

Transcriptional landscape of fate choices in the sensory lineages

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Corresponding author: Saida Hadjab



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Igor Adameyko



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Bioinformatics Seminar – Louis Faure
7/17/2022



Karolinska
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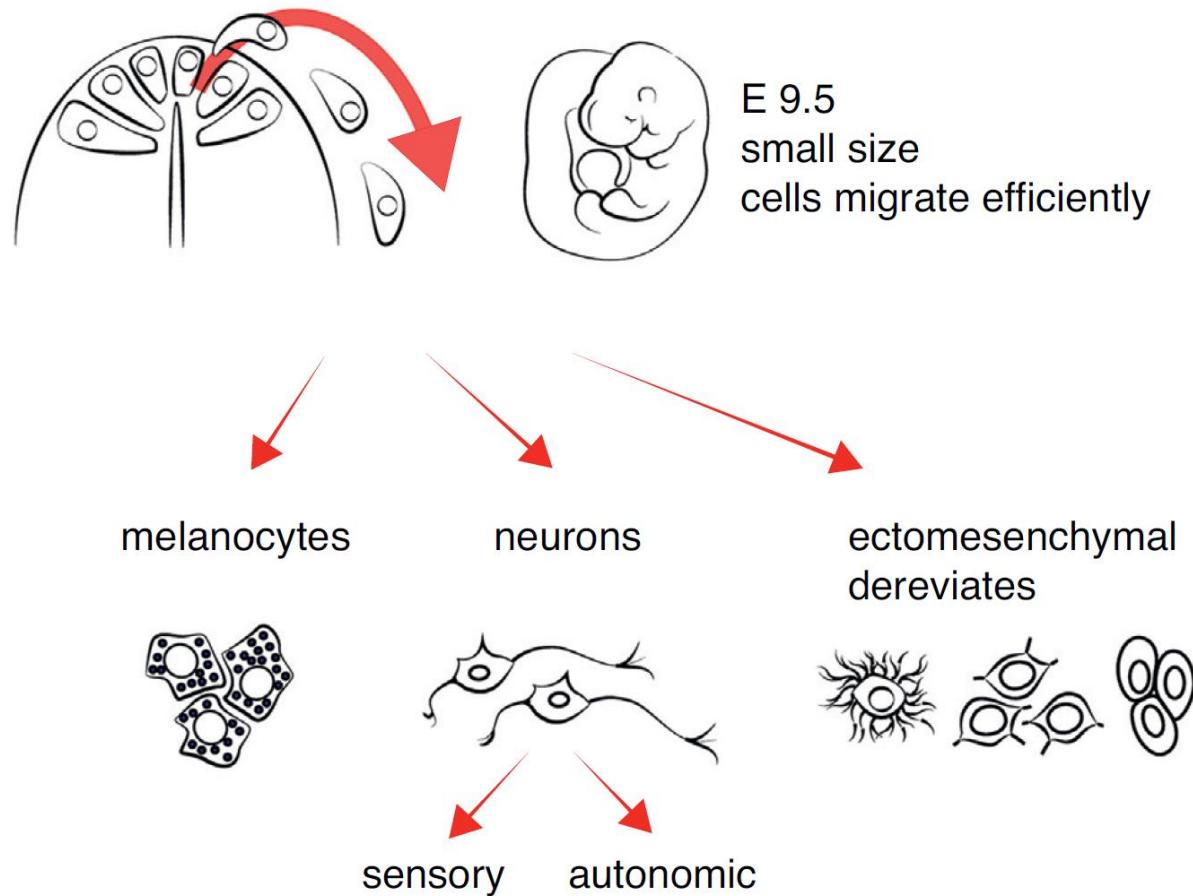
Saida Hadjab



François Lallemend



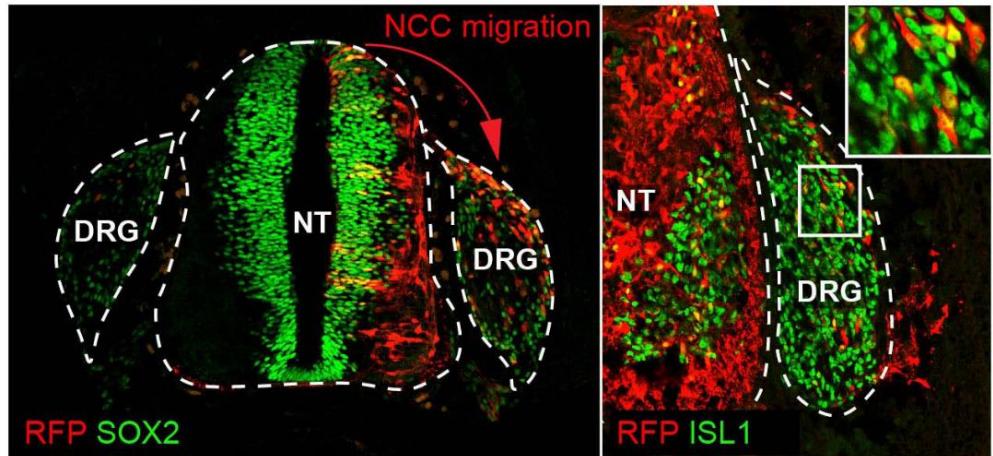
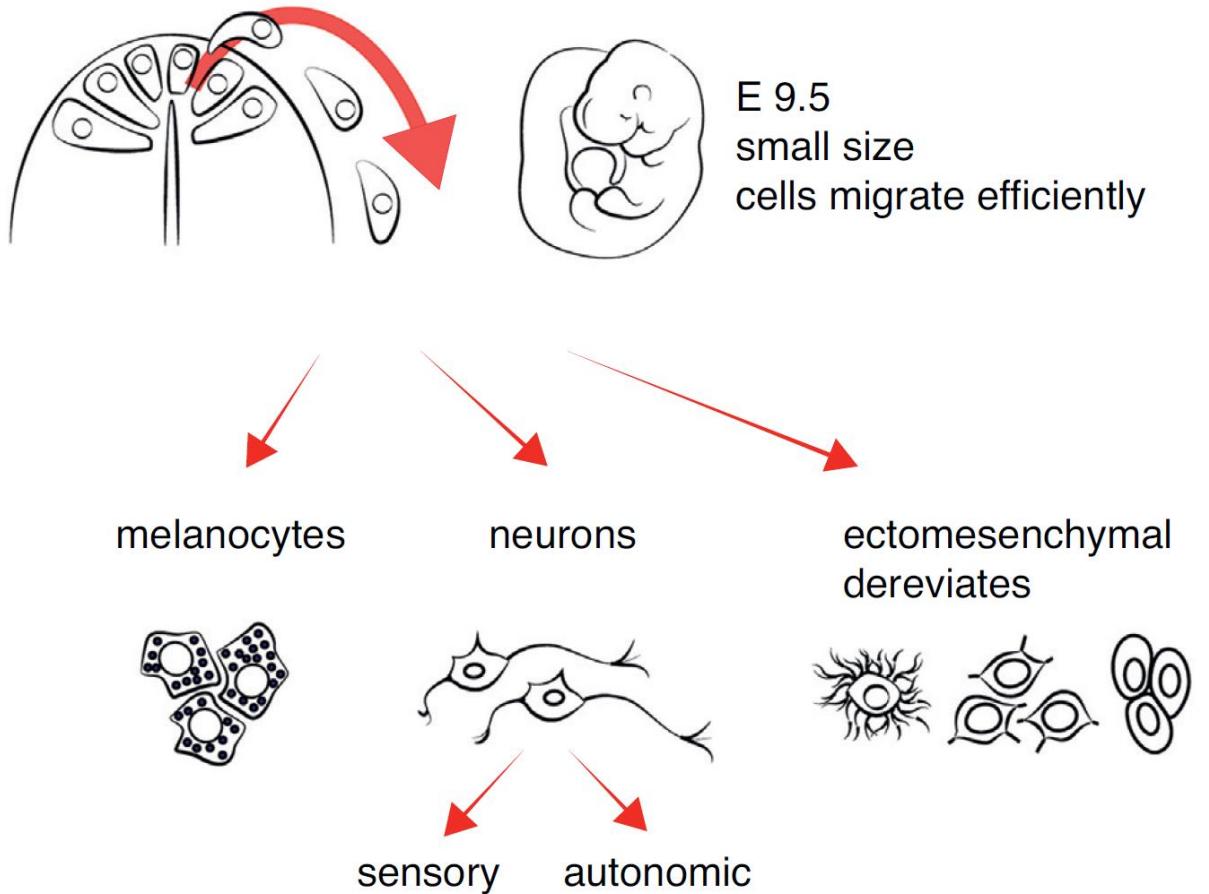
Neural crest



Petersen, J. & Adameyko, I. Nerve-associated neural crest: peripheral glial cells generate multiple fates in the body. *Curr. Opin. Genet. Dev.* 45, 10–14 (2017).



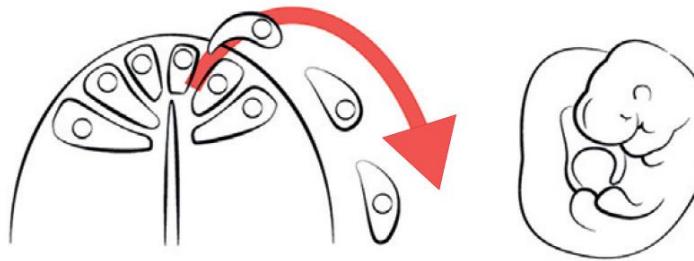
Neural crest



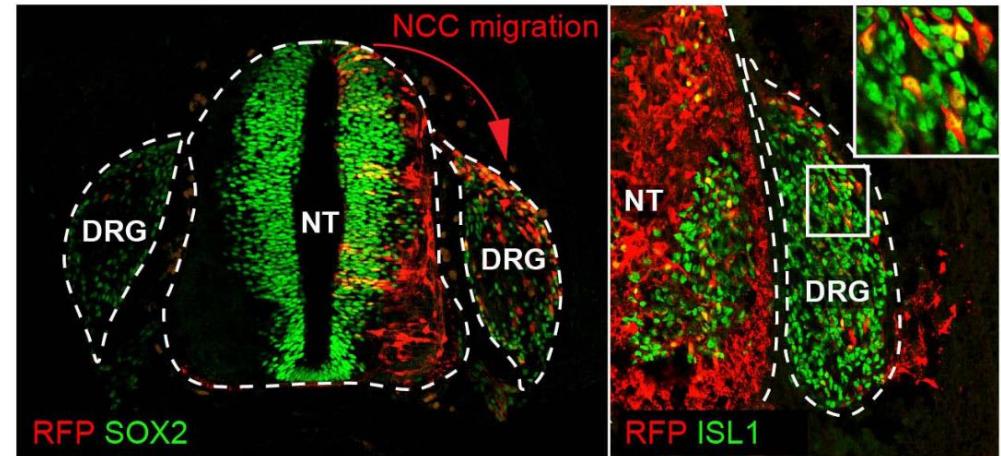
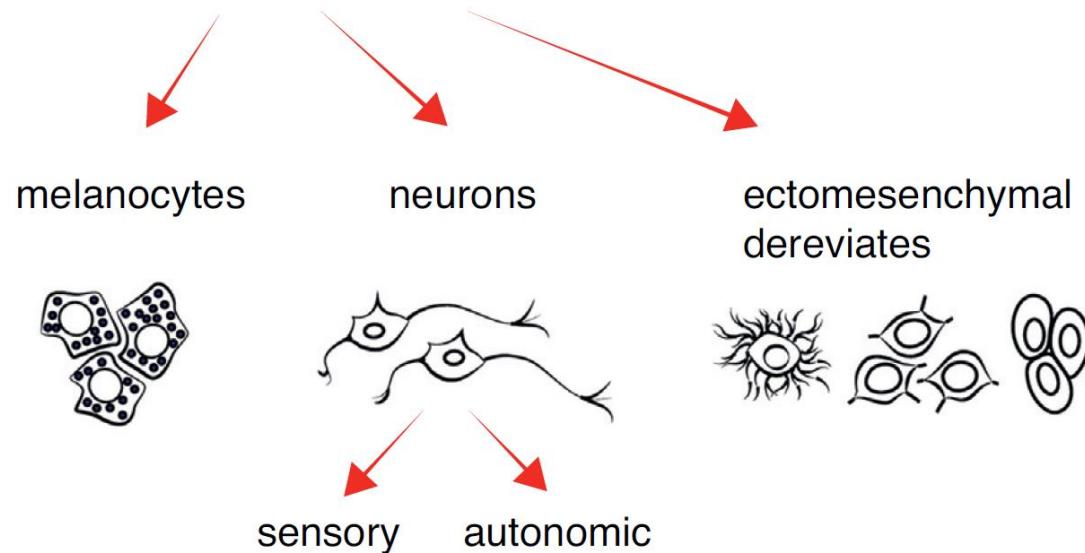
Soldatov, R. et al. Spatiotemporal structure of cell fate decisions in murine neural crest. *Science* (80-). 364, (2019).

Petersen, J. & Adameyko, I. Nerve-associated neural crest: peripheral glial cells generate multiple fates in the body. *Curr. Opin. Genet. Dev.* 45, 10–14 (2017).

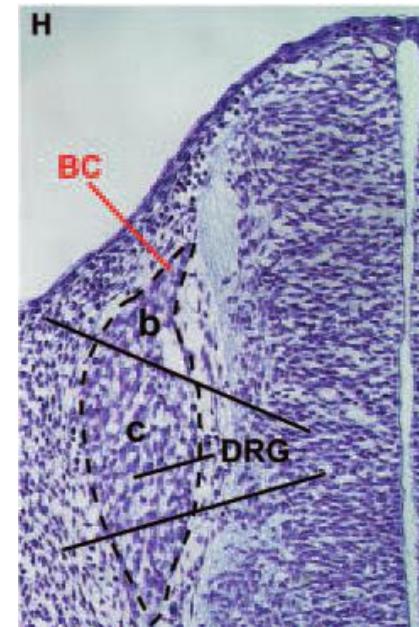
Neural crest



E 9.5
small size
cells migrate efficiently



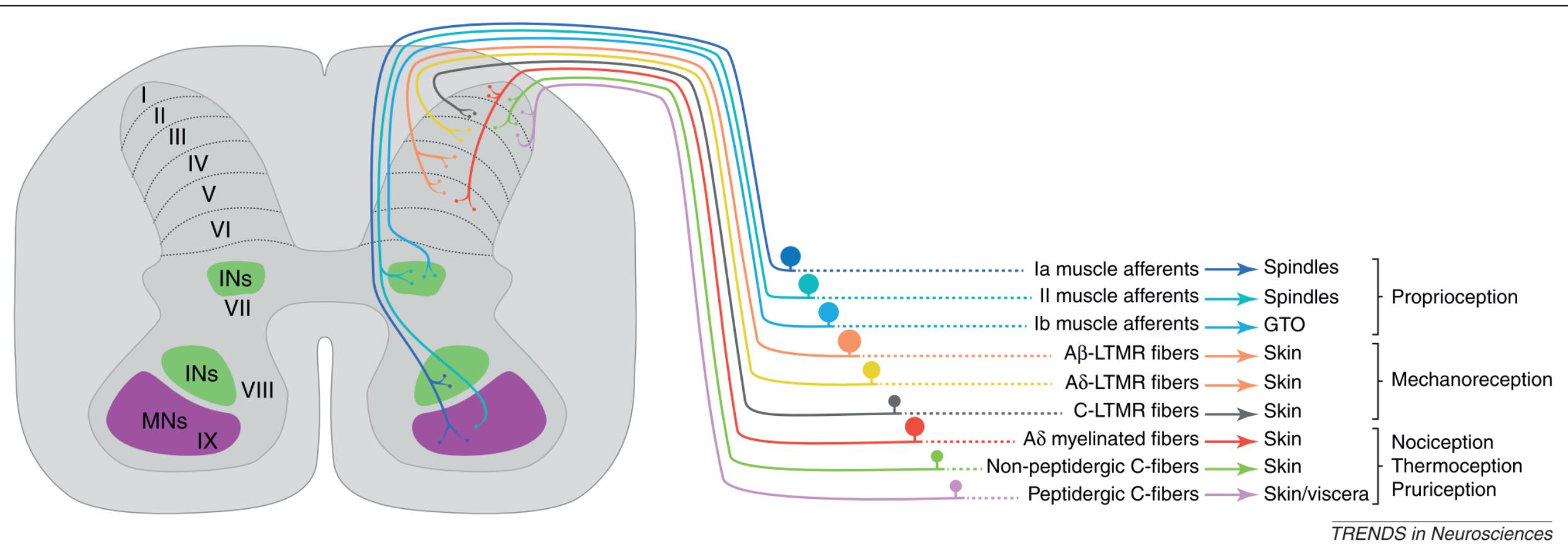
Soldatov, R. et al. Spatiotemporal structure of cell fate decisions in murine neural crest. *Science* (80-.). 364, (2019).



Petersen, J. & Adameyko, I. Nerve-associated neural crest: peripheral glial cells generate multiple fates in the body. *Curr. Opin. Genet. Dev.* 45, 10–14 (2017).

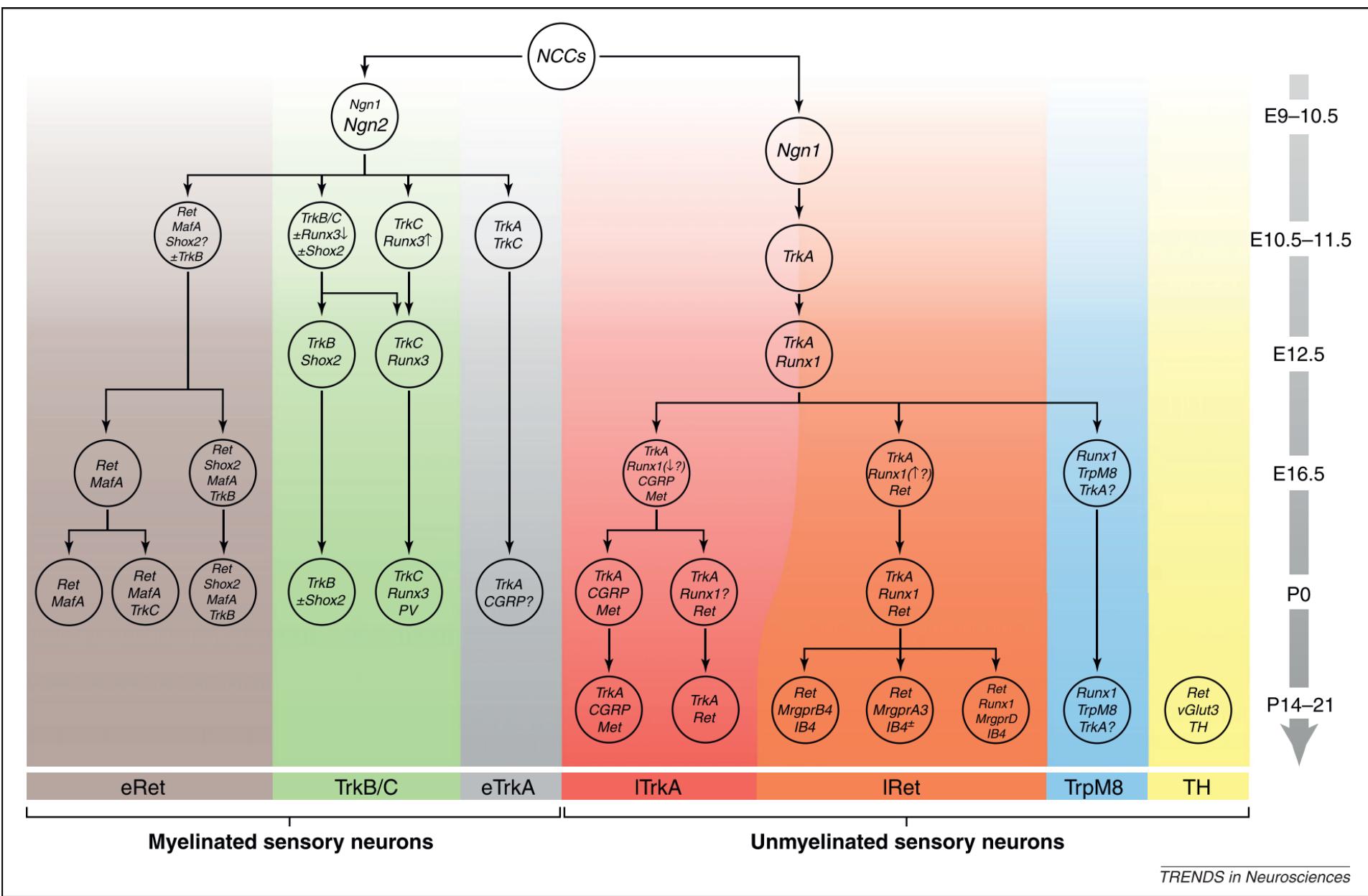


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Lallemand, F. & Ernfors, P. Molecular interactions underlying the specification of sensory neurons



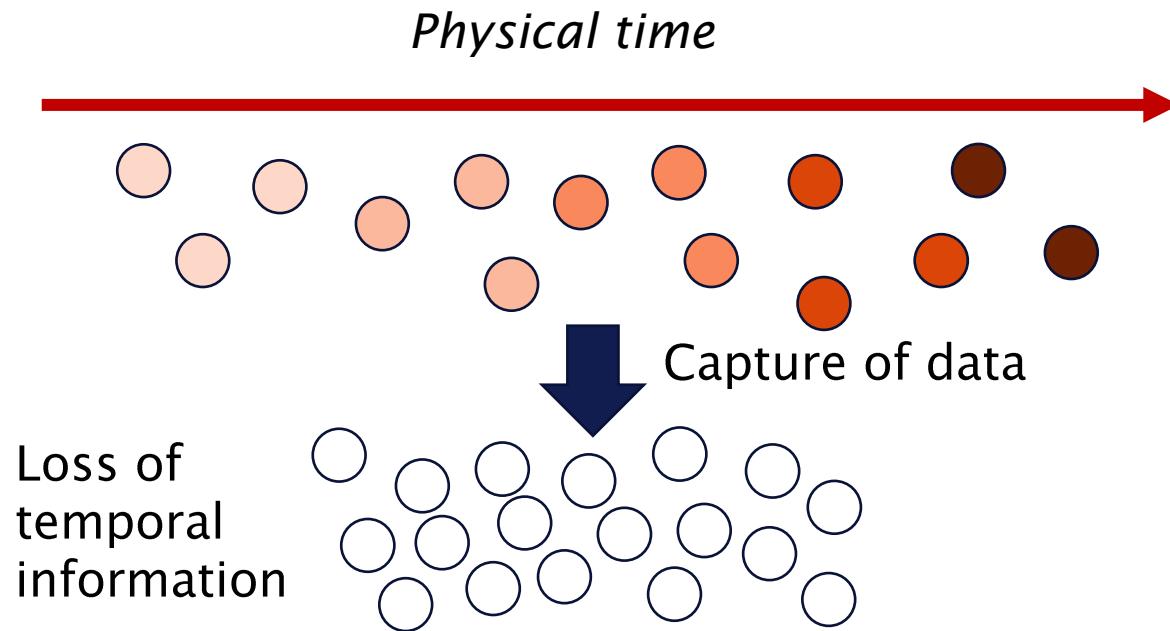


Lallemand, F. & Ernfors, P. Molecular interactions underlying the specification of sensory neurons



