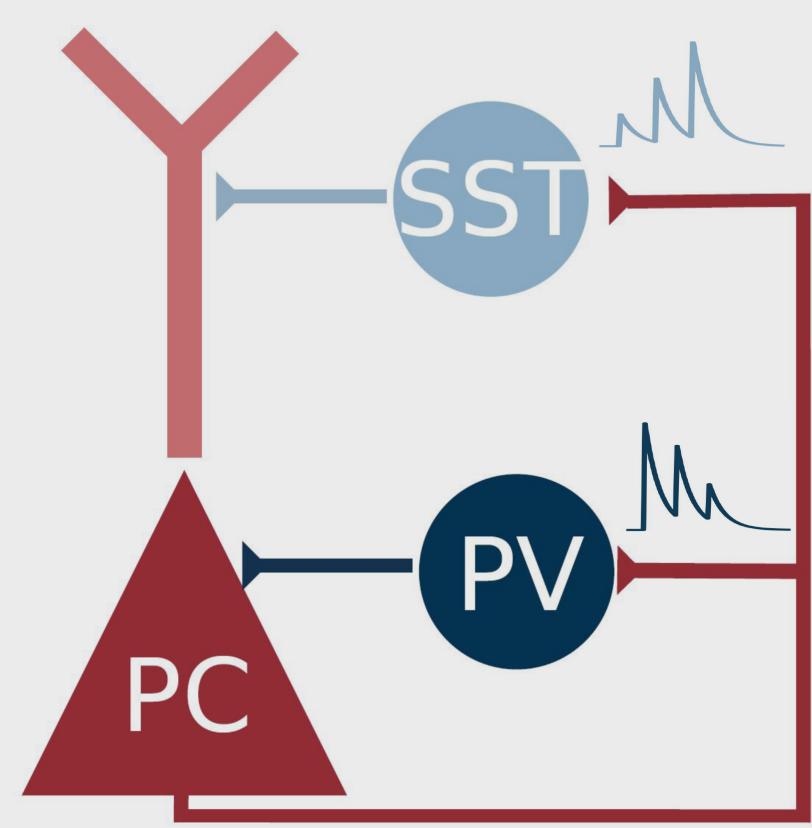




Interneuron diversity: optimization vs evolution

What is the function of different interneuron types?

