Dense Inhibitory Connectivity in Neocortex

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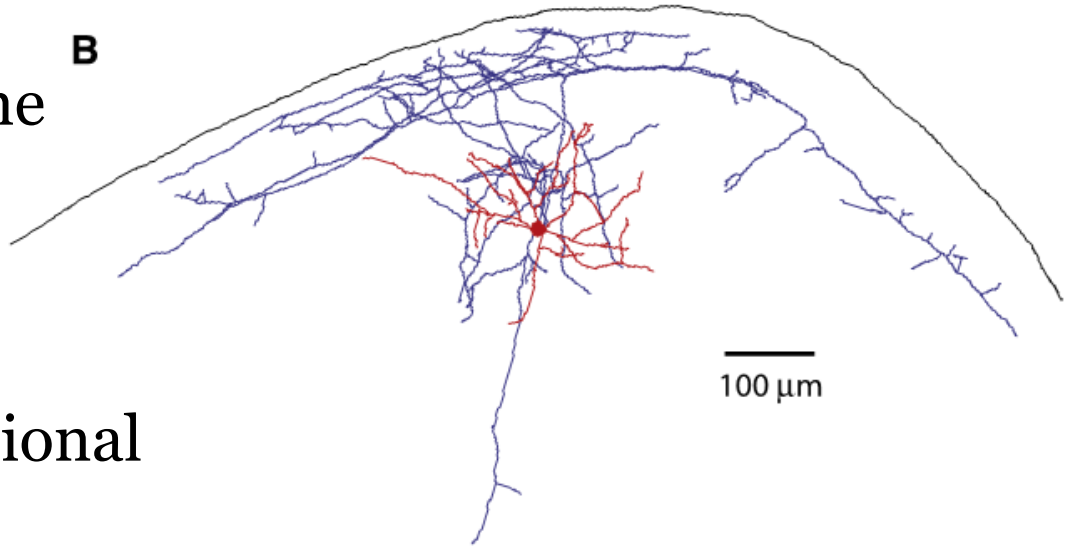
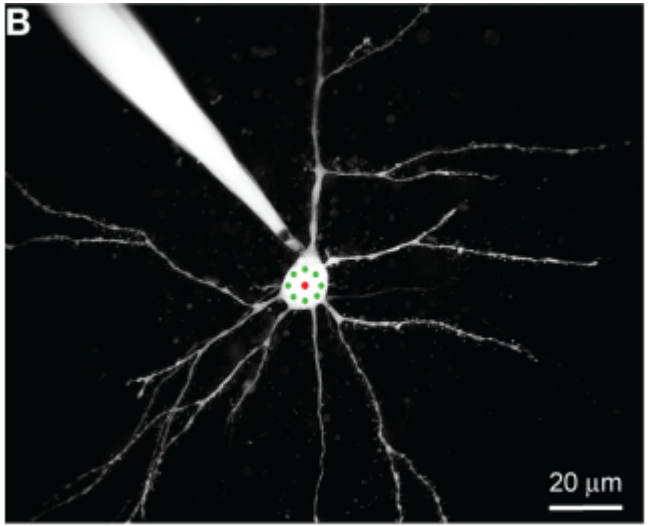
Opportunity

