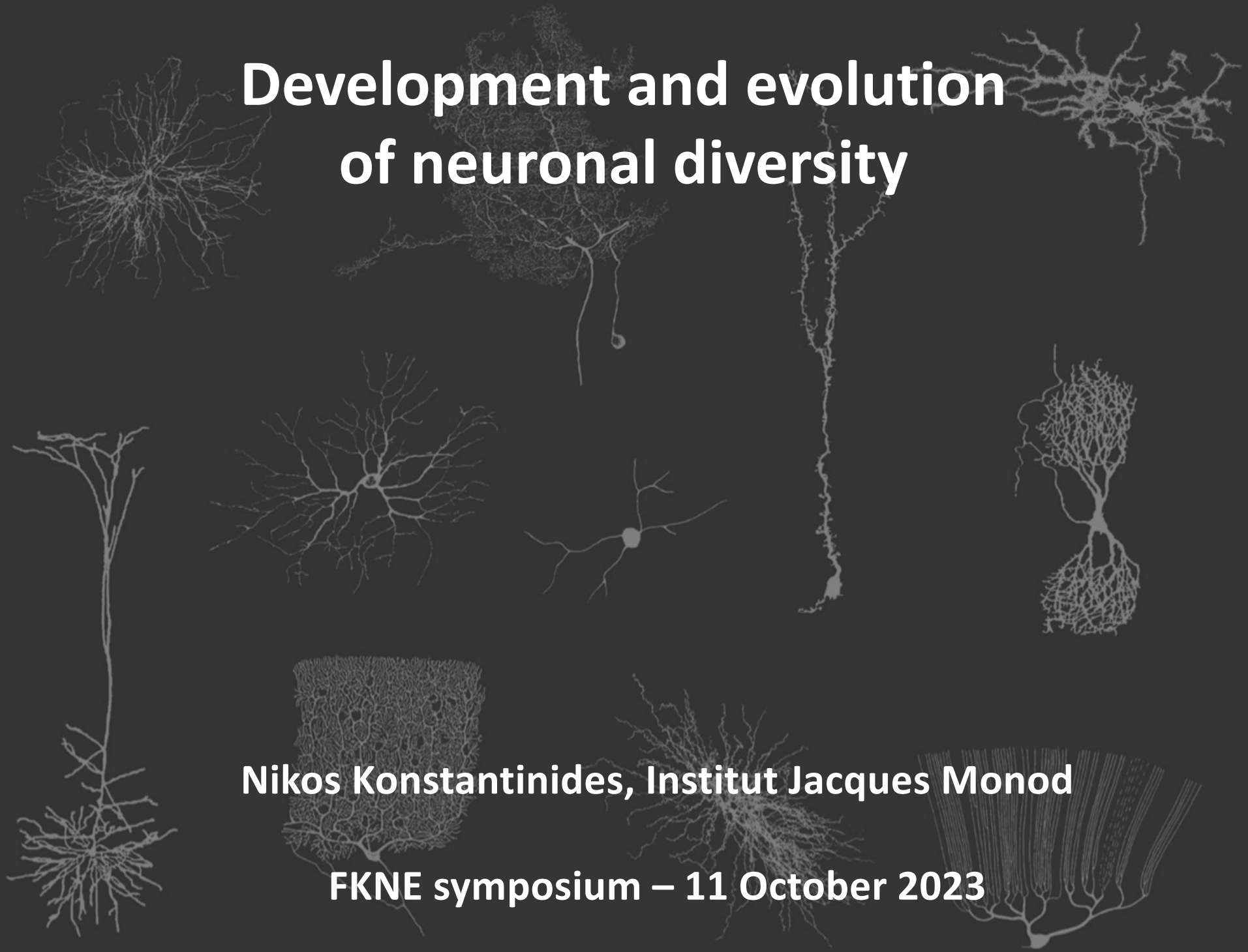
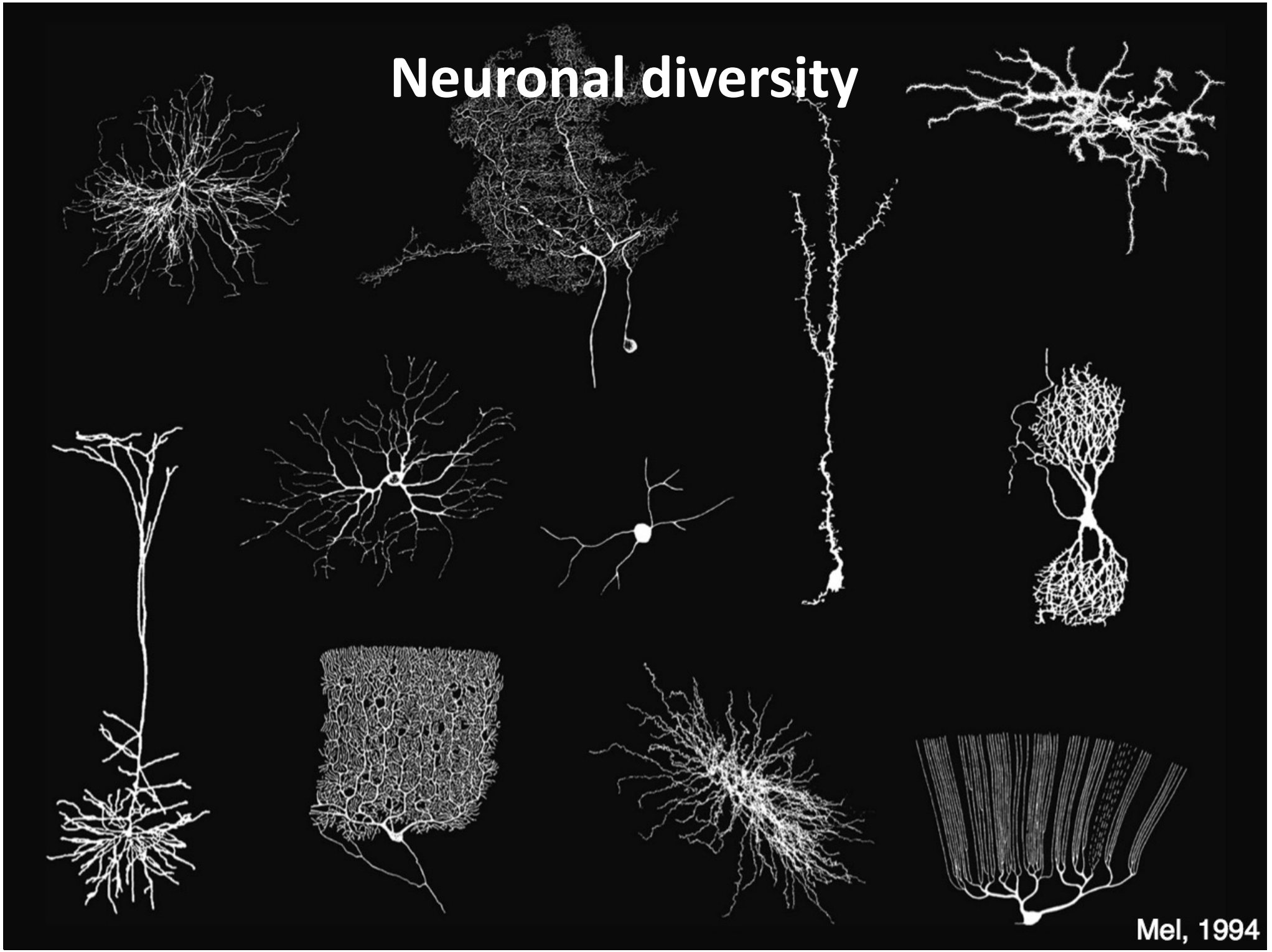
Development and evolution of neuronal diversity

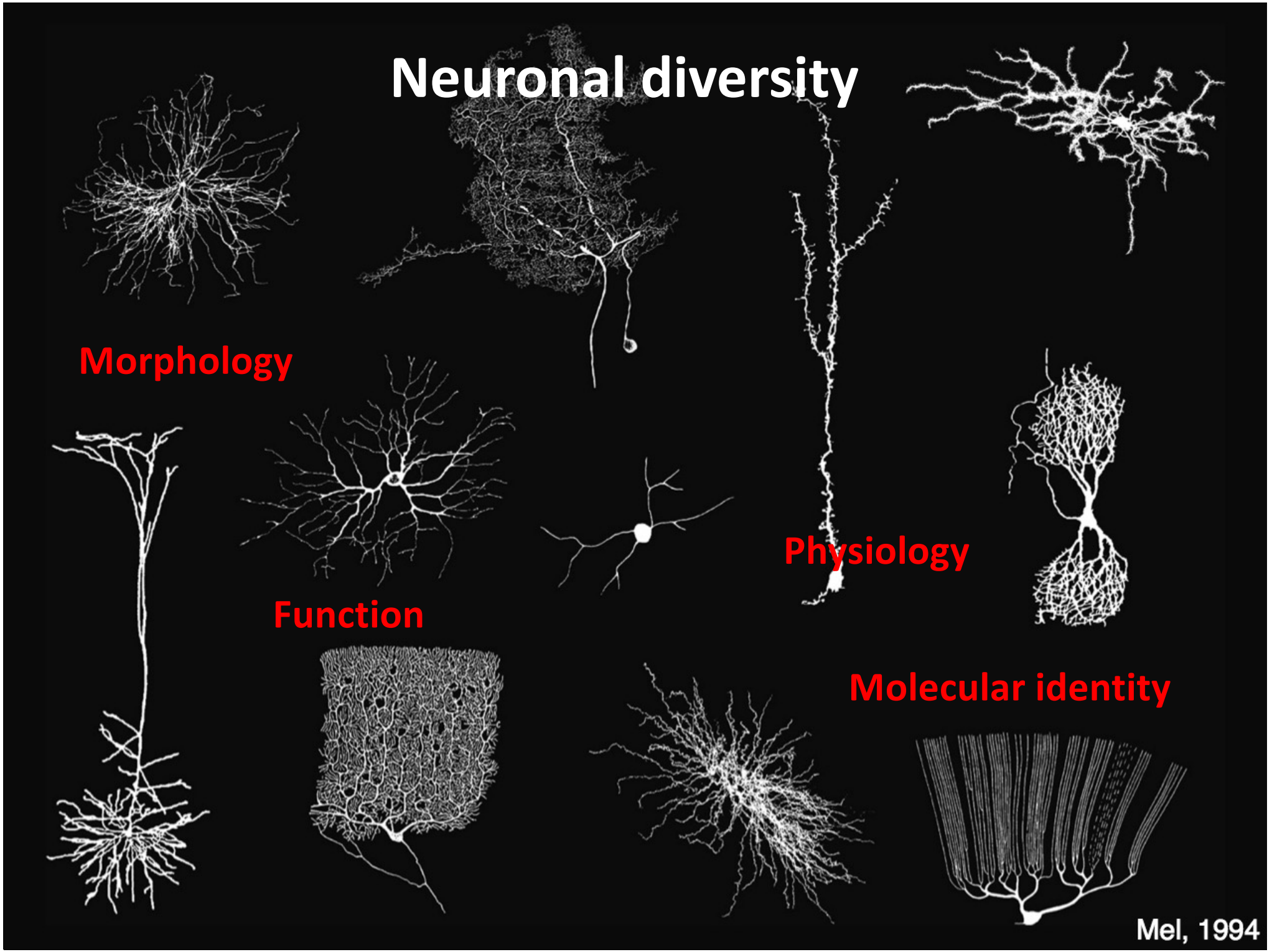


Nikos Konstantinides, Institut Jacques Monod

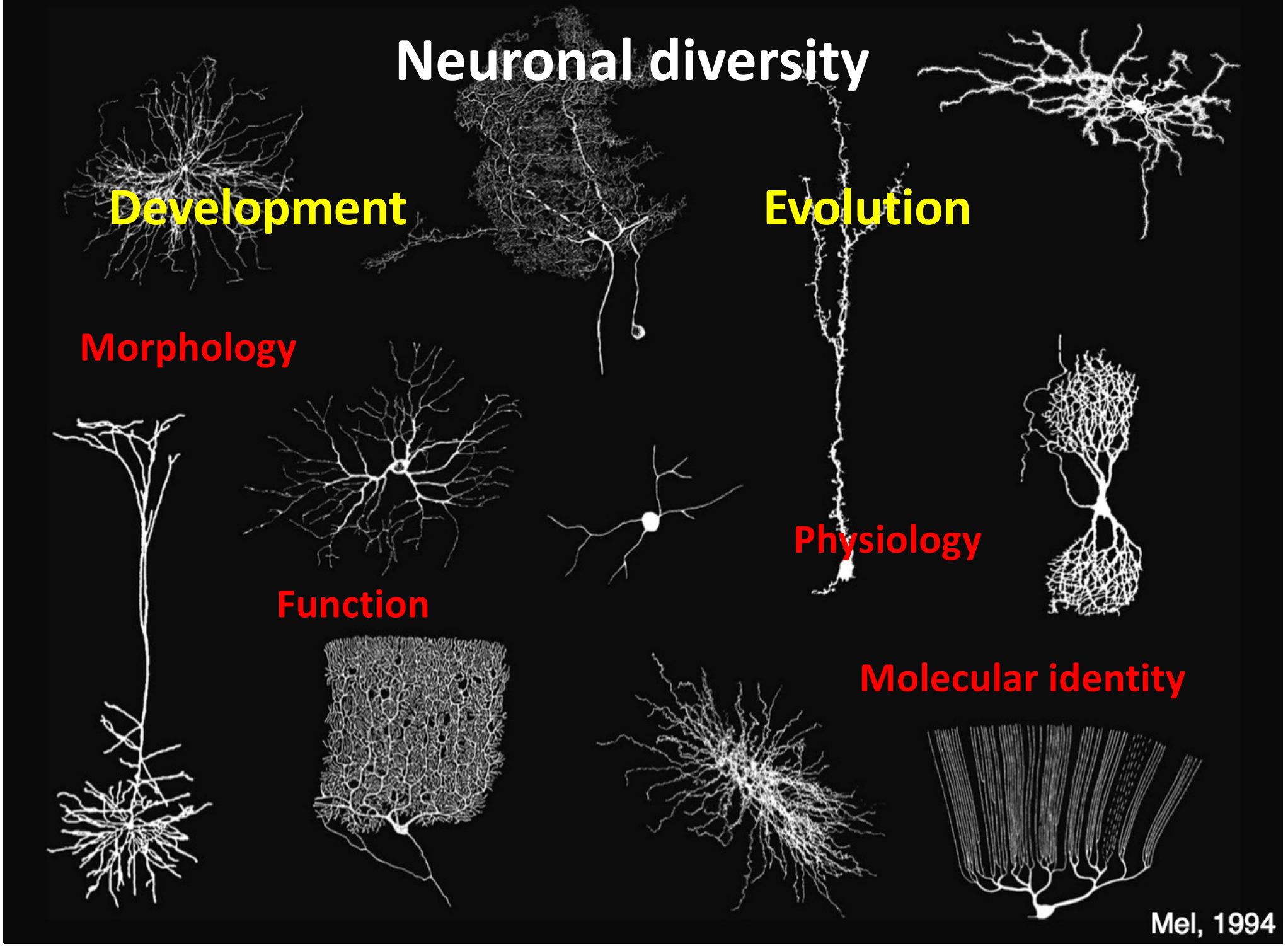
FKNE symposium – 11 October 2023

Neuronal diversity



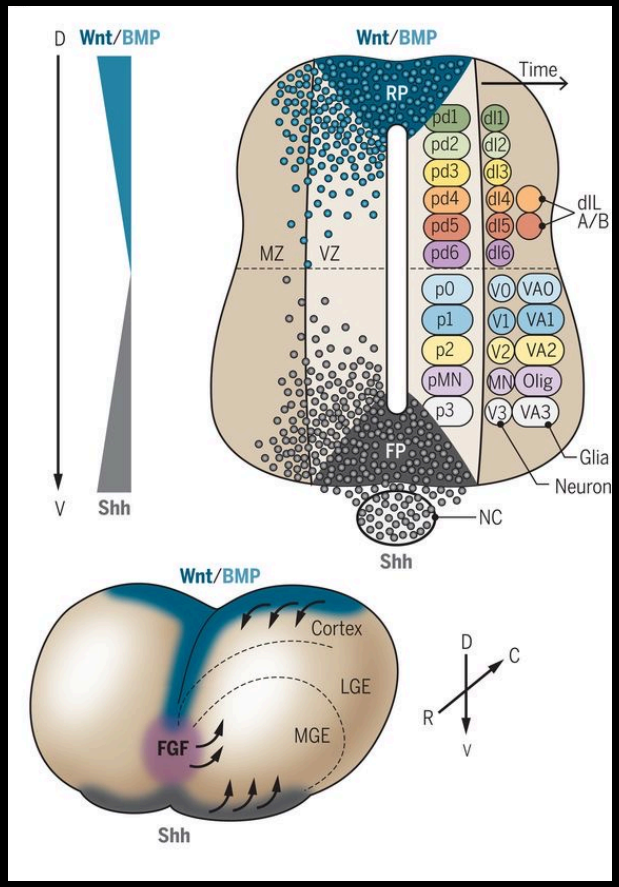

Neuronal diversity
Morphology
Physiology
Function
Molecular identity
Mel, 1994

Neuronal diversity



Two mechanisms generate neuronal diversity

Spatial patterning



reviewed in Holguera and Desplan, Science 2018
original data: Jessell, Briscoe, Hippenmeyer and many other labs

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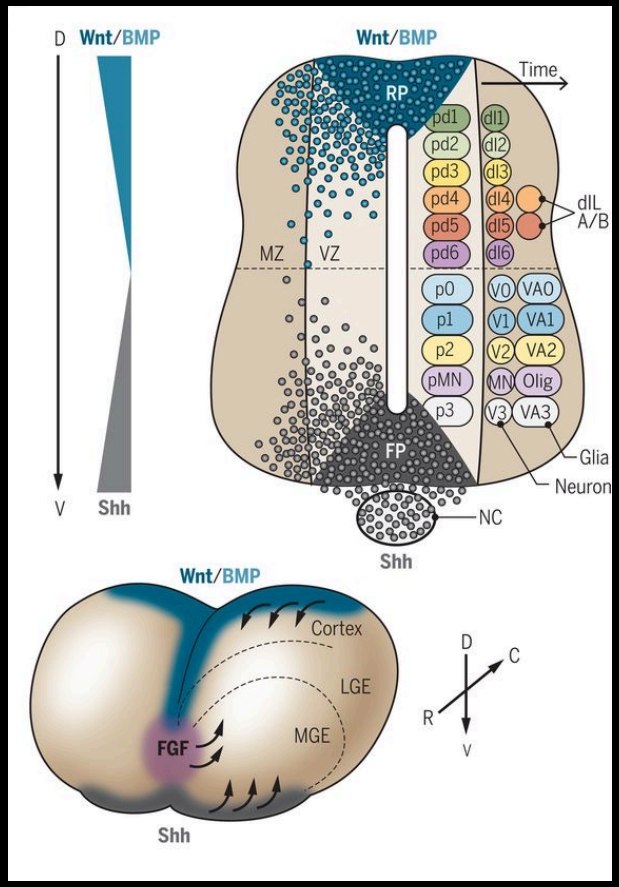
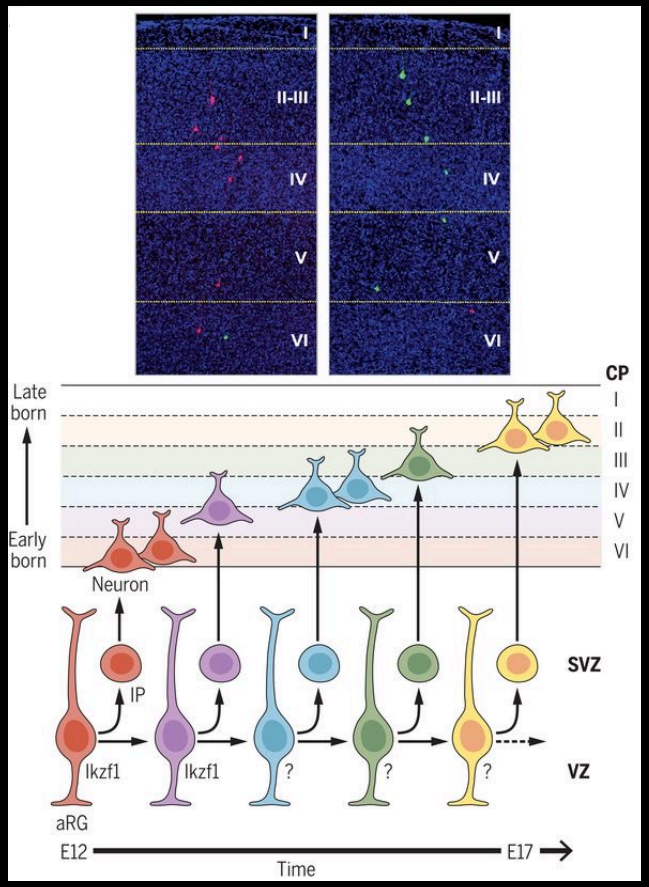