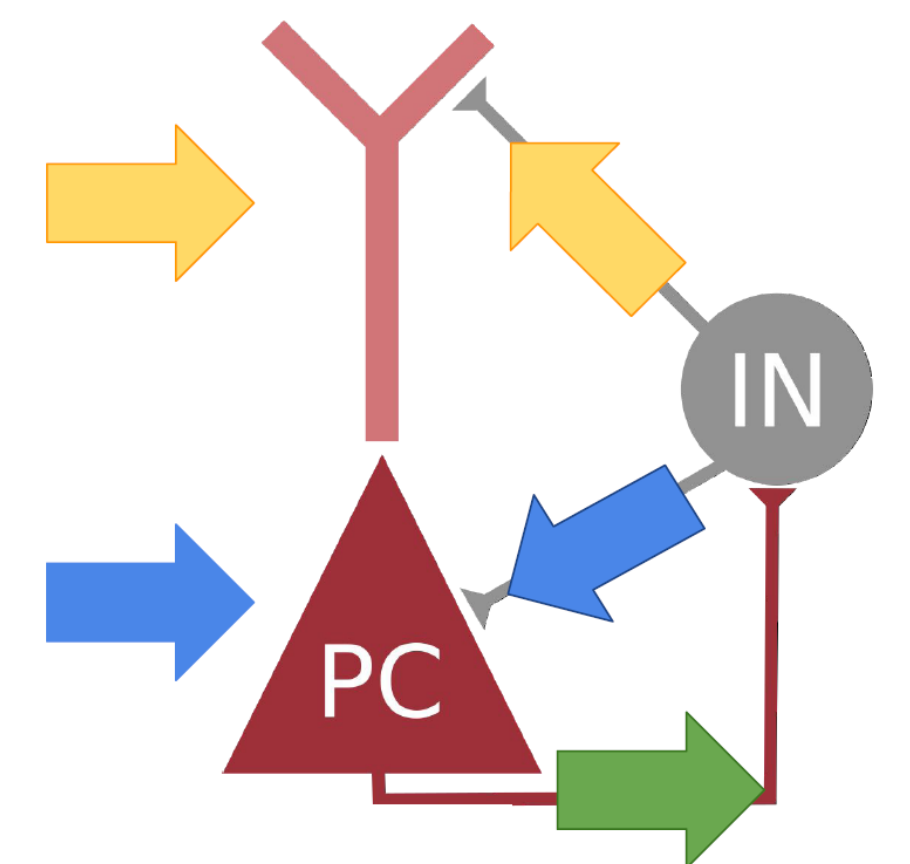
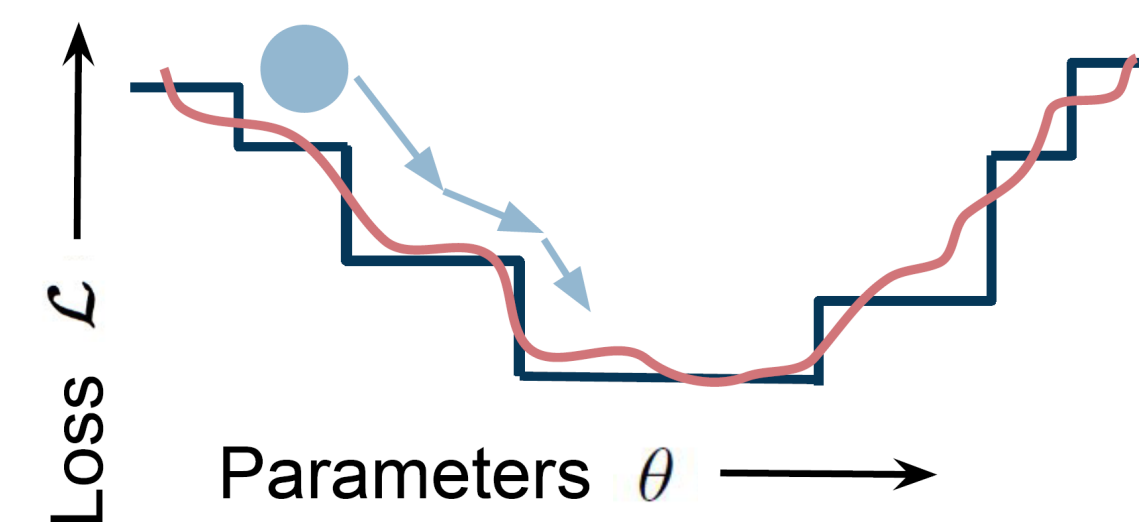


- PV & SST interneurons differ in:
 - Input: depressing vs facilitating
 - Output: cell body vs dendrites
- For what function?
- Hypothesis:** Specialized control of pyramidal cell (PC) compartments
- Test: Optimize cell types for function
- Prediction:** Optimization generates PV & SST cells