- desire to map larger regions of brain at the single cell level

- apply mapping to understanding functional roles: GABAergic interneurons



Challenge

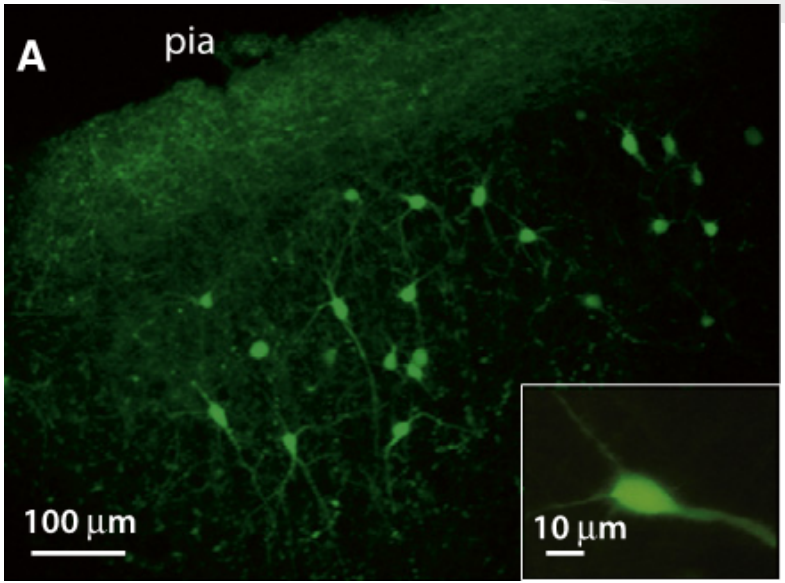


- create more high-throughput imaging system to explore connections on single cell level: two-photon stimulation
- modify system for use with interneurons

Figure: Fino et al. 2009

Action

- transgenic mouse model: GFP in somatostatin-positive interneurons



Action

- mapped sGFP cells onto PCs using two-photon photostimulation: RuBi-glutamate

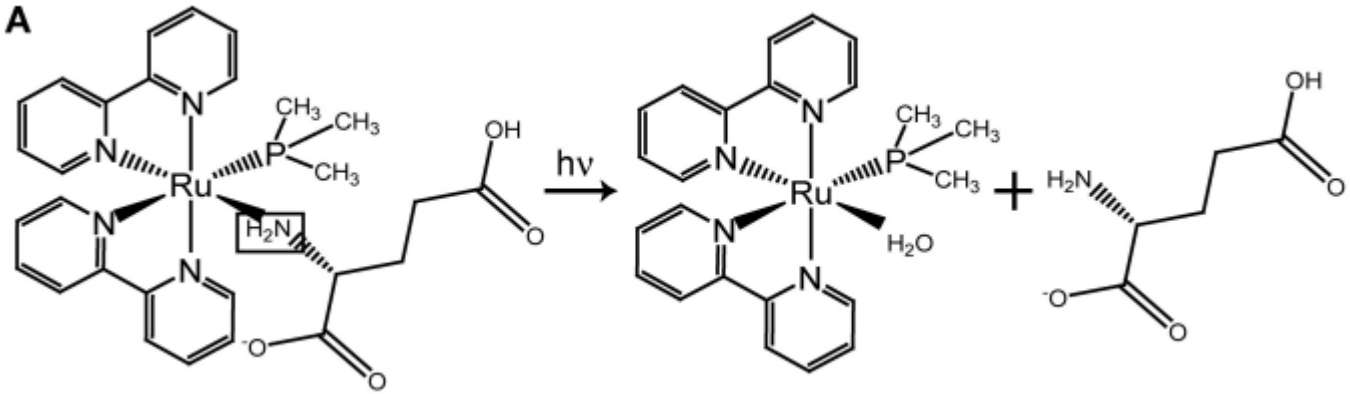
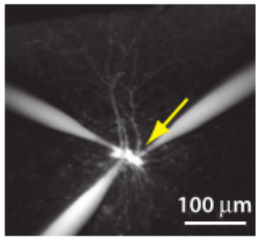


