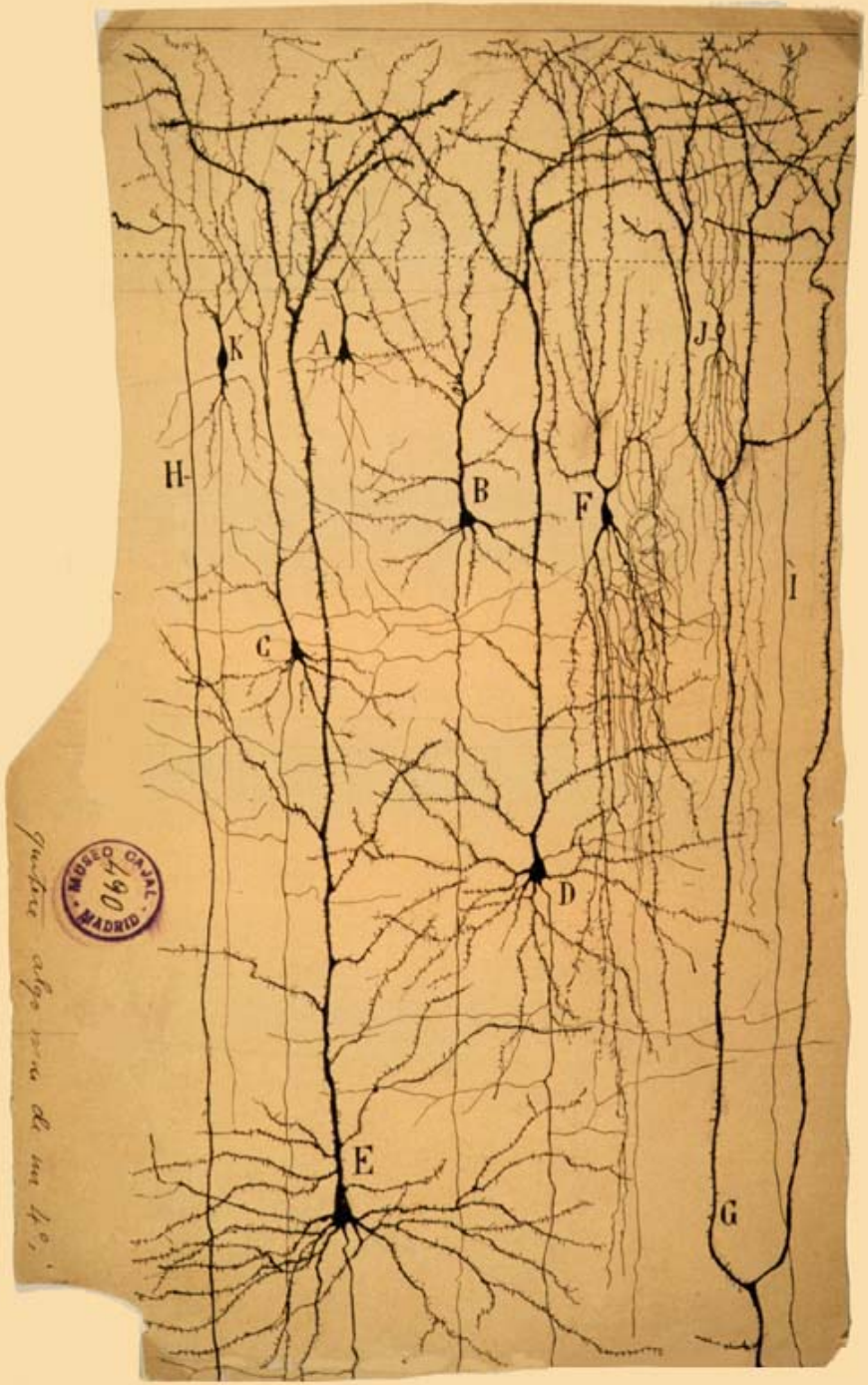
Why study circuits?

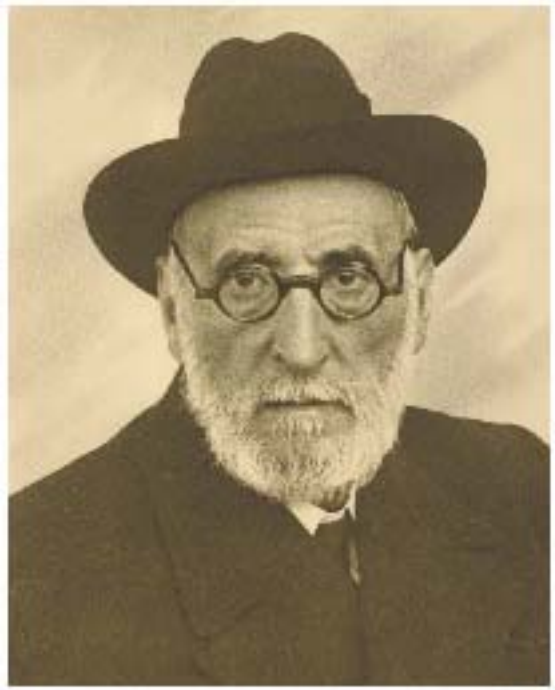
- There are distinct classes of neurons
- Defining them is essential to understand the circuit
- Connectivity is not random
- Work at the same level that the circuit uses



Santiago Ramon y Cajal (1852-1934)

•Cortical microcircuit is an “impenetrable jungle”

•Difference in cell types between species



A hundred classes of neocortical neurons

Lorente de Nó, 1922 (1902-1990)

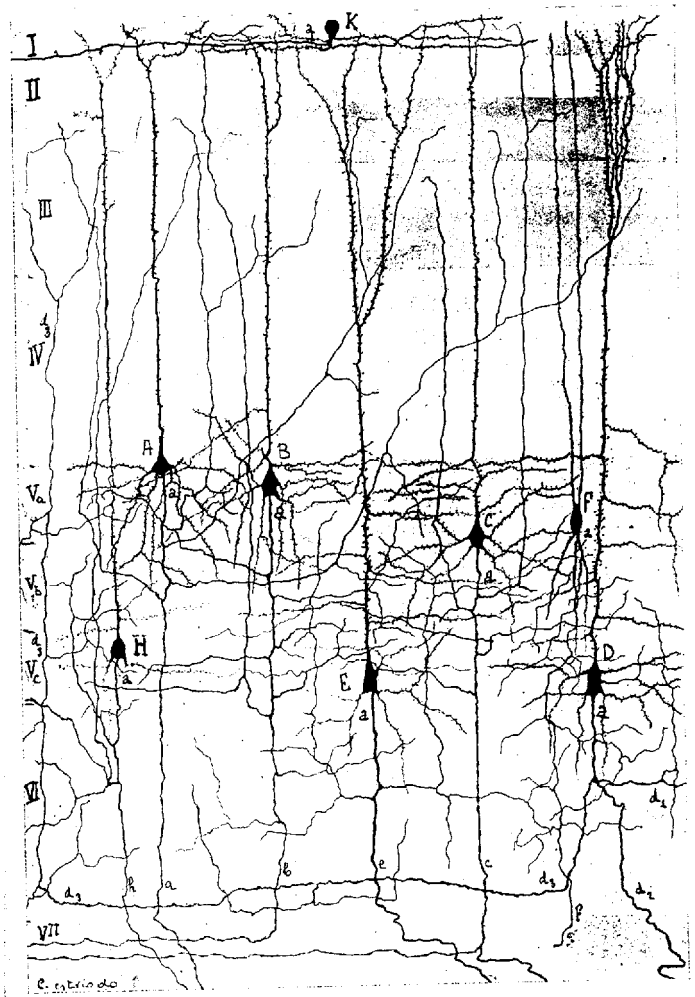


Fig. 15. — Capa de las células piramidales grandes; *A, H, E*, pirámides con axon de proyección; *B*, idem de axon calloso; *C*, idem de axon bifurcado en ramo calloso y ramo de proyección; *D*, idem de axon complicado; *F*, célula fusiforme de axon largo (análoga a las de la figura 10); *K*, célula de Cajal.

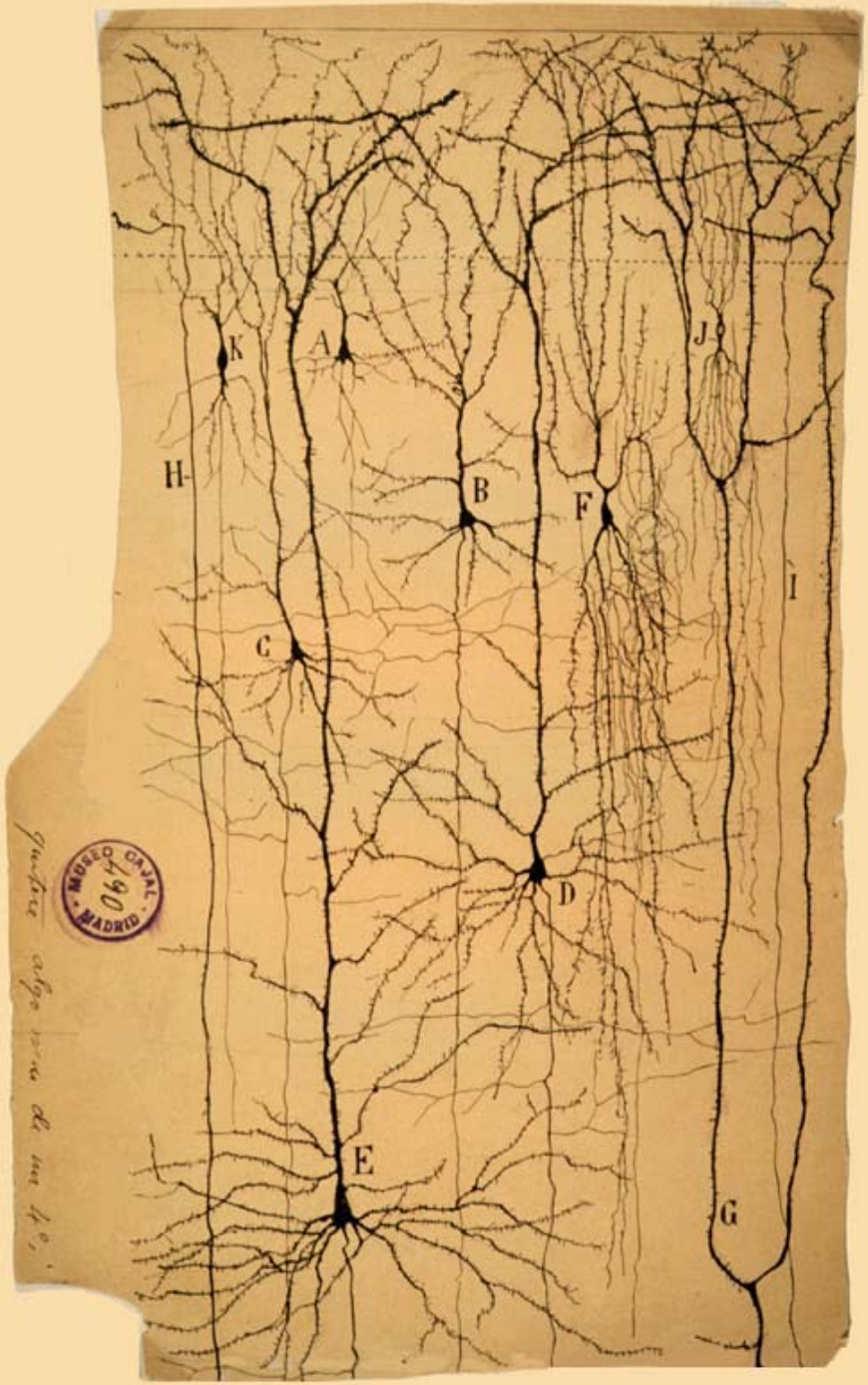
LA CORTEZA CEREBRAL DEL RATÓN

(Primera contribución. — La corteza acústica.)

POR R. LORENTE DE NÓ.

(DEL INSTITUTO CAJAL.)

QuickTime™ and a
TIFF (LZW) decompressor
are needed to see this picture.