Optimize interneurons for compartment-specific E/I balance

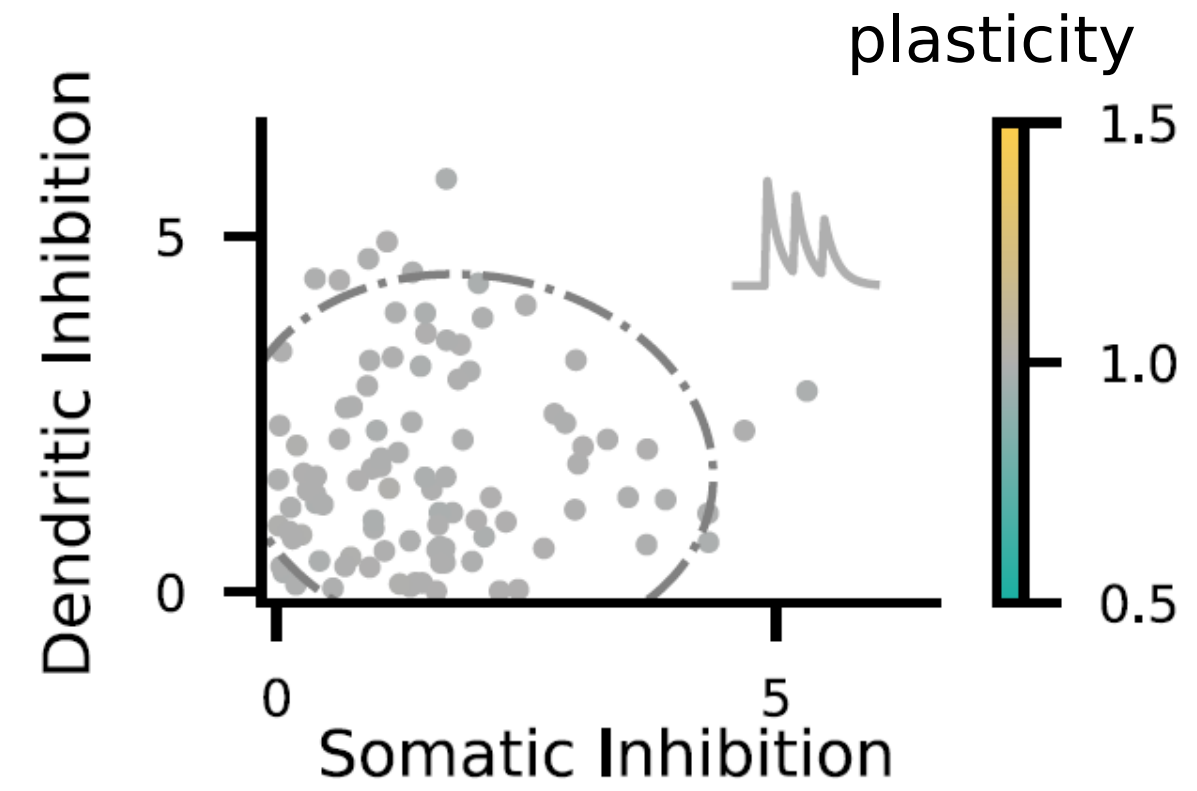
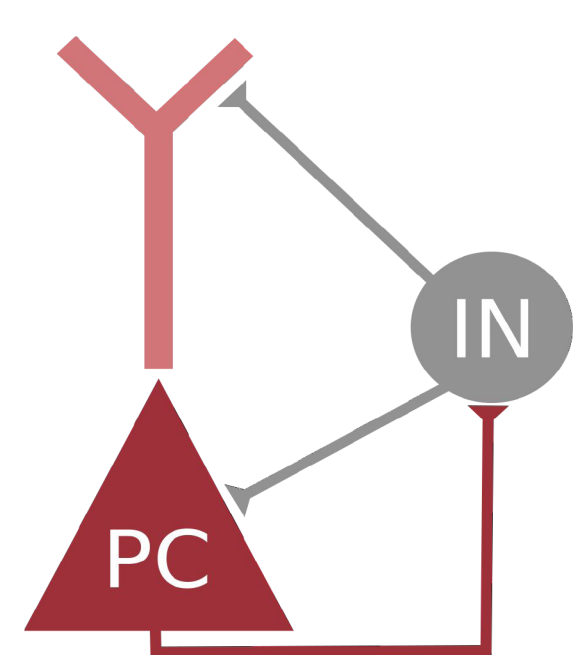
$$\mathcal{L} = \sum_t (W^{\text{soma}} r_{IN}(t) - I_{\text{soma}}(t))^2 + (W^{\text{dend}} r_{IN}(t) - I_{\text{dend}}(t))^2$$

Optimize connectivity & short-term plasticity
- surrogate gradient descent [1]