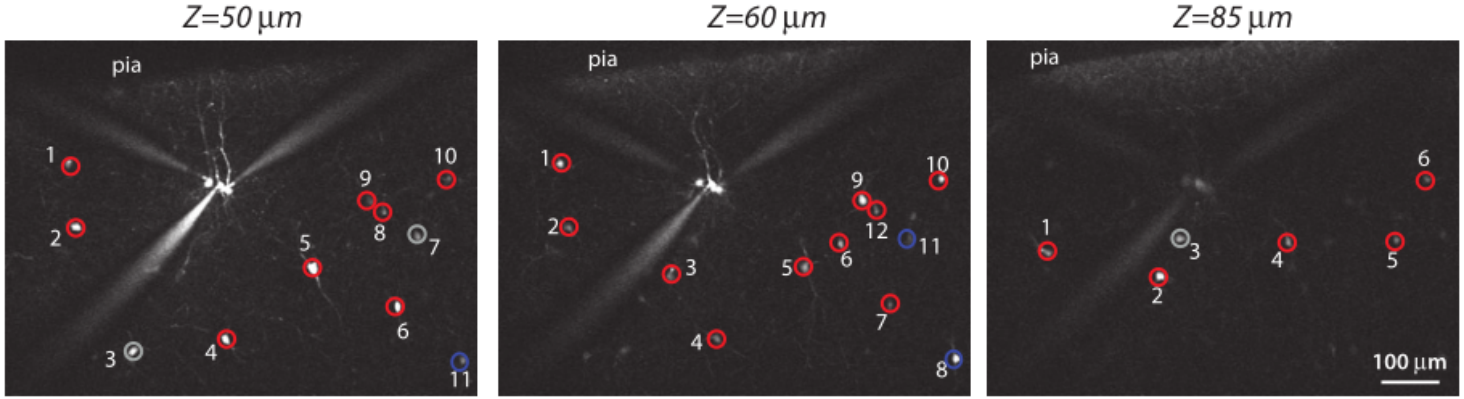
Figure: Fino et al. 2009

Action

- patched layer 2/3 PCs (+40 mV or -40 mV) and recorded while sequentially stimulating each sGFP cell with variety of laser powers

