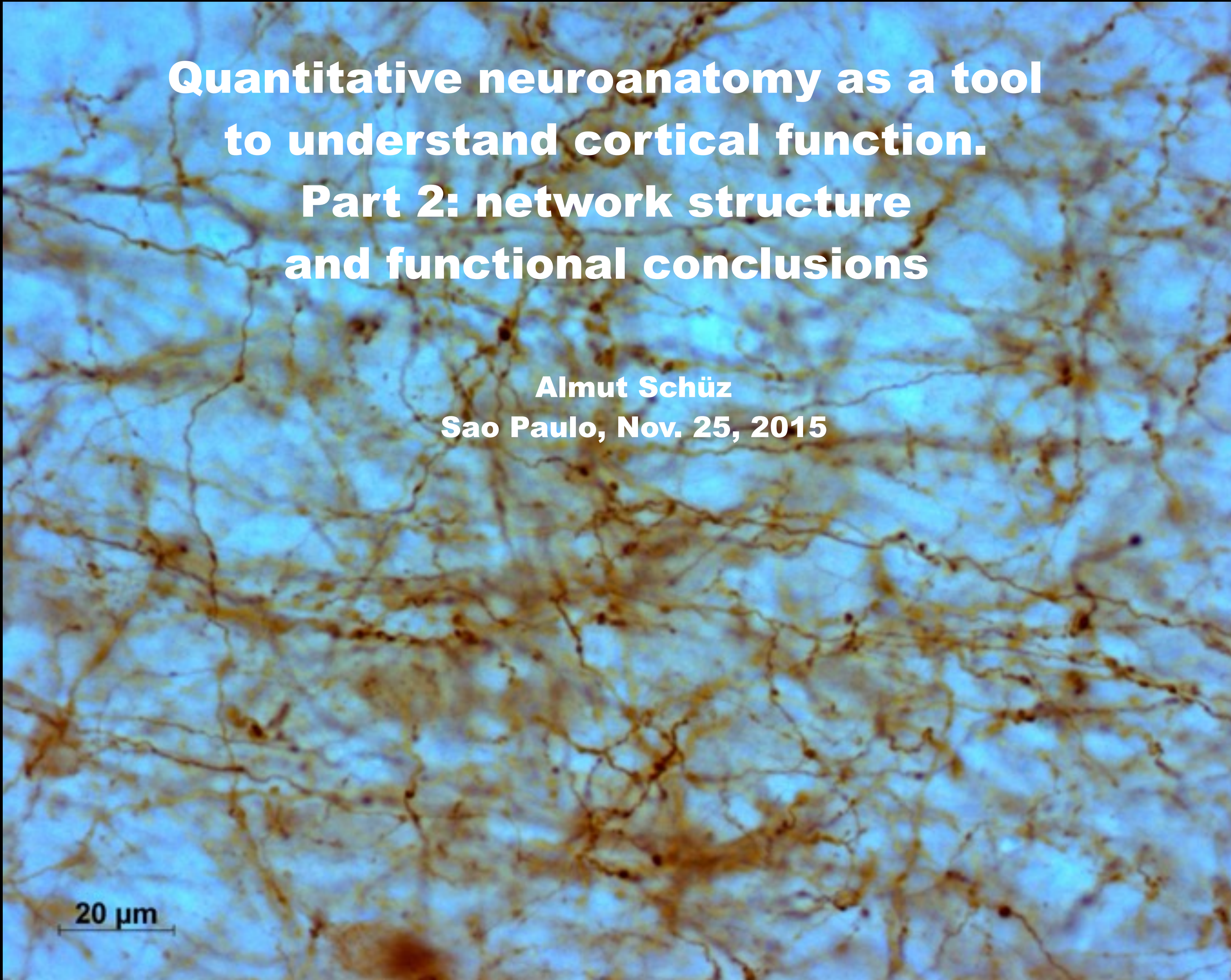
Quantitative neuroanatomy as a tool to understand cortical function. Part 2: network structure and functional conclusions