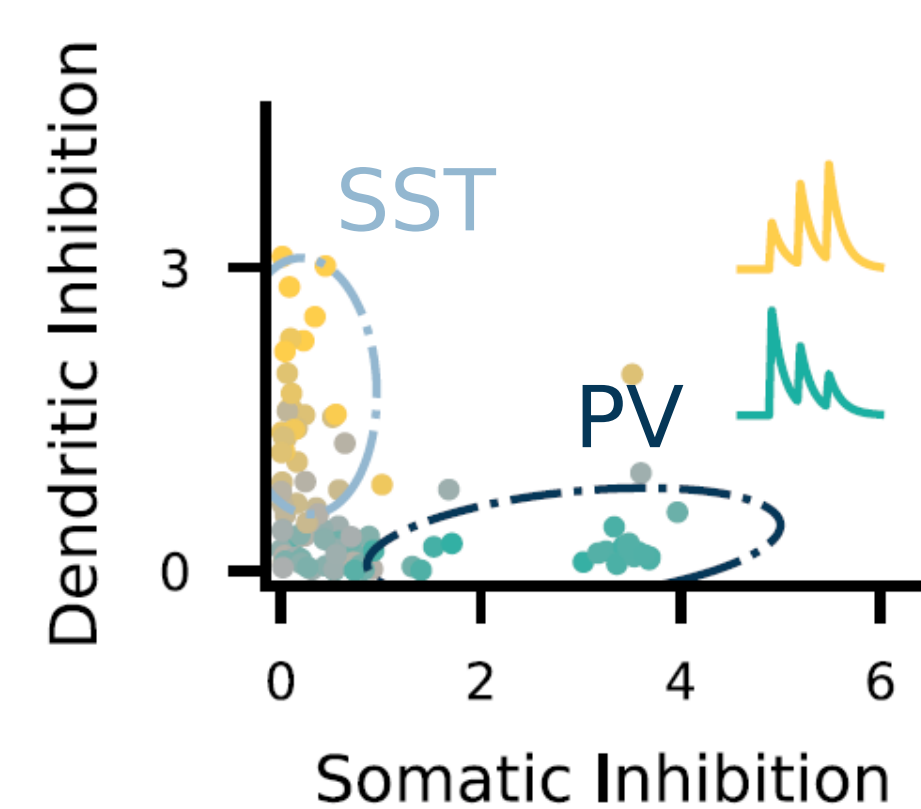
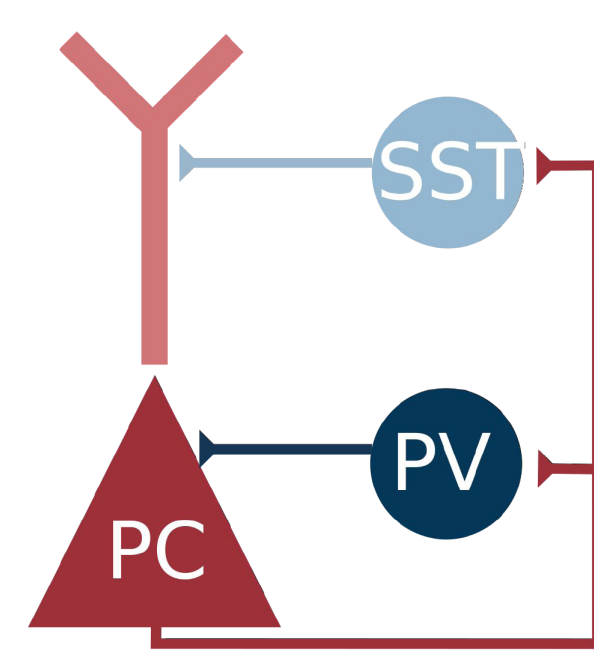
Interneuron types emerge from optimization