Temporal patterning



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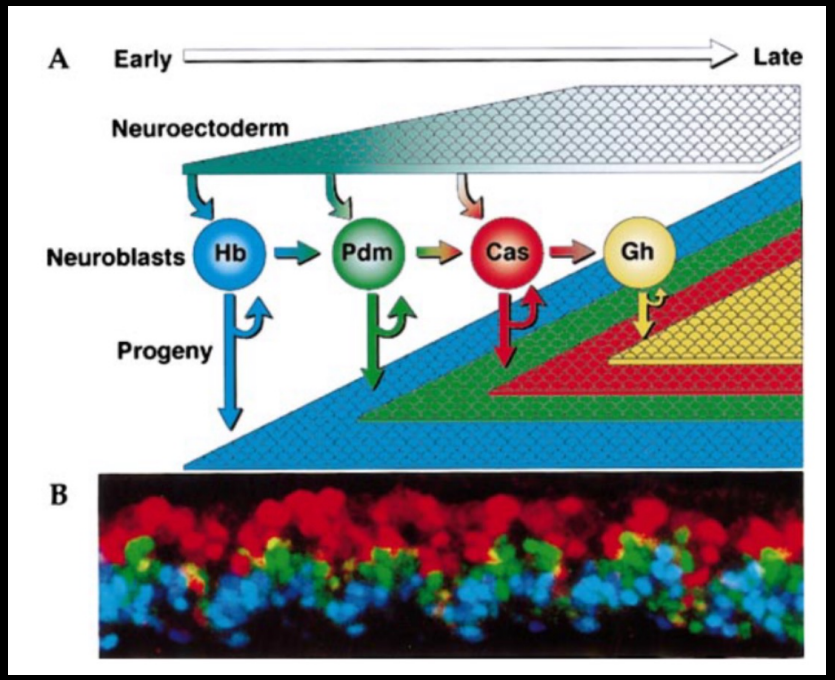
Temporal transcription factors



Brody and Odenwald, Dev Biol 2000

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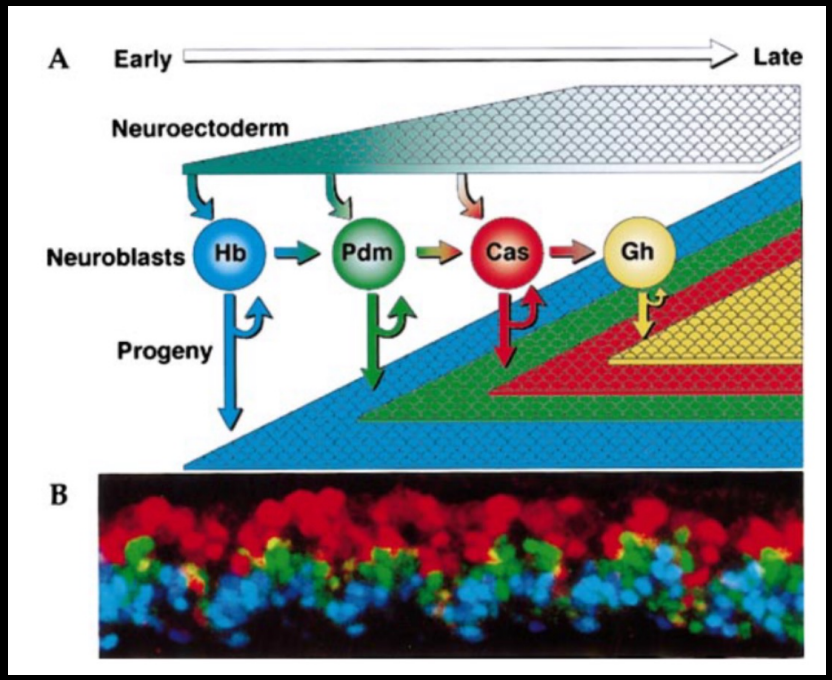

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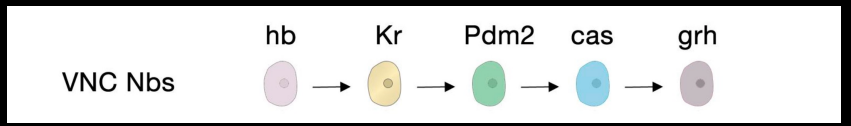

reviewed in Mira and Morante,
Front Cell Dev Biol 2020

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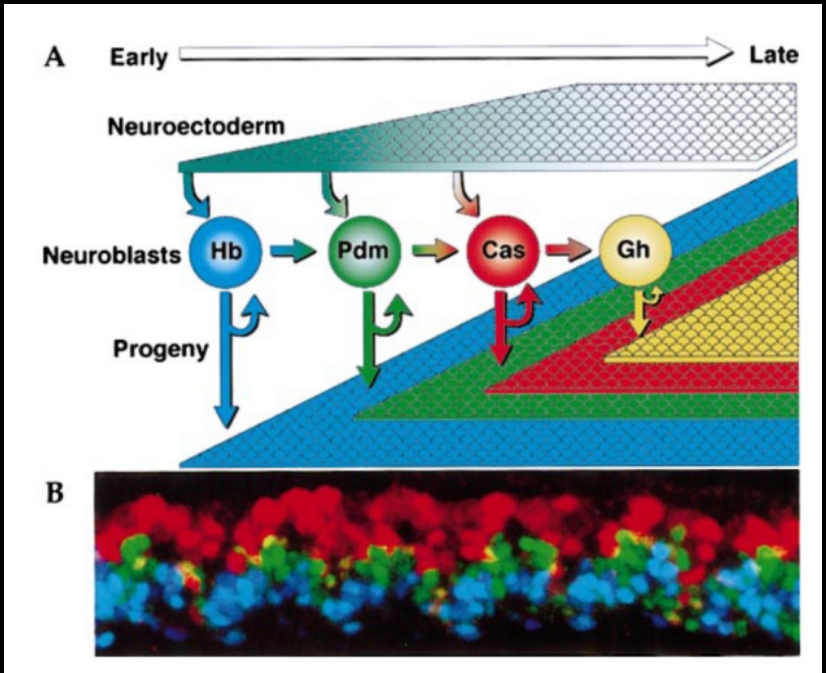

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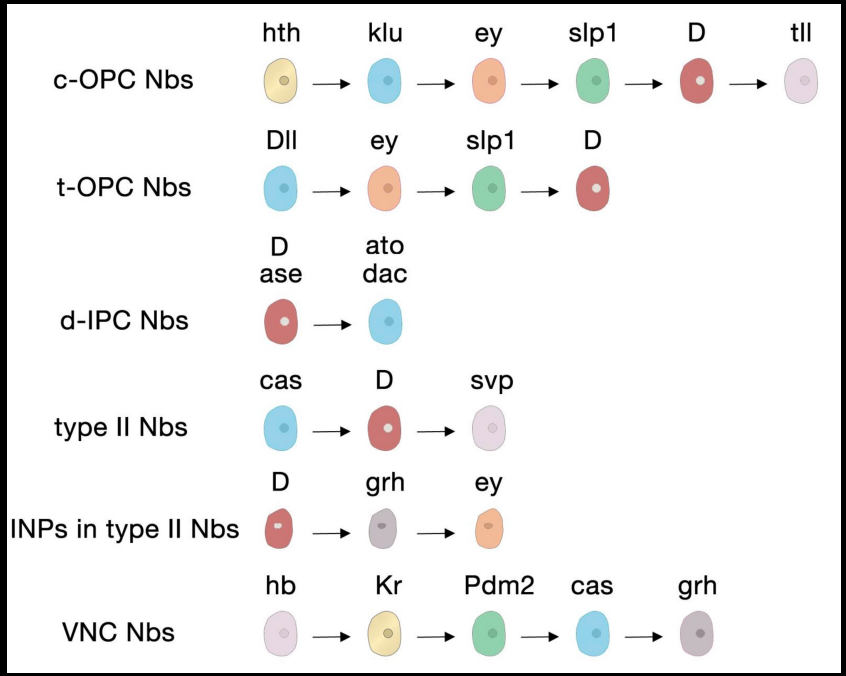

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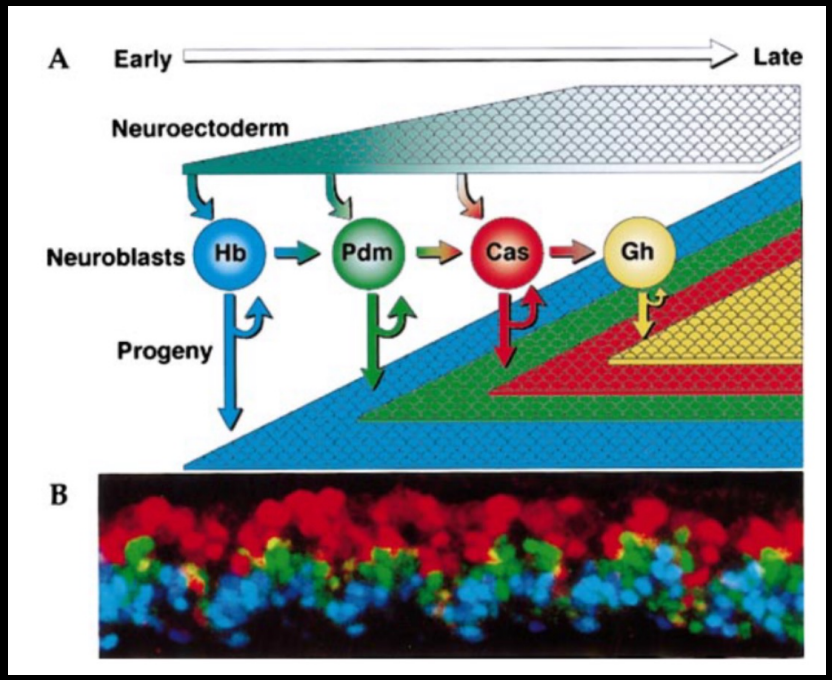
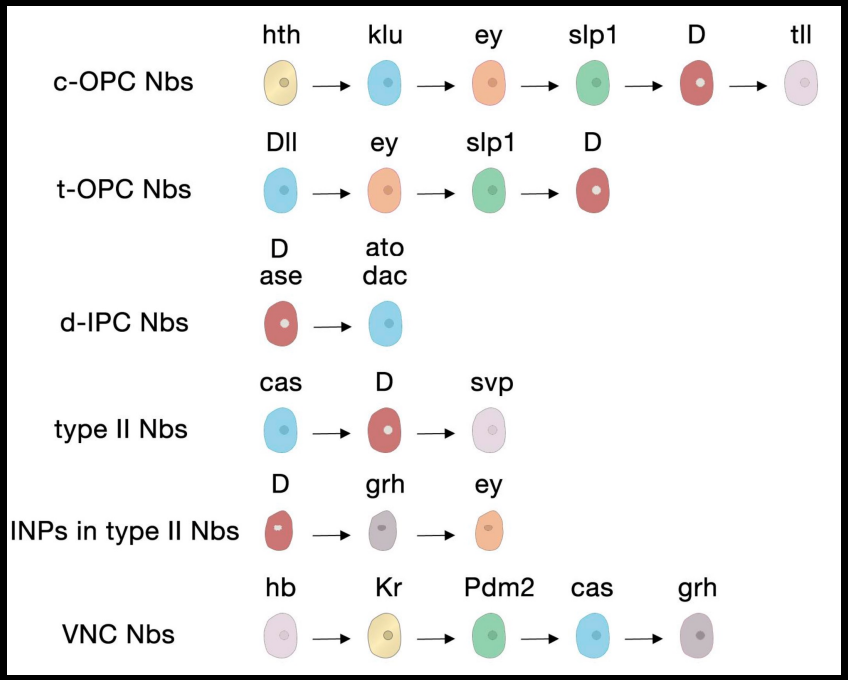


Brody and Odenwald, Dev Biol 2000



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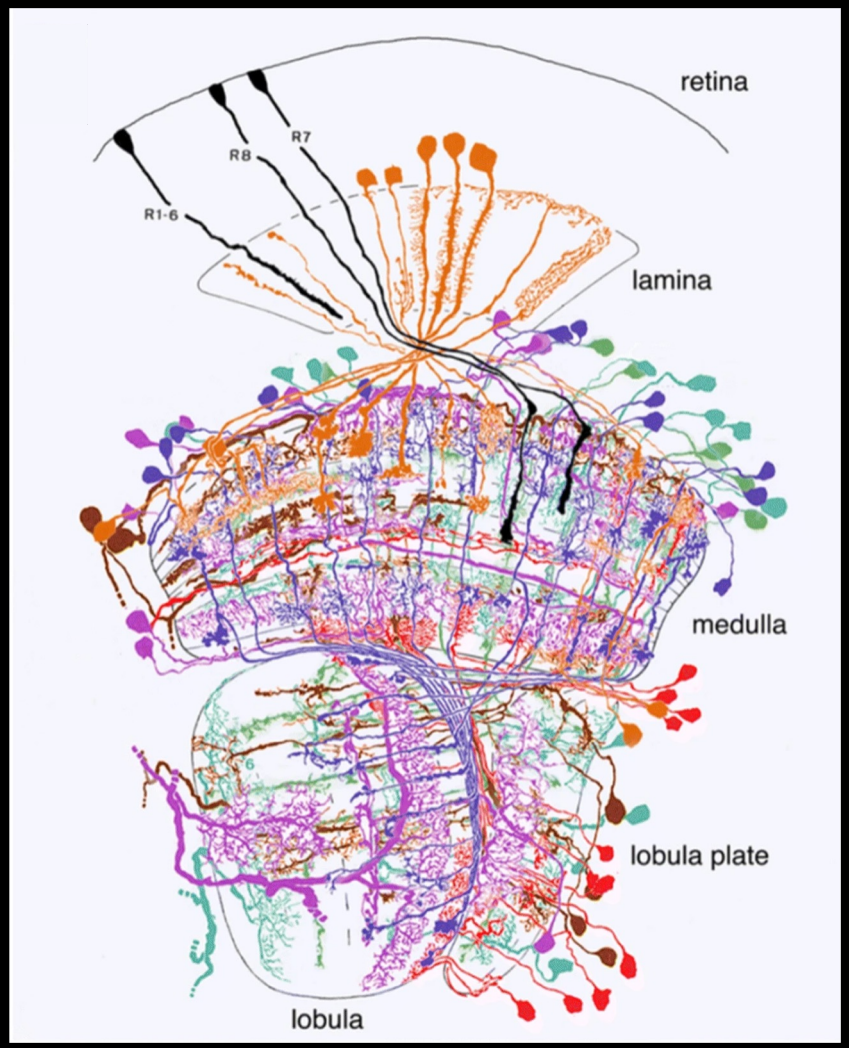
Temporal transcription factors were identified by antibody screens and informed guesses

Our model system: *Drosophila* optic lobe



Fischbach and Dittrich, 1989, Borst et al 2020

Ozel, Simon, et al, 2022

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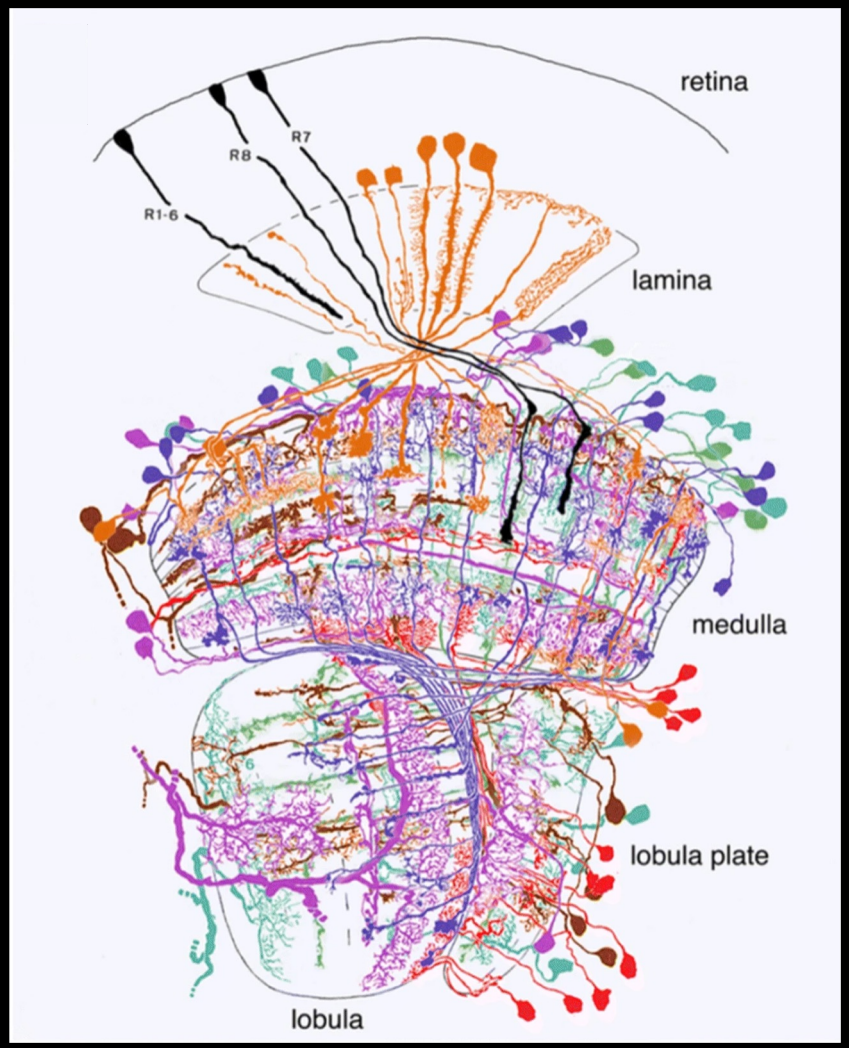