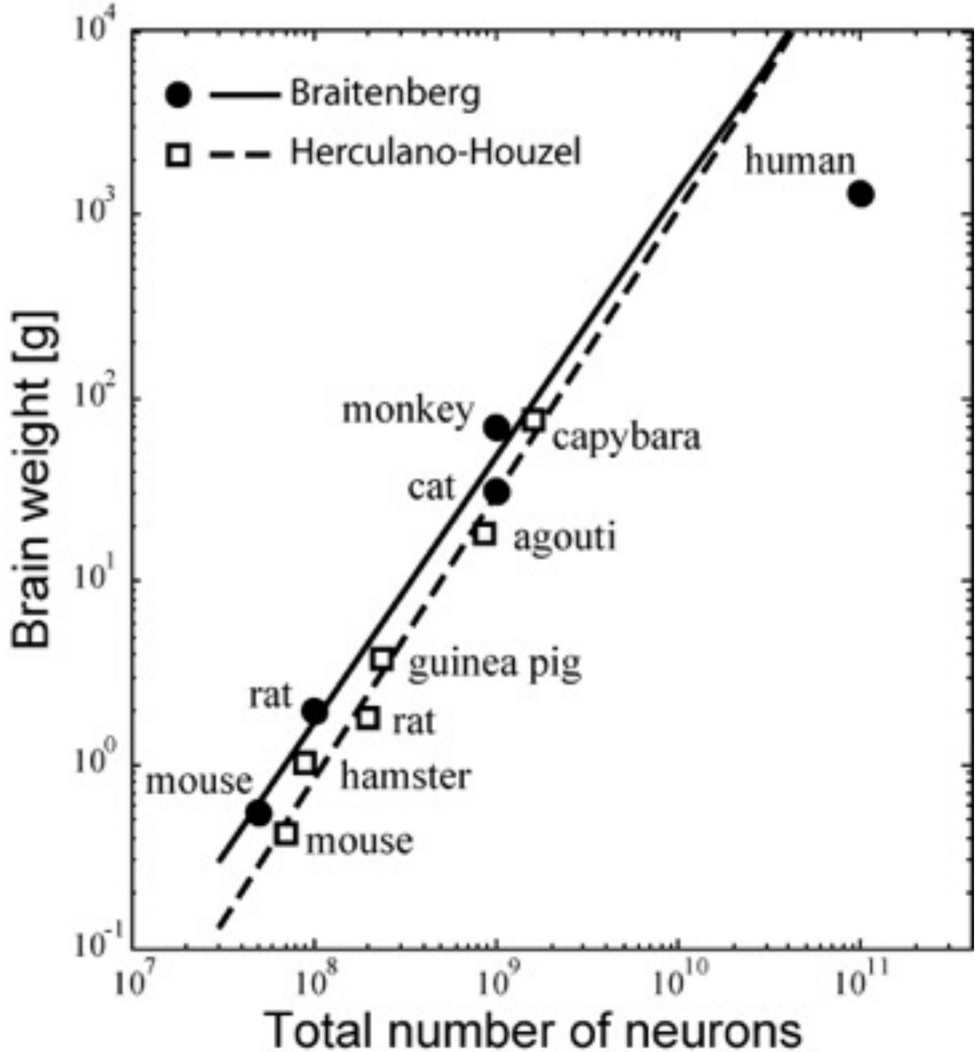
Almut Schüz

Sao Paulo, Nov. 25, 2015

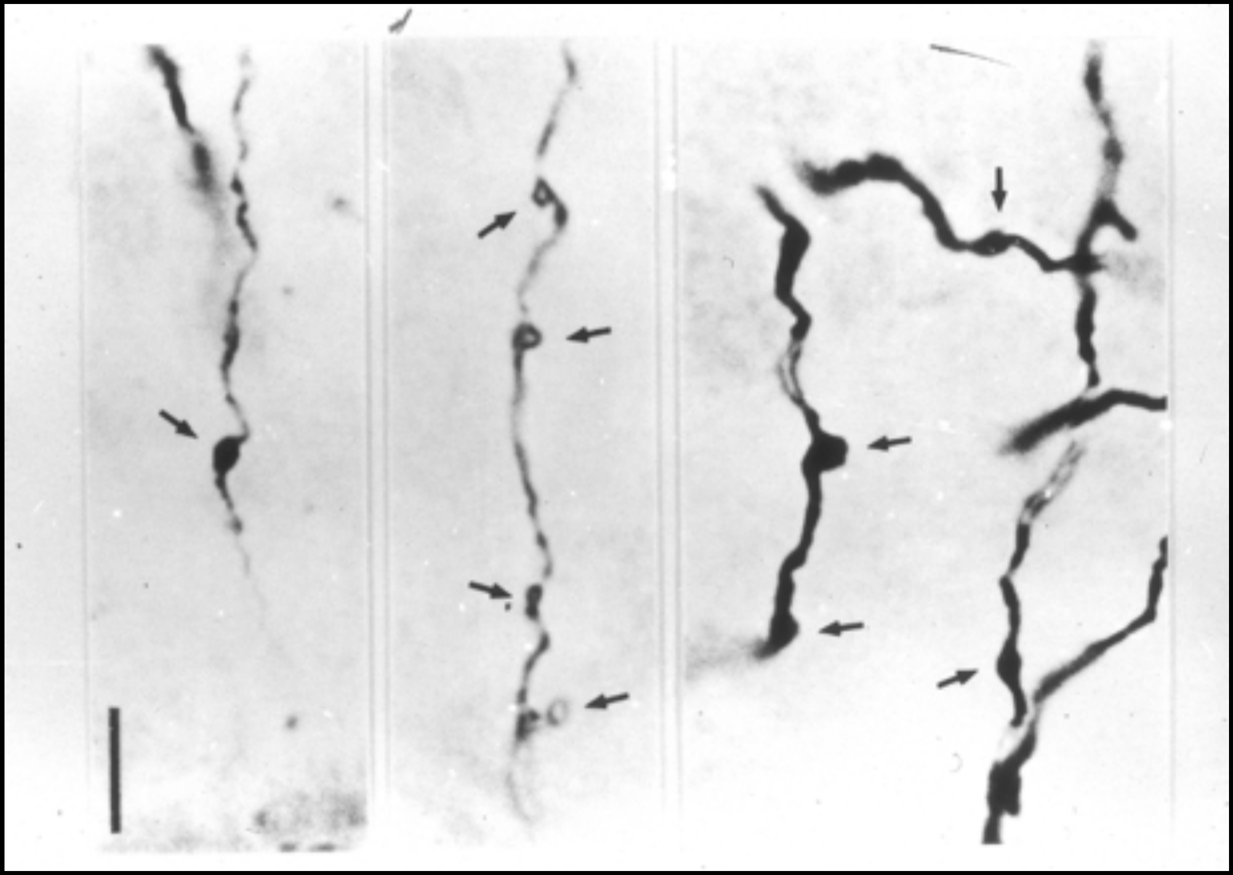


Density of synapses along axons

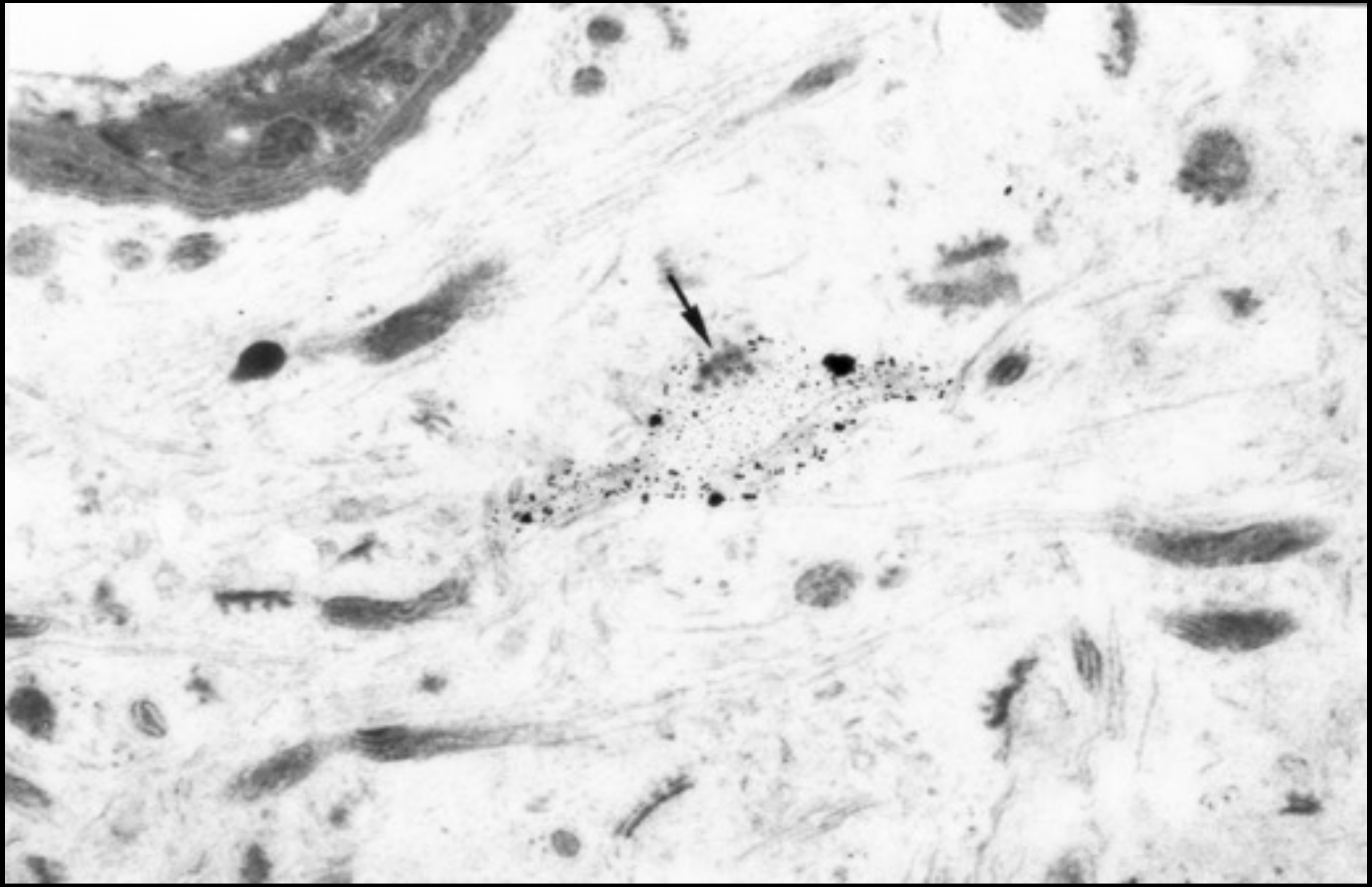
Probability of connections between neurons



Braitenberg
Herculano-Houzel
human
monkey
capybara
cat
agouti
guinea pig
rat
rat
mouse
hamster
mouse
Brain weight [g]
Total number of neurons
10^4
10^3
10^2
10^1
10^0
10^{-1}
10^7
10^8
10^9
10^{10}
10^{11}



From Schüz and Münster (1985)



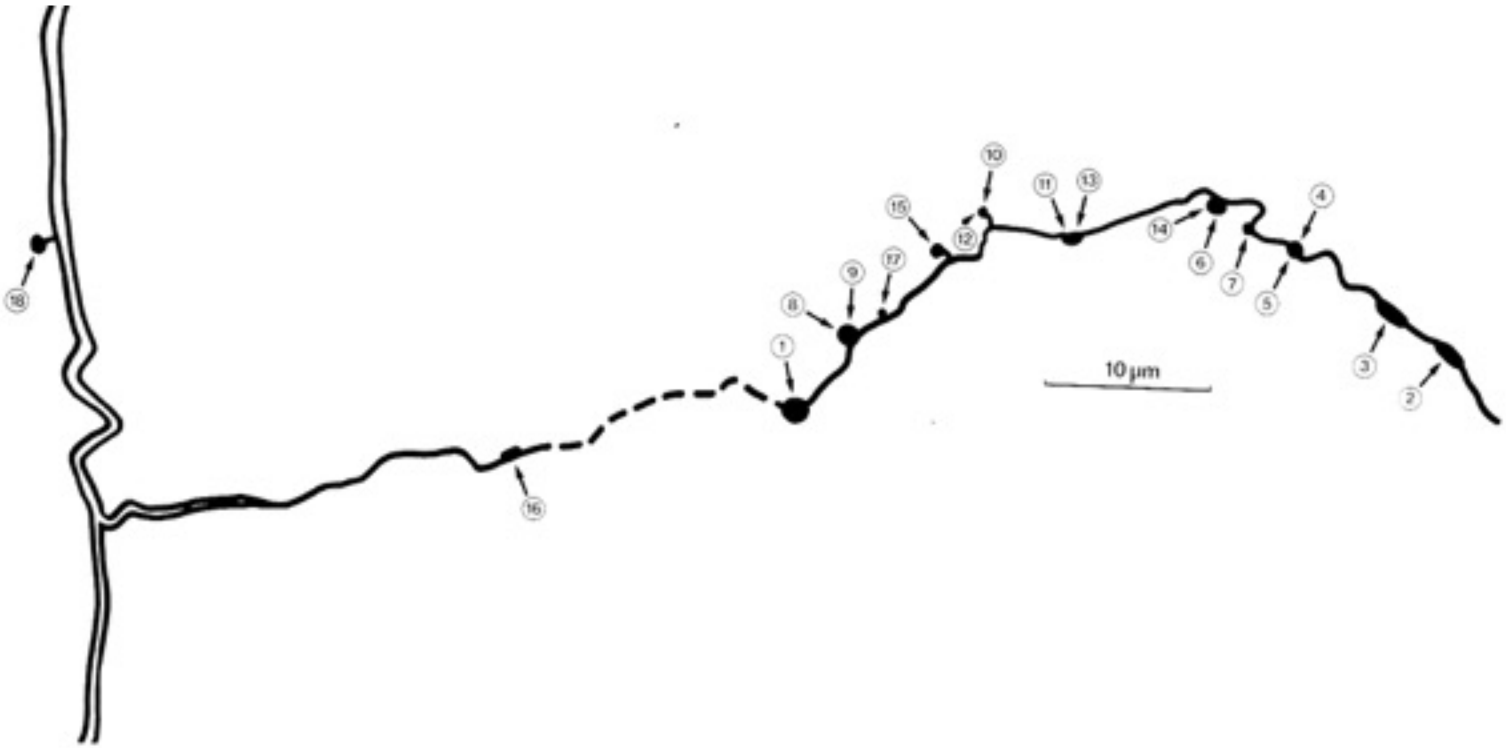
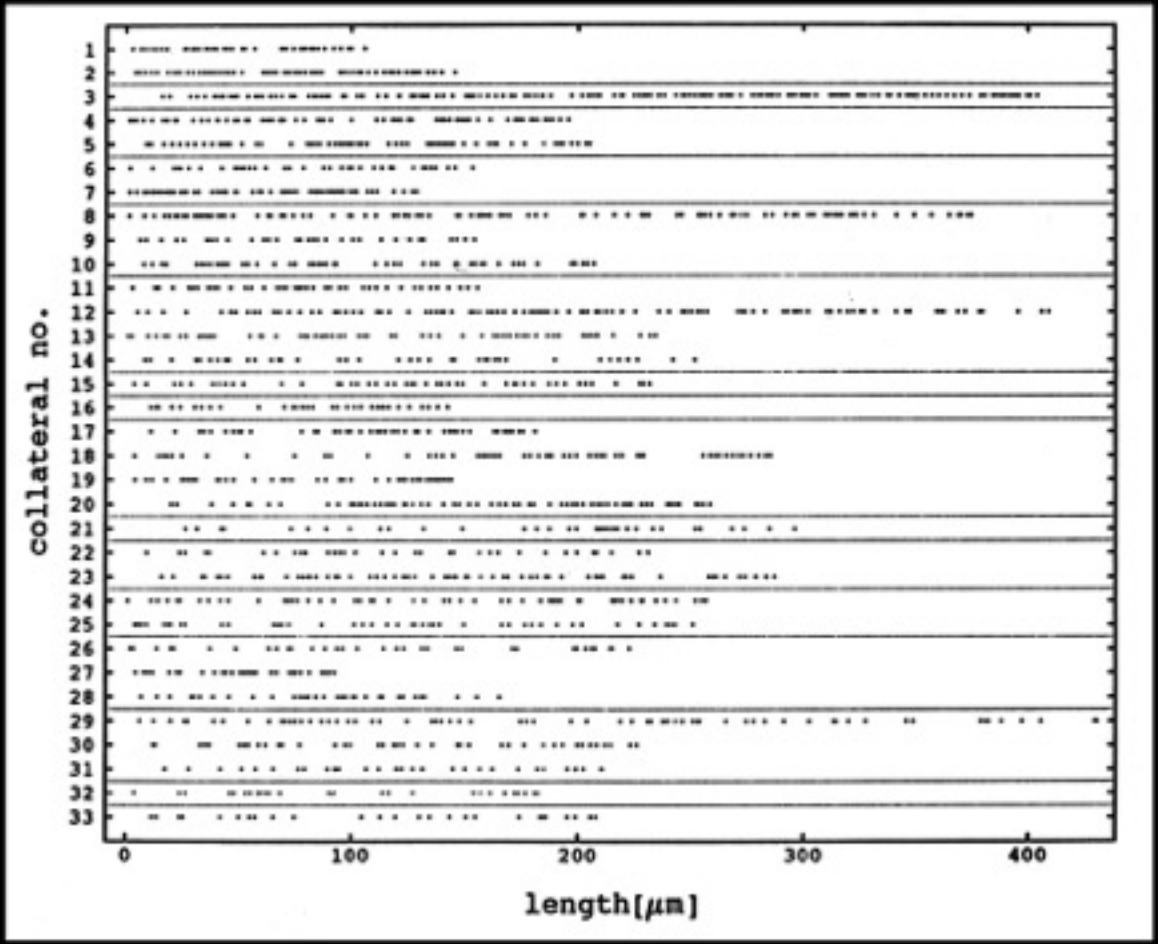


Abb. 34: *rechte Kollaterale des Axonbaumes in Abb. 33. Die Pfeile weisen auf (durchnumerierte) Synapsen hin. Alle befinden sich auf Verdickungen oder kleinen Fortsätzen. Aus Schüz und Münster (1985).*

