Can a conserved transcriptomic axis predict state modulation of cortical interneurons?

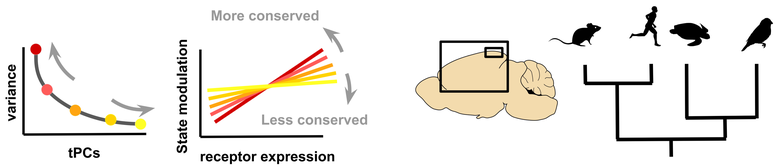
Joram Keijser, Loreen Hertaeg, Henning Sprekeler
Technical University Berlin, BCCN Berlin, ECN Berlin

Comparative scRNAseq

In mouse visual cortex, interneuron subtypes differ in their modulation with **behavioural state**. State modulation can be predicted from the first transcriptomic principal component (**tPC1**), possibly due to **cholinergic receptors** [1].

Question: How general is this link between transcriptome and state-dependent processing?

Approach: Reanalyse scRNA-seq datasets [2-6]: mouse, human, turtle, songbird



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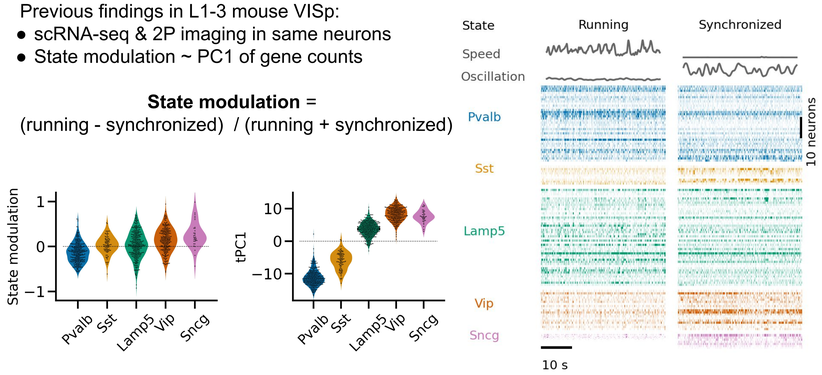

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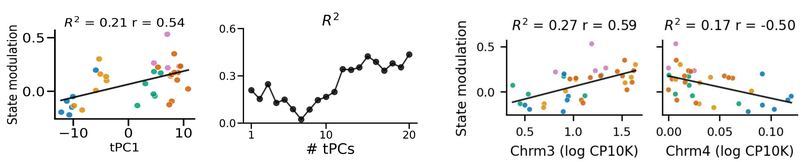

References

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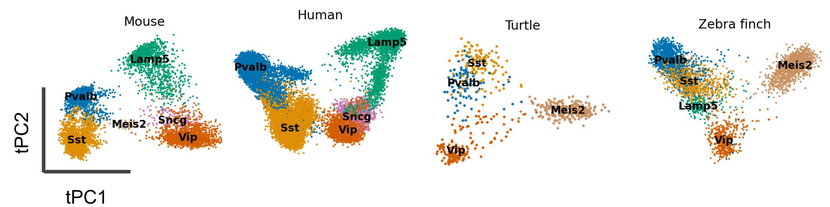
tPC similarity decreases with evolutionary distance

Apply PCA to each dataset. Quantify similarity using principal angles & variance explained

Human -but not turtle and finch - tPCs similar to mouse tPCs

Divergent gene expression between **homologous** cell types.



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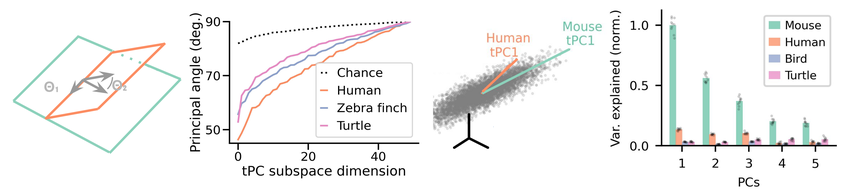