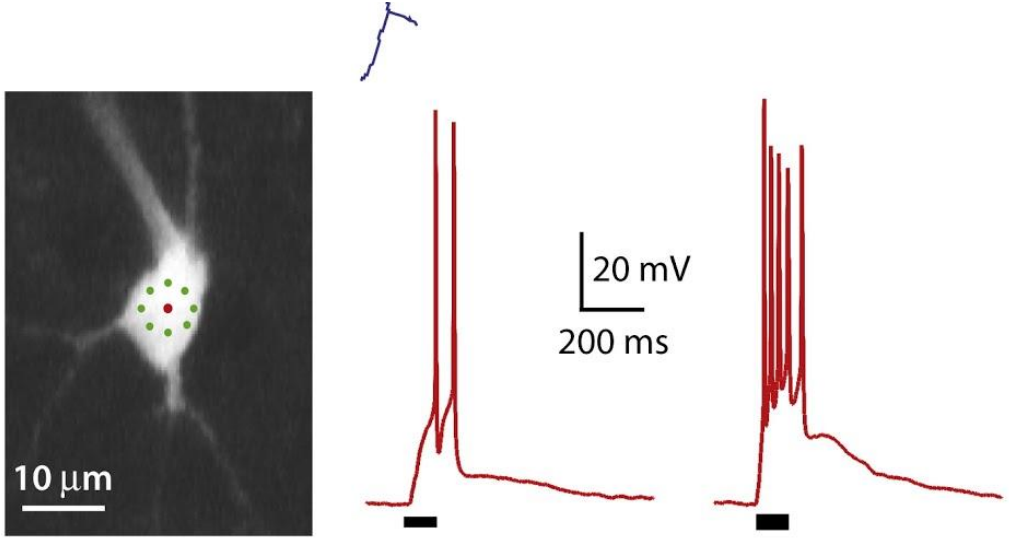


Pyramidal cell 1



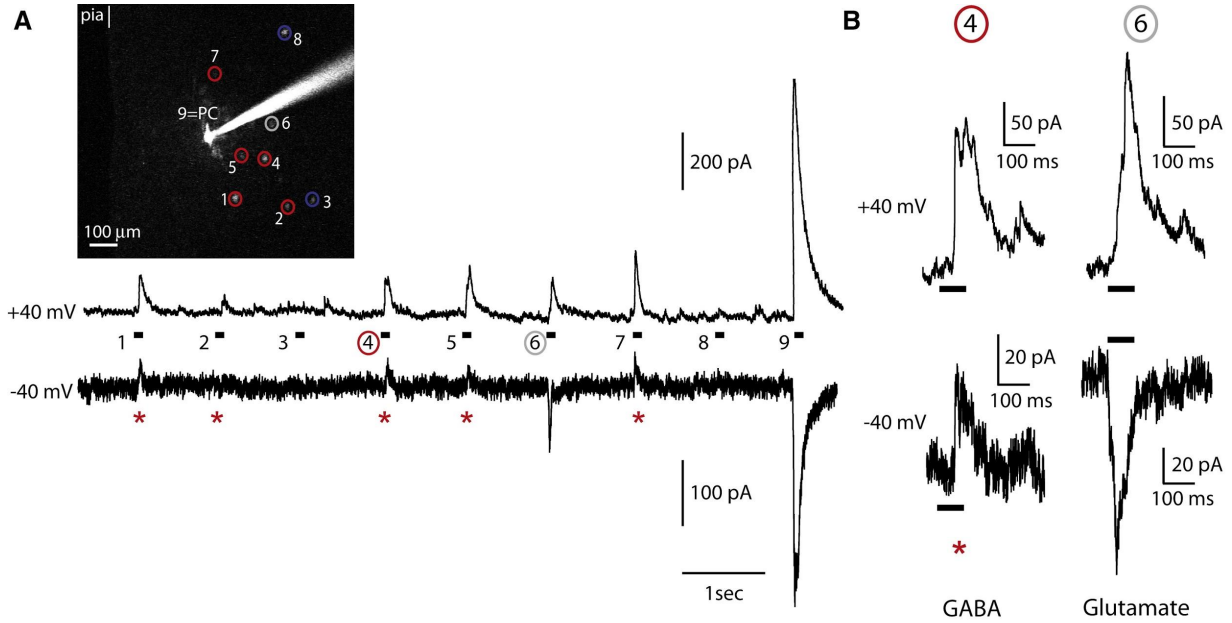
Action

- uncaging laser targeting: temporal and spatial multiplexing of two-photon laser



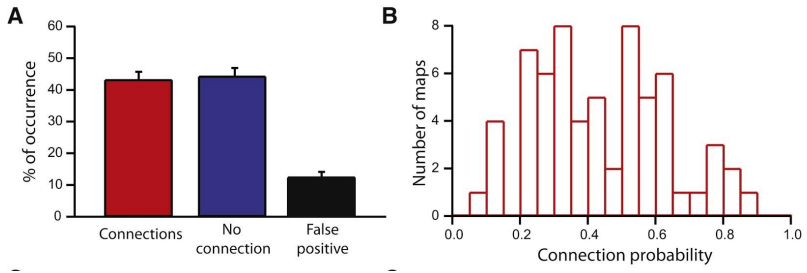
Resolution

- Induced IPSCs(Inhibitory Post synaptic potential) in postsynaptic PCs through photoactivation of presynaptic inhibitory neurons.



