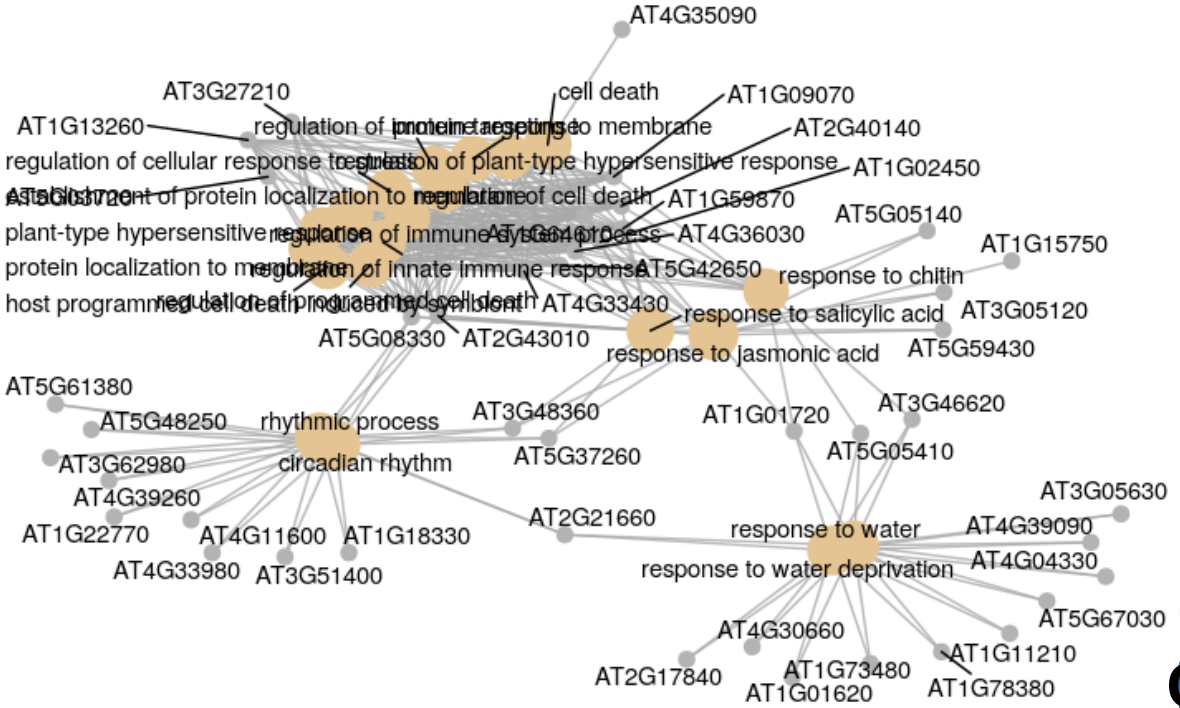
AT4G35090
AT3G27210
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AT1G09070
AT1G13260
AT2G40140
AT1G02450
AT1G59870
AT5G05140
AT4G36030
AT1G15750
AT5G42650
response to chitin
AT4G33430
AT3G05120
response to salicylic acid
AT5G08330
AT2G43010
response to jasmonic acid
AT5G59430
AT5G61380
AT5G48250
rhythmic process
AT3G48360
AT1G01720
AT3G46620
AT5G05410
AT3G62980
circadian rhythm
AT5G37260
AT4G39260
AT3G05630
AT2G21660
response to water
AT4G39090
AT1G22770
AT4G11600
AT1G18330
AT4G04330
AT4G33980
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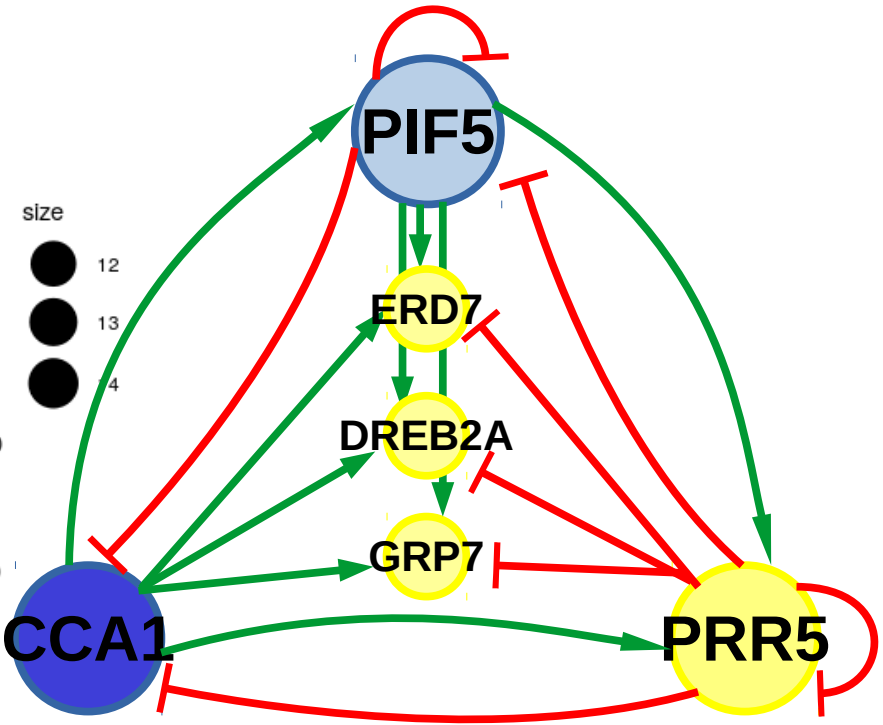