Cortical microcircuit (~1mm^3)

-Structure:

- Cell types
- Connections
  - Random
  - Specific
    - Canonical
    - Areal/Species

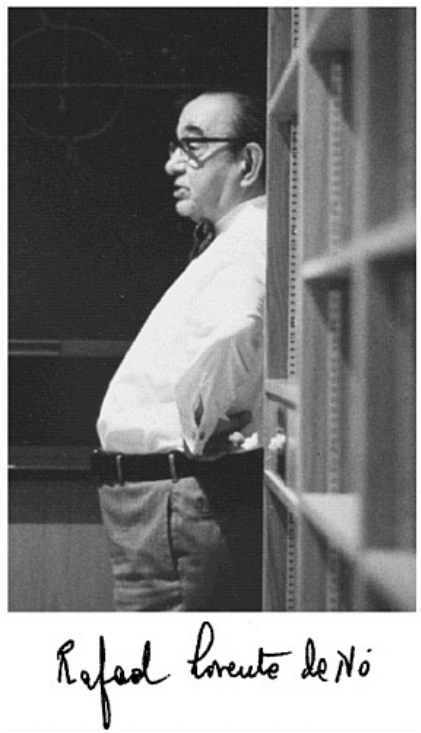
-Function:

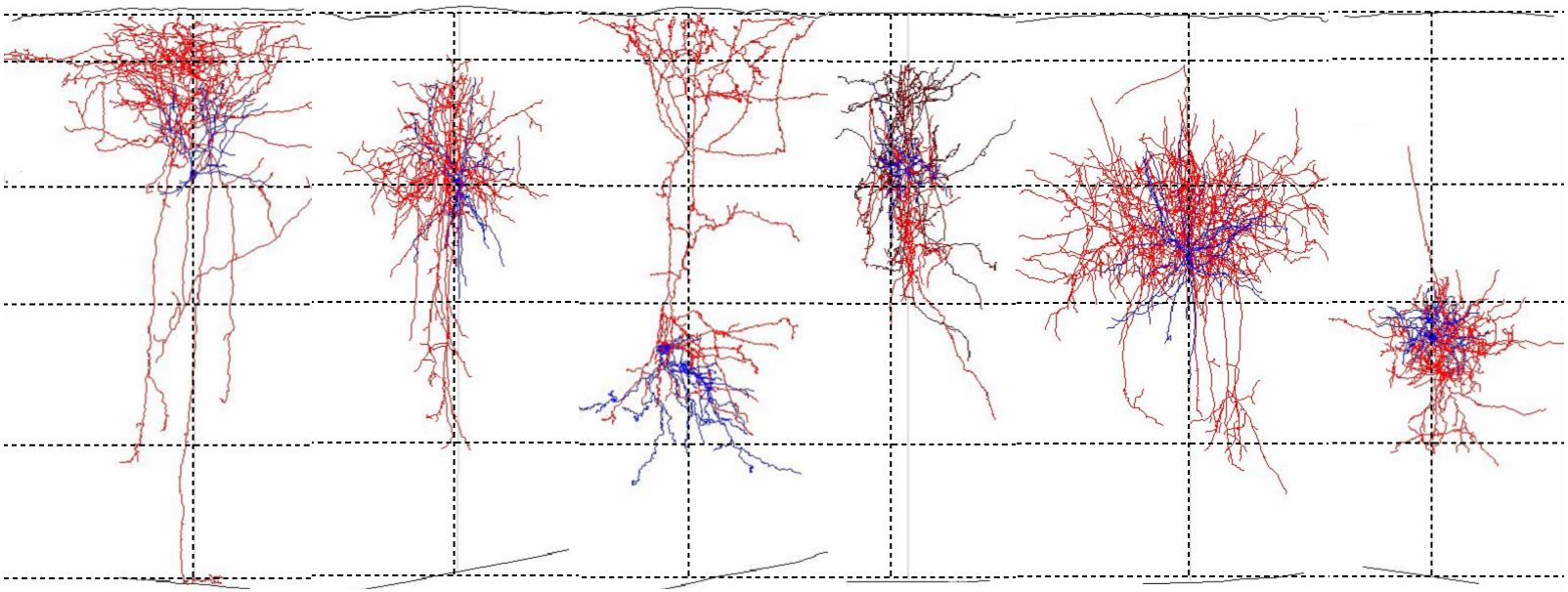
- Feedforward
- Feedback

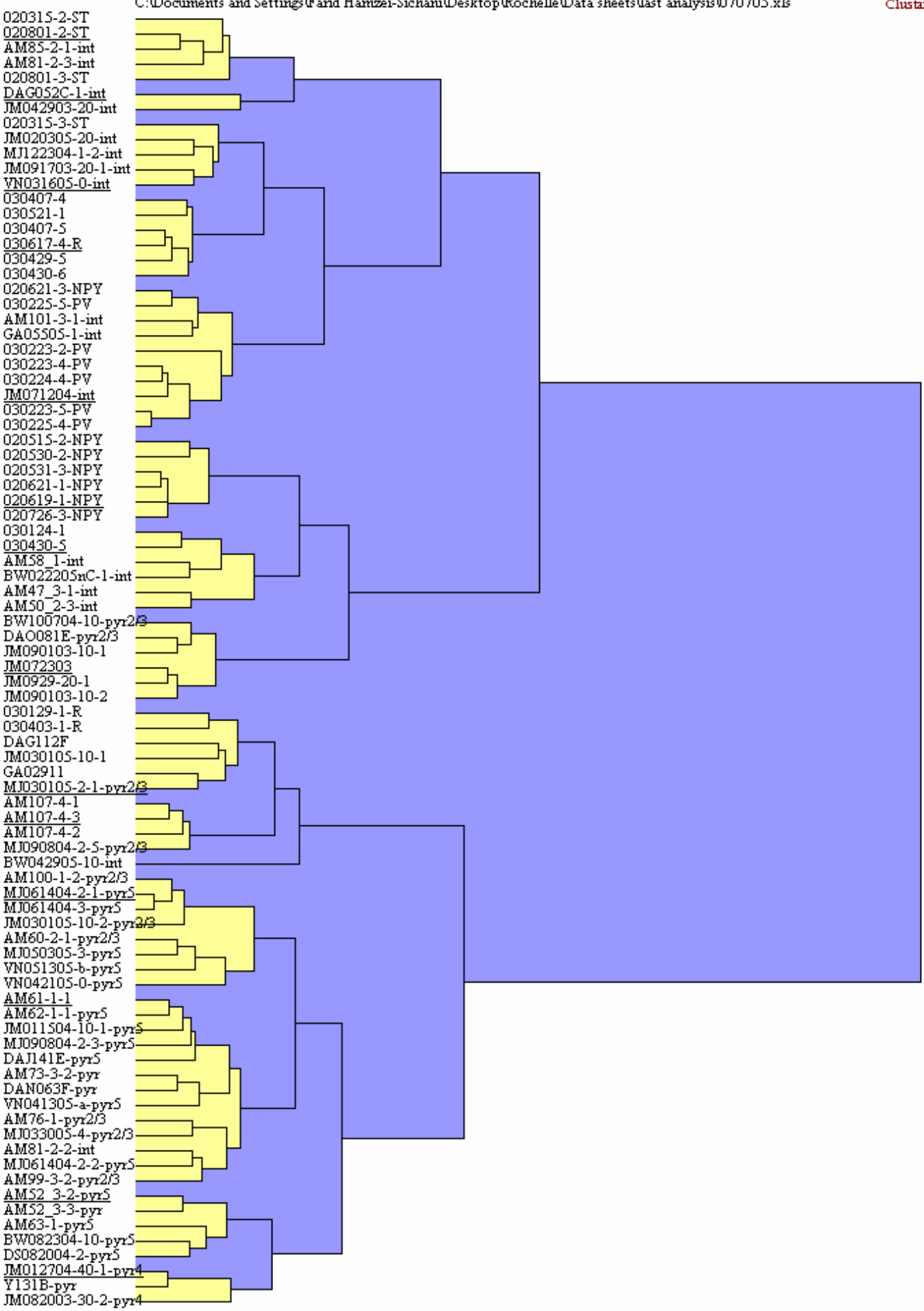
Two theories of cortical function:

Feed-forward: Single cell
- Sherrington
- Hubel &Wiesel
- Receptive fields
- Speed of processing

Feed-back: Neuronal ensembles
- Brown
- Lorente/Hebb
- Llinás
- Recurrent connectivity
- Spontaneous activity



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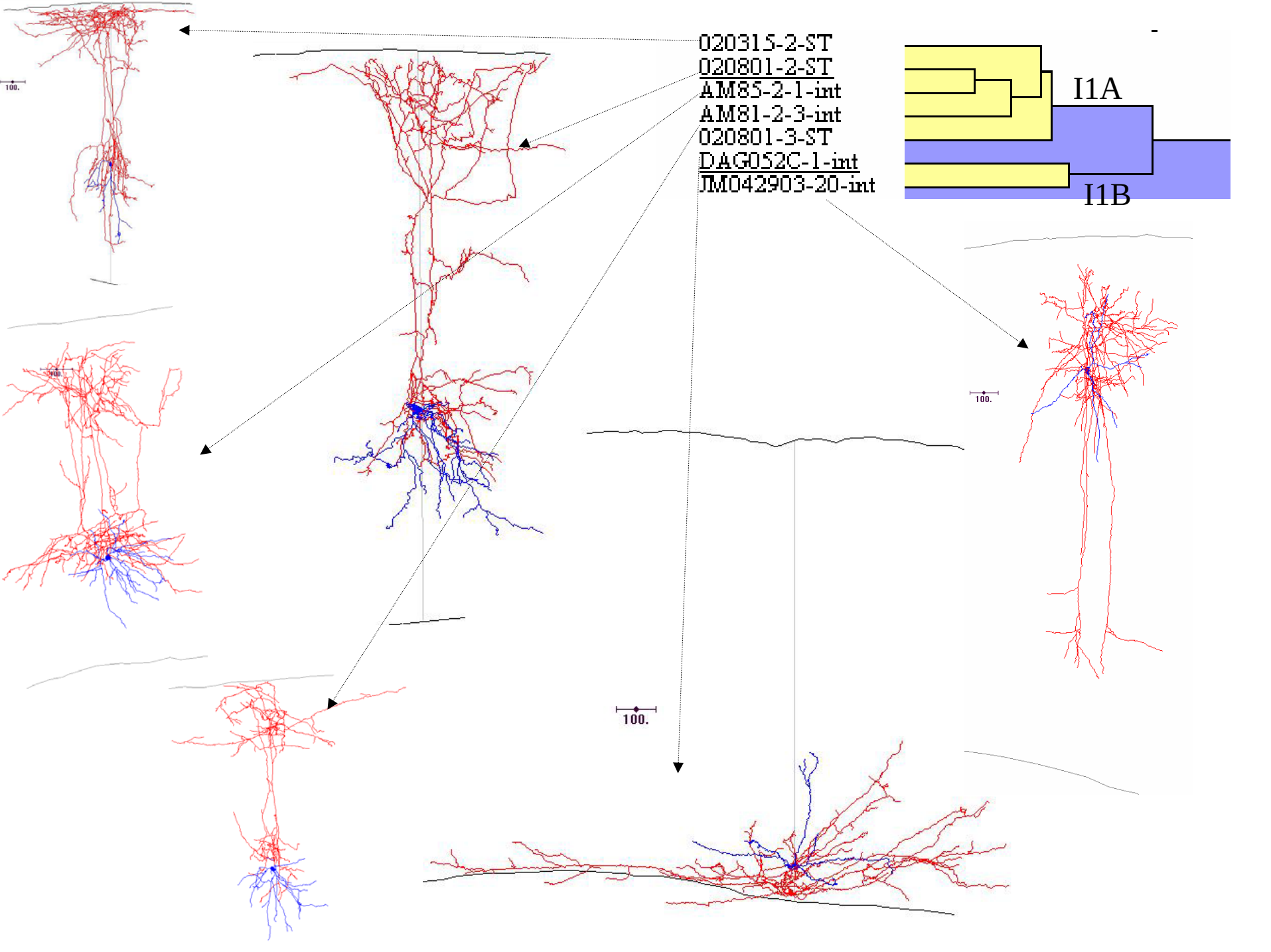
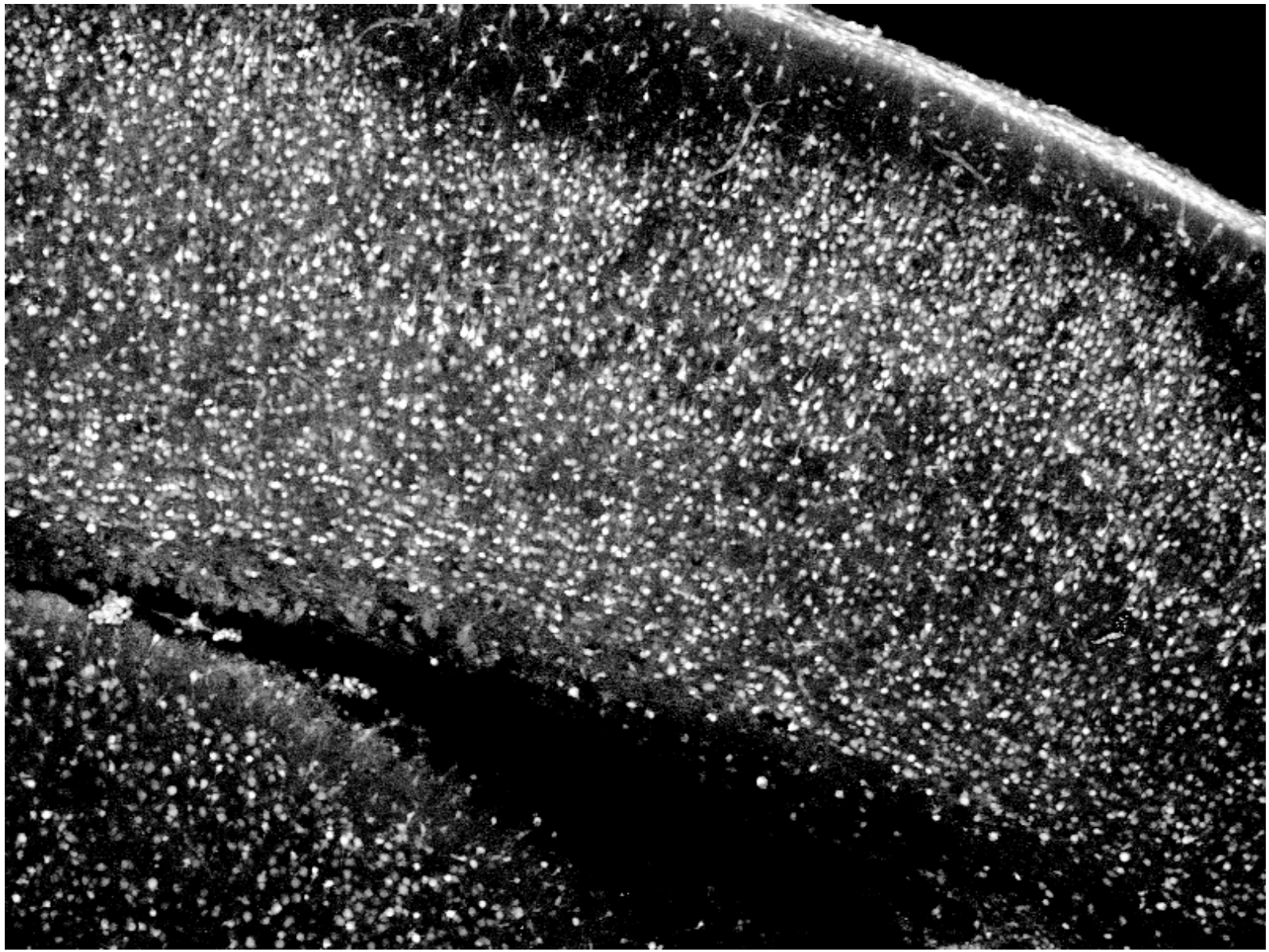
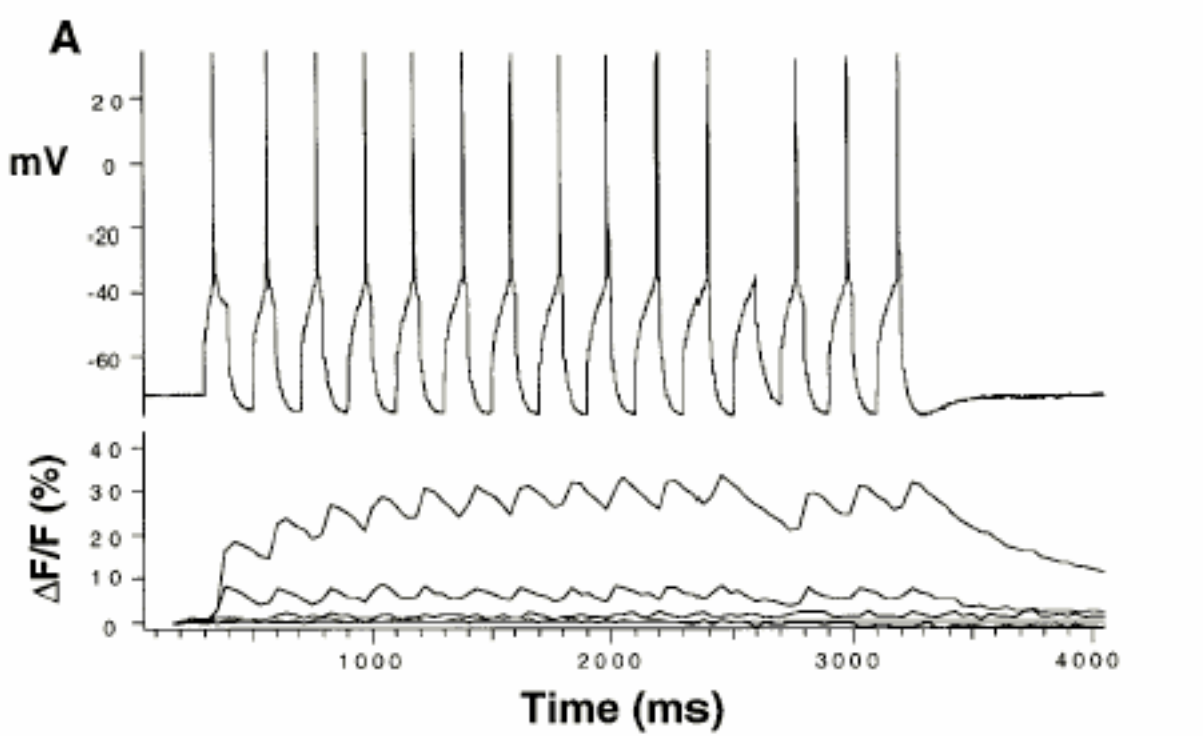
020801-2-ST
AM85-2-1-int
AM81-2-3-int
020801-3-ST
DAG052C-1-int
JM042903-20-int
020315-3-ST
JM020305-20-int
MJ122304-1-2-int
JM091703-20-1-int
VN031605-0-int
030407-4
030521-1
030407-5
030617-4-R
030429-5
030430-6
020621-3-NPY
030225-5-PV
AM101-3-1-int
GA05505-1-int
030223-2-PV
030223-4-PV
030224-4-PV
JM071204-int
030223-5-PV
030225-4-PV
020515-2-NPY
020530-2-NPY
020531-3-NPY
020621-1-NPY
020619-1-NPY
020726-3-NPY
030124-1
030430-5
AM58_1-int
BW022205nC-1-int
AM47_3-1-int
AM50_2-3-int
BW100704-10-pyr2/3
DAO081E-pyr2/3
JM090103-10-1
JM072303
JM0929-20-1
JM090103-10-2
030129-1-R
030403-1-R
DAG112F
JM030105-10-1
GA02911
MJ030105-2-1-pyr2/3
AM107-4-1
AM107-4-3
AM107-4-2
MJ090804-2-5-pyr2/3
BW042905-10-int
AM100-1-2-pyr2/3
MJ061404-2-1-pyr5
MJ061404-3-pyr5
JM030105-10-2-pyr2/3
AM60-2-1-pyr2/3
MJ050305-3-pyr5
VN051305-b-pyr5
VN042105-0-pyr5
AM61-1-1
AM62-1-1-pyr5
JM011504-10-1-pyr5
MJ090804-2-3-pyr5
DAJ141E-pyr5
AM73-3-2-pyr
DAN063F-pyr
VN041305-a-pyr5
AM76-1-pyr2/3
MJ033005-4-pyr2/3
AM81-2-2-int
MJ061404-2-2-pyr5
AM99-3-2-pyr2/3
AM52_3-2-pyr5
AM52_3-3-pyr
AM63-1-pyr5
BW082304-10-pyr5
DS082004-2-pyr5
JM012704-40-1-pyr4
Y131B-pyr
JM082003-30-2-pyr4