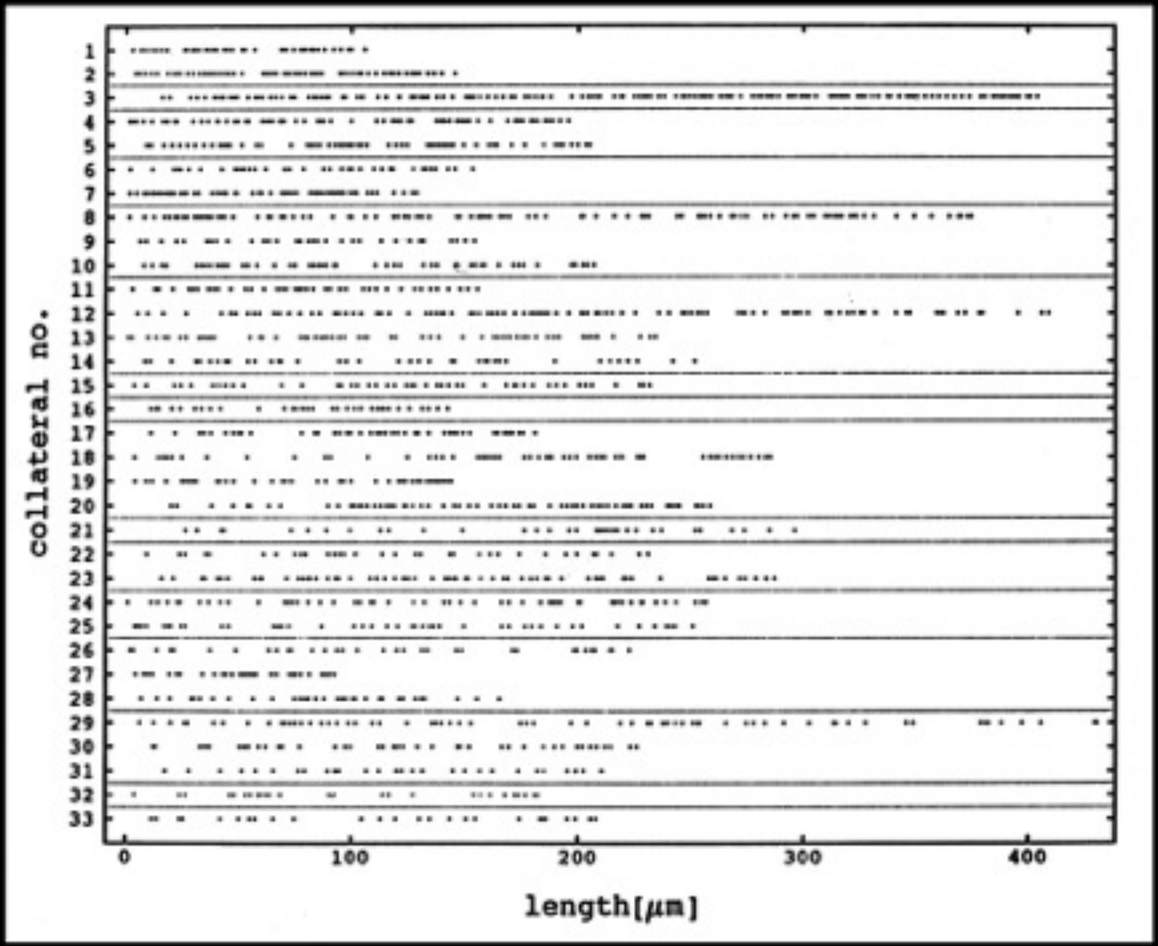
Distribution of synaptic boutons along collaterals



From: Hellwig et al. (1994)

Average: 1 synapse every 5 μm

Distribution of synaptic boutons along collaterals



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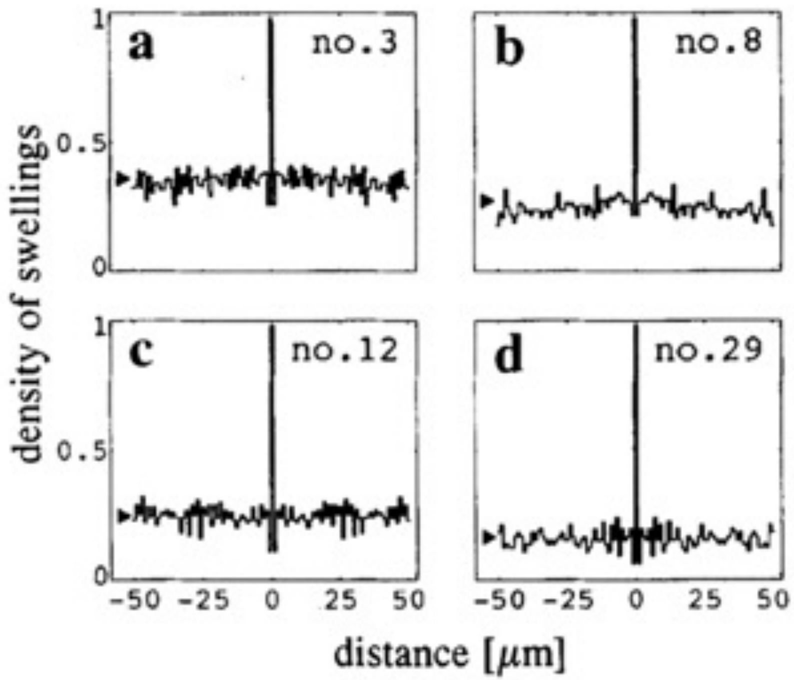


Fig. 10a–d. Autocorrelograms for the same collaterals as in Fig. 7. The *abscissa* shows distances between swellings, the *ordinate* the density of swellings per bin (bin size 1 μm). The density of swellings per bin can be interpreted as the probability of finding a swelling as a function of a certain distance to any given swelling. Apart from the trivial peak at position 0 and the small dip surrounding it, the autocorrelograms are essentially constant. Moreover, they equal the value, predicted on the basis of the average interswelling interval (*arrowheads*), which argues against the presence of any long-range trends in synaptic density along the axon collateral

pyramidal cell,
rat cortex.
intracellular injection
of biocytin

From:
Bernhard Hellwig
(2000)

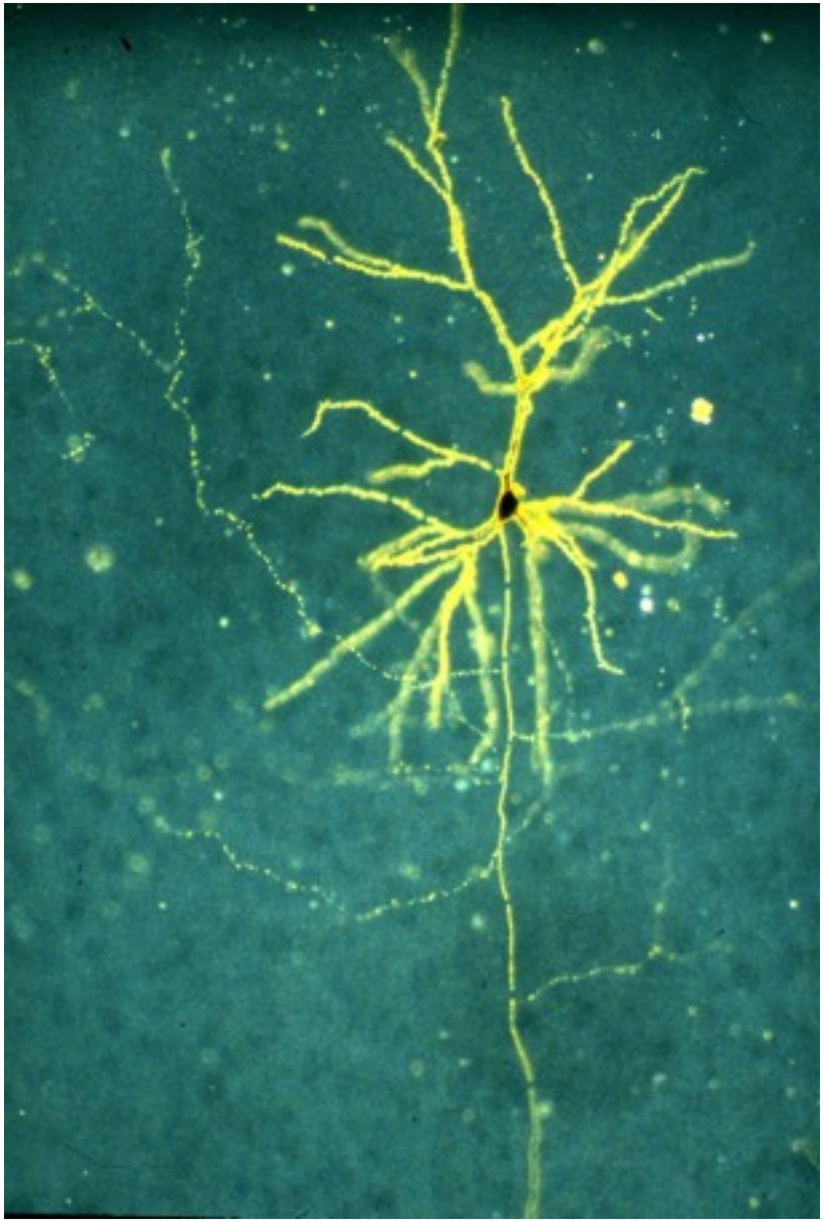


Fig. 3. Camera lucida drawings of dendritic arborizations of layer-2 pyramidal neurons. The position of the cortical surface is indicated by the corners in the upper right and upper left parts of the diagram. *Bar* 100 µm

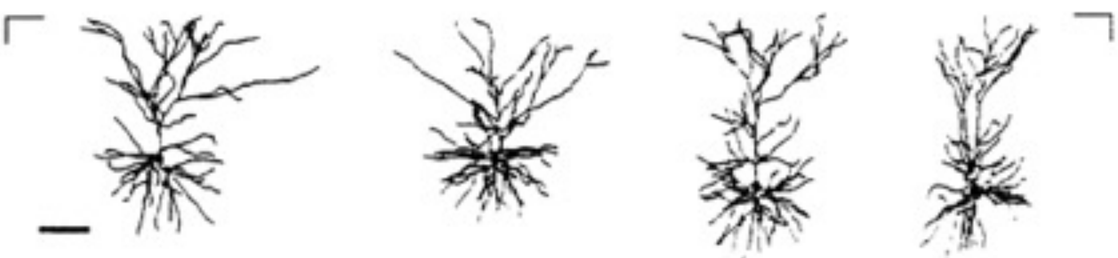


Fig. 4. Camera lucida drawings of dendritic arborizations of layer-3 pyramidal neurons. The position of the cortical surface is indicated by the corners in the upper right and upper left parts of the diagram. *Bar* 100 µm From Hellwig (2000)