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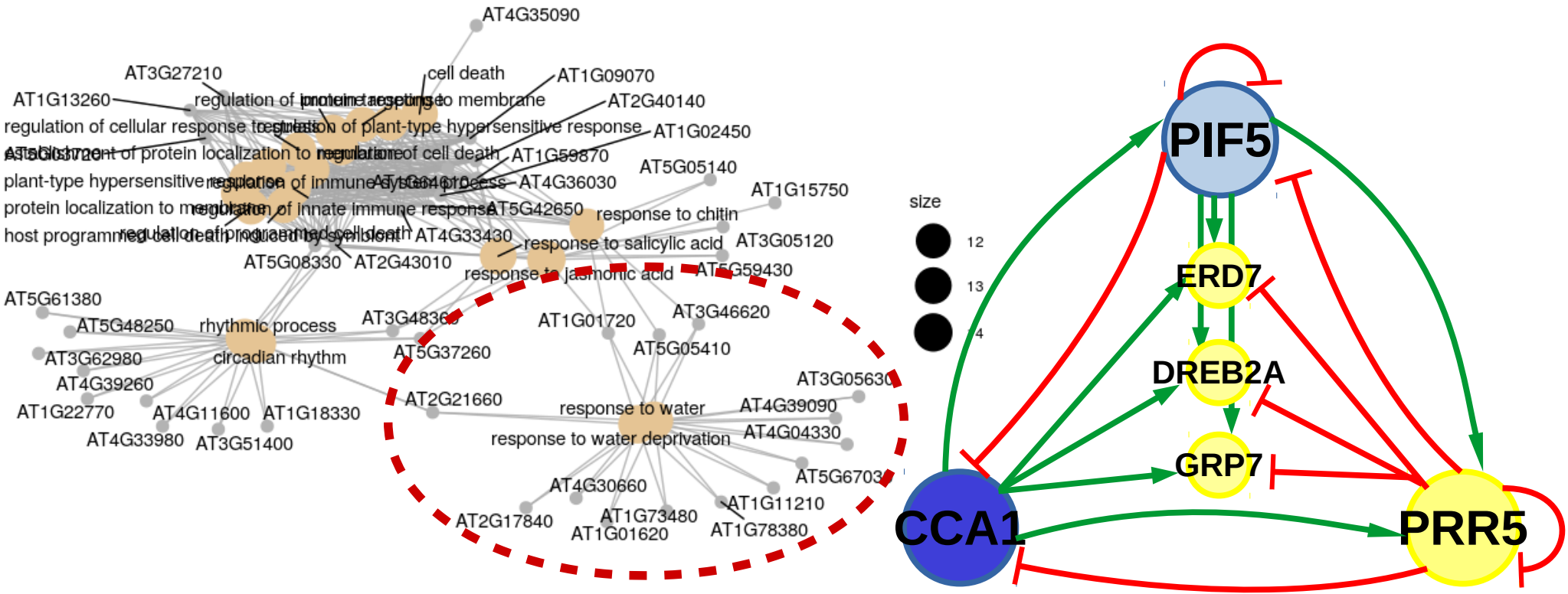