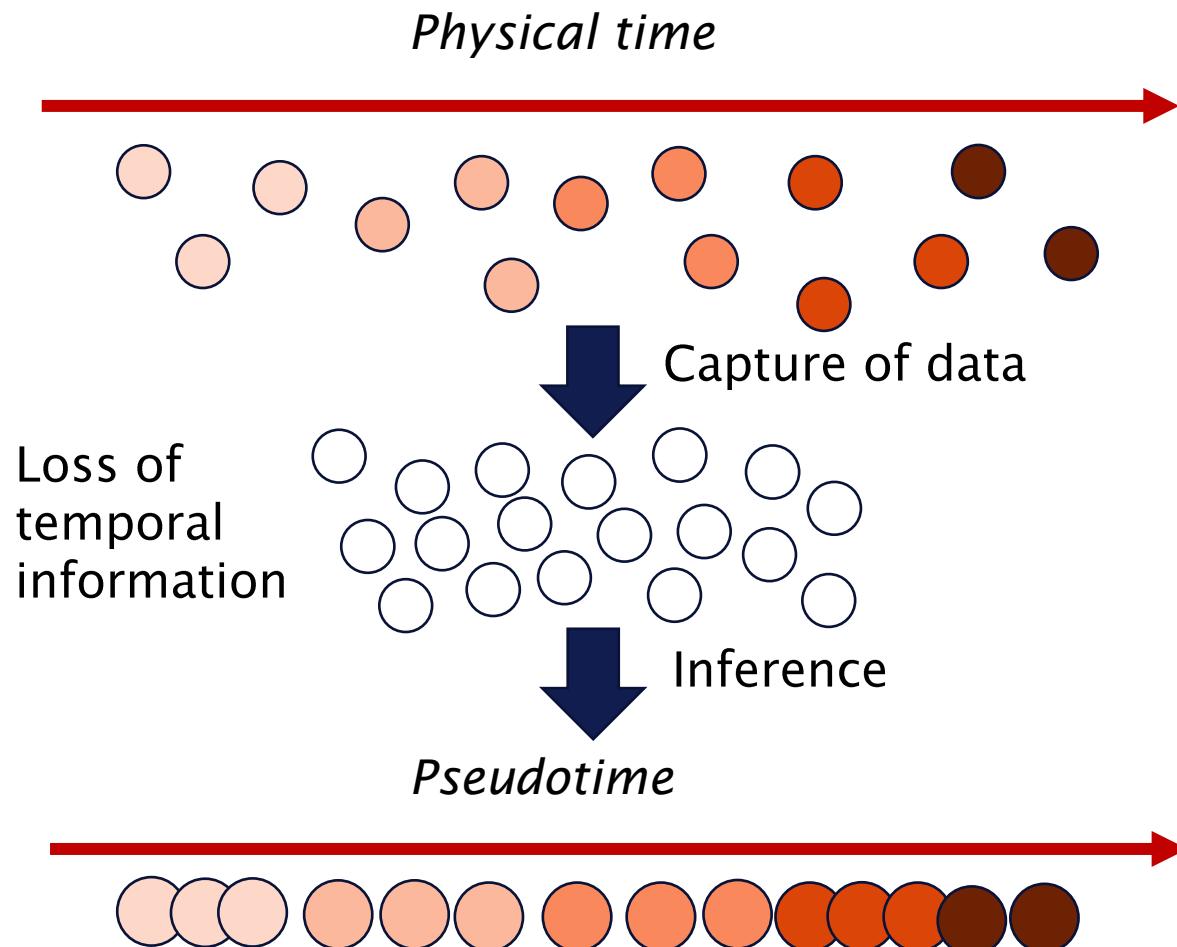
Pseudotime ordering

Ordering of the cell along a trajectory inferred in transcriptional space (Curve, Branching)



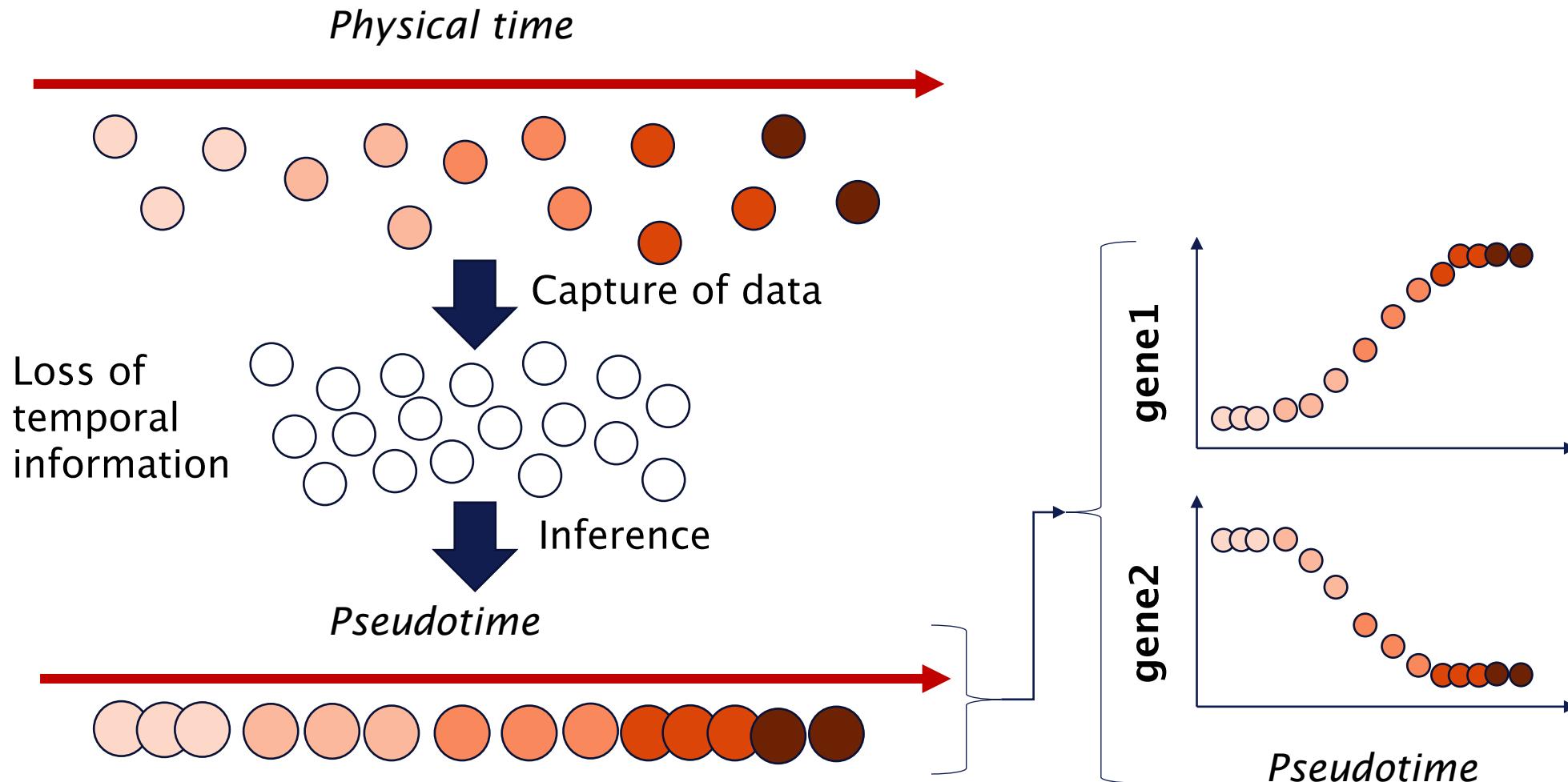
Pseudotime ordering

Ordering of the cell along a trajectory inferred in transcriptional space (Curve, Branching)

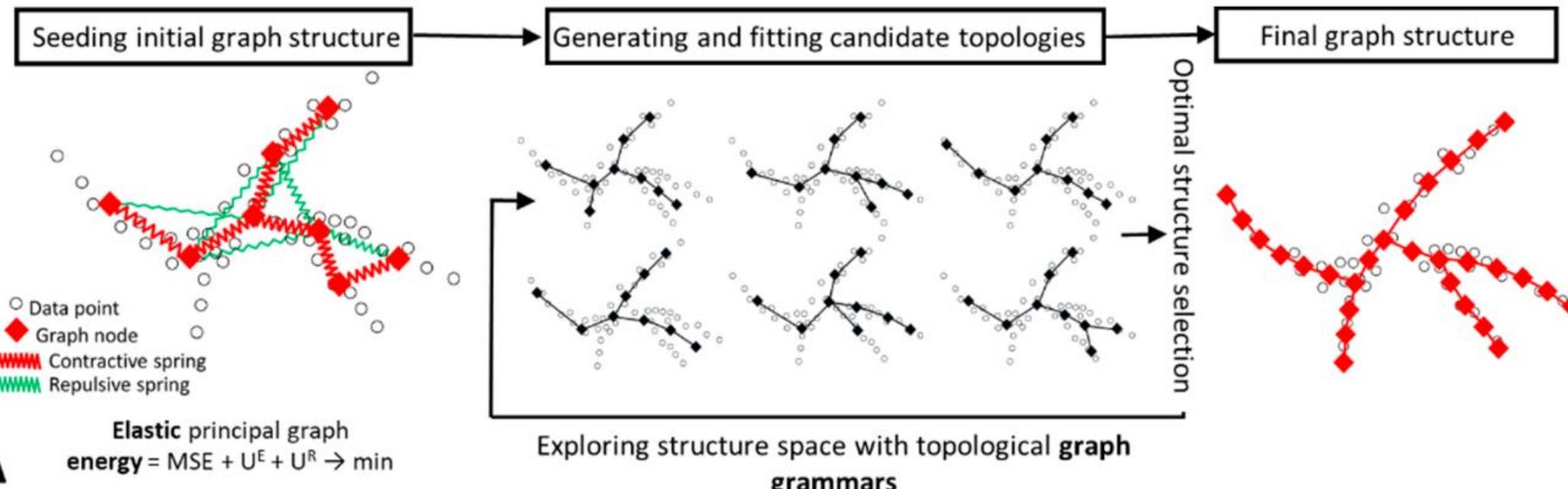


Pseudotime ordering

Ordering of the cell along a trajectory inferred in transcriptional space (Curve, Branching)



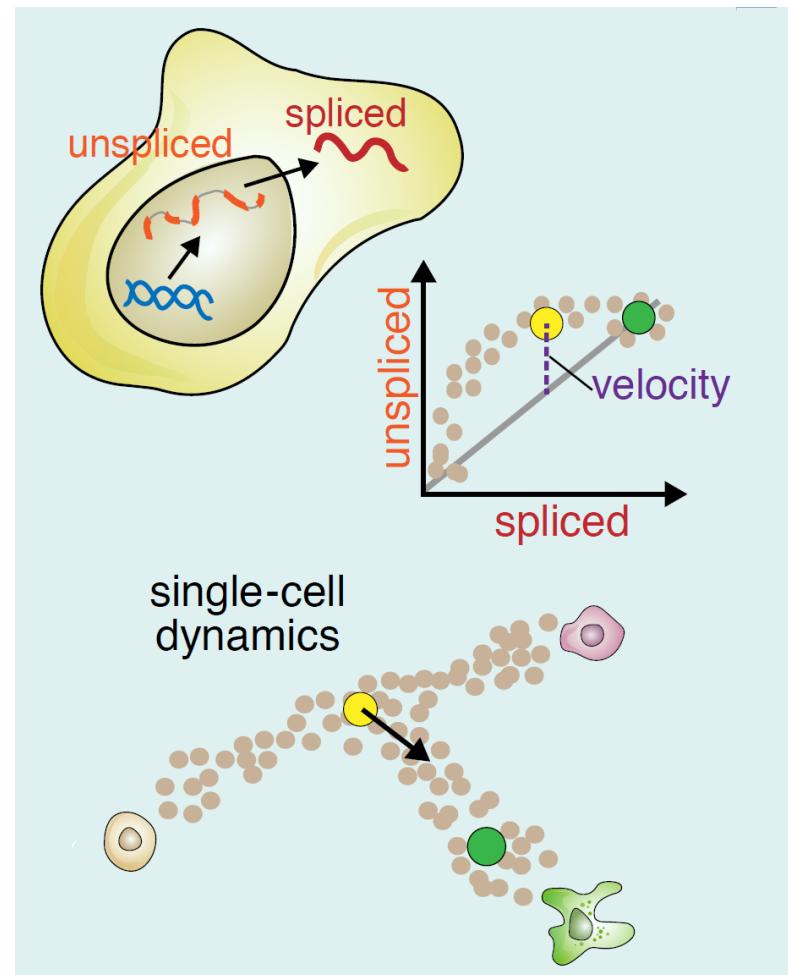
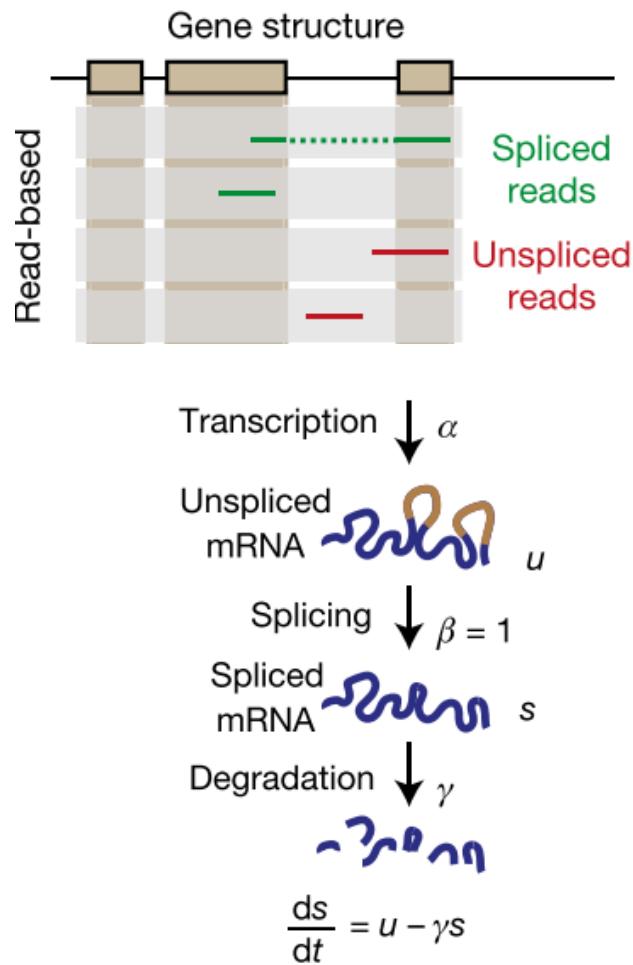
Inferring latent space in high dimensions: ElPiGraph



Albergante, L. *et al.* Robust And Scalable Learning Of Complex Dataset Topologies Via Elpigraph. *Entropy* **22**, 296 (2020).



RNA velocity: inferring cell's future state



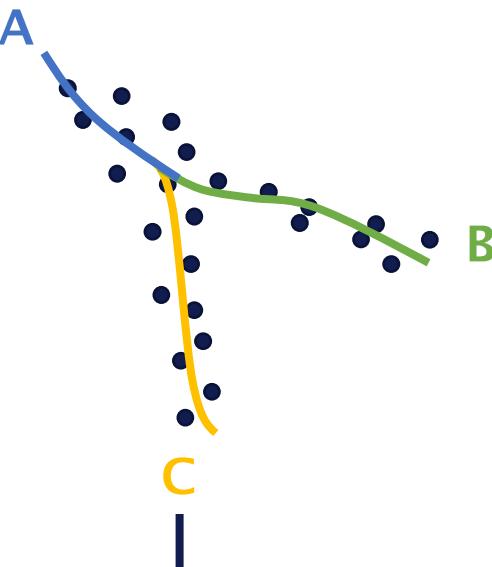
Edited from: Lederer, A. R. & La Manno, G. The emergence and promise of single-cell temporal-omics approaches. *Current Opinion in Biotechnology* (2020). doi:10.1016/j.copbio.2019.12.005



Uncovering trajectories: two complementary methods

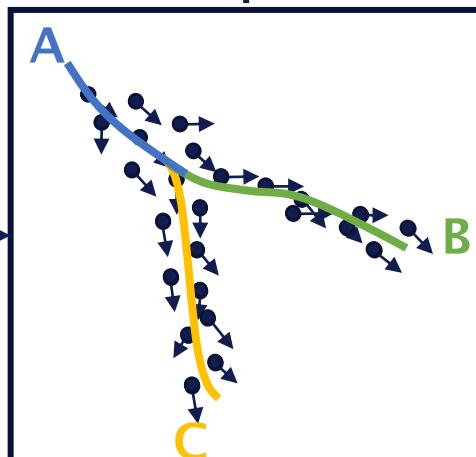
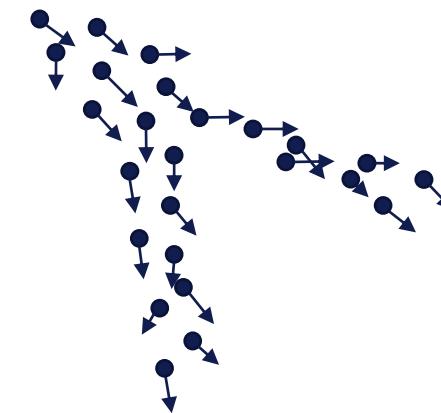
Pseudotime

Ordering of the cell along a trajectory
inferred in transcriptional space
(Curve, Branching)



RNA Velocity

Inferring the next state of a cell by
using balance between spliced and
unspliced RNA



Single-cell sequencing strategy

Cell selection

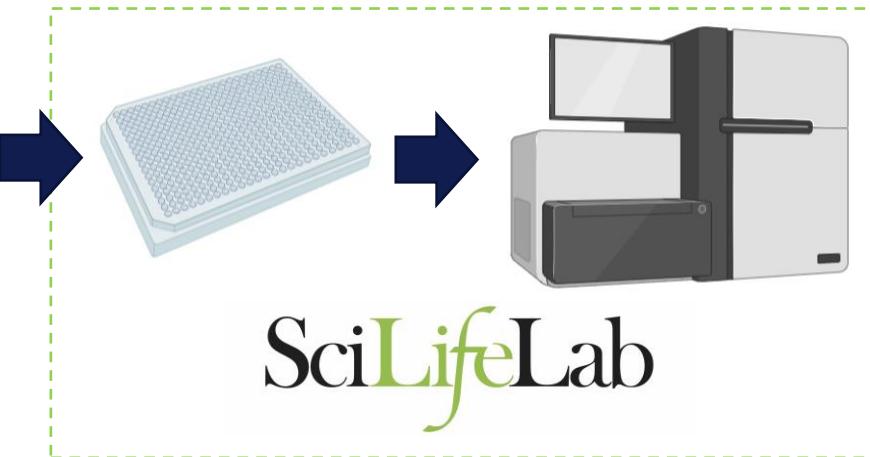
Brachial DRGs
Isl1Cre (E10.5)
Ntrk3Cre (E11.5-12.5)

Whole Trunk
Wnt1Cre (E9.5-10.5)

Above Otic vesicle
Pip1CreERT2 (E12.5)



FACS



Dissociated cells

Reverse transcription of mRNA

cDNA amplification and sequencing

Gene x cell matrix

Dimensionality reduction

Trajectory inference

Ordering of cells along trajectory
(a cell= a pseudotime value)



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Single-cell sequencing strategy

Cell selection

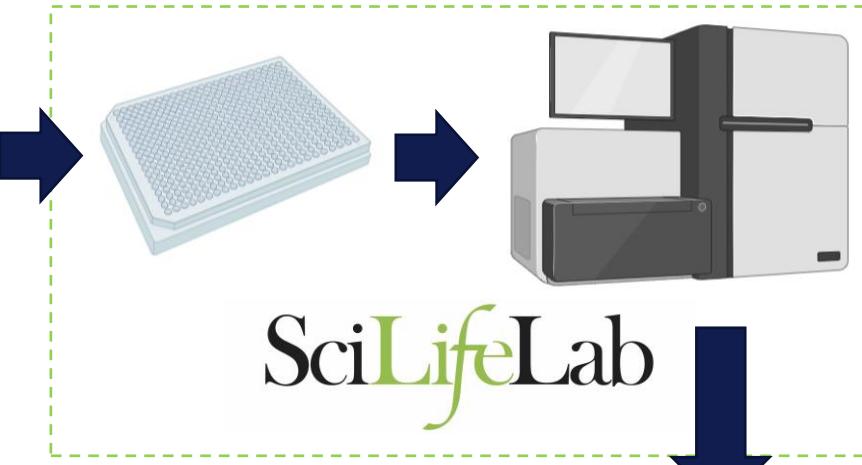
Brachial DRGs
Isl1Cre (E10.5)
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Whole Trunk
Wnt1Cre (E9.5-10.5)

