Large Scale Models of the Neocortex

Computational Models of Neural Systems

Lecture 8.3

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Outline

- Cortical layers and cell types
- Basic model of cortical microcircuitry
- Allen Institute for Brain Science: modeling mouse V1
- Blue Brain Project: modeling rat S1

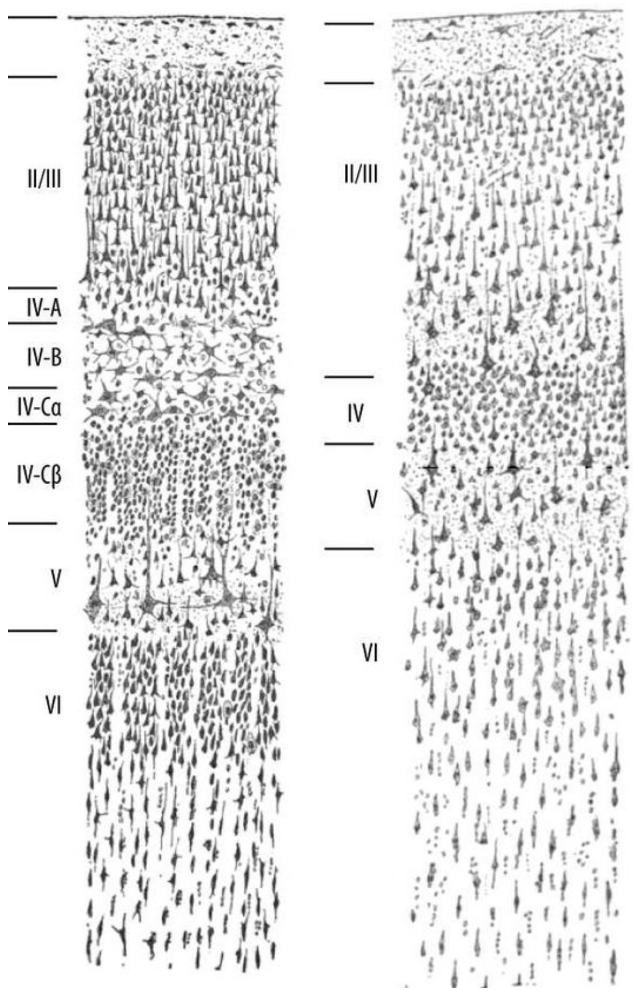
Neocortex Has Six Layers

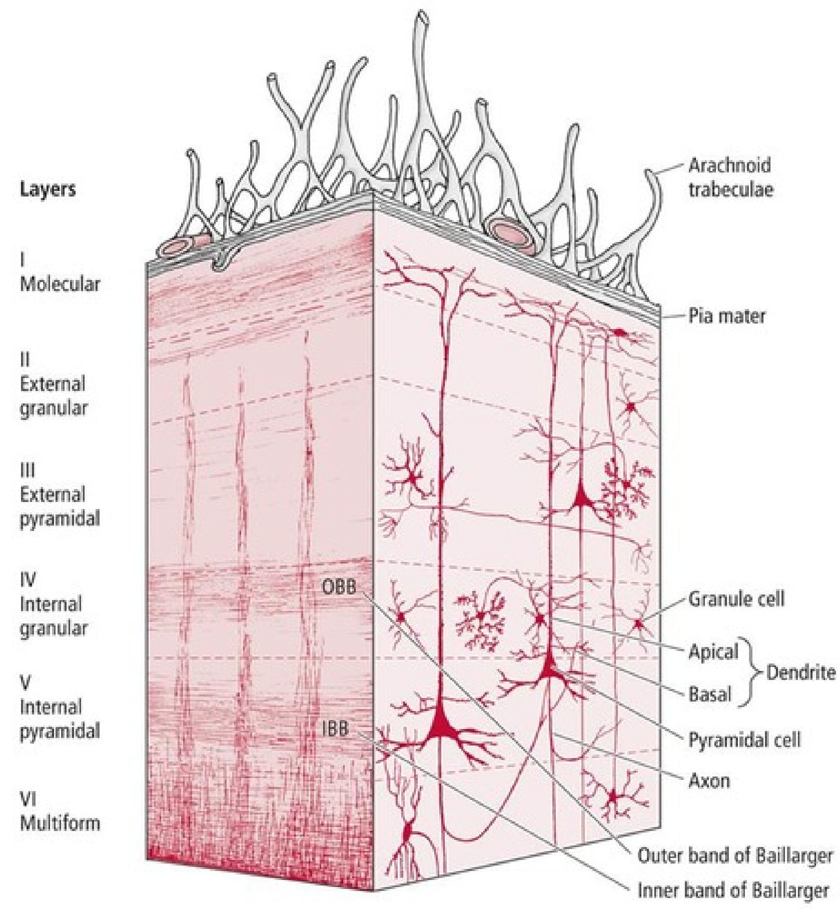
- Total thickness is roughly 1 mm (rats) to 3 mm (humans)
- Thickness of each layer varies between brain areas
- Some layers have sublayers

Ramon y Cajal (2011)