Before



Optimize

After

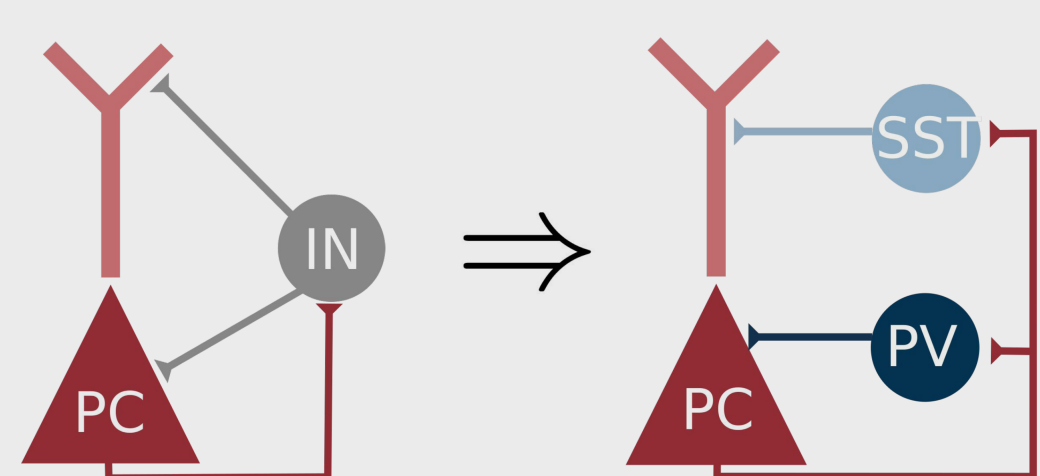


- Optimization splits INs into 2 groups, corresponding to SST & PV types
- Types specialize for different PC compartments
- SSTs select dendritic bursts via short-term facilitation [2]

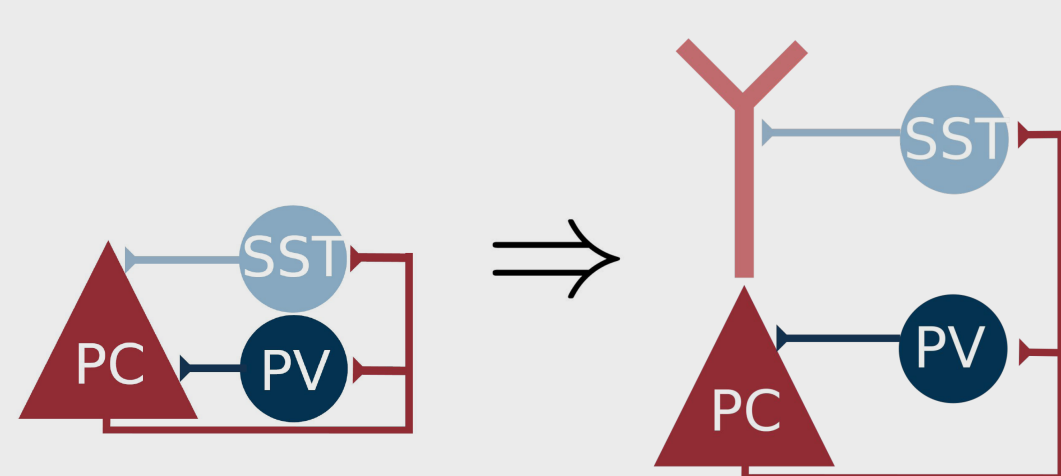
evolution = optimization ?

How did interneuron types evolve?