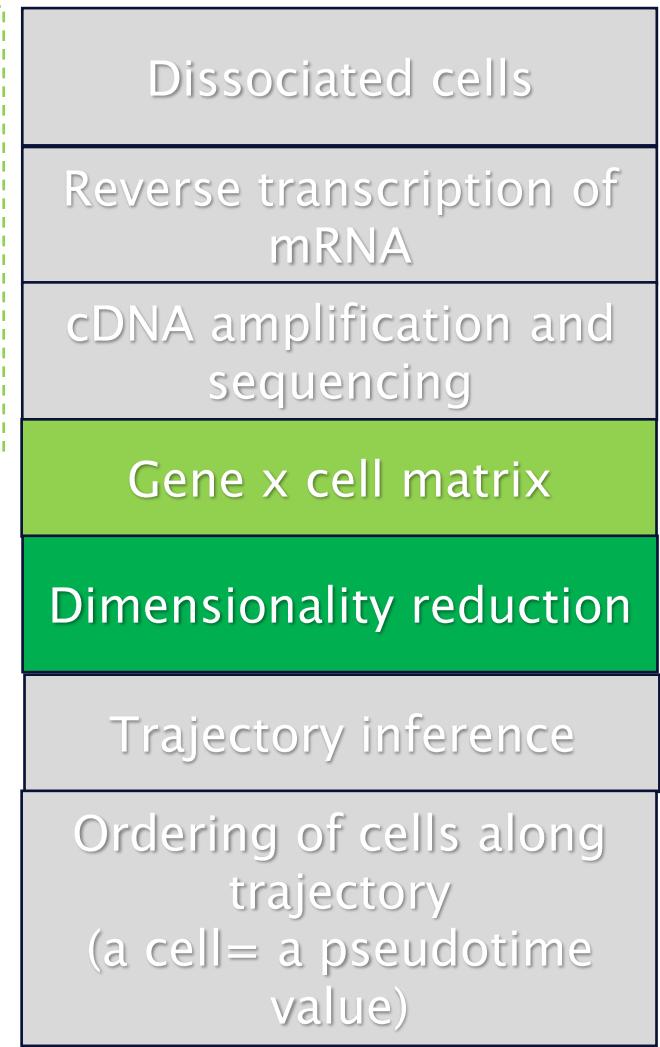
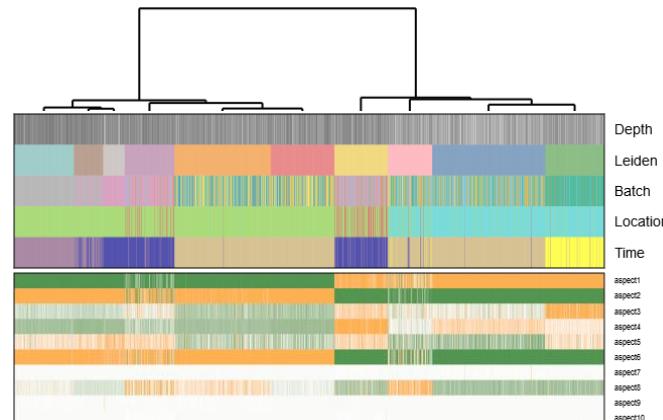
Above Otic vesicle
Pip1CreERT2 (E12.5)



FACS



Processing data using
Pagoda2 and scvelo



Single-cell sequencing strategy

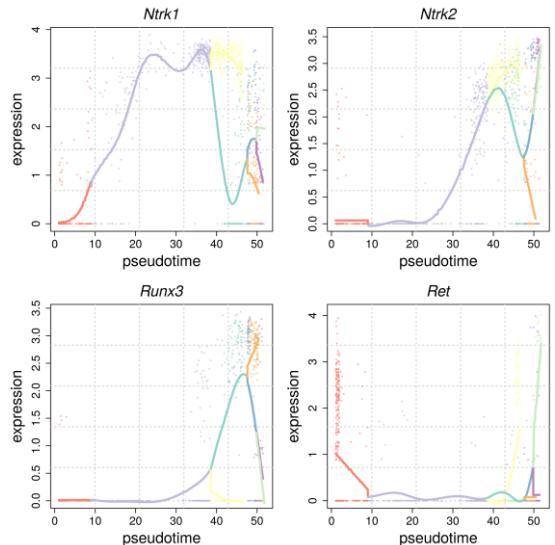
Cell selection

Brachial DRGs
Isl1Cre (E10.5)
Ntrk3Cre (E11.5-12.5)

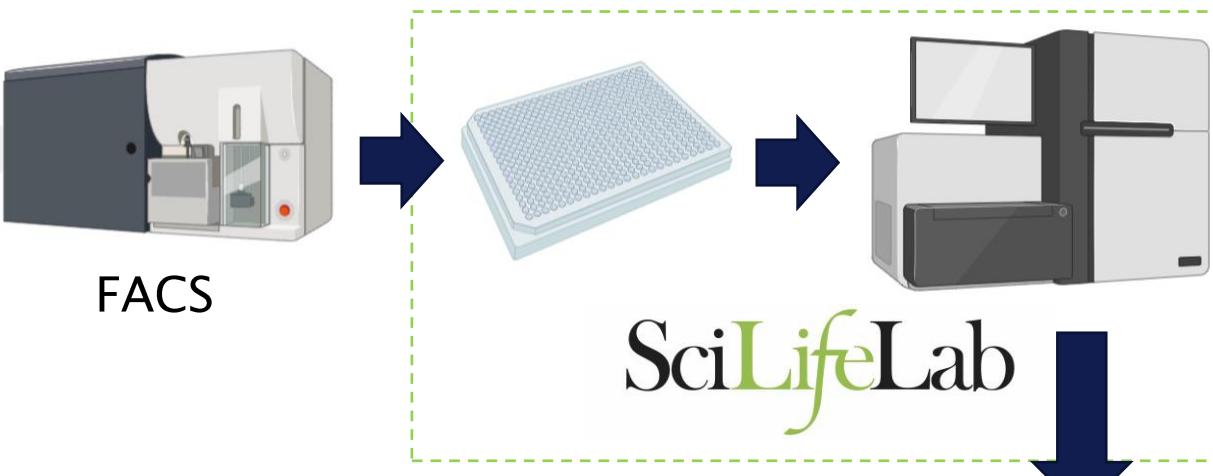
Whole Trunk
Wnt1Cre (E9.5-10.5)

Above Otic vesicle
Pip1CreERT2 (E12.5)

Dynamical gene Expression analysis

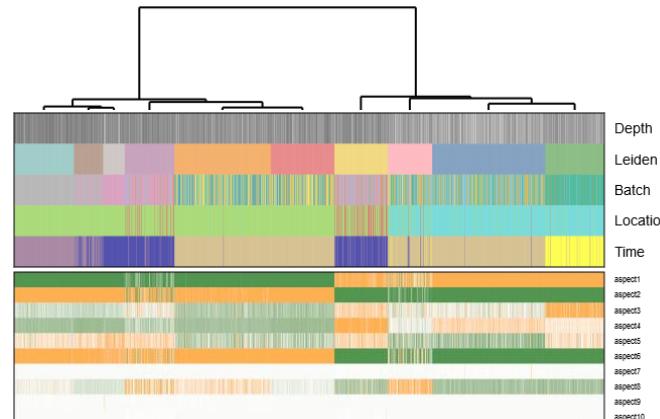


ElPiGraph on diffusion maps
(Palantir)



SciLifeLab

Processing data using
Pagoda2 and scvelo



Dissociated cells

Reverse transcription of mRNA

cDNA amplification and sequencing

Gene x cell matrix

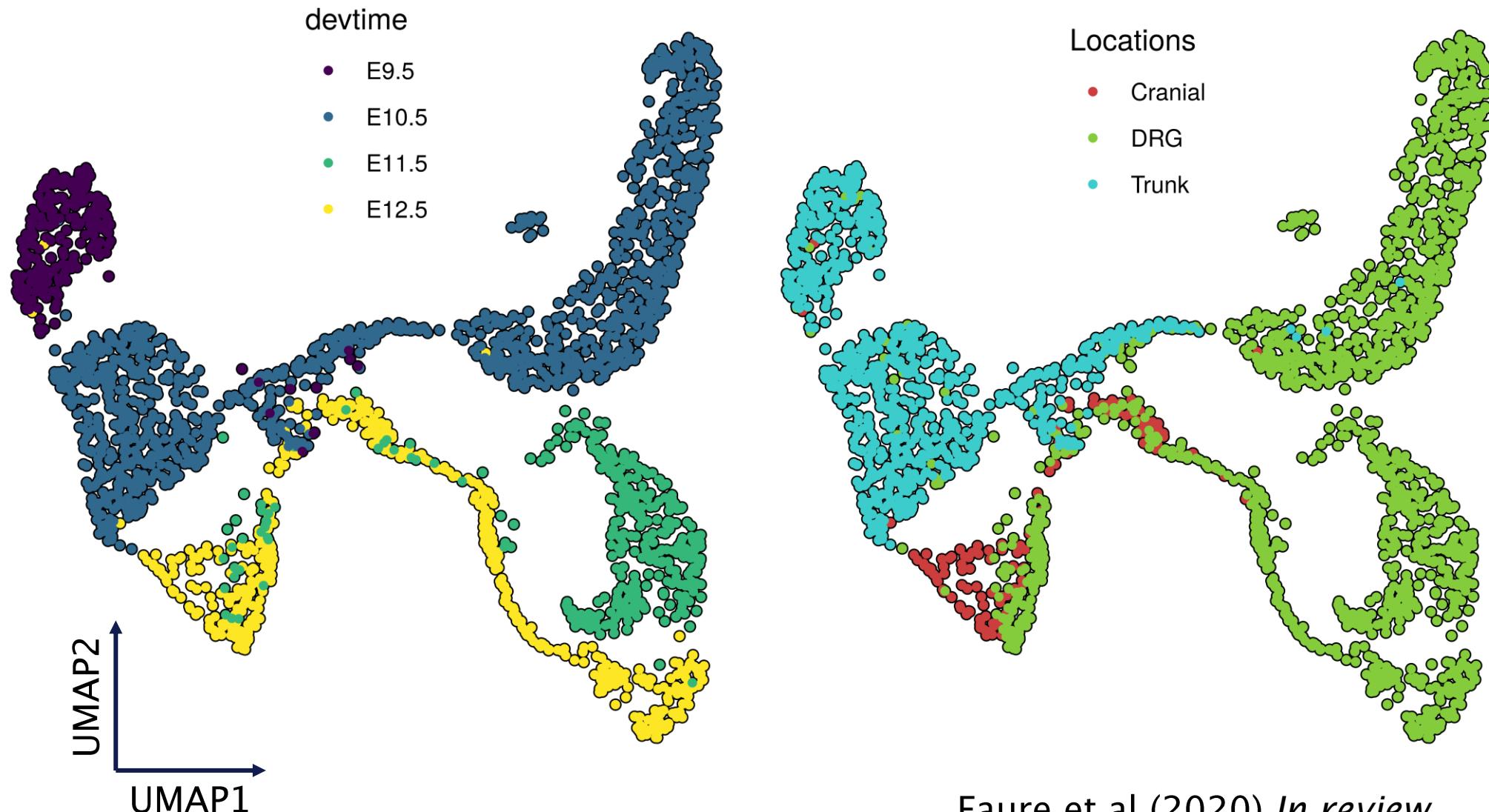
Dimensionality reduction

Trajectory inference

Ordering of cells along trajectory
(a cell = a pseudotime value)



Overview of the sequencing data



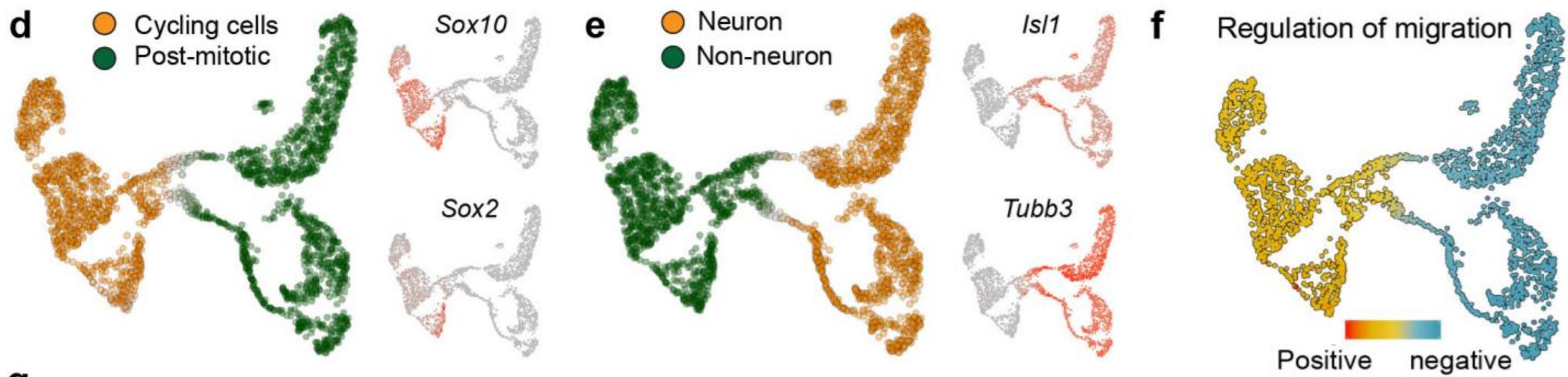
Overview of the sequencing data



Faure et al (2020) *In review*

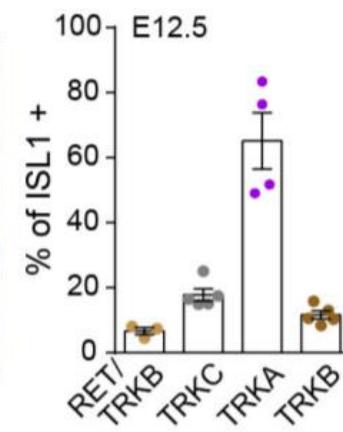
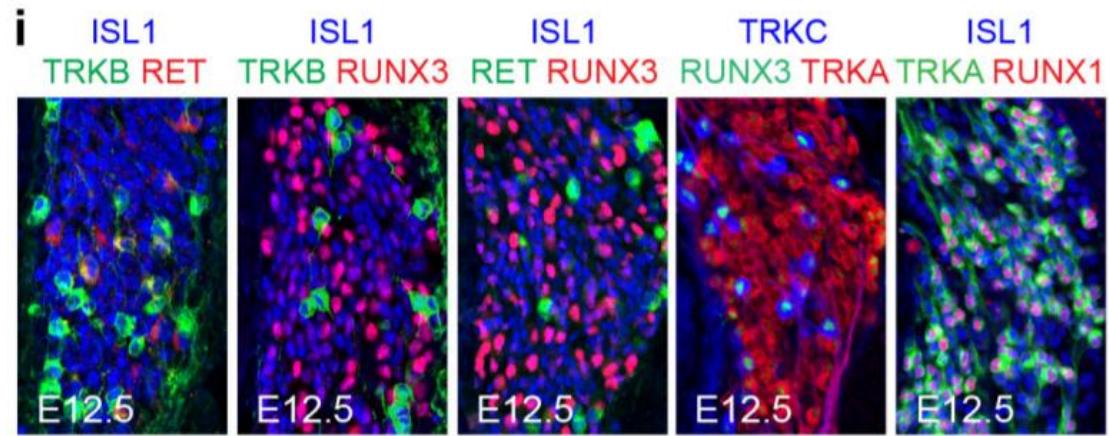
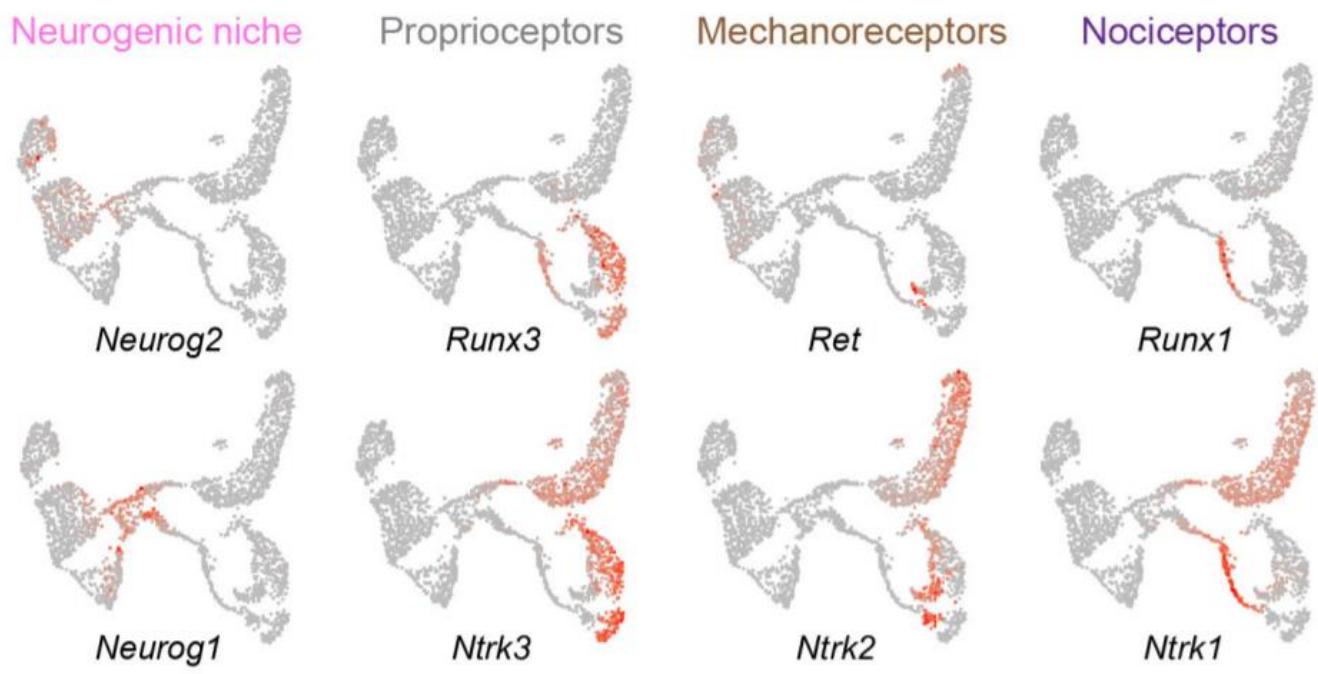


Main sources of variation and relevant biological aspects



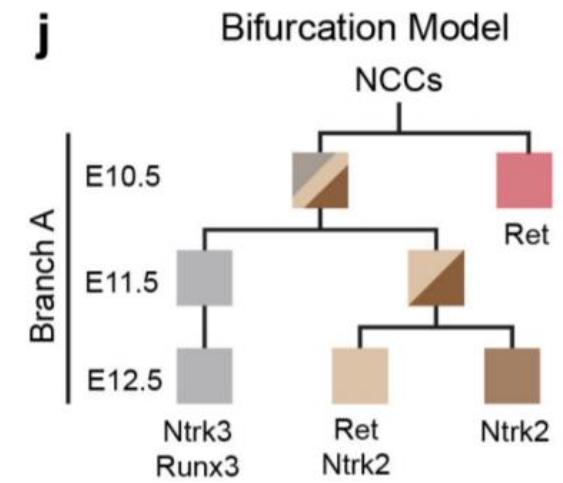
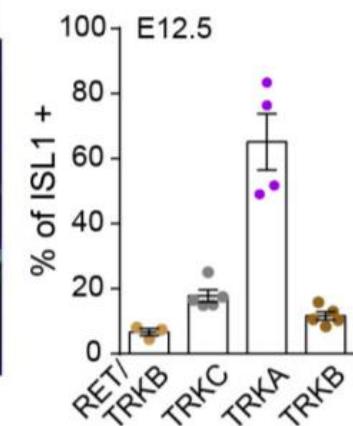
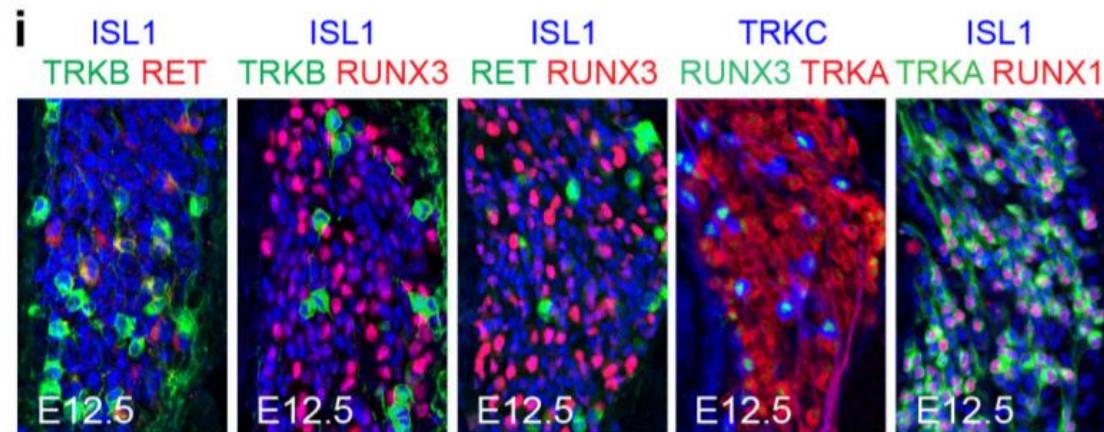
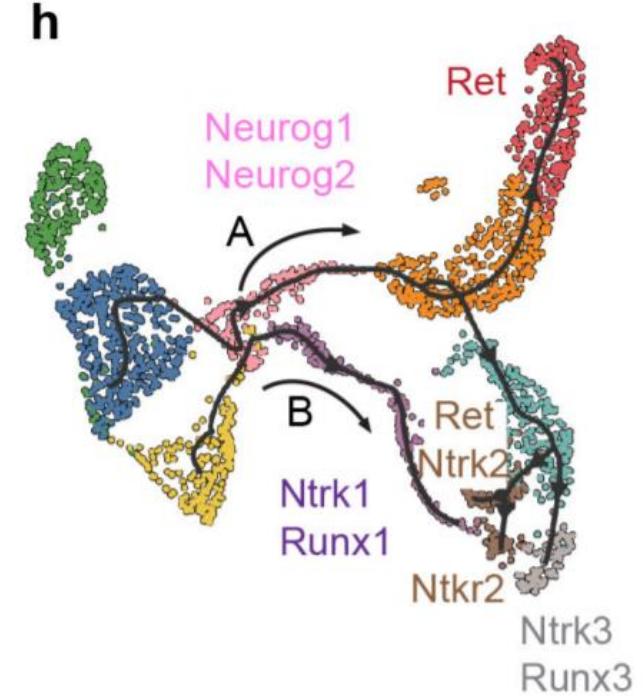
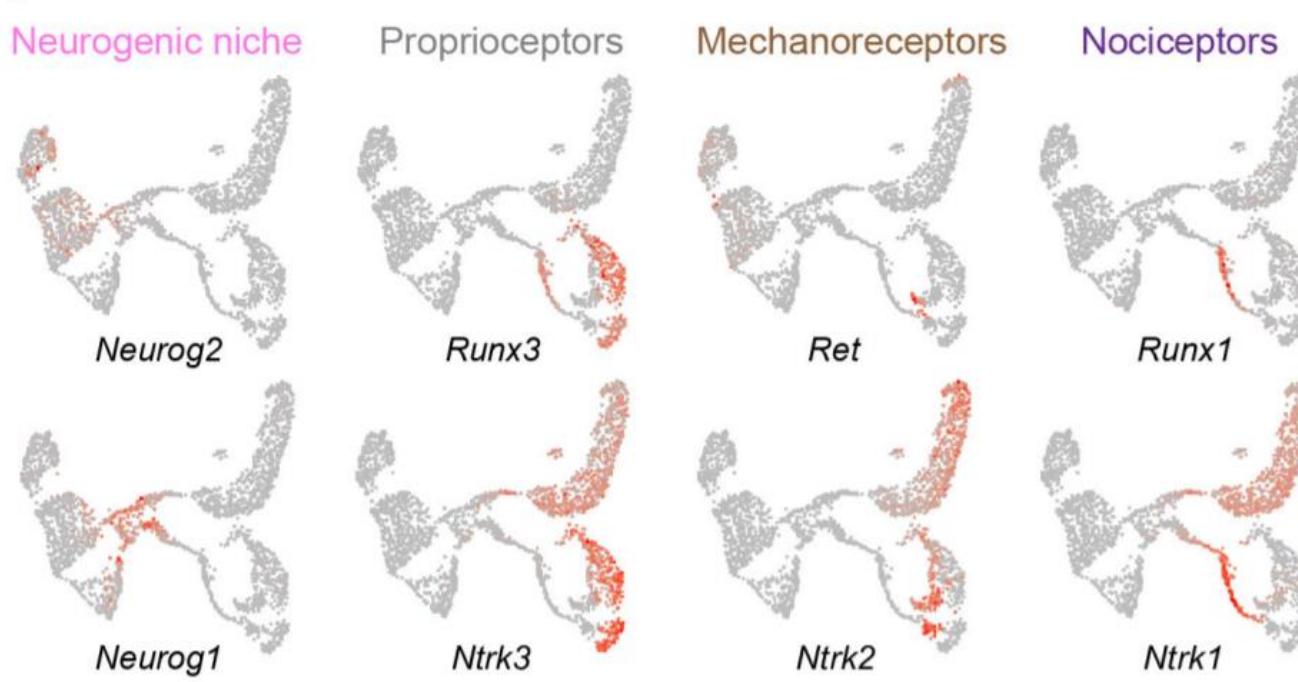
Faure et al (2020) *In review*