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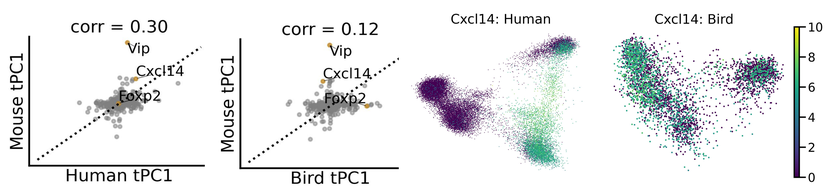

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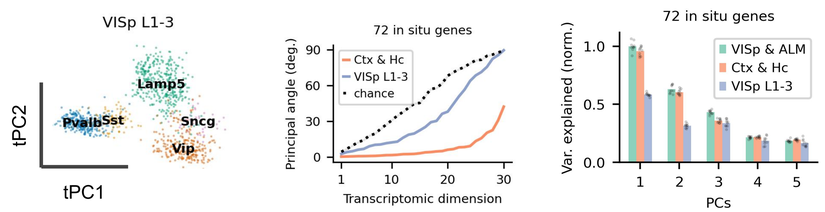
Subtle differences due to missing **subtypes** and undetected **genes**



Conclusion

Transcriptomic PCs diverge with evolutionary distance.

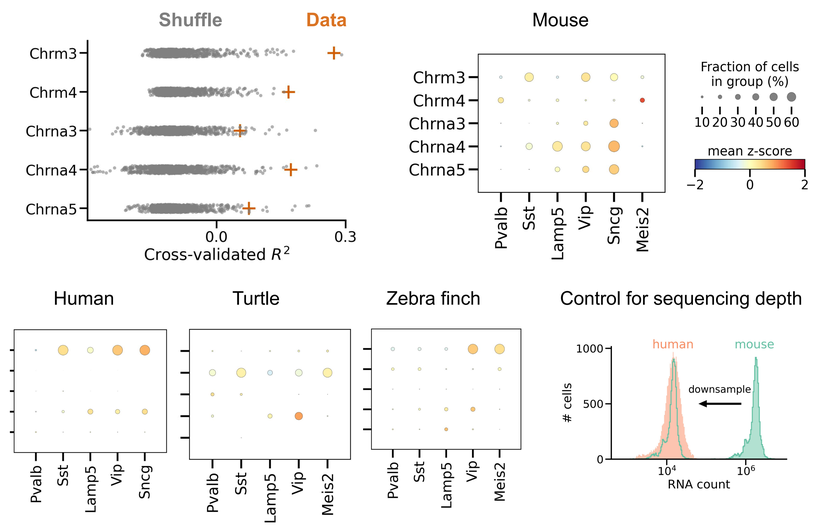
Homologous interneurons thus express different sets of genes. Homology ≠ identity.

Conserved modulation of human interneurons due to connectivity

Divergent modulation of turtle & bird interneurons consistent with conserved function: acetylcholine emphasizes sensory inputs

Divergent cholinergic receptor expression

5 cholinergic receptors predict state modulation in mice. Their expression is **not conserved**



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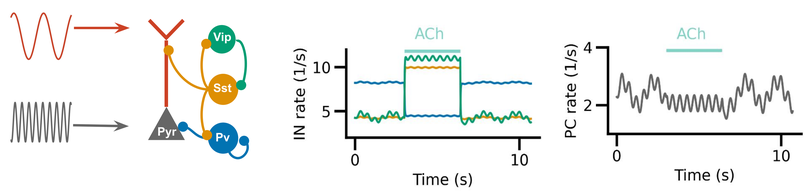

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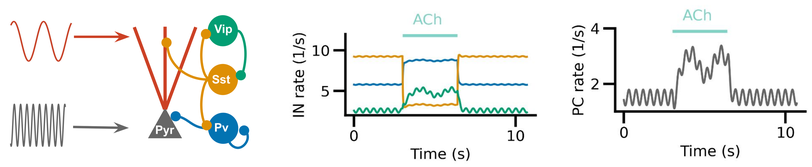

