

# Inhibition of inhibition in visual cortex: the logic of connections between molecularly distinct interneurons

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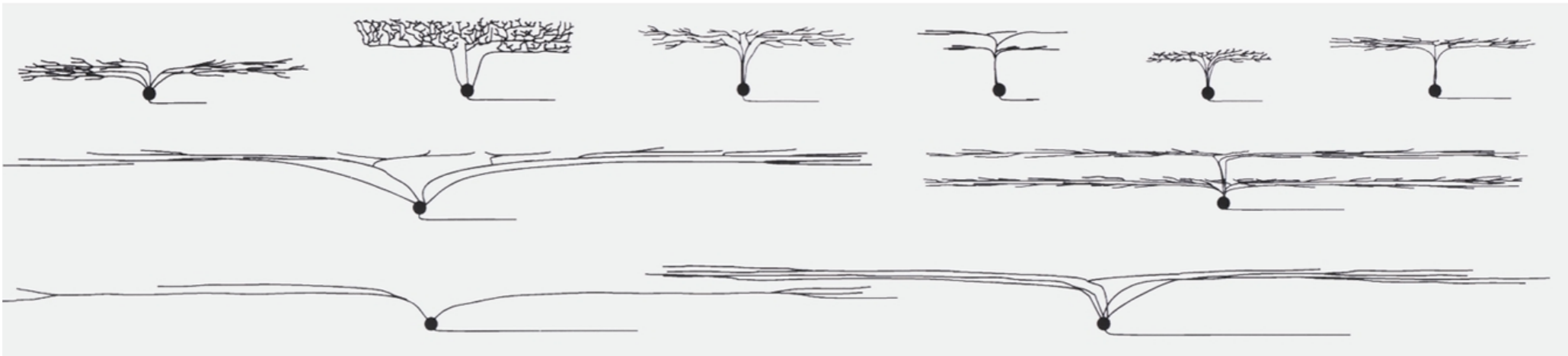
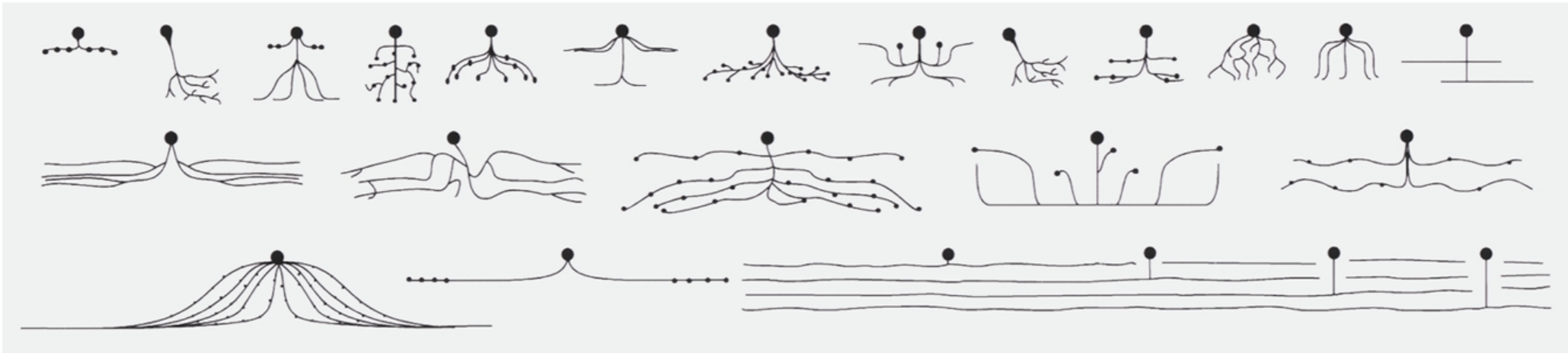