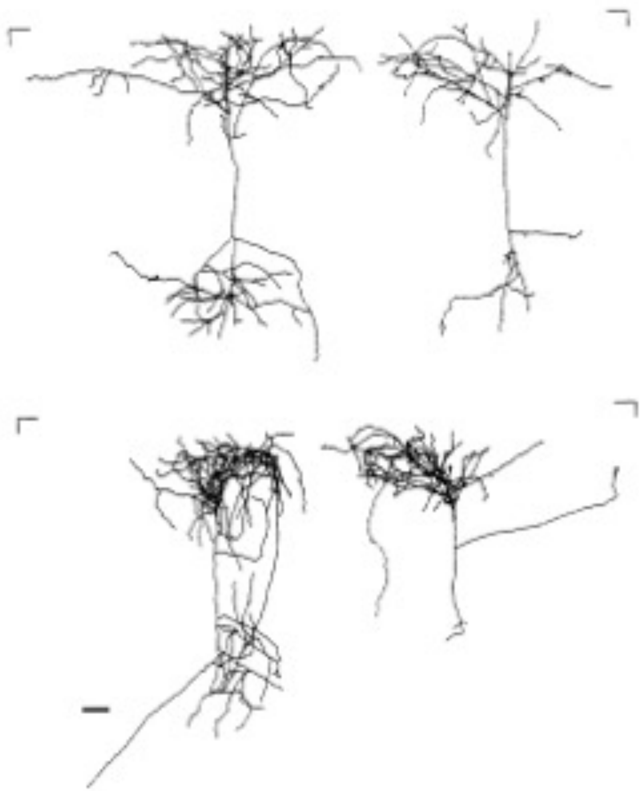


Fig. 5. Camera lucida drawings of axonal arborizations of layer-2 pyramidal neurons. The corners indicate the position of the cortical surface. *Bar* 100 µm

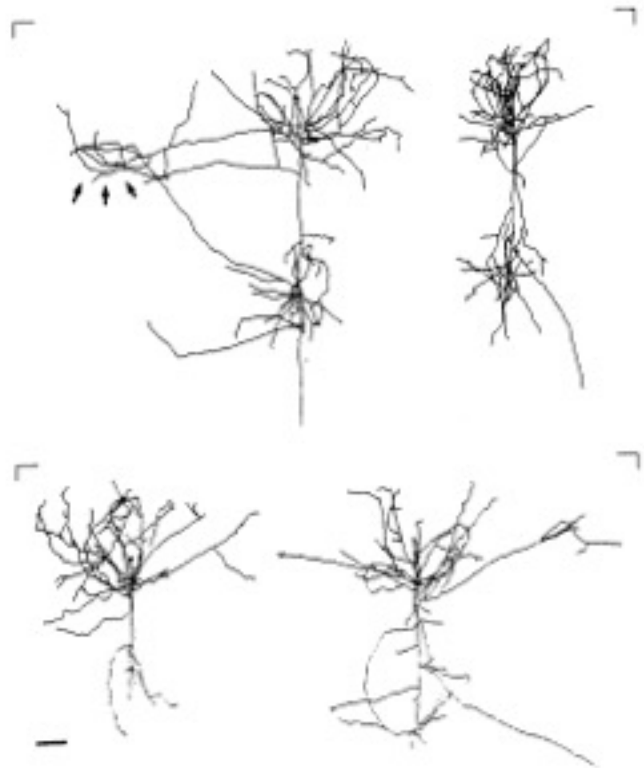
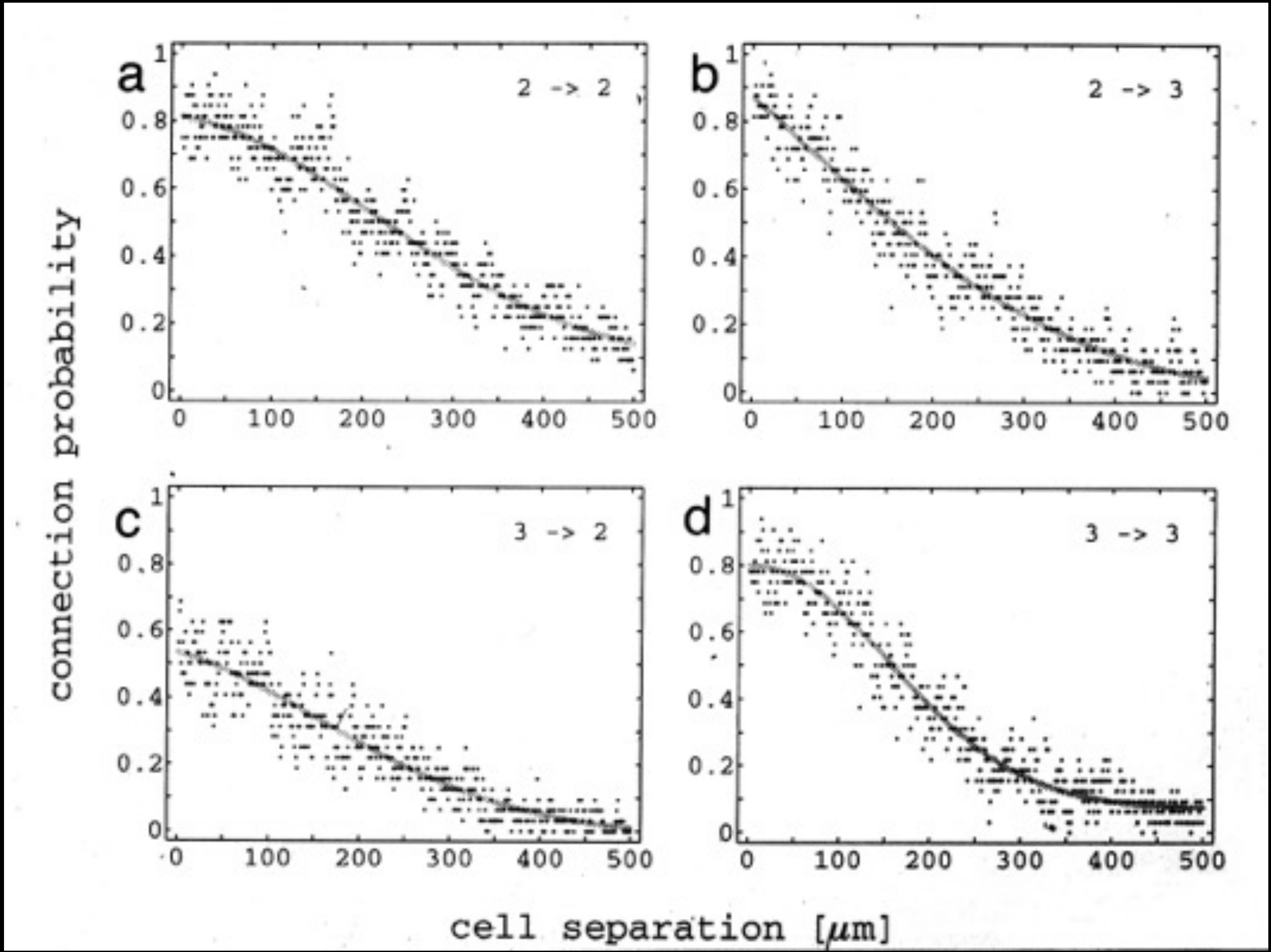
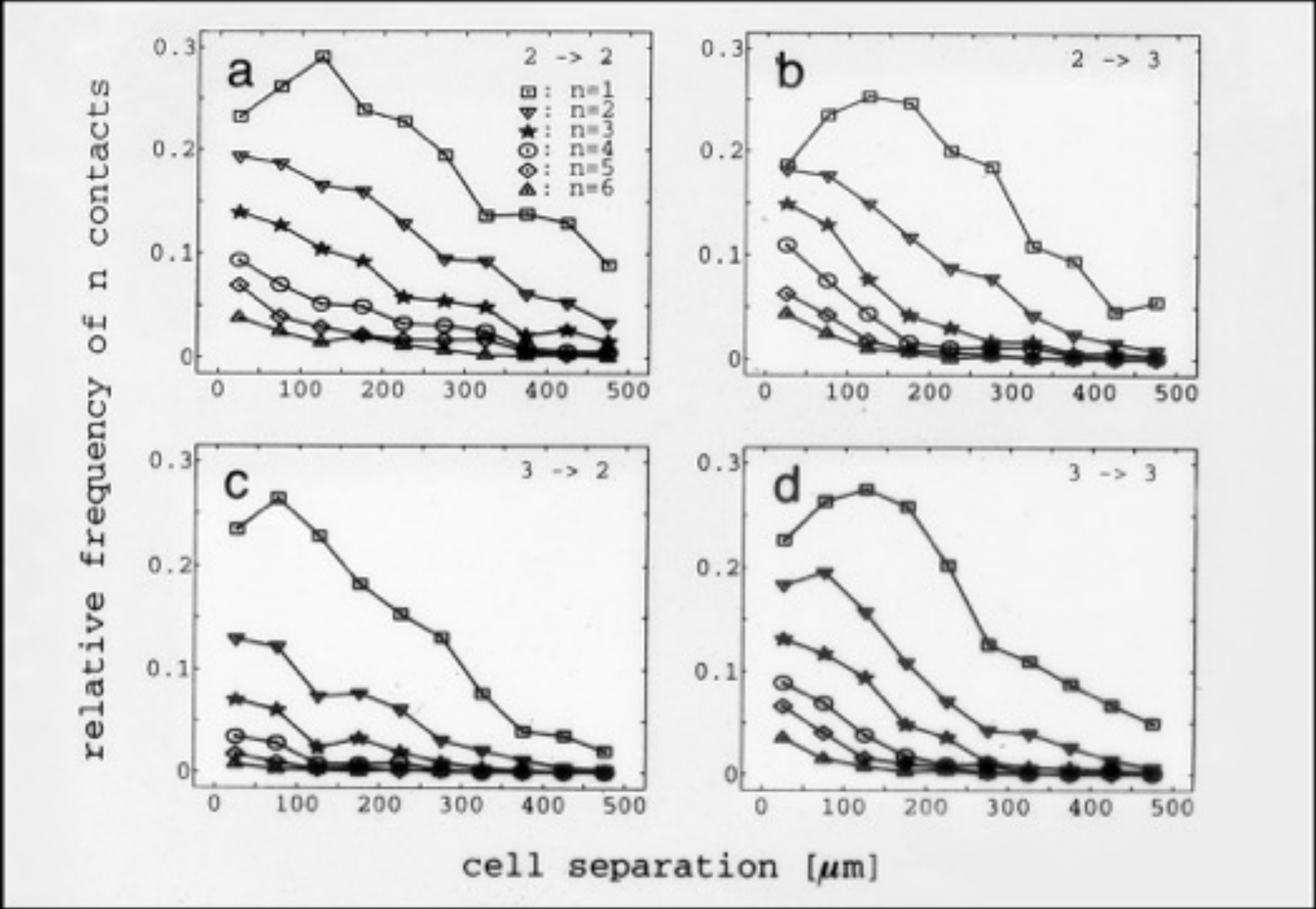


Fig. 6. Camera lucida drawings of axonal arborizations of layer-3 pyramidal neurons. The corners indicate the position of the cortical surface. *Arrows* point to a cluster of axon collaterals. *Bar* 100 µm