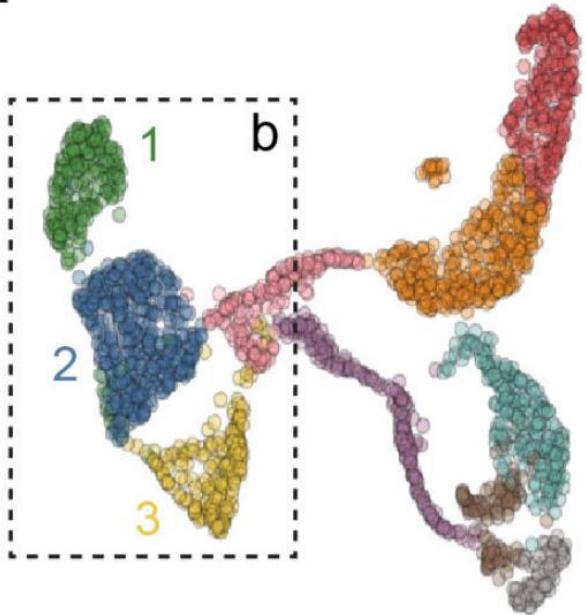
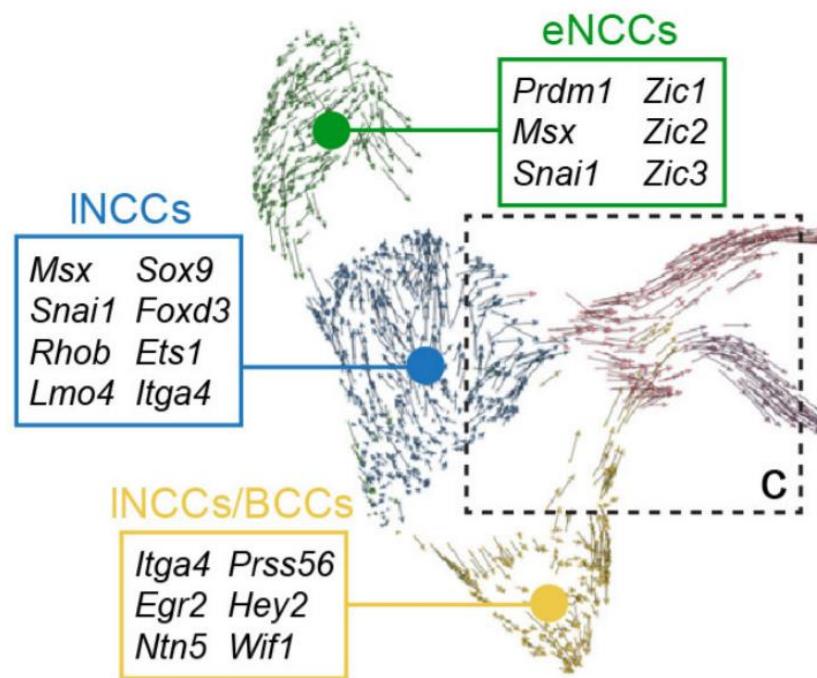
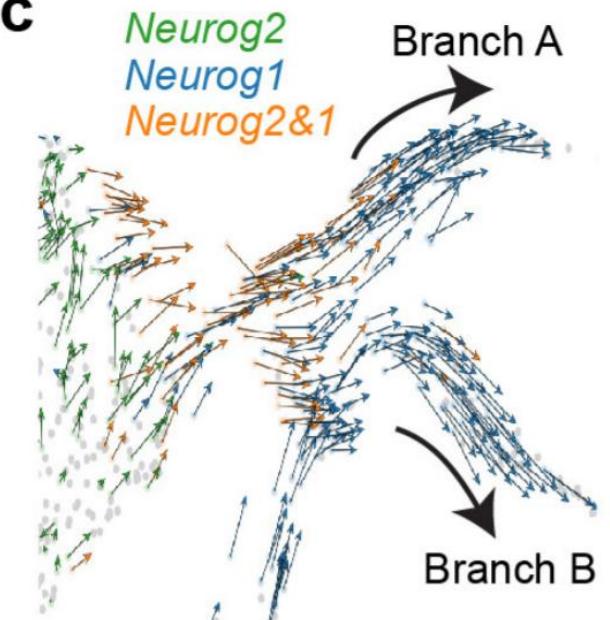