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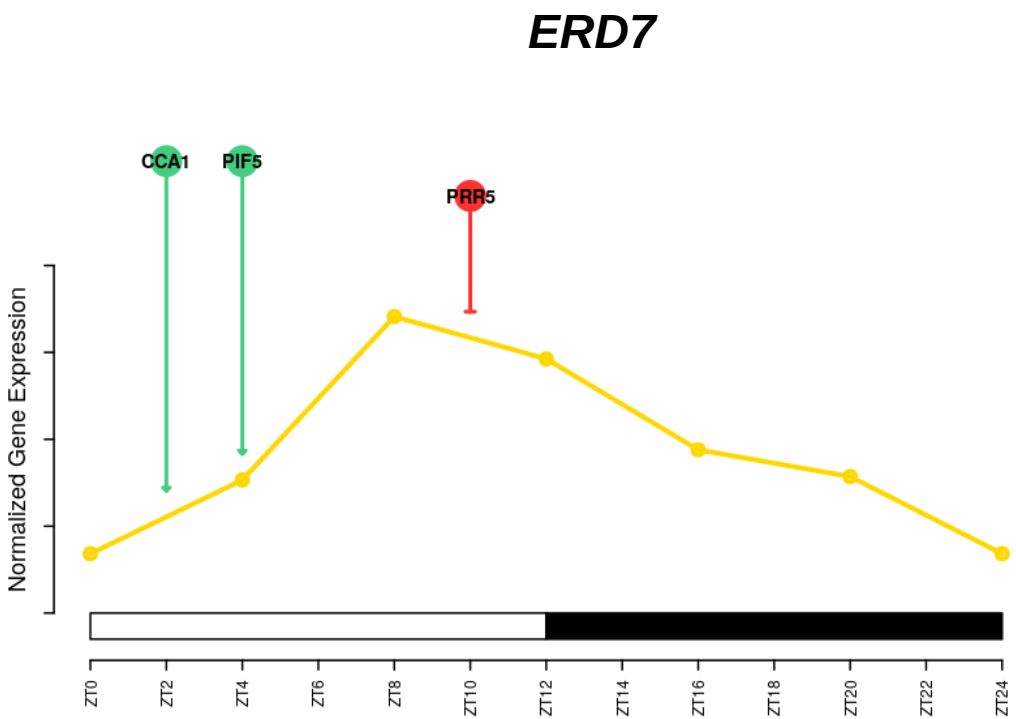