Left: adult human visual cortex

Right: adult human motor cortex

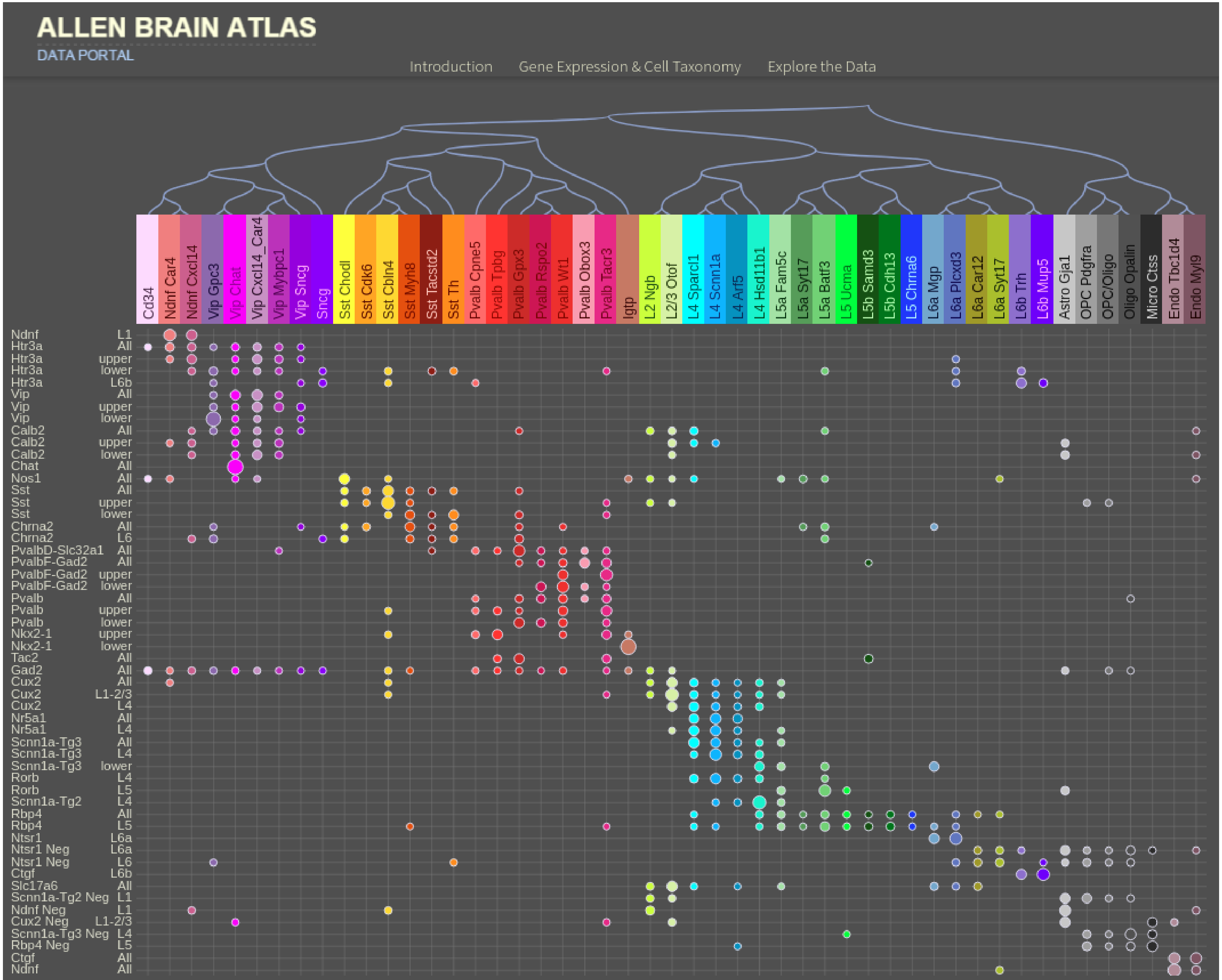




Roughly 50 Cell Types

- Allen Institute for Brain Science: 42 neuron types in mouse V1
  - 19 excitatory types
  - 23 inhibitory types
- Inhibitory cells: four major clusters labeled by molecular markers:
  - parvalbumin (Pvalb)
  - somatostatin (Sst)
  - vasoactive intestinal polypeptide (Vip)
  - neuron-derived neurotrophic factor (Ndnf)
- Excitatory types are specific to each layer
  - pyramidal cells, star pyramidal cells, stellate cells
- Another 7 cell types are non-neurons, such as glial cells, astrocytes, and oligodendrocytes.

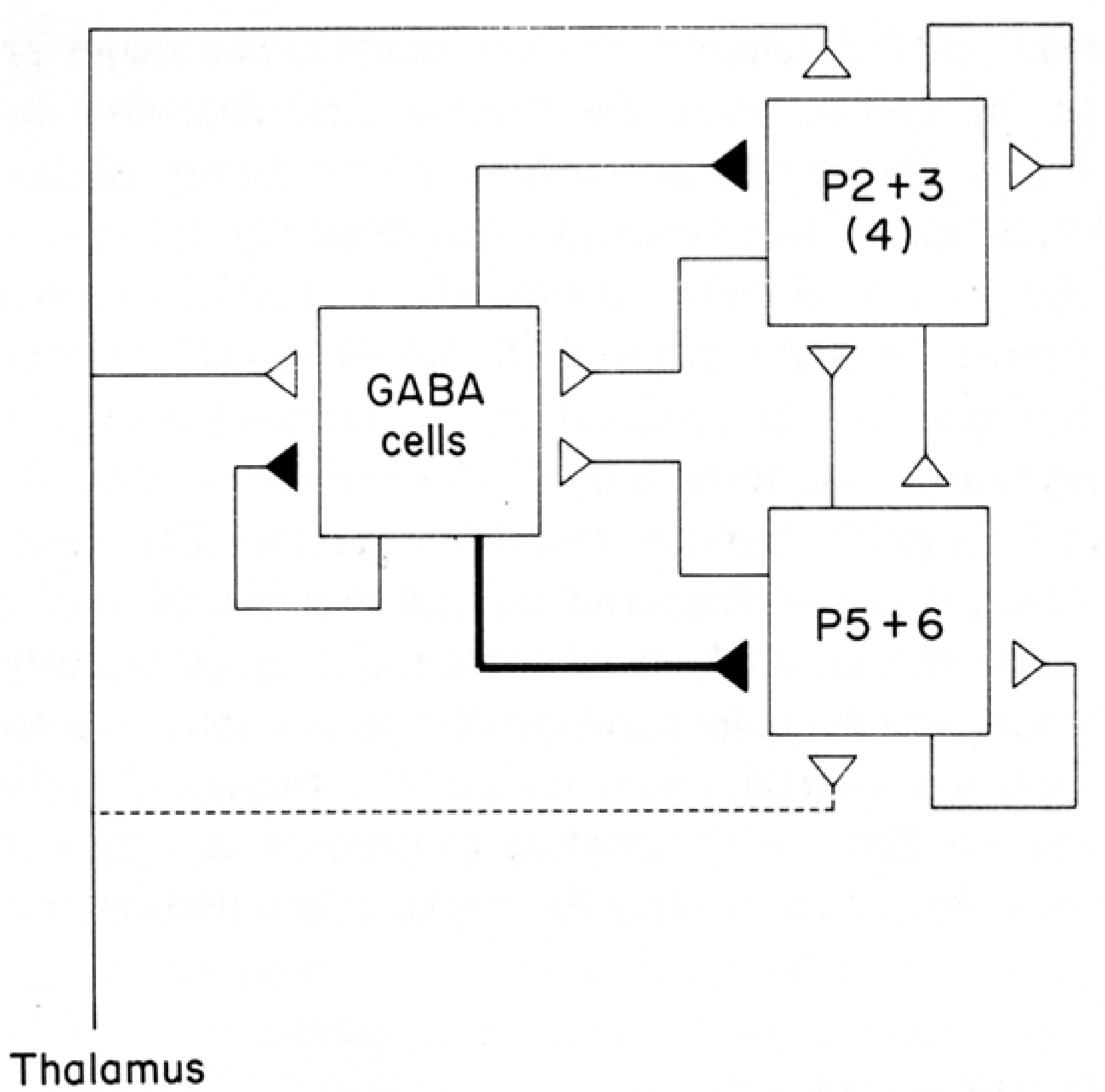
casestudies.bain-map.org/celltax



Cortical Micro-Columns

- First identified in somatosensory cortex by Mountcastle; confirmed in visual cortex by Hubel and Wiesel.
- 1 cubic mm of cortex contains cells that share the same receptive field and are mutually connected by local interneurons
- Other cell types provide long-range connections between micro-columns.
- Organizing principles include:
  - Recurrent excitation
  - Feedforward, feedback, and recurrent inhibition
  - Lateral inhibition