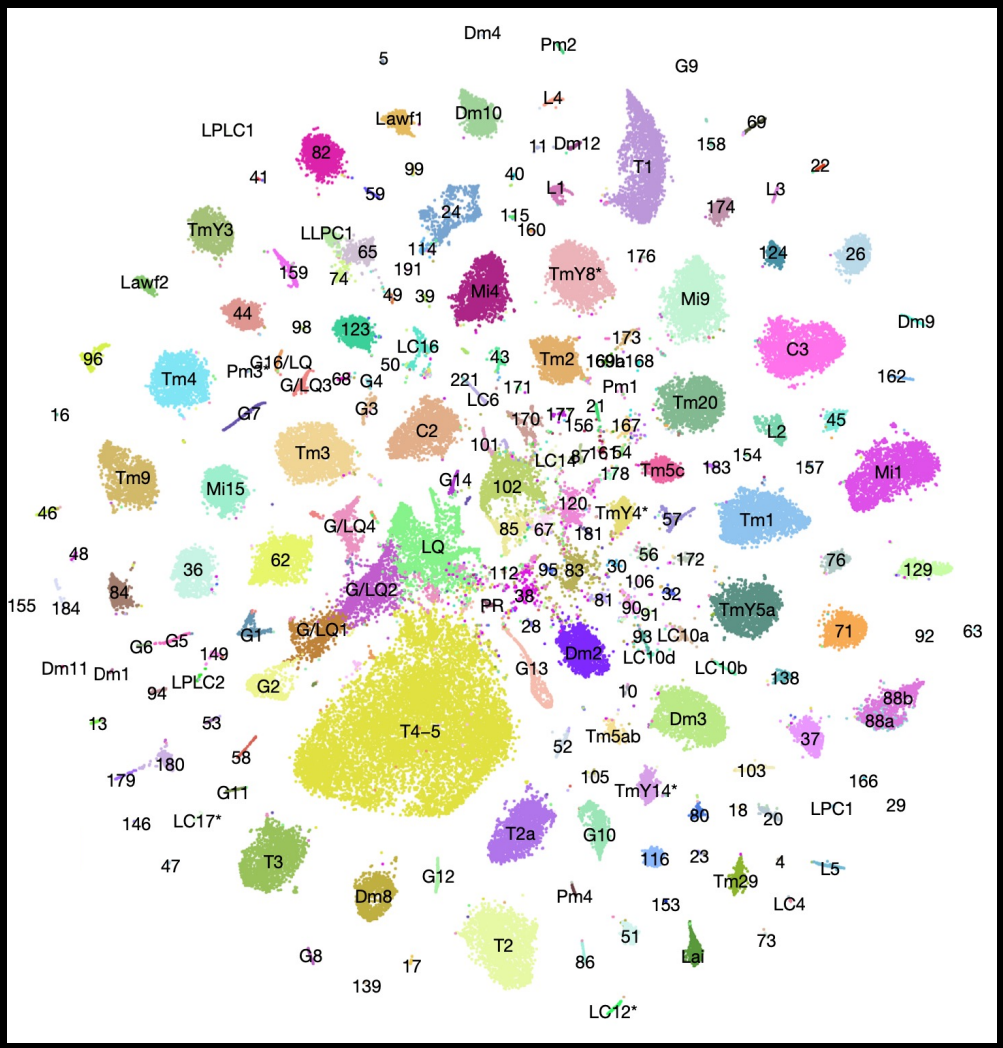

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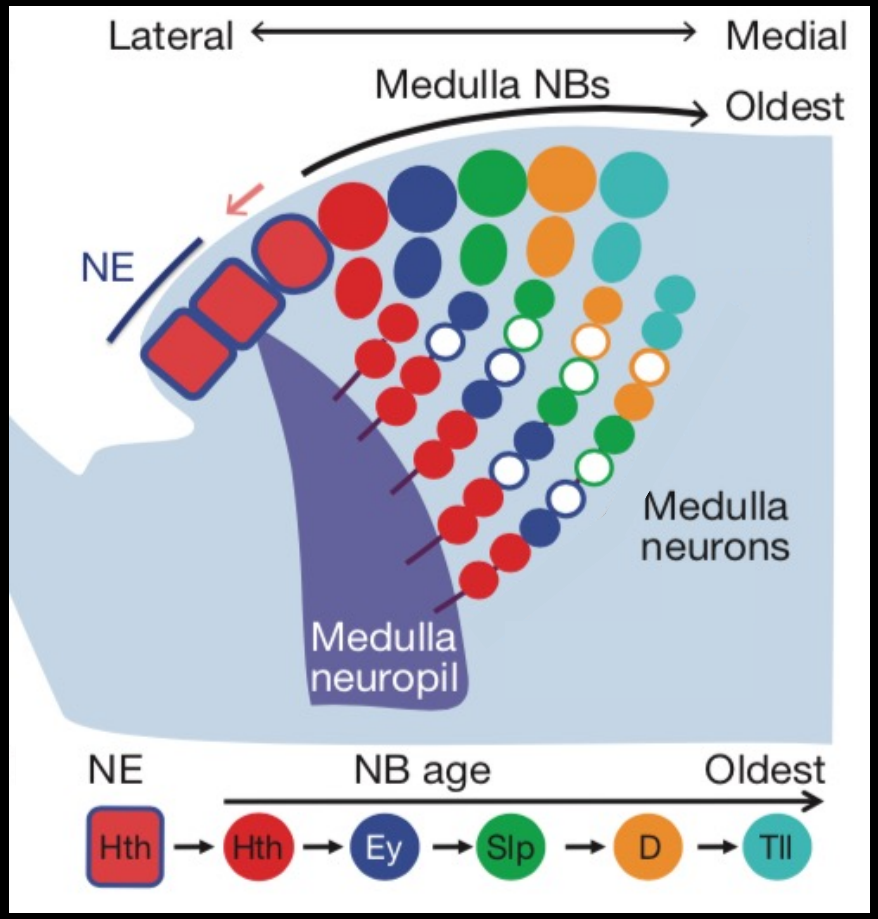
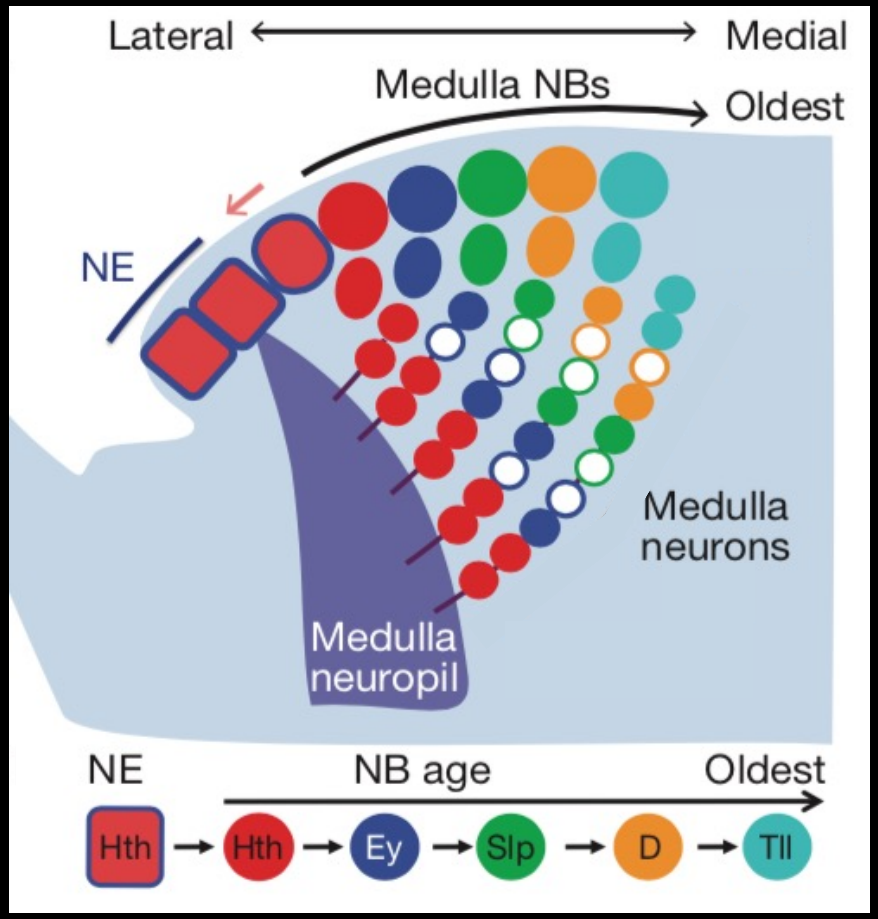
Drosophila optic lobe development



Li, Erclik, et al, Nature 2013

A comprehensive approach to identify temporal transcription factors



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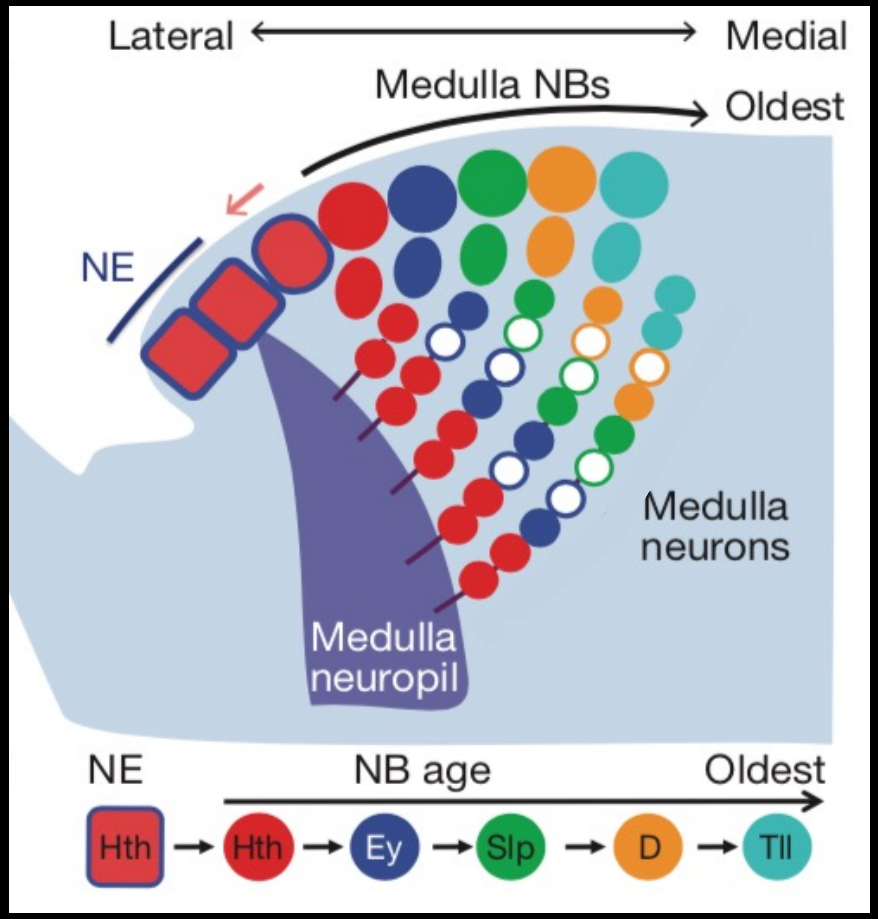

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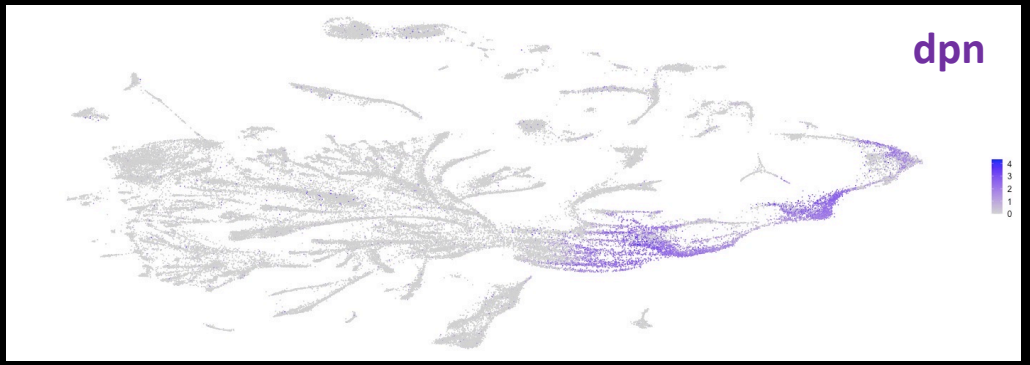
Single-cell sequencing of the larval optic lobe



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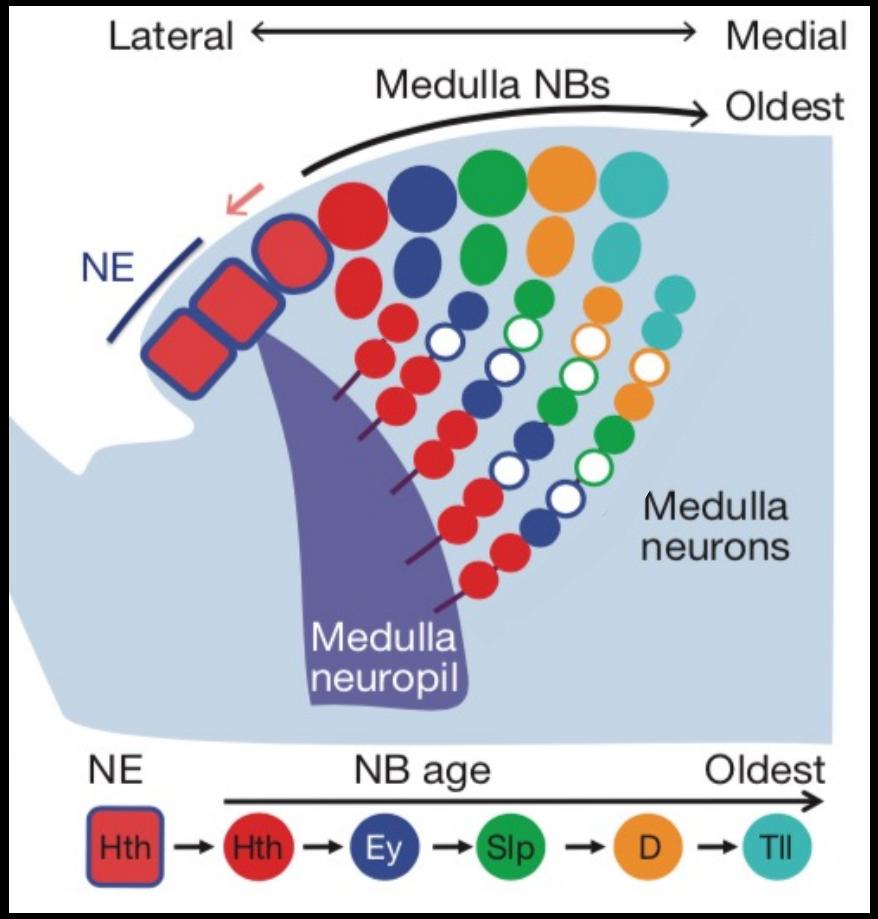

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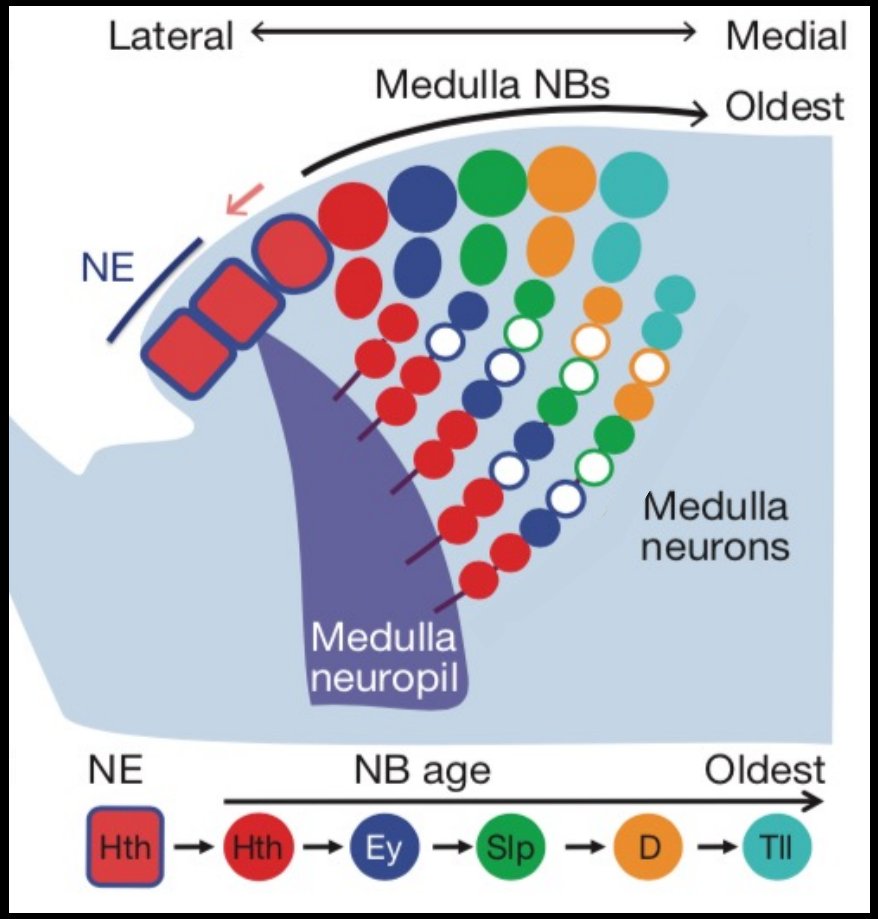

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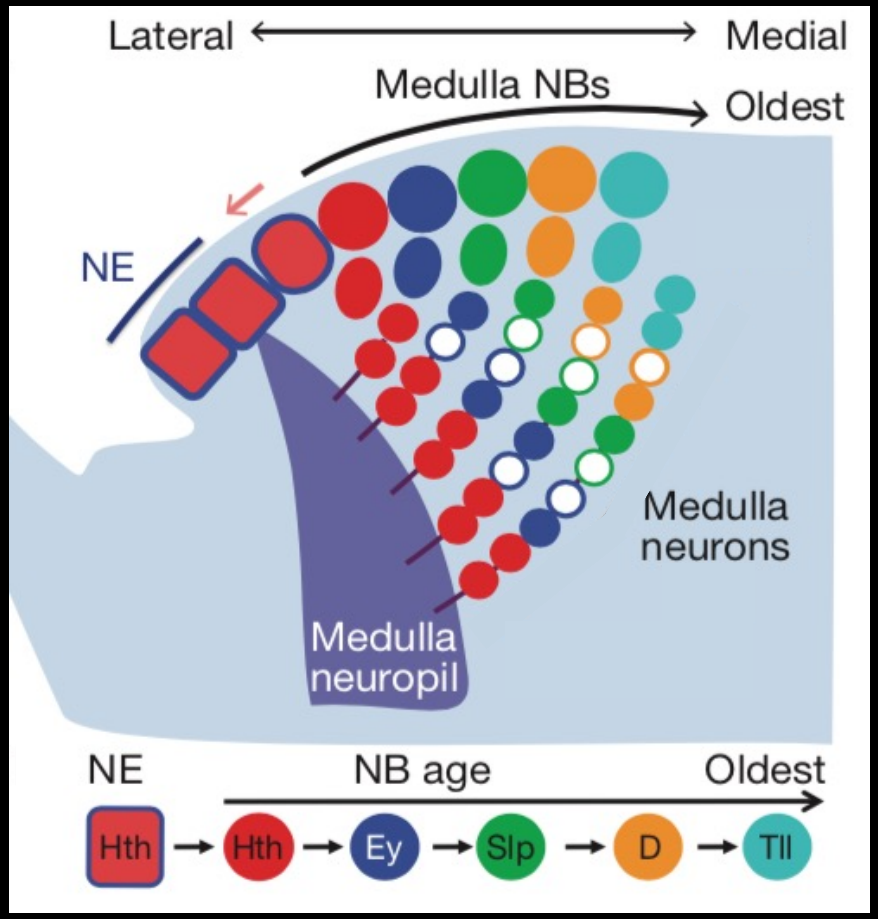

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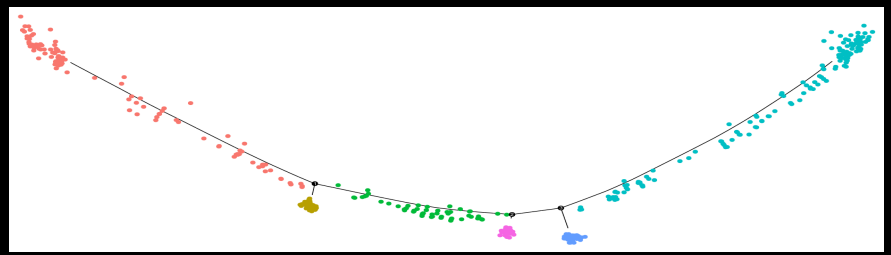