Hypothesis 1: Optimization

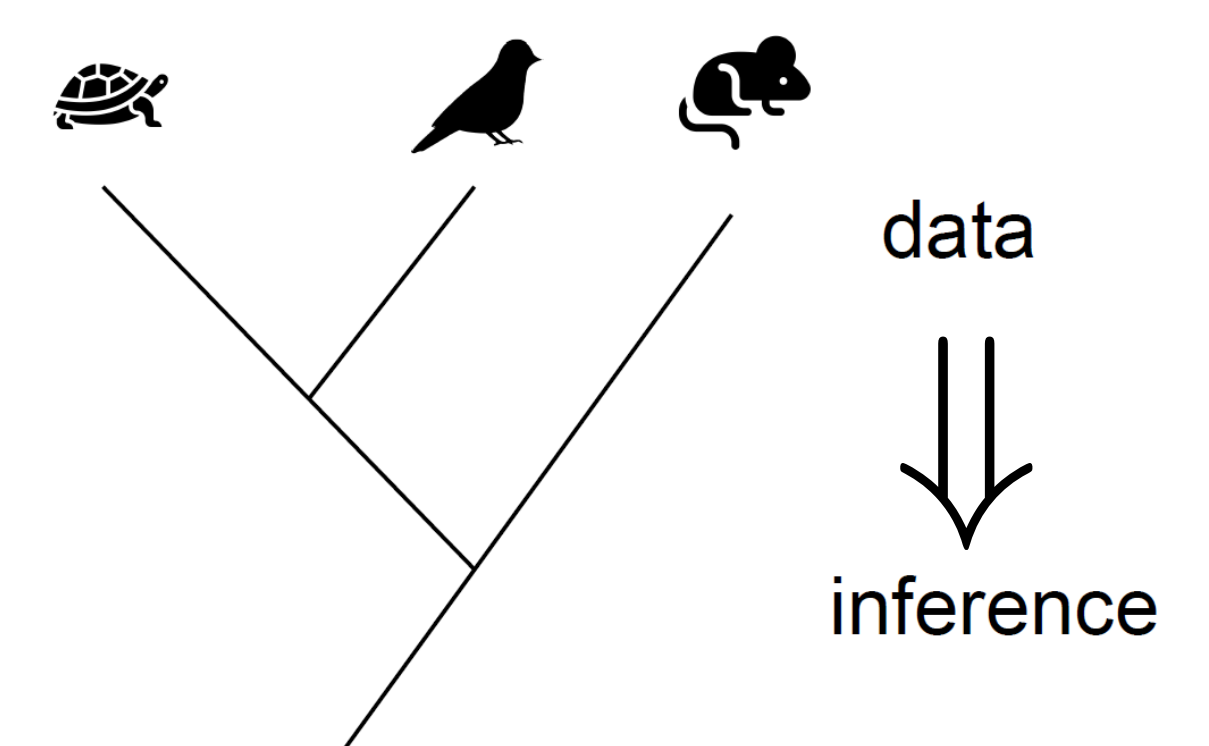


Hypothesis 2: Reuse

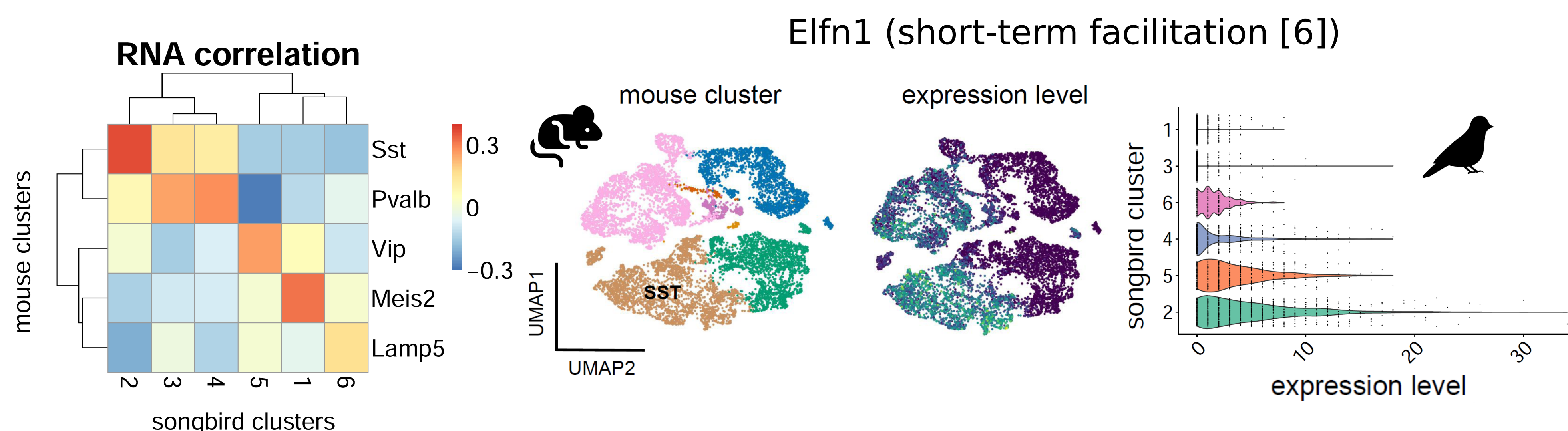


Reconstruct evolutionary history