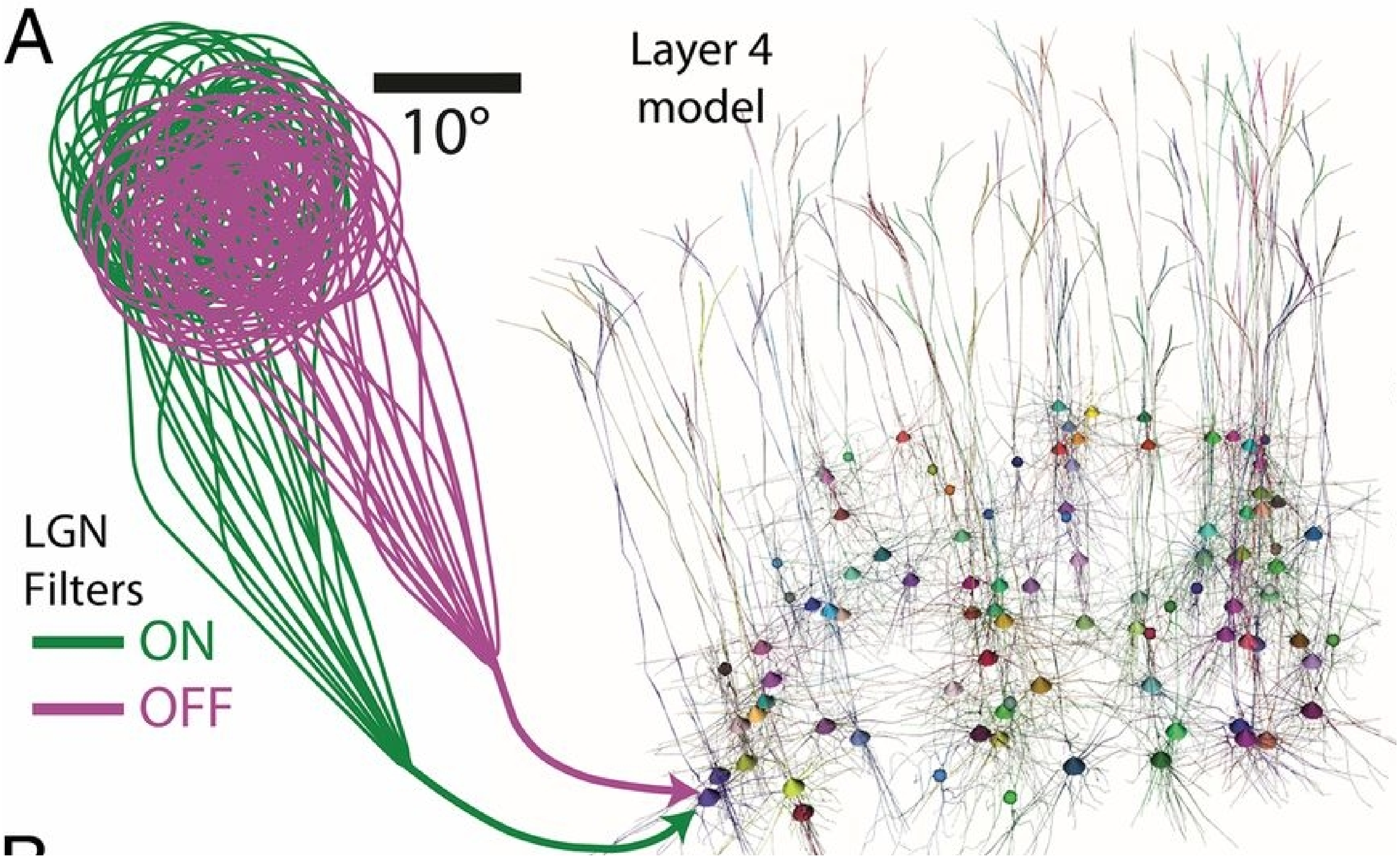
Early Microcircuit Model (Douglas et al. 1989)



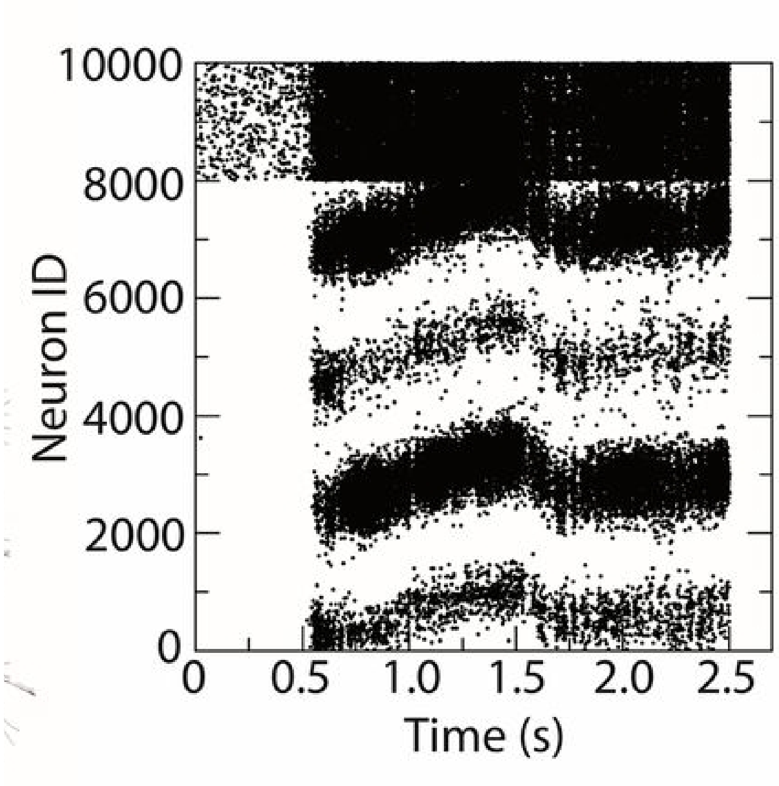
Allen Institute: Modeling Mouse V1

- Models of individual neurons
  - Point neuron models: LIF and GLIF (generalized leaky integrate and fire)
  - Biophysical models: explicit representations different conductances: 15-16 free parameters optimized by genetic algorithm; passive dendrites
  - More detailed biophysical models with active dendritic conductances
- System-Level models: three levels of granularity
  - Population representation (mean firing rate)
  - Point neuron representation: each neuron is a GLIF model
  - Models with biophysically realistic neurons (expensive!)

10,000 Layer 4 Cells (1% shown)