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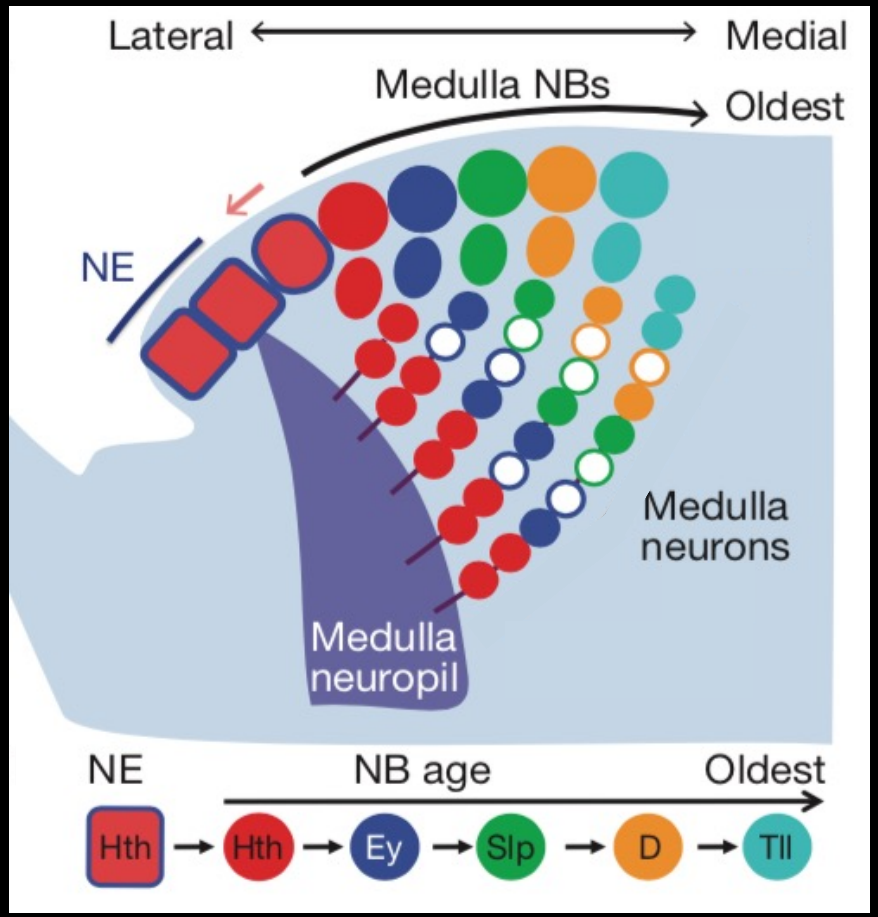

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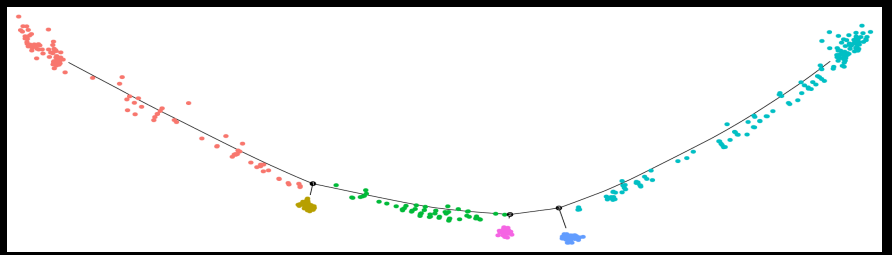
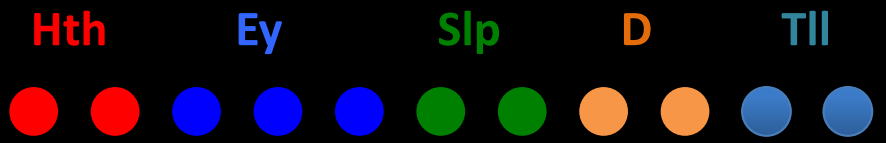
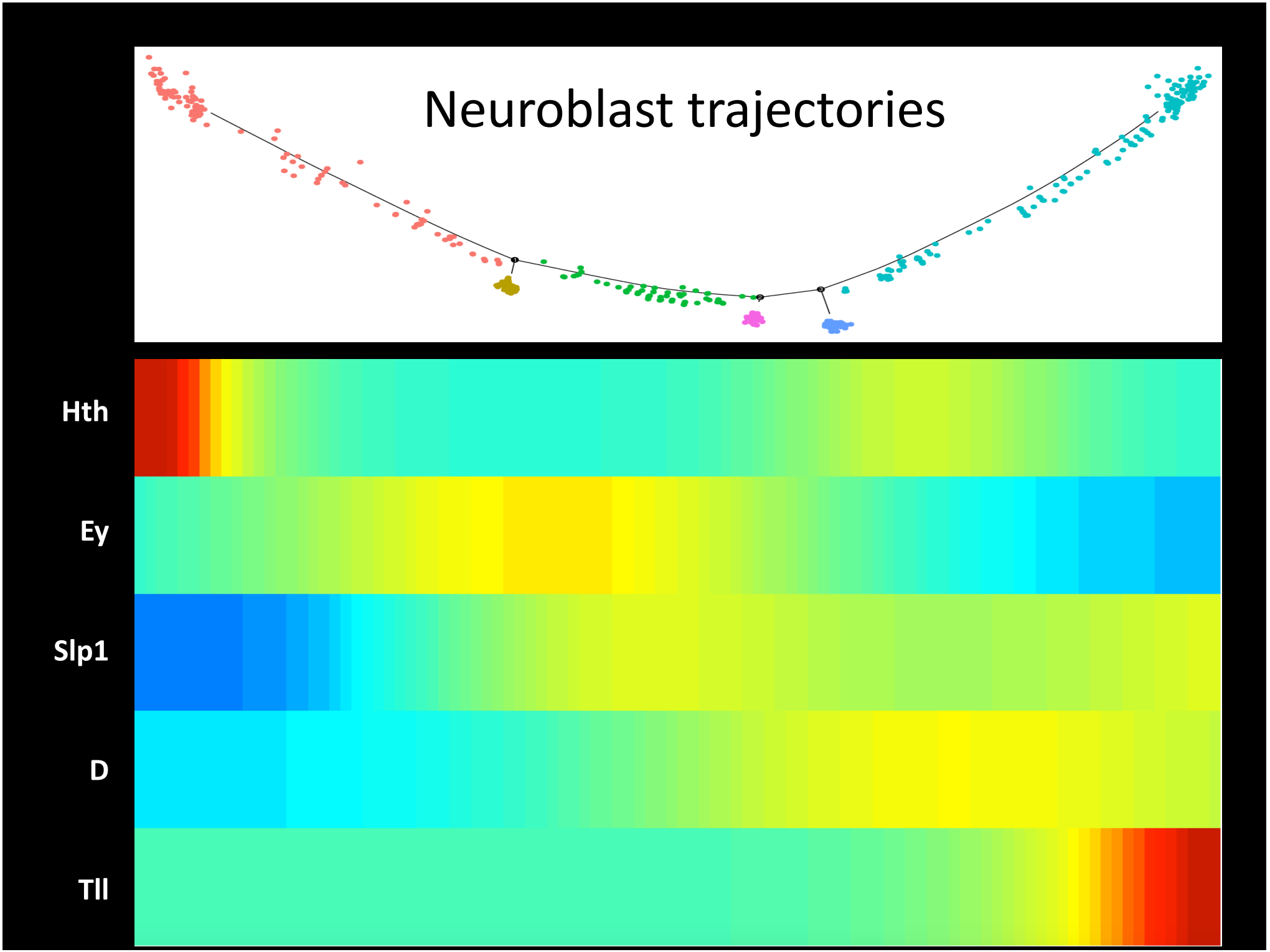
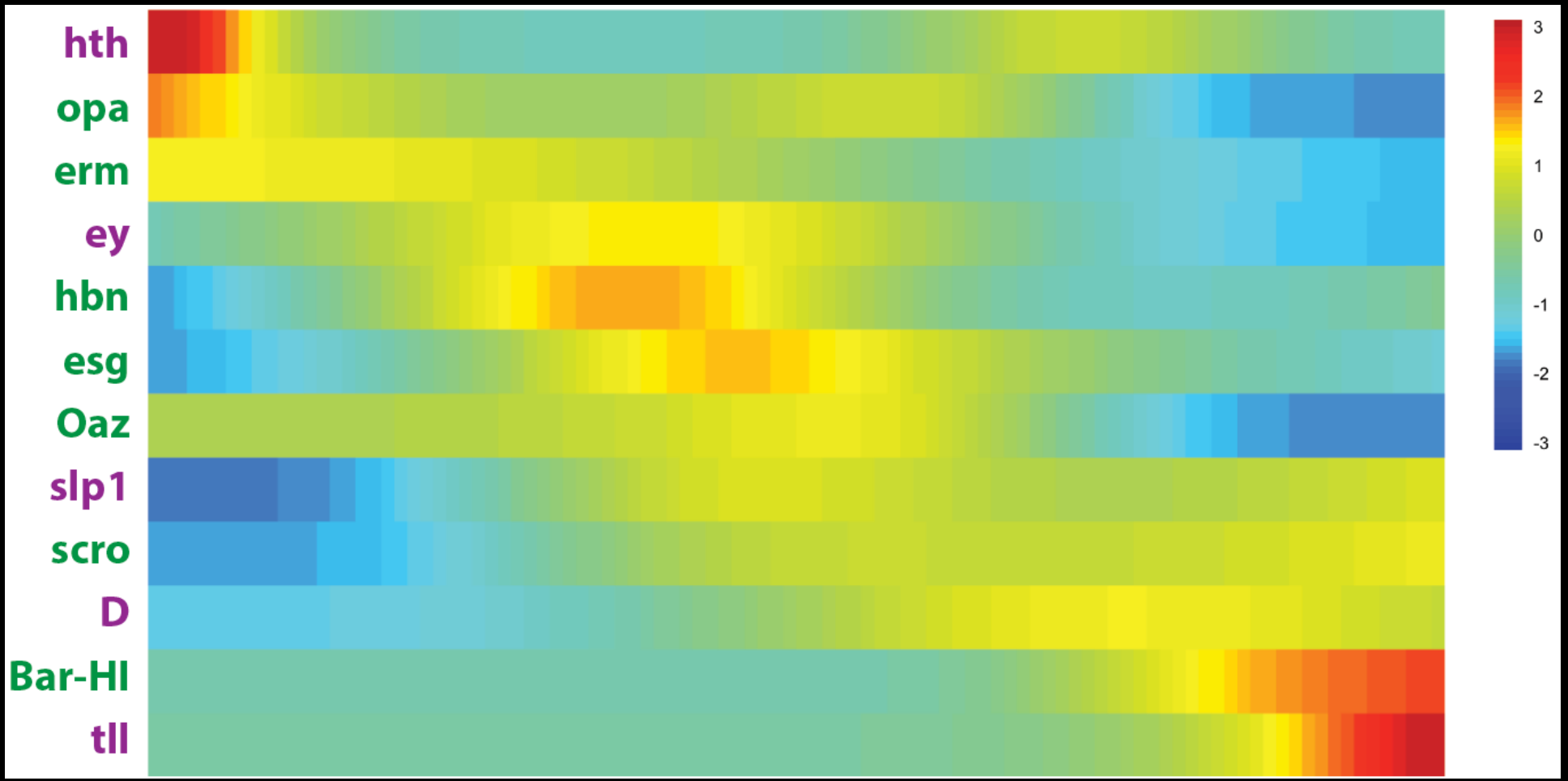




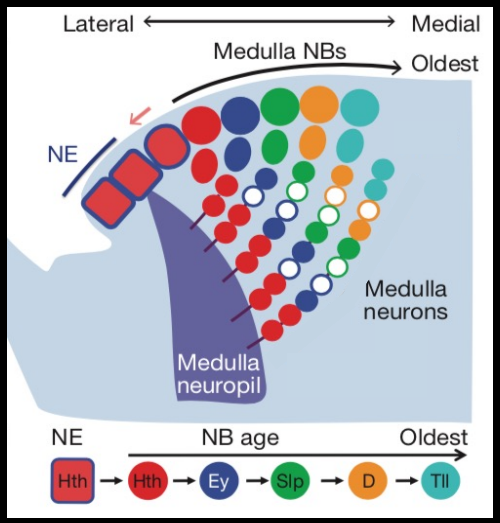

Neuroblast trajectories
Hth
Ey
Slp1
D
Tll

Identify new tTFs



Konstantinides, Holguera, Rossi et al, 2022

How do tTFs affect neuronal diversity?



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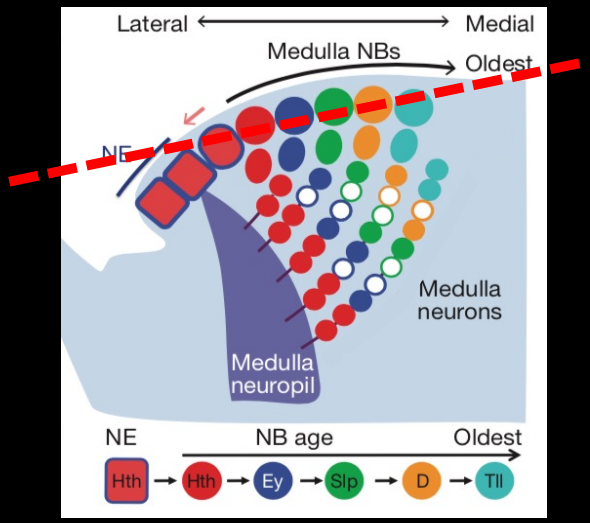

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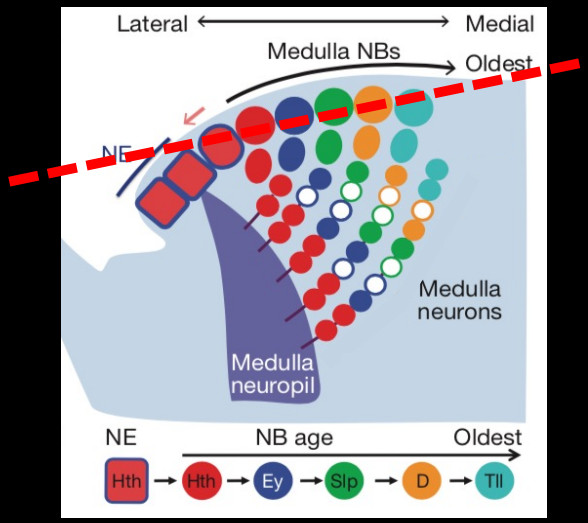
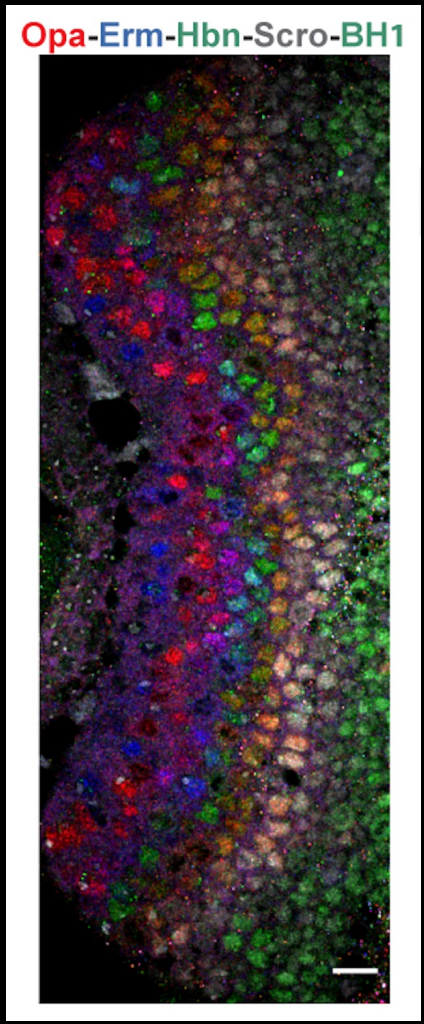
Temporal transcription factor expression in **neuroblasts**





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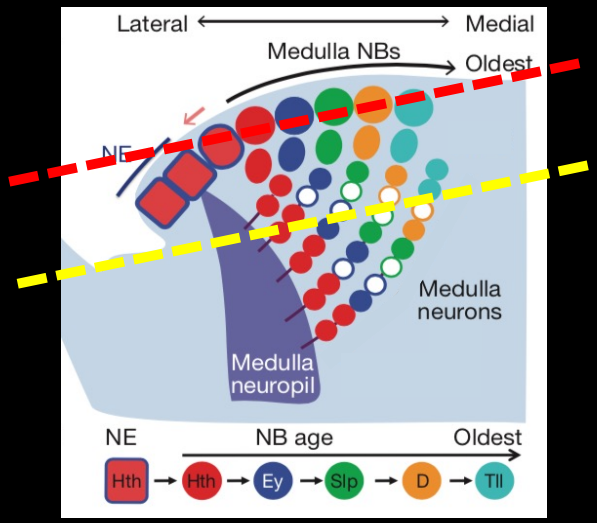

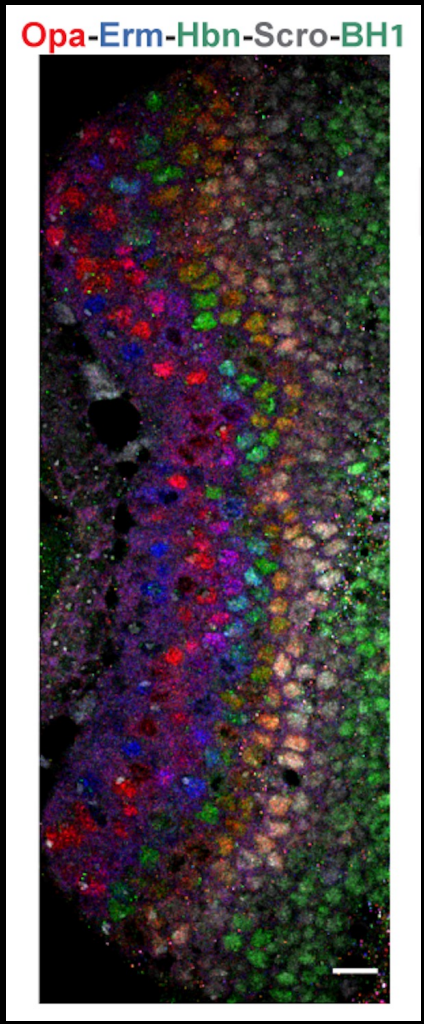

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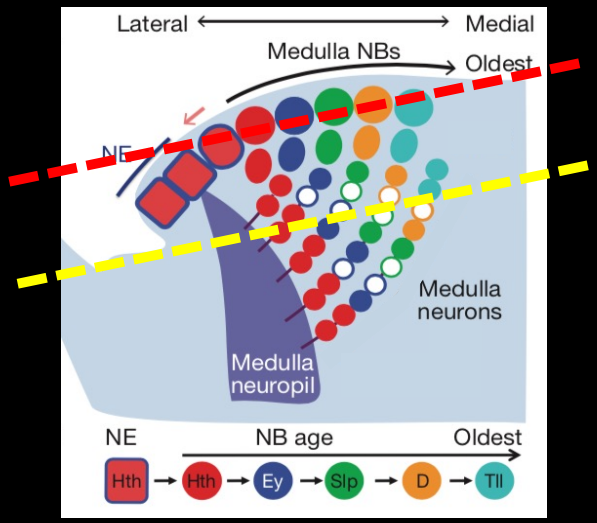
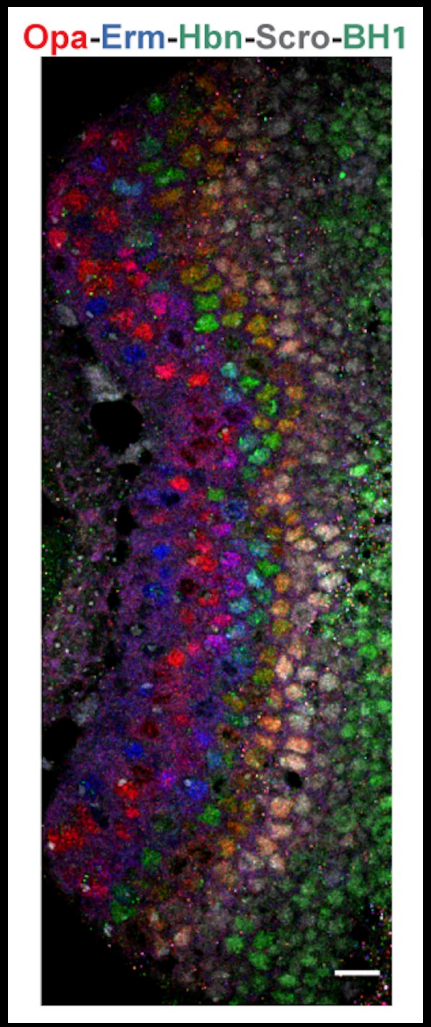
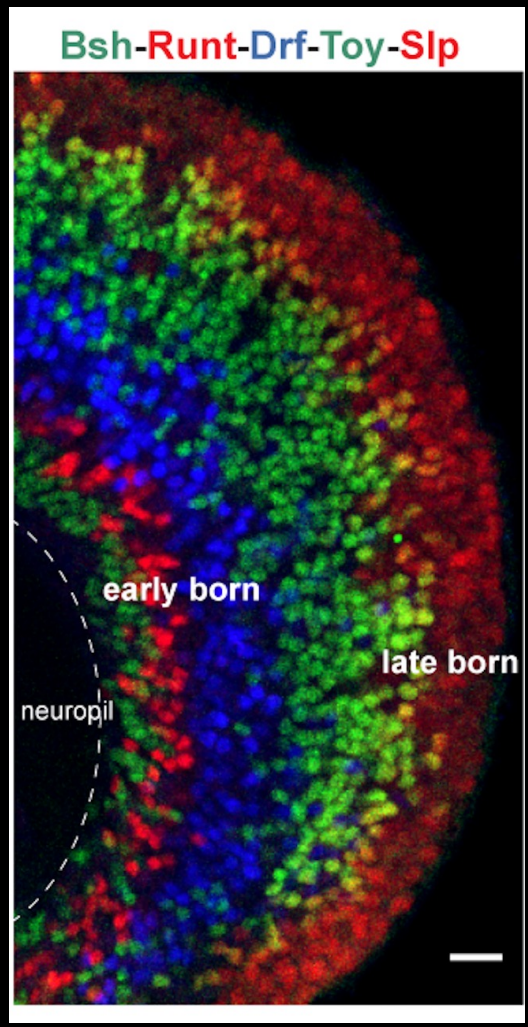