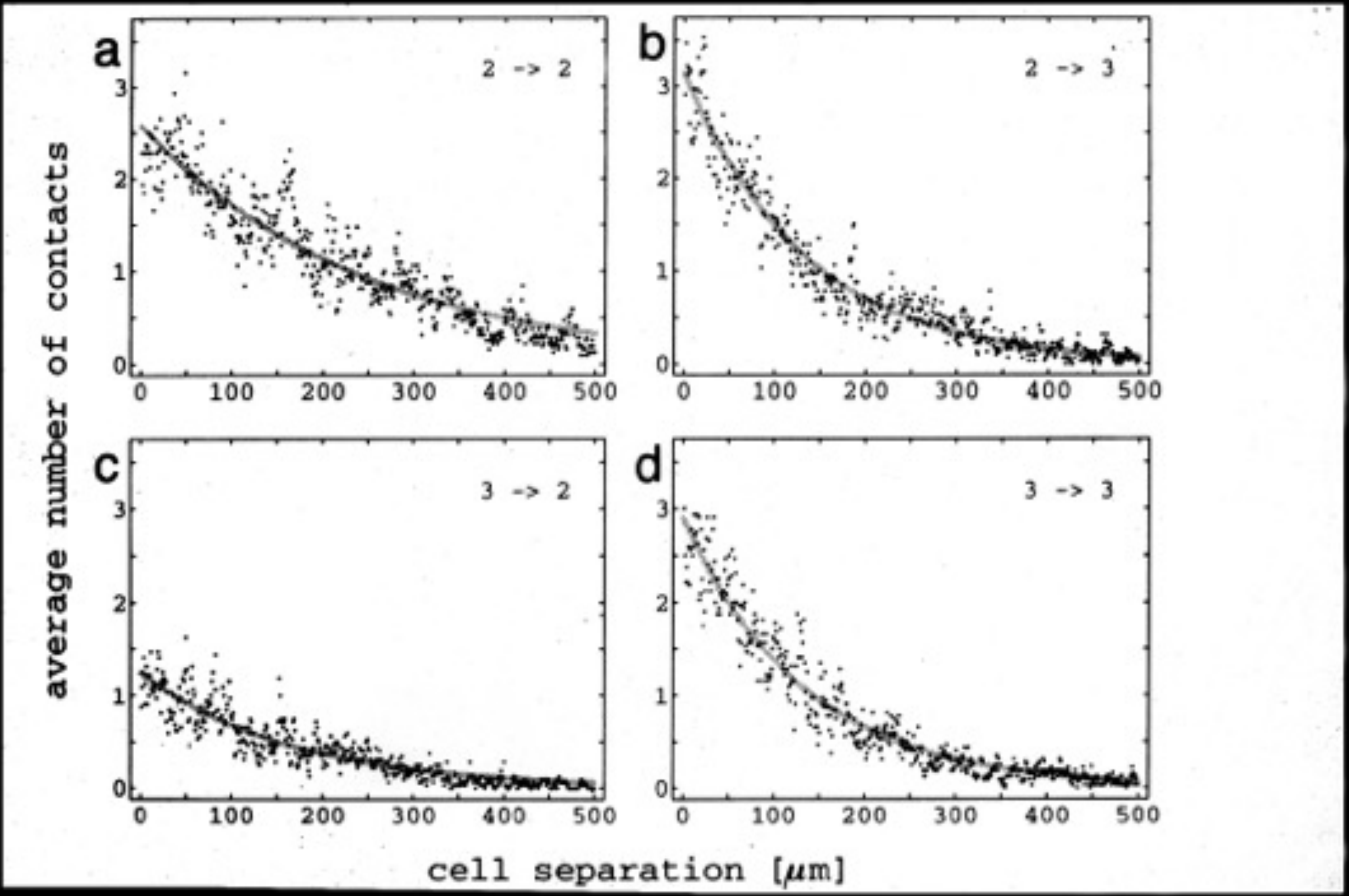
From Hellwig (2000)

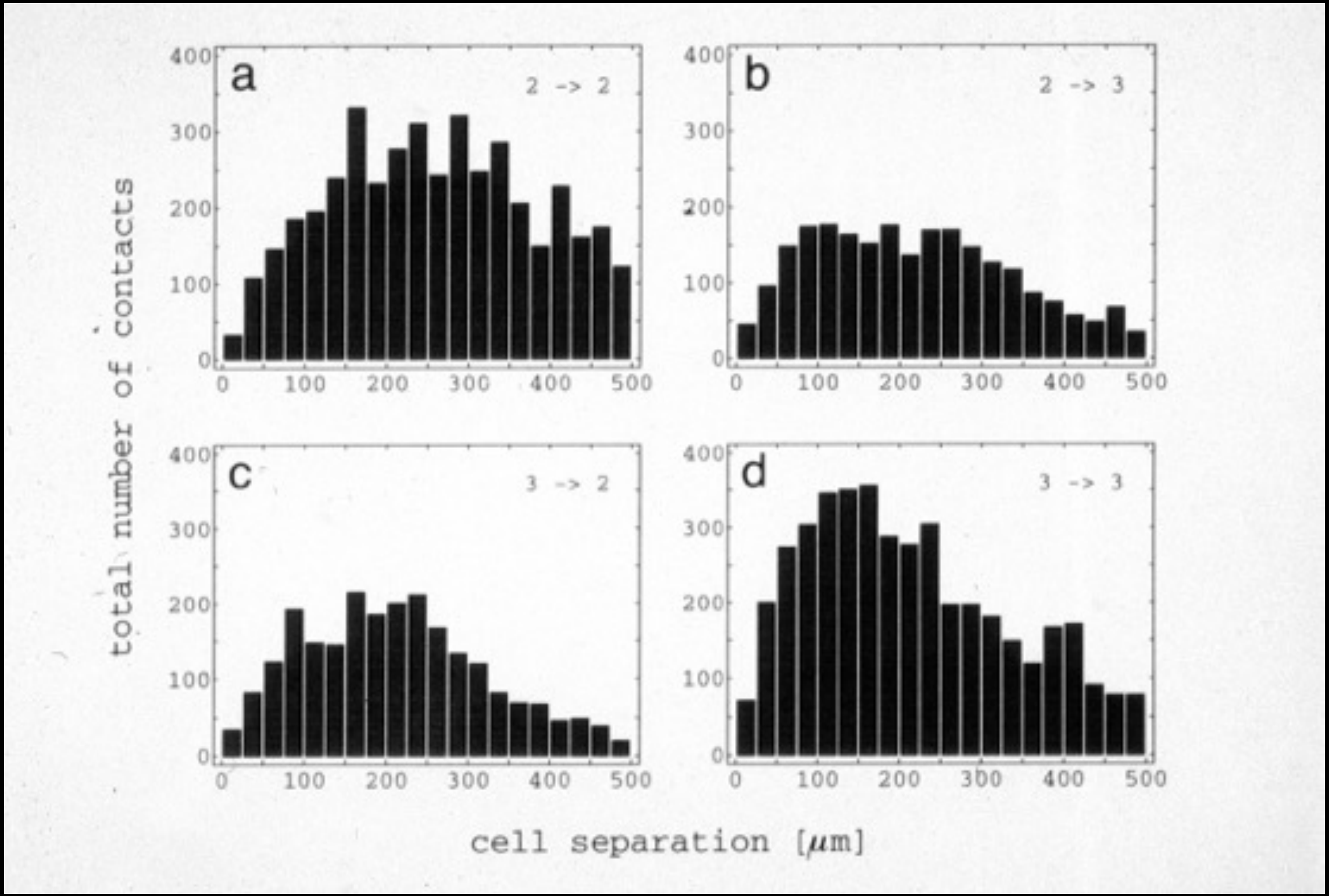


From: Bernhard Hellwig (2000)



From: Bernhard Hellwig (2000)


a
2 -> 2
b
2 -> 3
c
3 -> 2
d
3 -> 3
average number of contacts
cell separation [μm]
0
1
2
3
0
100
200
300
400
500



From: Bernhard Hellwig (2000)

Results

Input neurons (mouse cortex) < 10^6

Neurons in the cortex: 1.6×10^7

Input neurons (mouse cortex) $< 10^6$

Neurons in the cortex: 1.6×10^7

(human cortex)

Input neurons: order of 10^8

Neurons in the cortex: order of 10^{10} (Haug)

Input neurons (mouse cortex) < 10^6

Neurons in the cortex: 1.6 x 10^7

(human cortex)

Input neurons: order of 10^8

Neurons in the cortex: order of 10^{10} (Haug)

1. The cortex is mainly connected in itself

Pyramidal cells:

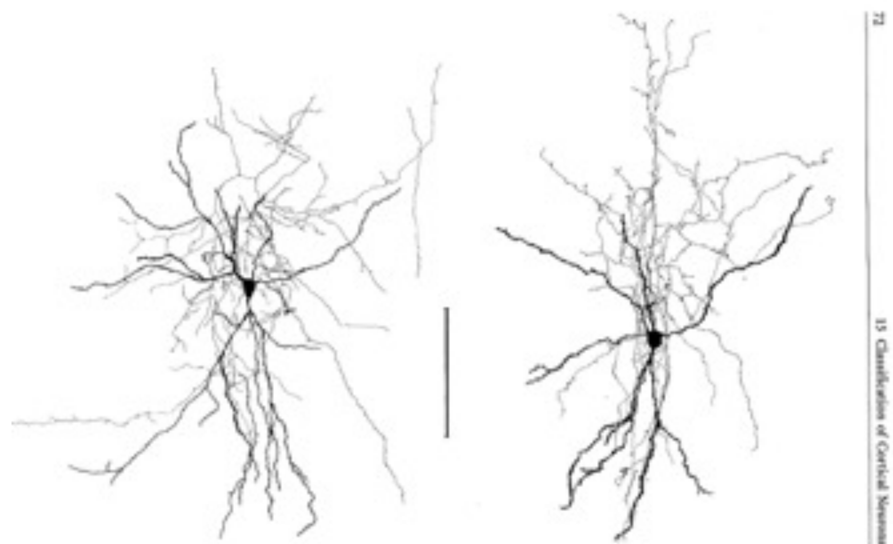
Dendritic spines

Local and distant axonal ramifications

Non-pyramidal cells:

Smooth dendrites

Local axonal ramifications



Pyramidal cells:

Dendritic spines

Local and distant axonal ramifications

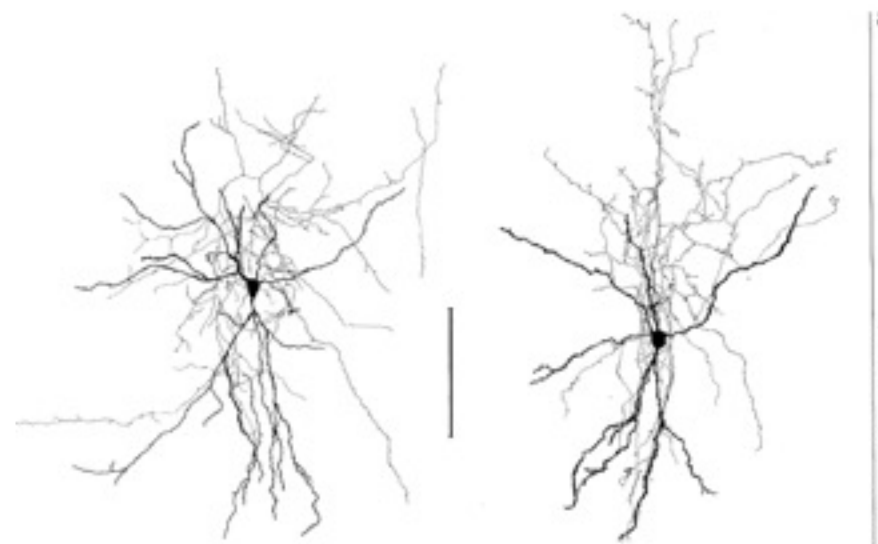
Excitatory

Non-pyramidal cells:

Smooth dendrites

Local axonal ramifications

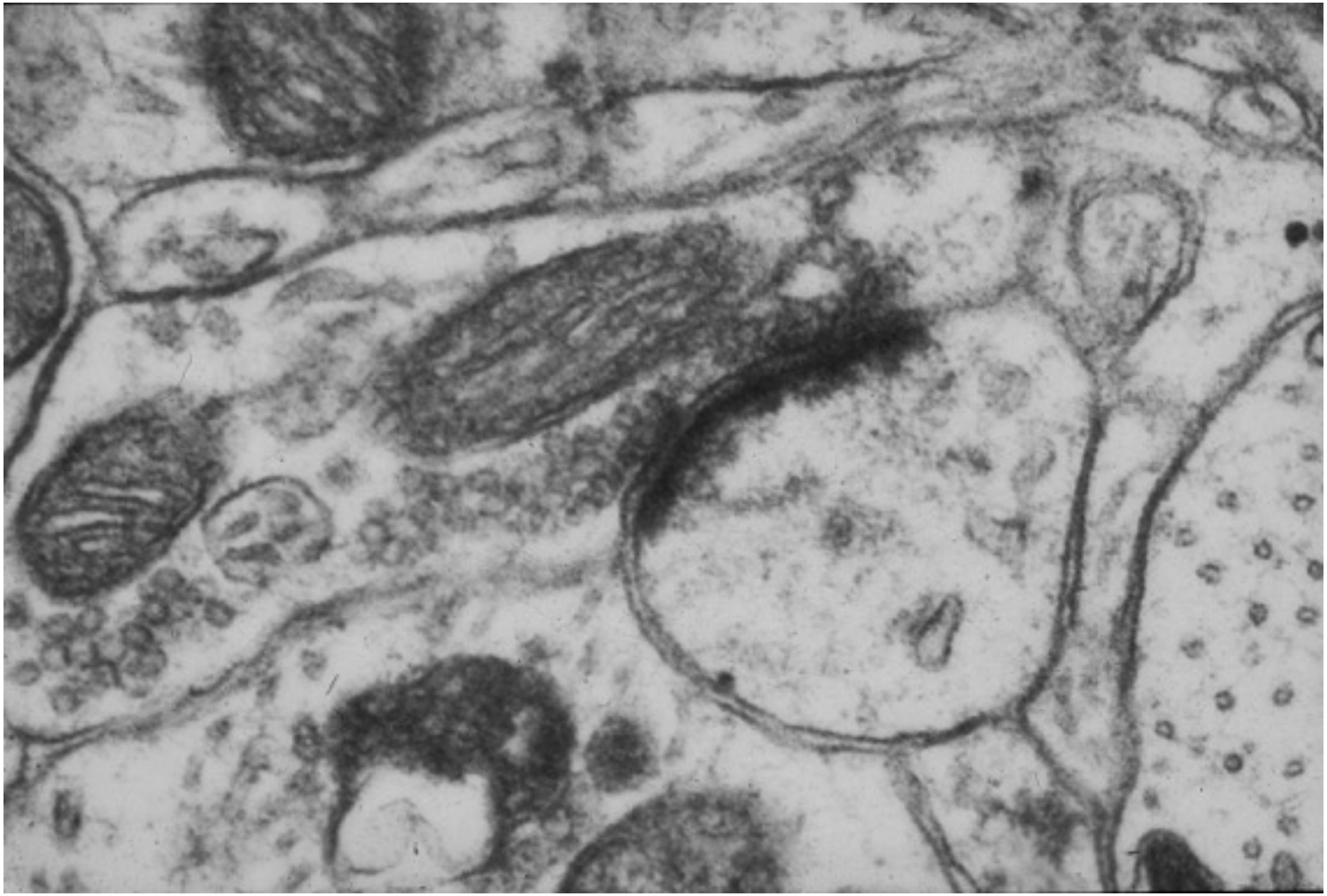
inhibitory



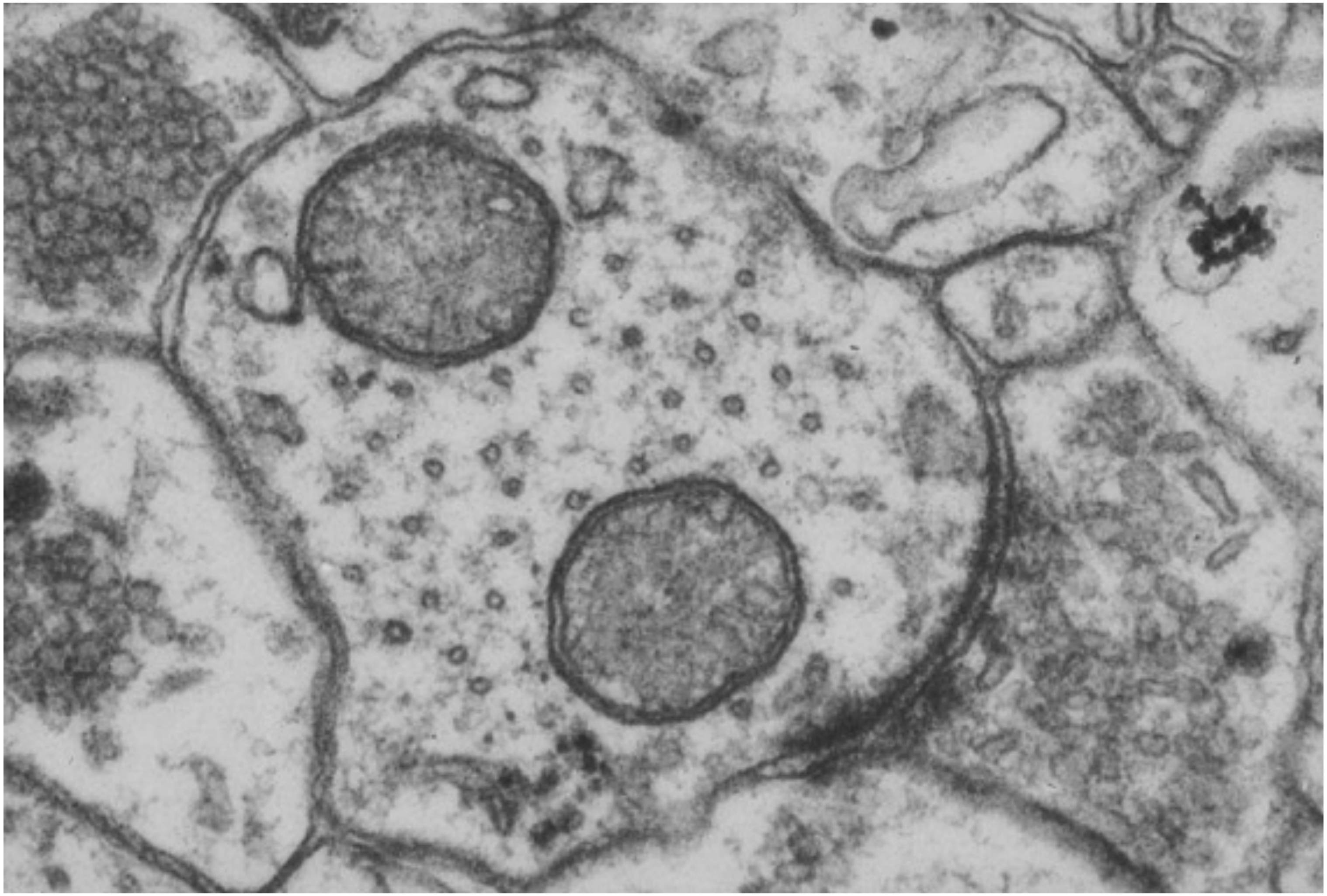
Pyramidal cells:

→ about 85 % of all neurons (Peters)

2. The vast majority of neurons of one main type (pyramidal cells, including spiny stellate cells) and is excitatory.



Type I synapse



Type II synapse

2. The vast majority of neurons is of one main type (pyramidal cells, including spiny stellate cells) and is excitatory.

3. Most of the synapses in the cortex are excitatory (about 90 %)

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75 % of synapses on dendritic spines (i.e. on pyramidal cells)