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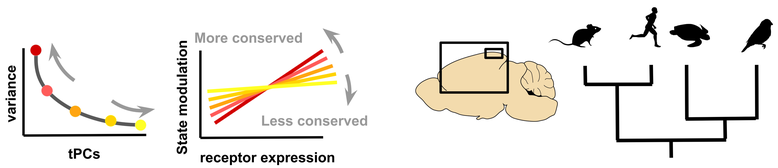

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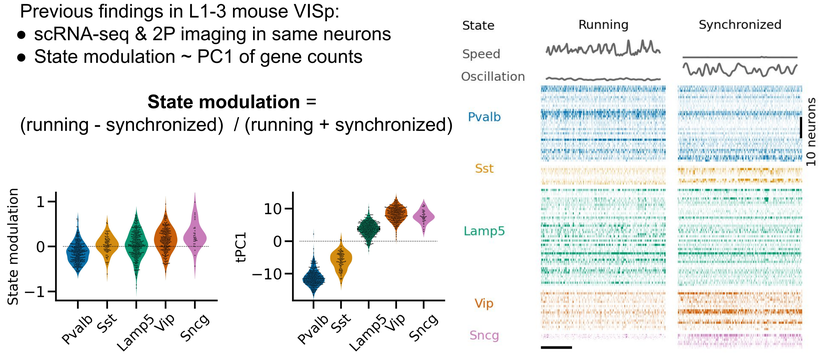

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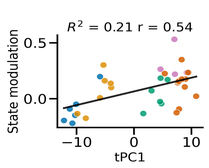

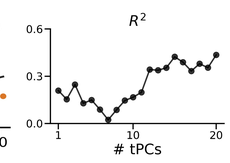

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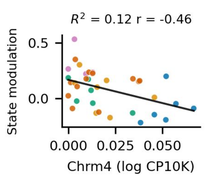

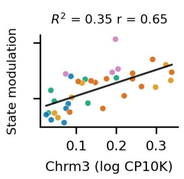

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State modulation of mammalian interneurons could be conserved due to connectivity

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Need more data from non-model organisms

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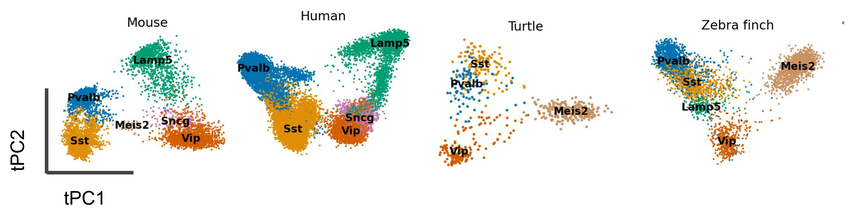

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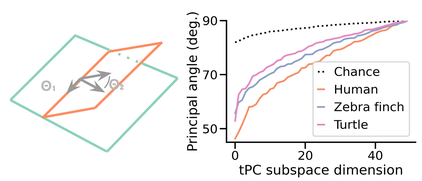

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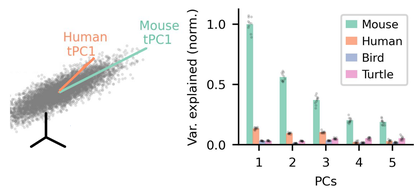

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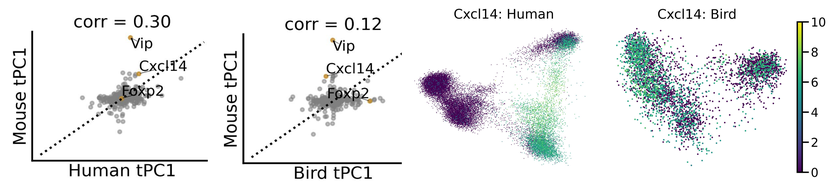

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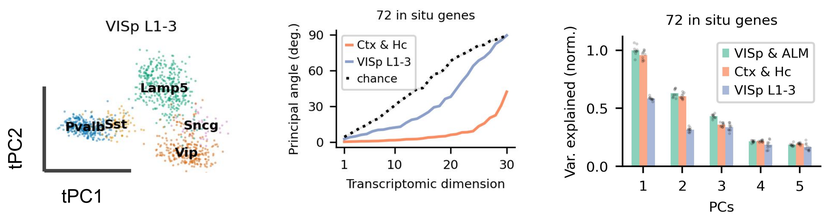