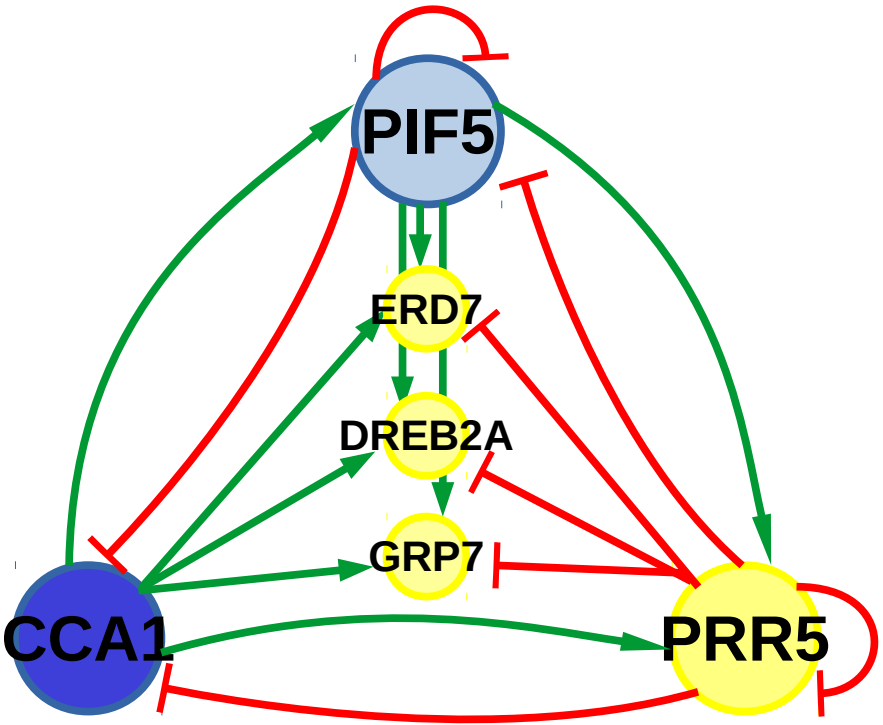

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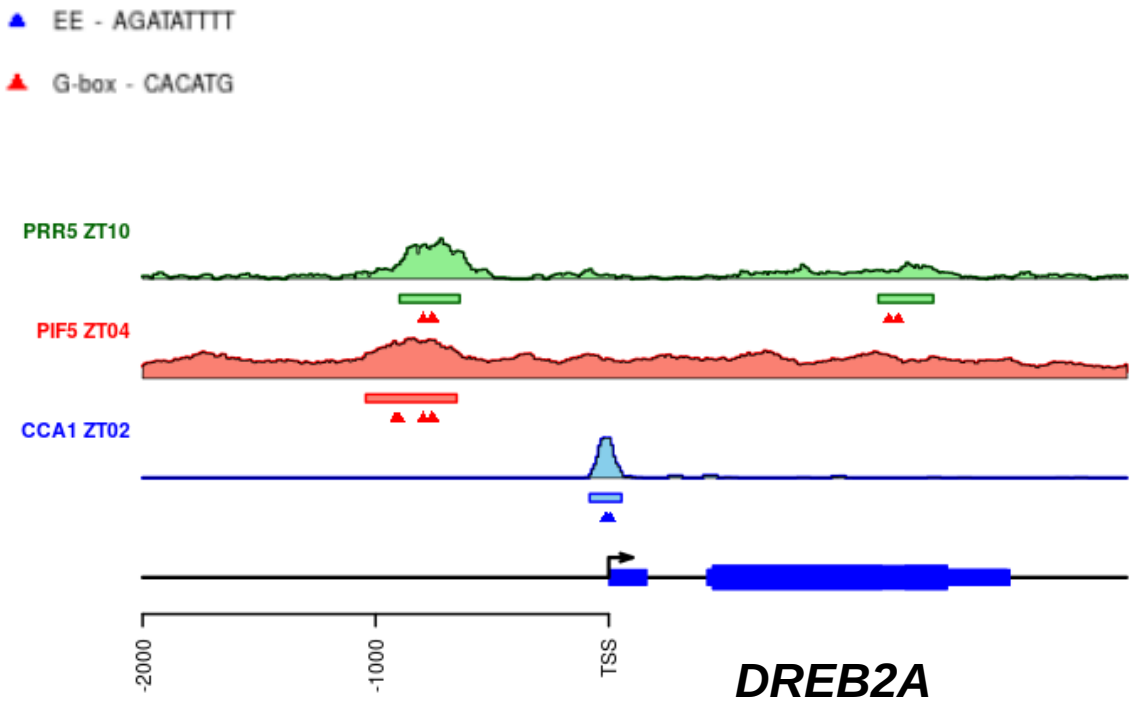