Faure et al (2020) *In review*



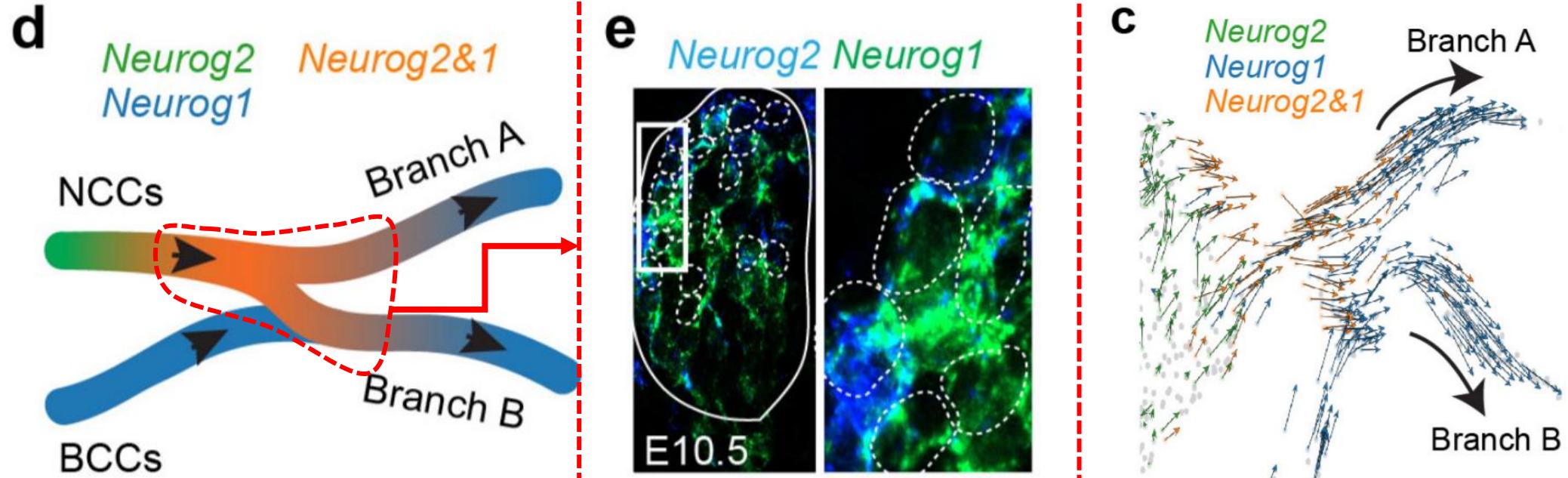


Faure et al (2020) *In review*

a**b****c**

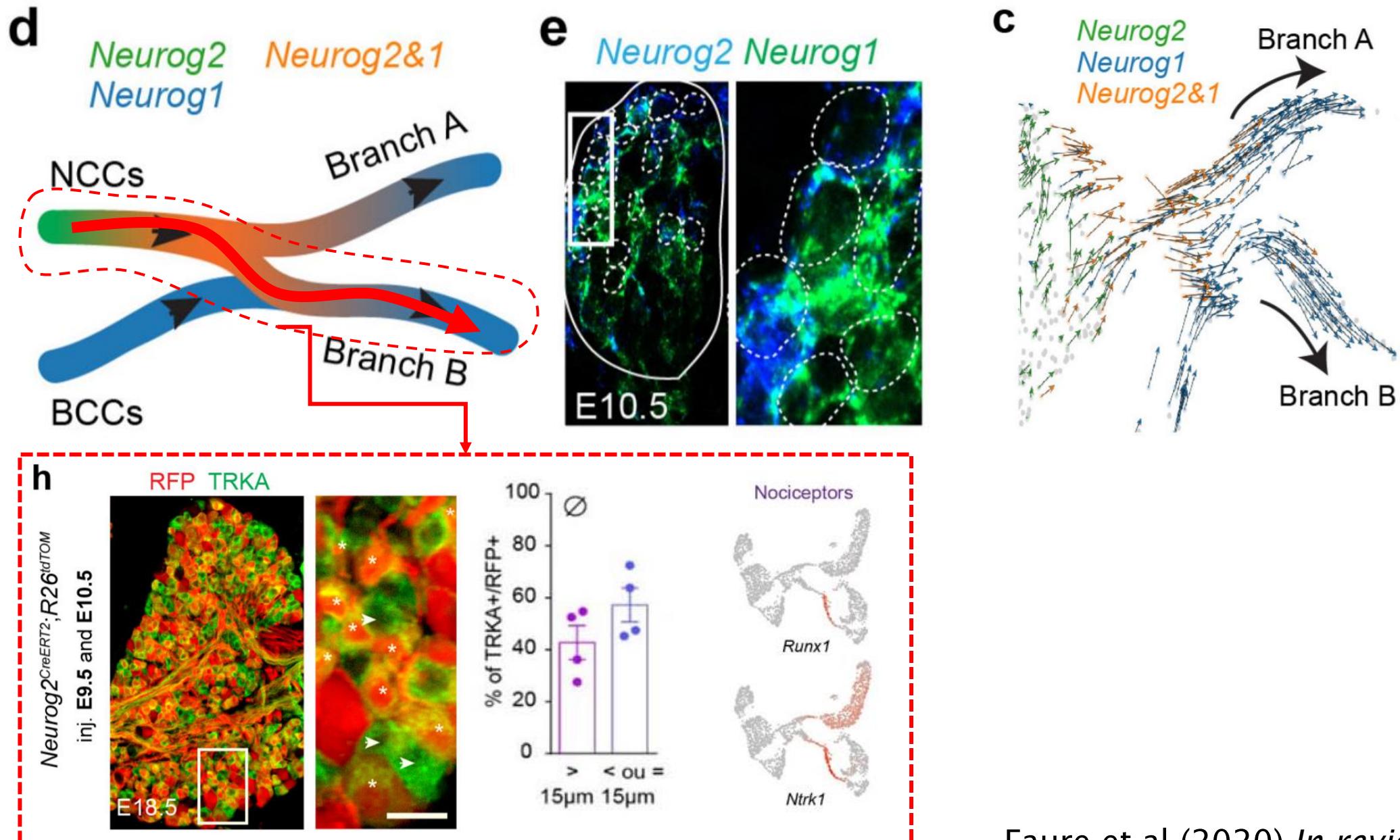
Faure et al (2020) *In review*





Faure et al (2020) *In review*

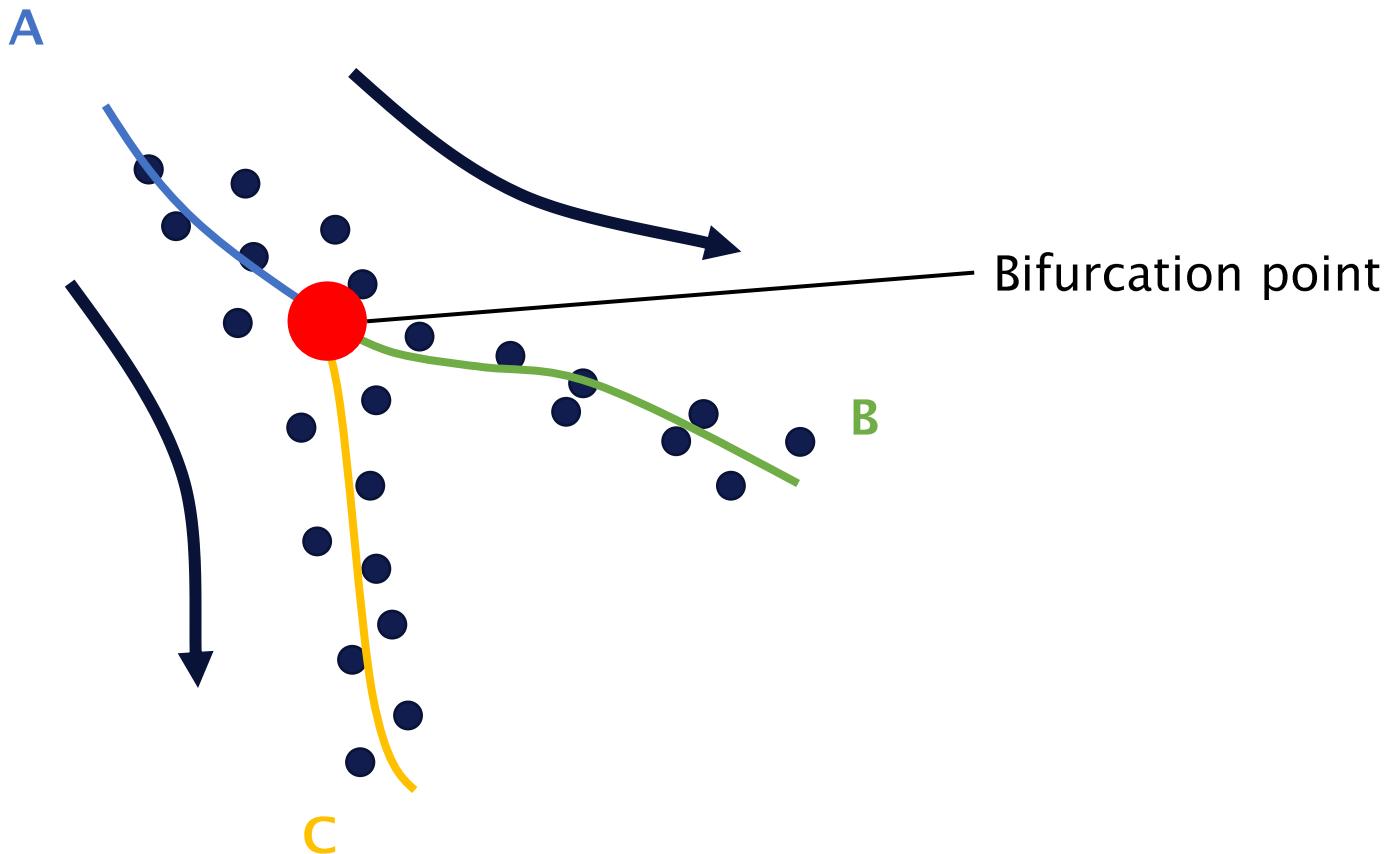




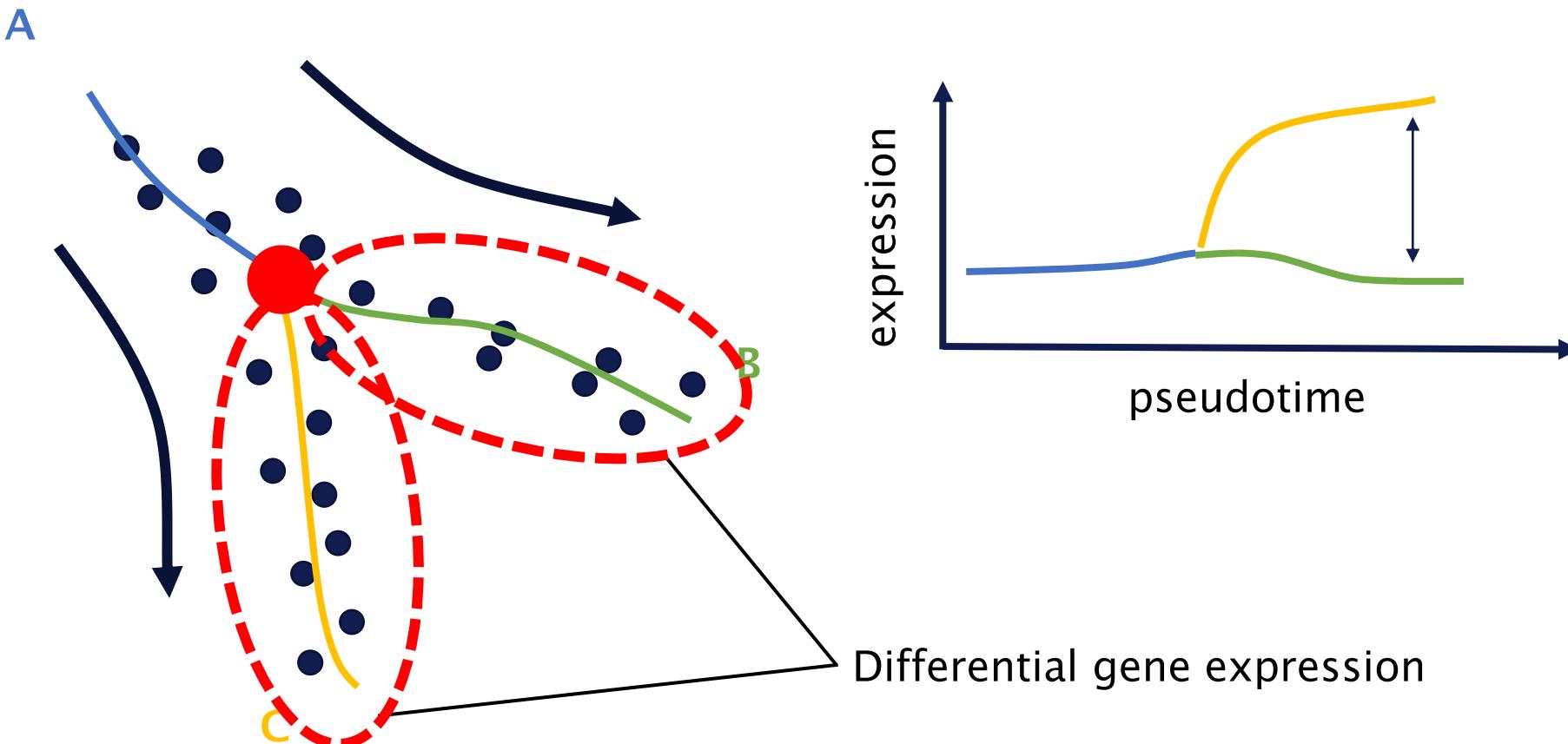
Faure et al (2020) *In review*



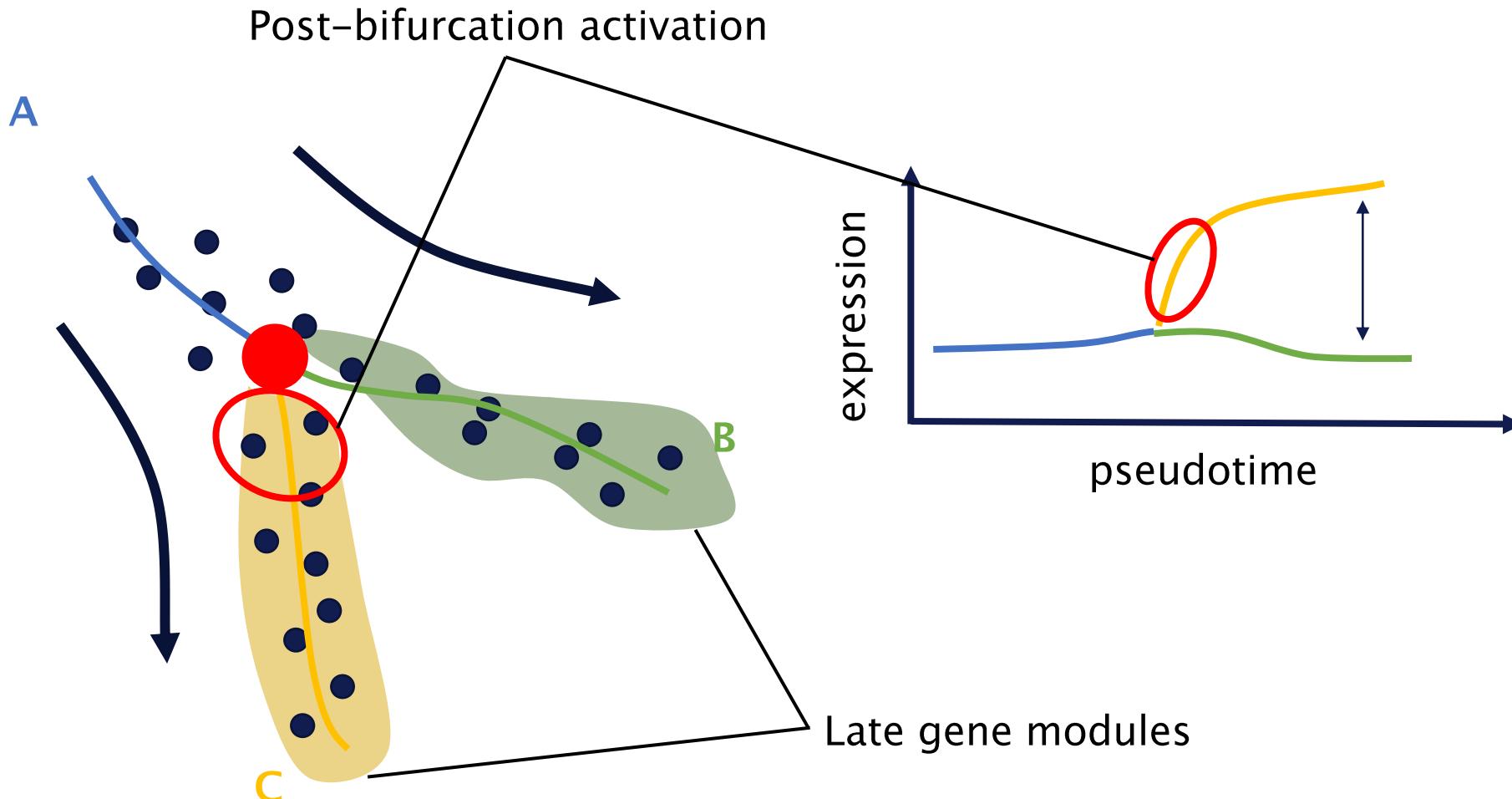
Bifurcation analysis



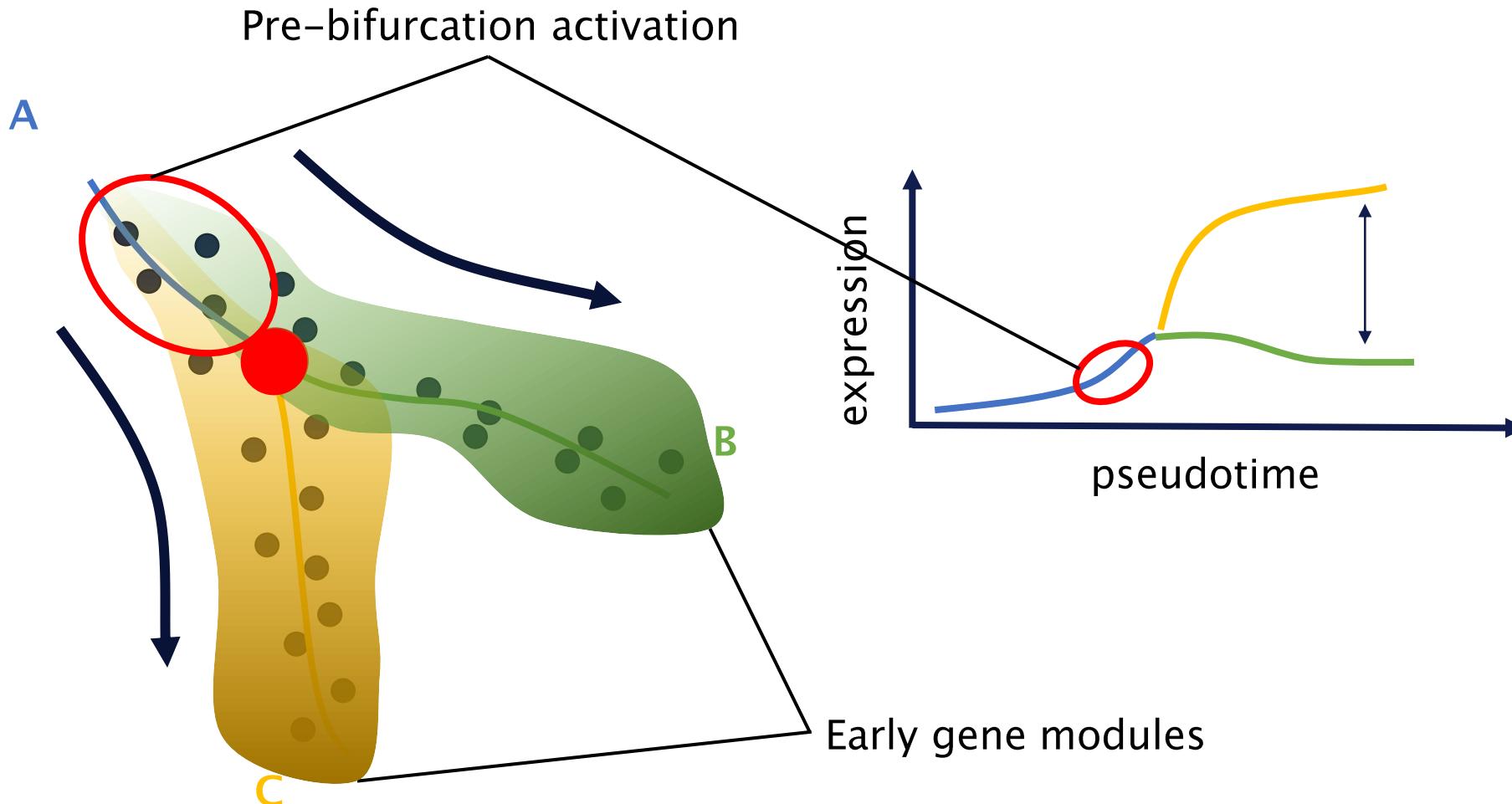
Bifurcation analysis

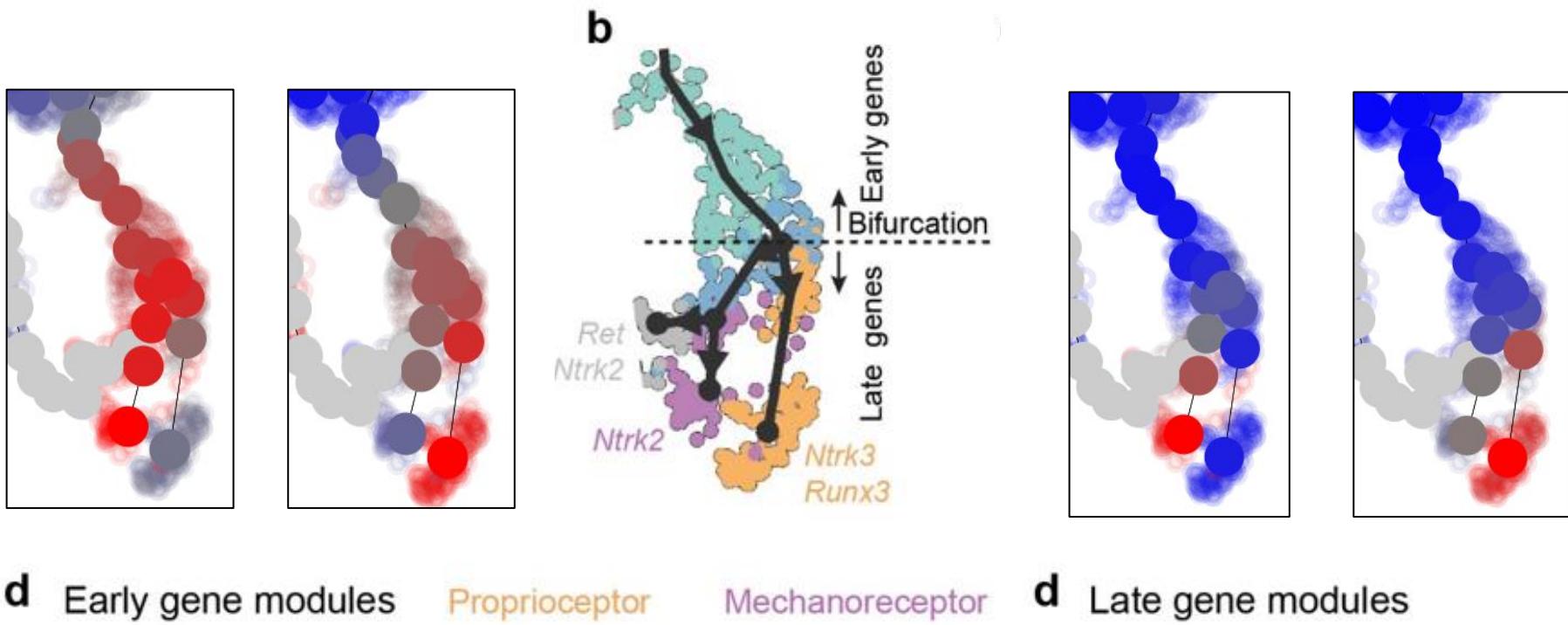


Bifurcation analysis



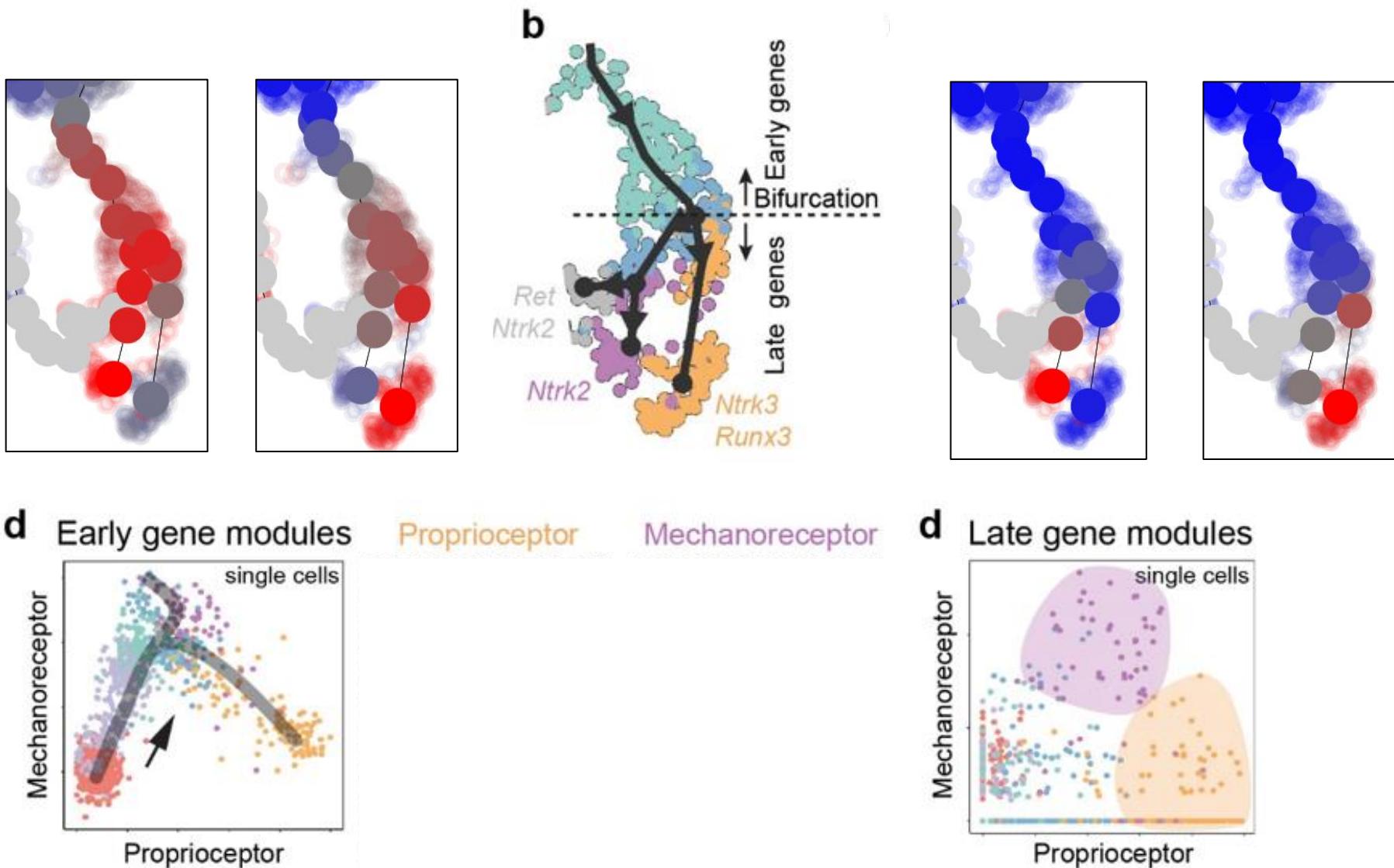
Bifurcation analysis





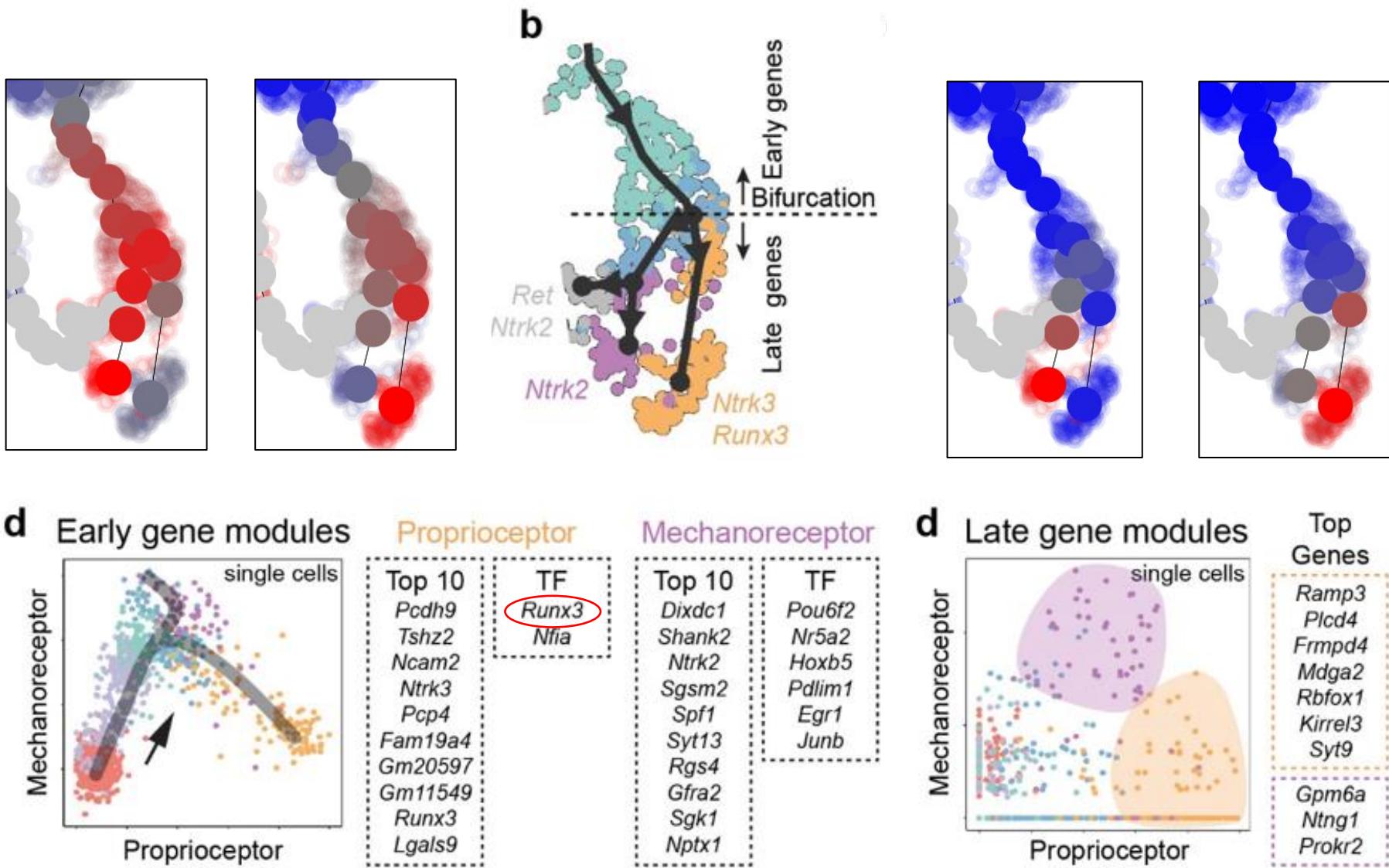
Faure et al (2020) *In review*





Faure et al (2020) *In review*

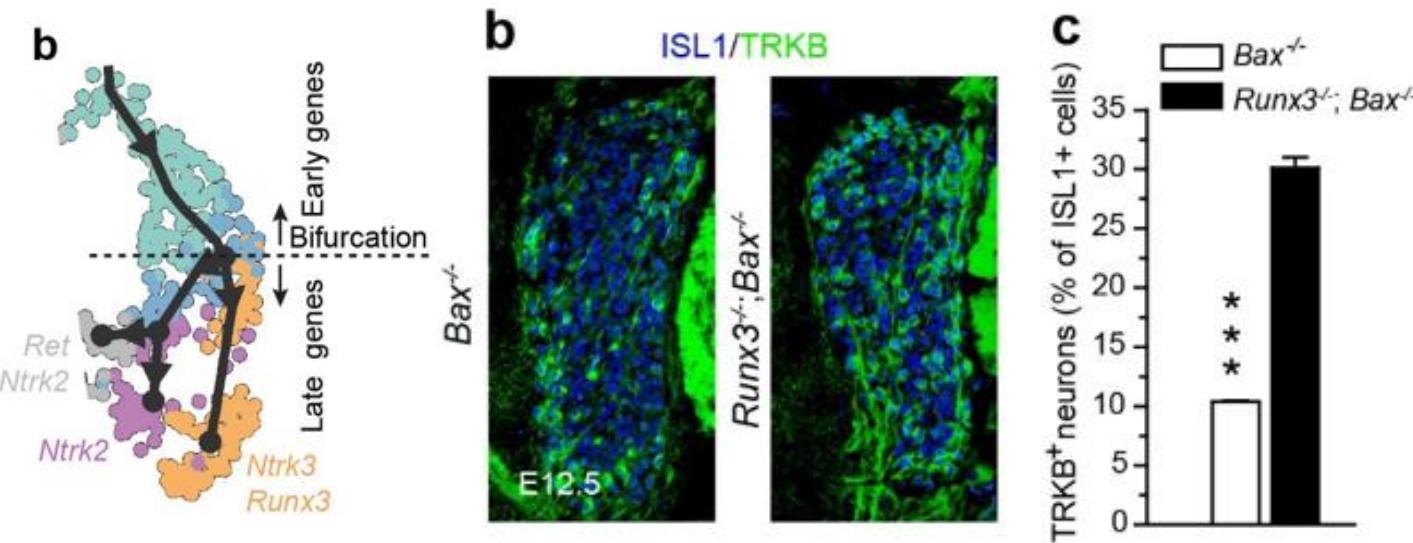




Faure et al (2020) *In review*



In vivo validation of gene module involved in fate decision

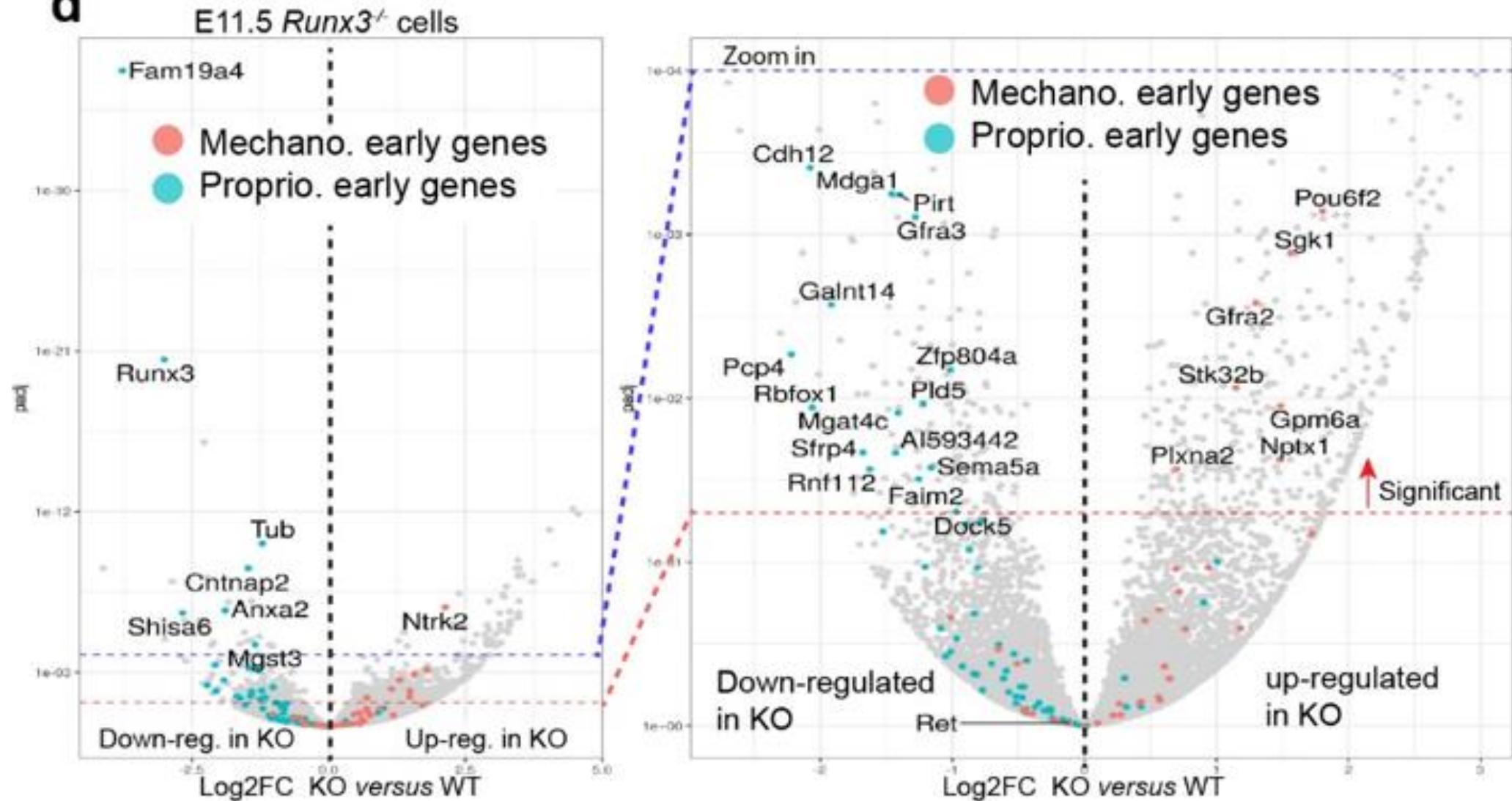


Faure et al (2020) *In review*



In vivo removal of TF of pro-proprioceptive fate lead to mechanoreception fate

d

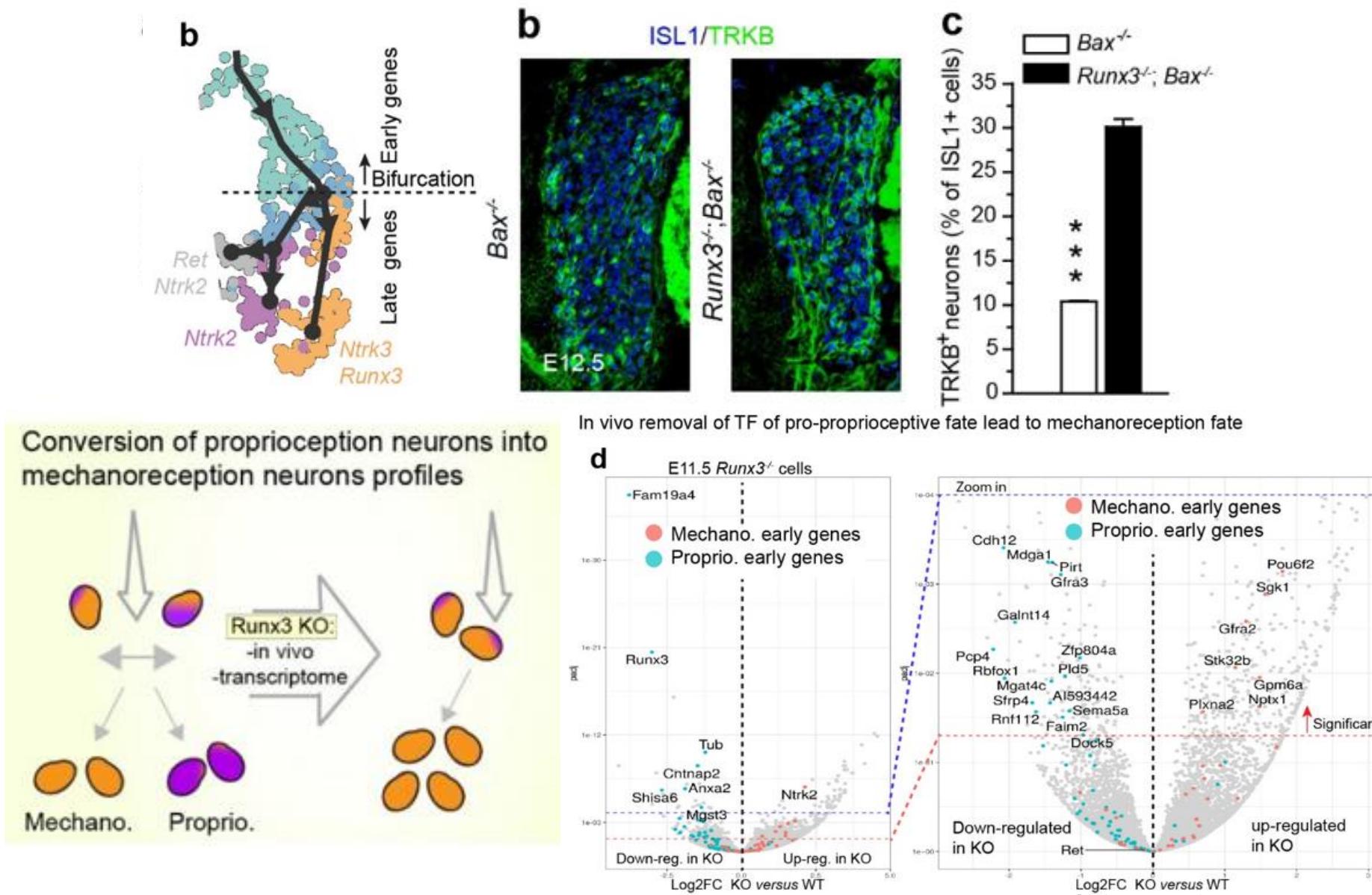