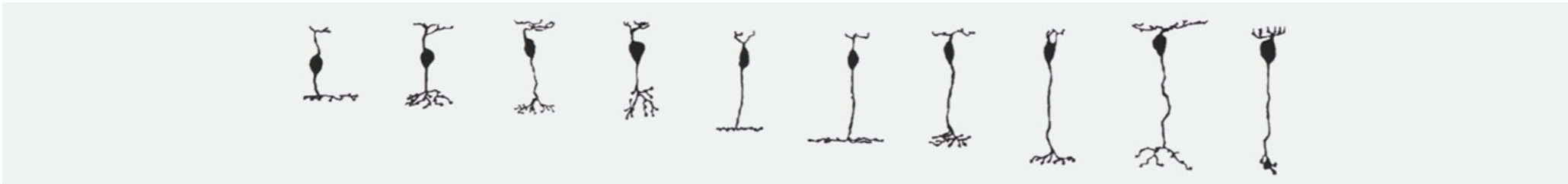
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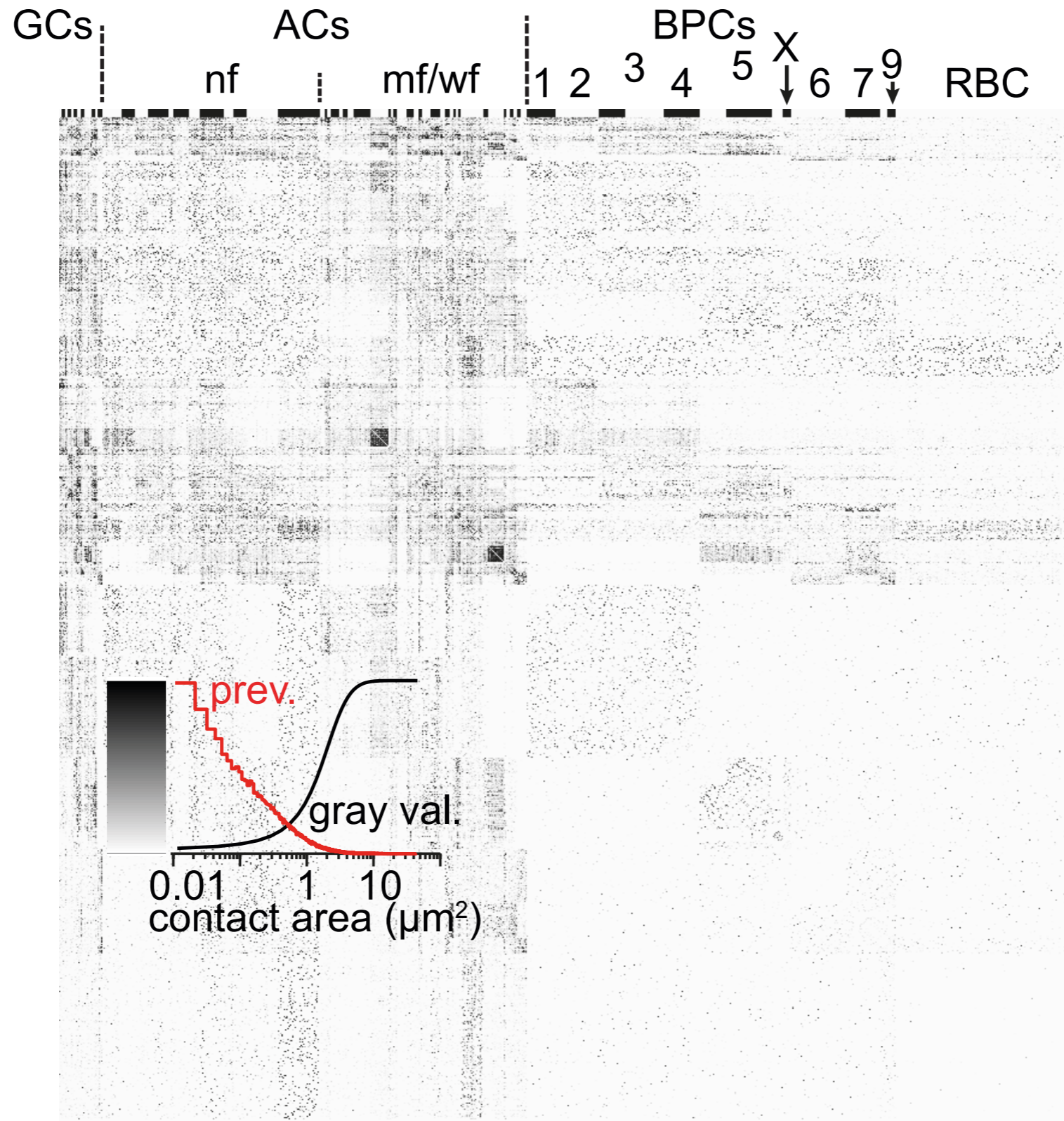
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# there are lots of different cell types