Neuronal transcription factor expression



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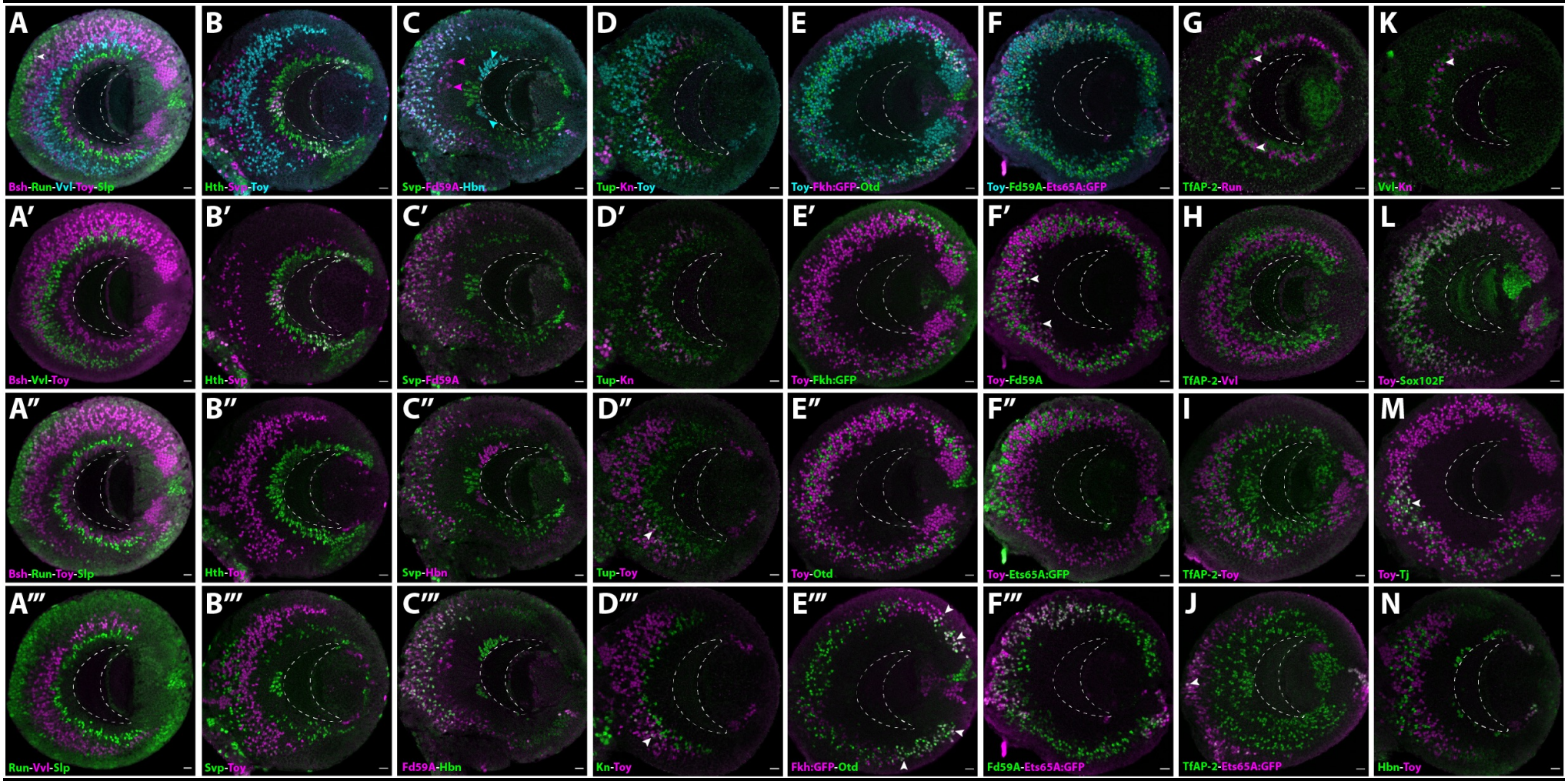

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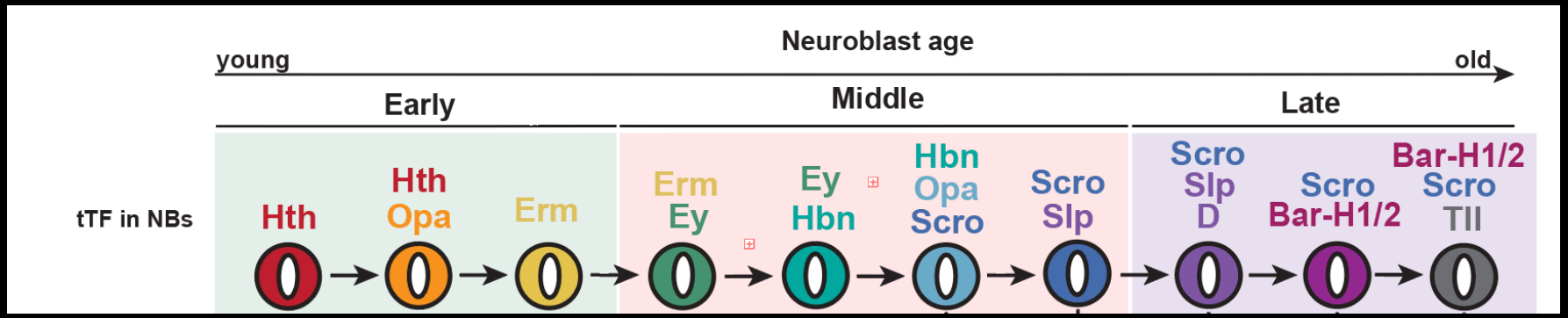

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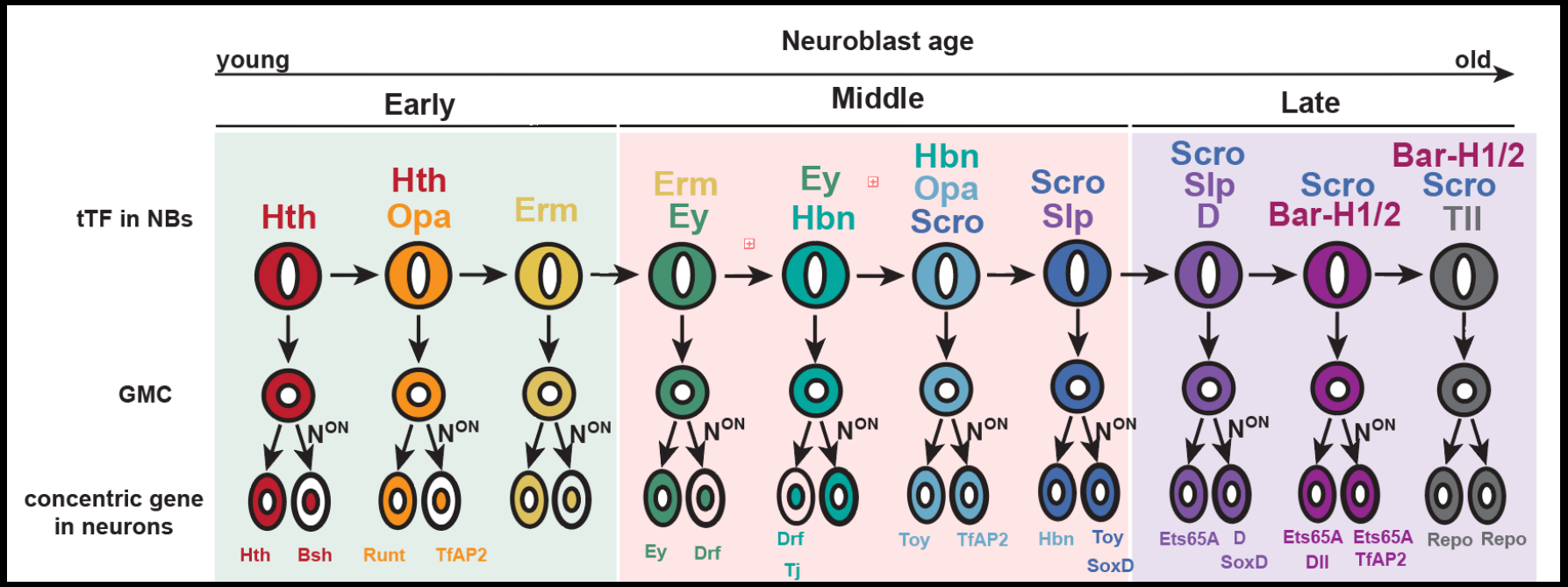

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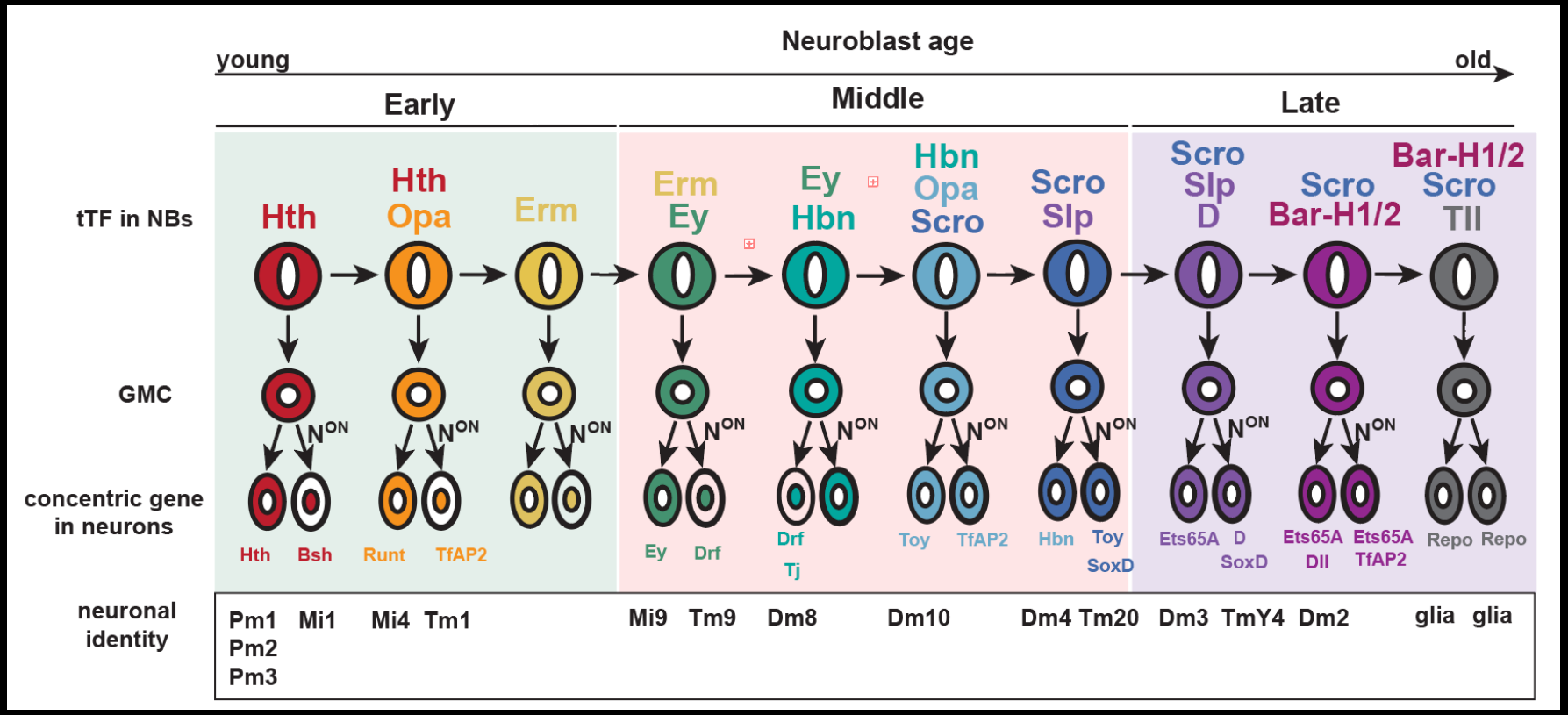

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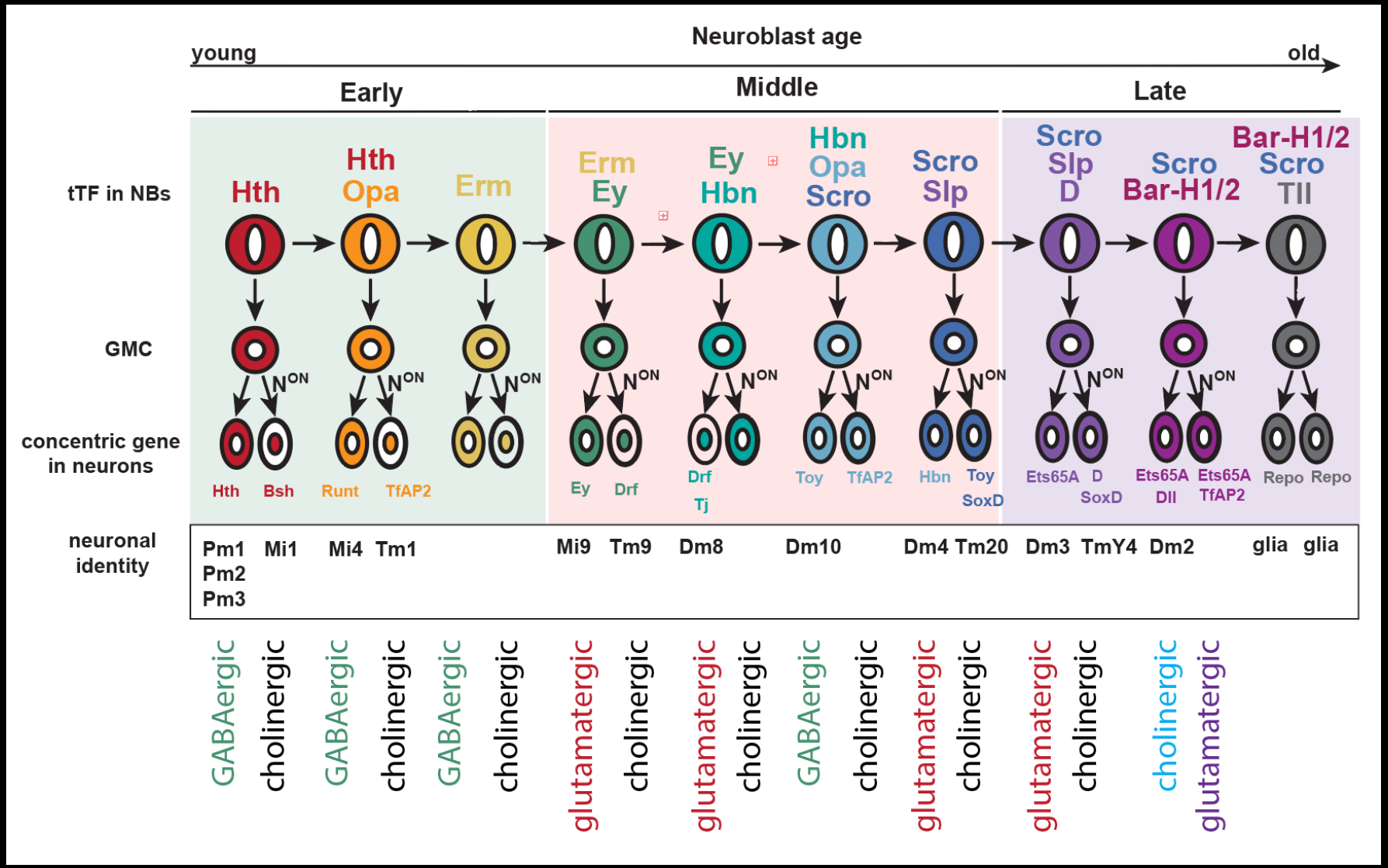

Konstantinides, Holguera, Rossi et al, 2022

Take-home message

- We identify a complete (?) temporal series in the optic lobes
- We establish the birth order and temporal window of origin of each neuronal type in the medulla
- Proof of principle for use of similar techniques in non-genetic models

How do neurons that are tightly interconnected in circuits evolve to output new behaviours?

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1. Evolution of a new cell type (Pop et al, 2020; Prieto-Godino et al, 2020)
2. Genetic drift - changes in terminal features (Ding et al, 2016)
3. Circuitry change – synaptic partners or synaptic strength (Seeholzer et al, 2018)

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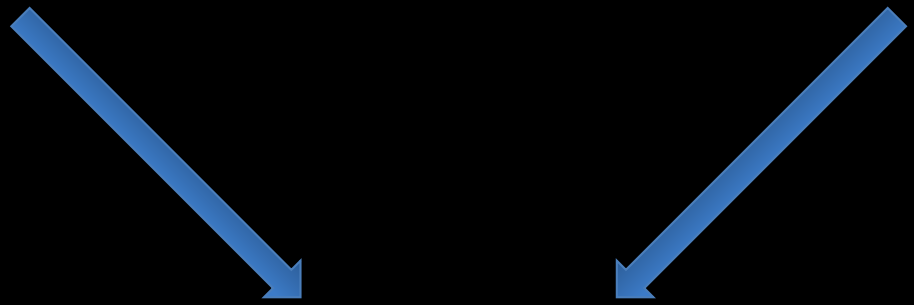

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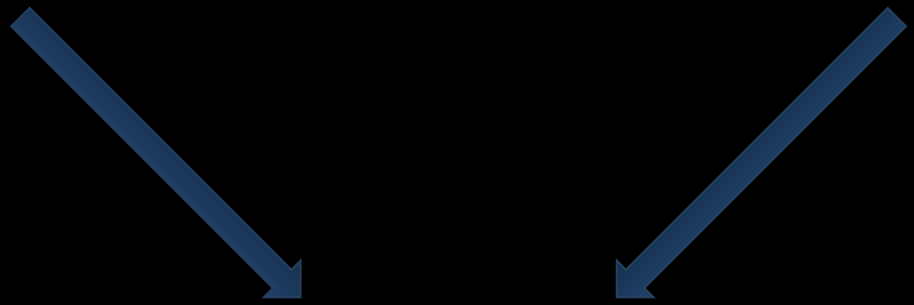