020315-2-ST
020801-2-ST
AM85-2-1-int
AM81-2-3-int
020801-3-ST
DAG052C-1-int
JM042903-20-int
I1A
I1B
100.

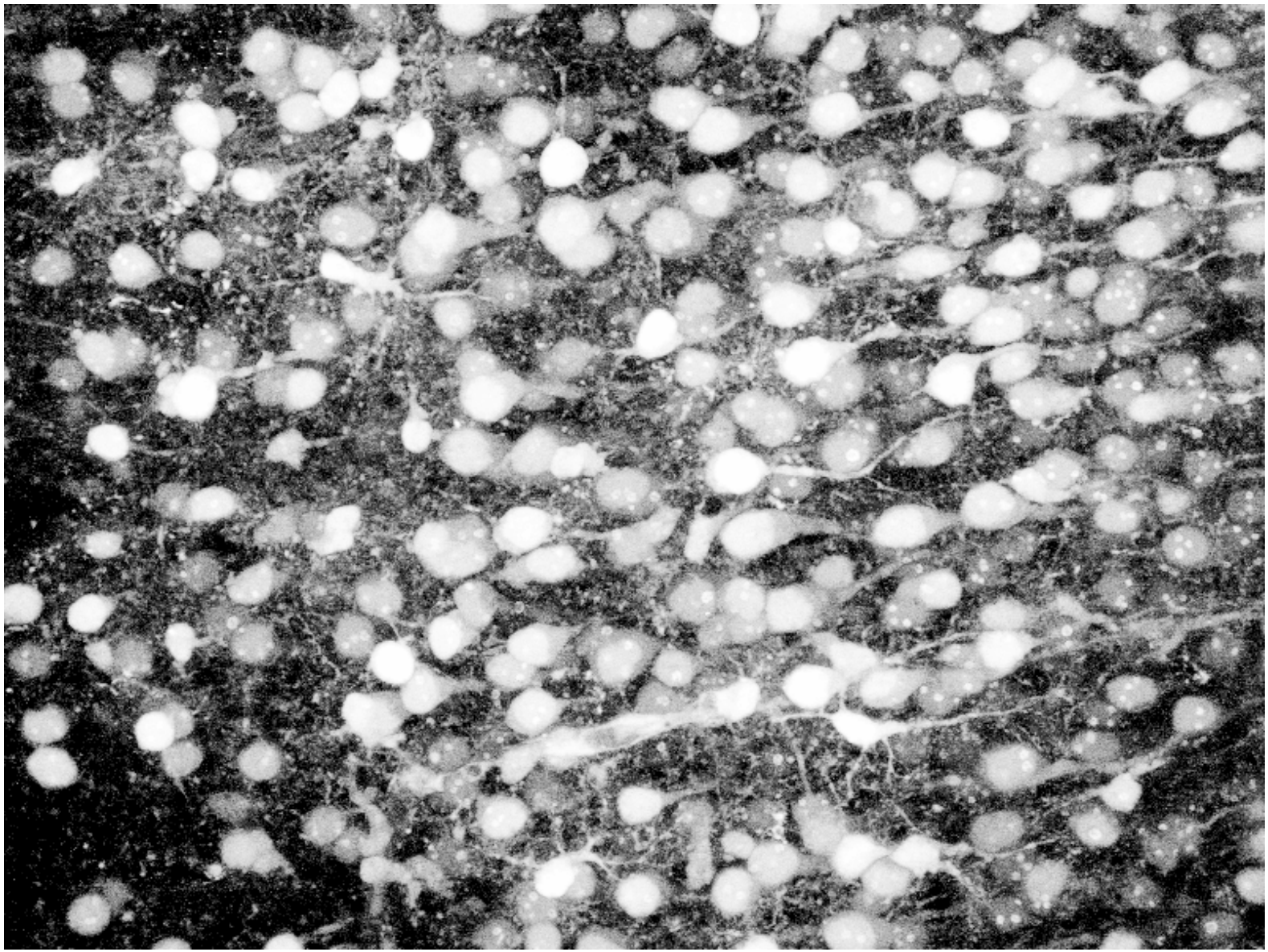
Calcium imaging of cortical microcircuits



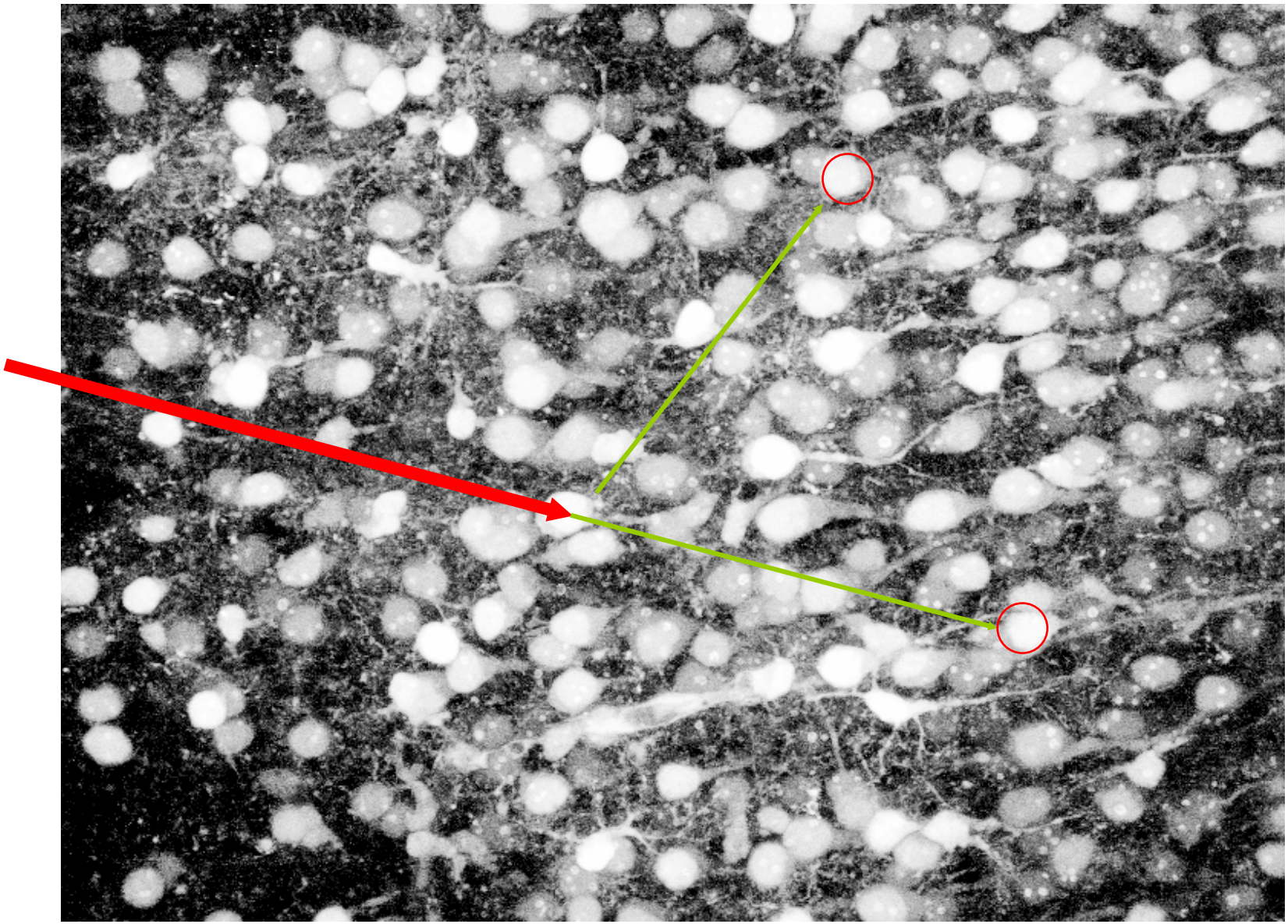
Single-cell resolution imaging of Ca^{2+} influx due to action potentials