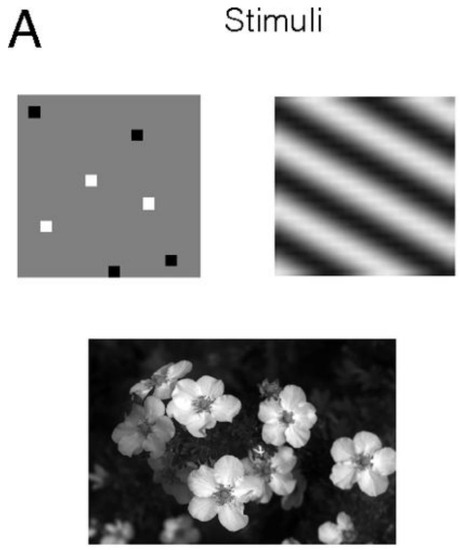


Response to Visual Stimulation

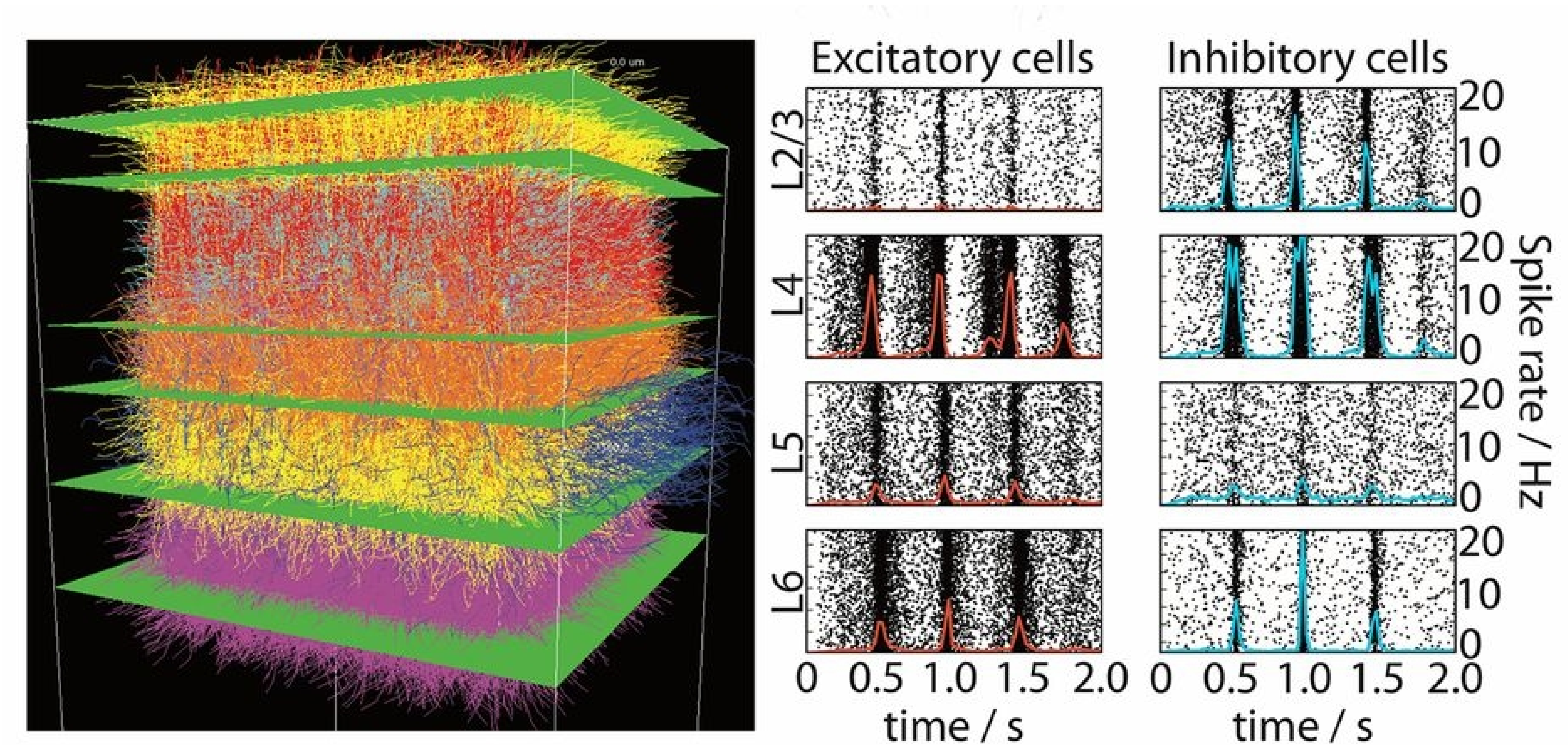


Fast-spike interneurons

Pyramidal cells grouped by orientation pref.

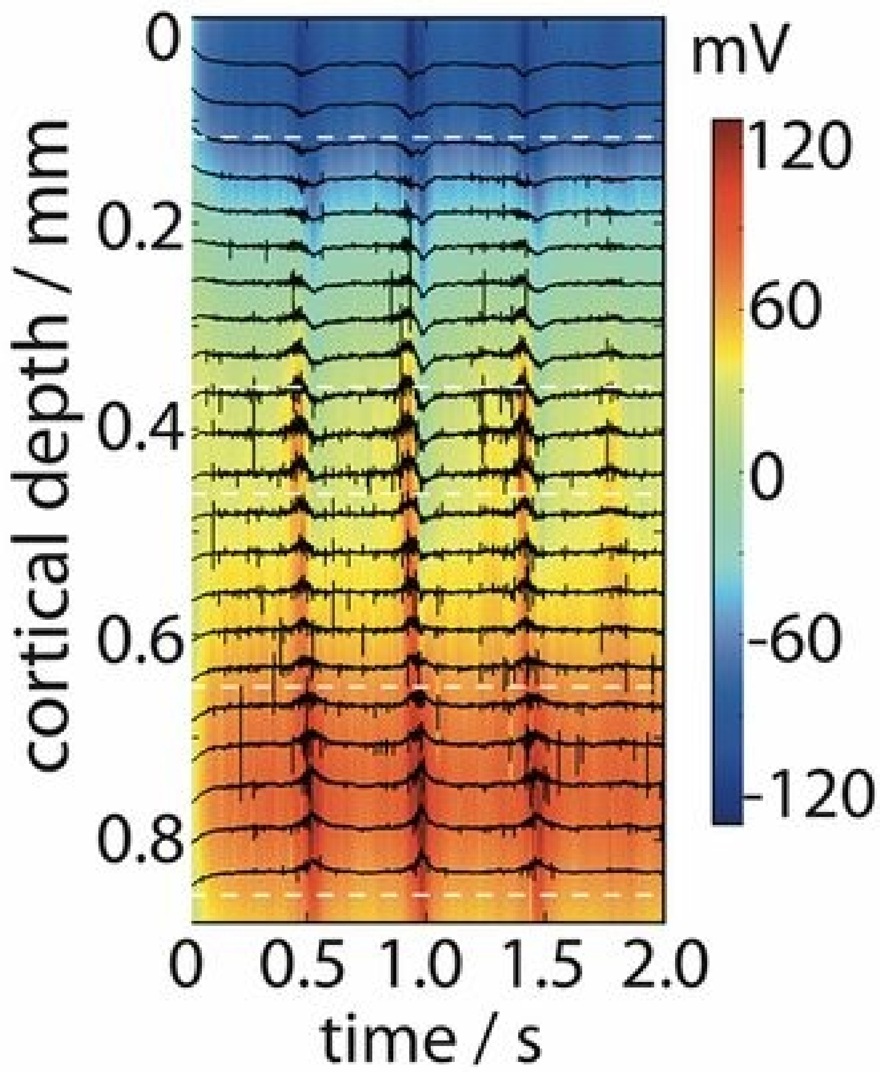


Multilayer Network Model (24,000 cells)



Response to drifting grating

Local Field Potential At Depth



What Can These Models Do?

The models can fit statistical physiological data such as:

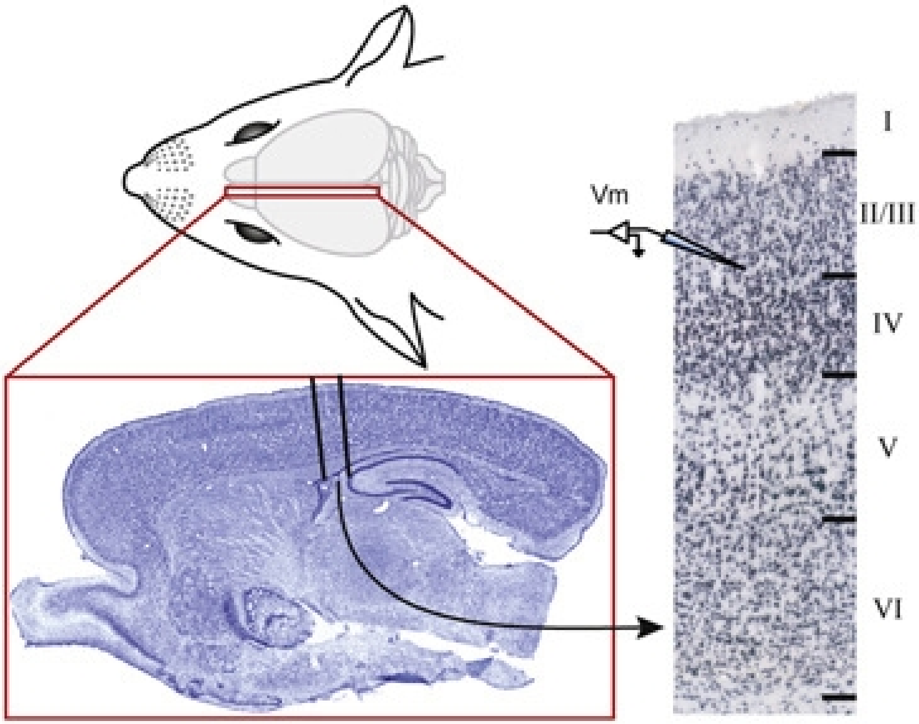
- Firing rates of various cell types
  - Baseline rates
  - Responses to stimuli
- Spike correlations between neurons, or with LFP
- Extracellular voltage (LFP: local field potential) at various cortical depths