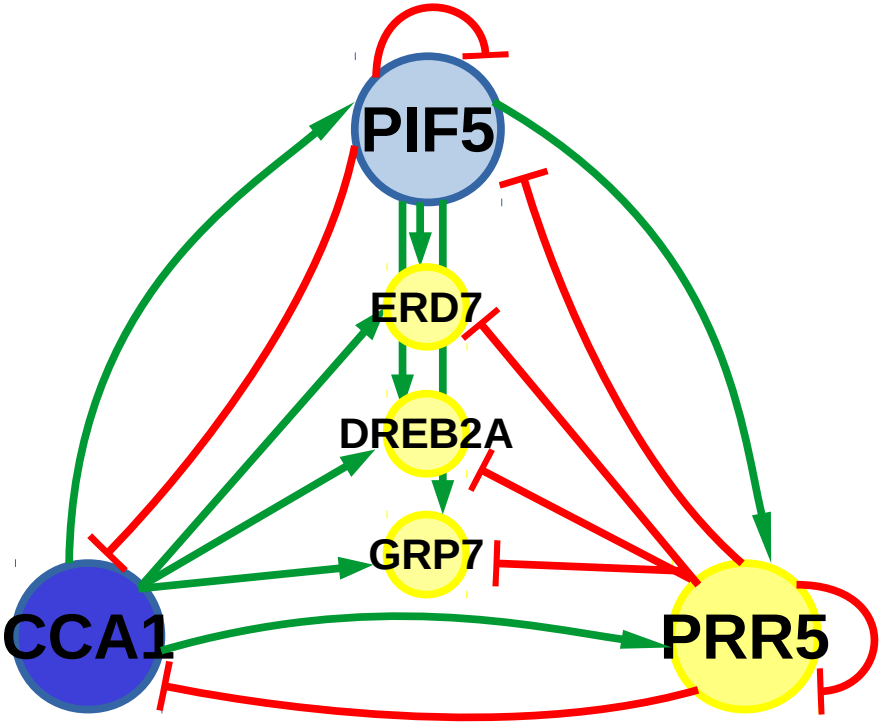

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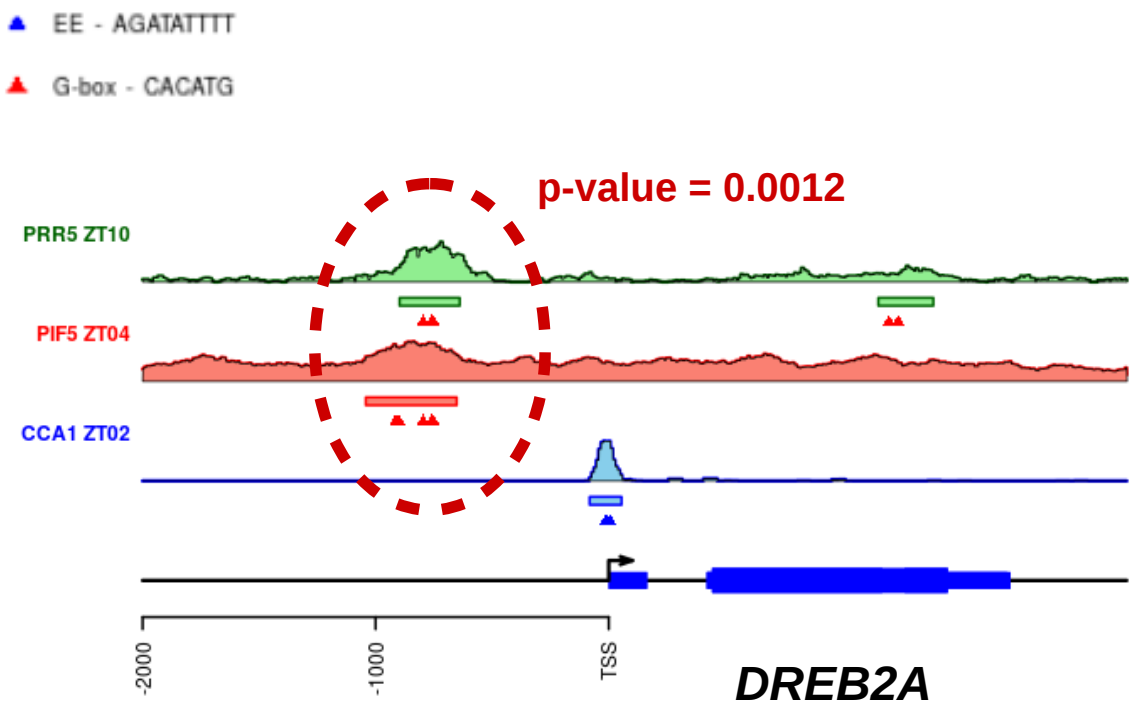