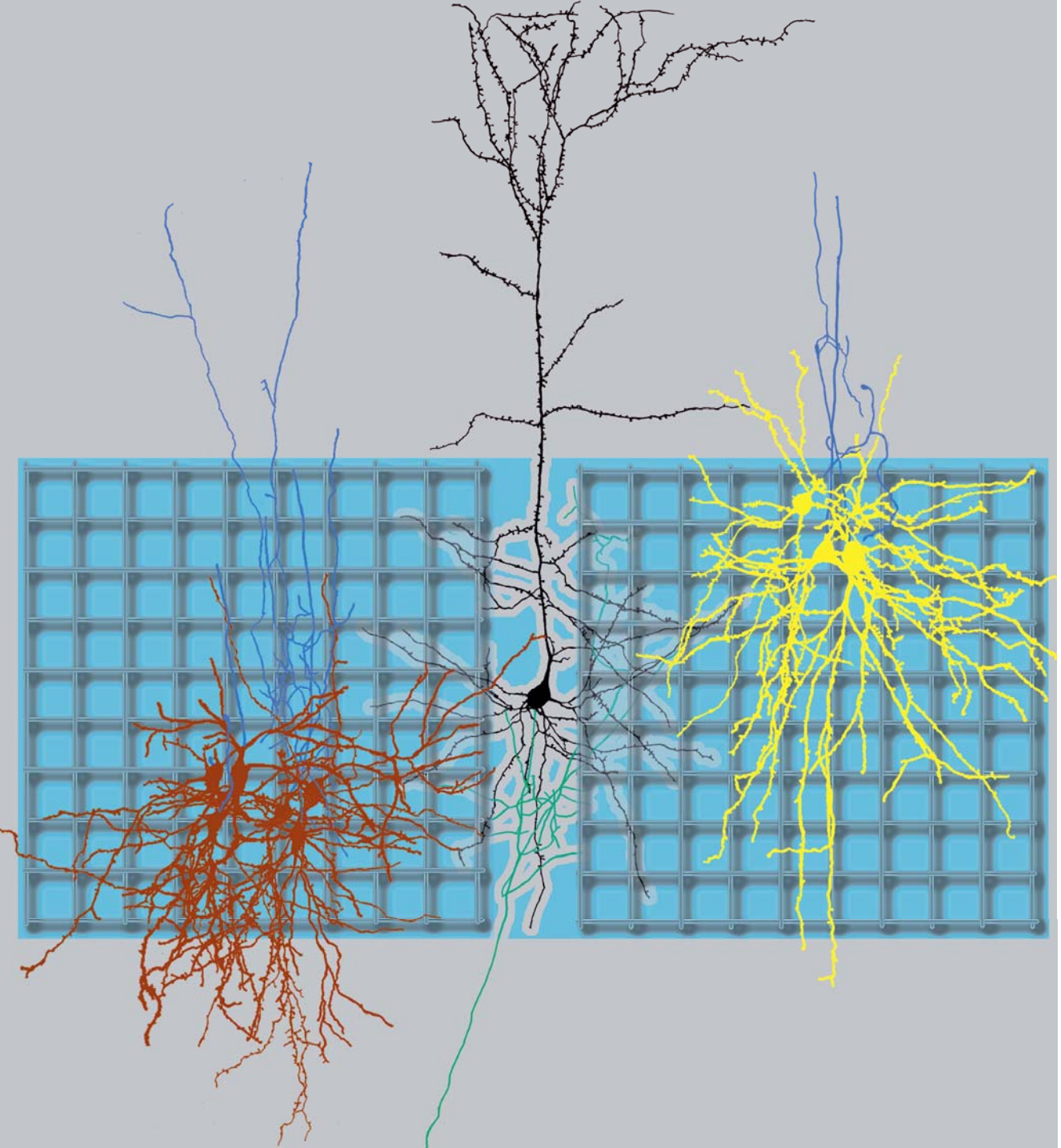


Optical tracking of synaptic connections



Stimulation of presynaptic cell can reveal postsynaptic targets

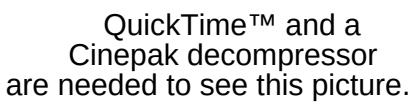




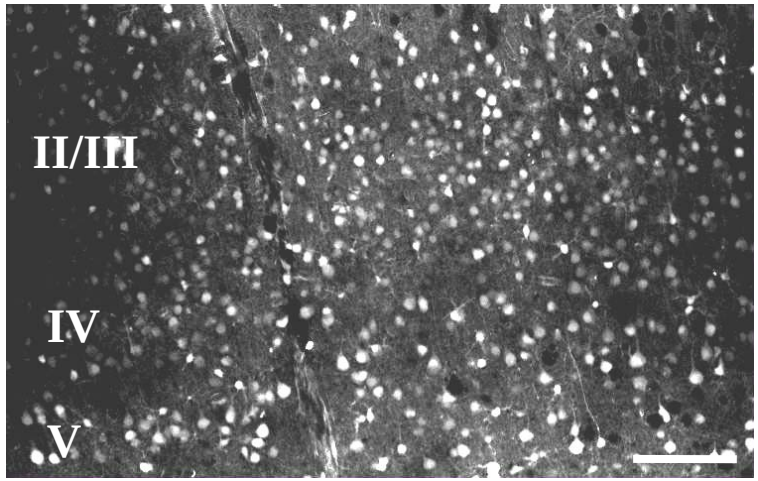
Specificity across different animals:

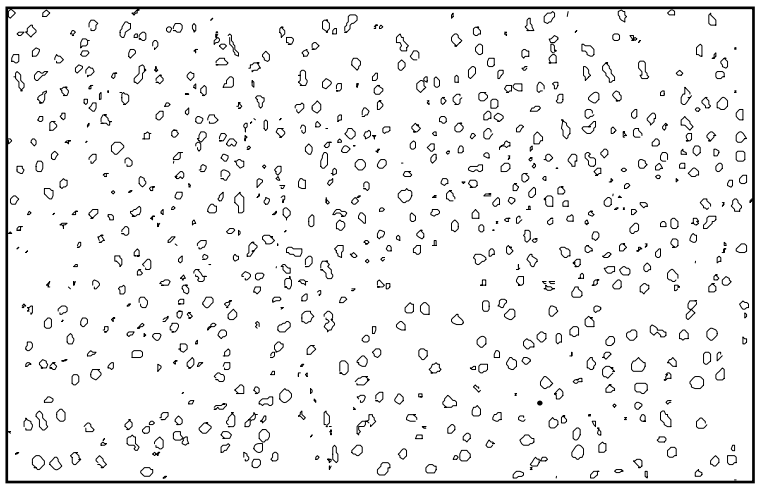
- in cell type
- in cell position
- in contact
  - number
  - position
- in axon shape

Cortical circuits in vitro are spontaneously active: spontaneous activity as a tool, let the circuit speak