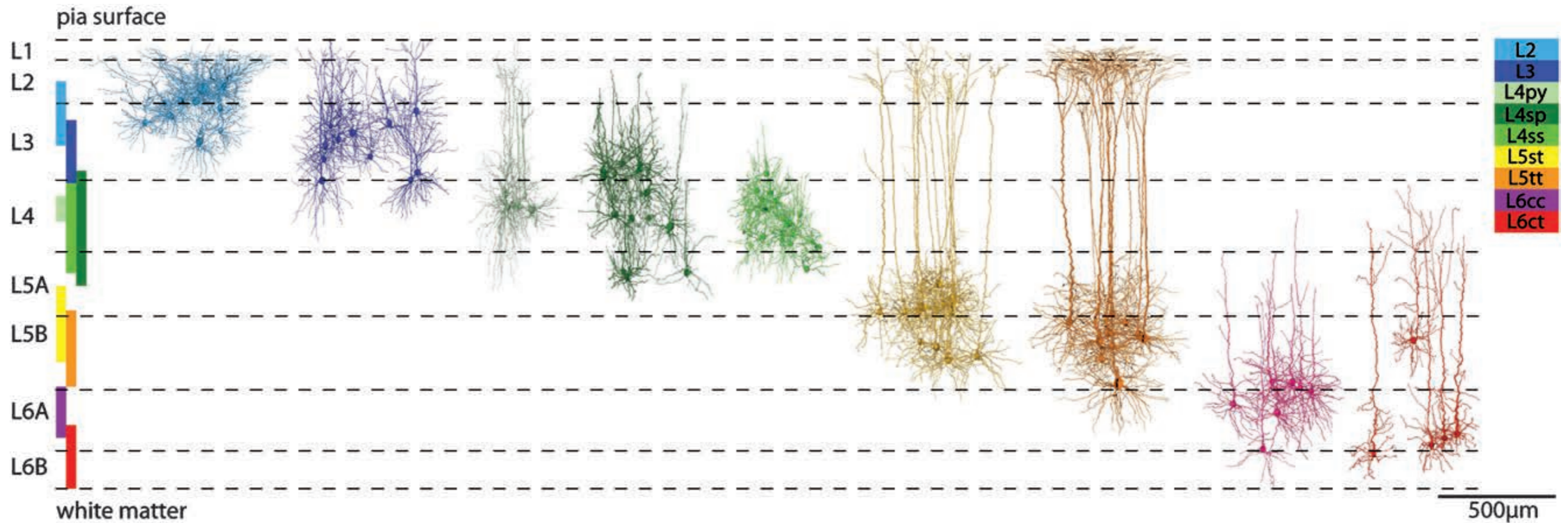
# we know that cell type patterns neural connectivity