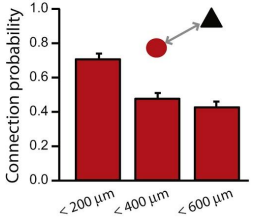
Resolution - Connectivity

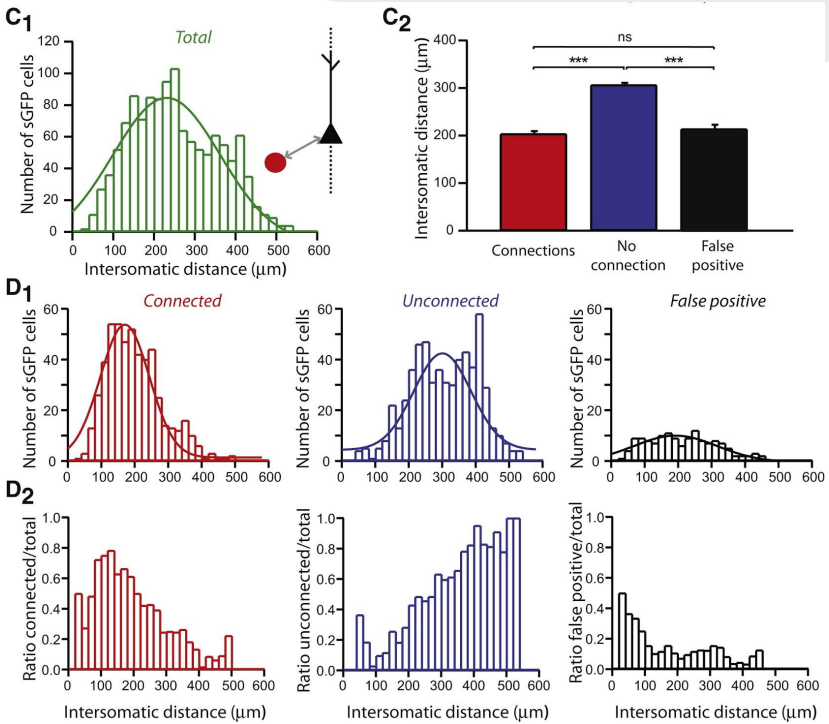
- Recorded 20 pairs and 7 triplets of PCs
  - 43.2% of stimulated sGFP interneurons were connected
  - Individually, connection probability ranged from .1 to .9



Resolution - Connectivity

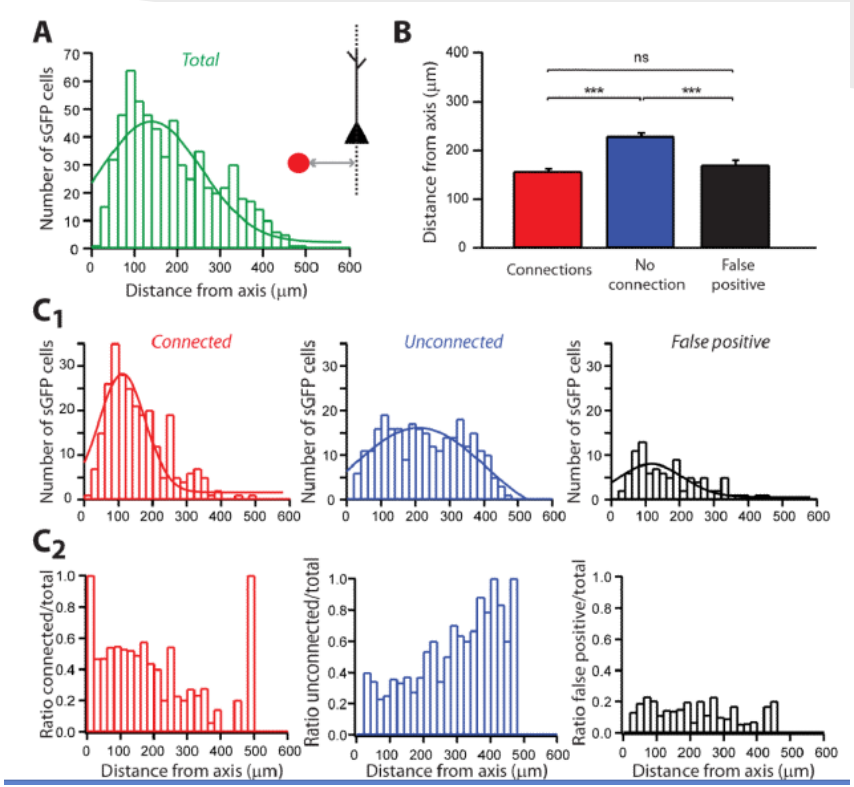
- Connected interneurons were significantly closer to recorded PCs than unconnected ones(203.9+-5.5 microm vs. 306.9+-4.1microm)