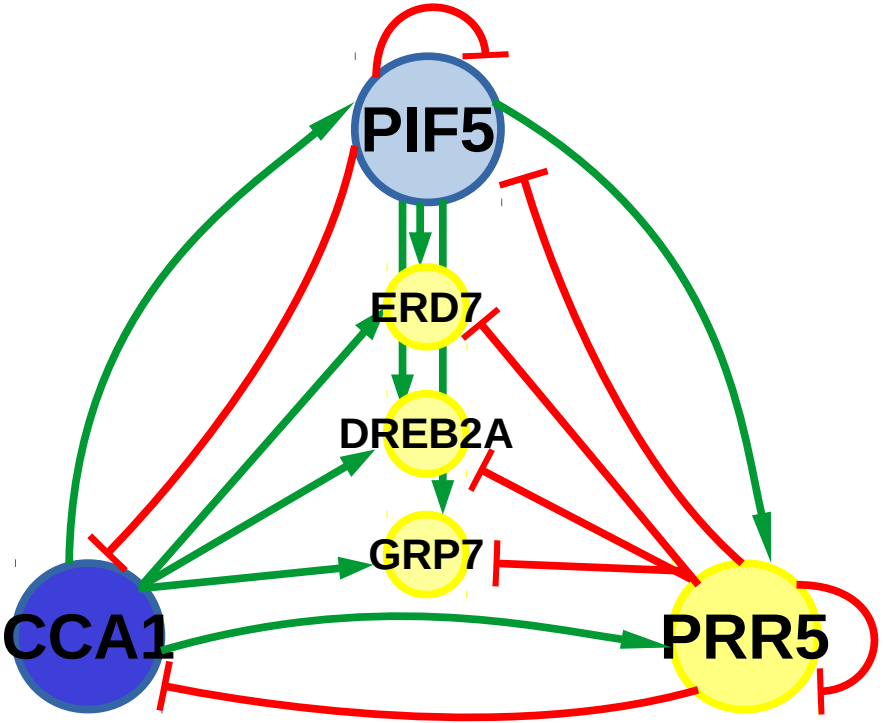

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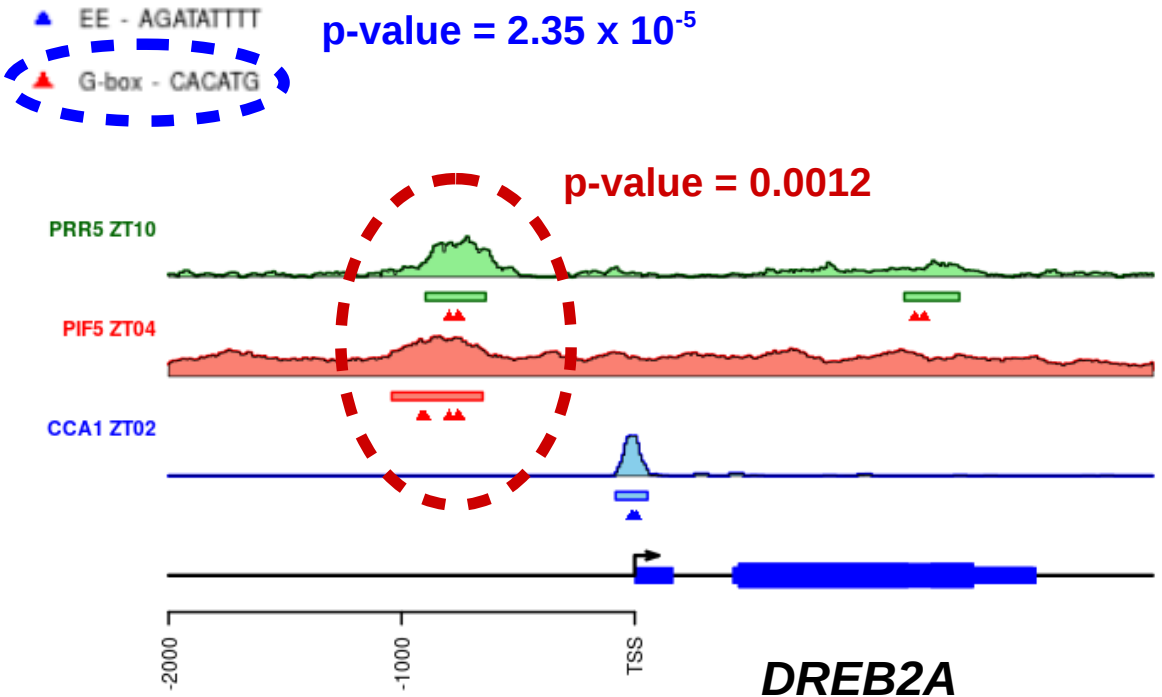
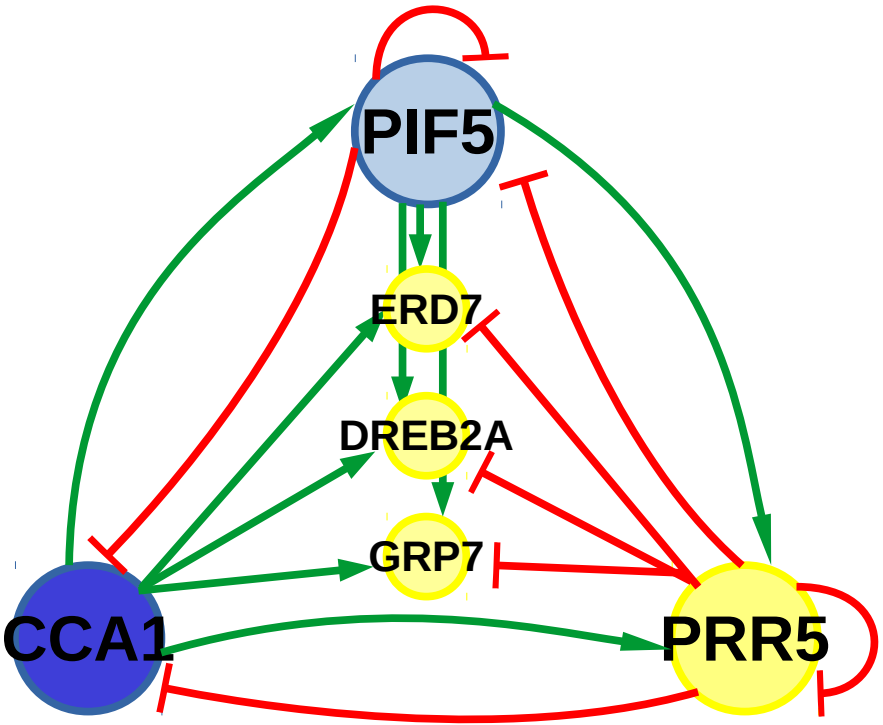
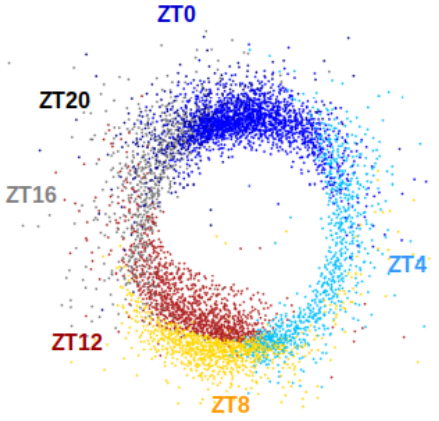


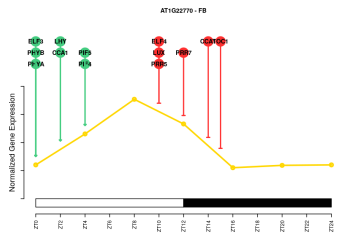


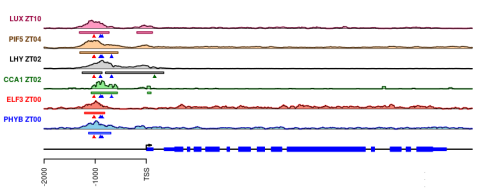
Summary

- **ATTRACTOR** is a **transcriptional network** capturing the synergistic regulation exerted by the circadian clock and light signaling that unveils a system simultaneously **robust to random perturbations and sensitive to directed tuning**.

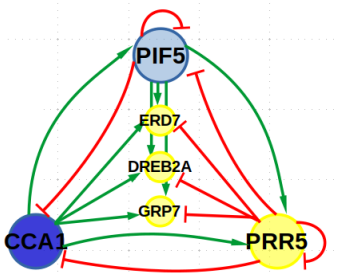


- **ATTRACTOR** is a web based tool that **enables researchers to explore** the expression profile, regulators and their binding sites of **individual genes** as well as the **coordinated regulation** of multiple transcription factors over common target genes.