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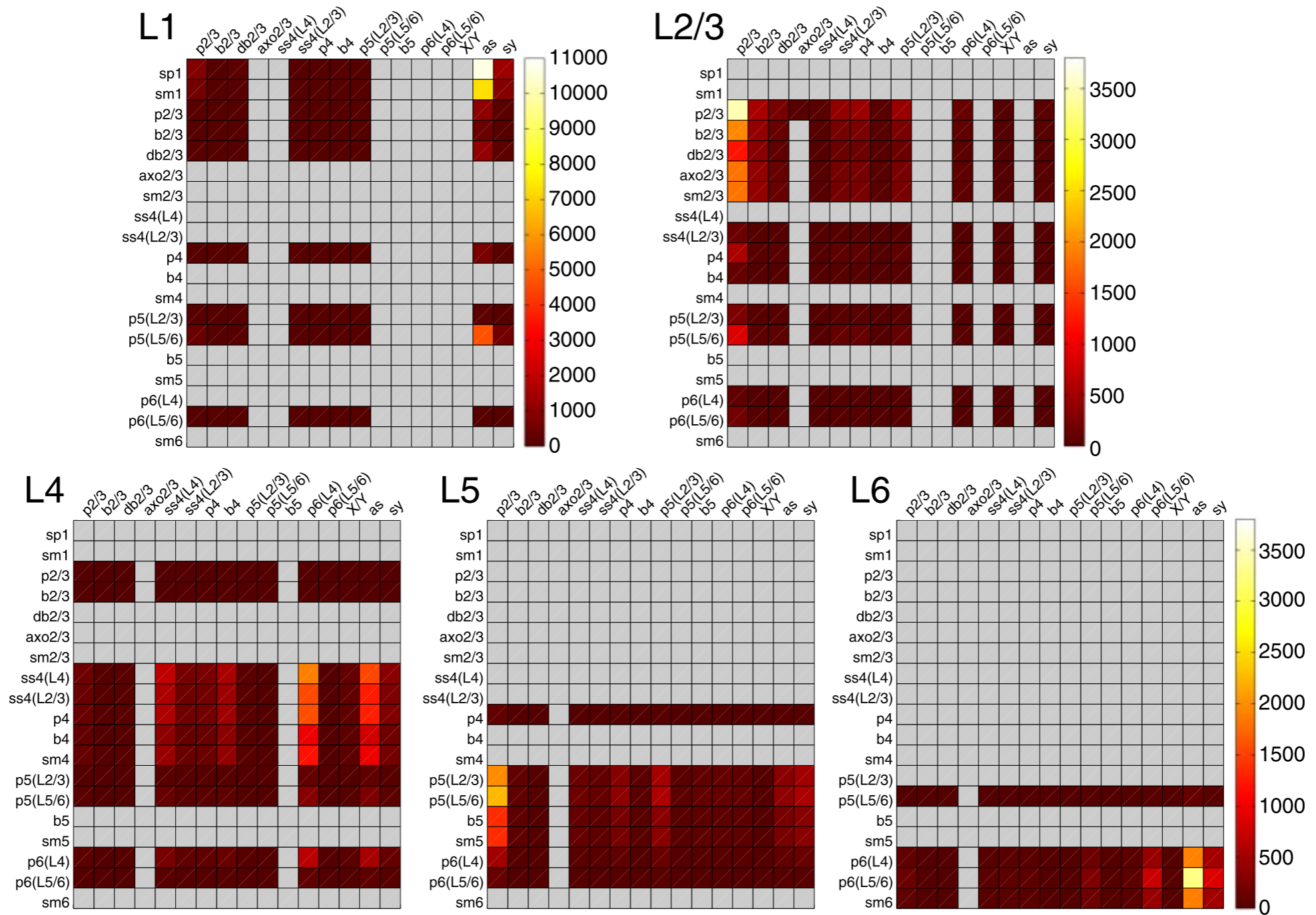
- what are the rules of neural connectivity in cortex?

# the excitatory cell types in barrel cortex



**Figure 2.** Definition of excitatory cell types in a barrel column. Cluster analysis of morphological features identified 9 excitatory cell types. Registration allowed determining the vertical extent of the cell type-specific soma locations (colored vertical bars). These cell-type borders were not sharp and complement cytoarchitectonic definitions of cortical layers (e.g., using soma density as indicated by the horizontal dashed lines; adopted from Meyer, Wimmer, Oberlaender, et al. (2010)). Some of the cell-type borders determined here did not match cytoarchitectonic layer borders (e.g., L4 neurons may be located in cytoarchitectonic layers 3 and 5) and some cell types intermingled within layers (e.g., thick-tufted and slender-tufted neurons in L5).

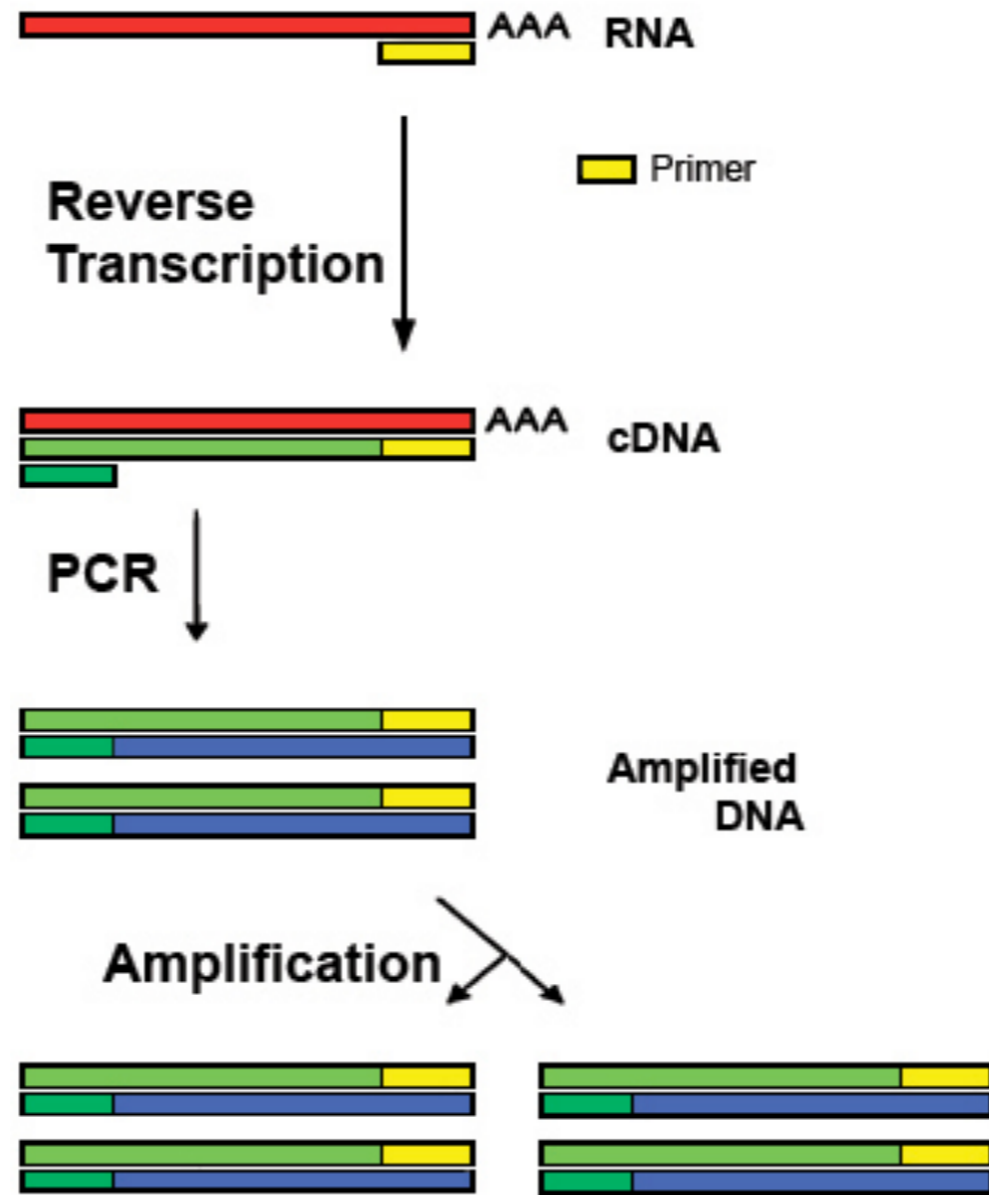
# “potential” connectivity based on Peters’ rule