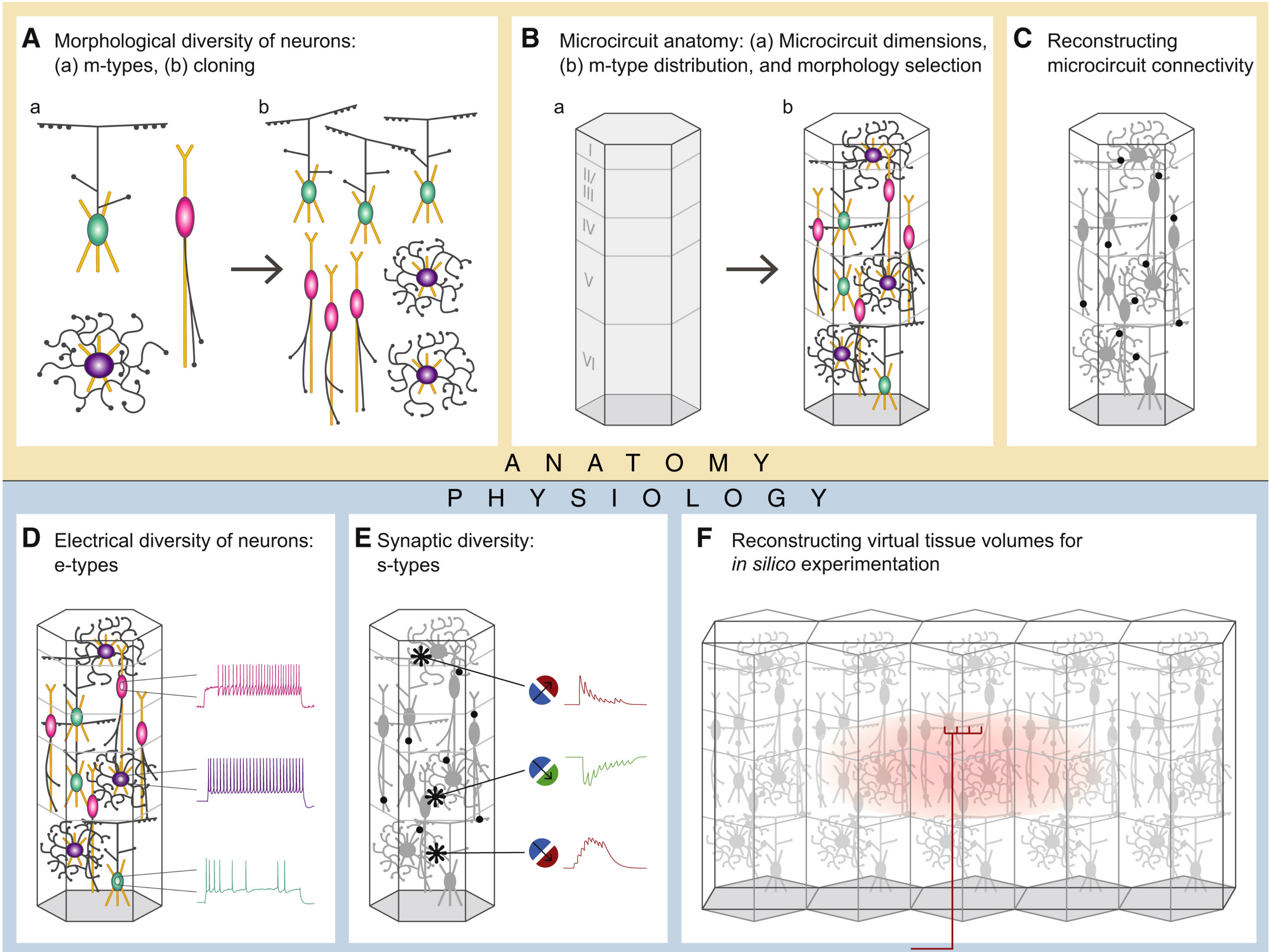
What these models cannot do:

- Perform computations comparable to real V1 neurons
- We don't know the actual wiring diagram for V1
- We don't have models for the top-down inputs to V1

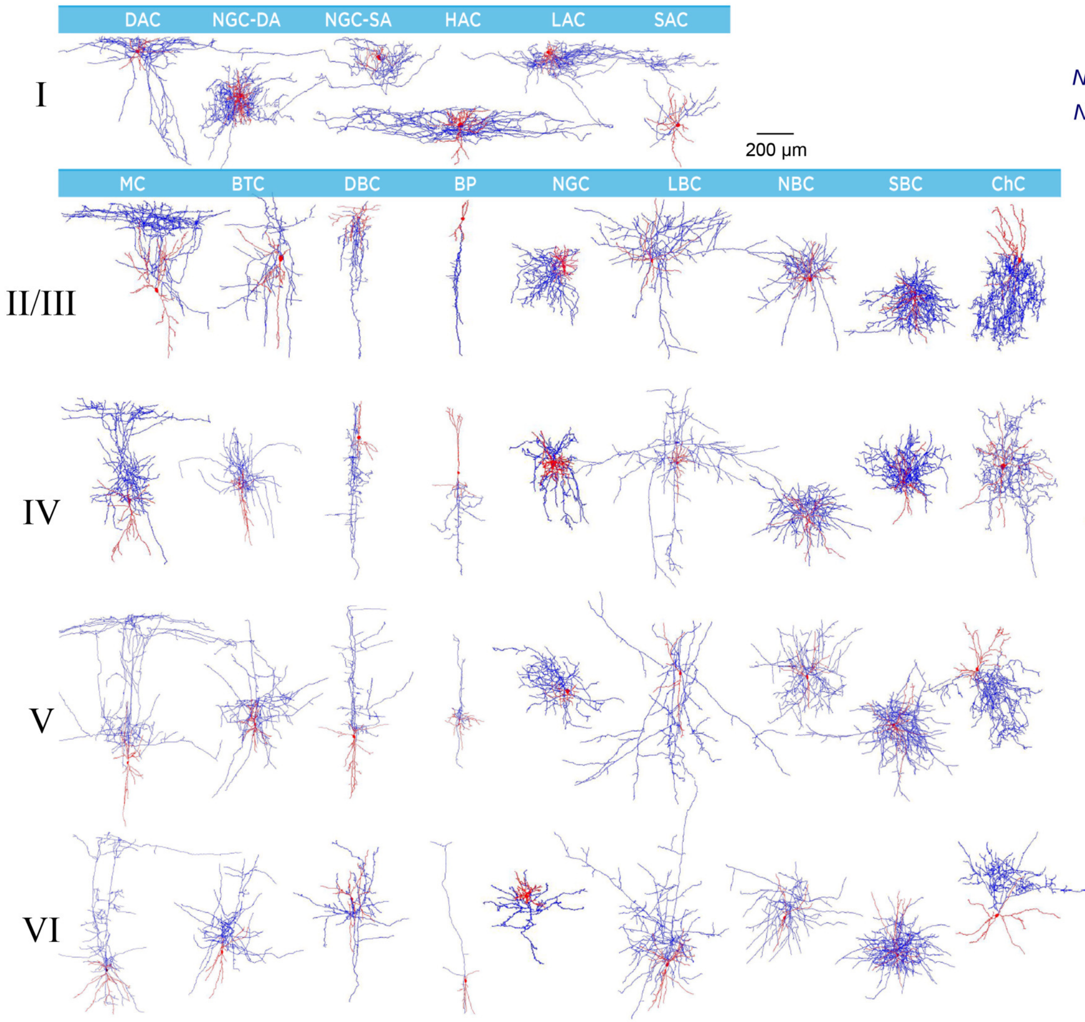
Henry Markram: Blue Brain Project

- Goal: reconstruct roughly 0.3 mm^3 of rat somatosensory cortex.
- About 31,000 neurons:
  - 55 layer-specific morphological subtypes, or
  - 207 morpho-electrical subtypes
- Rich connectivity:
  - roughly 8 million connections
  - roughly 37 million synapses