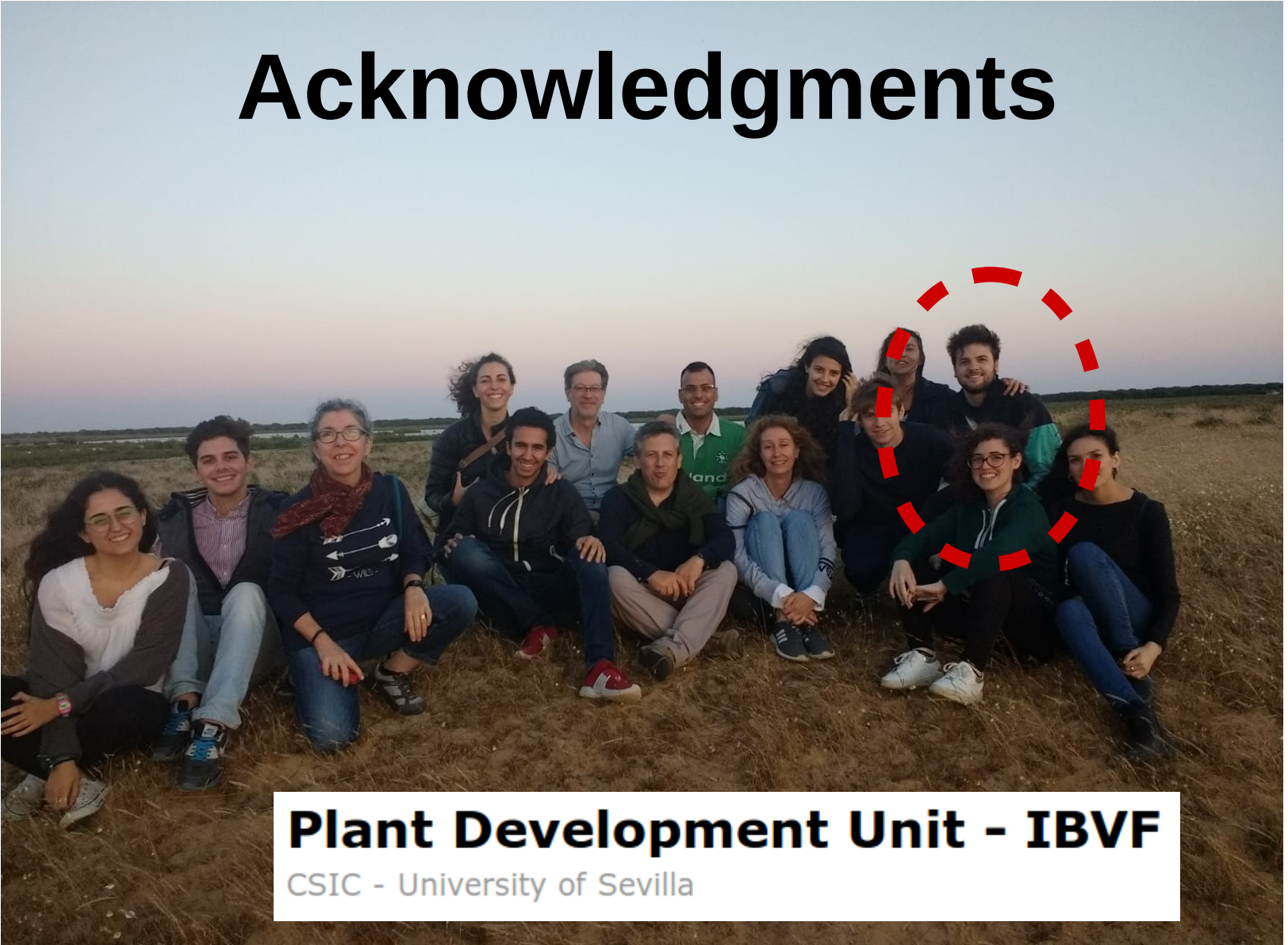




- **Network motive** analysis reveals that PIFs, PRRs and CCA1/LHY form linked **controlling response to drought**.



Acknowledgments



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