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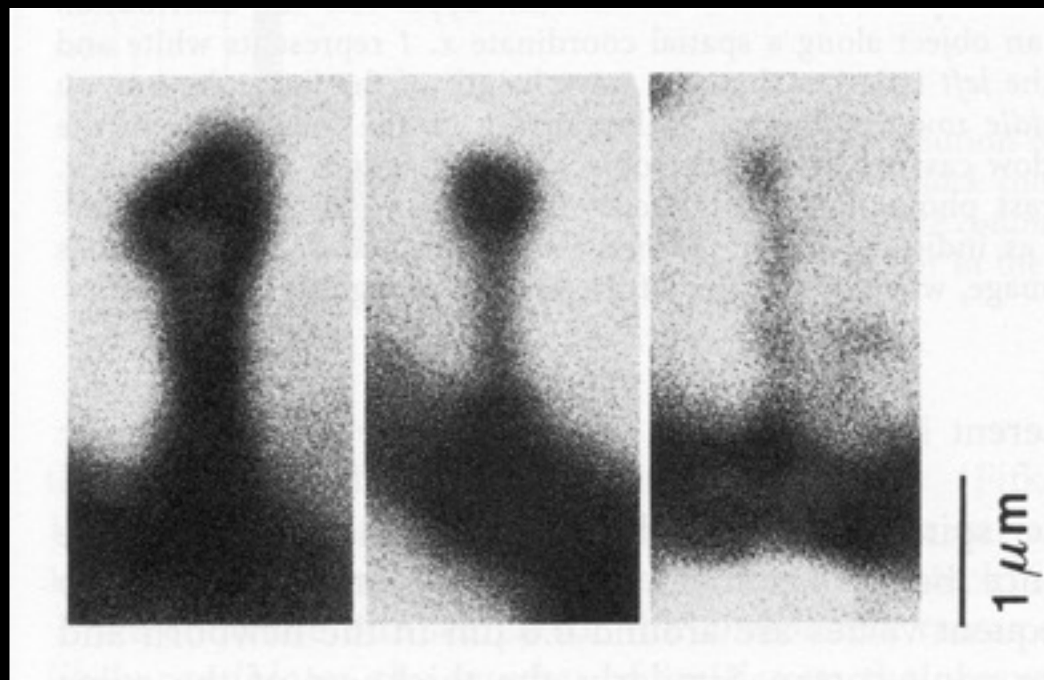
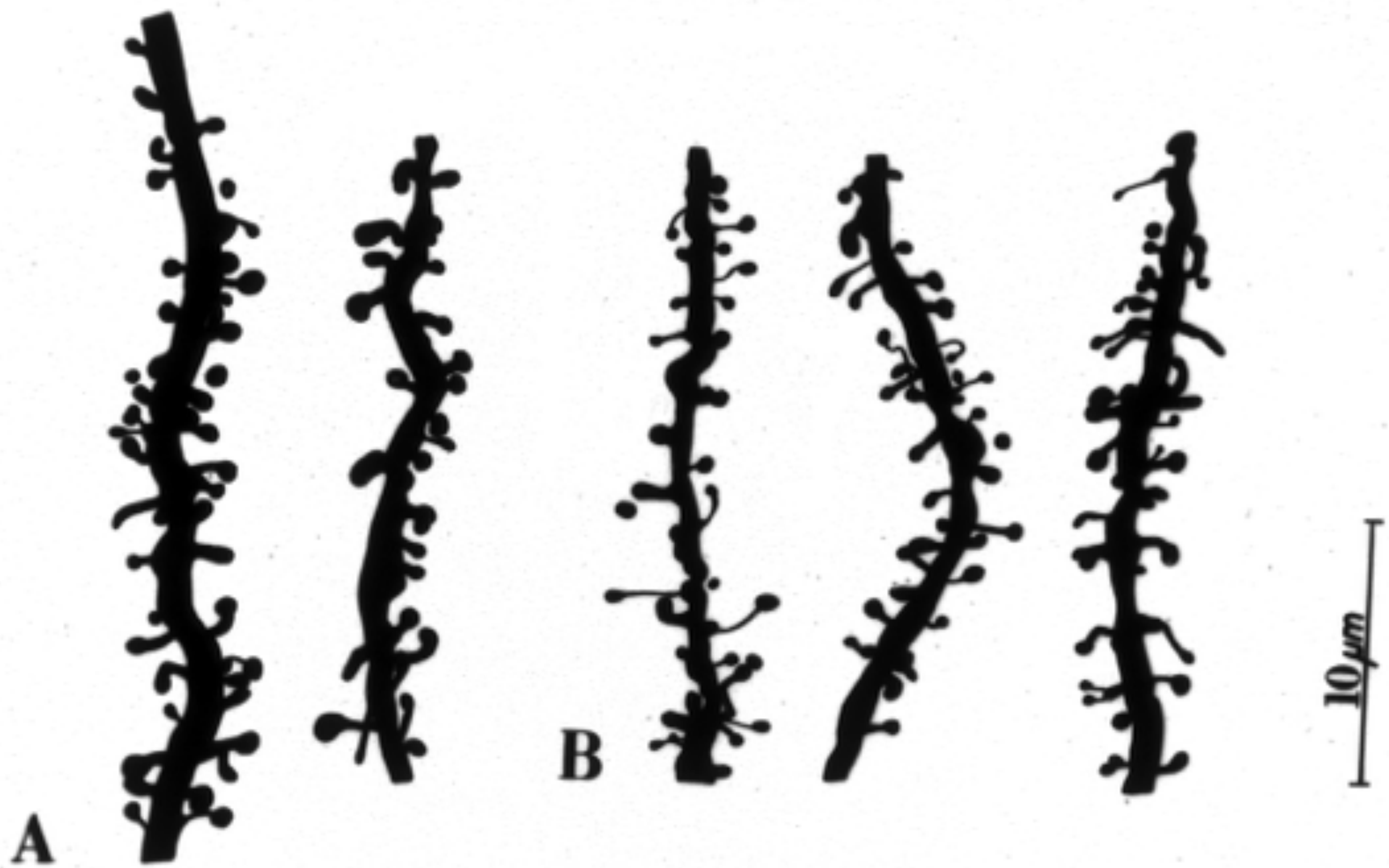
3. Most of the synapses in the cortex are excitatory (about 90 %)

75 % of synapses on dendritic spines (i.e. on pyramidal cells)

4. Most of the synapses are synapses between pyramidal cells



Dendritic spines, guinea pig
From: Schüz (1986)


A
B
10 μm

5. Most of the synapses are learning elements

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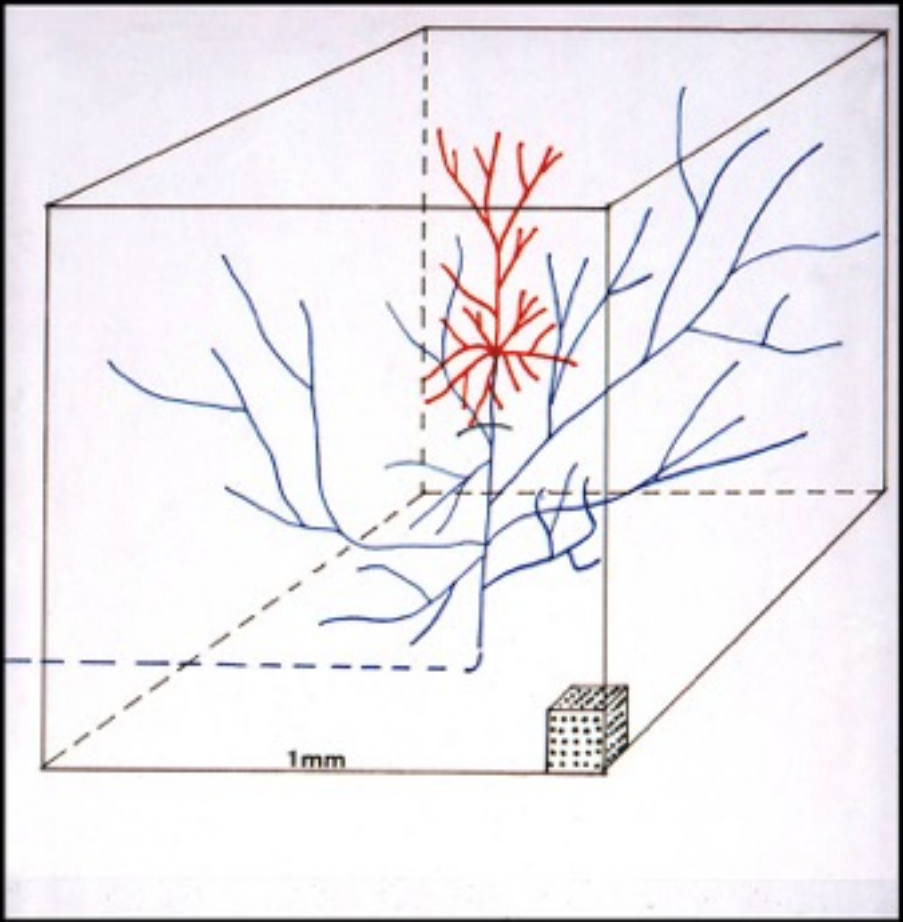
(mouse cortex)

