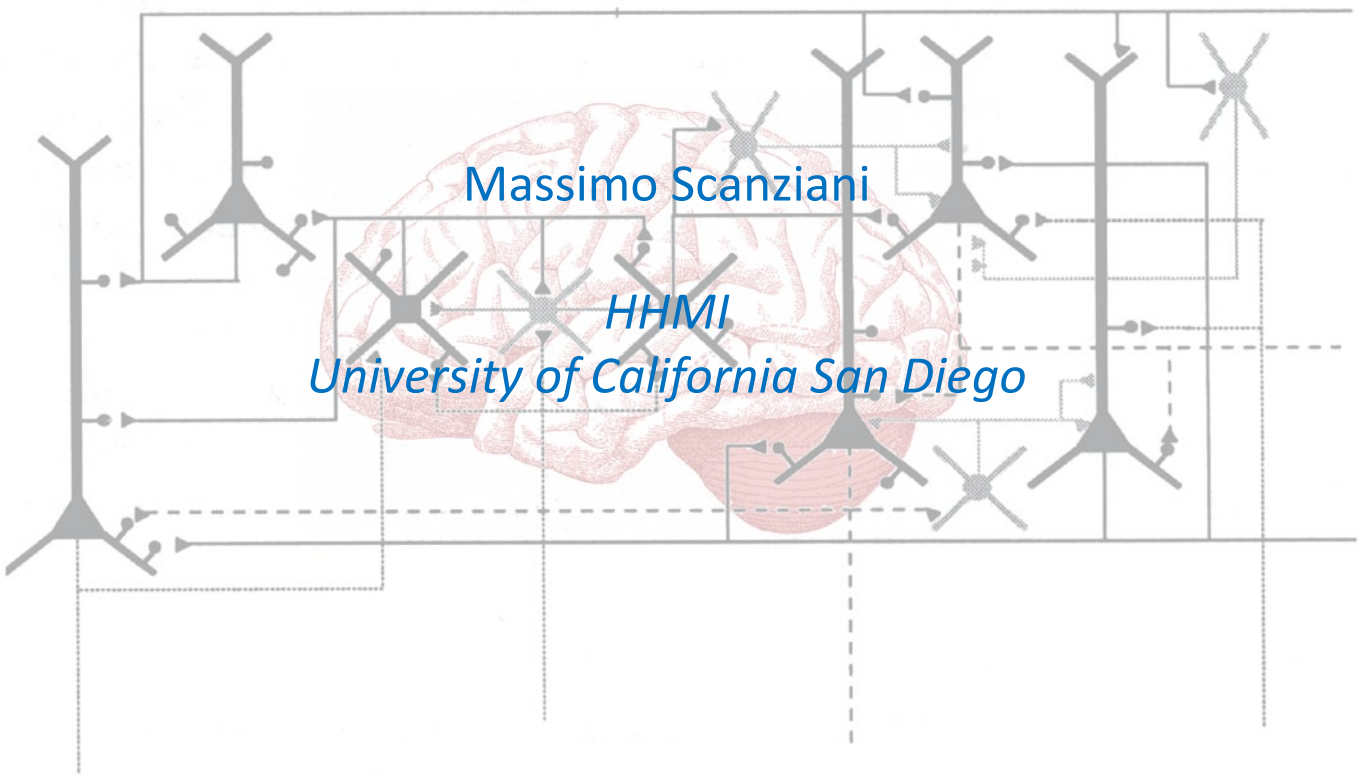
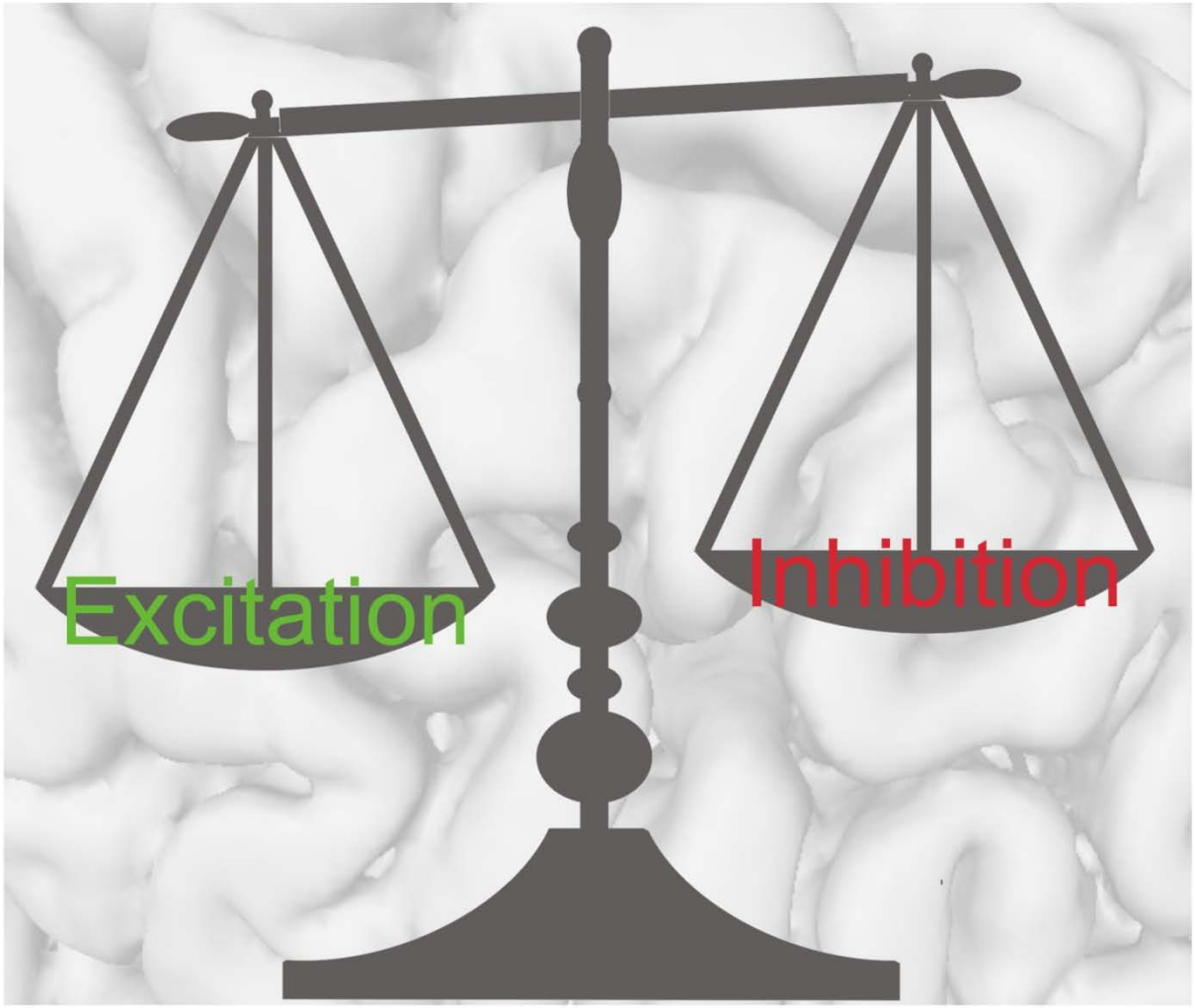
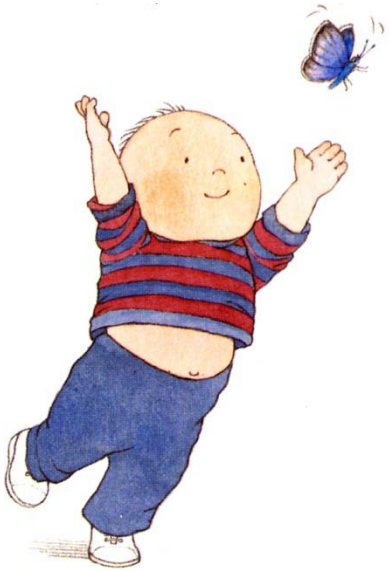
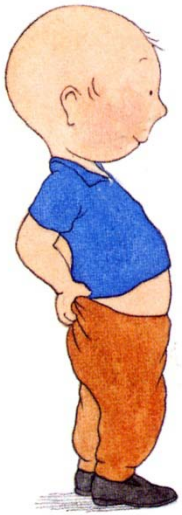