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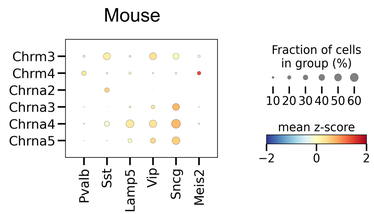

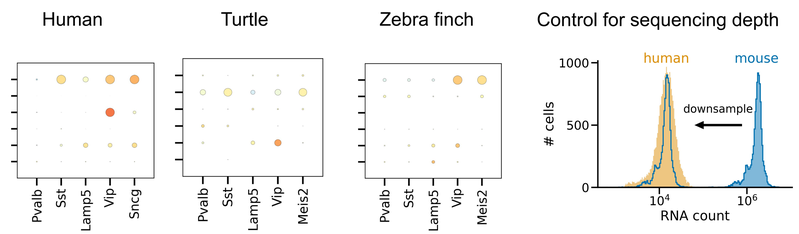

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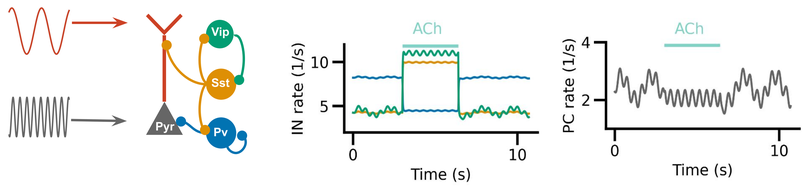

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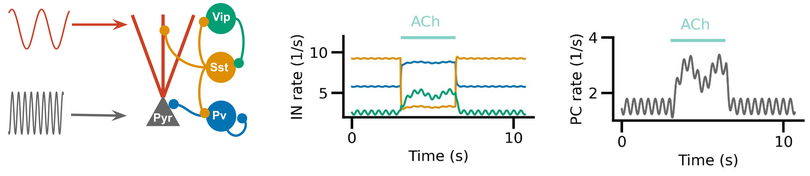

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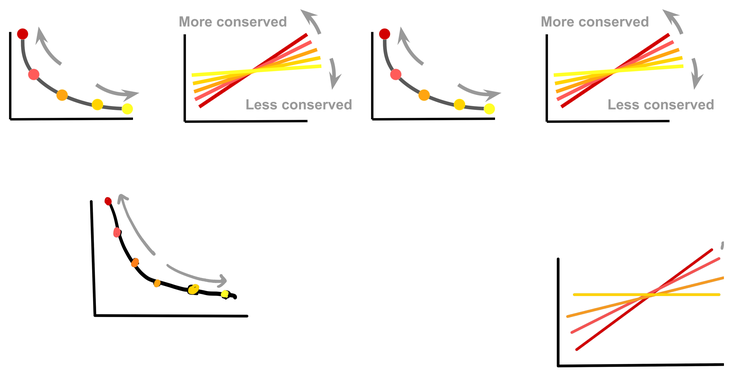
More conserved
Less conserved
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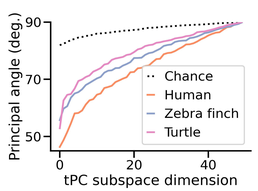
Principal angle (deg.)
90
70
50
0
20
40
tPC subspace dimension
Chance
Human
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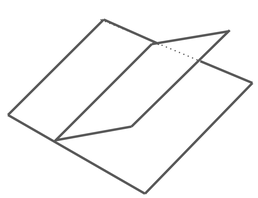
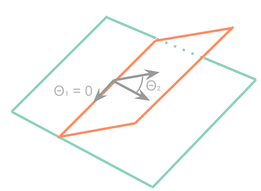
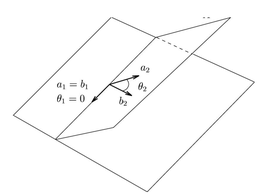
Turtle




$\Theta_1 = 0$
Θ_2


$a_1 = b_1$
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a_2
θ_2
b_2