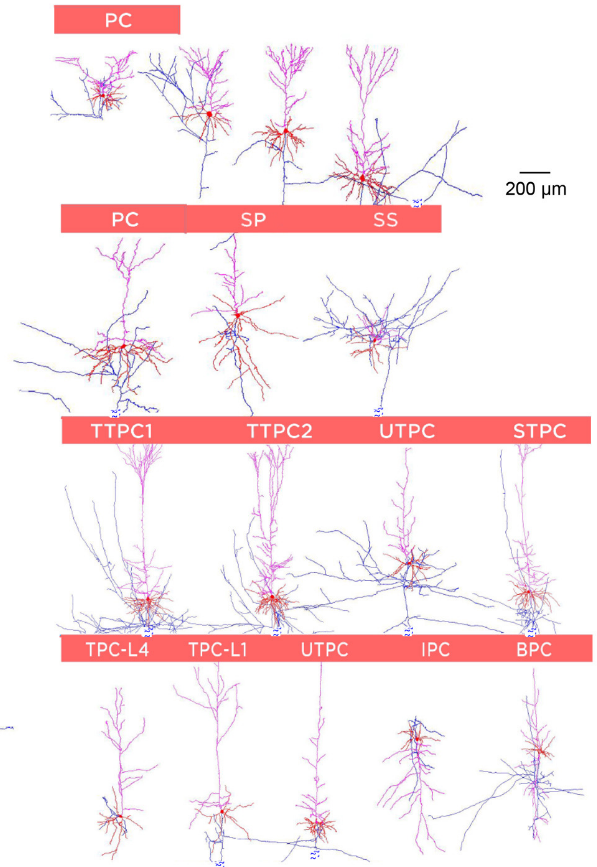

A Morphological diversity of neurons:
(a) m-types, (b) cloning
a
b
B Microcircuit anatomy: (a) Microcircuit dimensions,
(b) m-type distribution, and morphology selection
a
b
I
II/
III
IV
V
VI
C Reconstructing
microcircuit connectivity
A N A T O M Y
P H Y S I O L O G Y
D Electrical diversity of neurons:
e-types
E Synaptic diversity:
s-types
F Reconstructing virtual tissue volumes for
in silico experimentation

Cell Morphologies



DAC	Descending Axon Cell
NGC-DA	Neurogliaform Cell with dense axonal arborization
NGC-SA	Neurogliaform Cell with slender axonal arborization