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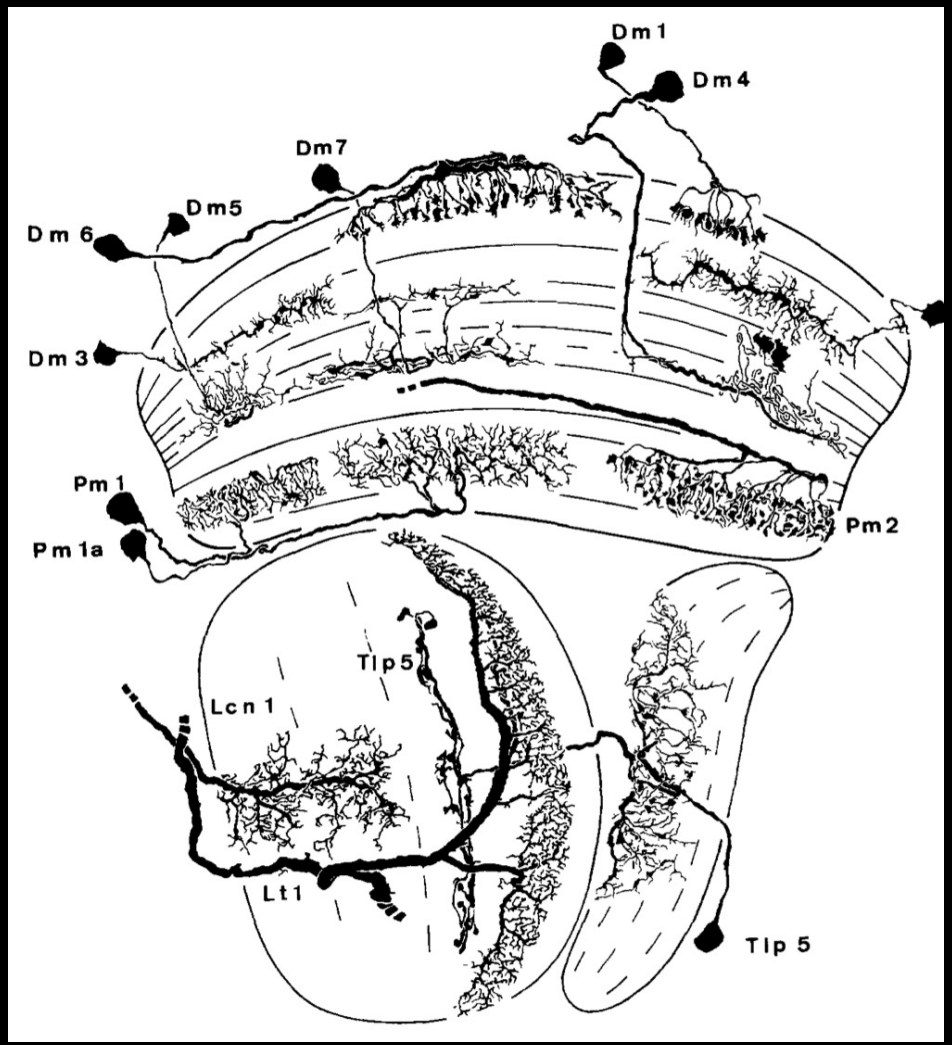
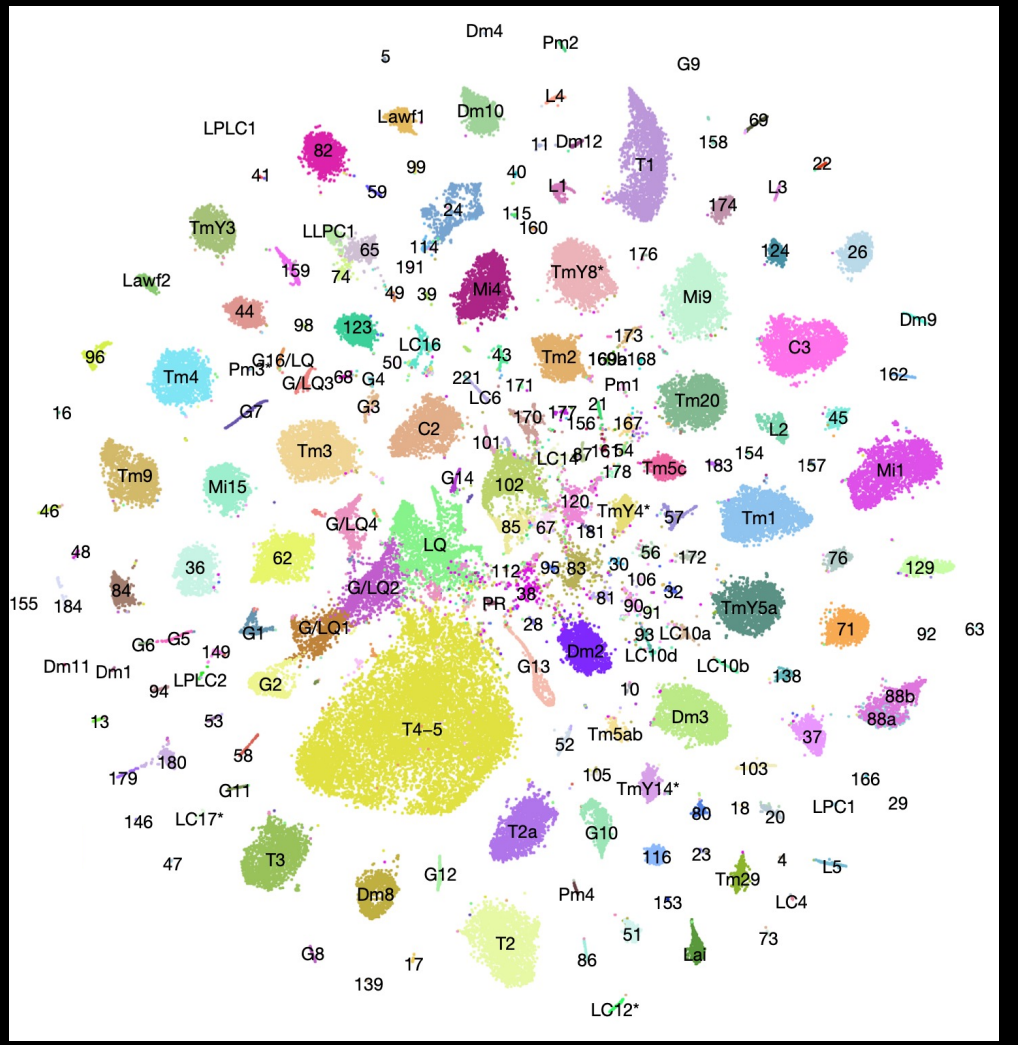
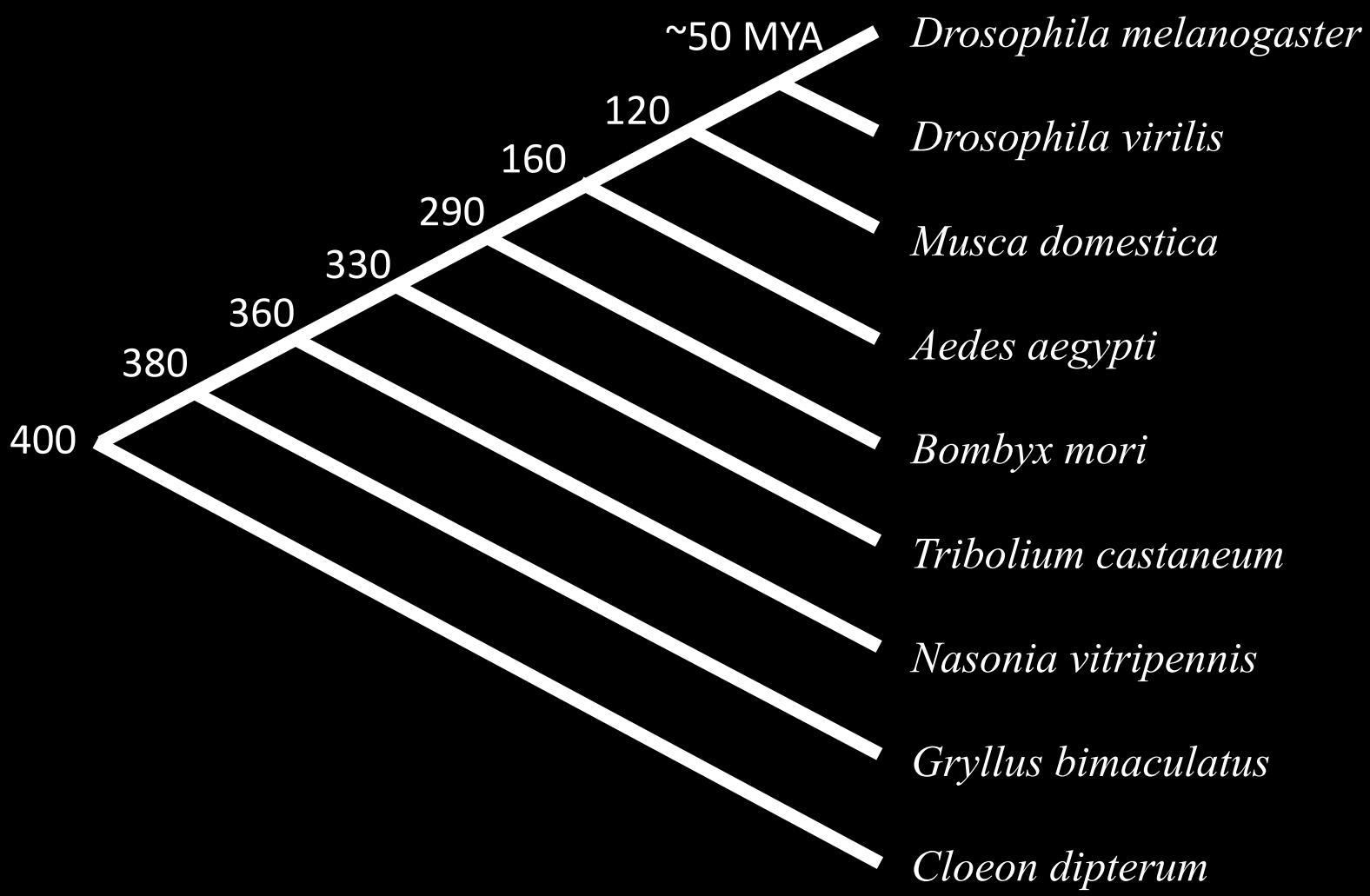