**Figure 7.** Estimated number of synapses formed by one type of neuron with another type in the cortical layer indicated based on Peters’s rule (Eqs. 2, 3). L1–L6, Presynaptic cell types are indicated on the top, postsynaptic cell types are indicated along the y-axis. For a presynaptic cell type  $j$  and a postsynaptic cell type  $i$ , the color of the corresponding square indicates the number of synapses that all neurons of type  $j$  form in layer  $u$  (indicated on the top left corner) with an individual neuron of type  $i$ . This number is denoted by  $\bar{s}_{ij}^u$  in Figure 1. Light gray squares indicate zero values. sy and as indicate the number of unassigned asymmetric and symmetric synapses on the dendritic trees of each cell type. Color bars are shown.

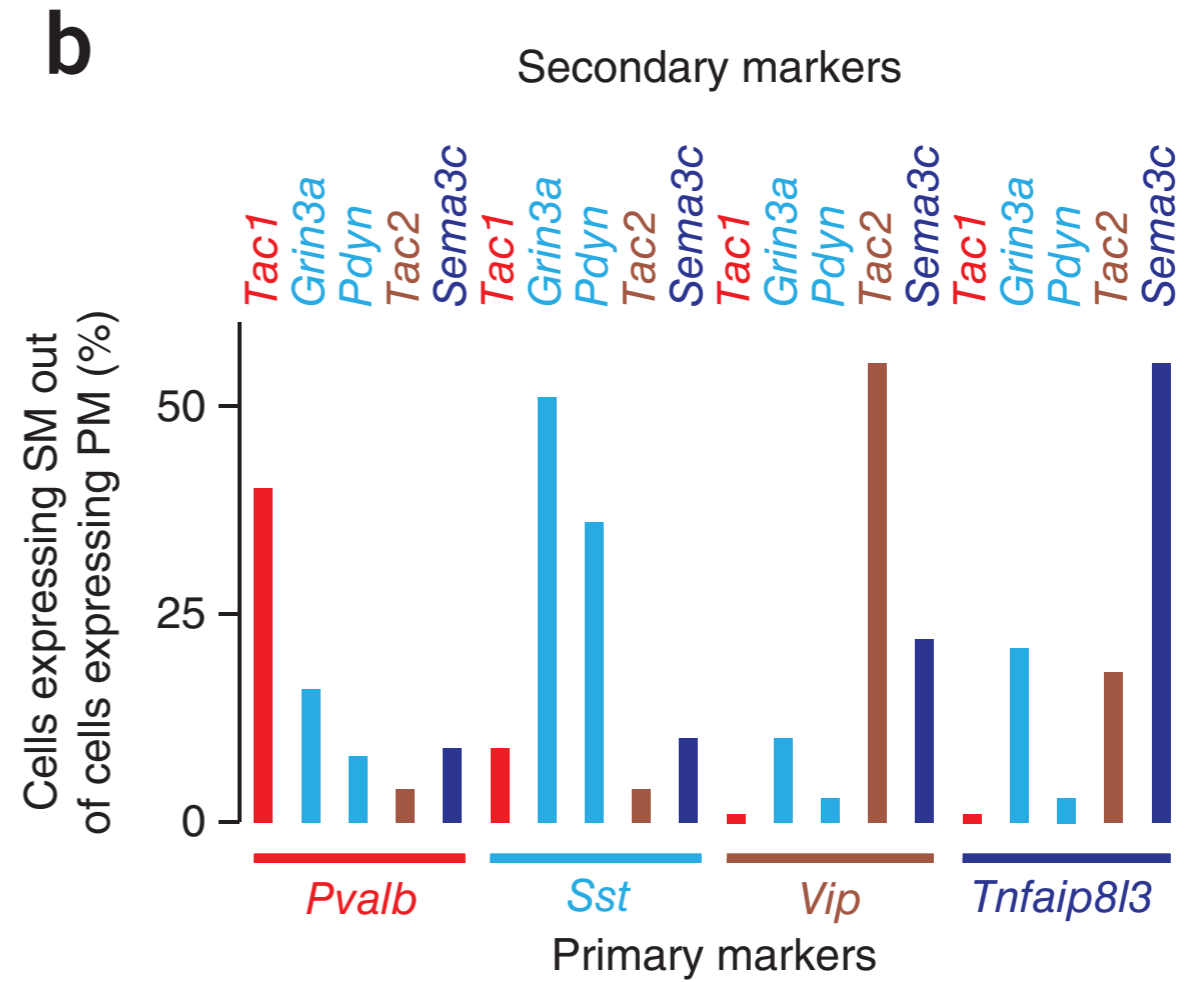
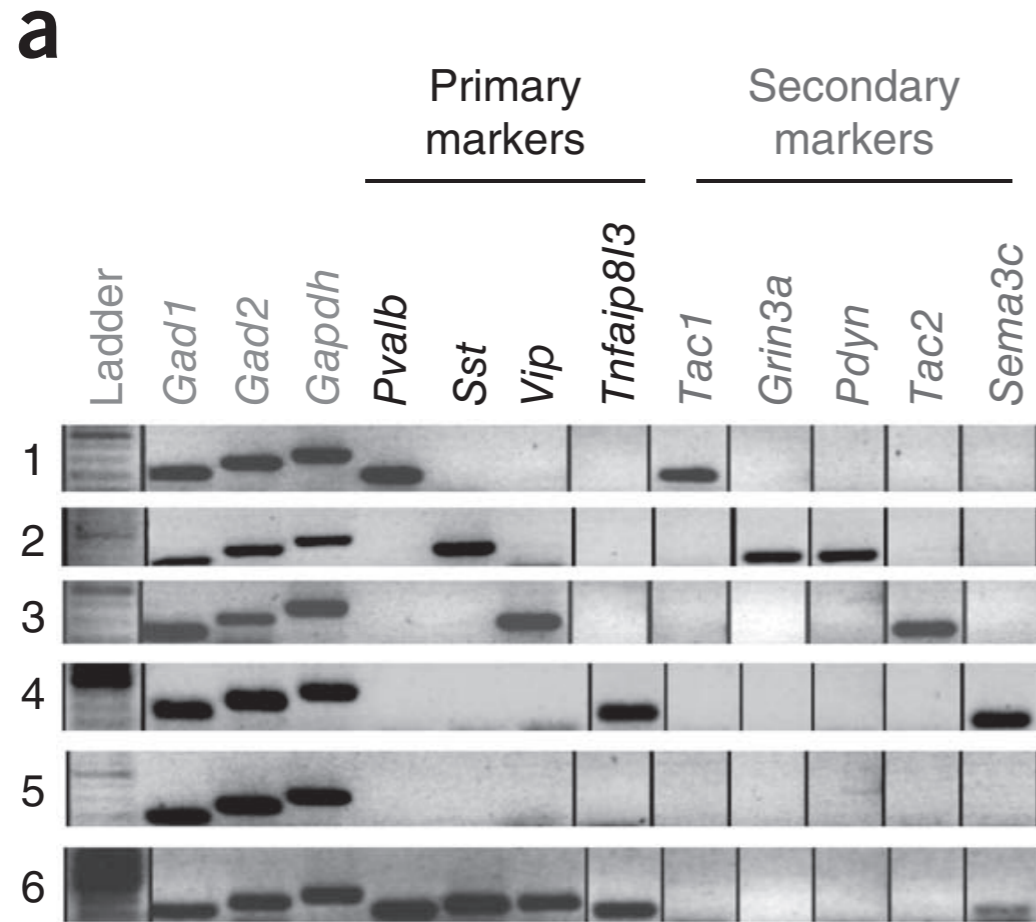
- what is the actual connectivity of inhibitory cell types in visual cortex?
- what are the inhibitory cell types?
  - let's use molecular markers