Massimo Scanziani

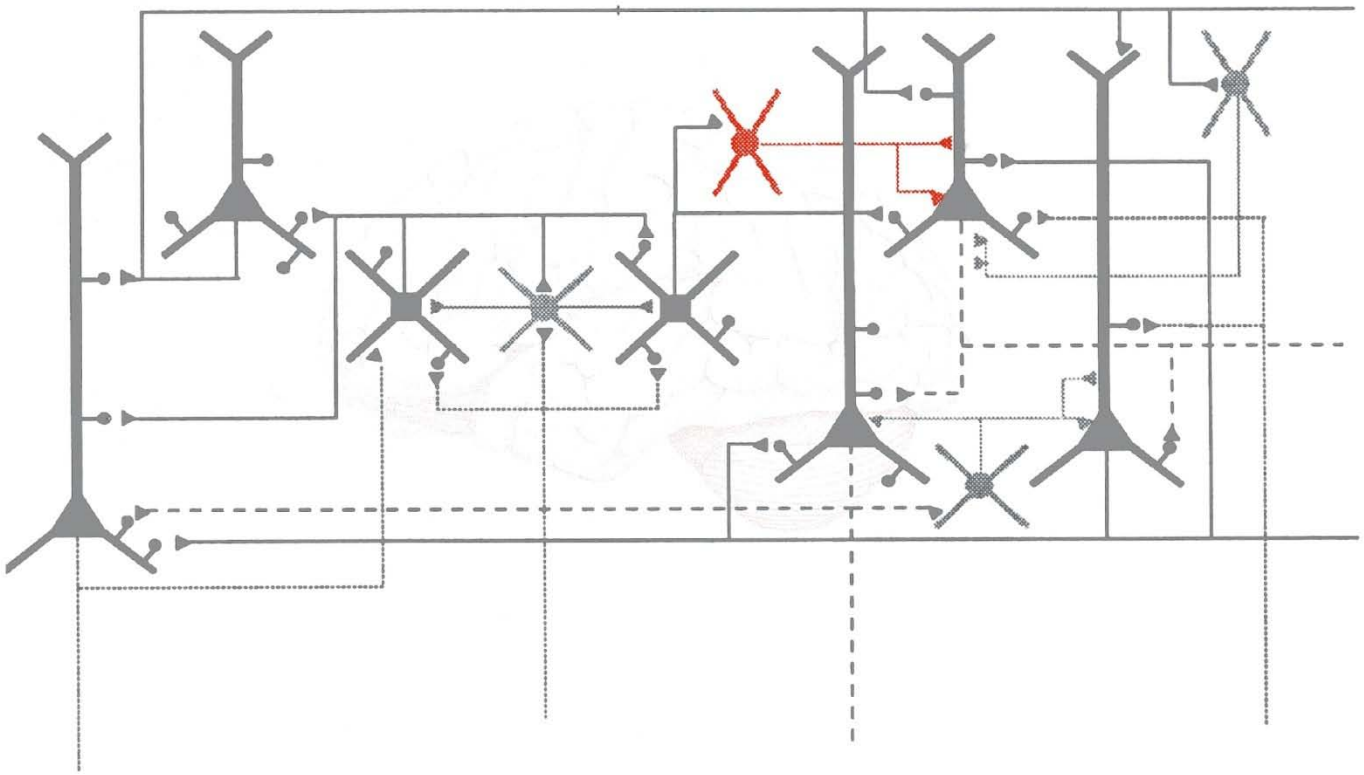
HHMI
University of California San Diego

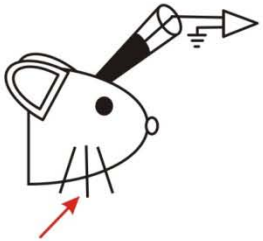

Excitation
Inhibition





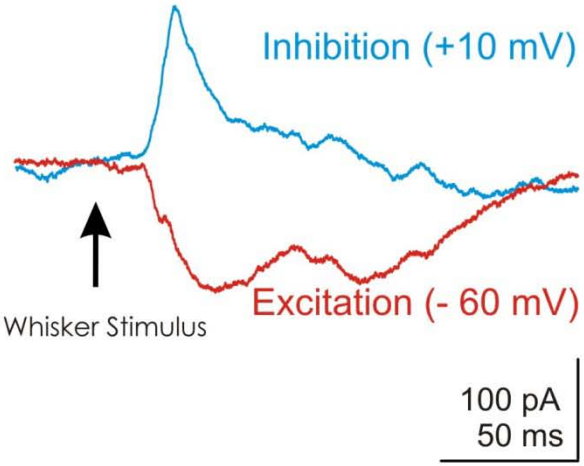
H. Oxenbury 1985

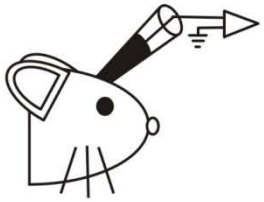




Somatosensory cortex (layer 2/3)
Whisker stimulation

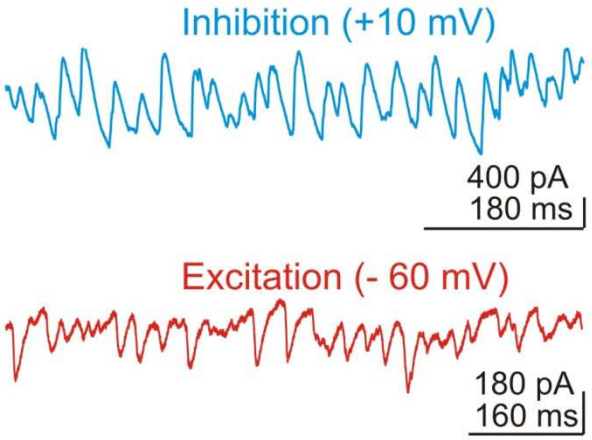
Whole-cell Voltage-clamp



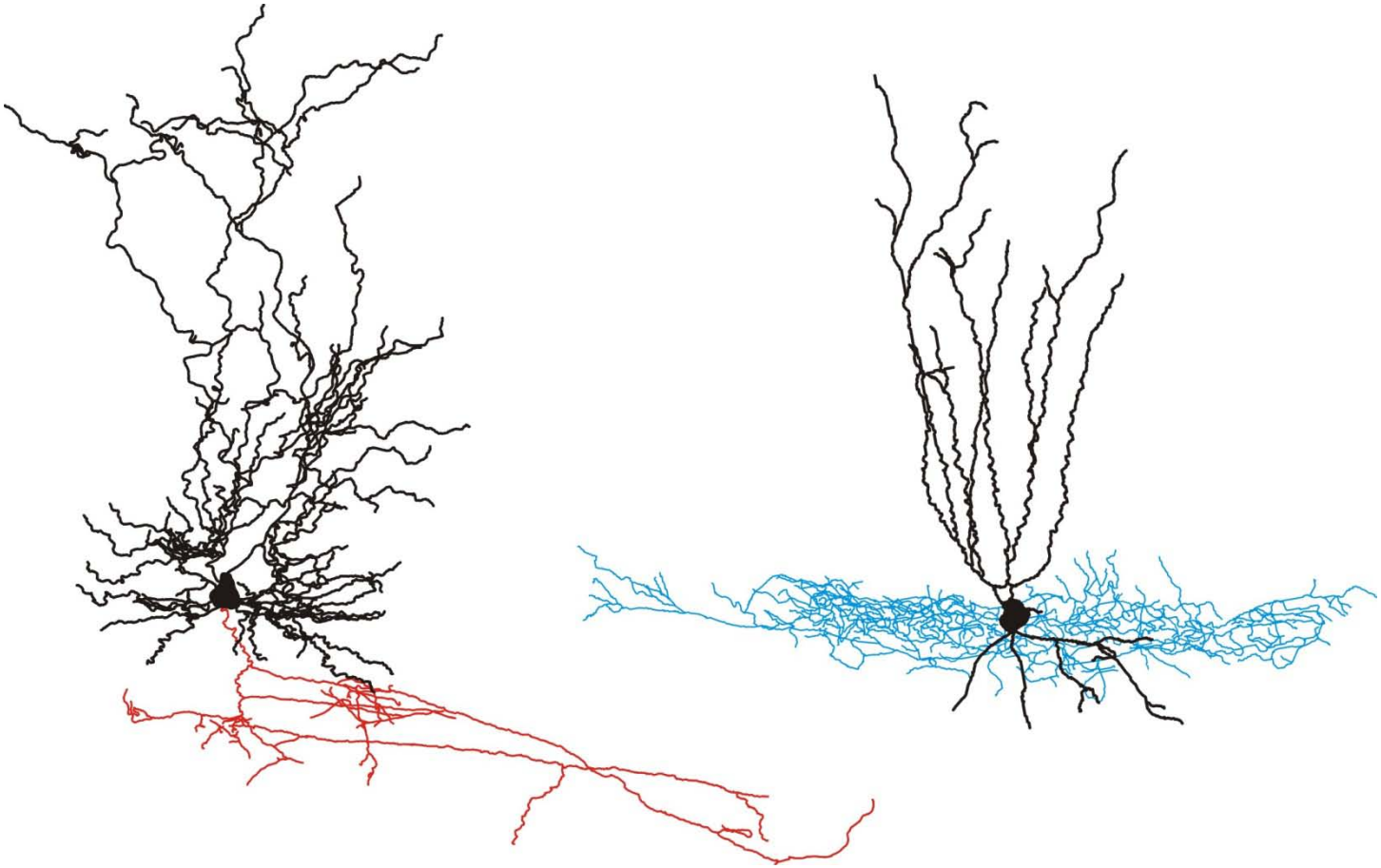


Hippocampus (CA3)
Spontaneous Gamma oscillations

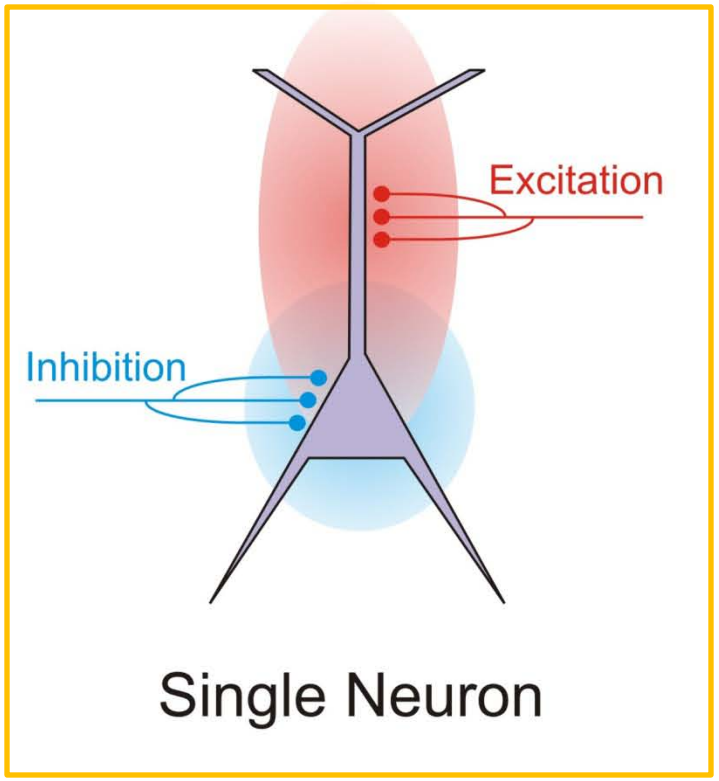
Whole-cell Voltage-clamp

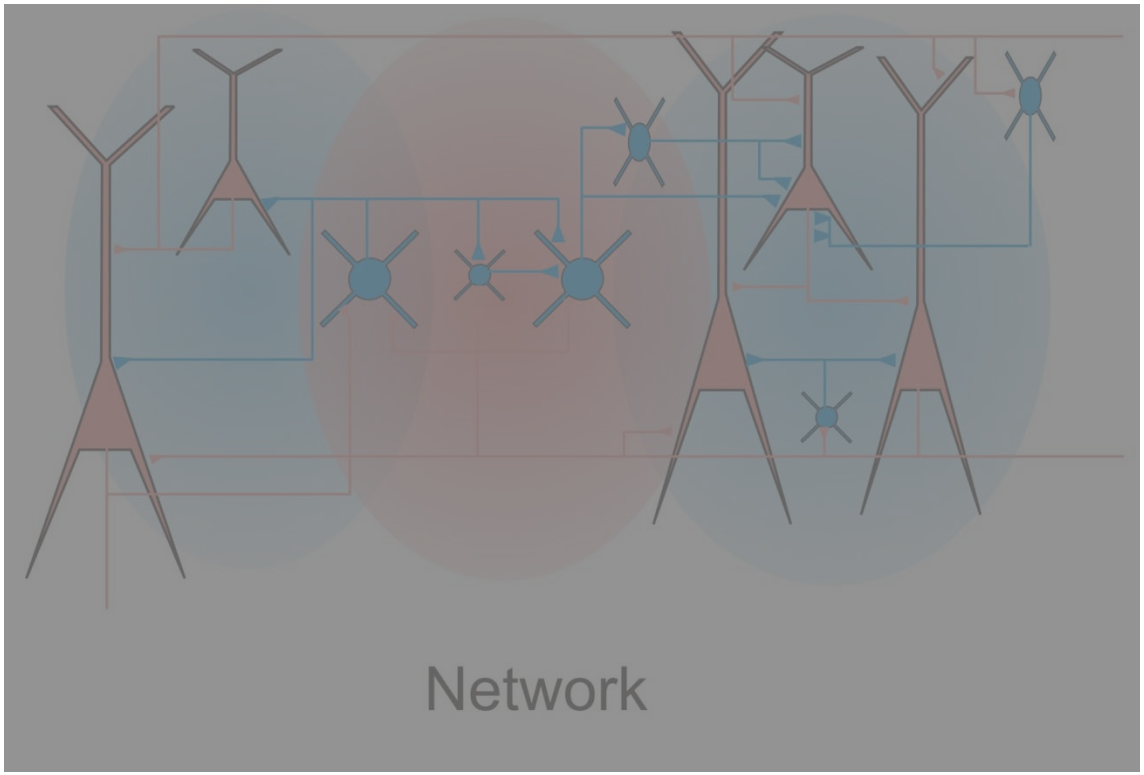


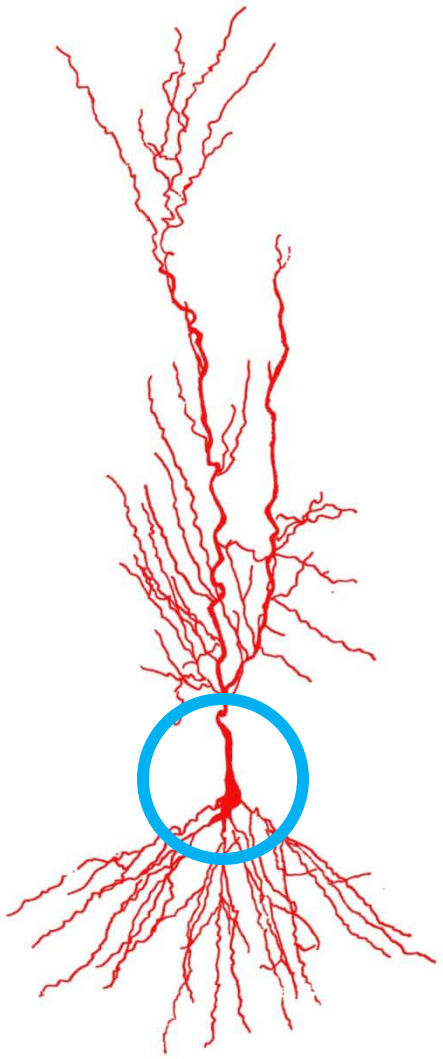
Excitatory and Inhibitory Neurons

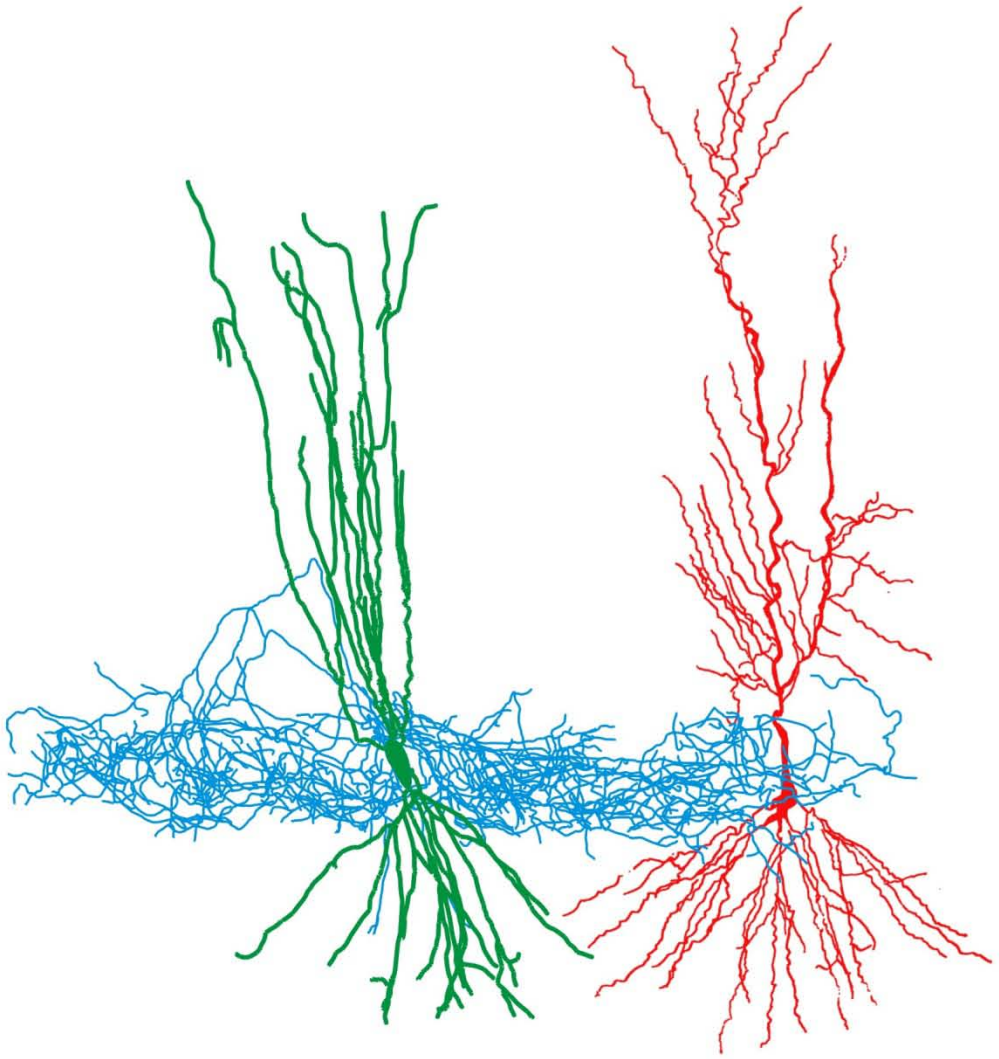


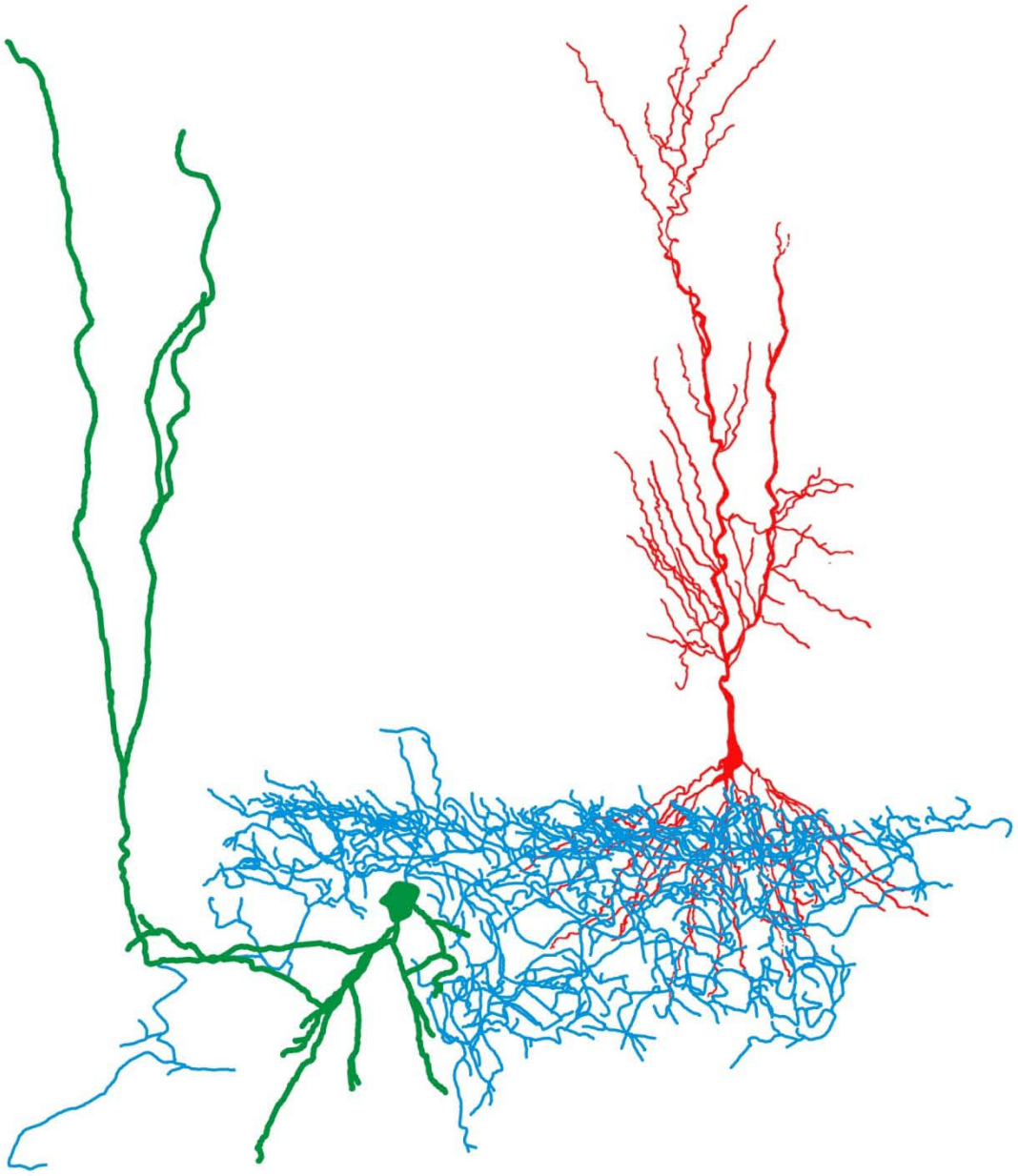
Coordination of Excitation and Inhibition in Cortical Space