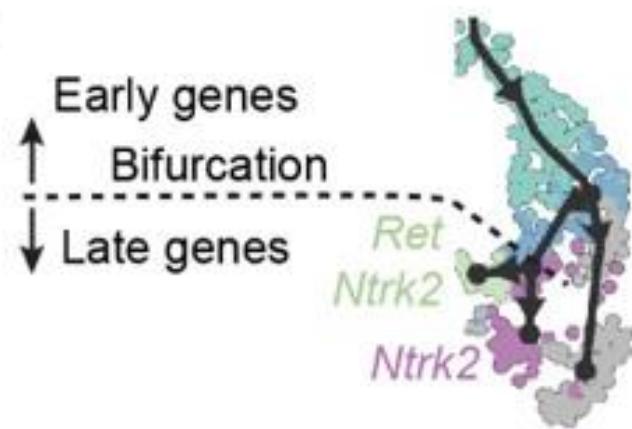
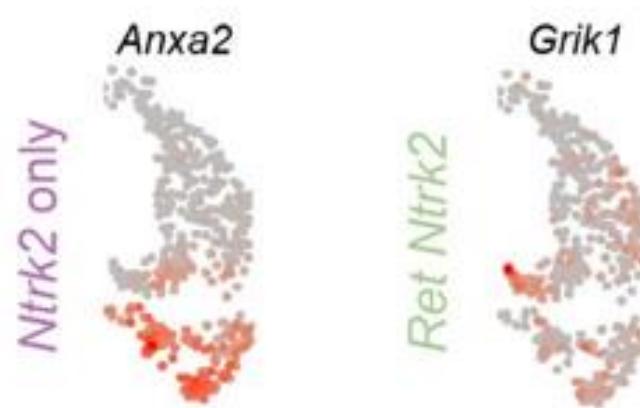
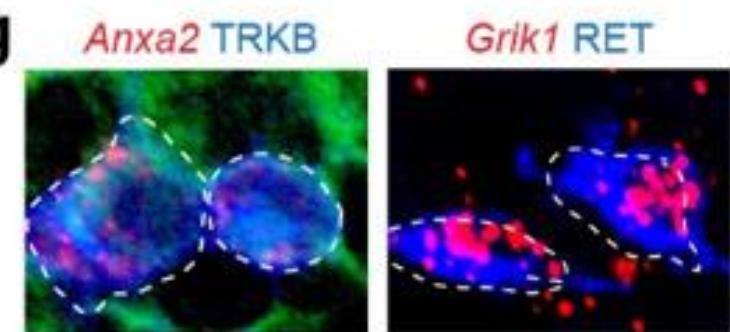
Faure et al (2020) In review



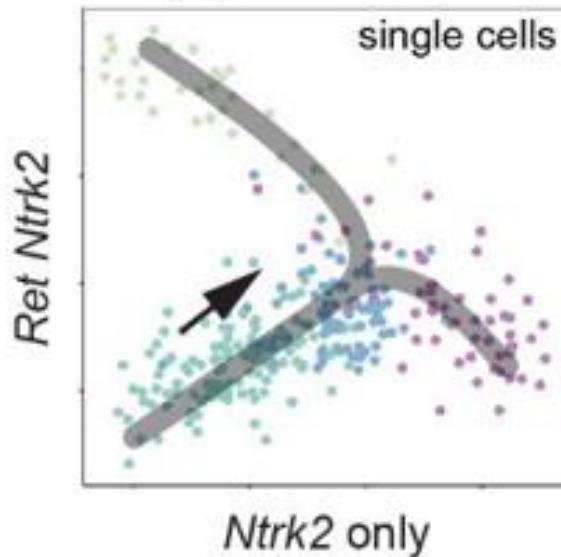
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In vivo validation of gene module involved in fate decision



e**f****g**

h Early gene modules

*Ntrk2 only*

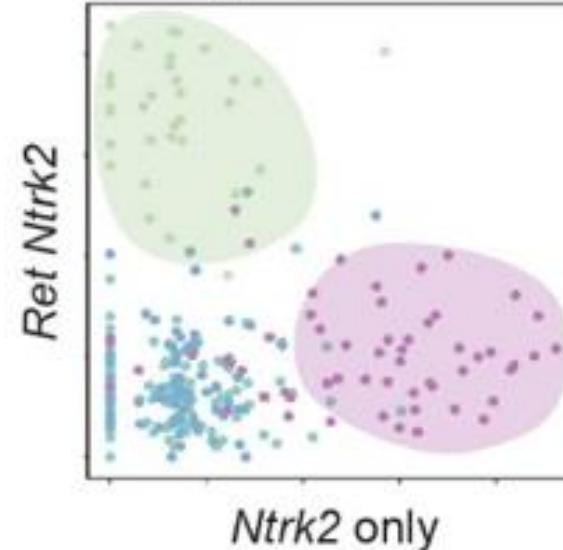
Top 10
Fxyd7
Nrsn2
Chd5
Tmem63c
Paqr9
Sema3f
Dmrtb1
Rab15
Sybu
Fam189a2

TF
Myt1l
Dmrtb1
Tcf15
Pdlim

Top 10
Greb1l
Ptchd1
Calcb
Rgs20
Nt5dc3
Stk32b
Cacna2d3
Onecut3
Ptch2
Asic4

TF
Pou6f2
Onecut3
Dcc

h Late gene modules

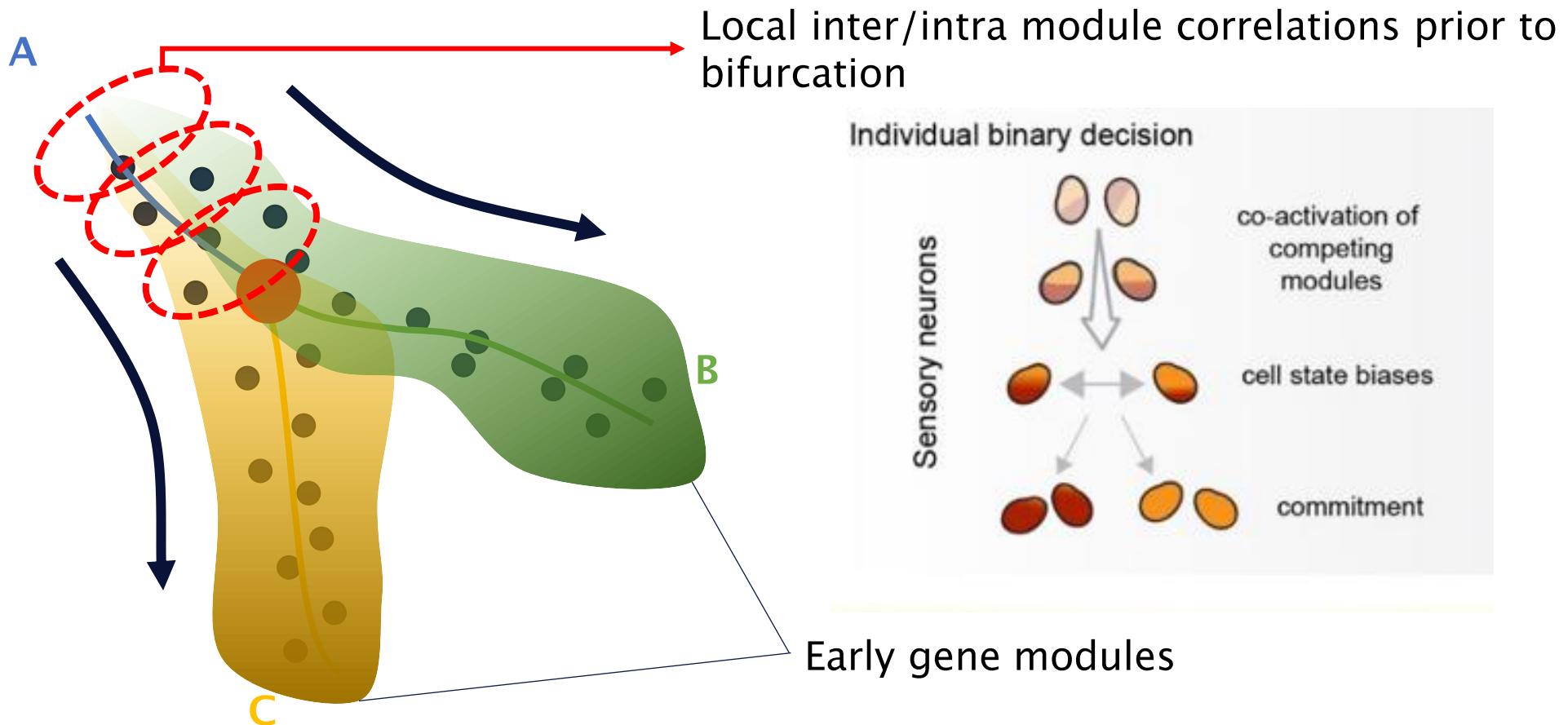


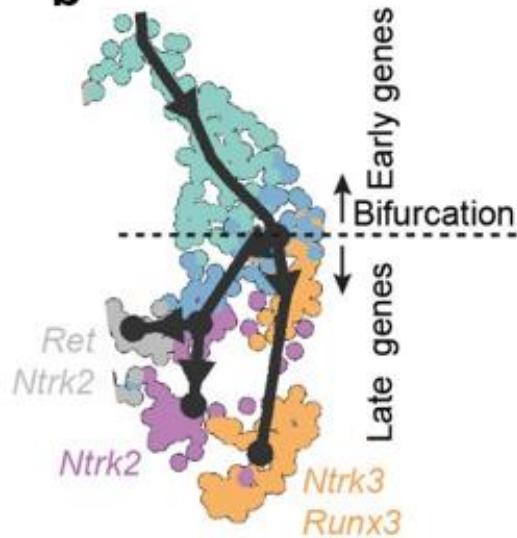
Top Genes

<i>Ddx3y</i>
<i>Adamts17</i>
<i>Igf1</i>
<i>Gbn3</i>
<i>Coch</i>
<i>Ptprt</i>
<i>Aff3</i>
<i>Rhpn1</i>
<i>Lin28a</i>
<i>Sox6</i>
<i>Ttr</i>

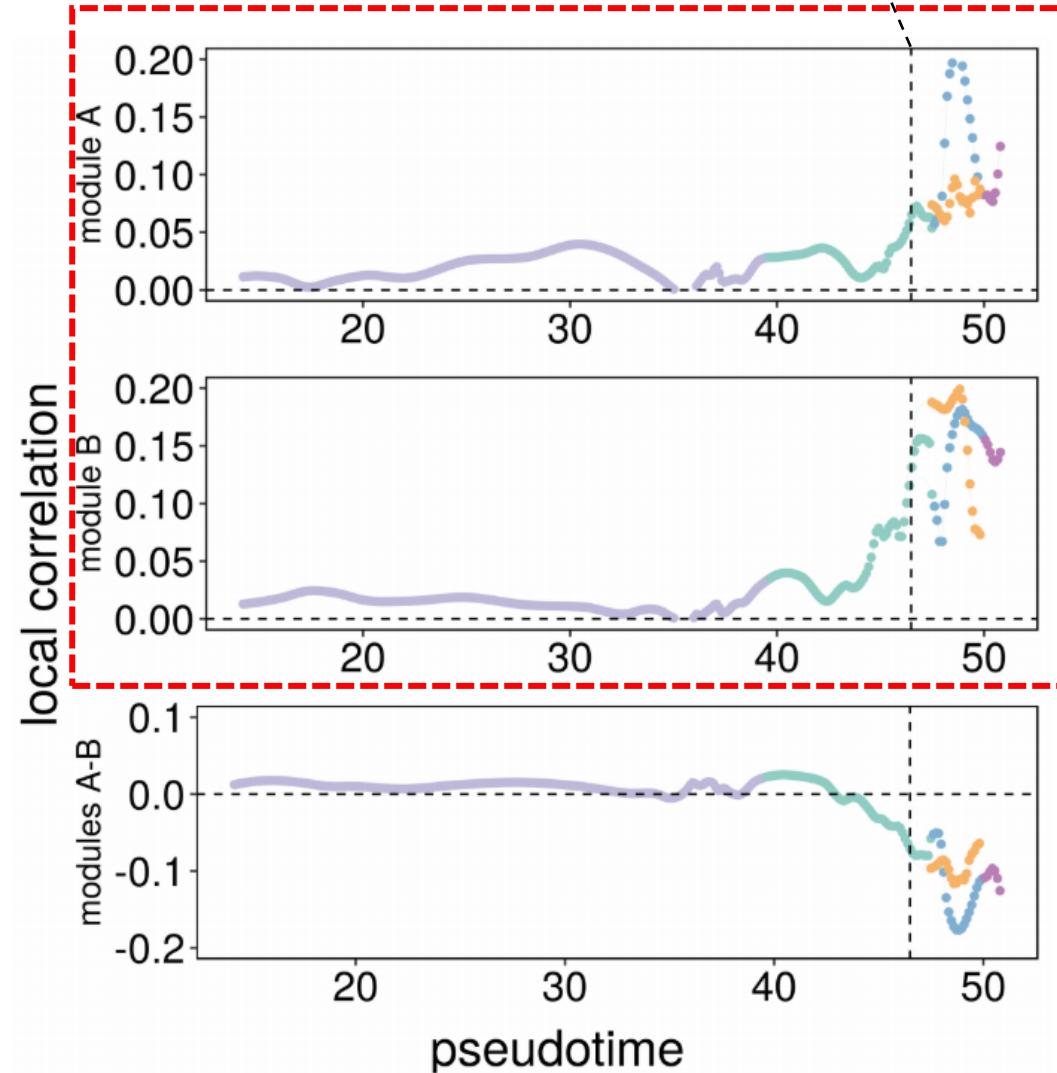


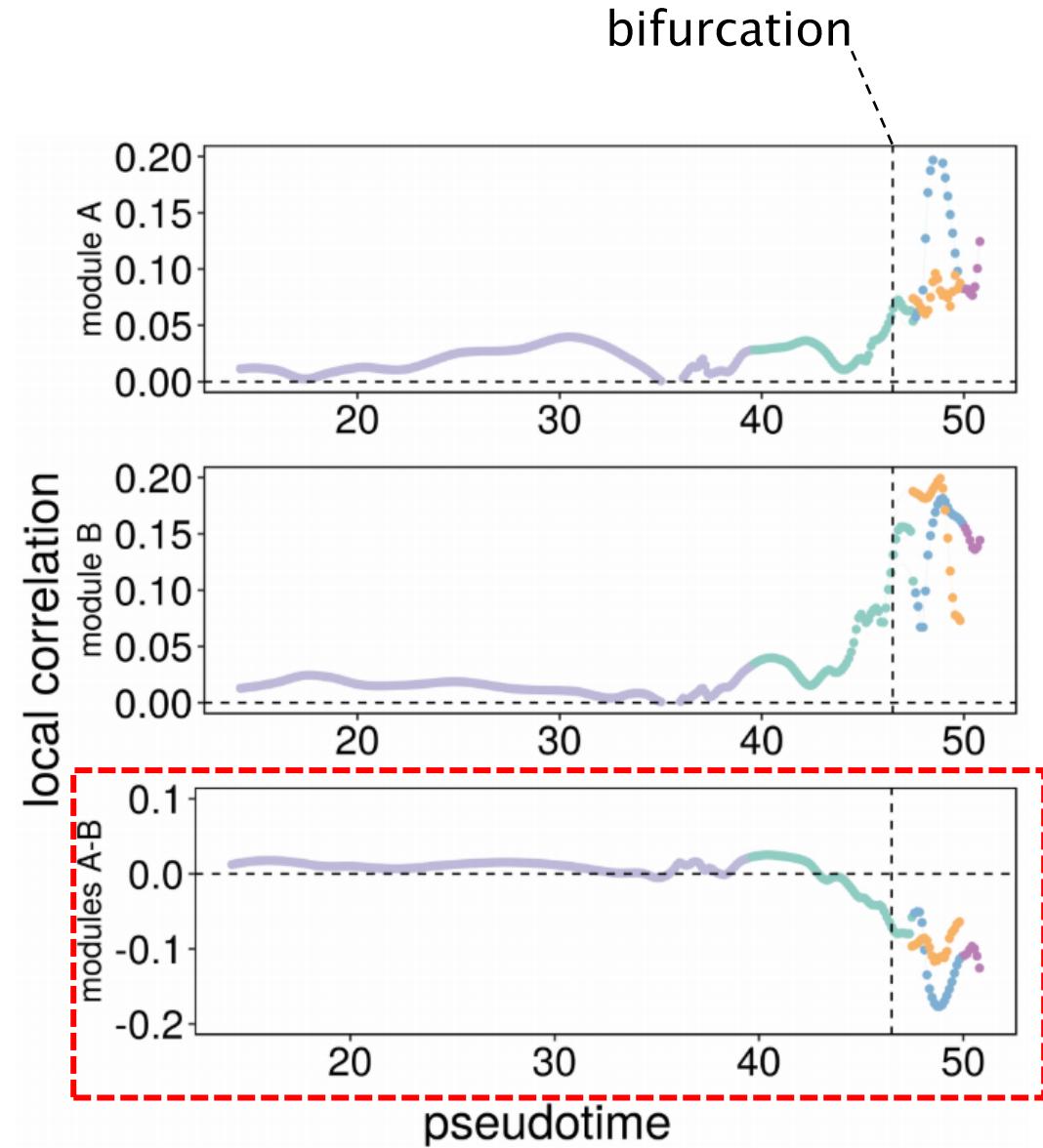
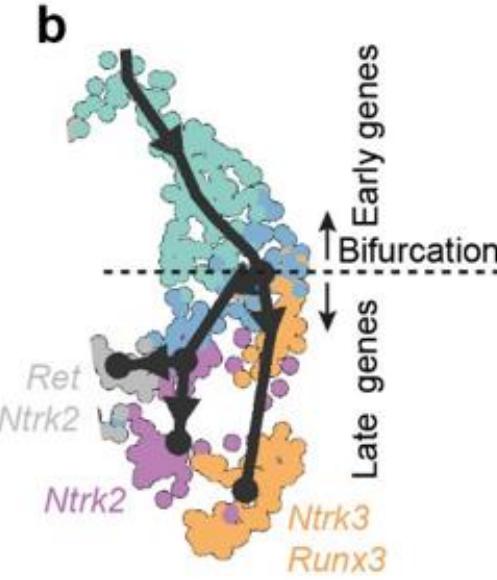
Inferring commitment prior to bifurcation