Fischbach and Dittrich, 1989

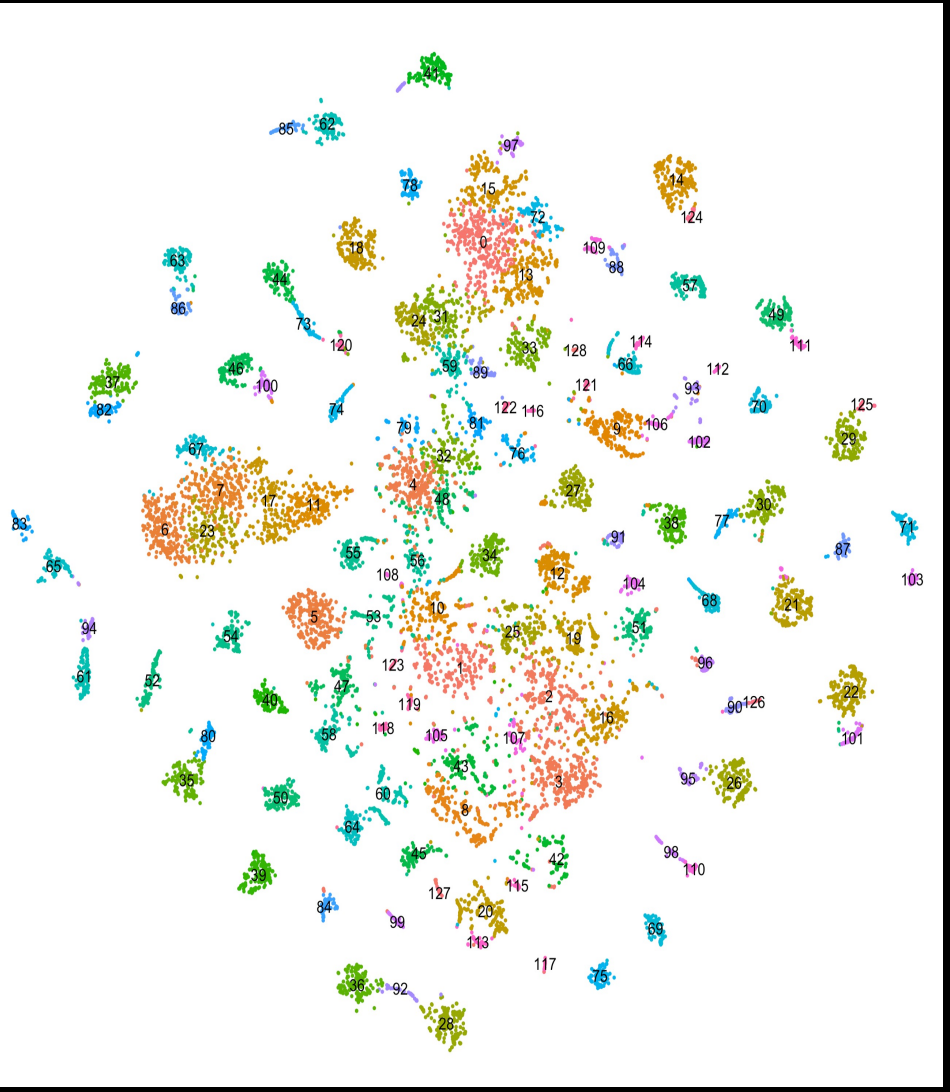
Ozel, Simon, et al, 2022

Comparative analysis of neuronal type composition

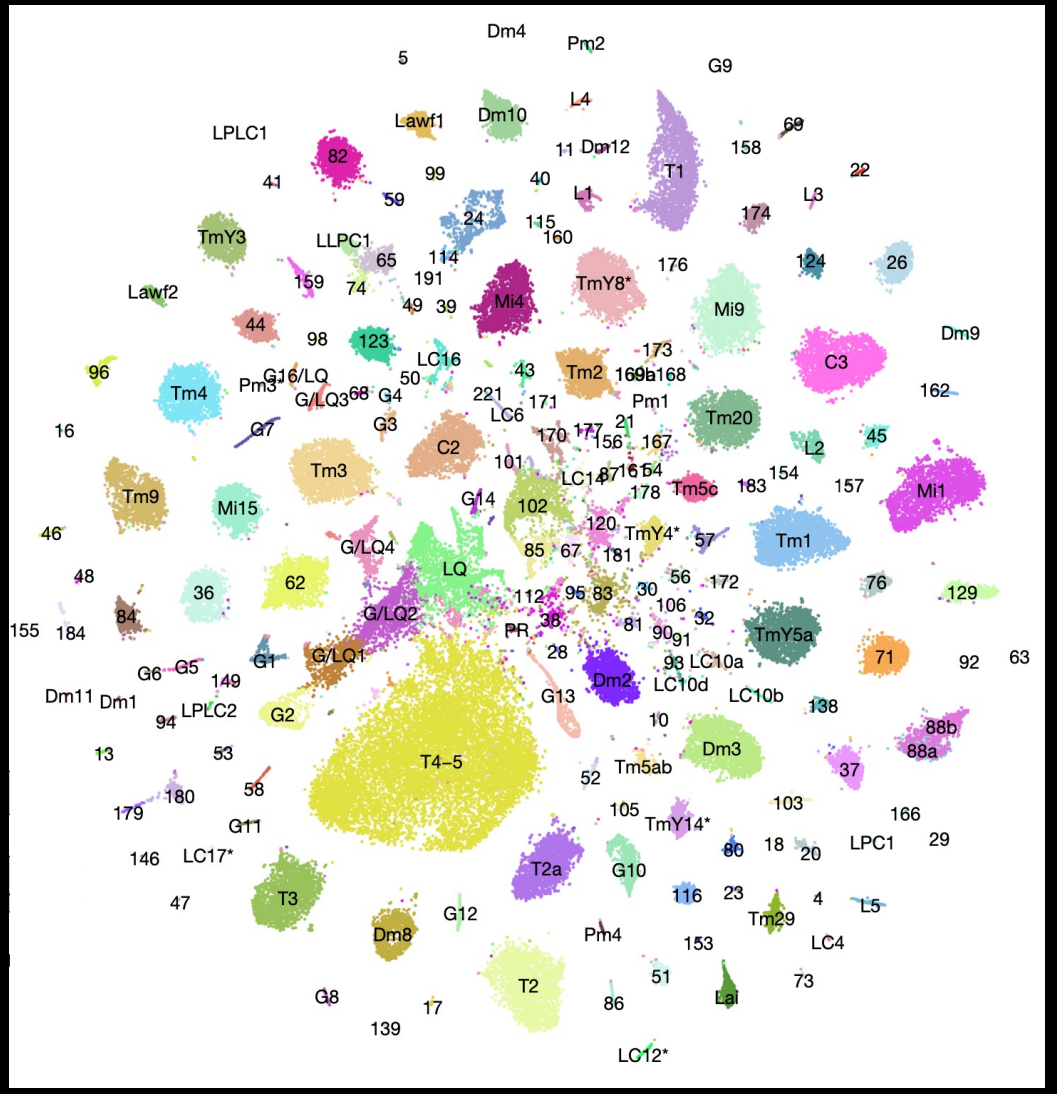


Comparison of cell-type composition in different brains

Drosophila virilis

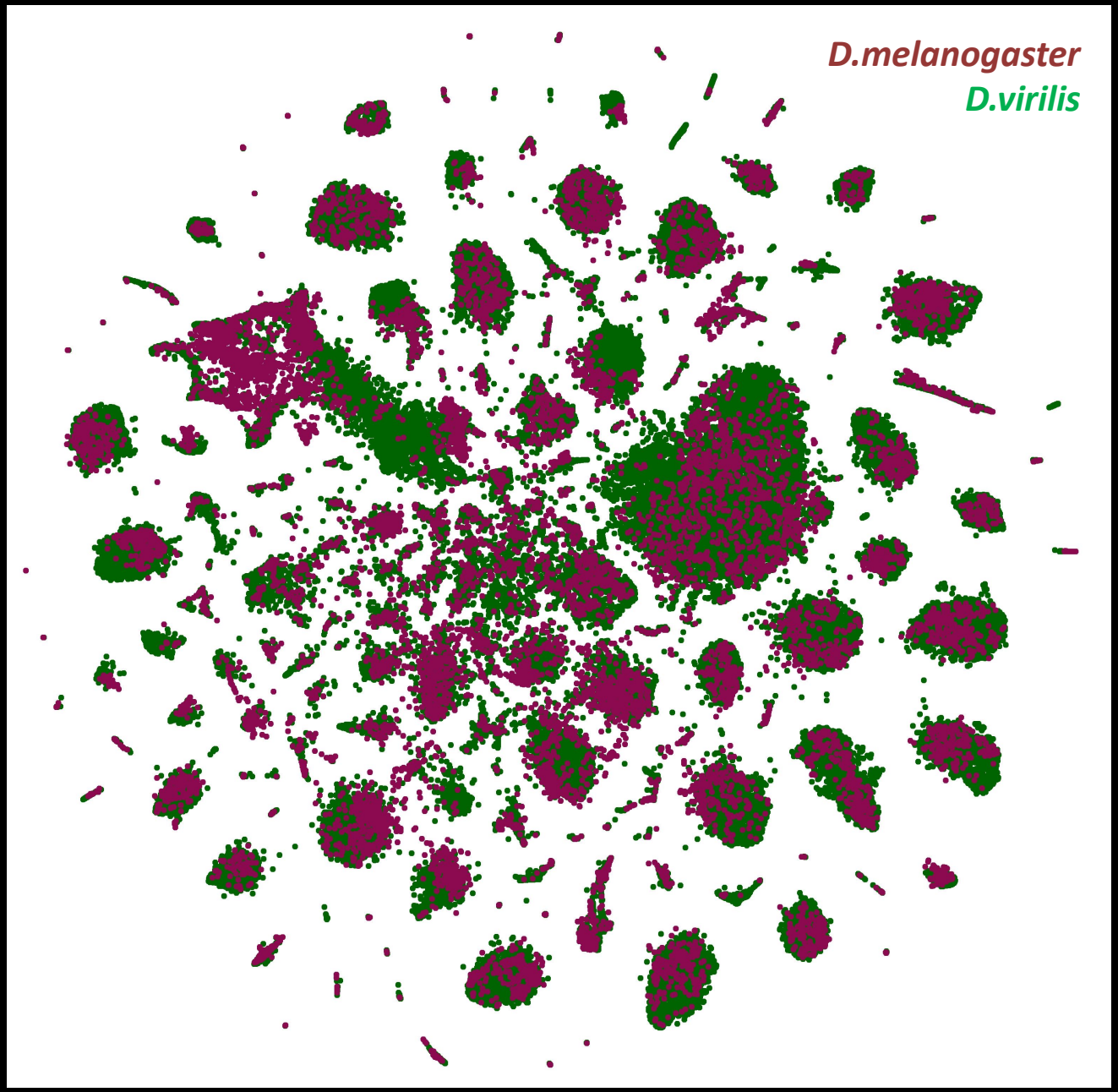


Drosophila melanogaster



Ozel, Simon, …, Konstantinides*, Desplan*, 2021

Comparison of cell-type composition in different brains



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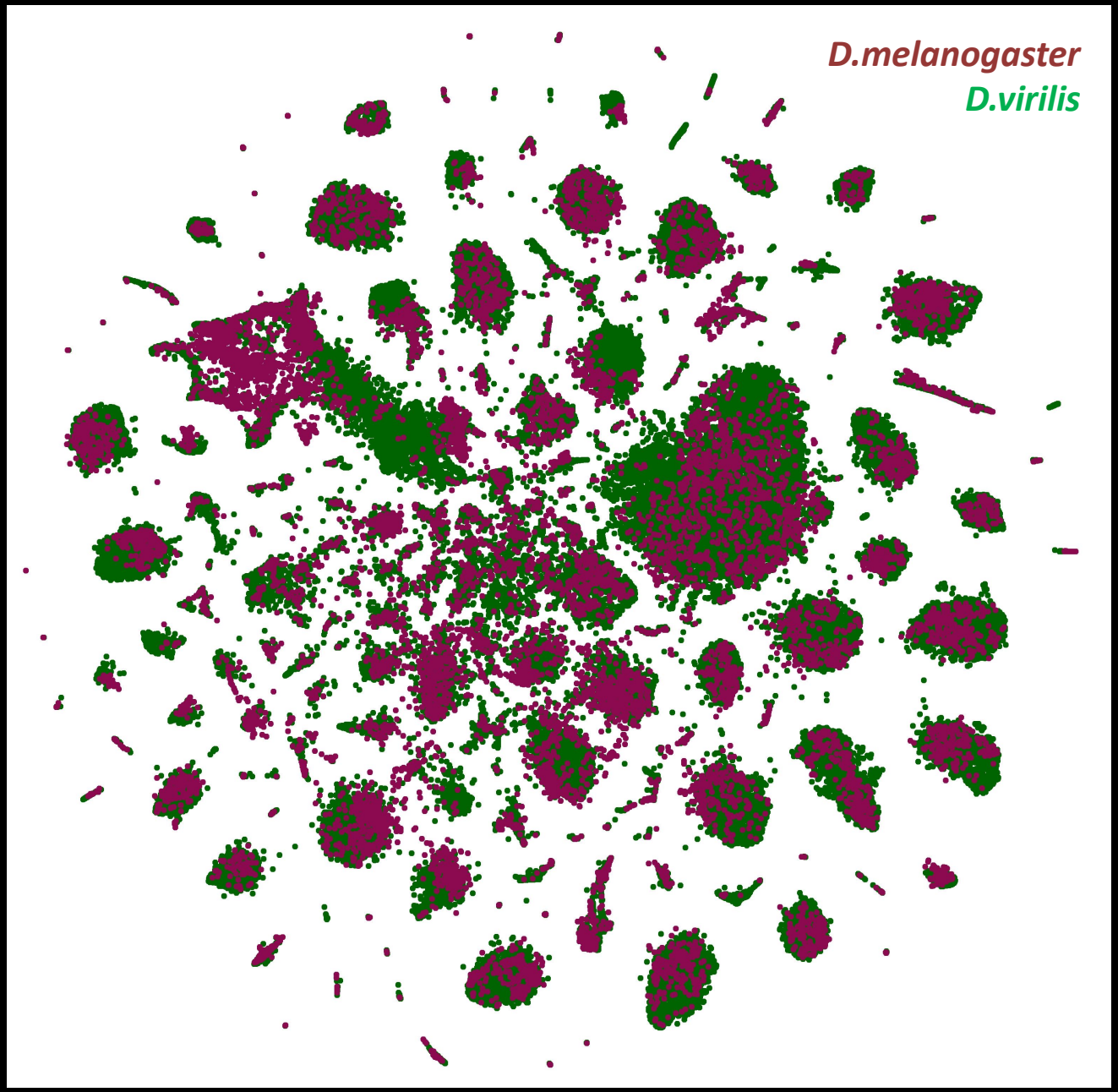

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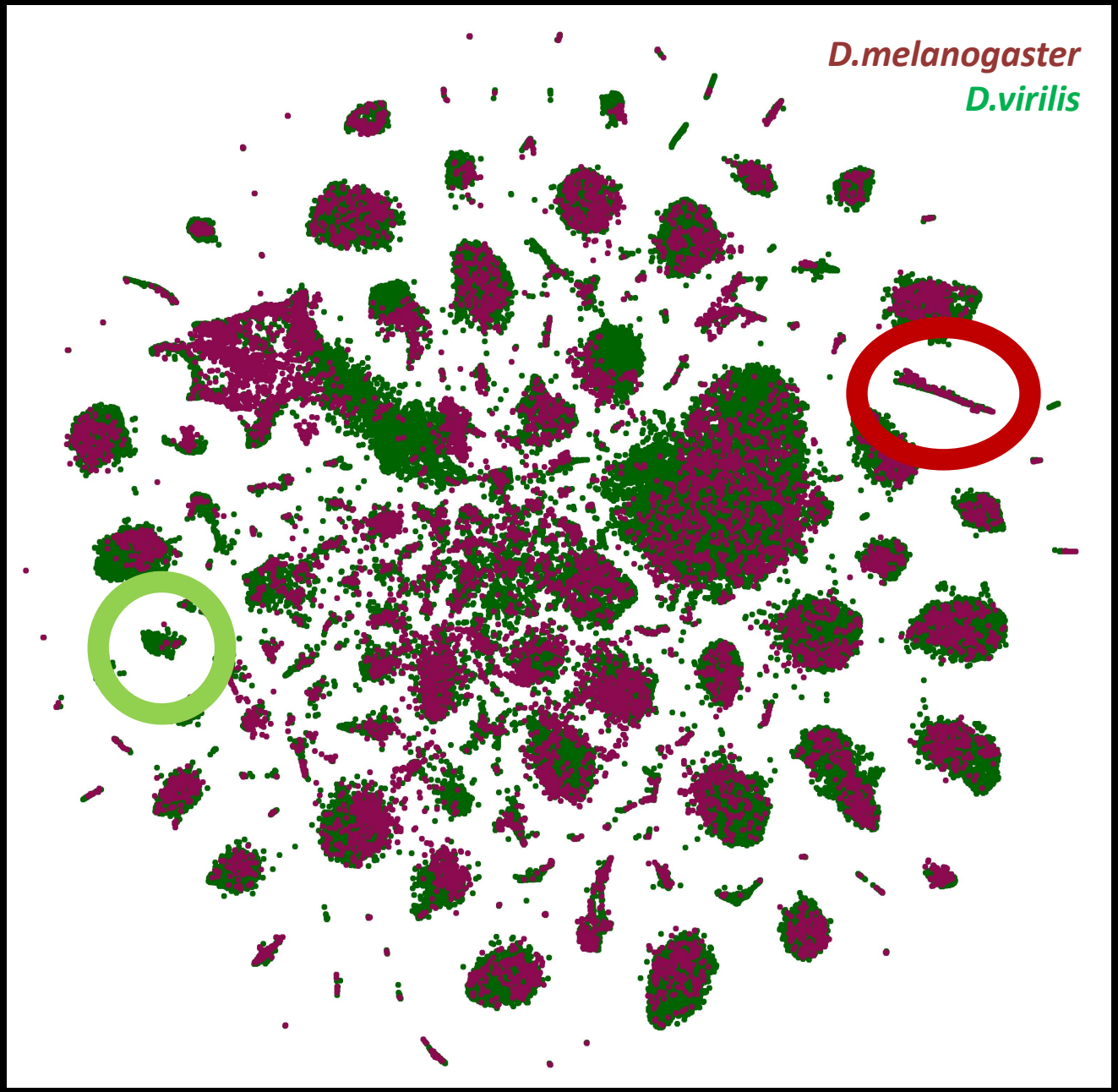
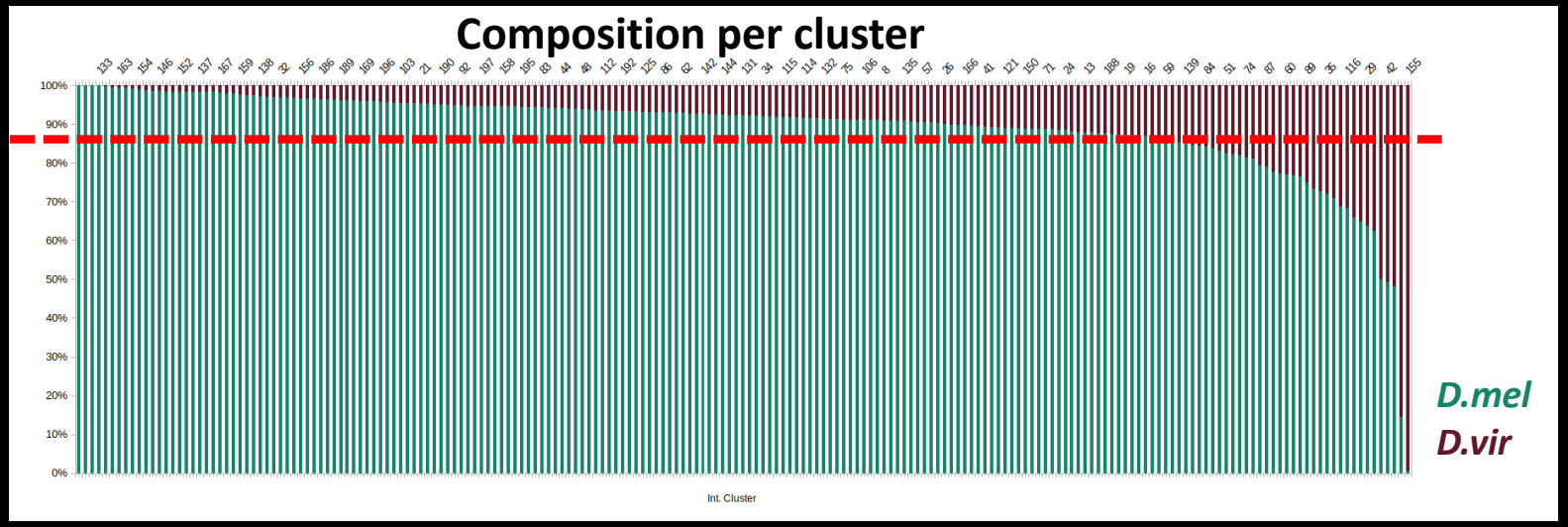


scCoda – Compositional analysis of single-cell data

87% of cells are melanogaster



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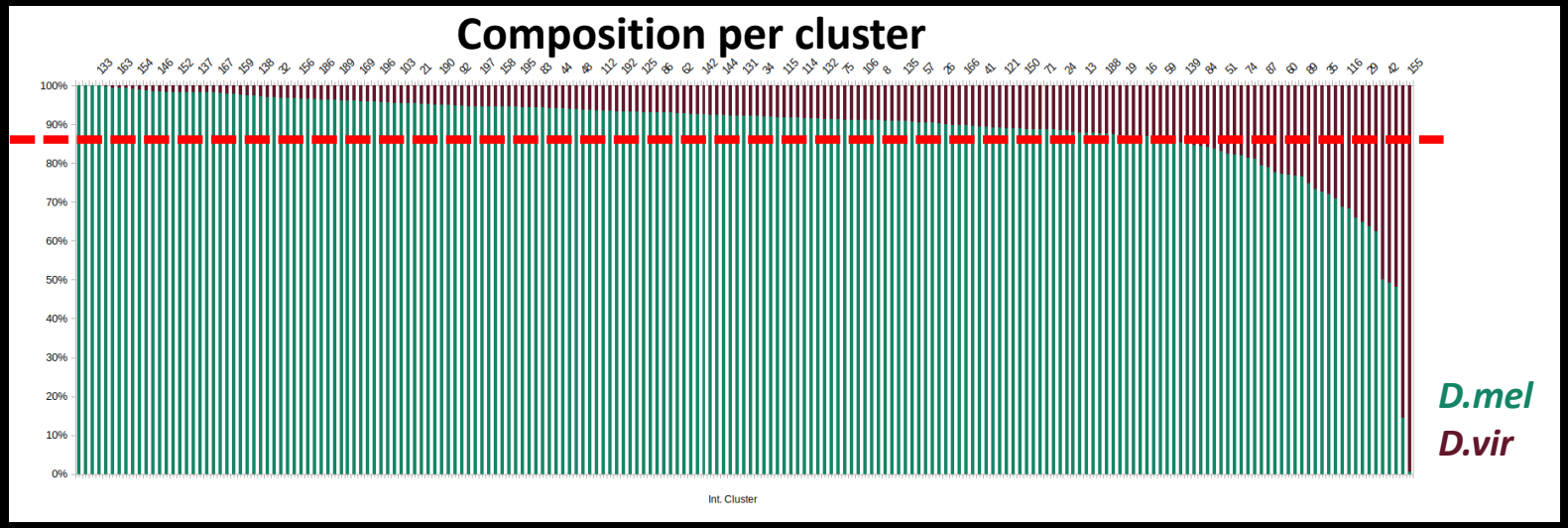

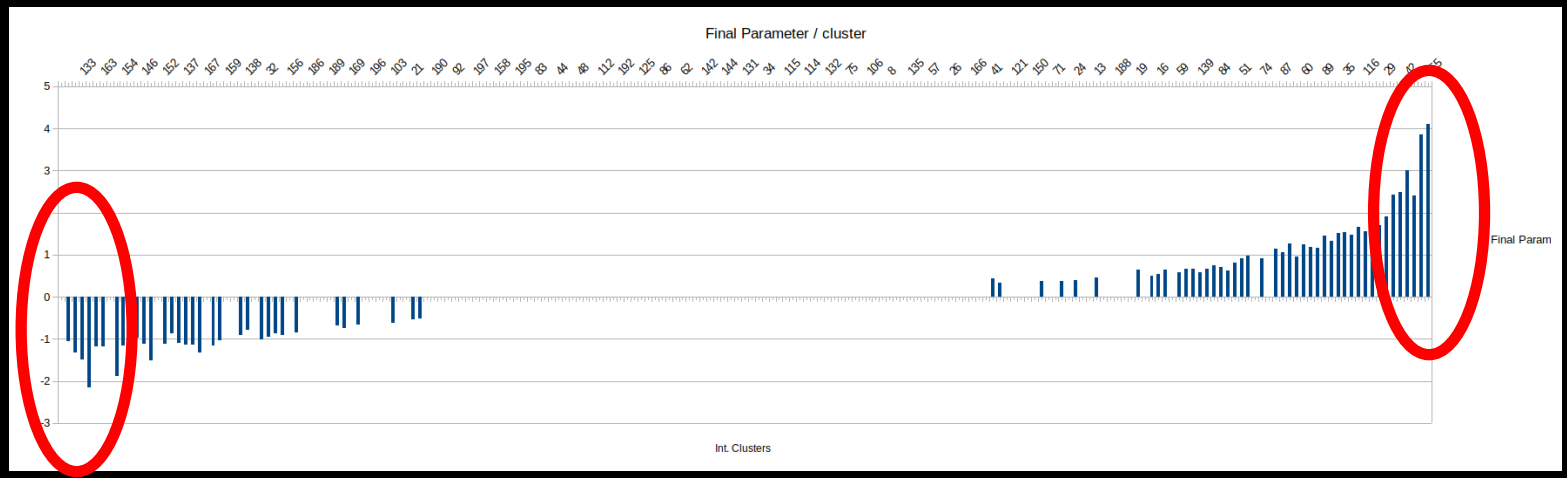

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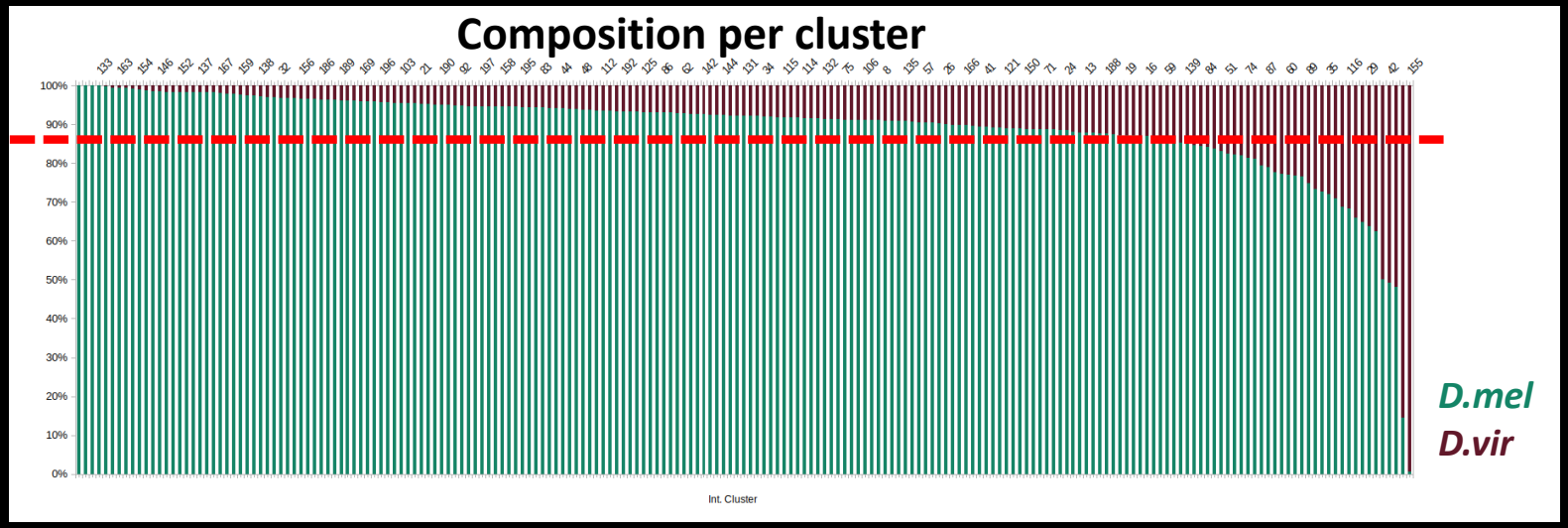

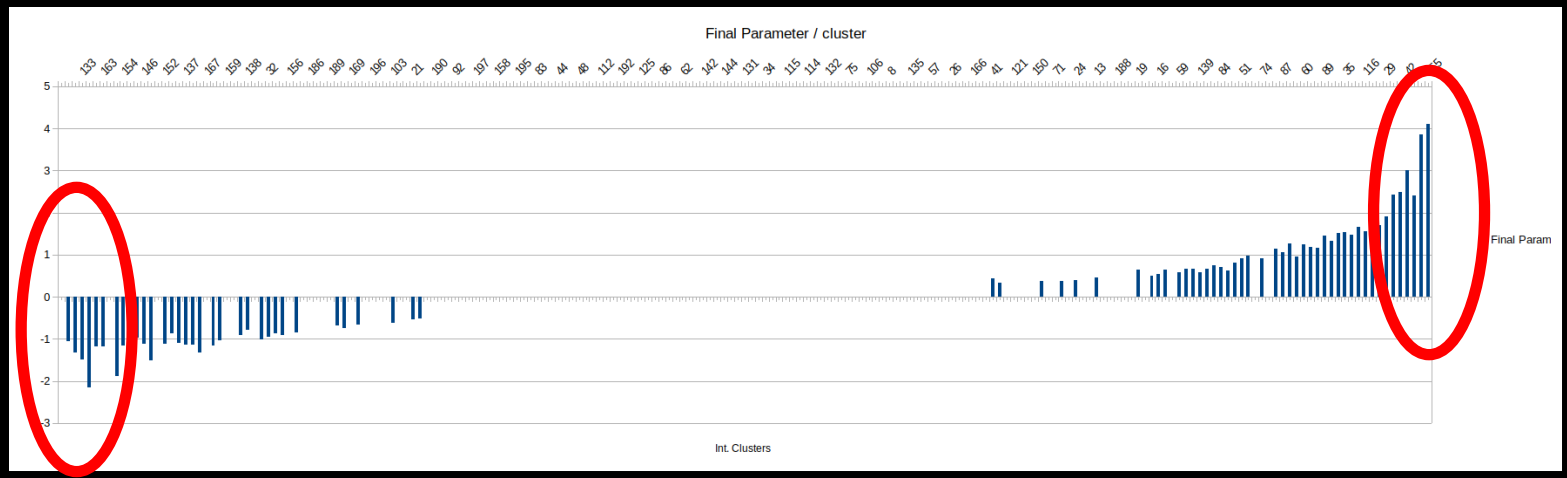

How do neurons that are tightly interconnected in circuits evolve to output new behaviours?