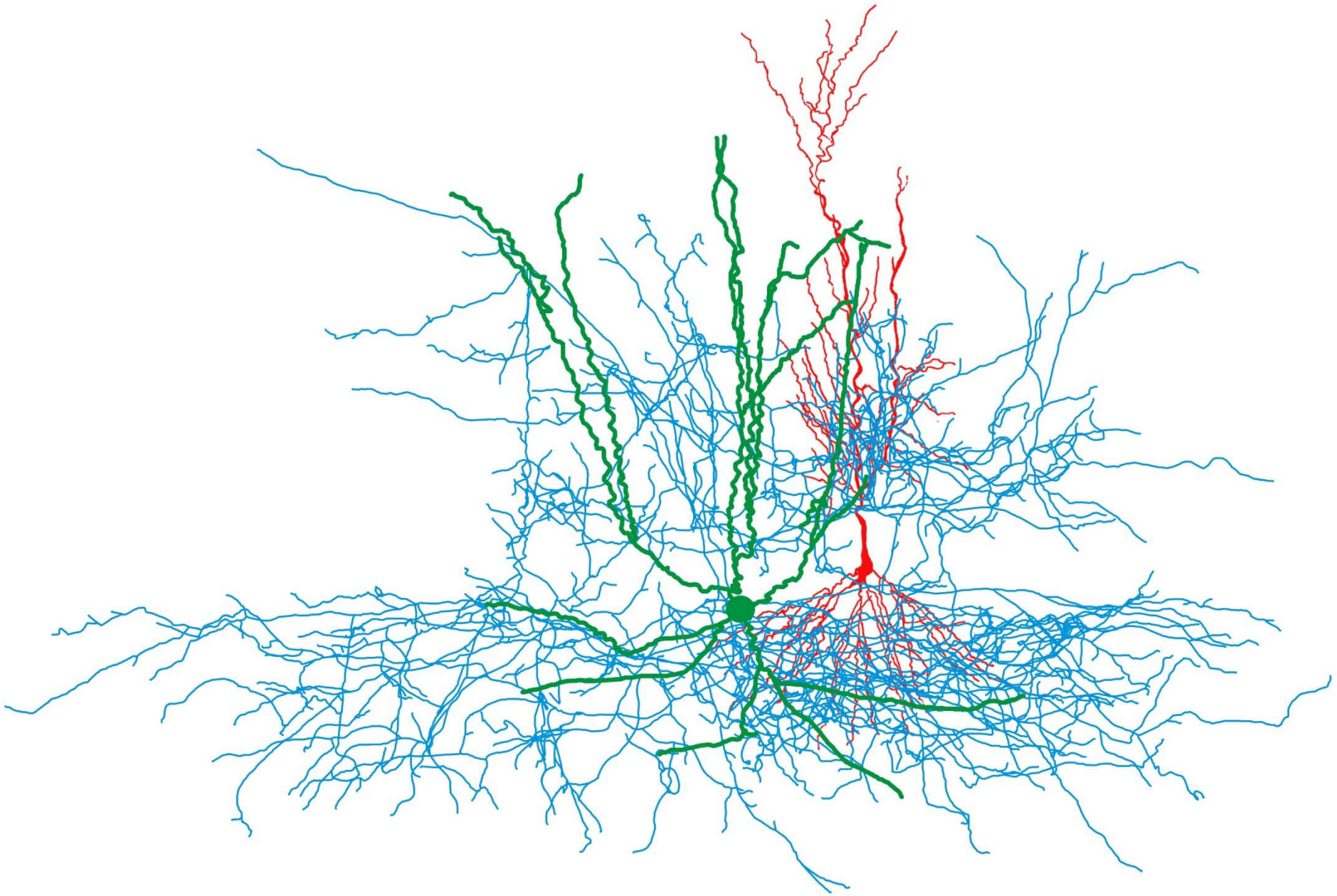


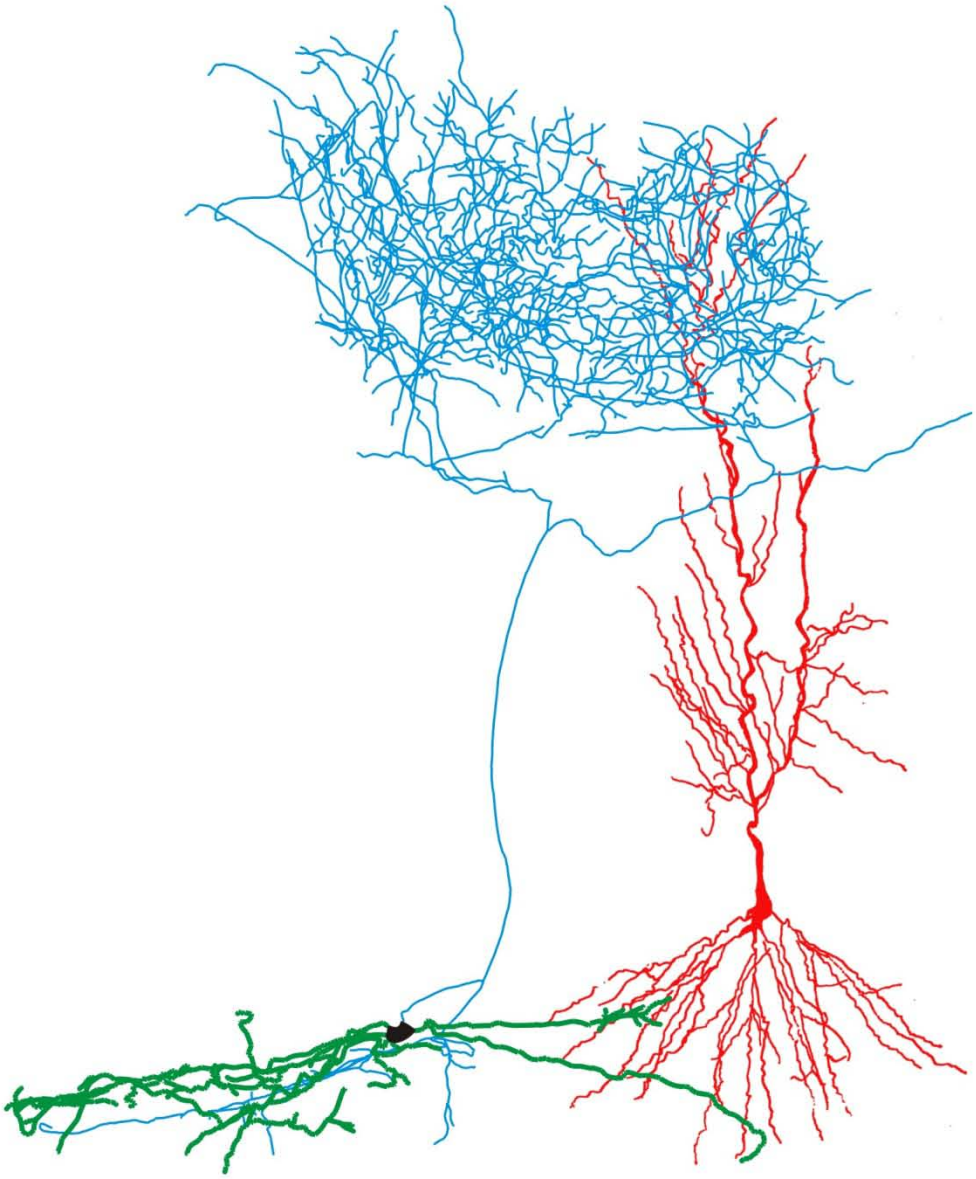




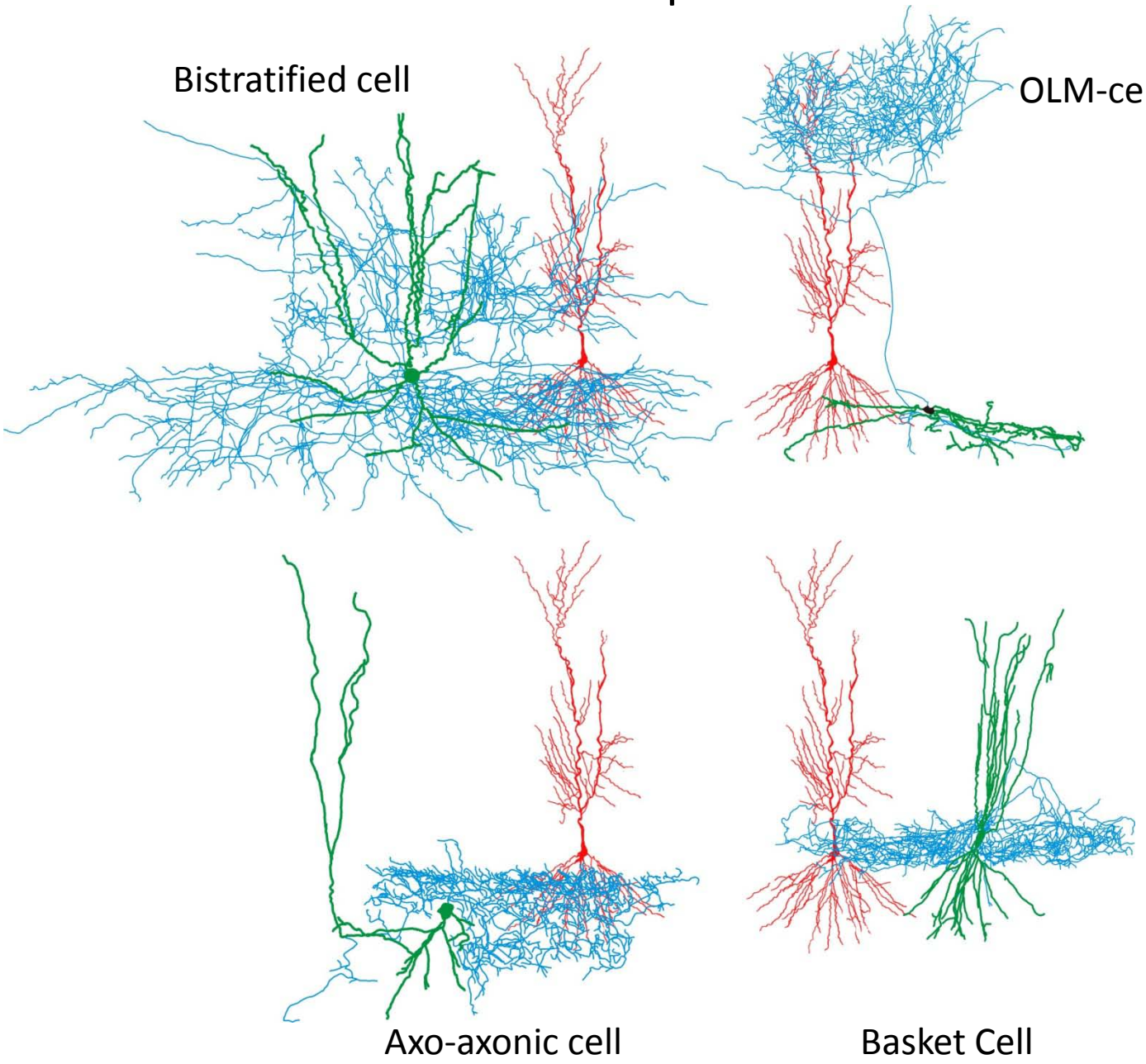






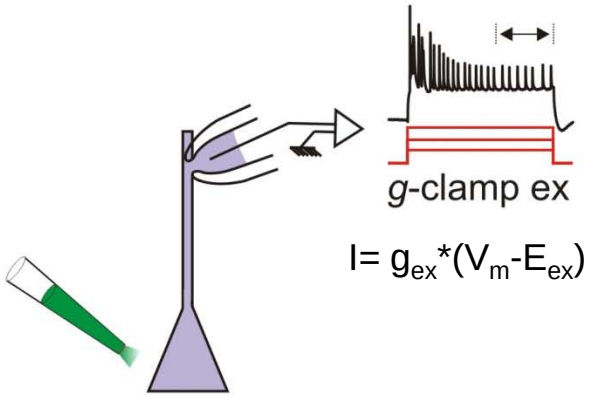


Inhibition is Compartmentalized

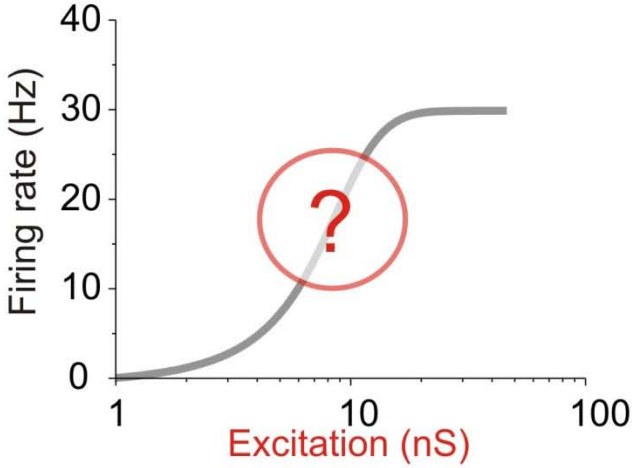


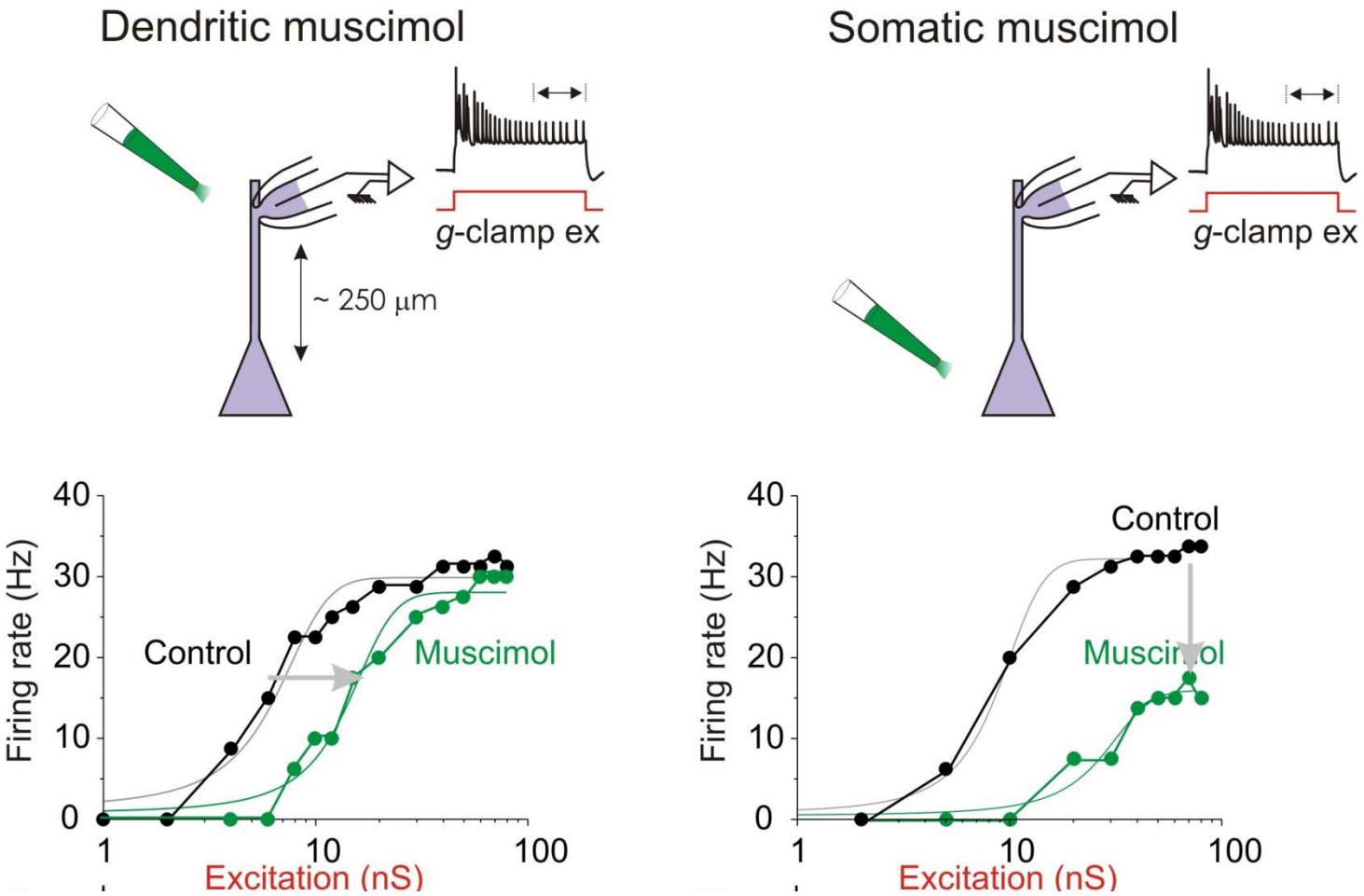
What is the role of the compartmentalization of inhibition on the output of the neuron?