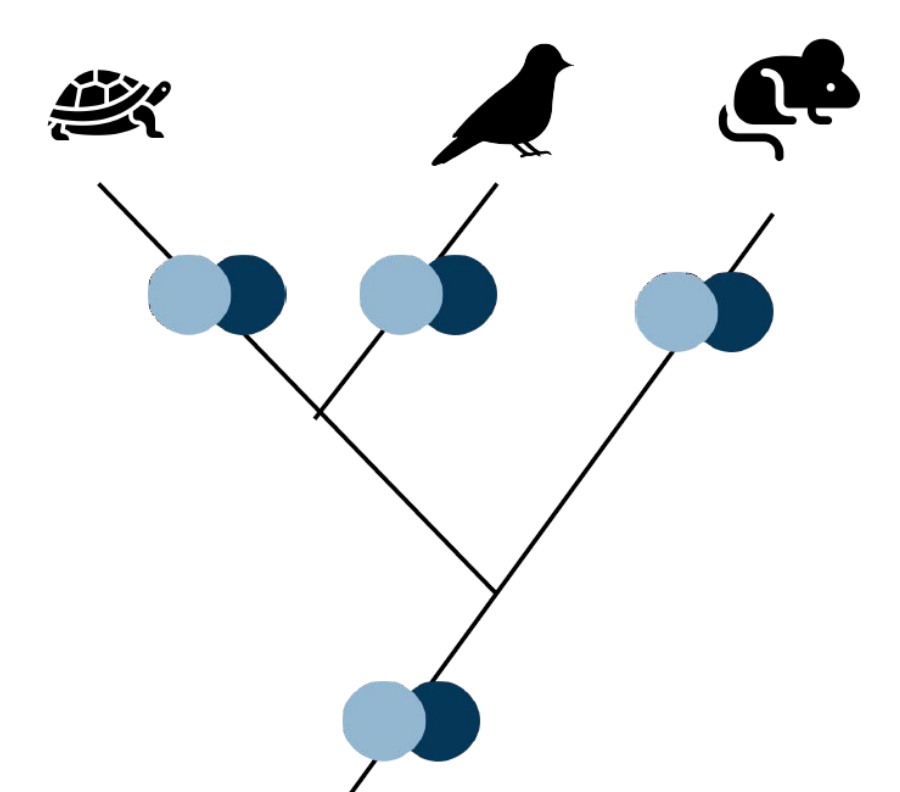
- Compare cell types across species
- Shared properties likely old
- Unique properties likely new
- Use scRNA-seq data [3,4,5]