b

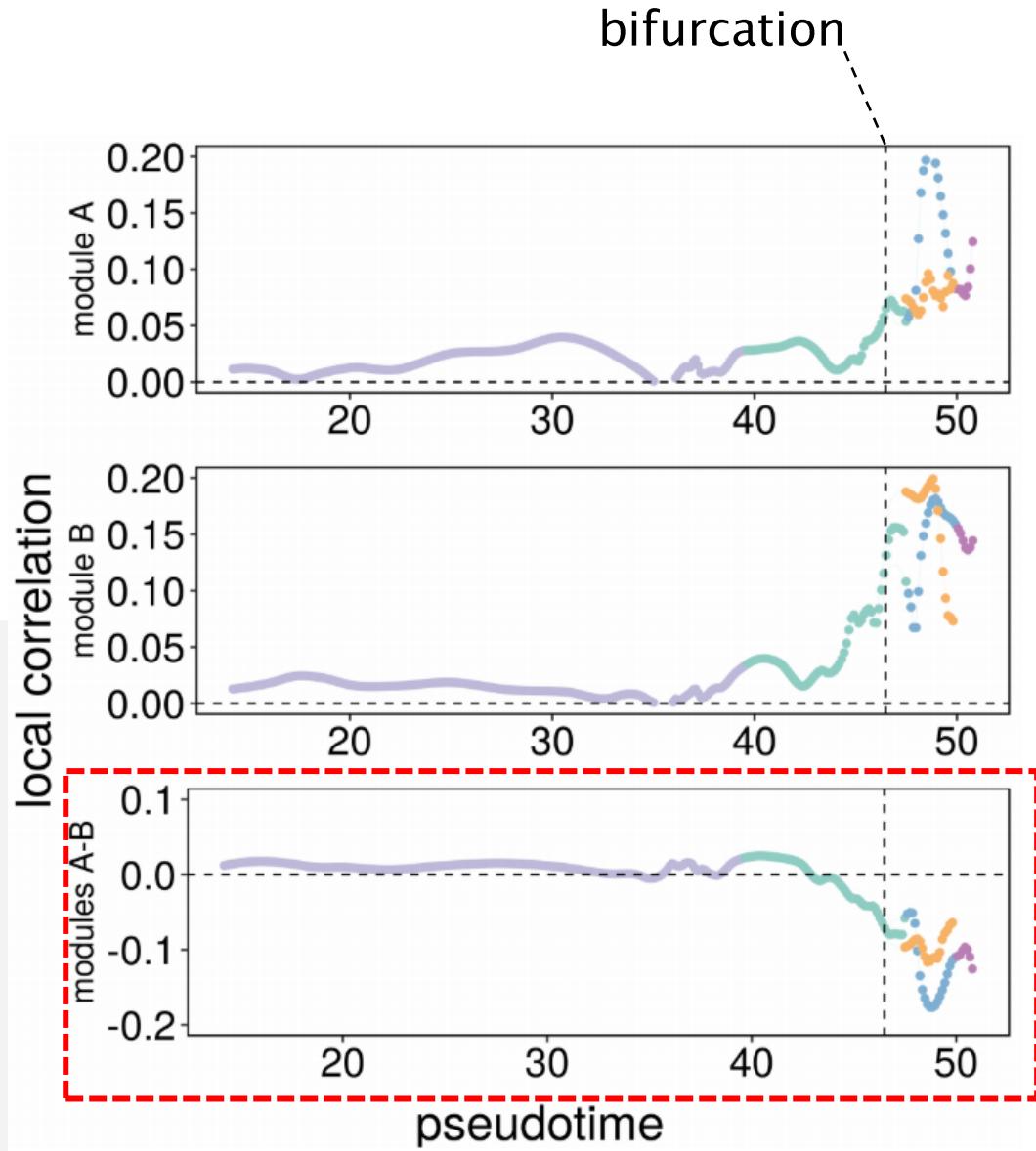
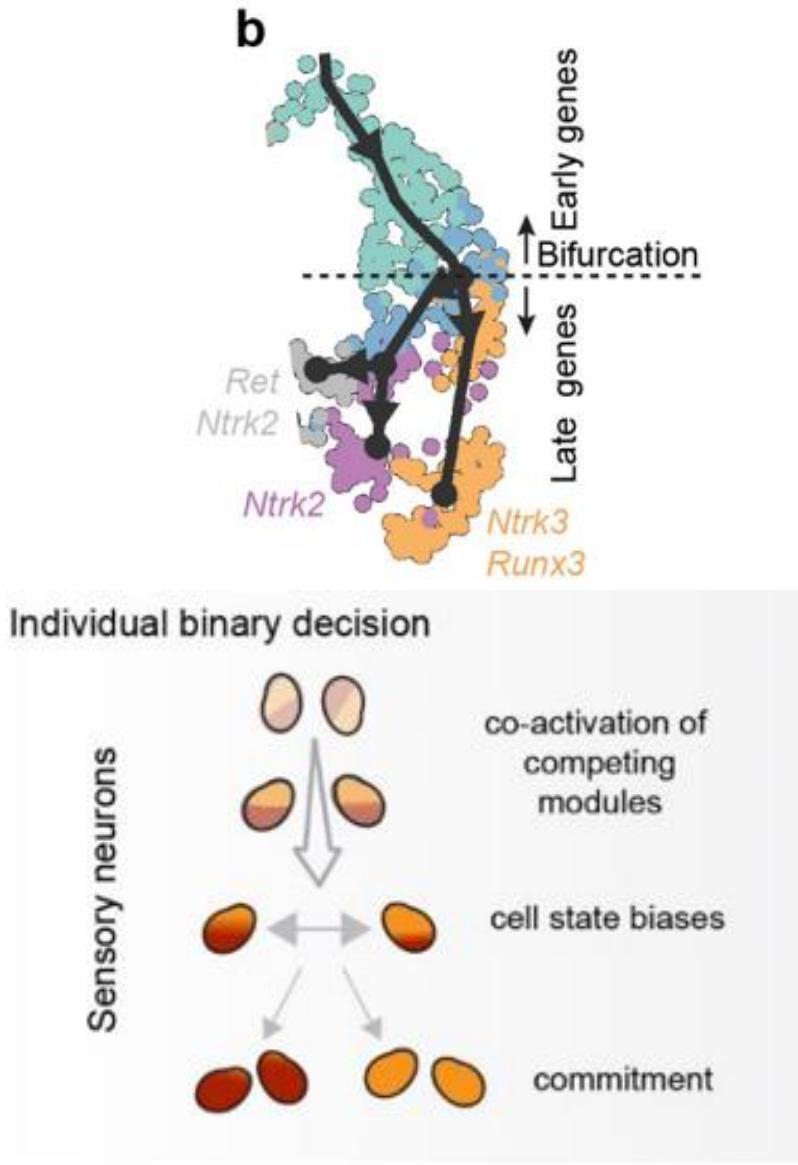
bifurcation

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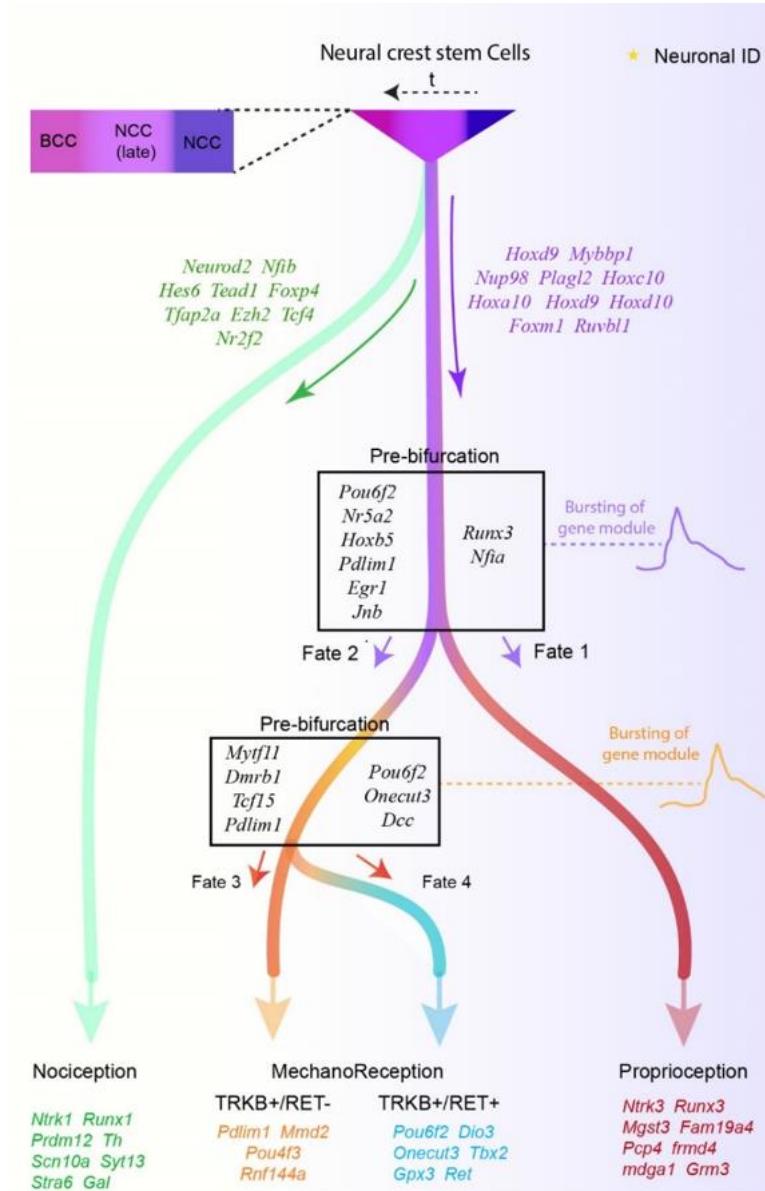
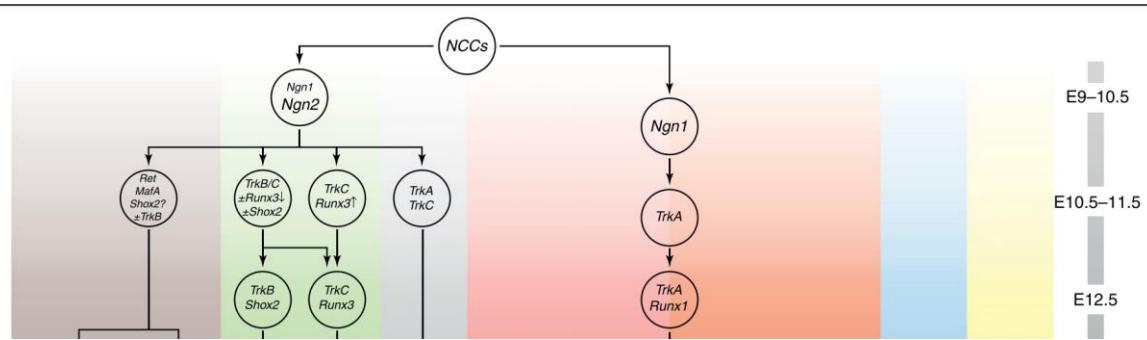




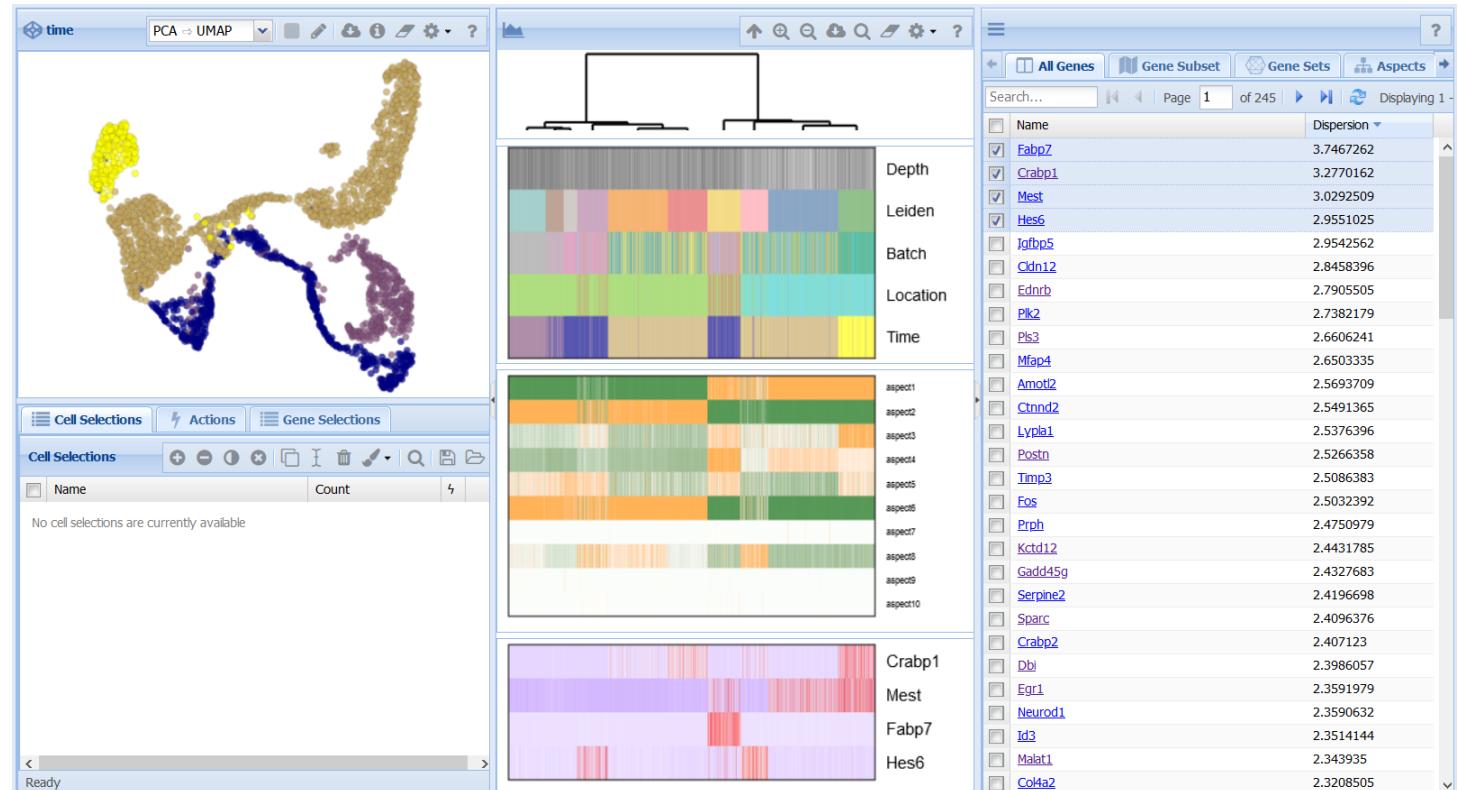
Faure et al (2020) *In review*

New model

Classical model



Data exploration and code reproducibility



Thank you!

Igor Adameyko



Saida Hadjab



François Lallemend



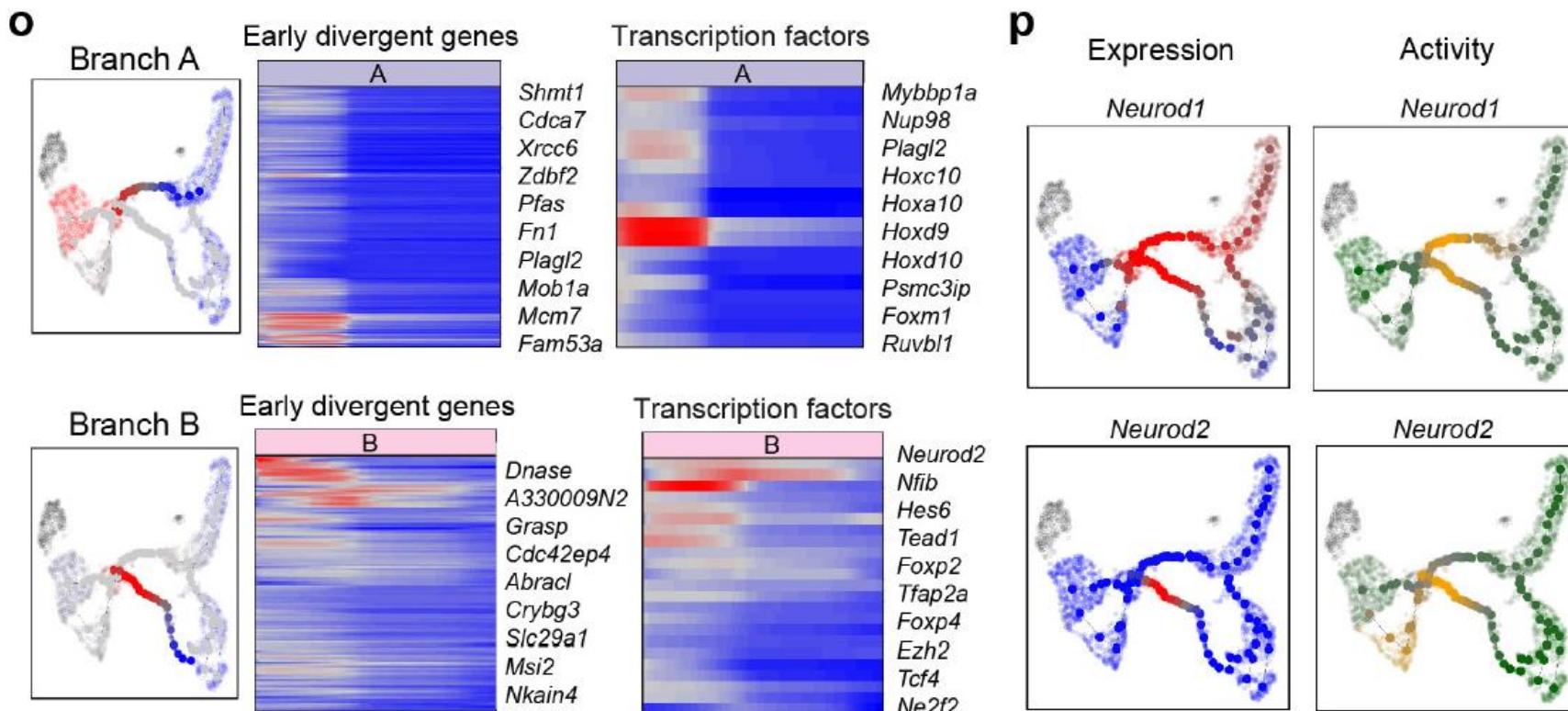
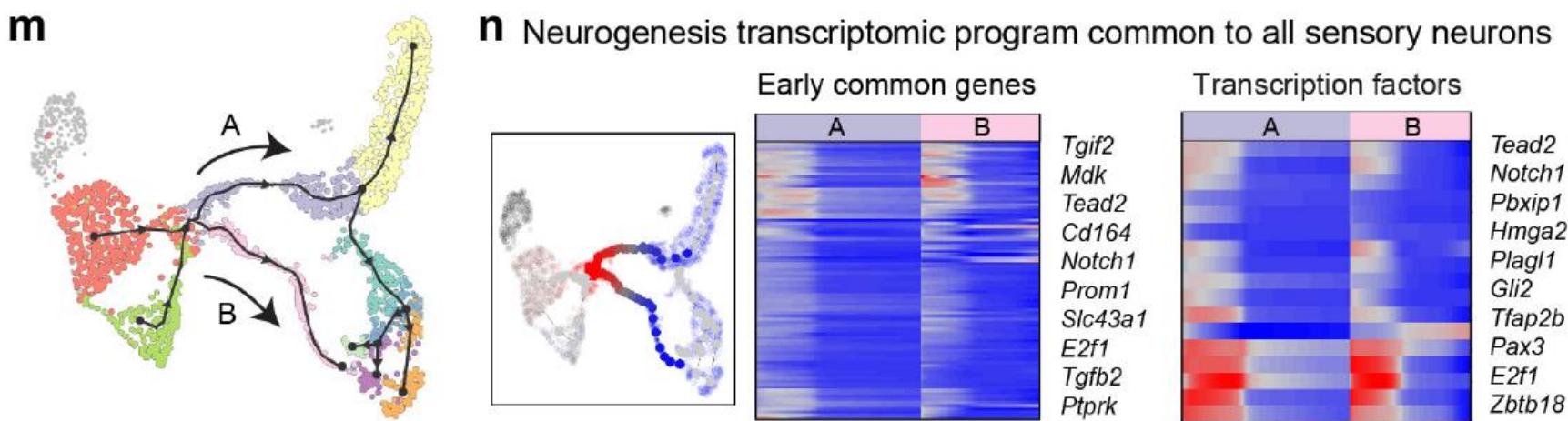
Maria Eleni Kastriti