Somatic muscimol



$I = g_{ex} * (V_m - E_{ex})$

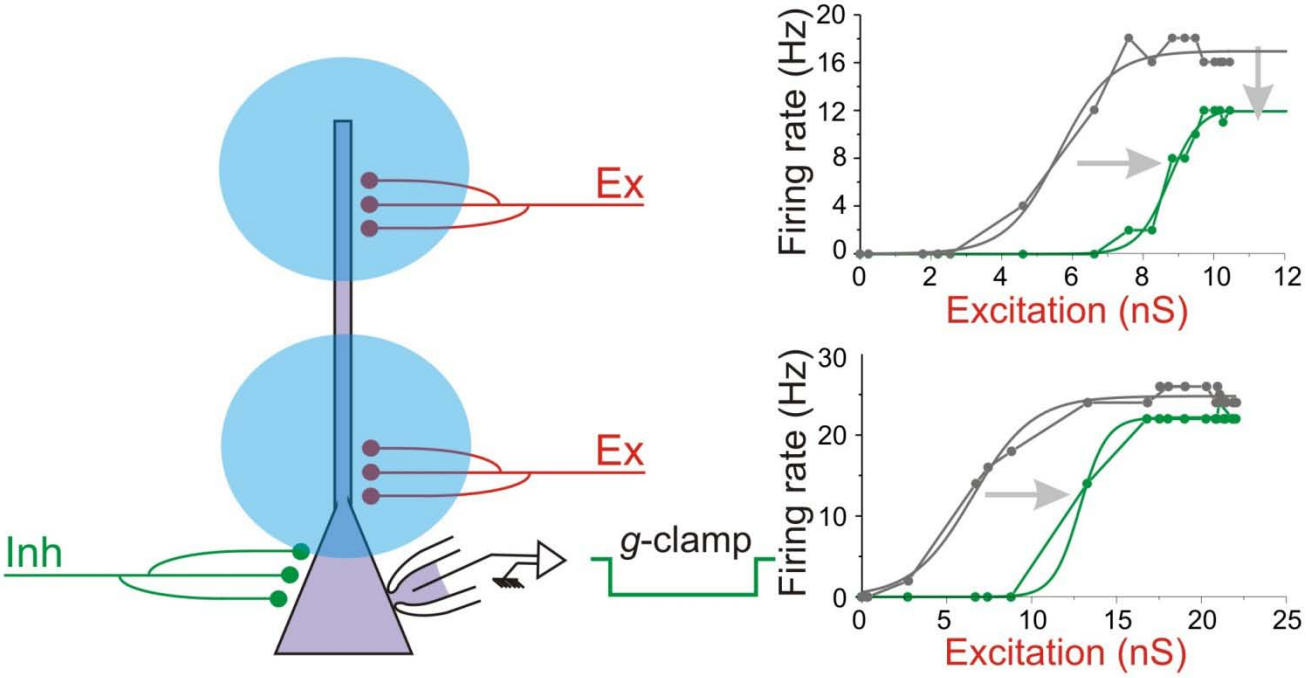




Dendritic inhibition shifts input-output to the right: Competitive action

Somatic inhibition reduces maximal firing rate: Non-competitive action

Somatosensory Cortex-Layer 5-Pyramidal cells-ChR2

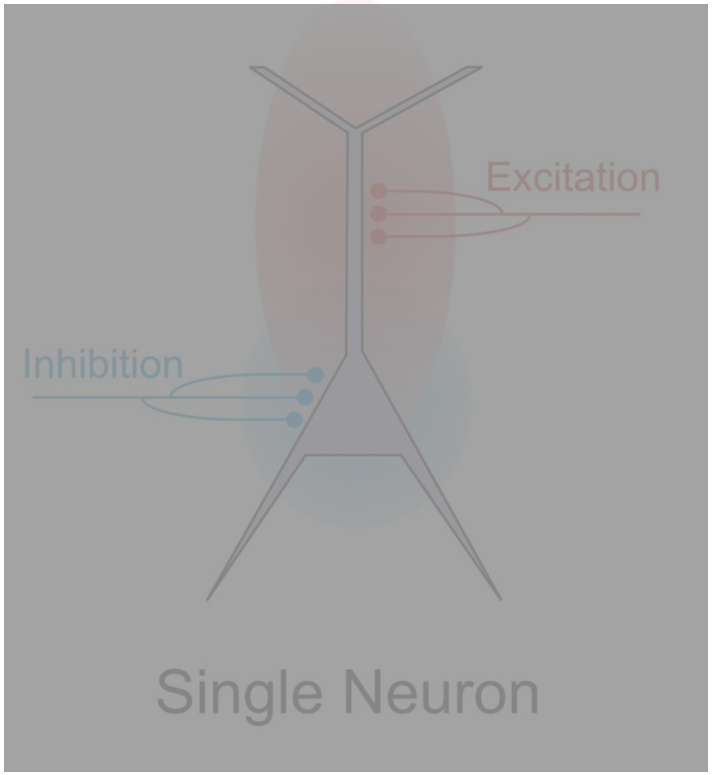


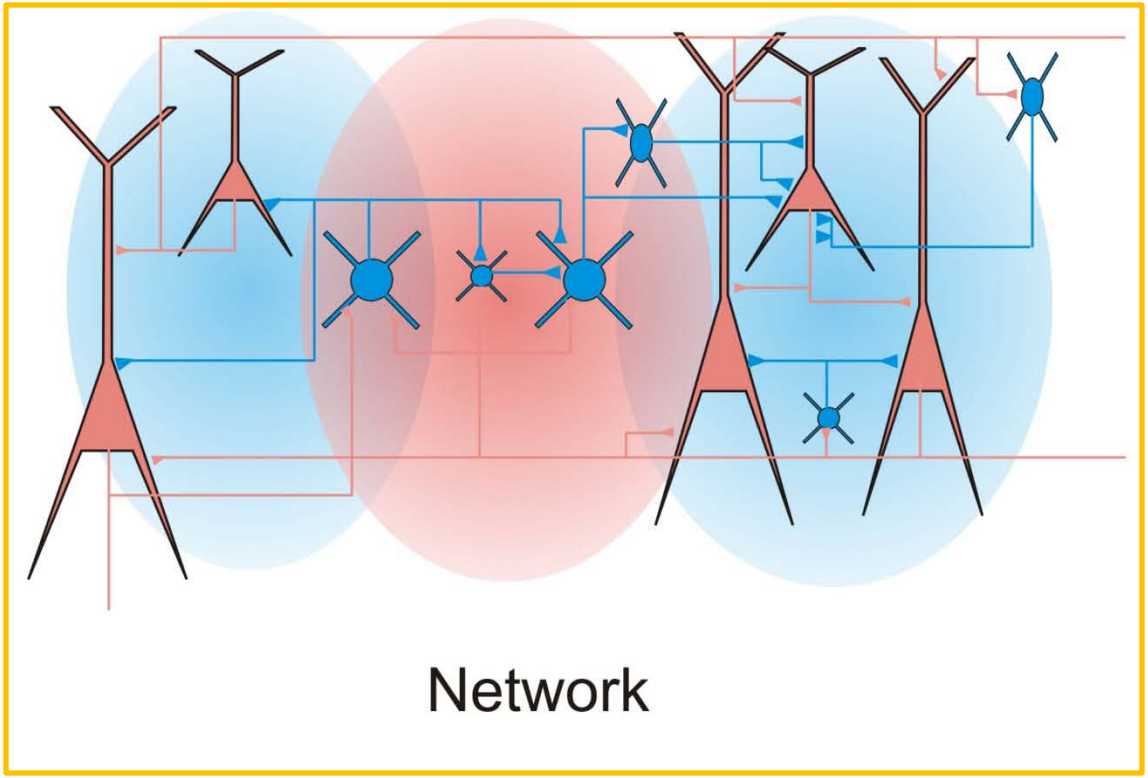
Proximal excitatory inputs: Somatic inhibition shifts input-output to the right

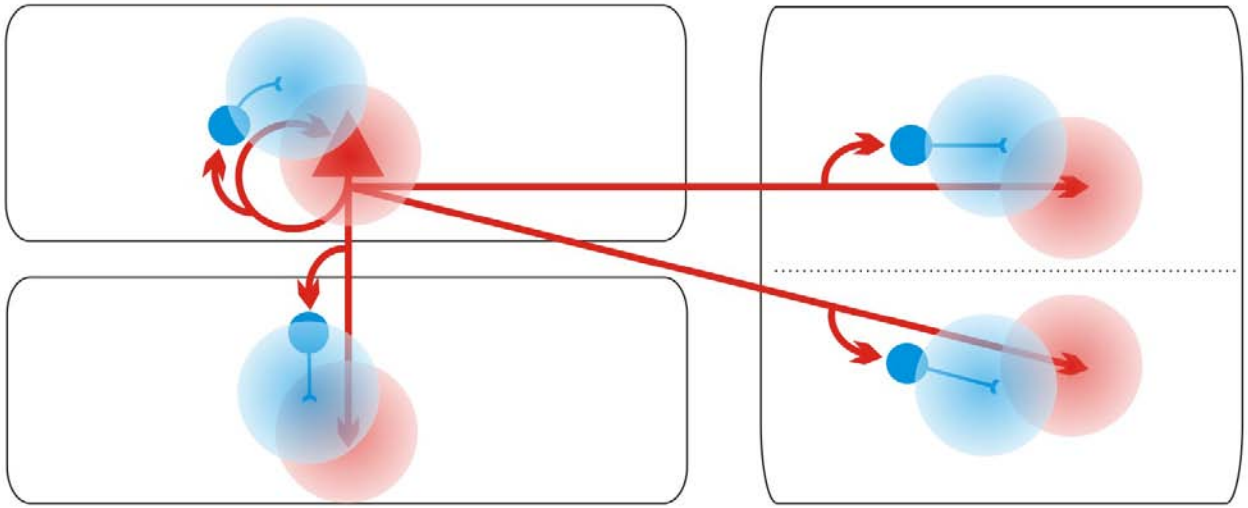
Distal excitatory inputs: Somatic inhibition also reduces maximal firing rate

See also Vu & Krasne 1992 in Crayfish

Coordination of Excitation and Inhibition in Cortical Space

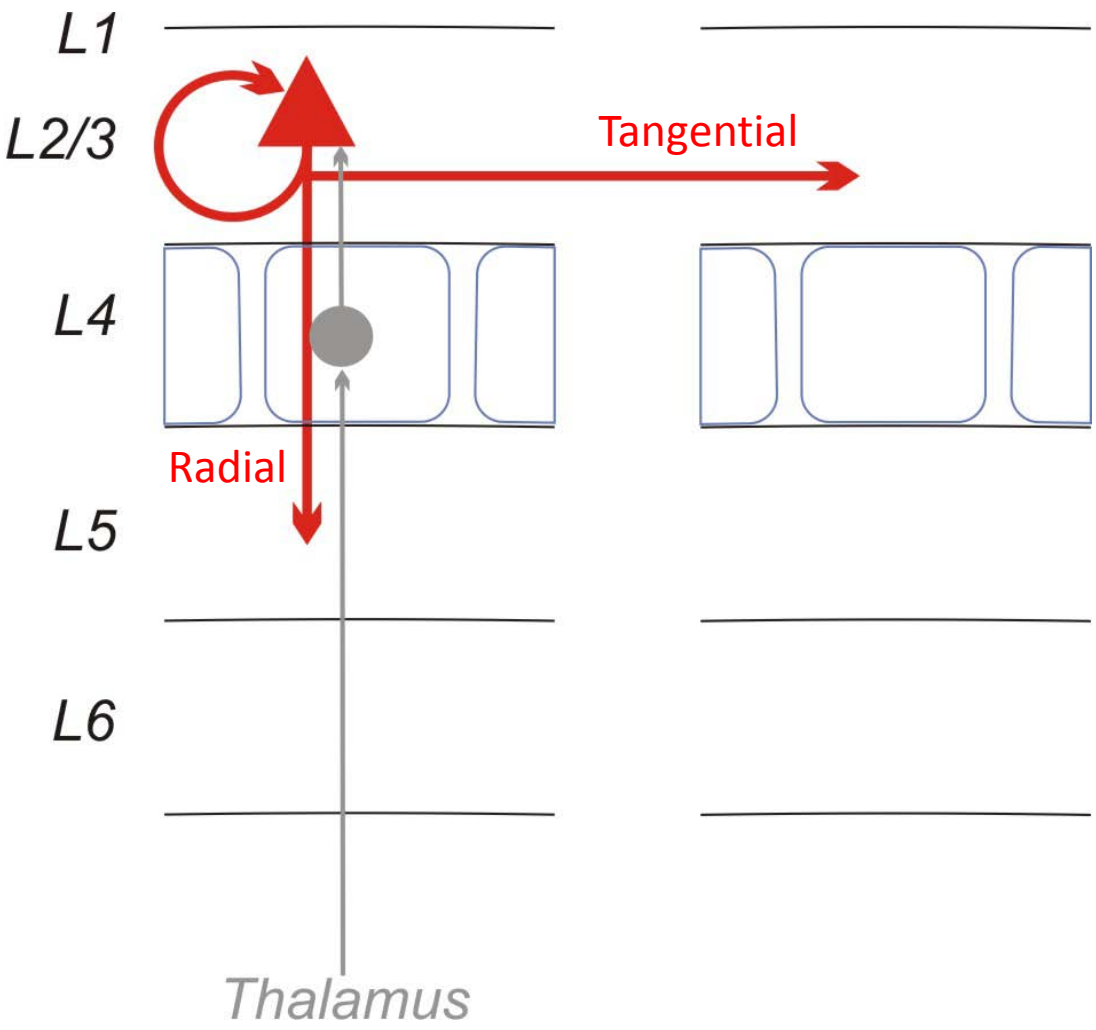




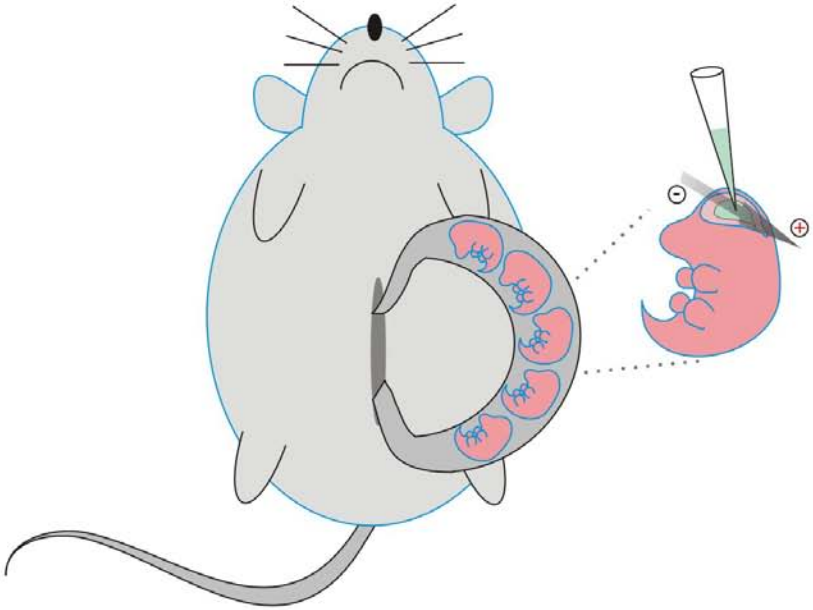


Spatial relationship between excitation and inhibition?