Resolution - Connectivity

- Higher probability of connections from sGFP interneurons to PCs within a local circuit(same “column”)



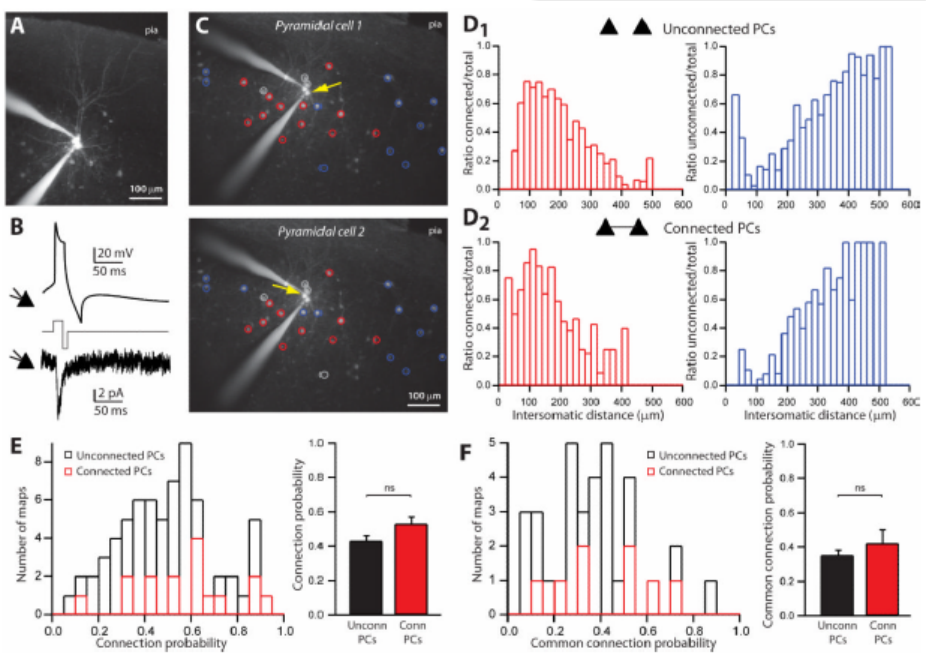
Resolution - Selectivity

- Wanted to know if Inhibitory neurons distinguished between circuits

- P(connection|Excitatory neuron is part of a cycle)
- P(connection|Inhibitory neuron is connected to second Excitatory neuron)

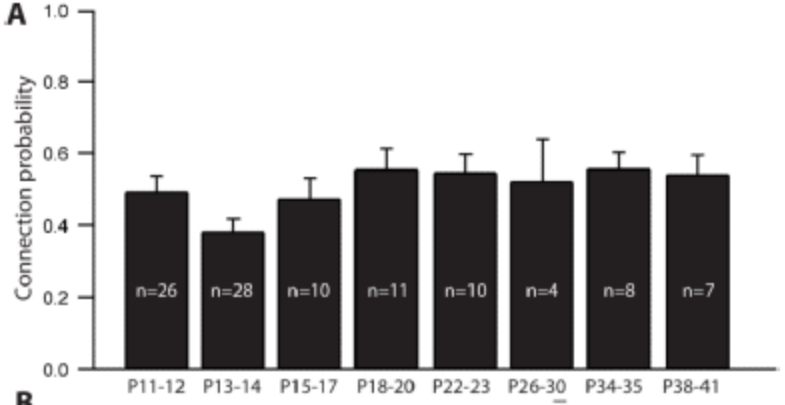
Resolution - Selectivity

- Compared connected pairs of PCs to unconnected PCs
  - Both had similar connection probability
  - Distributions of connected or unconnected cells were also similar
- Conclude that sGFPs connect with PCs without discriminating and therefore do not form specific subnetworks