# reverse transcriptase - polymerase chain reaction (RT-PCR)

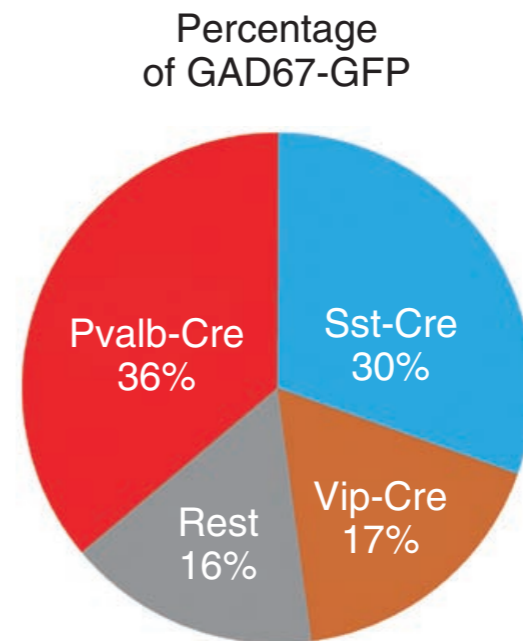
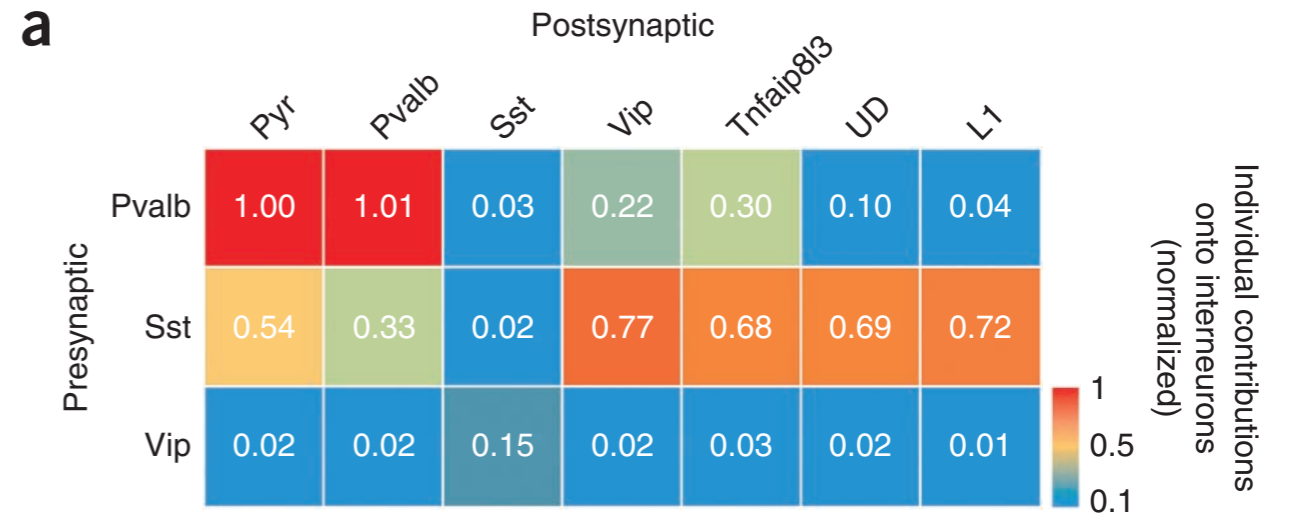
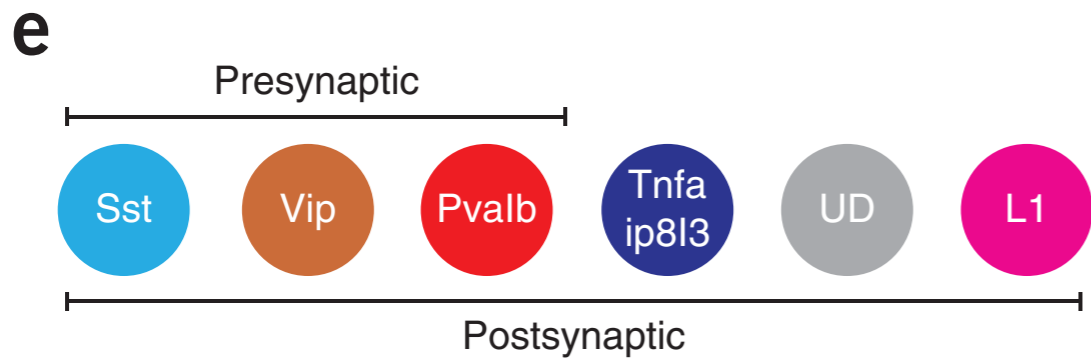
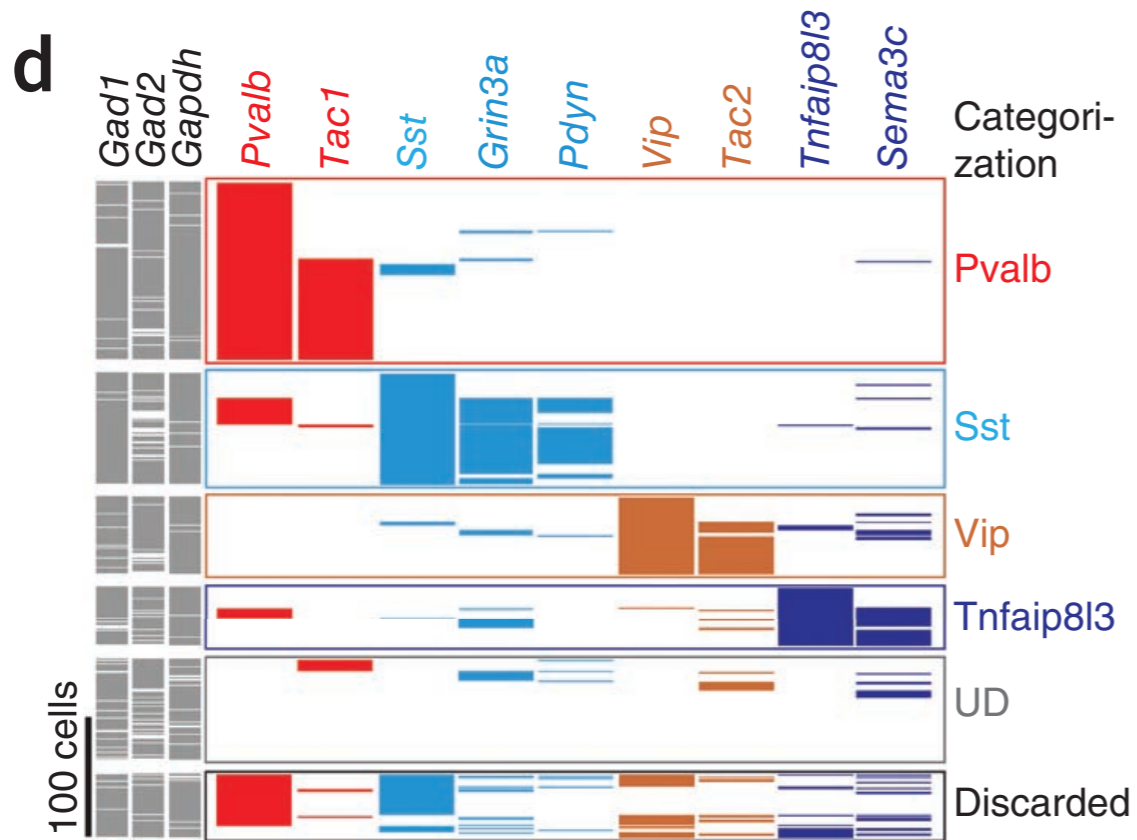