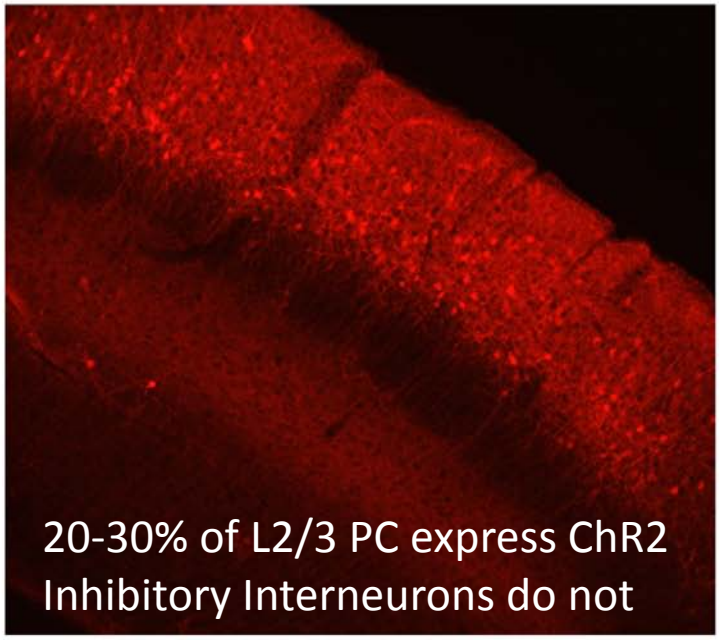
Net effect on neuronal output?

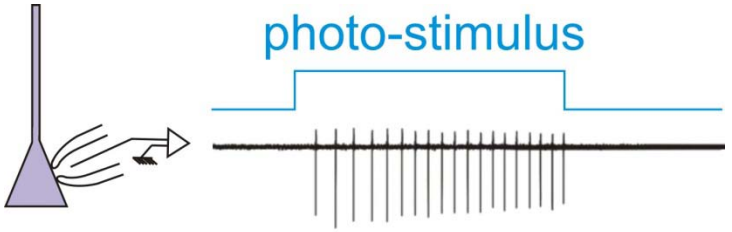

L1
L2/3
L4
L5
L6
Tangential
Radial
Thalamus

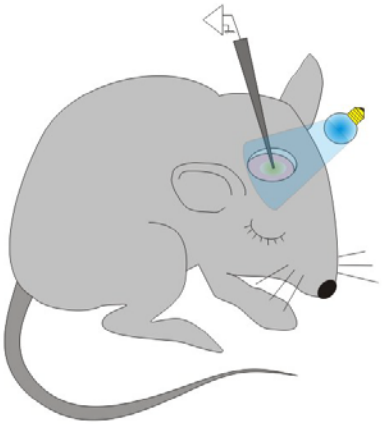
in utero electroporation
of ChR2 at E15

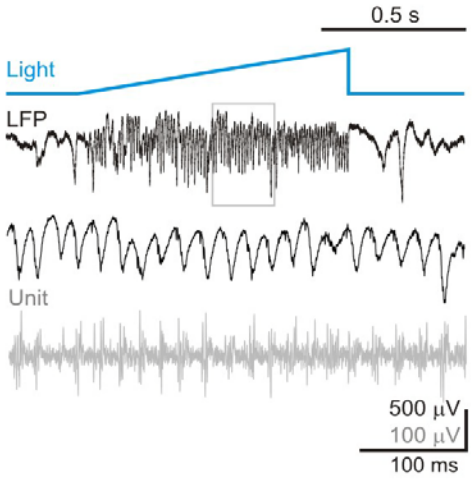


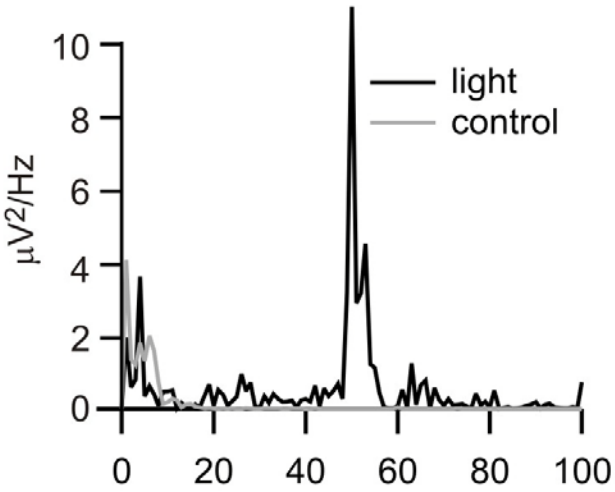
Allow to develop until P15-30

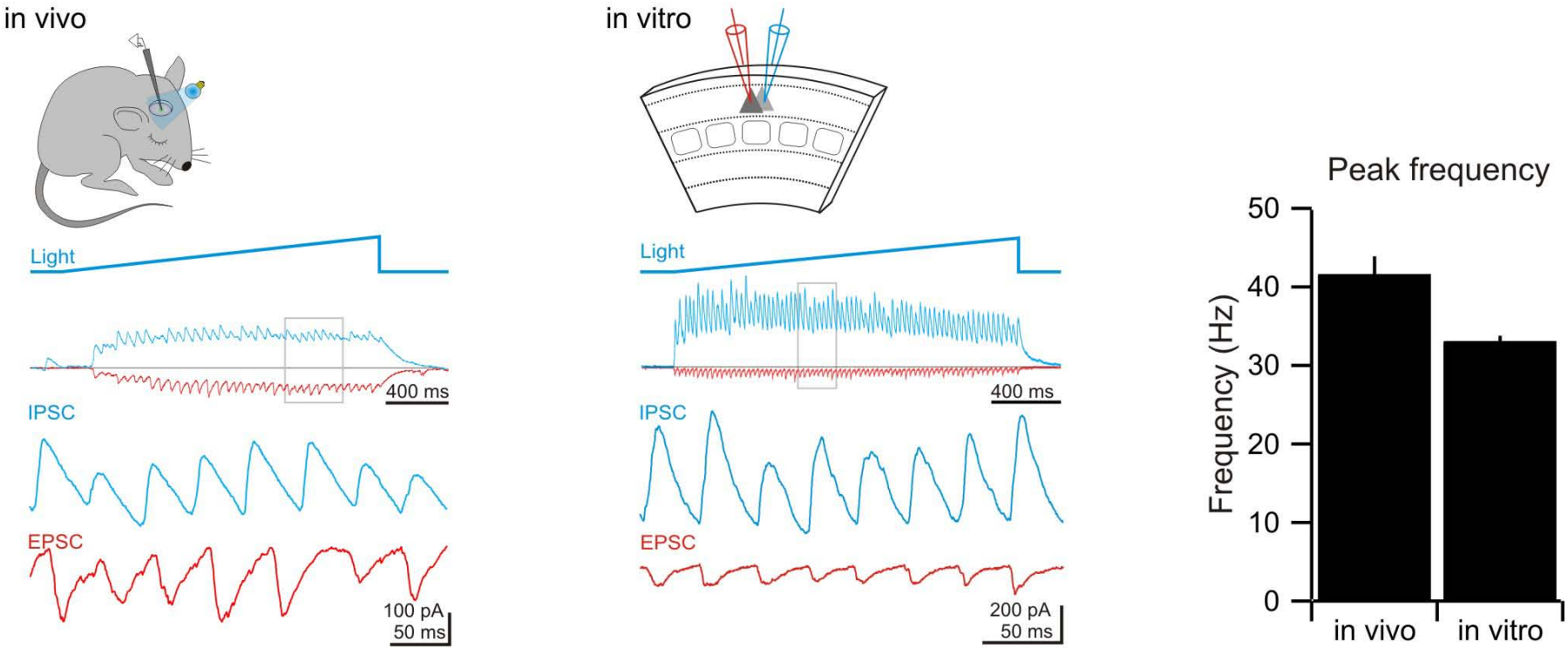




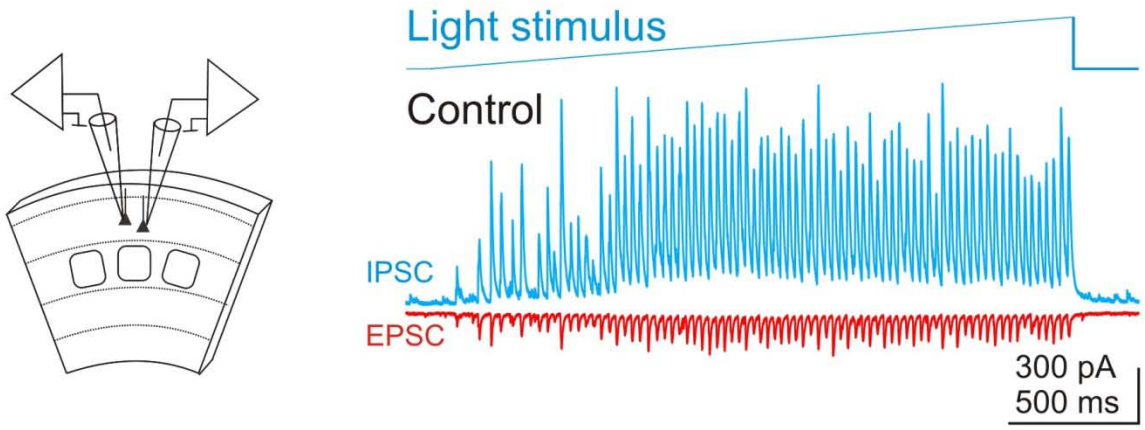



0.5 s
Light
LFP
Unit
500 µV
100 µV
100 ms


10
8
6
4
2
0
µV²/Hz
light
control
0
20
40
60
80
100

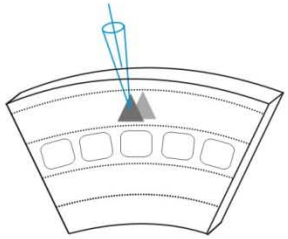


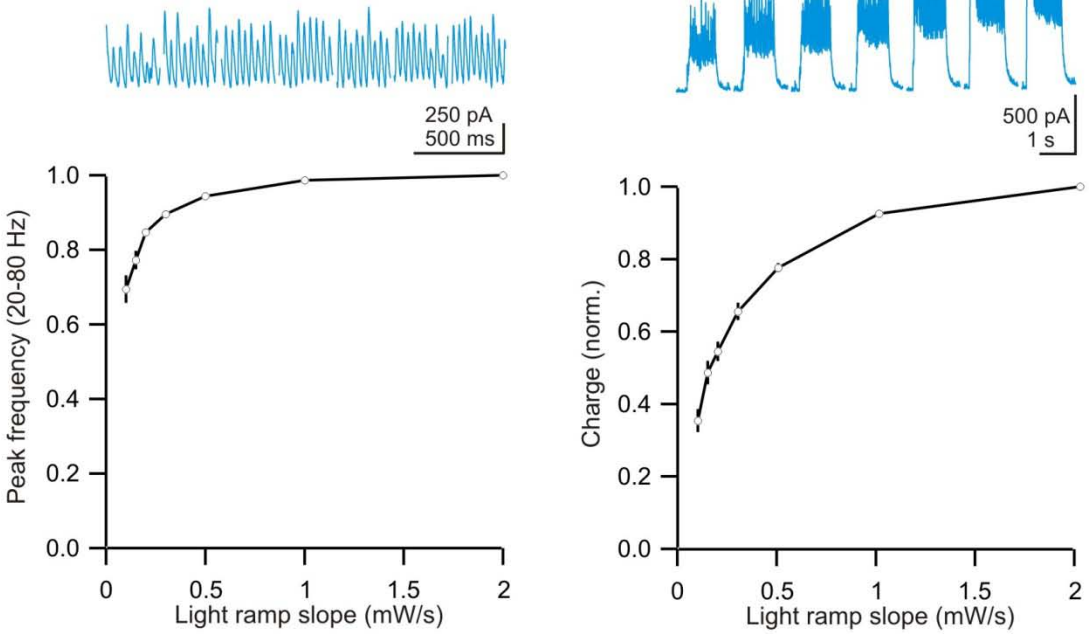
Light ramp generates oscillation at γ-frequency in layer 2/3 of somatosensory cortex



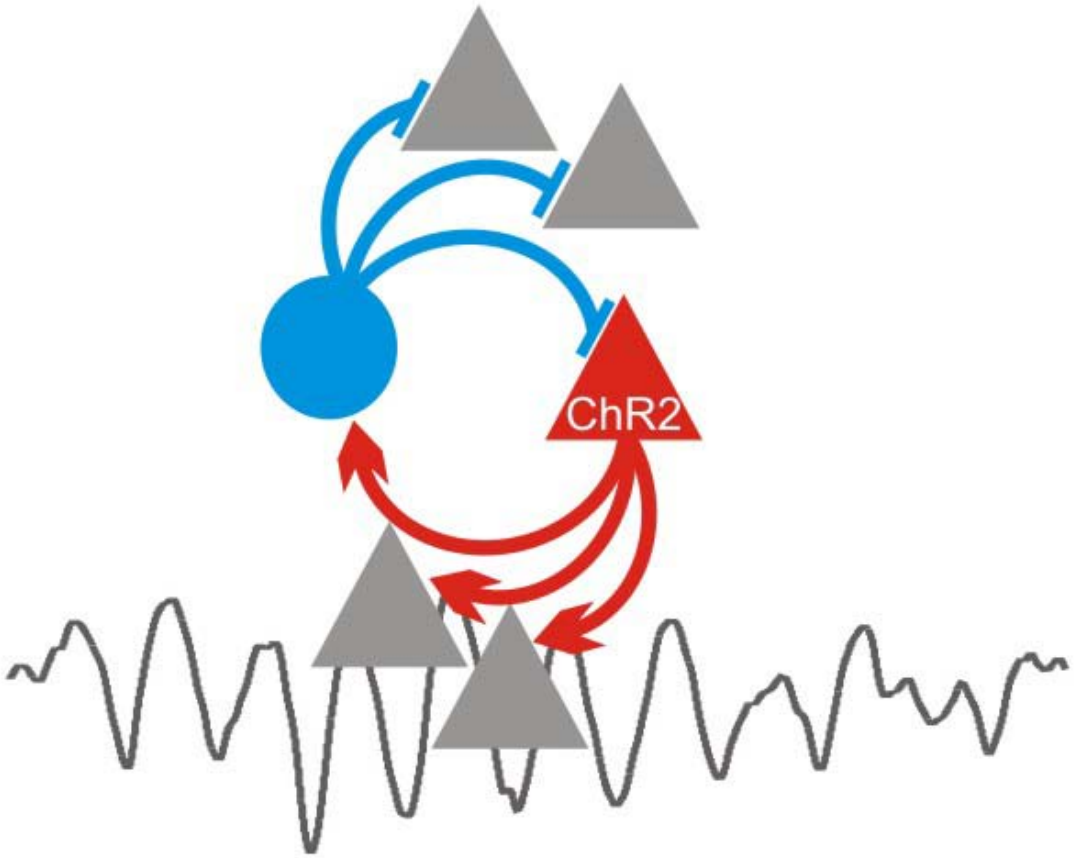
The oscillation relies on both Glutamatergic and GABAergic transmission

in vitro



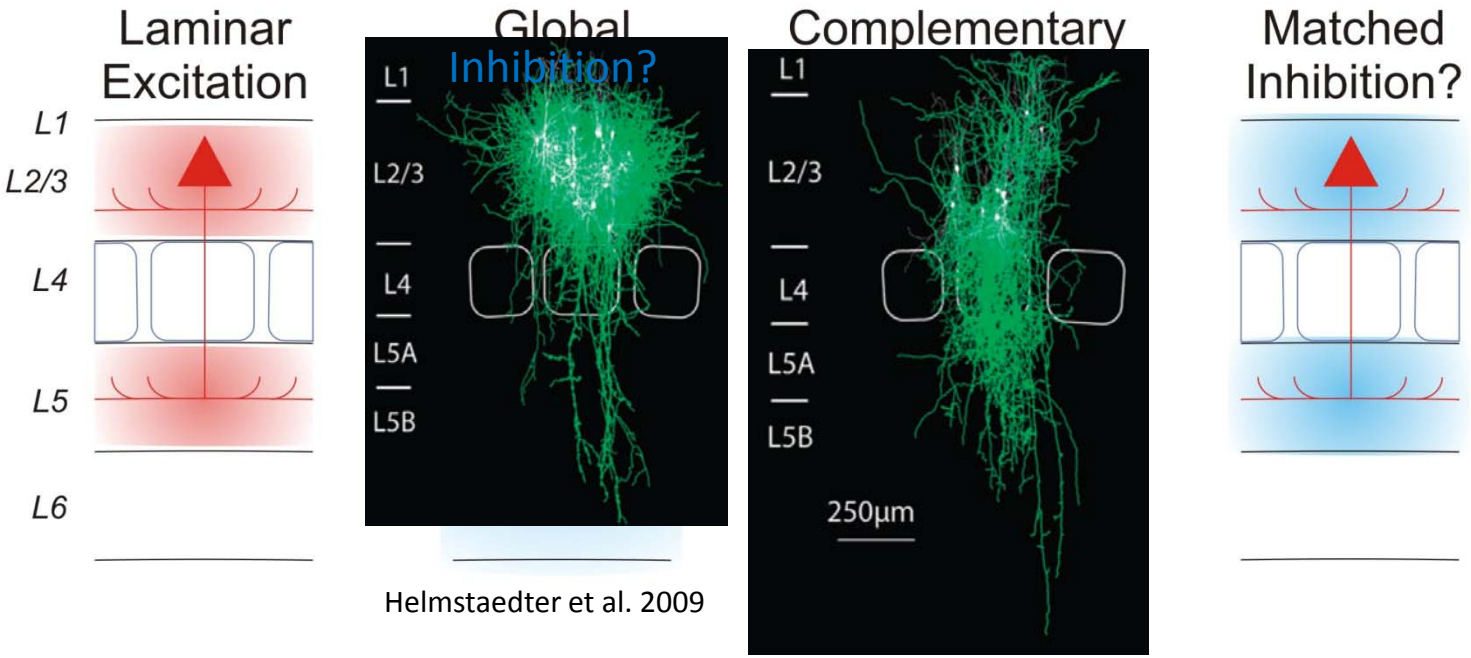


The frequency of the oscillations is only moderately sensitive to stimulus intensity