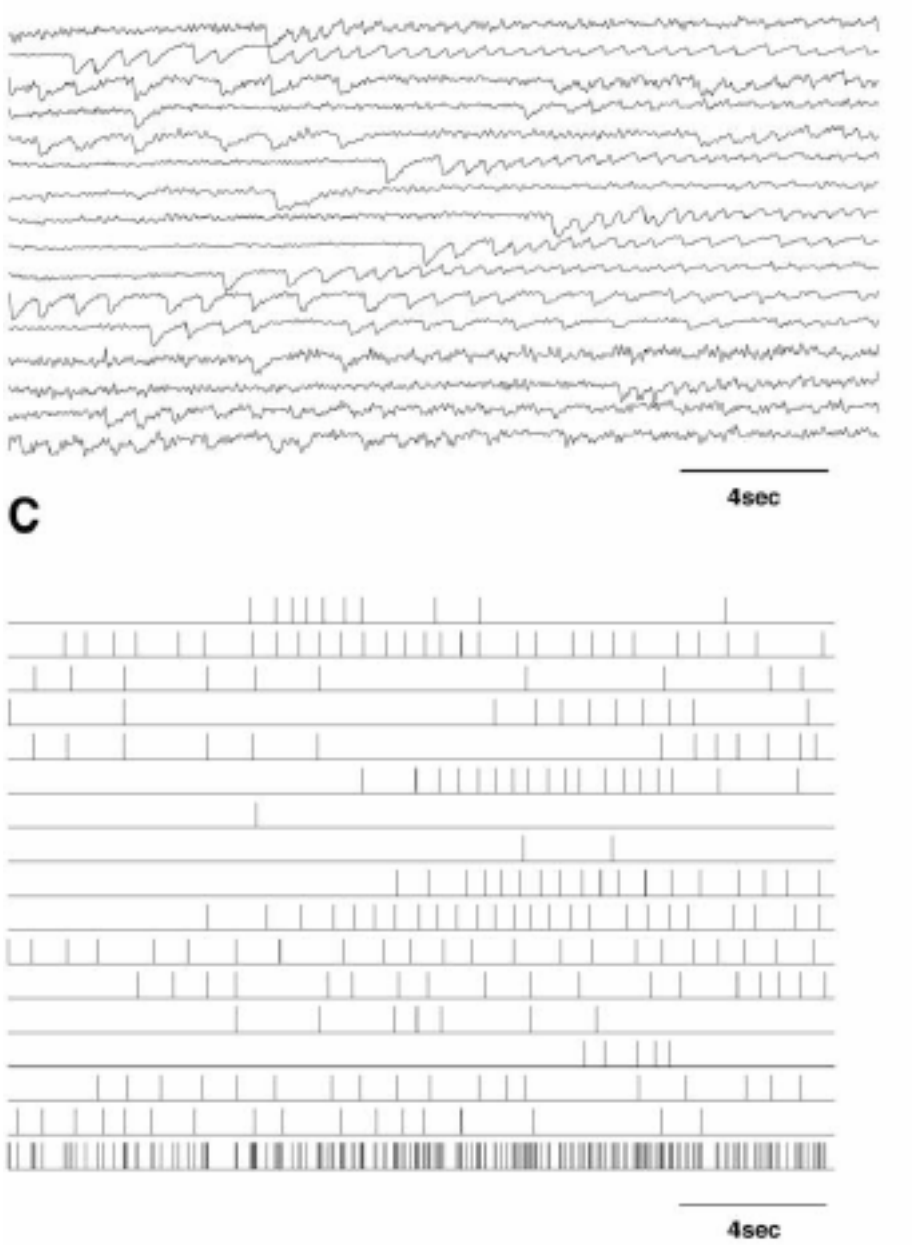


Automatic identification of cells



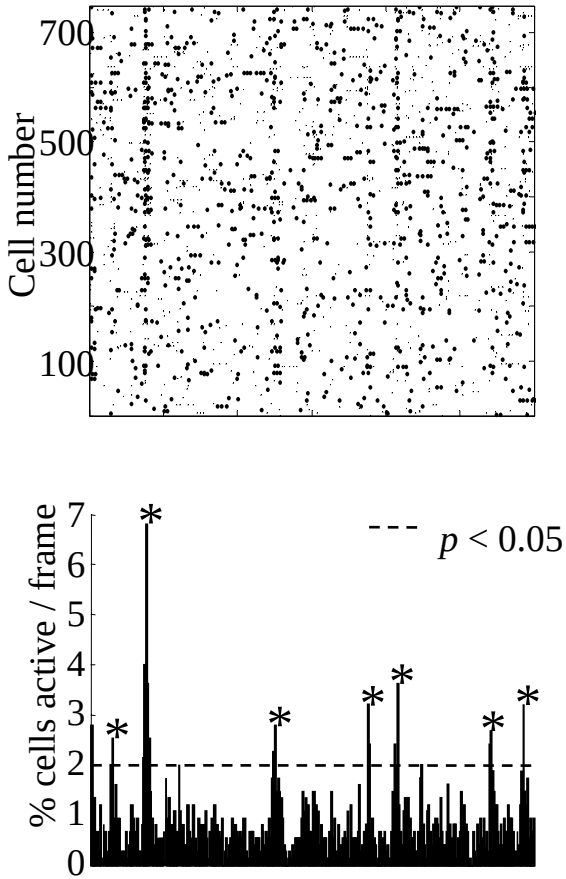


Detection of calcium transients

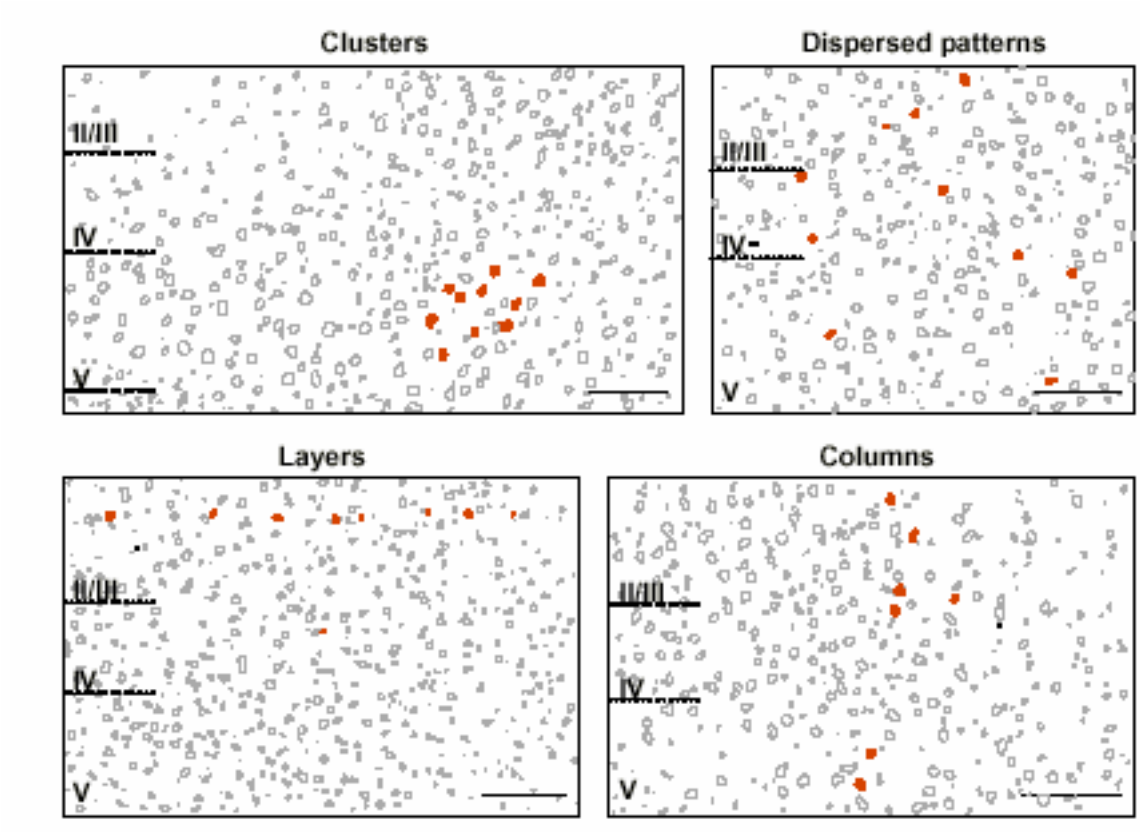


Spontaneous synchronizations of a small % of neurons

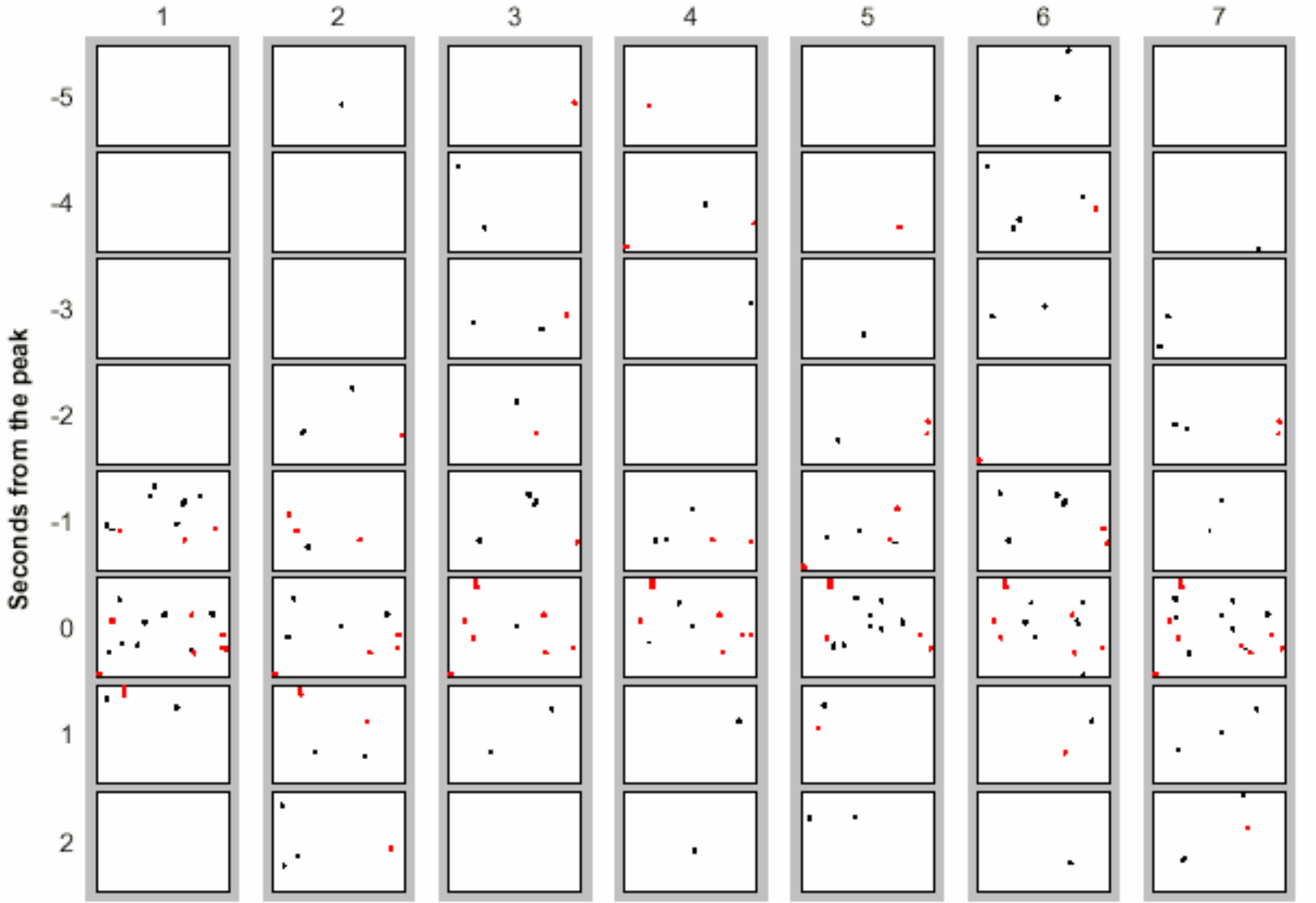
Low temporal resolution- 1sec/frame

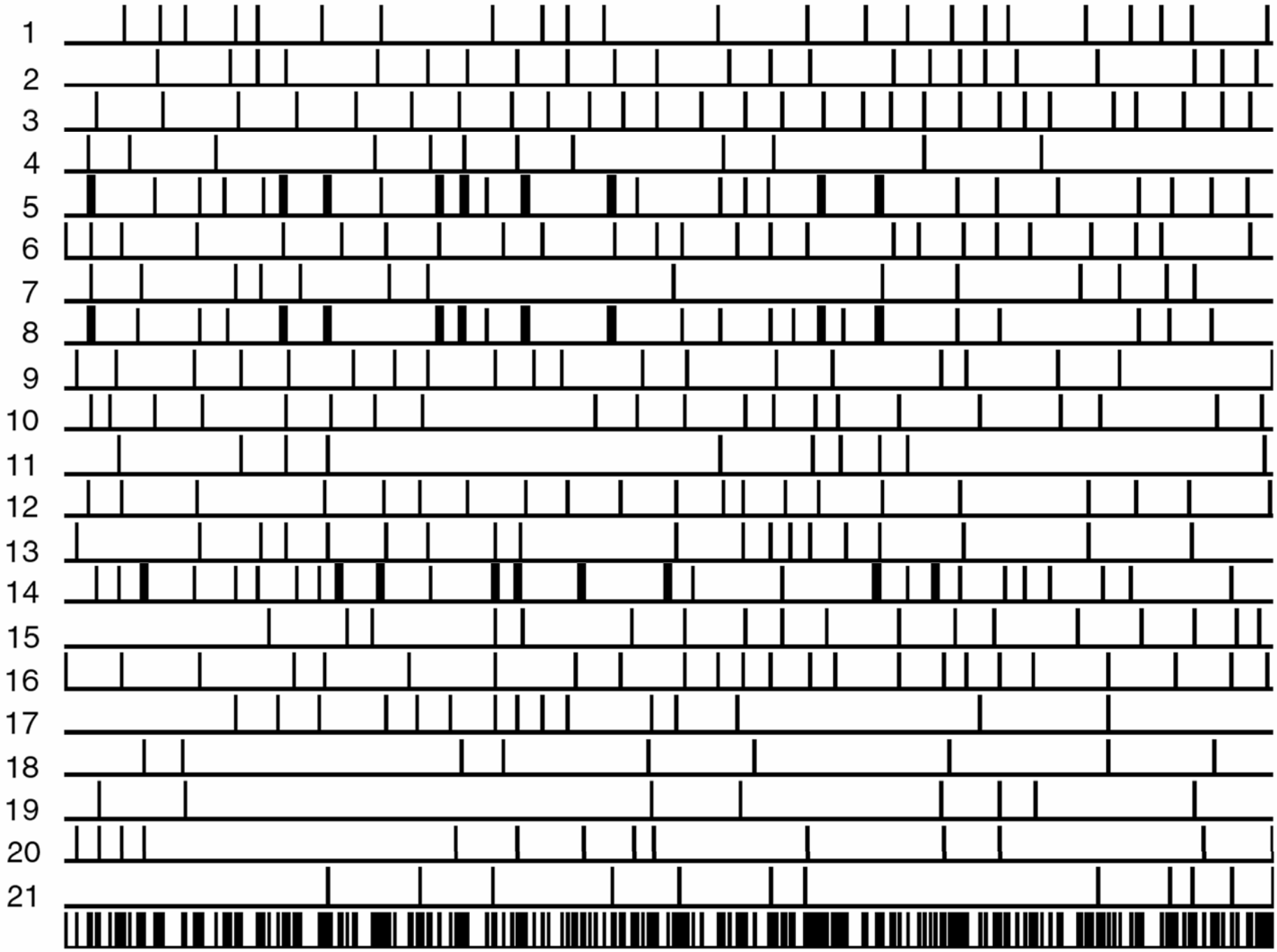


Spontaneous coactivations have specific spatial patterns



Patterns are never identical and have stereotyped dynamics




1
2
3
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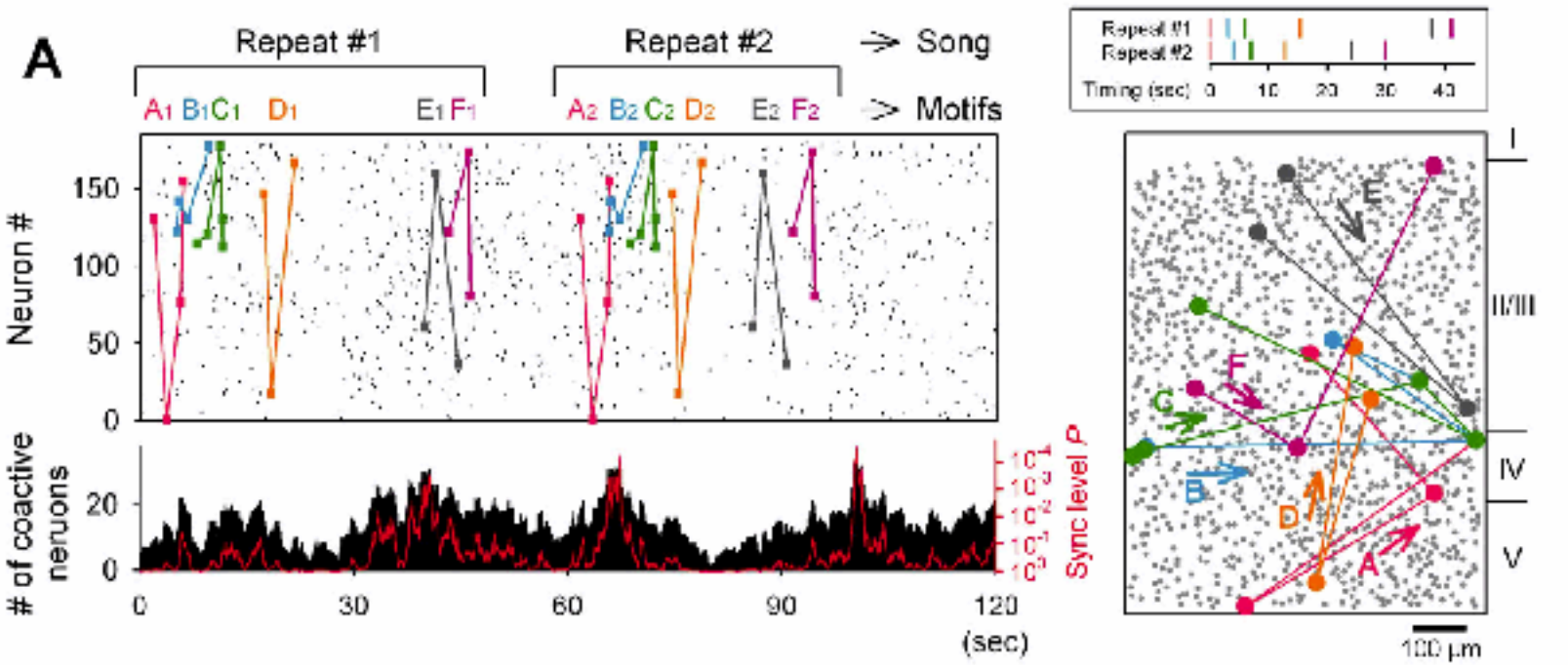
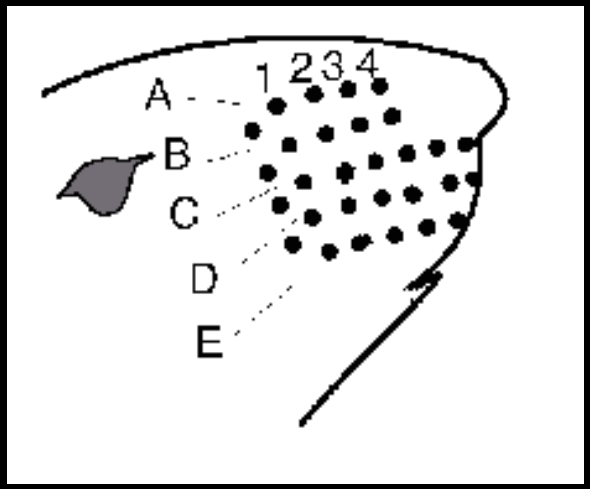
21

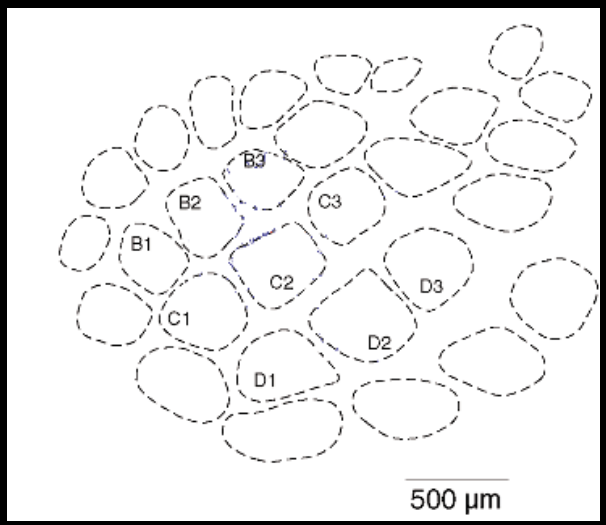
Cortical motifs and songs: repeated sequences of activity