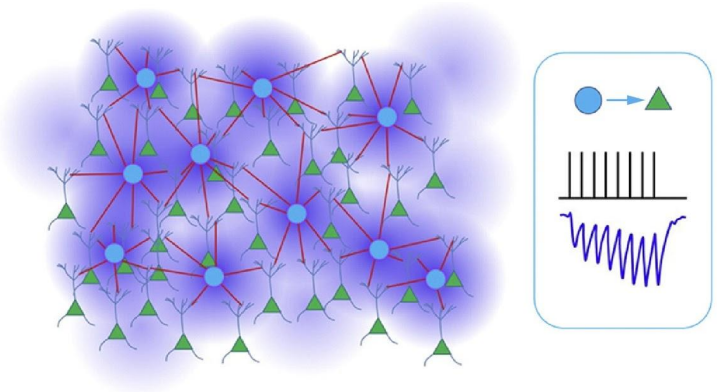


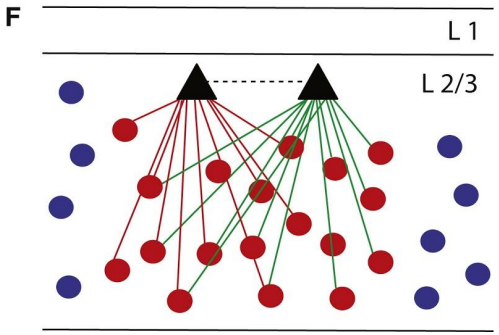
Resolution - Development

- Mapped animals at a range of developmental stages
- Found connection probability was similar throughout the ages



Resolution - Model





Karnani, Mahesh M., Masakazu Agetsuma, and Rafael Yuste. "A blanket of inhibition: functional inferences from dense inhibitory connectivity." *Current opinion in neurobiology* 26 (2014): 96-102.

Future

- Understanding of mechanisms behind dense connectivity

- Test whether these results in other populations
  - of inhibitory interneurons outside the frontal cortex
  - of neuronal cell types

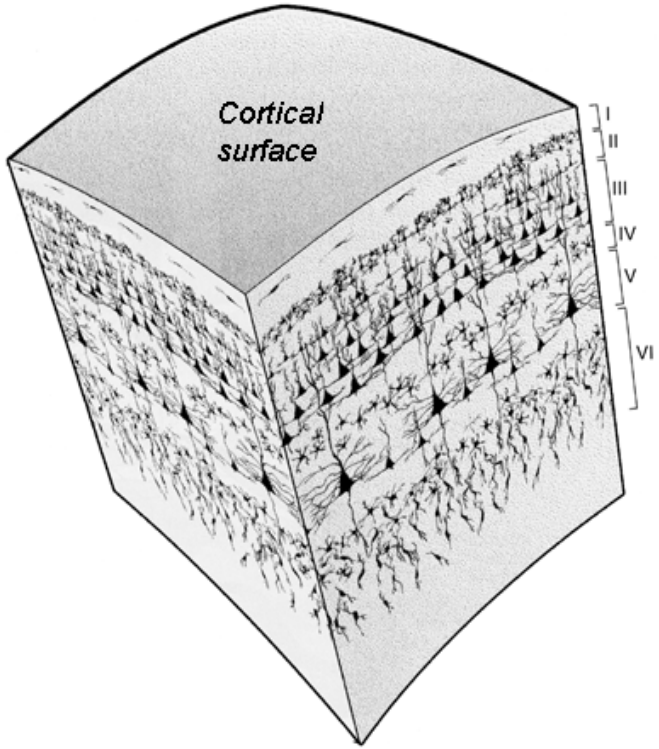
- Cortical modules

Works Cited

Fino E, Yuste R. Dense Inhibitory Connectivity in Neocortex. *Neuron*. 2011; 69: 1188-1203.

Thank you!

Supplemental



Supplemental