HAC	Horizontal Axon Cell
LAC	Large Axon Cell
SAC	Small Axon Cell

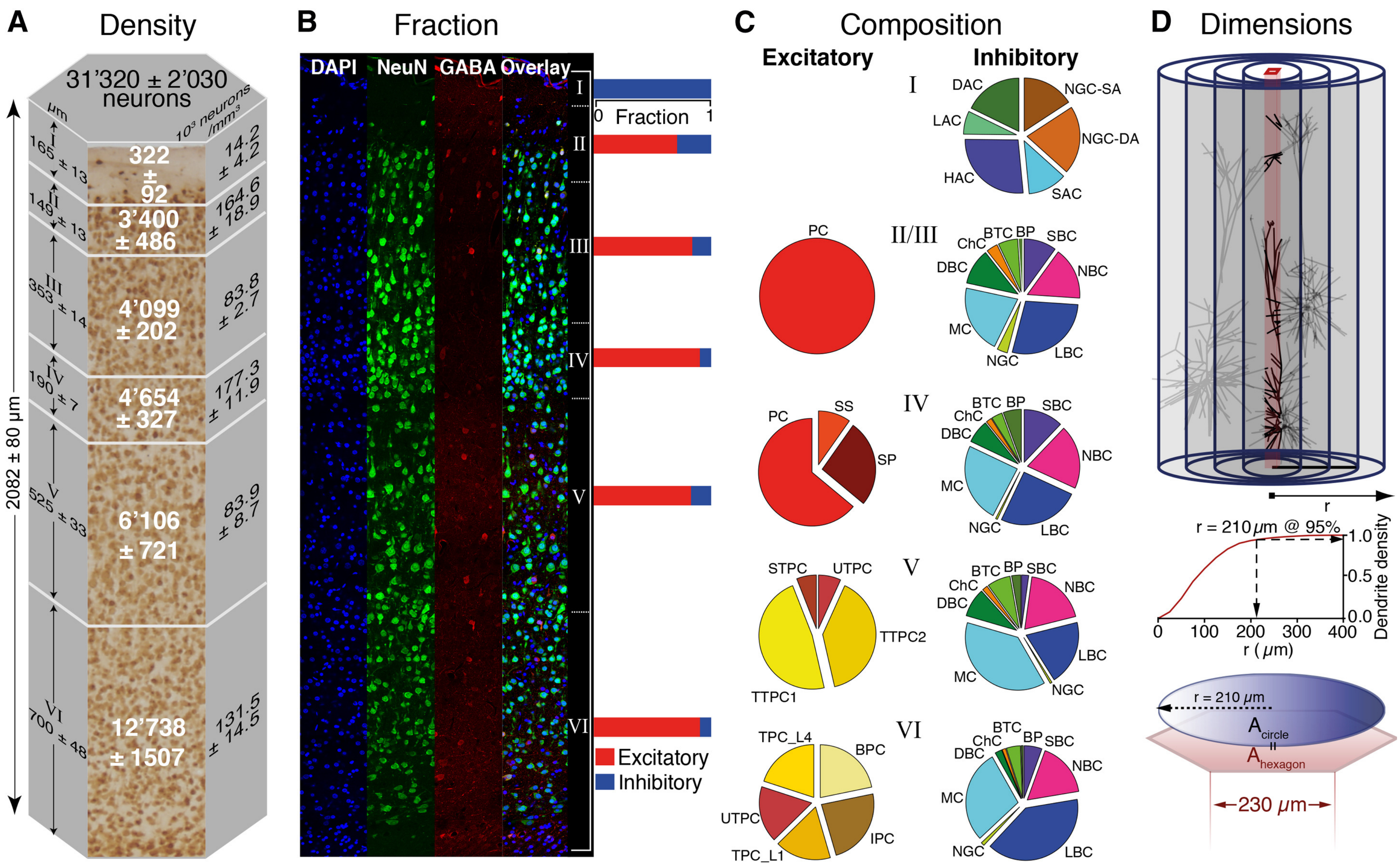


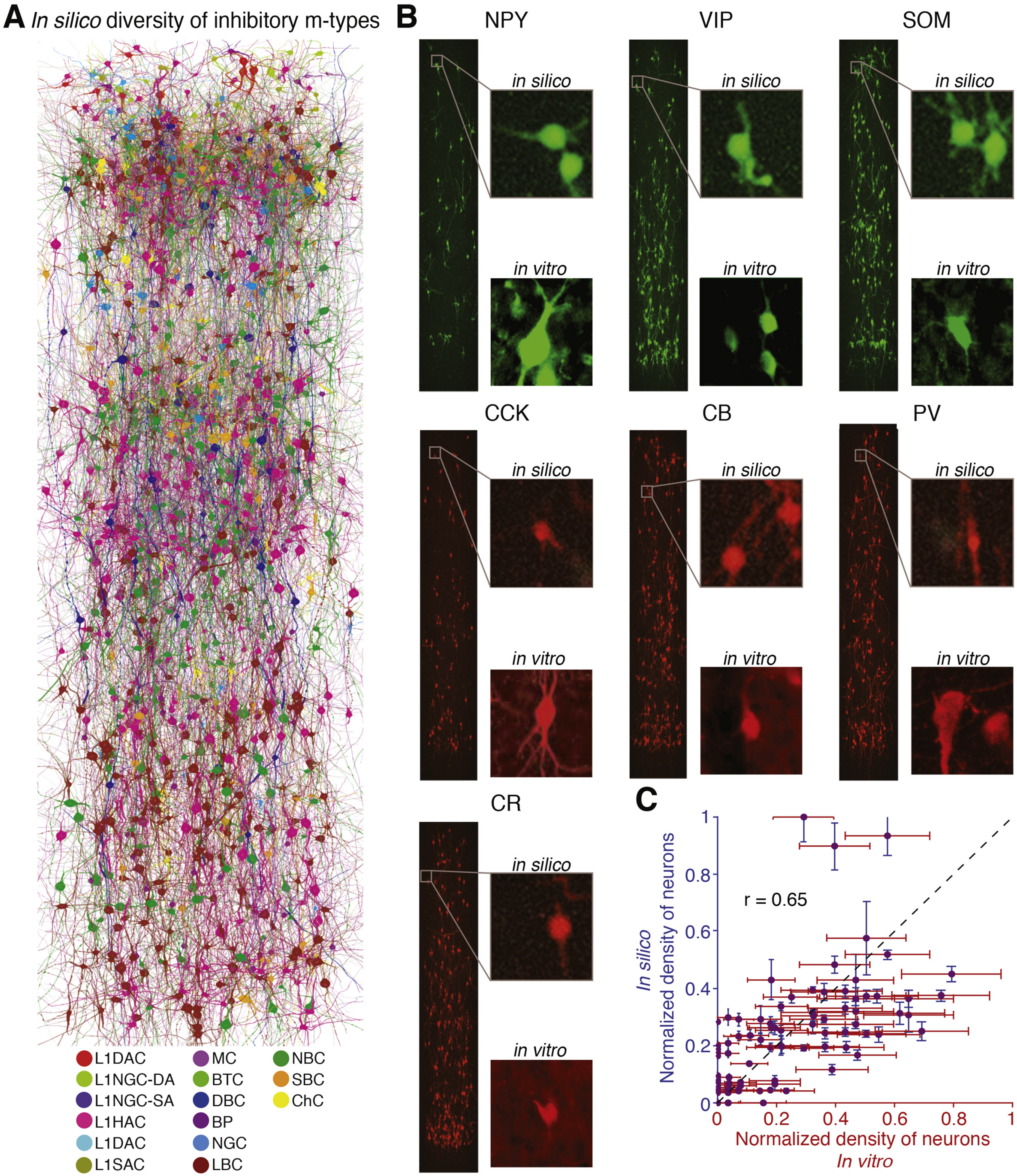
MC	Martinotti Cell
BTC	Bitufted Cell
DBC	Double Bouquet Cell
BP	Bipolar Cell
NGC	Neurogliaform Cell
LBC	Large Basket Cell
NBC	Nest Basket Cell
SBC	Small Basket Cell
ChC	Chandelier Cell

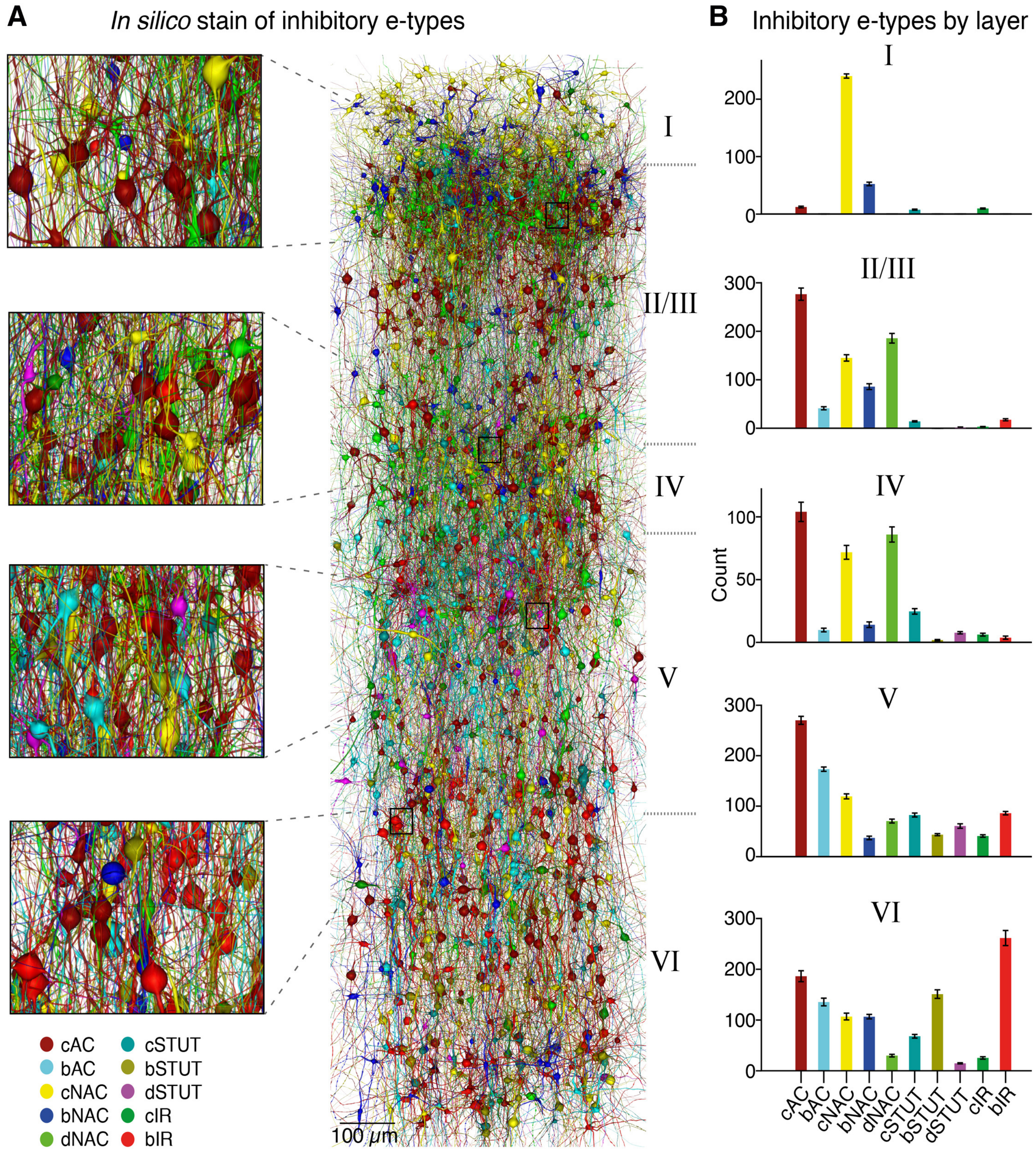
PC	Pyramidal Cell
SP	Star Pyramidal Cell
SS	Spiny Stellate Cell