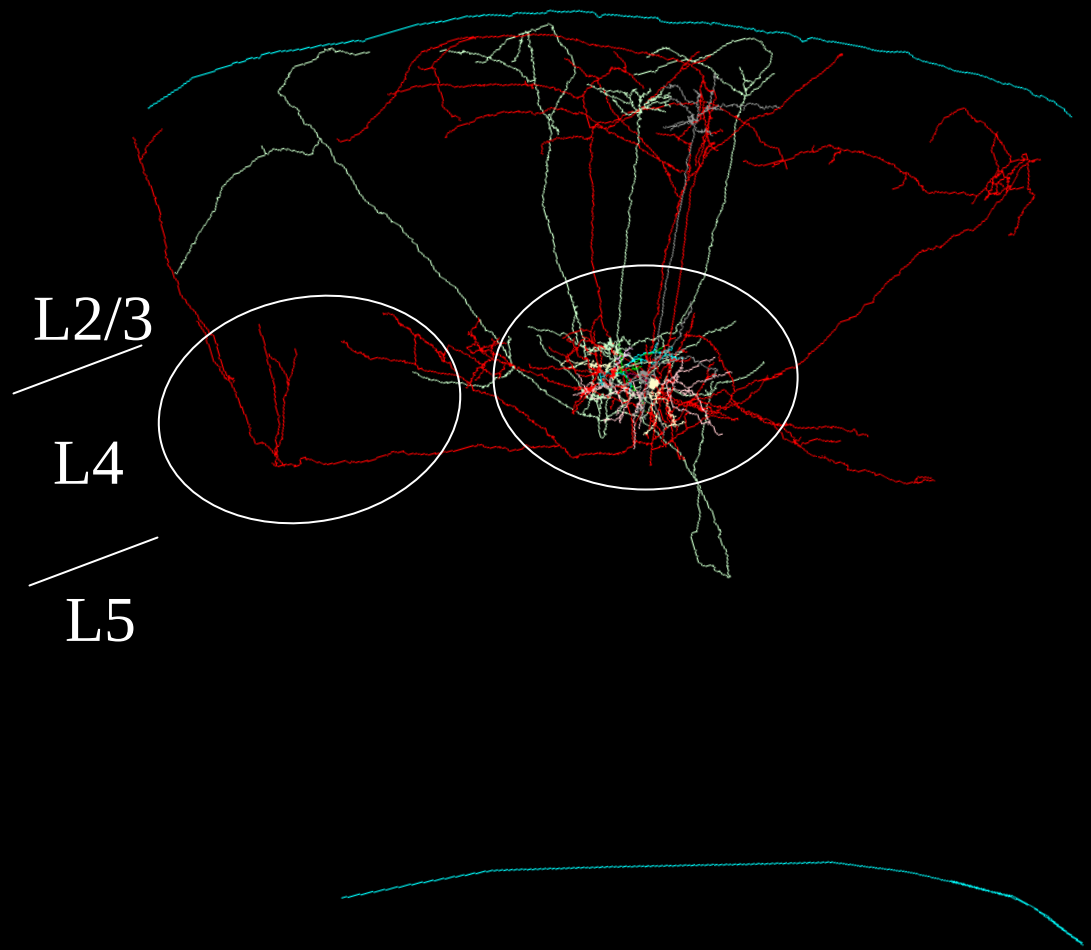
Intermediate temporal resolution- 50 msec/frame



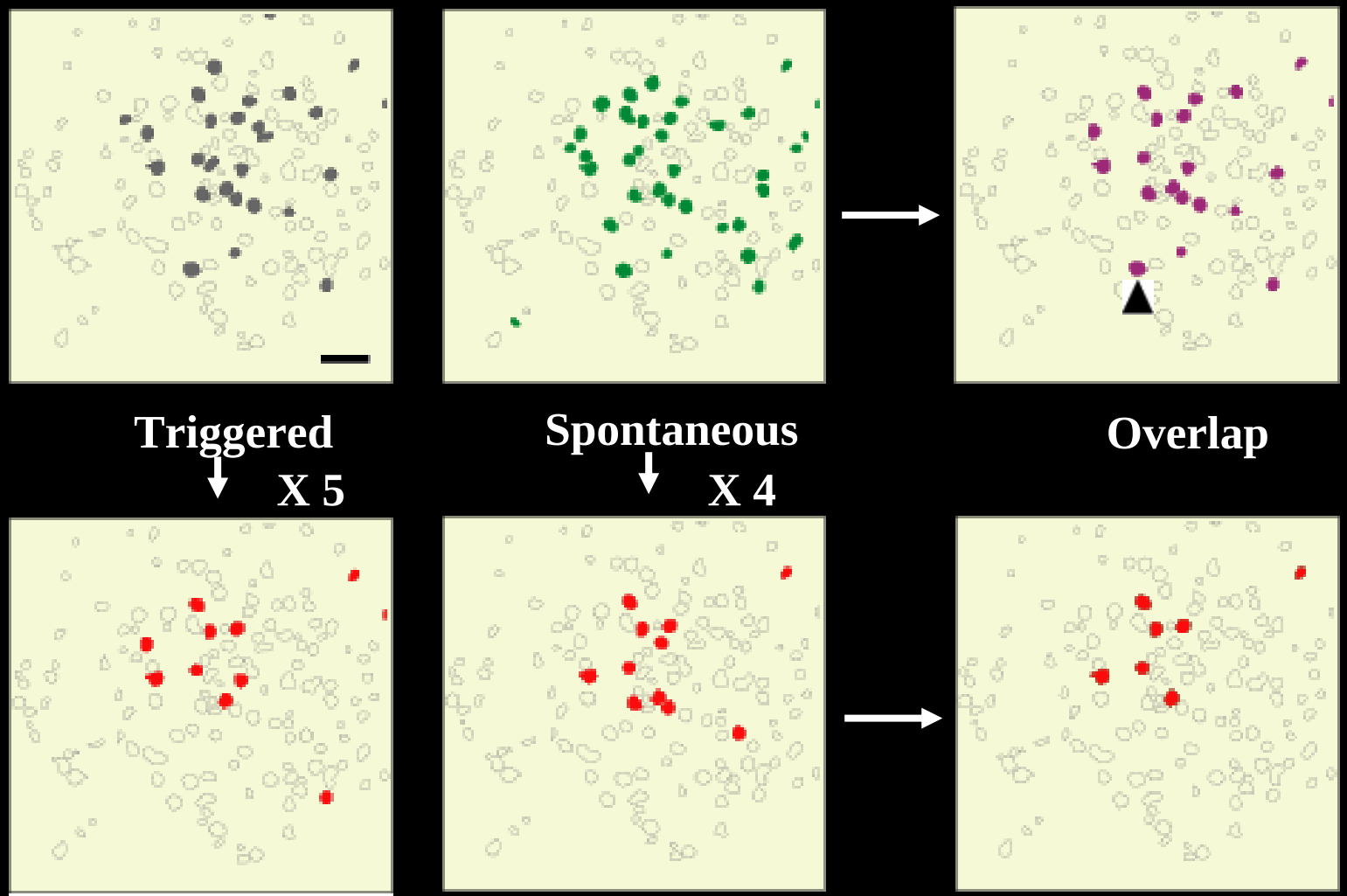
What cortical dynamics are trigered by thalamic stimulation?
Thalamocortical slices- layer 4





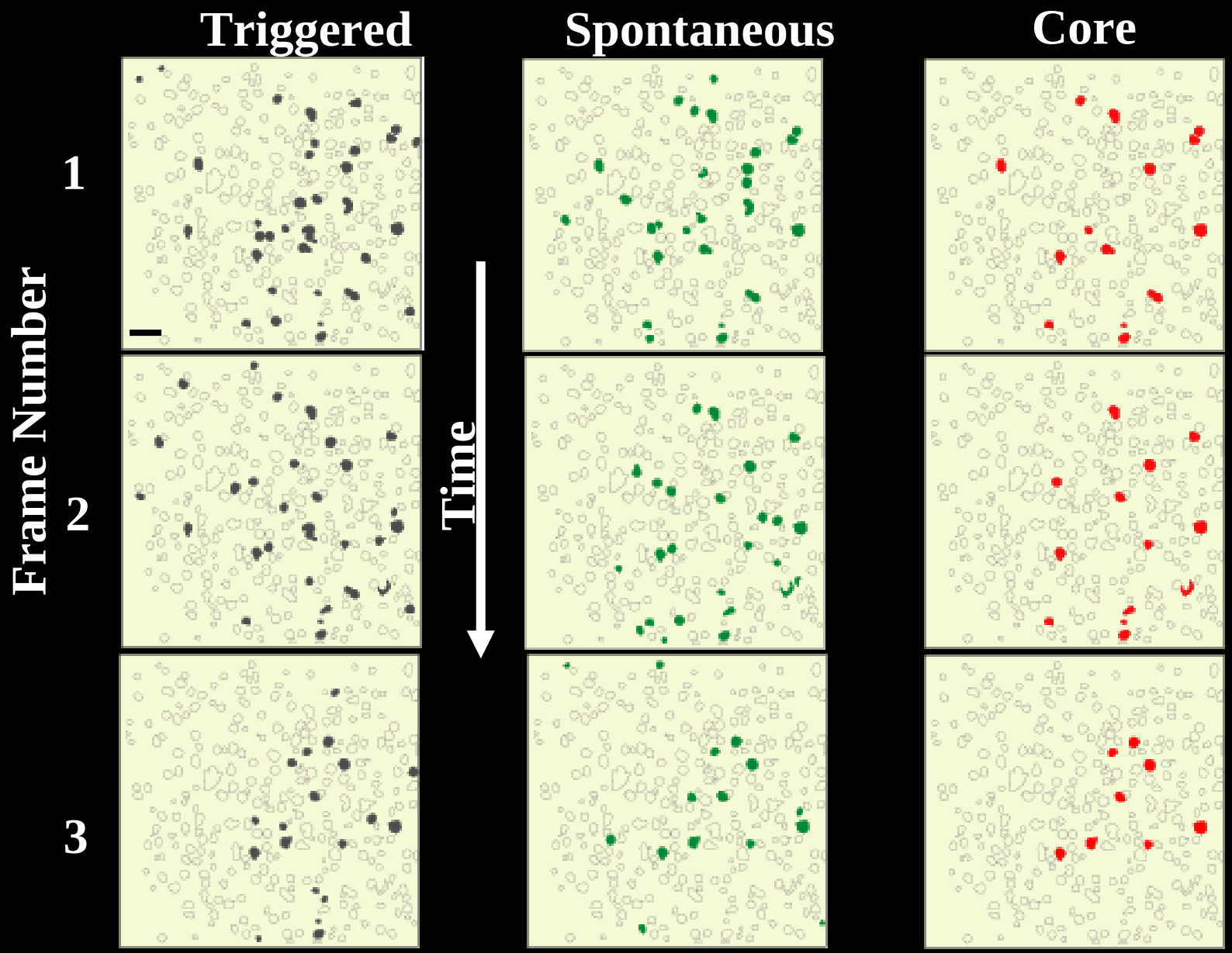


Spontaneous activity and thalamic stimulation engage the same neurons !!!



Identical Patterns during Spontaneous and Evoked Activity

100 msec/frame



Proc. Natl. Acad. Sci. USA
Vol. 79, pp. 2554–2558, April 1982
Biophysics

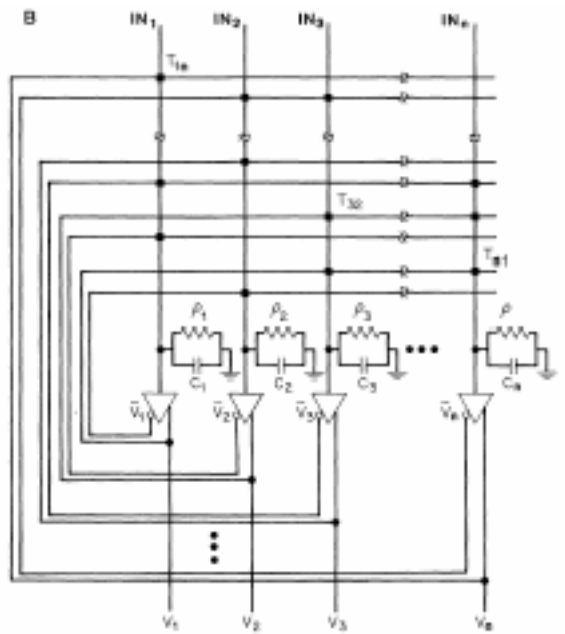
Neural networks and physical systems with emergent collective computational abilities

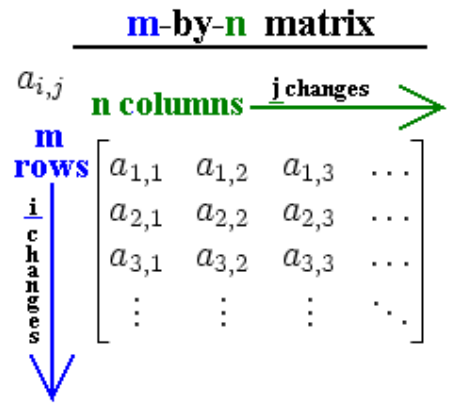
(associative memory/parallel processing/categorization/content-addressable memory/fail-soft devices)

J. J. HOPFIELD

Division of Chemistry and Biology, California Institute of Technology, Pasadena, California 91125; and Bell Laboratories, Murray Hill, New Jersey 07974