FWF

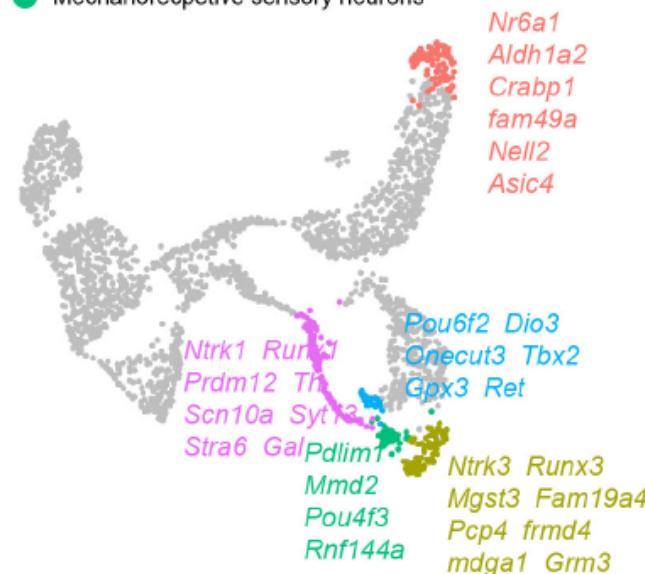


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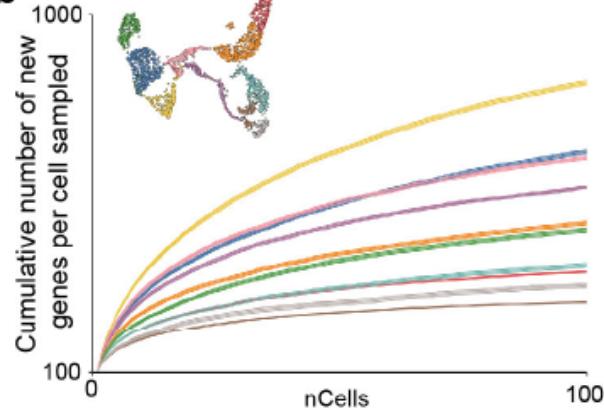


a Differentially expressed genes in sensory neurons lineages

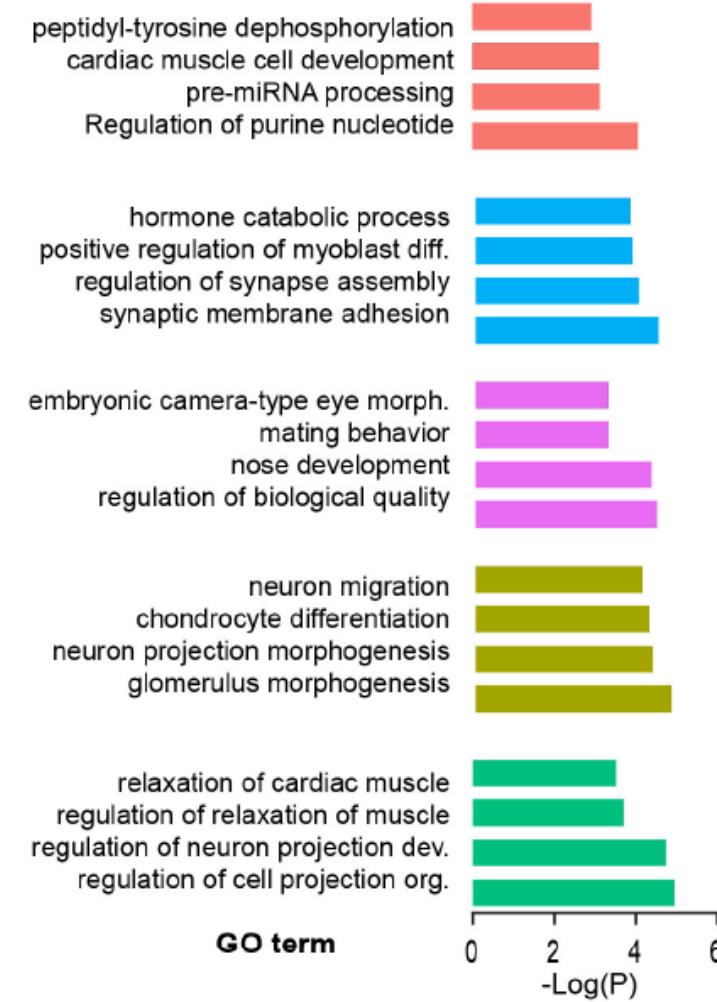
- Early divergent neurons
- Mechanoreceptive sensory neurons
- Nociceptive sensory neurons
- Proprioceptive sensory neurons
- Mechanoreceptive sensory neurons



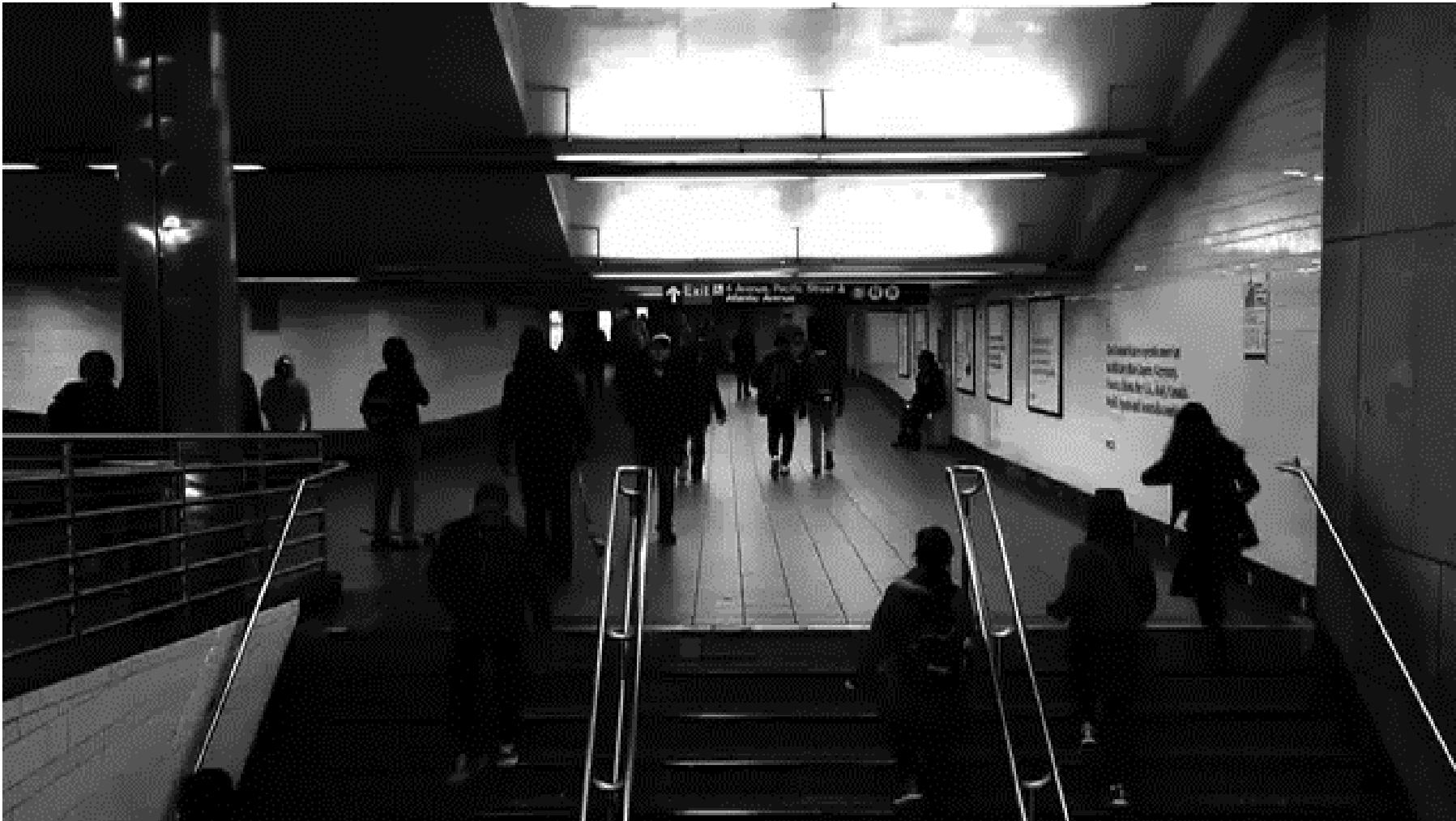
b



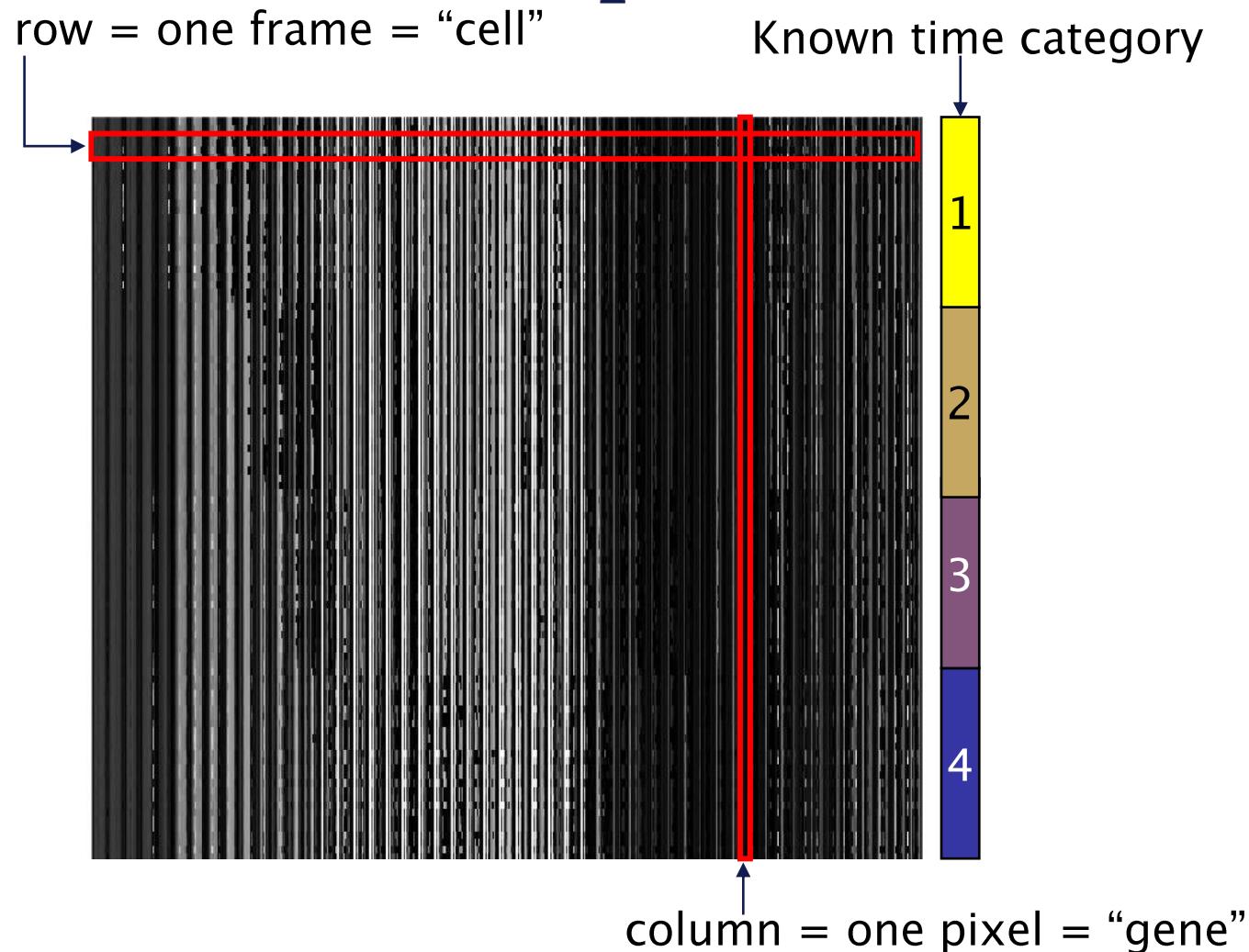
c Top GO term of sensory neurons lineages



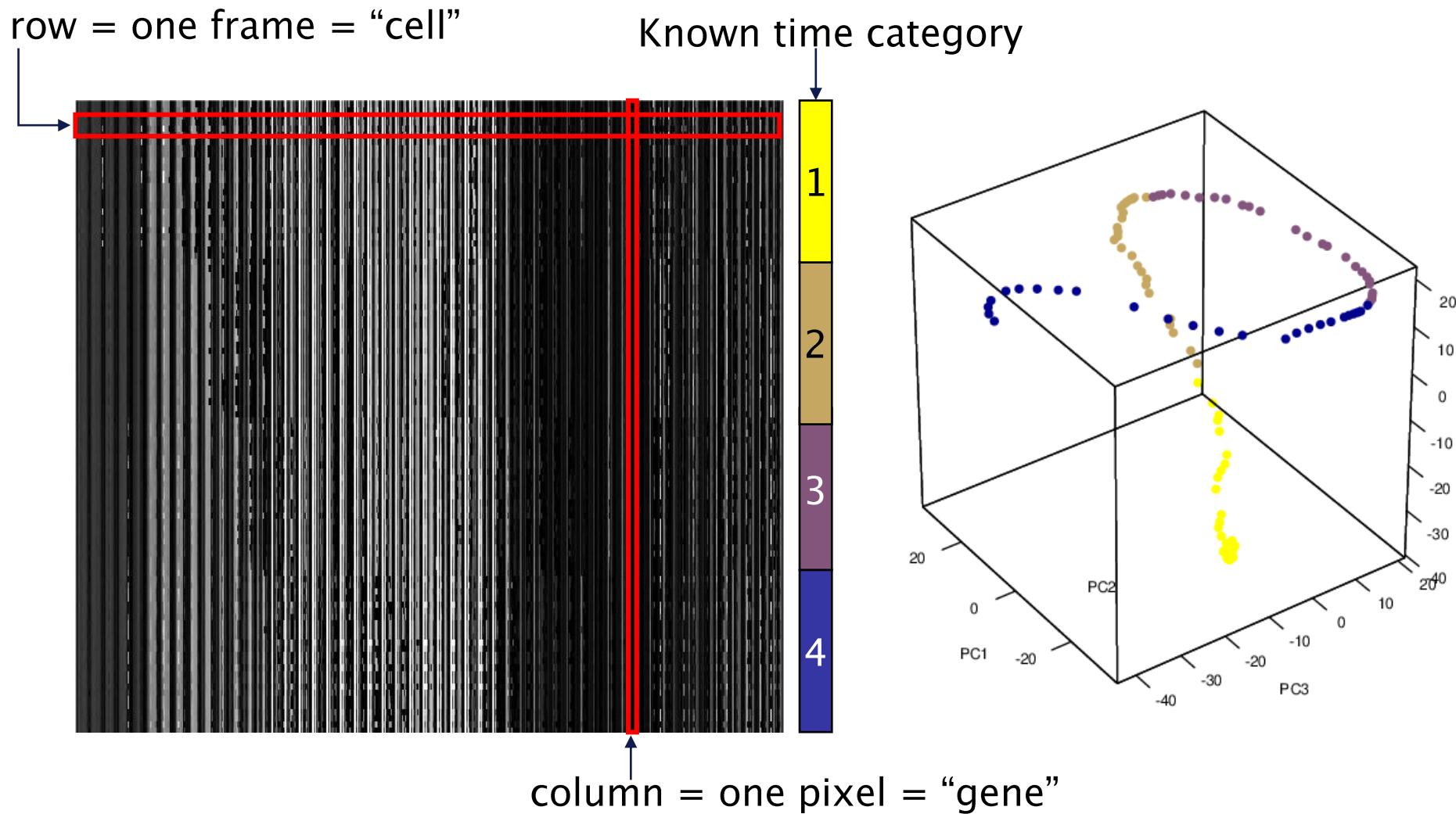
Concept of pseudotime: recovering lost time information



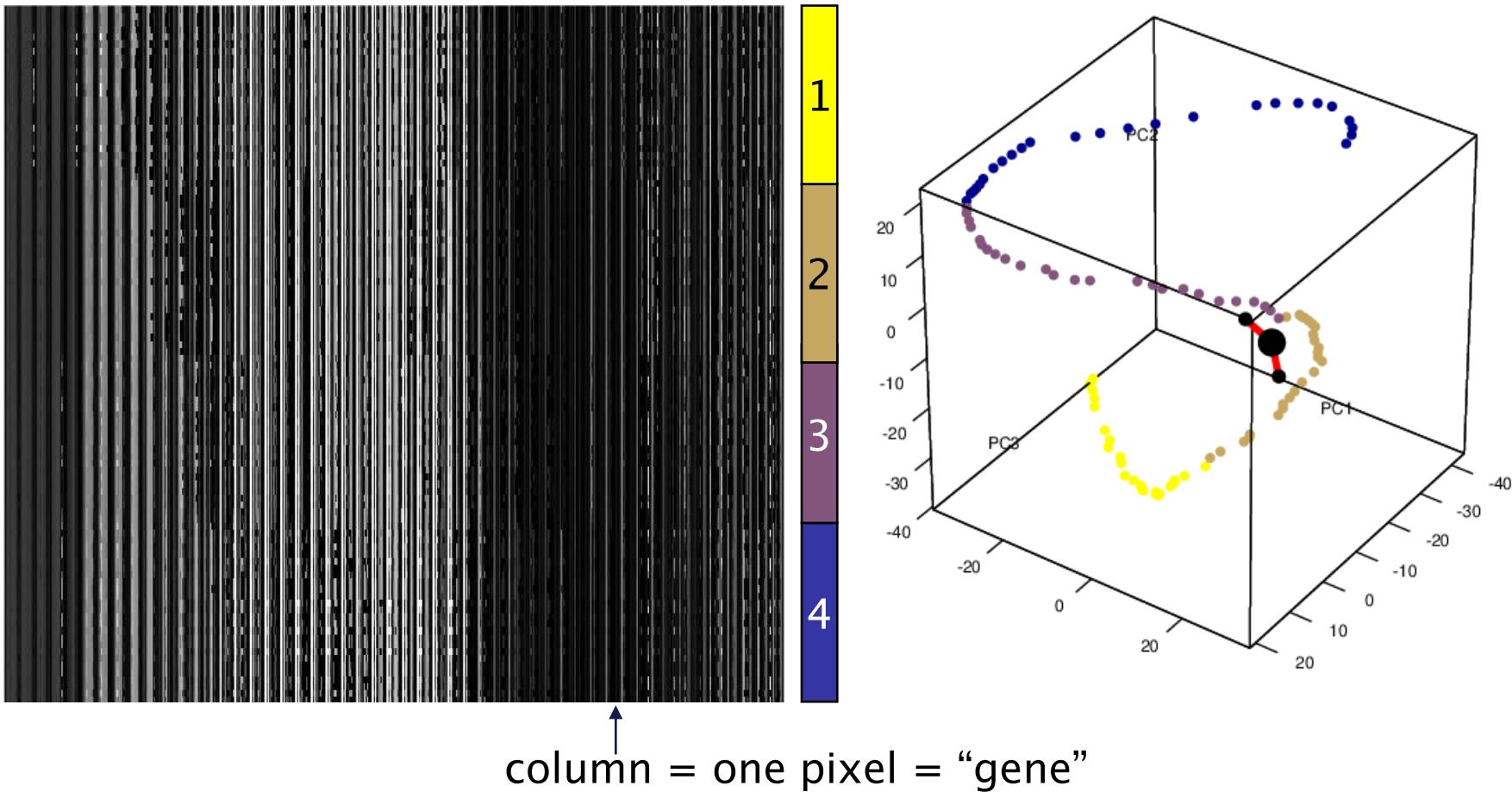
Considering the video as an expression matrix



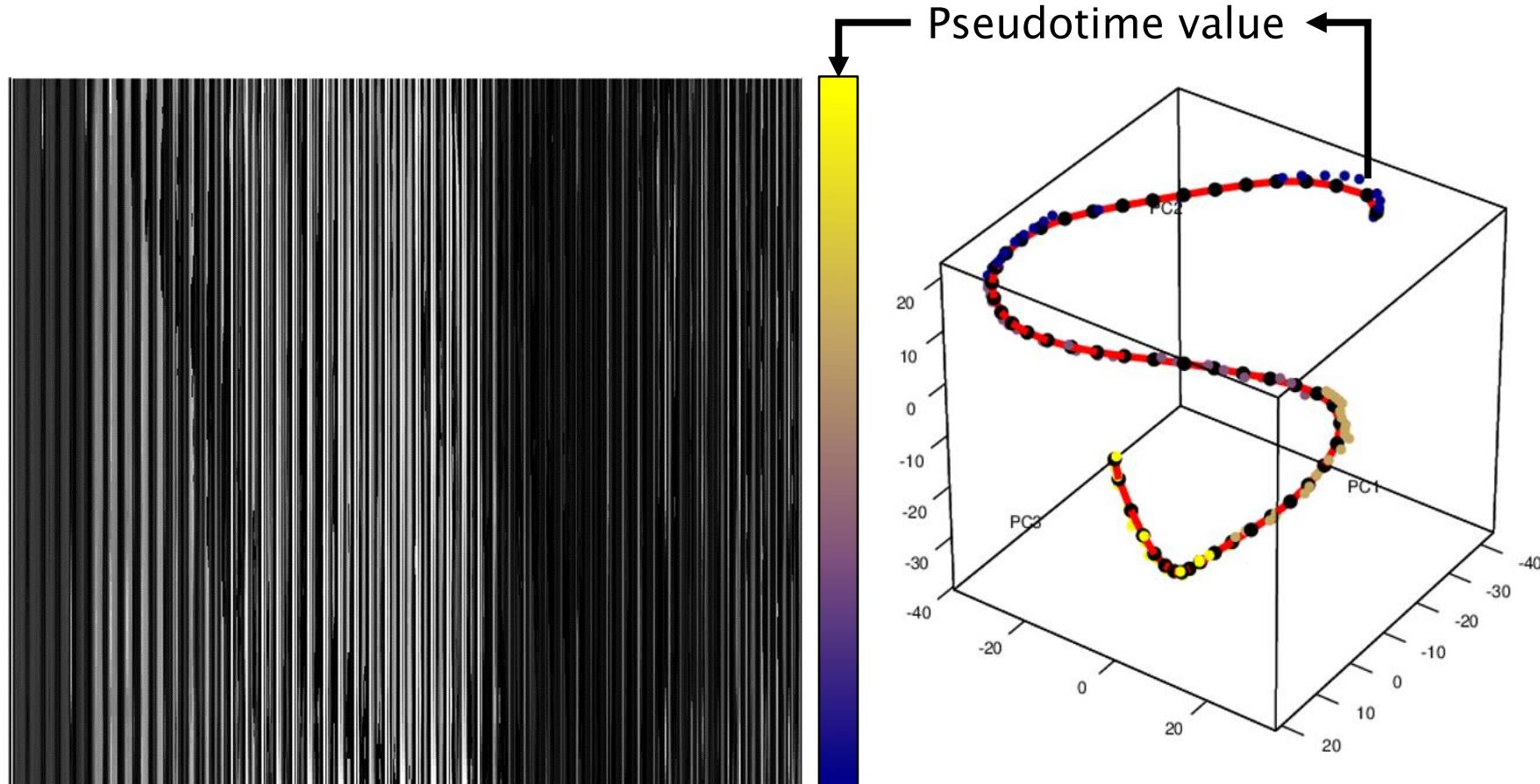
Applying PCA reveals low dimensional latent structure!



This latent structure can be approximated using principal curves



Ordering frames along the principal curve recovers lost time information!



Recovered time!