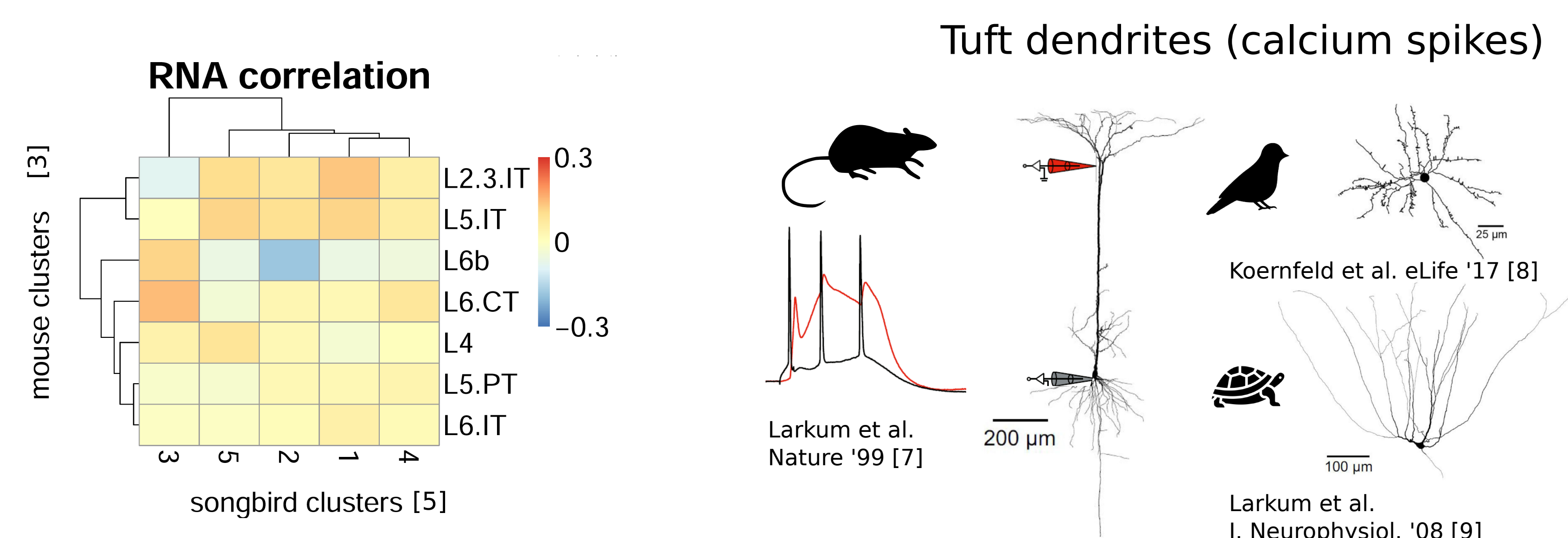
Interneurons conserved across species



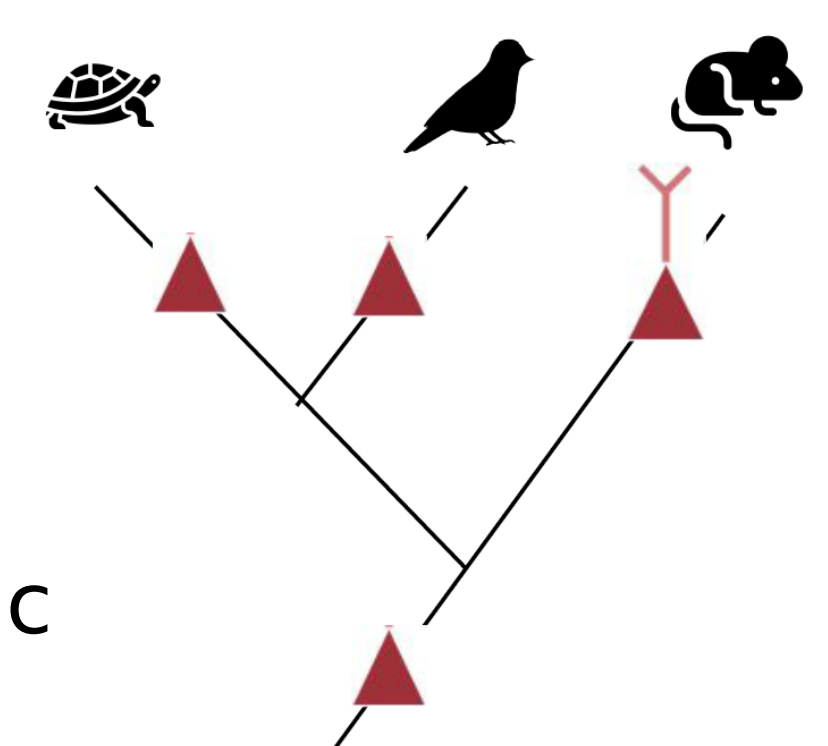
- Interneuron classes shared [3,4]
- Elfn1 gene shared
- PV & SST-like neurons likely ancestral



Pyramidal neurons not conserved



- Pyramidal classes not shared [3,4]
- Lack dendritic bursting (e.g. [9])
- Calcium spikes & dendritic bursting likely novel



- Interneurons provide specialized inhibition - but did not evolve for this function
- Instead: new function for existing interneurons
- What was (is) their original function ?