1. How different is the neuronal type composition of brain structures?

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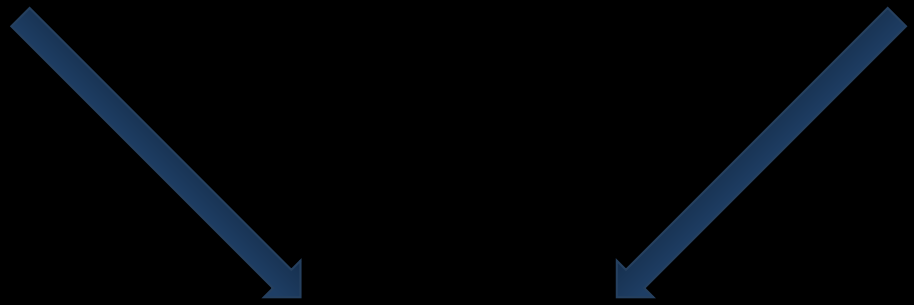

1. Evolution of a new cell type (Pop et al, 2020; Prieto-Godino et al, 2020)
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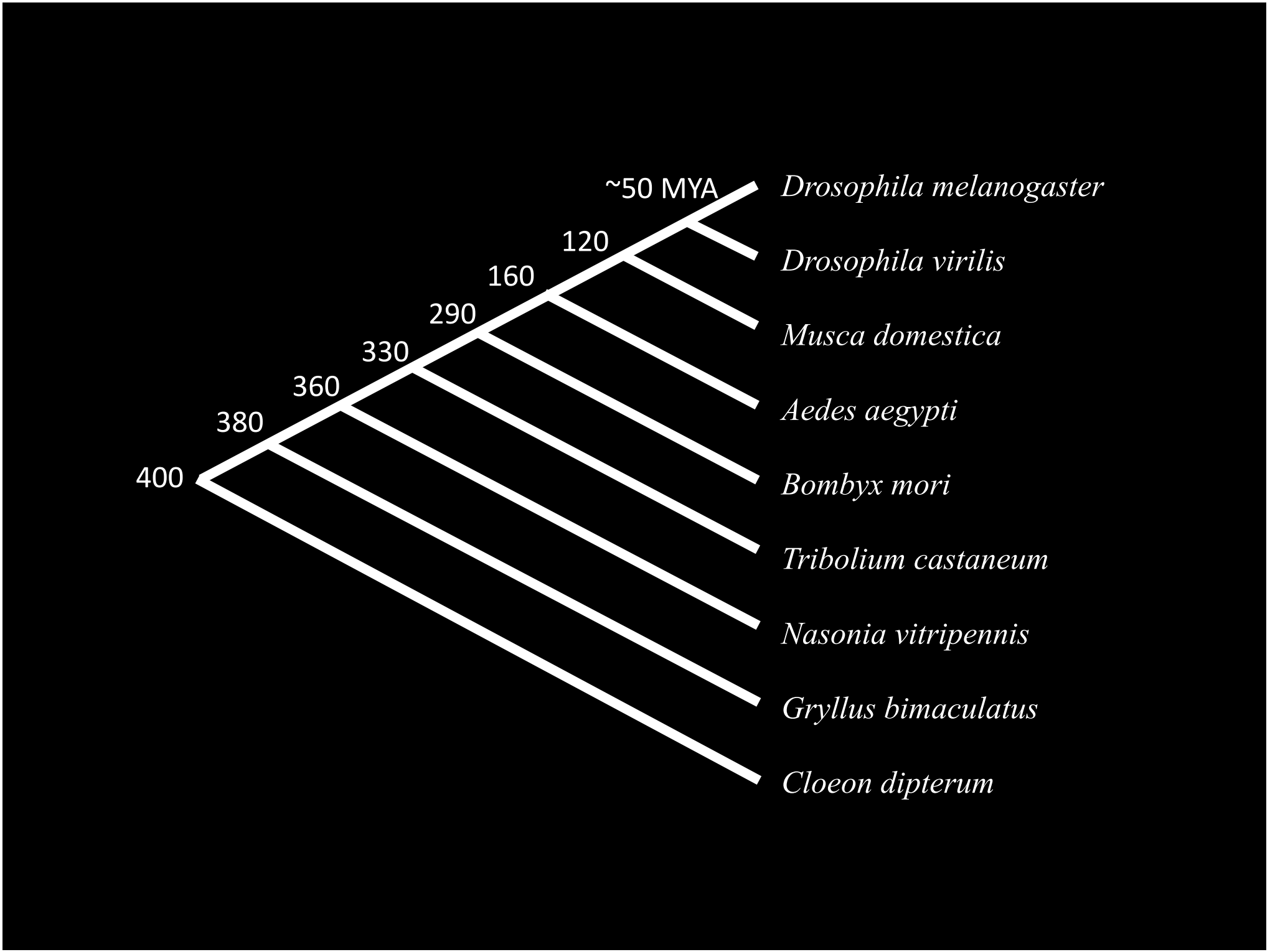
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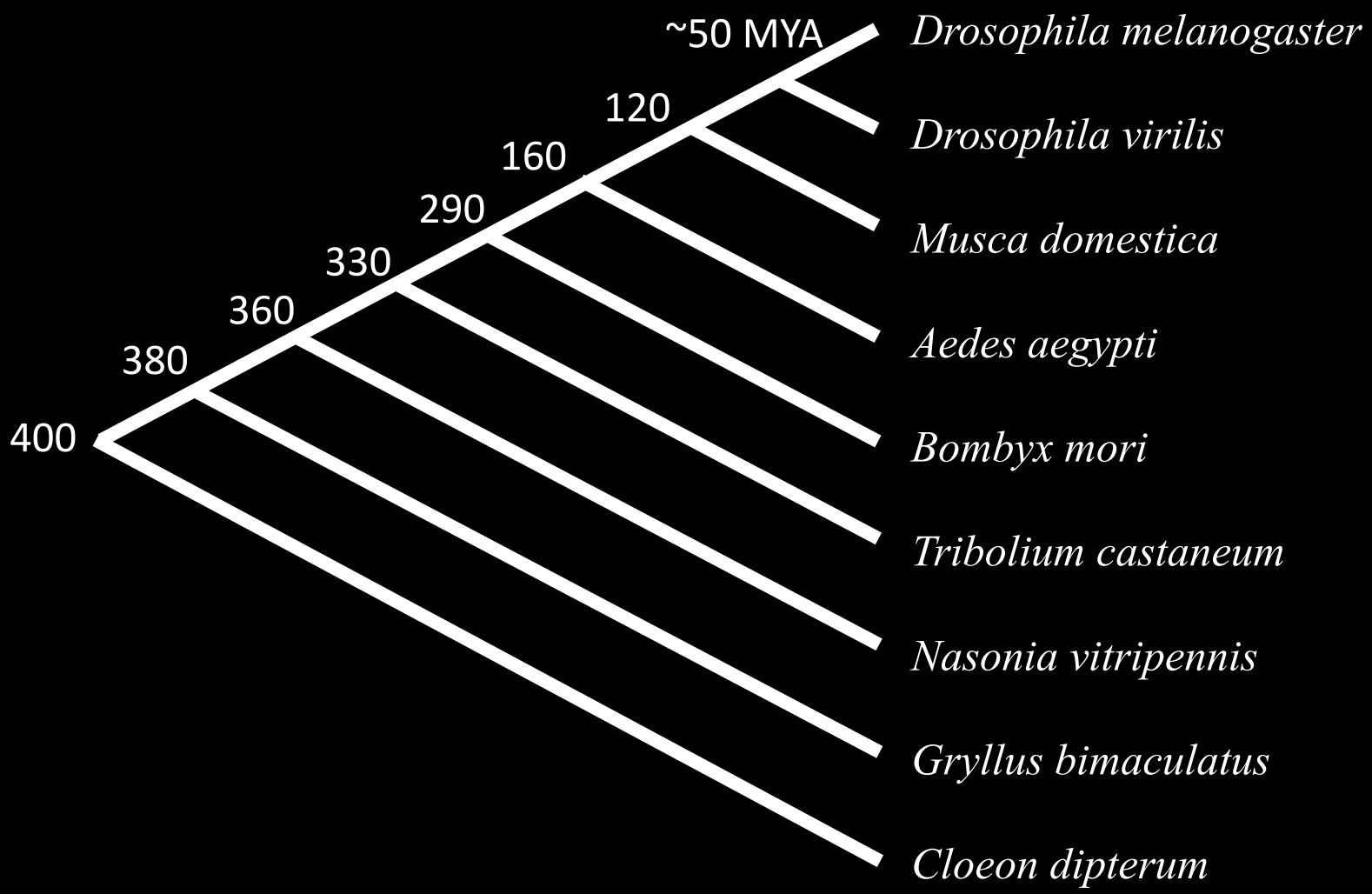
Cloeon dipterum

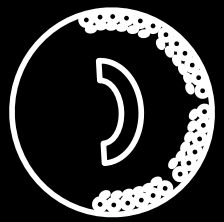


How similar are their developing visual systems and which stage is equivalent to the *Drosophila* third instar larva?

Edu staining at different stages to identify proliferating cells

D. melanogaster

3rd instar larvae



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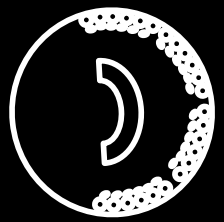
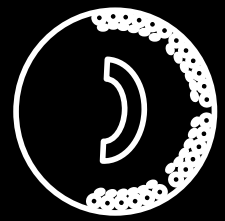
3rd instar larvae



D. virilis

3rd instar larvae



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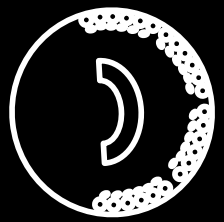

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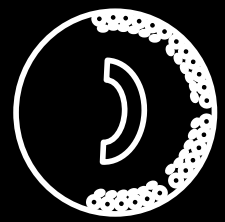
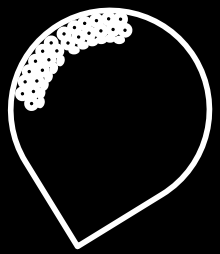


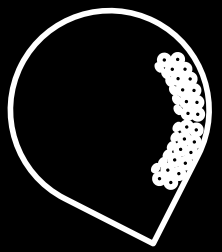
Bombyx mori

5th instar larvae



Tribolium castaneum

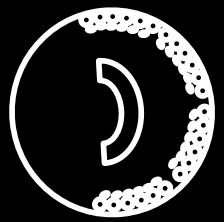
6th instar larvae



Edu staining at different stages to identify proliferating cells

D. melanogaster

3rd instar larvae



D. virilis

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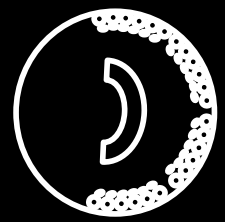

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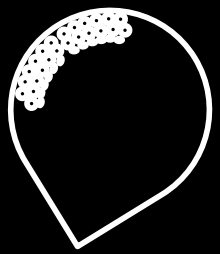

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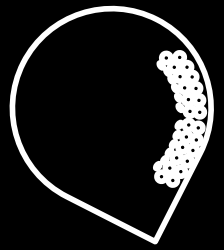
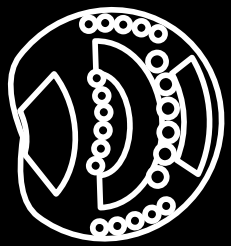


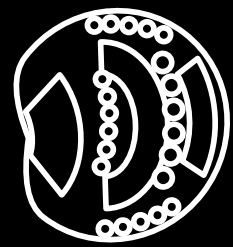
Gryllus bimaculatus

nympal stage 1,3,5



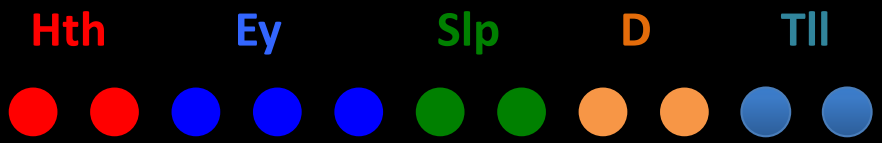
Cloeon dipterum

mid nympal stage



Evolution of temporal patterning

Drosophila melanogaster



Examples of differences

Addition or elimination of a temporal window

Duplication of part or all of the lineage

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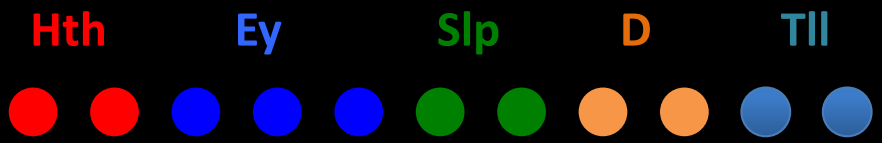


Examples of differences

Addition or elimination of a temporal window

Drosophila virilis?

Musca domestica?

Duplication of part or all of the lineage

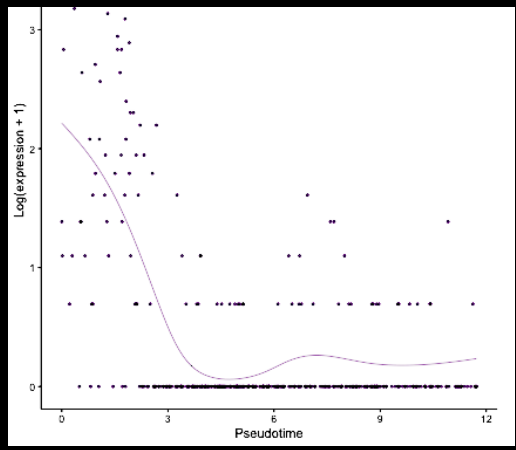
Experimental procedure

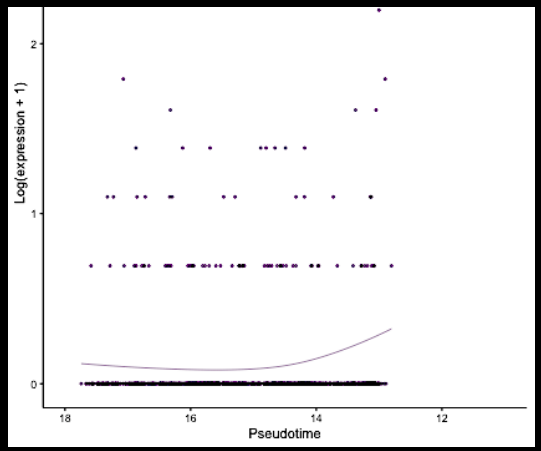
Trajectory inference: Slingshot

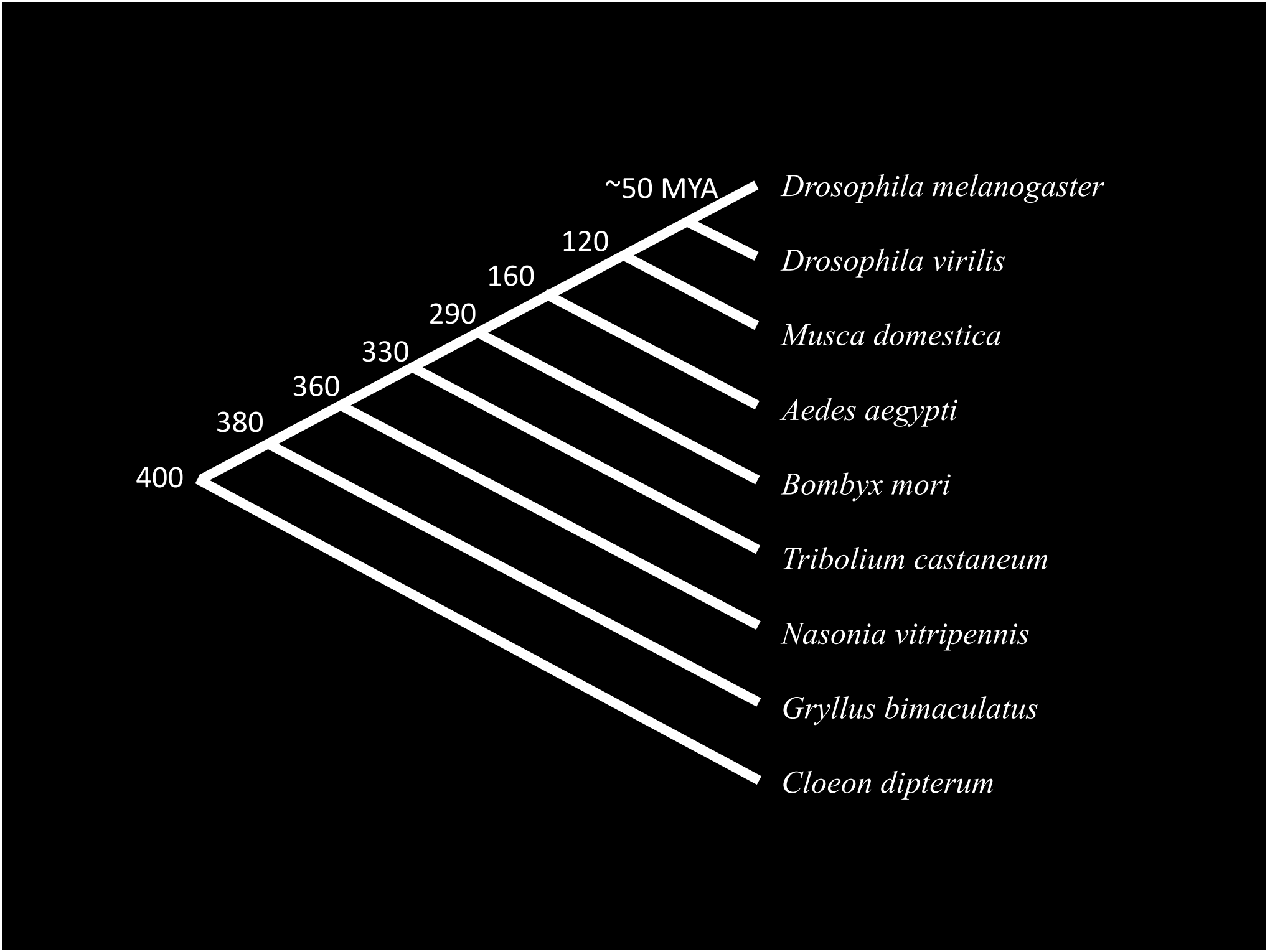
Generate transcription factor lists

Assess dynamic expression along pseudotime: Tradeseq

time



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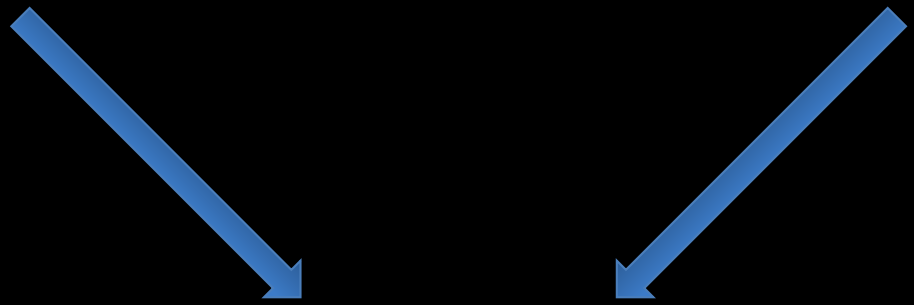

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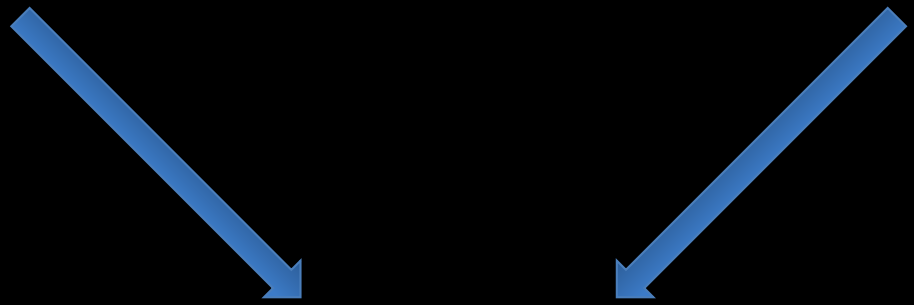

Circuitry and behavior?