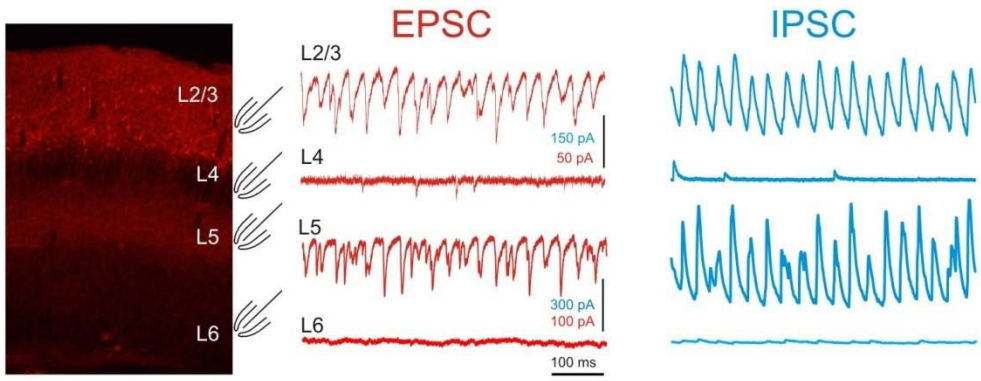

ChR2

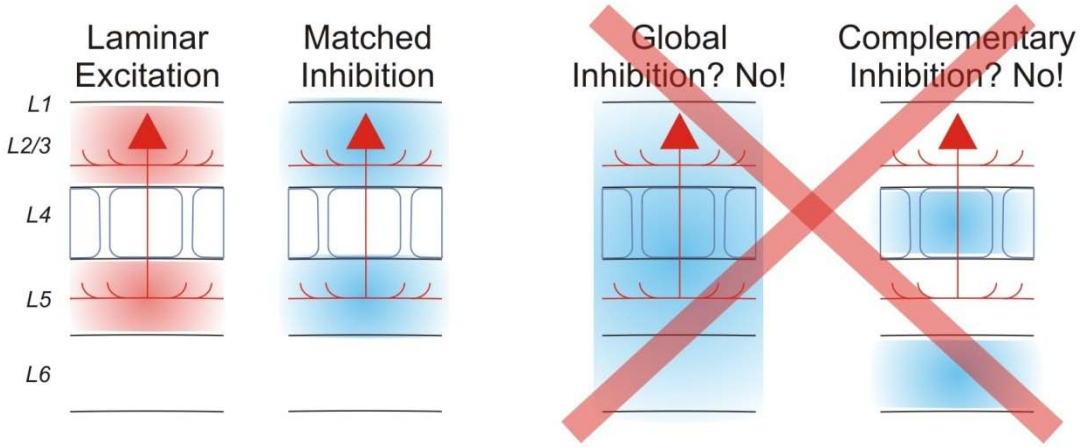
What is the Spatial Relationship between Excitation and Inhibition generated by Oscillatory activity in Layer 2/3?

Radial projections



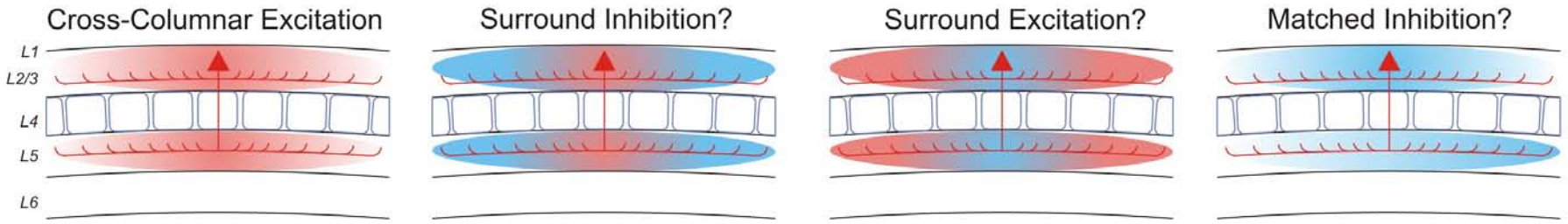
Helmstaedter et al. 2009

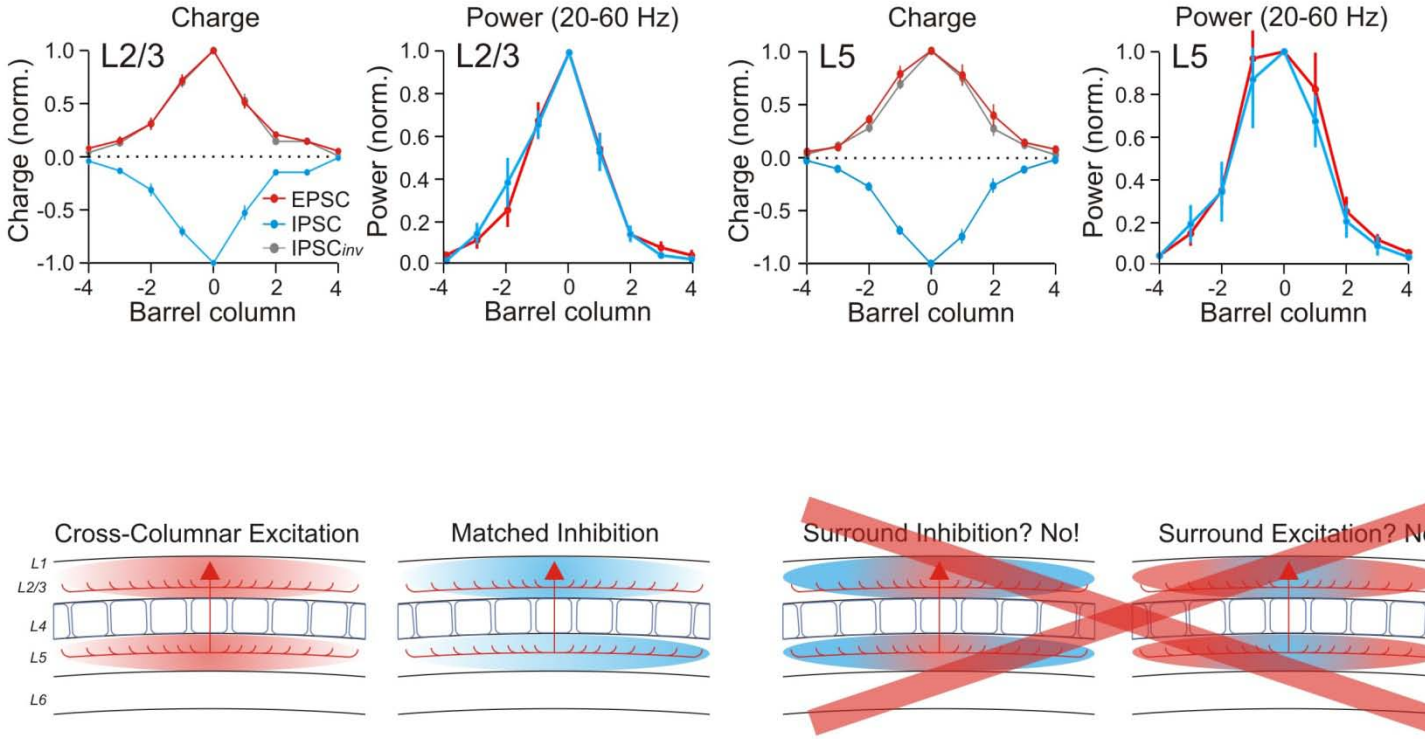




Inhibition generated by activity in layer 2/3 precisely matches excitation across **cortical layers**

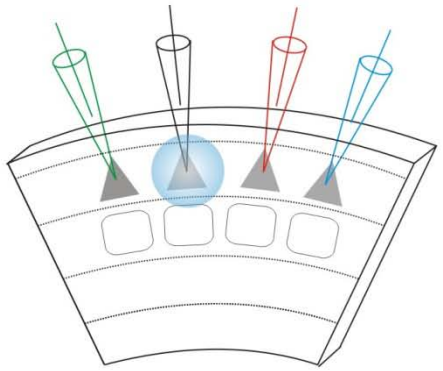
Tangential projections

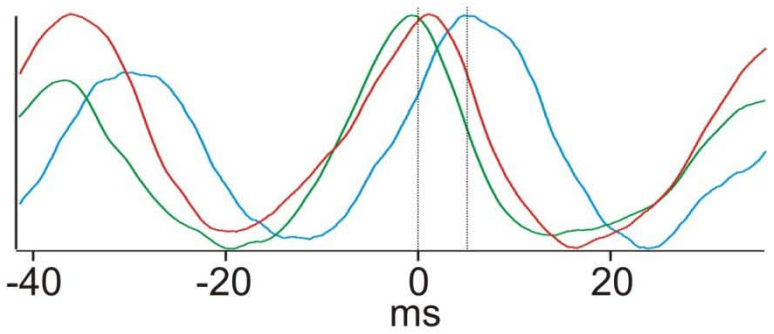



Charge
L2/3
Charge (norm.)
Barrel column
EPSC
IPSC
IPSCinv
Power (20-60 Hz)
L2/3
Power (norm.)
Barrel column
Charge
L5
Charge (norm.)
Barrel column
Power (20-60 Hz)
L5
Power (norm.)
Barrel column
Cross-Columnar Excitation
L1
L2/3
L4
L5
L6
Matched Inhibition
Surround Inhibition? No!
Surround Excitation? No!

Propagation speed of the wave:

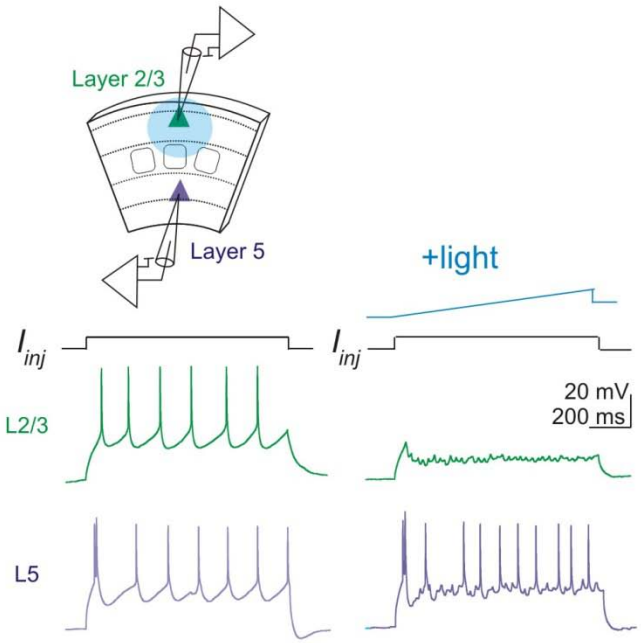
250 mm/s

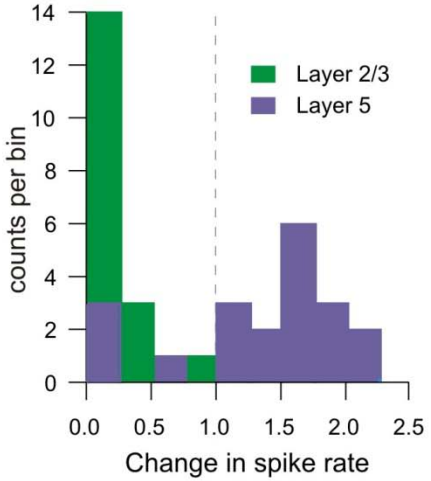


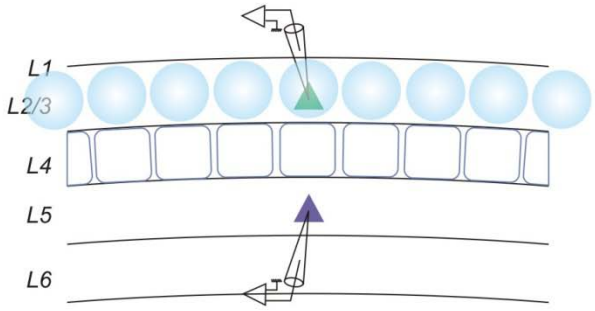


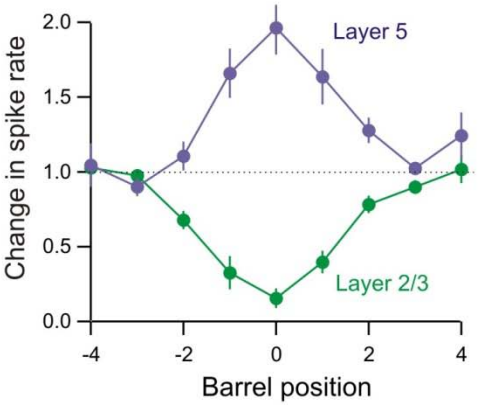
Excitation and Inhibition remain Proportional across Columns in both Layer 2/3 and 5

What is the functional consequence?