# molecular markers and single cell RT-PCR

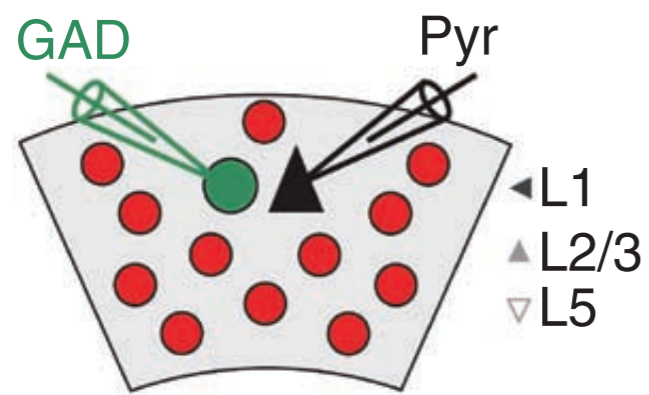


# 4 “defined” types + 2 “undefined” types

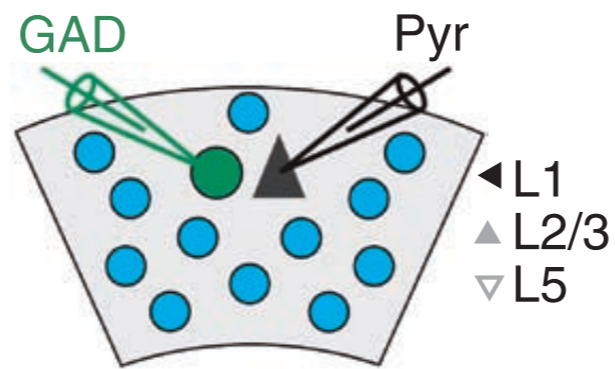


# 3 mice

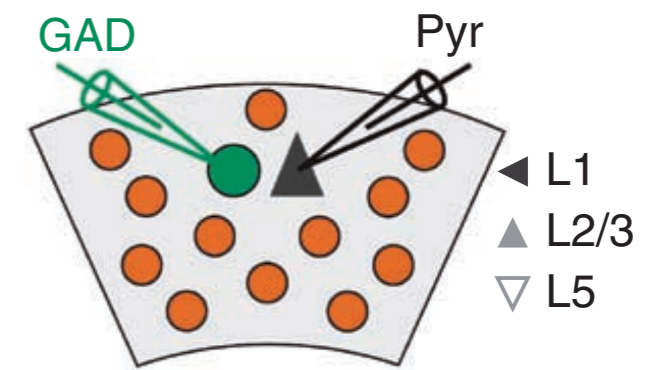
ChR2 in Pvalb

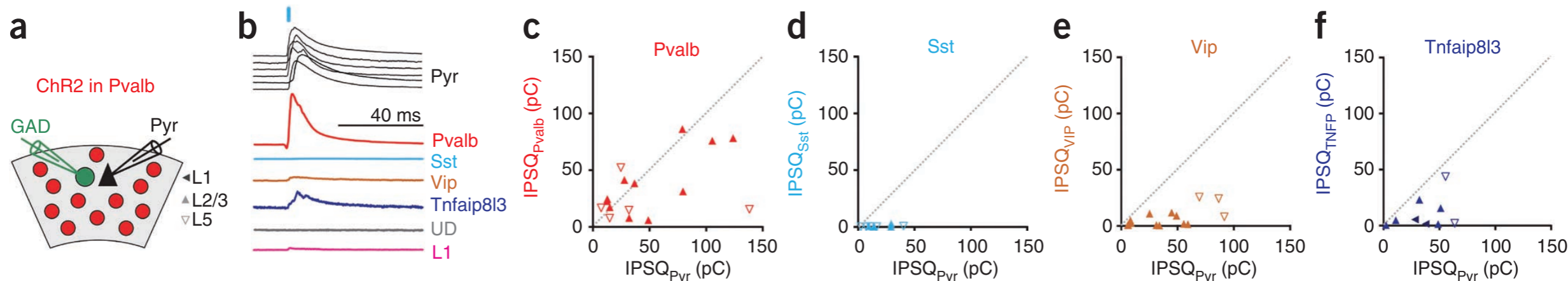


ChR2 in Sst

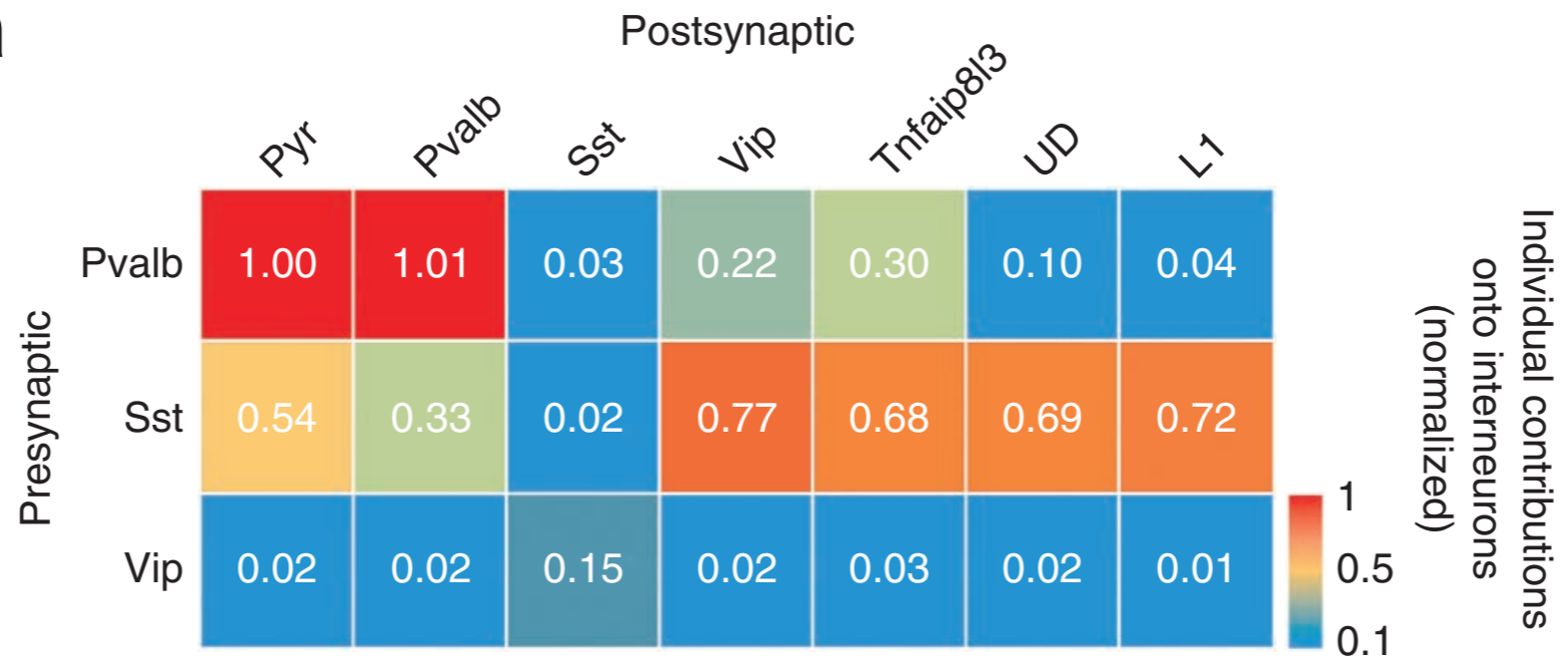
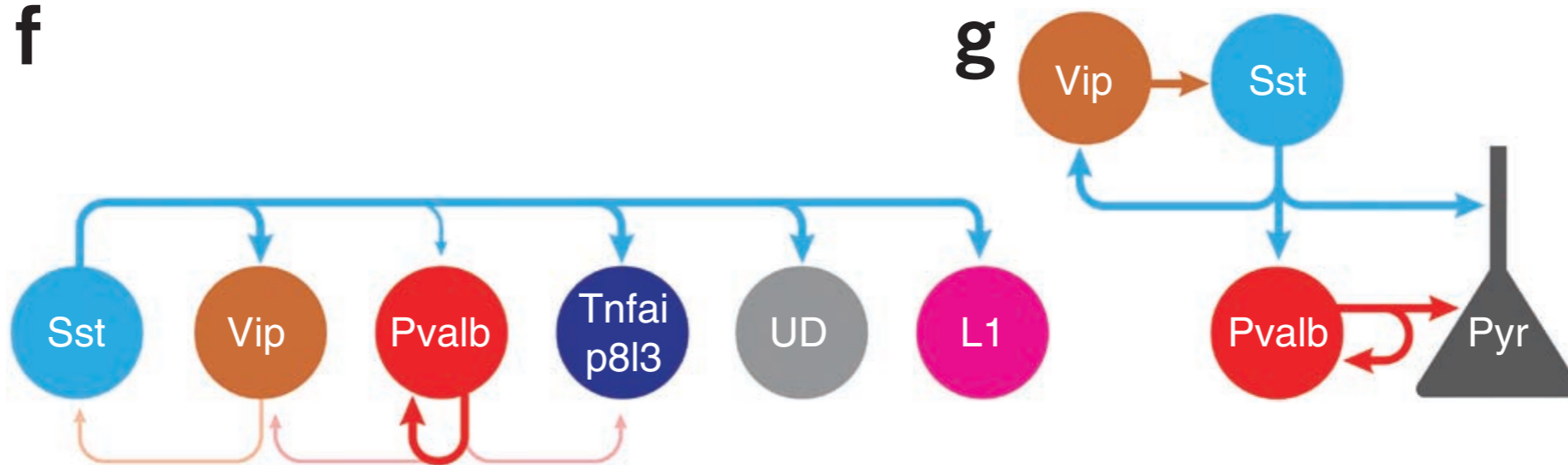
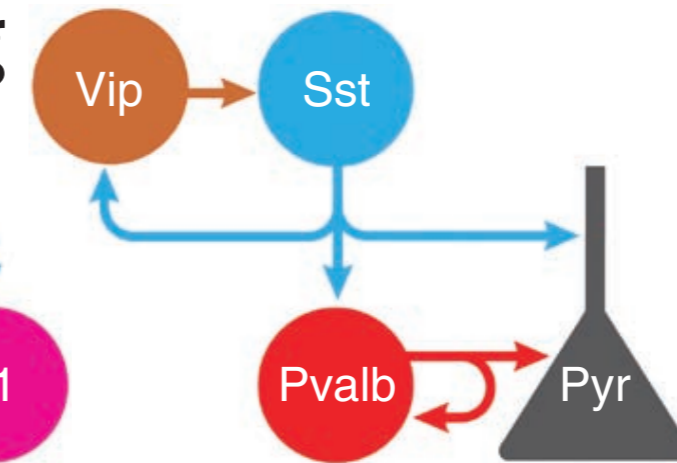


ChR2 in Vip





**Figure 4** Pvalb cells mainly inhibit one another. **(a)** Schematic of experimental configuration: ChR2-expressing Pvalb-Cre cells were photostimulated while we recorded from a pyramidal cell (Pyr) and a neighboring GAD65 and GAD67-expressing inhibitory neuron expressing GFP. **(b)** Example IPSCs simultaneously recorded in the reference pyramidal cell (black) and in one of the six different interneuron categories. Order of six pyramidal-cell IPSCs (top to bottom) matches the order of the IPSC simultaneously recorded in each of the six interneuron categories. For simplicity, all traces were scaled such that the pyramidal-cell IPSCs have the same peak amplitude. **(c–h)** IPSC evoked by Pvalb cell photostimulation and recorded in individual interneurons versus IPSC simultaneously recorded in a pyramidal cell ( $IPSC_{Pyr}$ ; symbols as in **a**). Dotted lines are unity lines. Pvalb: 16 cells, 15 slices, 10 mice; Sst: 9 cells, 9 slices, 6 mice; Vip: 15 cells, 12 slices, 9 mice, Tnfaip813: 9 cells, 5 slices, 5 mice; UD: 16 cells, 12 slices, 9 mice; L1: 7 cells, 5 slices, 5 mice. **(i)** Mean  $\pm$  s.e.m. of INC values of all recorded pairs of the respective category (Sst: 9 cells; Vip: 15 cells; Pvalb: 16 cells; Tnfaip813: 9 cells; UD: 16 cells; L1: 7 cells). **(j)** Schematic of the inhibition mediated by Pvalb cells onto each interneuron category.

**a****f****g**

## discussion

- cool technique
- surprisingly accurate
- potential space-clamping issues?
- poor estimates from low connectivity to Pyr
- massive averaging across animals and layers
- need presynaptic cell-type specific transgenic mice
- poor understanding of cell-types
- what about the other 80% of the cells?