TTPC1	Thick-tufted Pyramidal Cell with a late bifurcating apical tuft
TTPC2	Thick-tufted Pyramidal Cell with an early bifurcating apical tuft
UTPC	Untufted Pyramidal Cell
STPC	Slender-tufted Pyramidal Cell

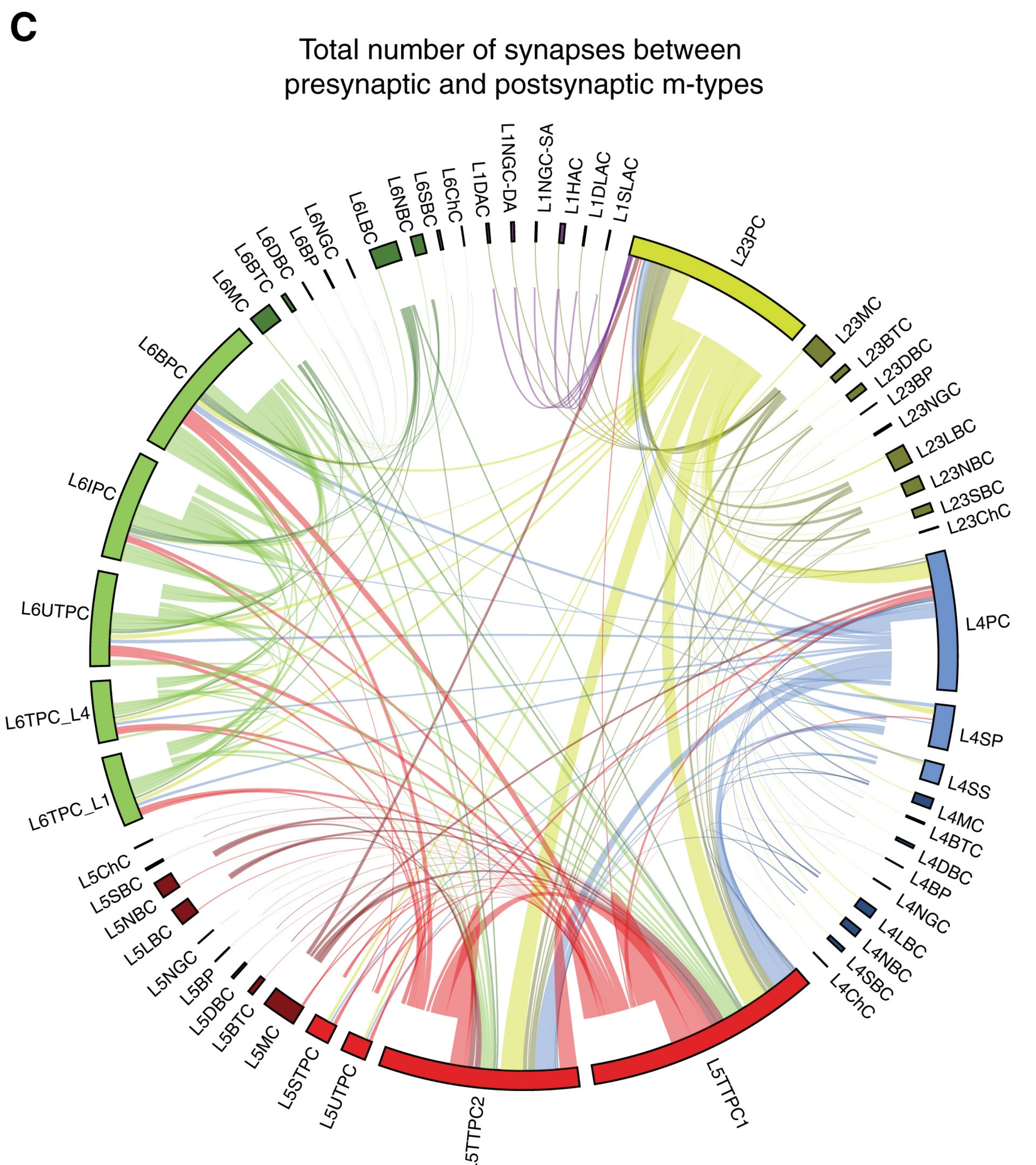
TPC_L4	Tufted Pyramidal Cell with dendritic tuft terminating in layer 4
TPC_L1	Tufted Pyramidal Cell with dendritic tuft terminating in layer 1
IPC	Pyramidal Cell with inverted apical-like dendrites
BPC	Pyramidal Cell with bipolar apical-like dendrites


A
Density
31'320 ± 2'030 neurons
μm
10^3 neurons /mm^3
I 165 ± 13
322 ± 92
14.2 ± 4.2
II 149 ± 13
3'400 ± 486
164.6 ± 18.9
III 353 ± 14
4'099 ± 202
83.8 ± 2.7
IV 190 ± 7
4'654 ± 327
177.3 ± 11.9
V 525 ± 33
6'106 ± 721
83.9 ± 8.7
VI 700 ± 48
12'738 ± 1507
131.5 ± 14.5
2082 ± 80 μm
B
Fraction
DAPI
NeuN
GABA
Overlay
I
II
III
IV
V
VI
0 Fraction 1
Excitatory
Inhibitory
C
Composition
Excitatory
Inhibitory
I
DAC
NGC-SA
LAC
NGC-DA
HAC
SAC
II/III
PC
BTC
BP
ChC
SBC
DBC
NBC
MC
NGC
LBC
IV
PC
SS
SP
BTC
BP
ChC
SBC
DBC
NBC
MC
NGC
LBC
V
STPC
UTPC
TTPC2
TTPC1
BTC
BP
SBC
ChC
NBC
DBC
LBC
MC
NGC
VI
TPC_L4
BPC
UTPC
IPC
TPC_L1
BTC
ChC
BP
SBC
DBC
NBC
MC
NGC
LBC
D
Dimensions
r
r = 210 μm @ 95%
1.0
0.5
0.0
Dendrite density
0
100
200
300
400
r (μm)
r = 210 μm
A_{circle}
=
$A_{hexagon}$
230 μm


A In silico diversity of inhibitory m-types
L1DAC
L1NGC-DA
L1NGC-SA
L1HAC
L1DAC
L1SAC
MC
BTC
DBC
BP
NGC
LBC
NBC
SBC
ChC
B
NPY
VIP
SOM
CCK
CB
PV
CR
in silico
in vitro
C
r = 0.65
In silico
Normalized density of neurons
Normalized density of neurons
In vitro
0
0.2
0.4
0.6
0.8
1


A
In silico stain of inhibitory e-types
B
Inhibitory e-types by layer
I
II/III
IV
V
VI
100 μm
cAC
bAC
cNAC
bNAC
dNAC
cSTUT
bSTUT
dSTUT
cIR
bIR
Count
0
50
100
200
300

Synapse Counts



Many Assumptions

- Data is lacking on most synapse types
- Assumptions have to be made about synapse properties, frequencies, spatial distribution
- Wiring is based on statistics and may be inaccurate

Simulations

- Simulations run on an IBM Blue Gene supercomputer.
- Various models used over the years.
- In 2015 their Blue Brain IV machine (IBM Blue Gene/Q) was the 100th most powerful supercomputer in the world.

Results

- Reproduces general response to thalamic input (whisker stimulation)
- “Soloists” vs. “Choristers”:
  - Choristers fire in synchrony with the LFP
  - Soloists are somewhat anti-correlated with LFP
  - Model predicts most soloists are interneurons
  - Changes in network state can affect chorister/soloist balance
- Predicts that anti-correlated inhibitory cancels out highly correlated excitatory activity
- Reproduces temporal sequential structure of L5 neurons during spontaneous activity