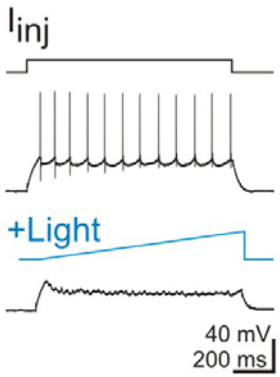

Layer 2/3
Layer 5
+light
I_{inj}
I_{inj}
20 mV
200 ms
L2/3
L5

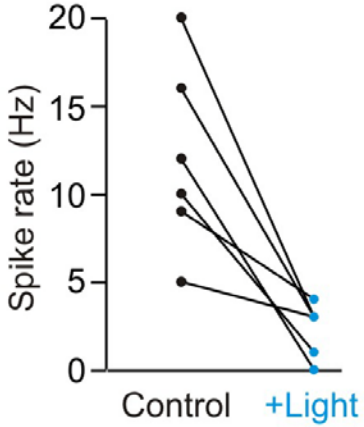

14
12
10
8
6
4
2
0
counts per bin
Layer 2/3
Layer 5
0.0
0.5
1.0
1.5
2.0
2.5
Change in spike rate


L1
L2/3
L4
L5
L6

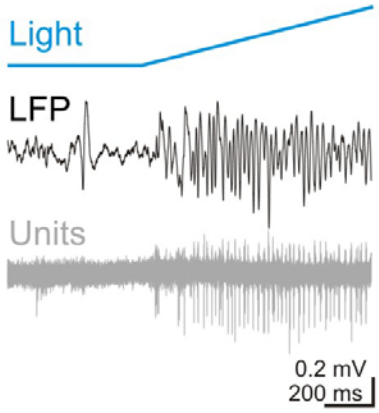

2.0
1.5
1.0
0.5
0.0
Change in spike rate
Layer 5
Layer 2/3
-4
-2
0
2
4
Barrel position

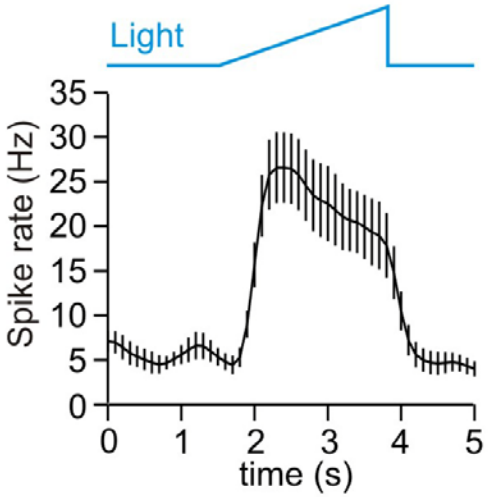
Whole-cell L2/3



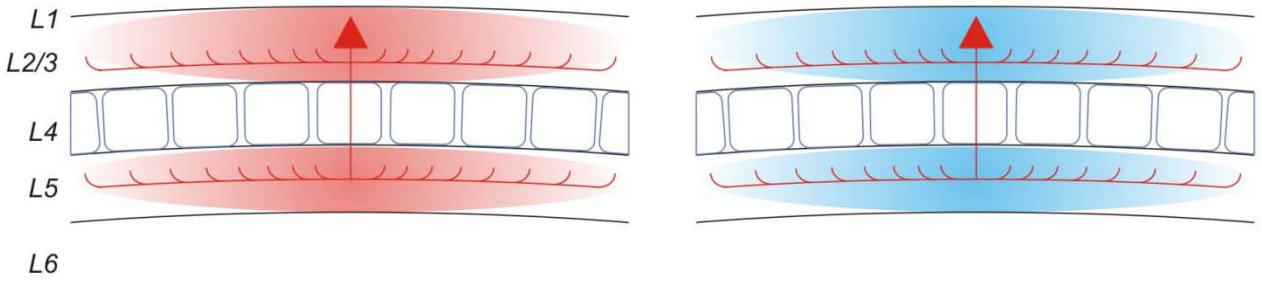


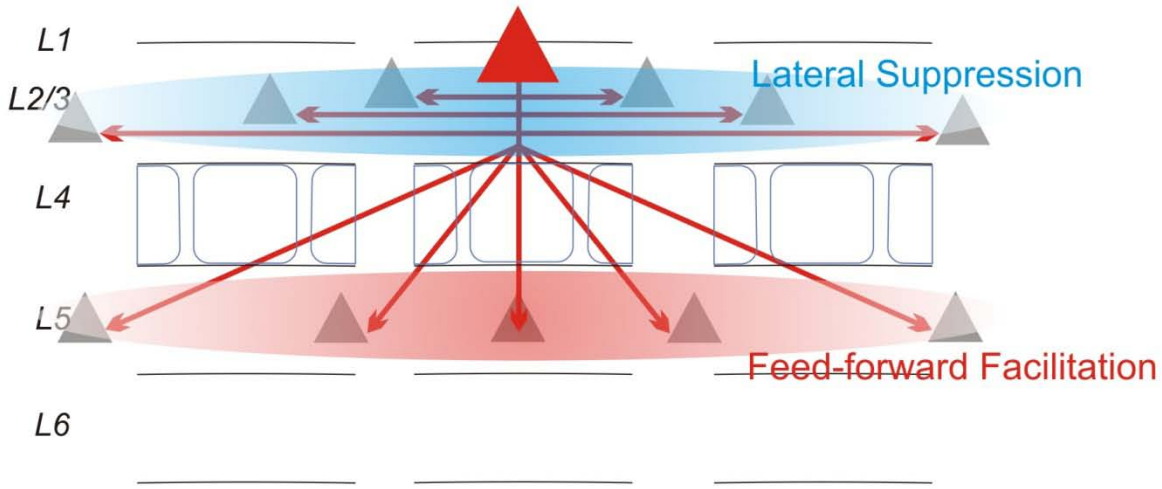
Units L5





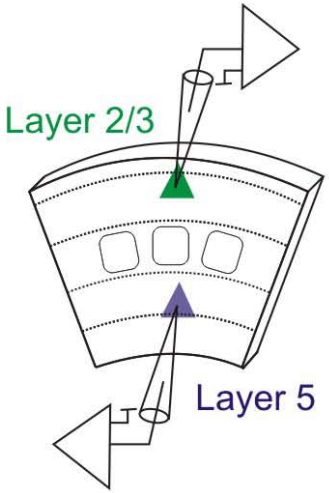
Excitation and Inhibition are Matched in Space Across Layers and Columns

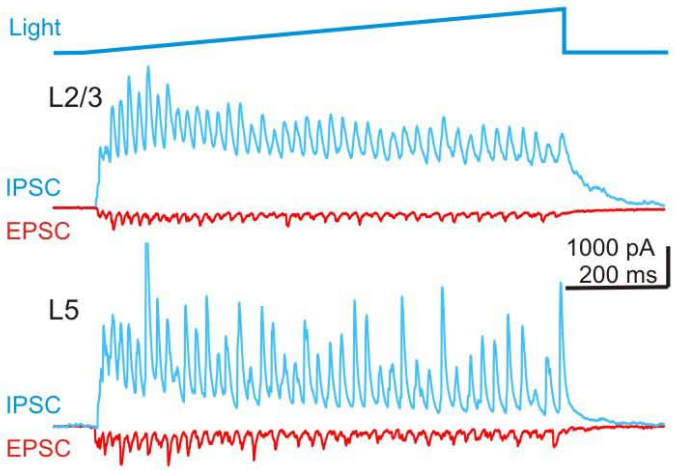


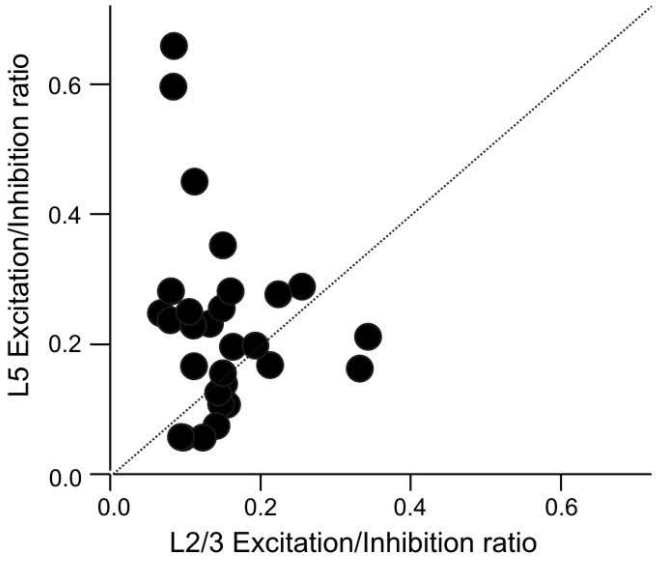


What is the mechanism?

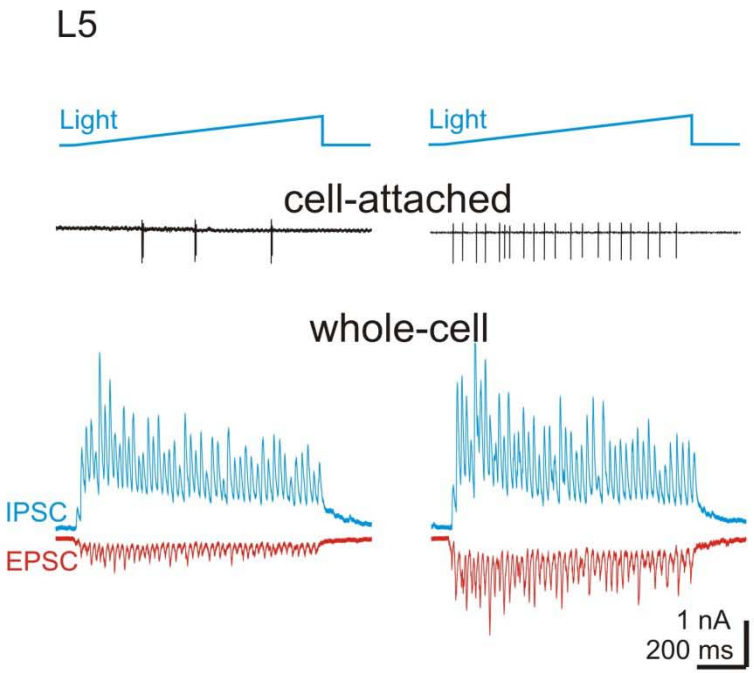
Excitation/Inhibition ratio is larger in Layer 5

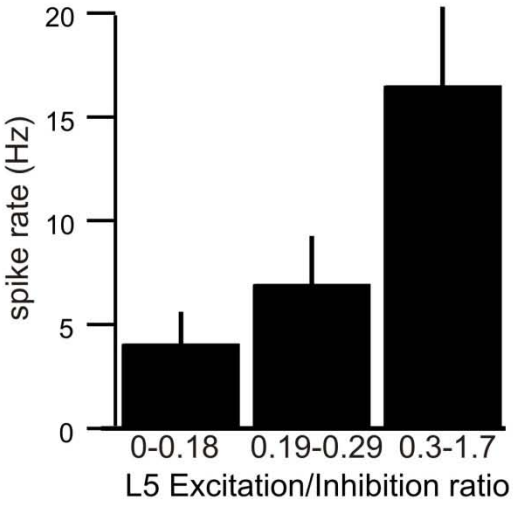




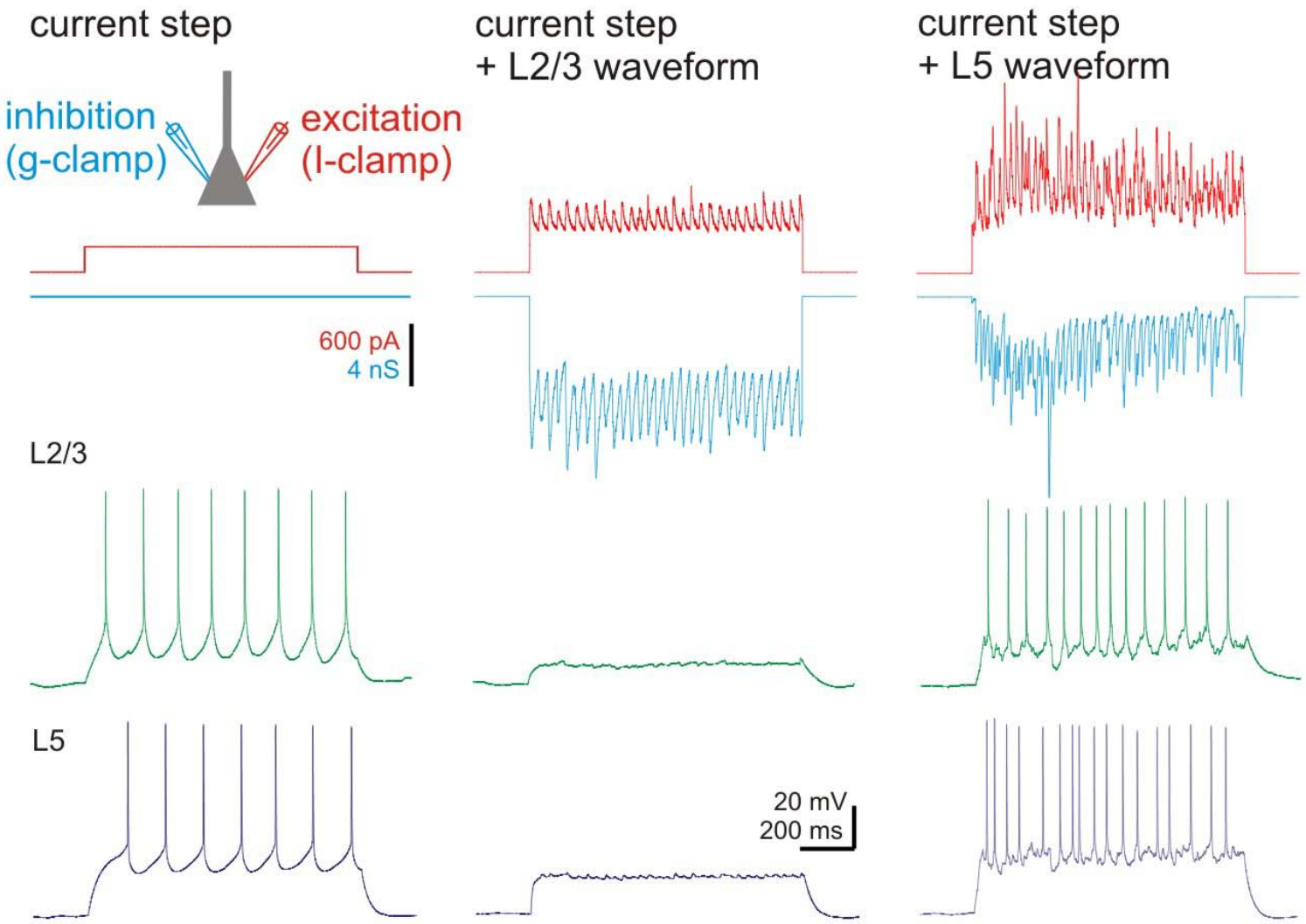


The larger the Excitation/Inhibition ratio the higher the Spike Rate

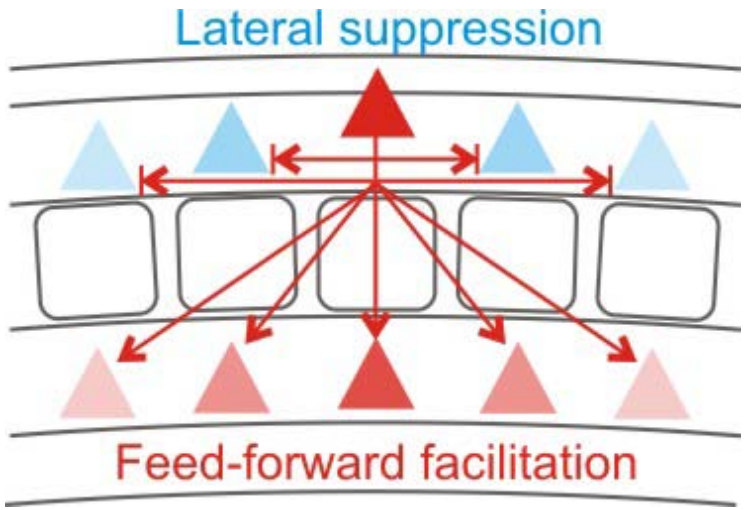




Can the difference in excitation-inhibition ratio account for
“lateral suppression” in layer 2/3
versus
“feed-forward facilitation” in layer 5?


current step
inhibition
(g-clamp)
excitation
(I-clamp)
600 pA
4 nS
L2/3
L5
current step
+ L2/3 waveform
20 mV
200 ms
current step
+ L5 waveform

Layer specific differences in Excitation/Inhibition Ratio generate
“lateral suppression” in layer 2/3
“feed-forward facilitation” in layer 5