Contributed by John J. Hopfield, January 15, 1982

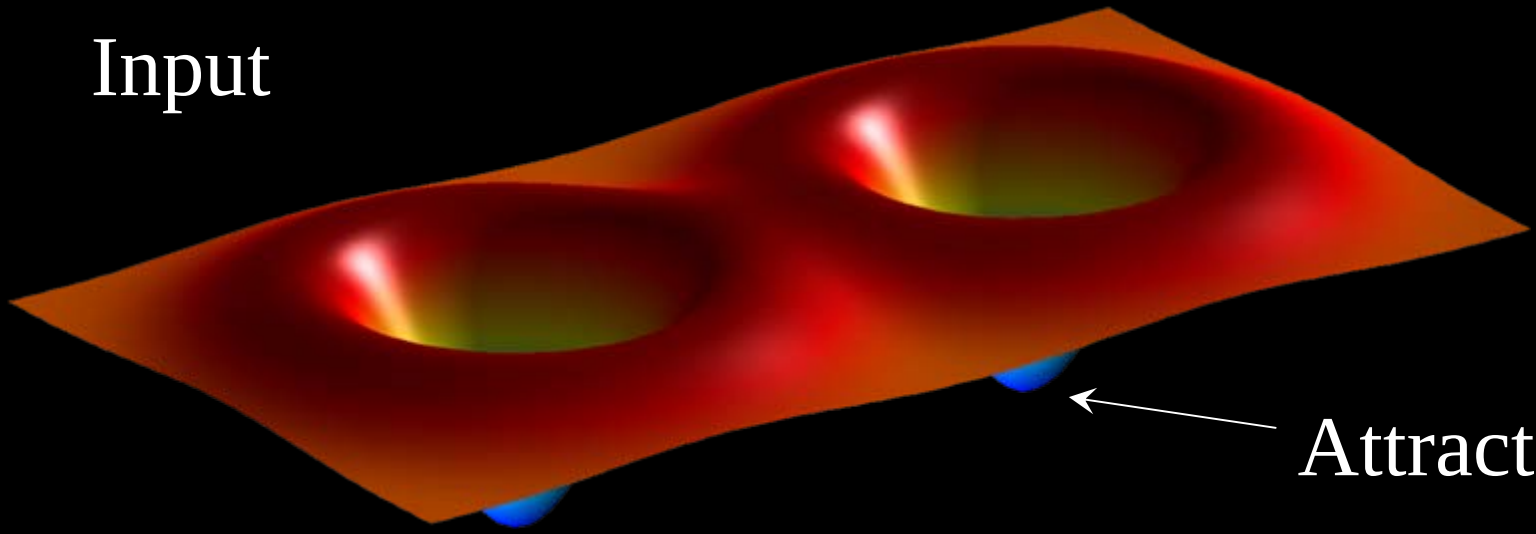


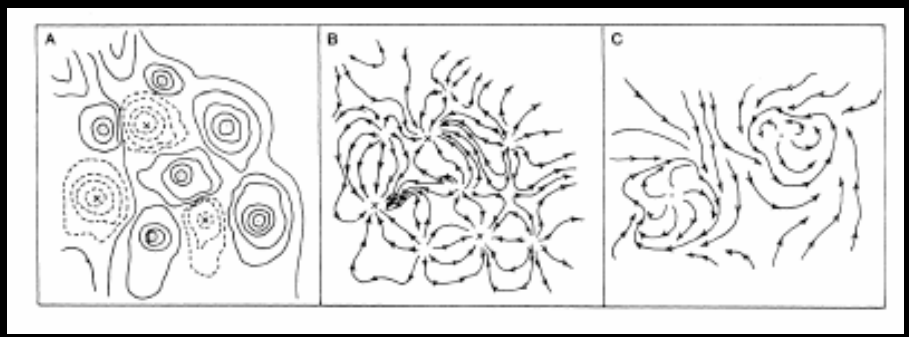


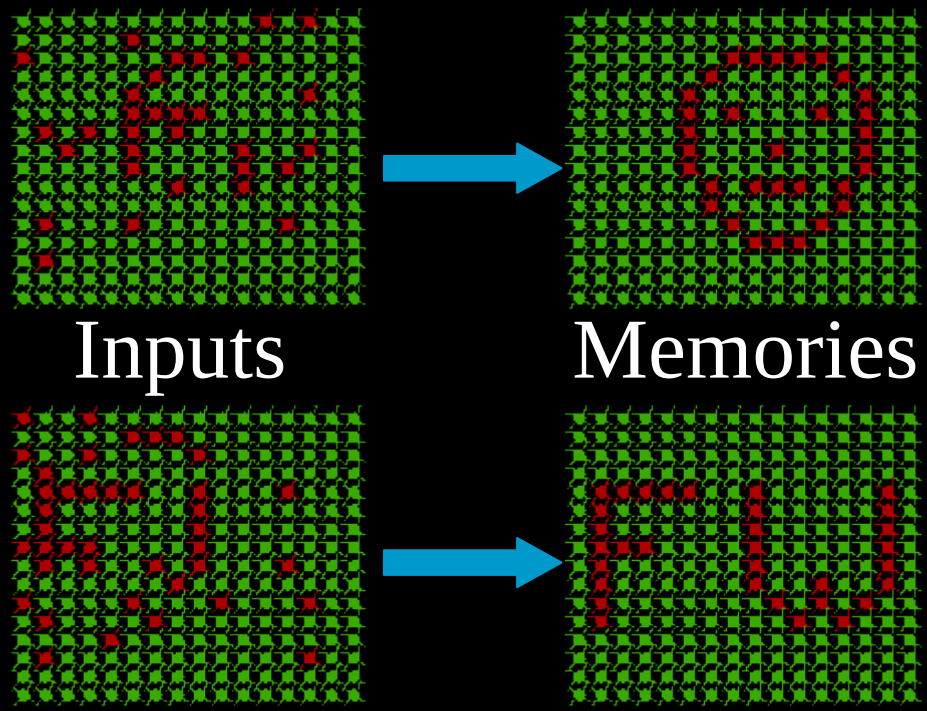
$$x_i(t+1) = \left(\sum_{j=1}^{N} a_{ij} x_j(t) - \theta_i \right)$$

(Excitatory connectivity in cortex is very distributed)

Circuit attractors : memories or solutions



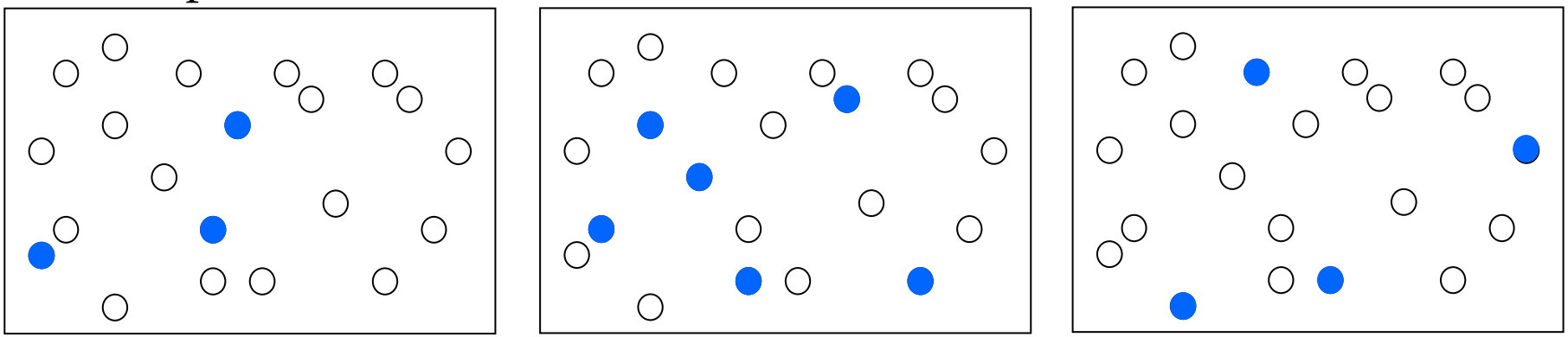




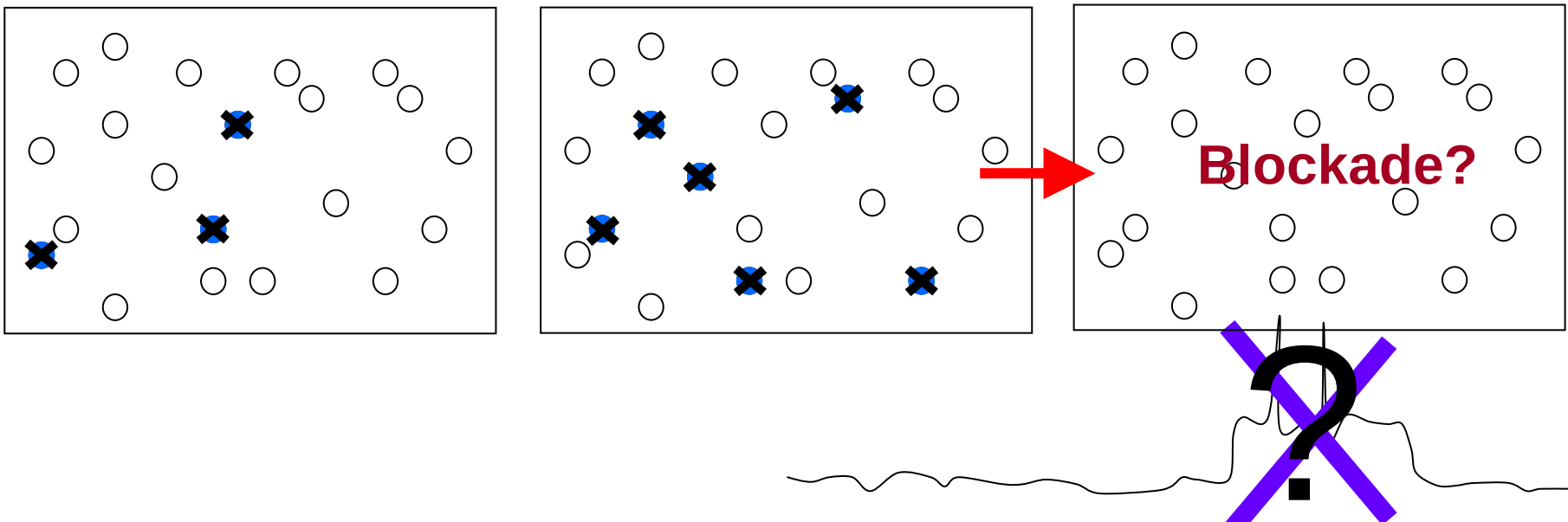
Controlling attractors:

Does ablation of cells prevent cortical pattern?

Record pattern

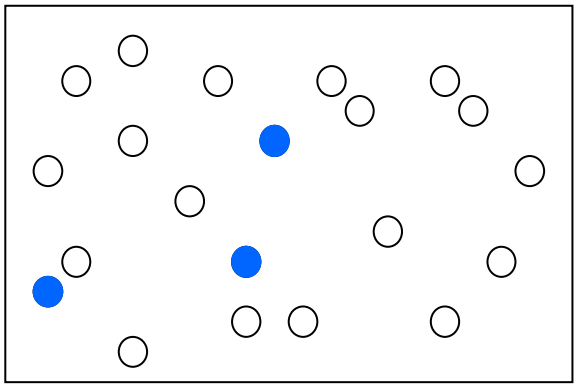


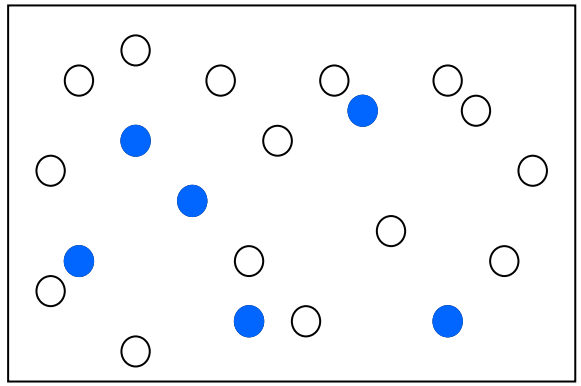
Ablate early-firing cells

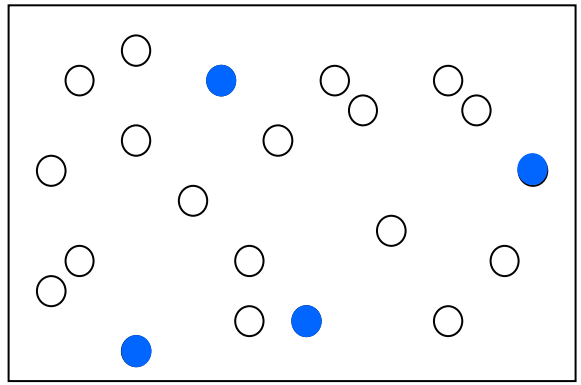


Triggering attractor dynamics with glutamate uncaging: Does the network complete patterns?