Conclusions

Single Neuron

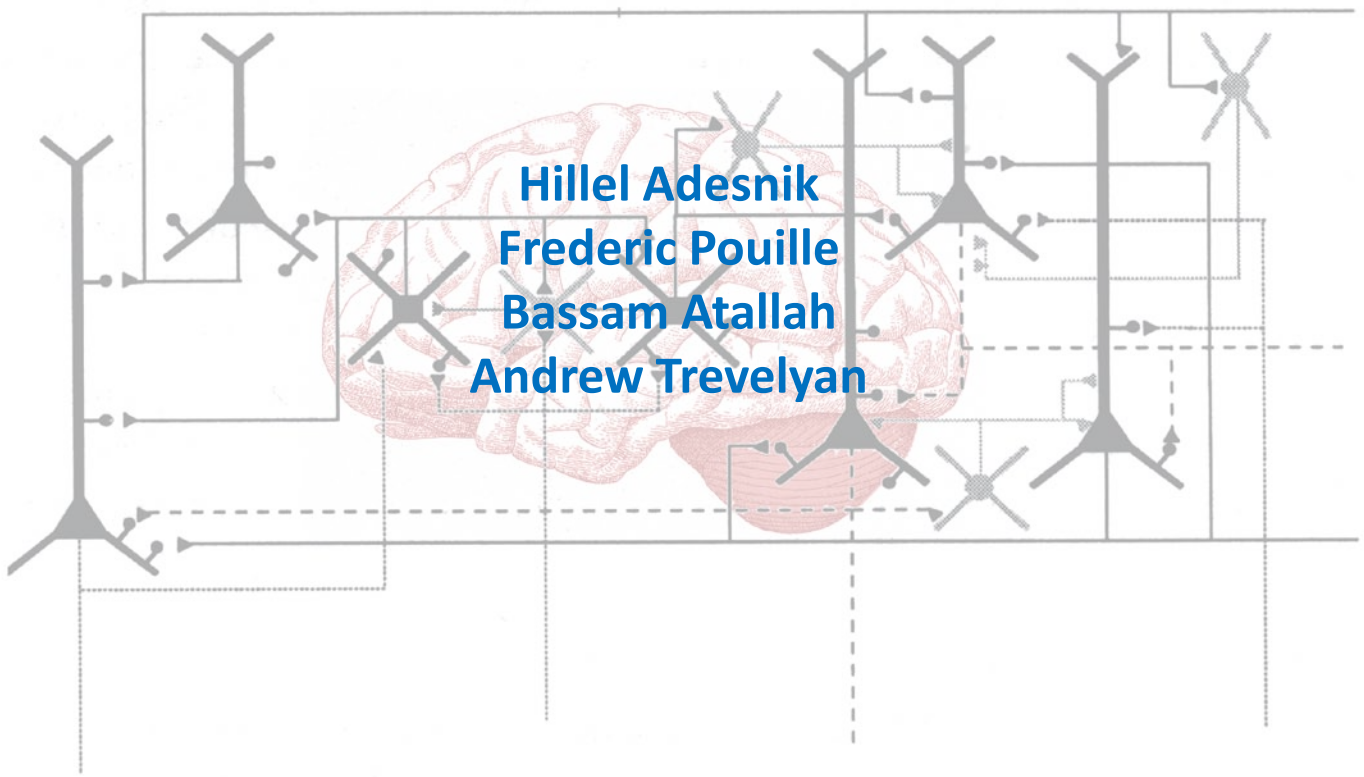
Spatial relationship between Excitation and Inhibition along the somatodendritic axis enables differential control of neuronal output:

Dendritic inhibition: rightward shift of input-output curve
Somatic inhibition: reduction in maximal firing rate

Network:

Excitation and Inhibition are matched in space:
Radially, across layers
Tangentially, across columns

Local differences in Excitation/Inhibition generate
"Lateral suppression" in layer 2/3
"Feed-forward facilitation" in layer 5
⟶ competition between columns for representation in cortical space



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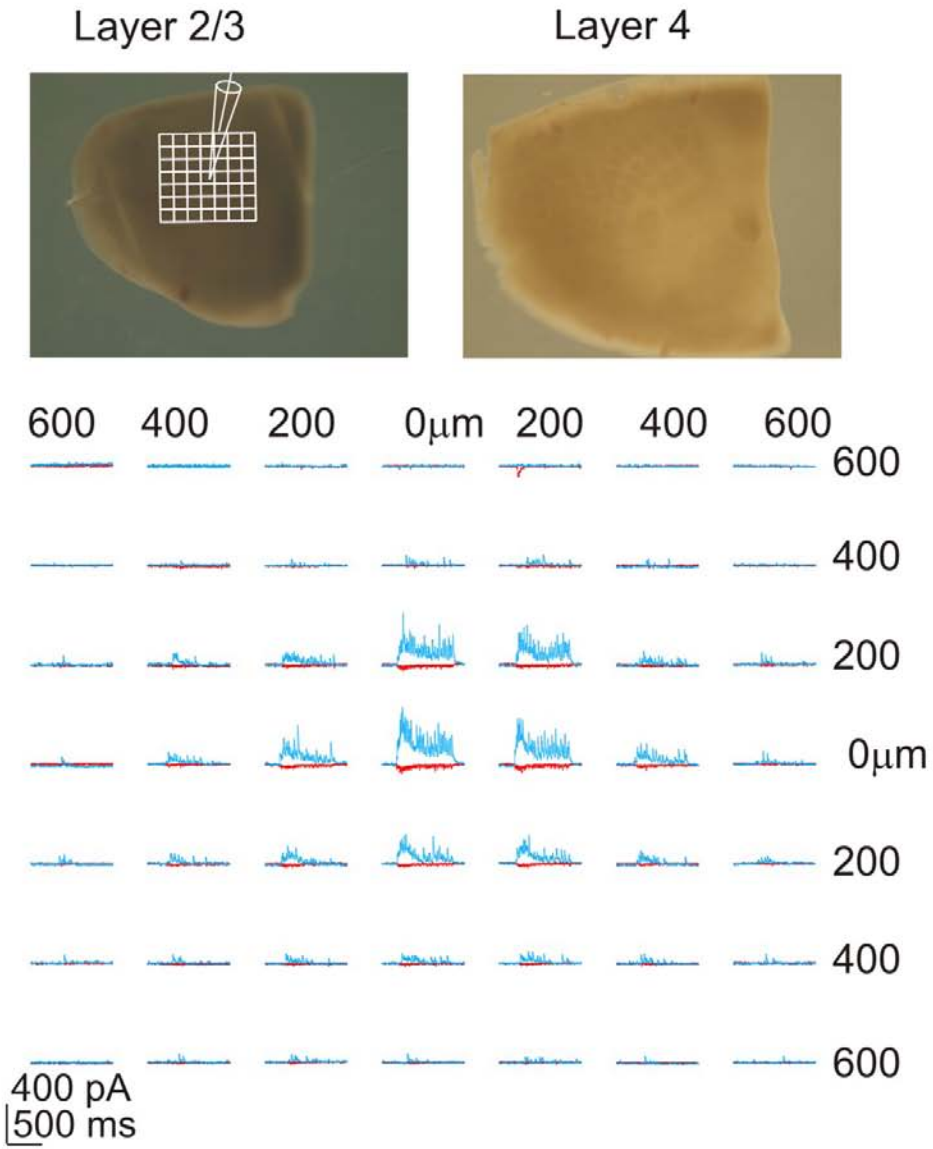
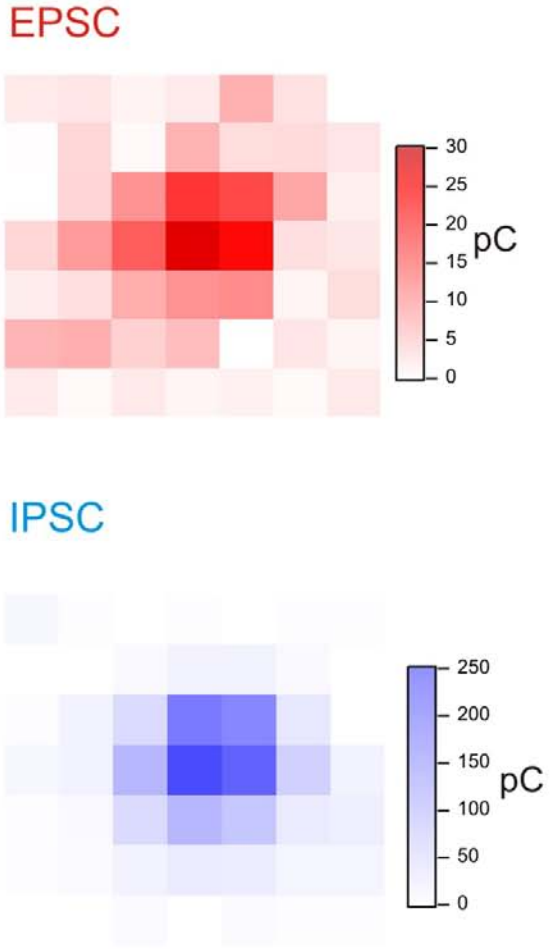
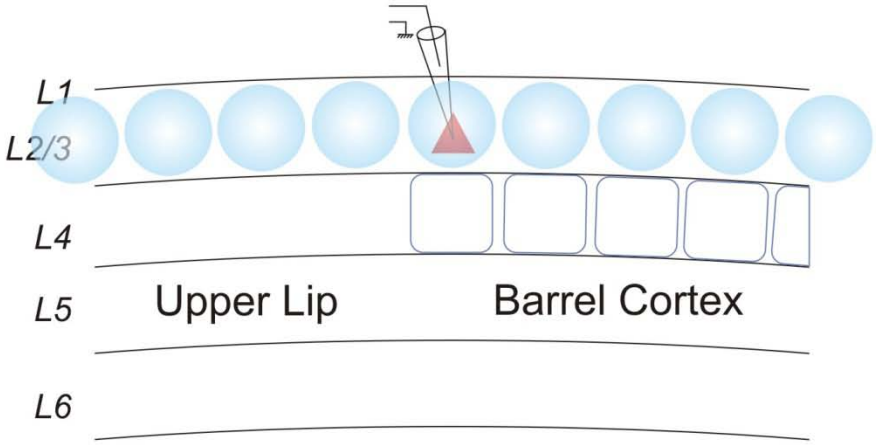
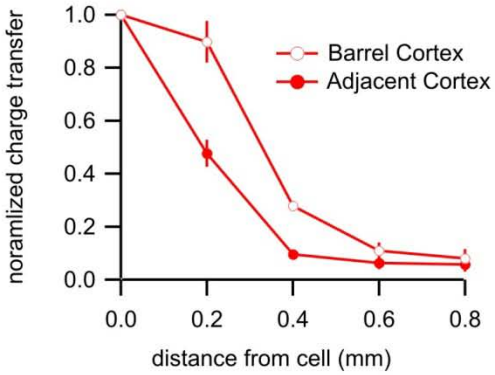

Layer 2/3
Layer 4
600
400
200
0μm
200
400
600
600
400
200
0μm
200
400
600
400 pA
500 ms

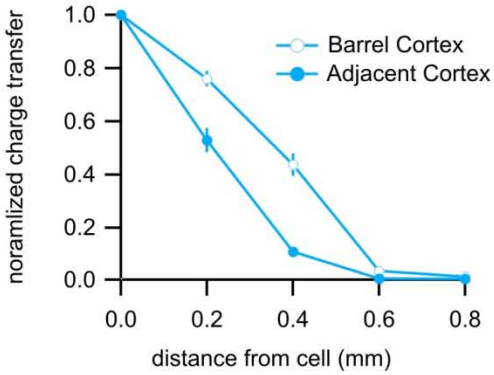

EPSC
30
25
20
15
10
5
0
pC
IPSC
250
200
150
100
50
0
pC

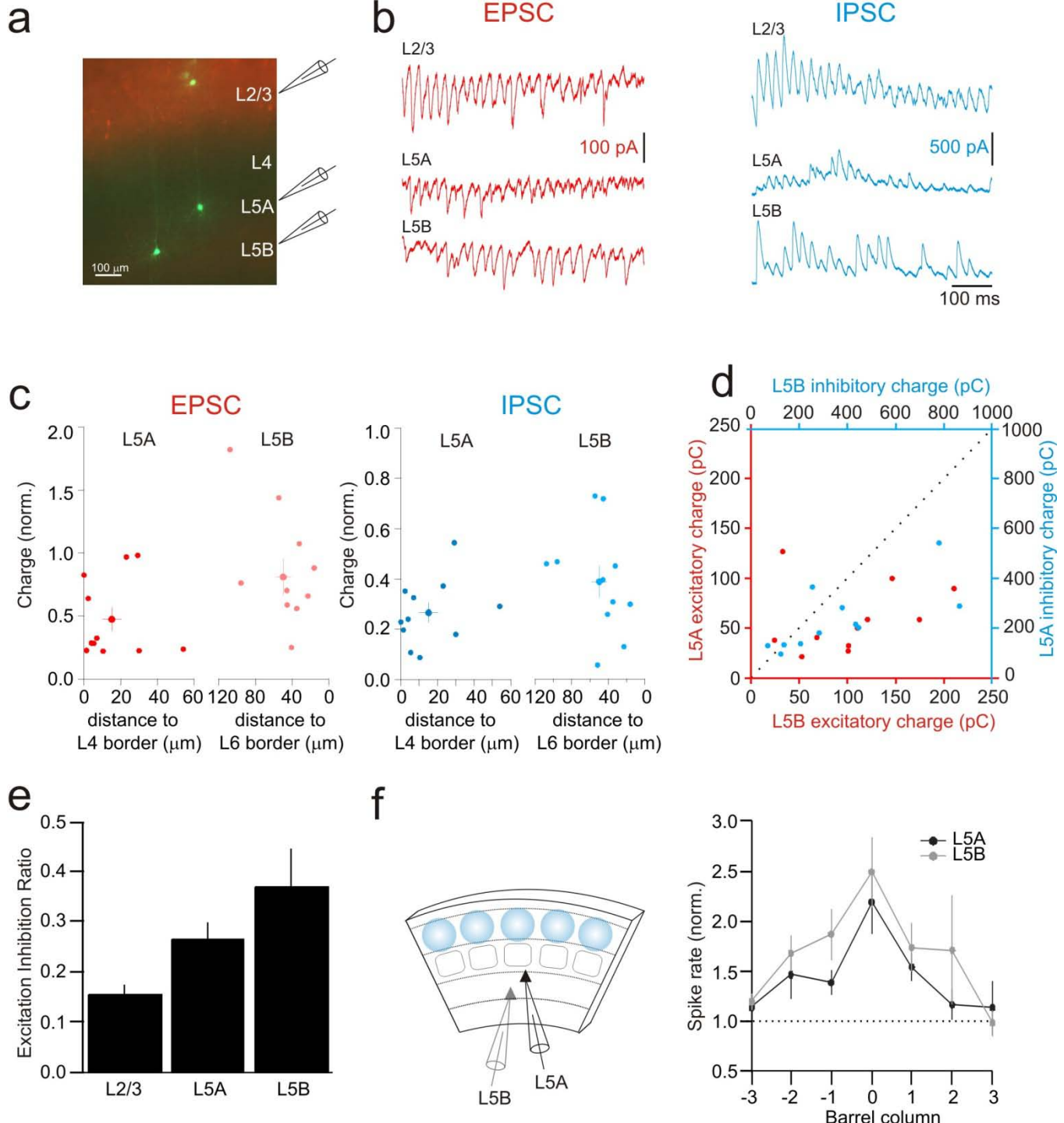
Control 2

How about neighboring cortices?








a
L2/3
L4
L5A
L5B
100 µm
b
EPSC
L2/3
100 pA
L5A
L5B
IPSC
L2/3
500 pA
L5A
L5B
100 ms
c
EPSC
L5A
L5B
Charge (norm.)
distance to L4 border (µm)
distance to L6 border (µm)
IPSC
L5A
L5B
Charge (norm.)
distance to L4 border (µm)
distance to L6 border (µm)
d
L5B inhibitory charge (pC)
L5A excitatory charge (pC)
L5A inhibitory charge (pC)
L5B excitatory charge (pC)
e
Excitation Inhibition Ratio
L2/3
L5A
L5B
f
L5B
L5A
Spike rate (norm.)
L5A
L5B
Barrel column