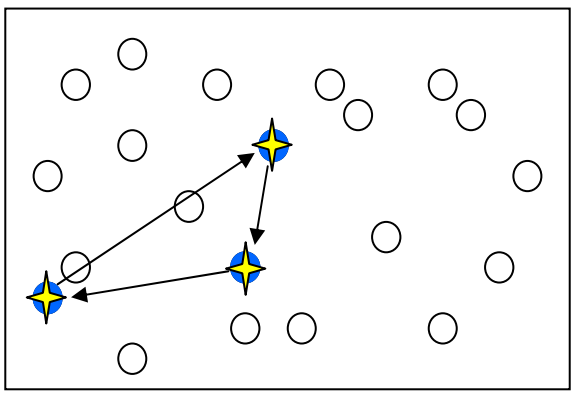
Record pattern

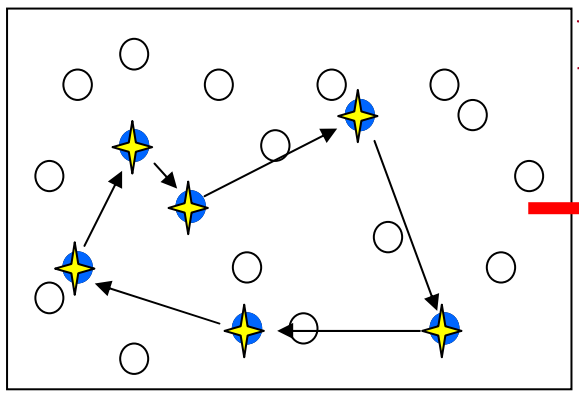




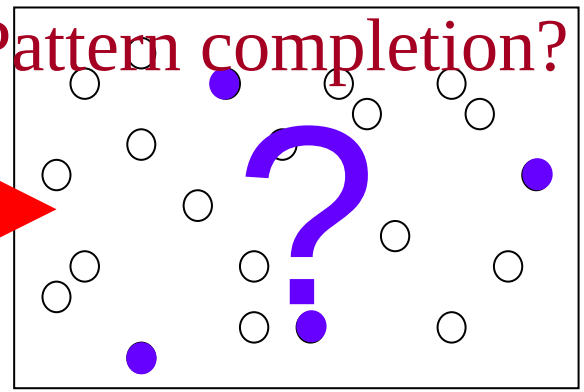


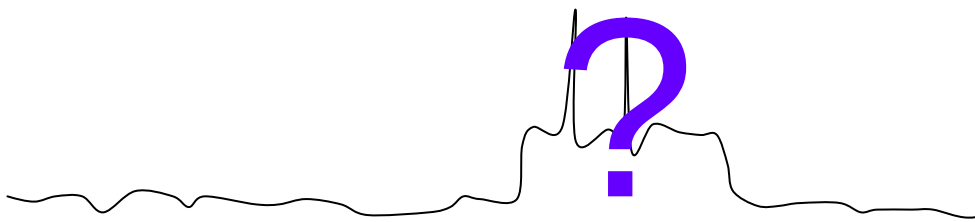
Stimulate to induce early observed sequence

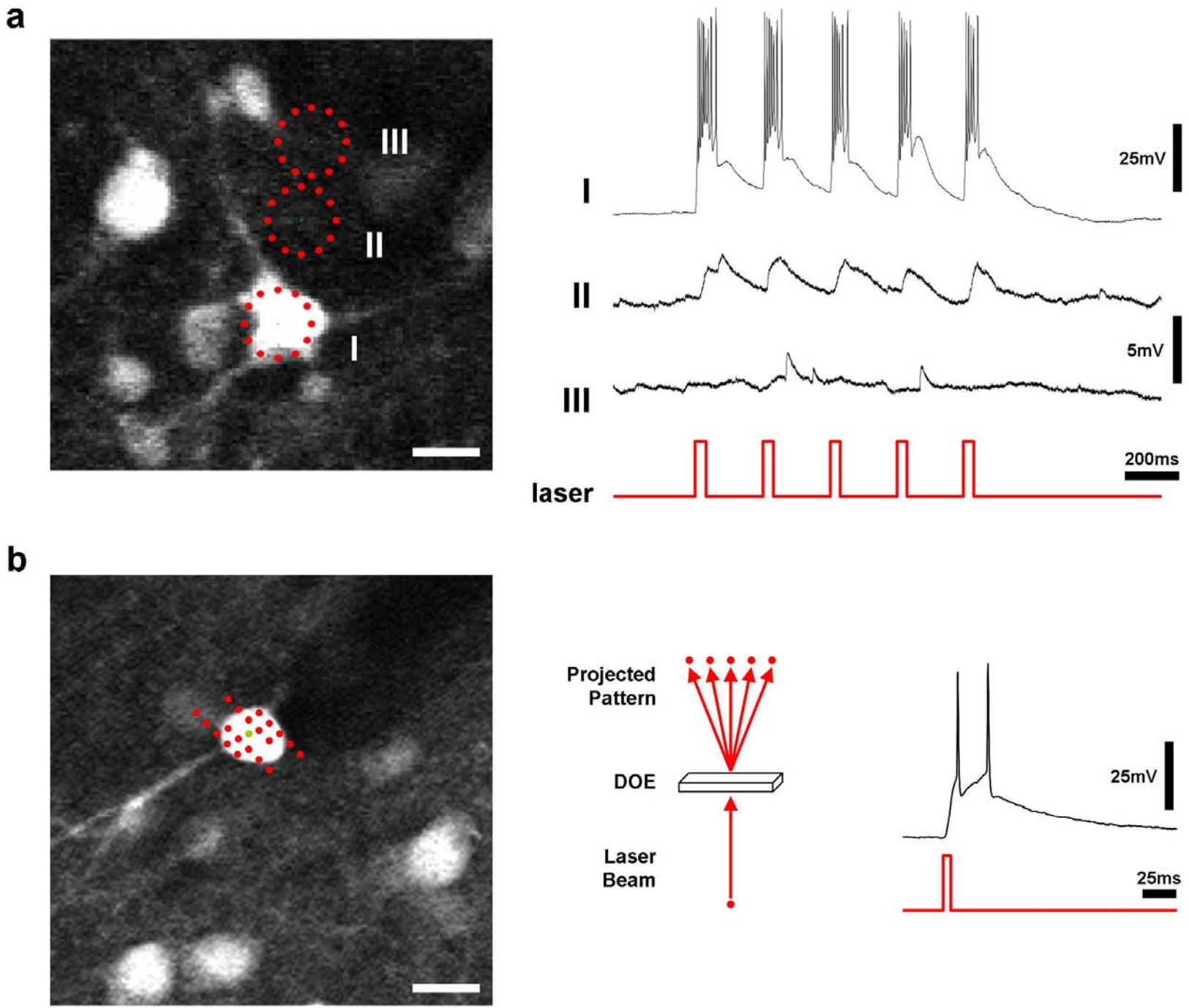




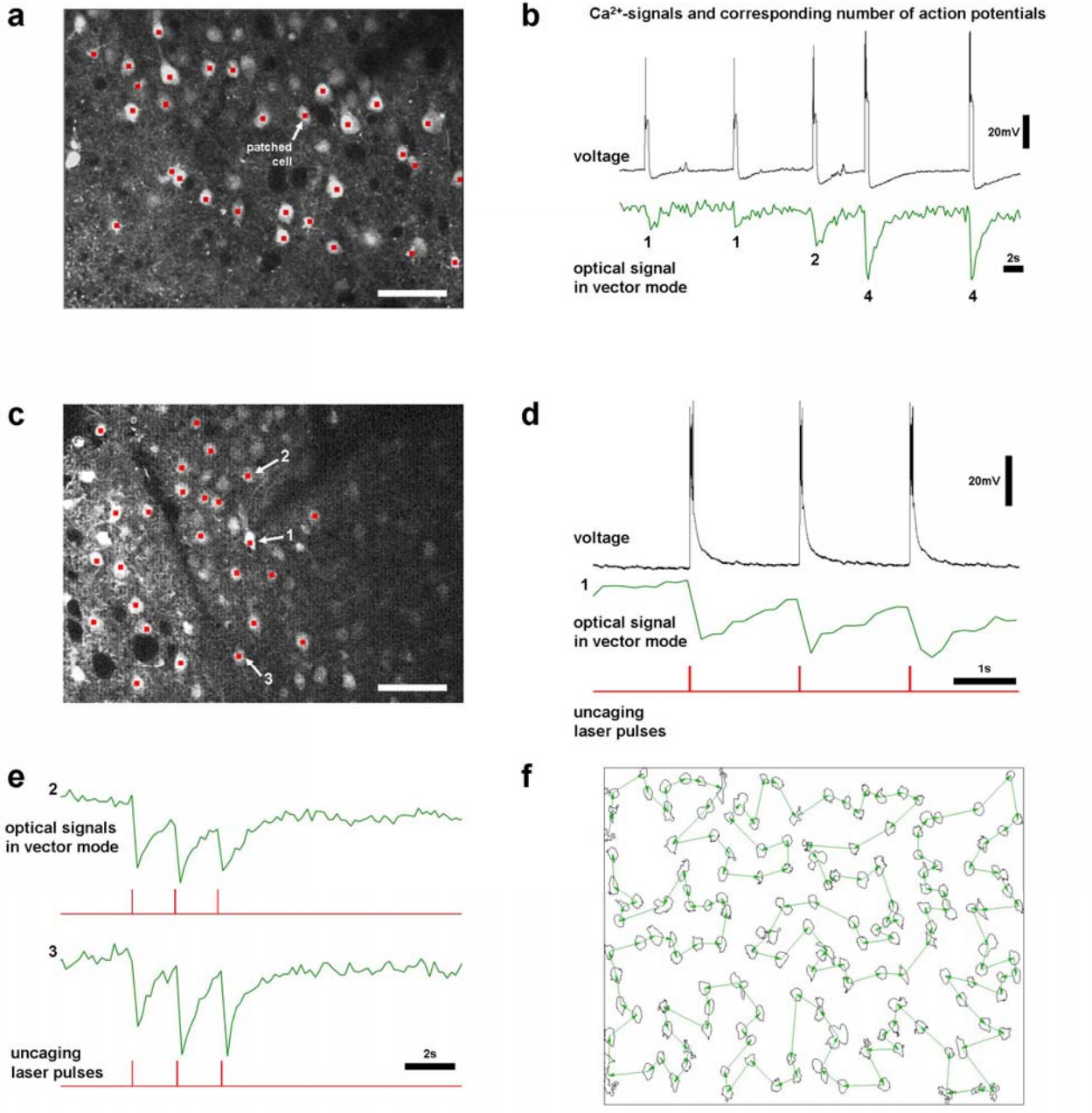
Pattern completion?

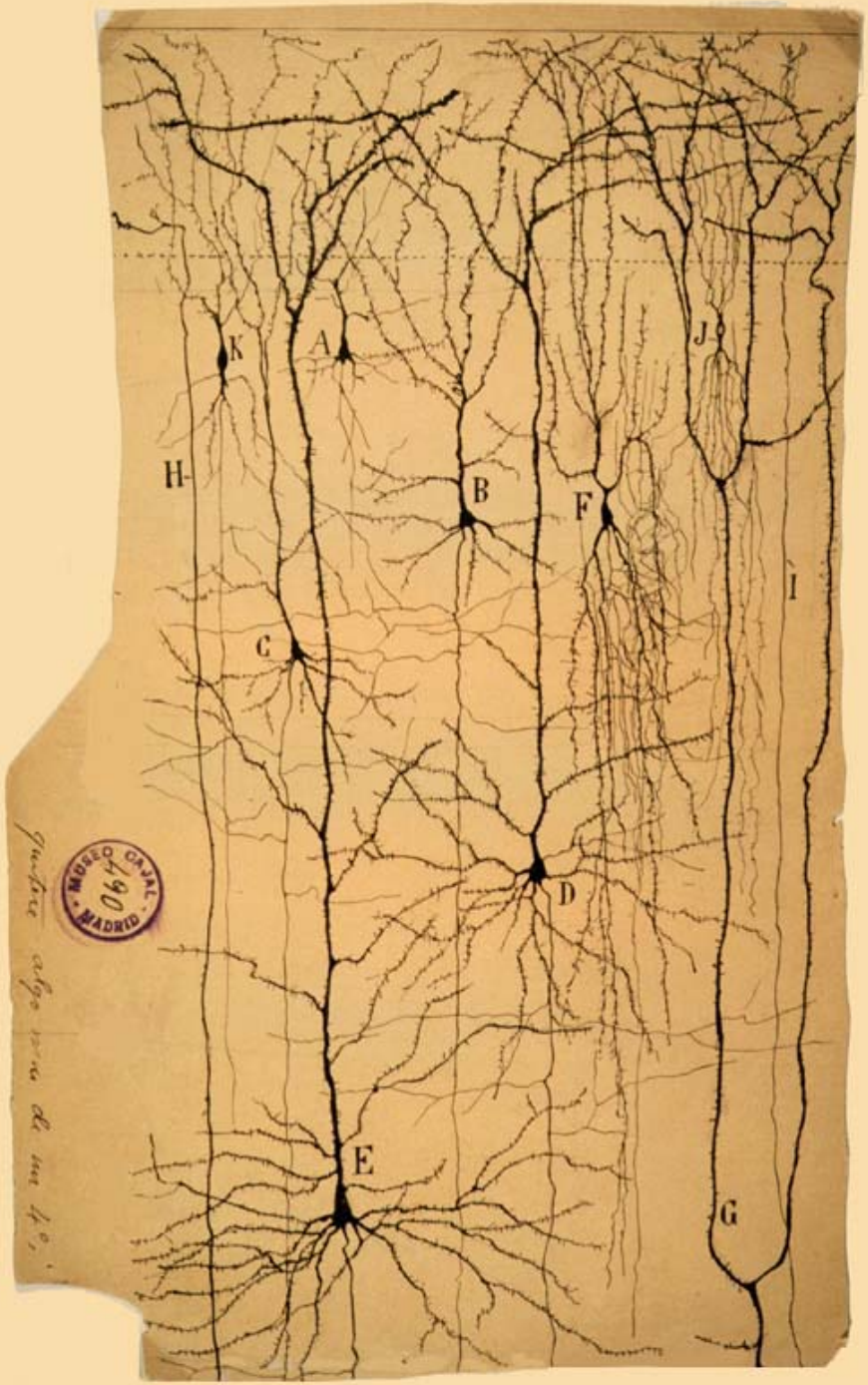





a
III
II
I
25mV
I
II
5mV
III
200ms
laser
b
Projected
Pattern
DOE
Laser
Beam
25mV
25ms

Playing the piano with the cortical microcircuit





Cortical microcircuit (~1mm^3)

-Structure:

Cell types

Connections

Random

⇒Specific

Canonical

Areal/Species

-Function:

Feedforward

⇒Feedback

Our research program:

- Define basic vocabulary of cell types in mouse cortex
- Identify down wiring diagram
- Characterize the basic grammar of activity patterns/ dynamics
  - Spontaneous activity
  - Thalamic-evoked (transfer function)
- Reverse-engineer the cortical microcircuit

Buqing Mao-postdoc (now U. Chicago)

Rosa Cossart-postdoc (now INSERM)

Dimitry Aronov-undergraduate (now MIT)

Yuji Ikegaya-visiting professor (now U. Tokyo)

Jason McLean-postdoc (now U. Chicago)

Vovan Nikolenko- PhD student

Brendon Watson-MD PhD student

National Eye Institute

- Reverberating activity is prevalent at all temporal scales

- Spatiotemporal patterns are real: statistics, two techniques, spatial profile, UP states, dopamine modulates, *they can be triggered*

- Sparse dynamics: small number of cells

- Single neurons can participate in many patterns: emergent code

- Repetitions never exact

- Thalamic stimulation triggers internal patterns/states

- Cortex is essentially “deaf” during spontaneous activity

- Pacemaker cells in neocortex