9×10^4 neurons/mm^3

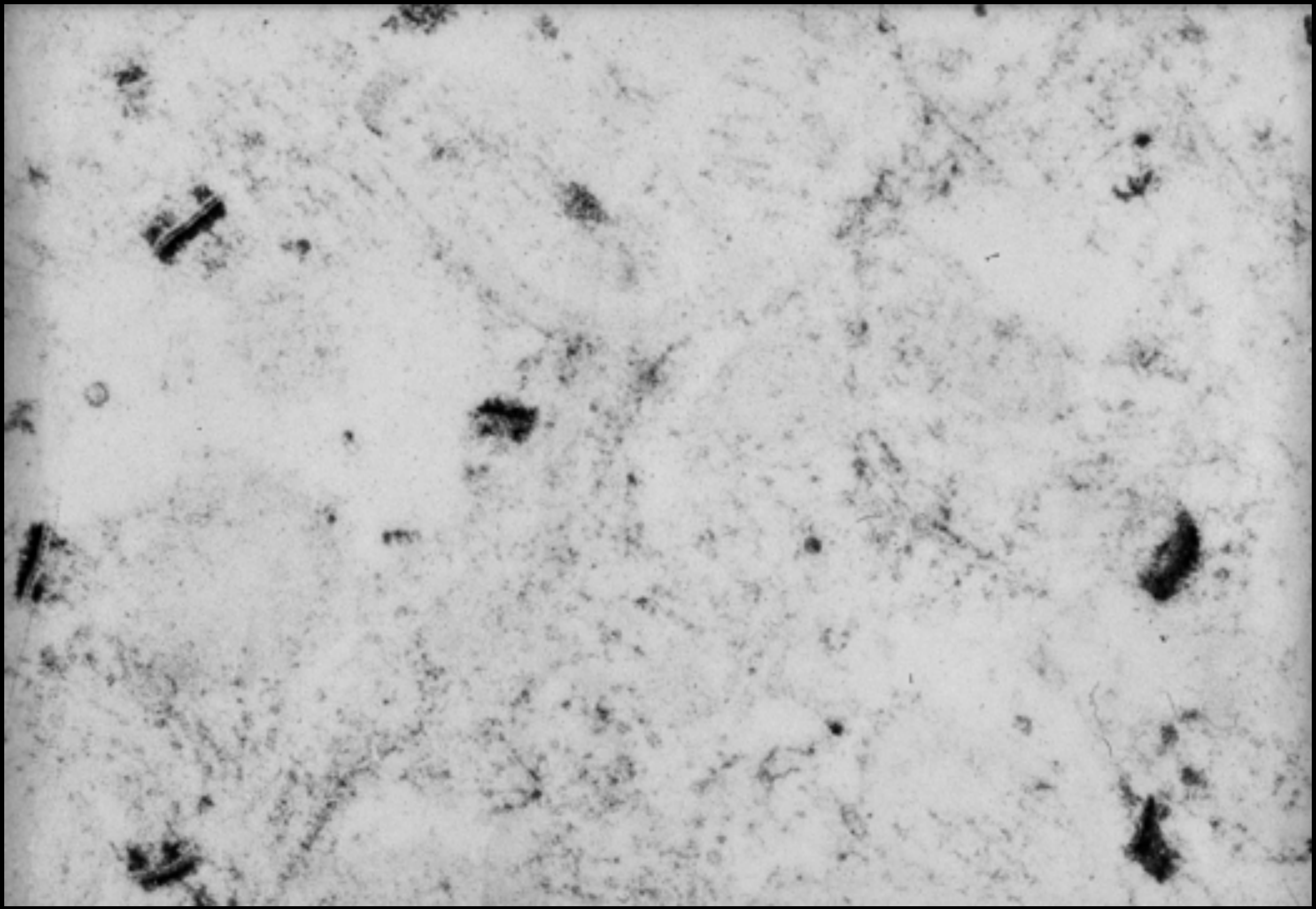
7.5×10^8 synapses/mm^3

} **8000 synapses per neuron**

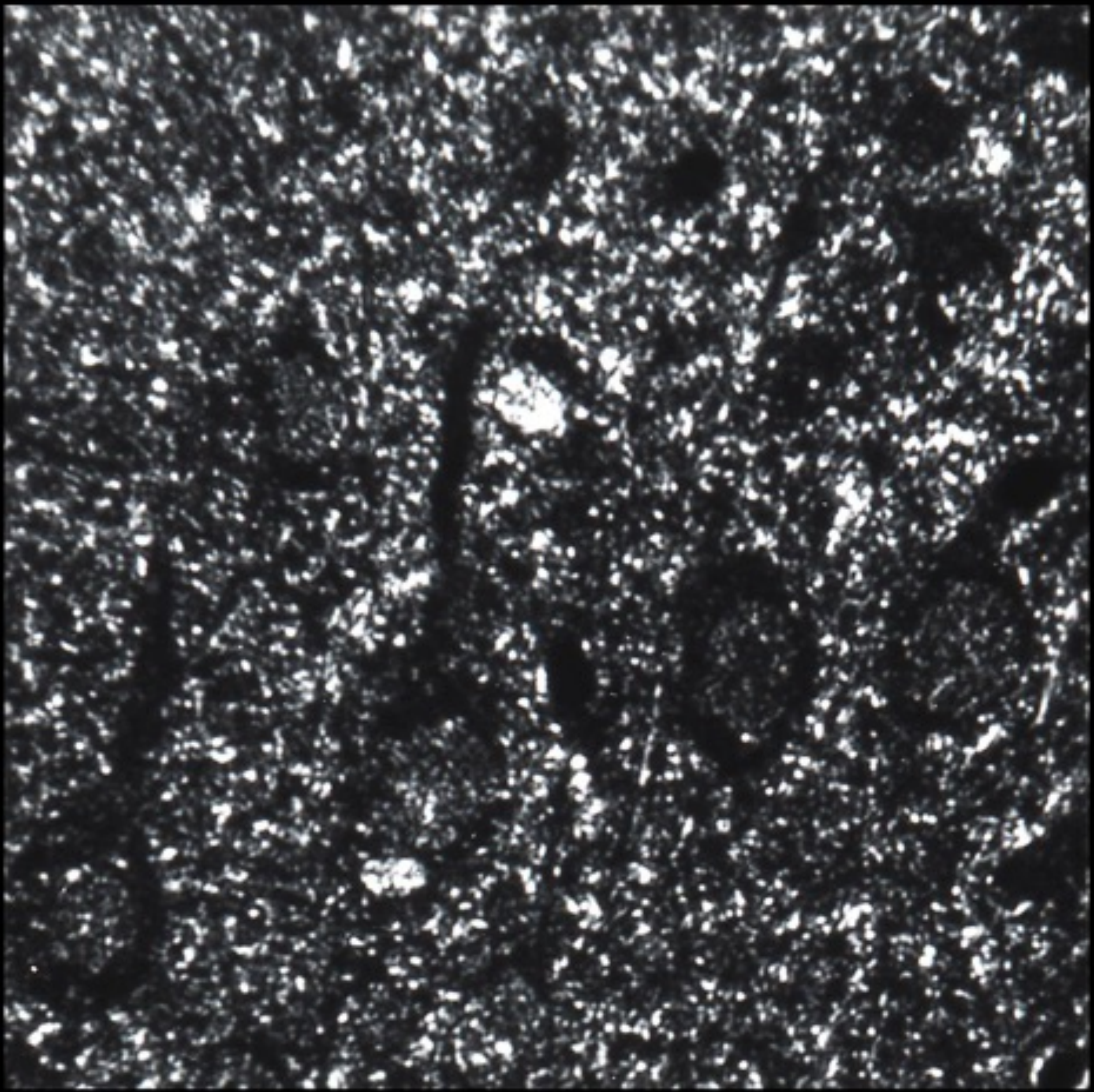
Each axonal tree traverses thousands of dendritic trees



Electron microscopy, phosphotungstic acid (PTA)



From: Schüz and Dortenmann, 1987



*From:
Braitenberg
and Schüz, 1991*

Probability of connections between 2 pyramidal cells:

At full overlap:

$p_0 = 0.1$, $p_1 = 0.27$, $p_2 = 0.27$, $p_3 = 0.18$

6. An individual pyramidal cell has thousands of synaptic targets (high degree of divergence of signals)

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8. Each neuron is connected with every other cortical neuron via one or a few synaptic steps

at most 3 – 4 steps (Greilich, 1984; Palm, 1986)

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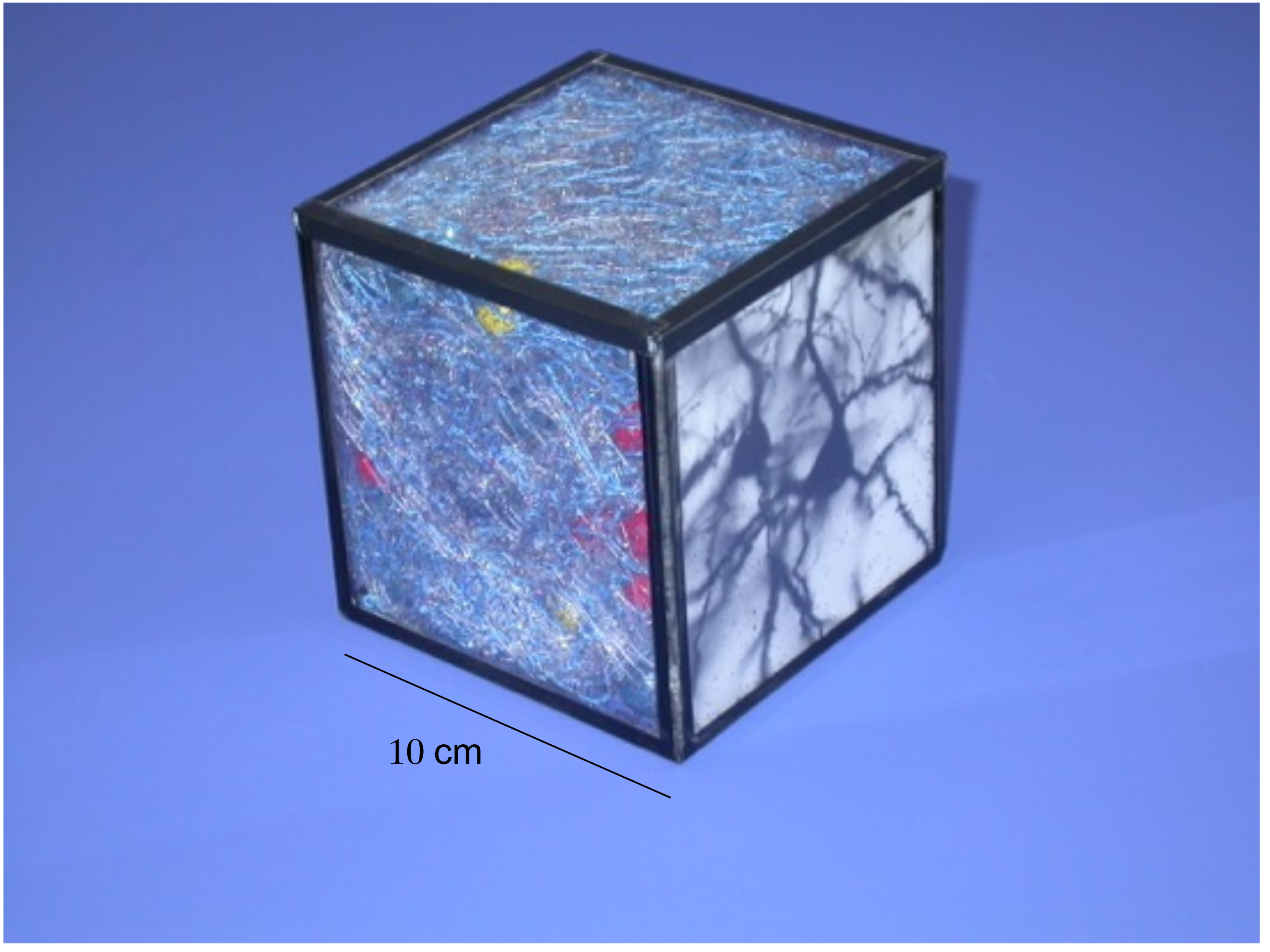
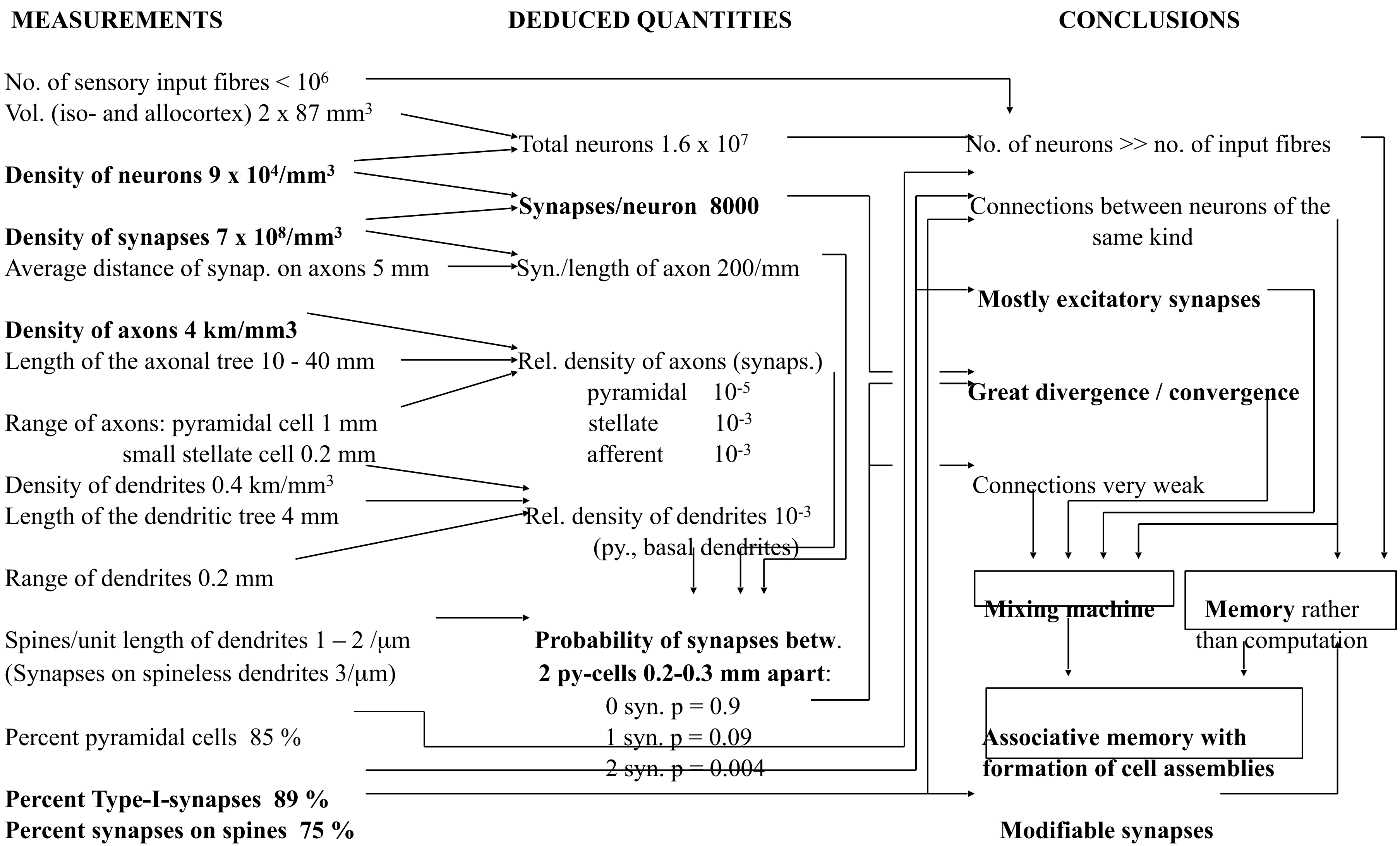
at most 3 – 4 steps (Greilich, 1984; Palm, 1986)

9. Connectivity between individual neurons largely statistically predetermined

1/1000 mm^3 cortex X 1000



What is such a network suited for?



From: Braitenberg and Schüz (1991/1998)

What is such a network suited for?

Mixing machine

Learning

What is such a network suited for?

Mixing machine

Learning

by association

What is such a network suited for?

Mixing machine

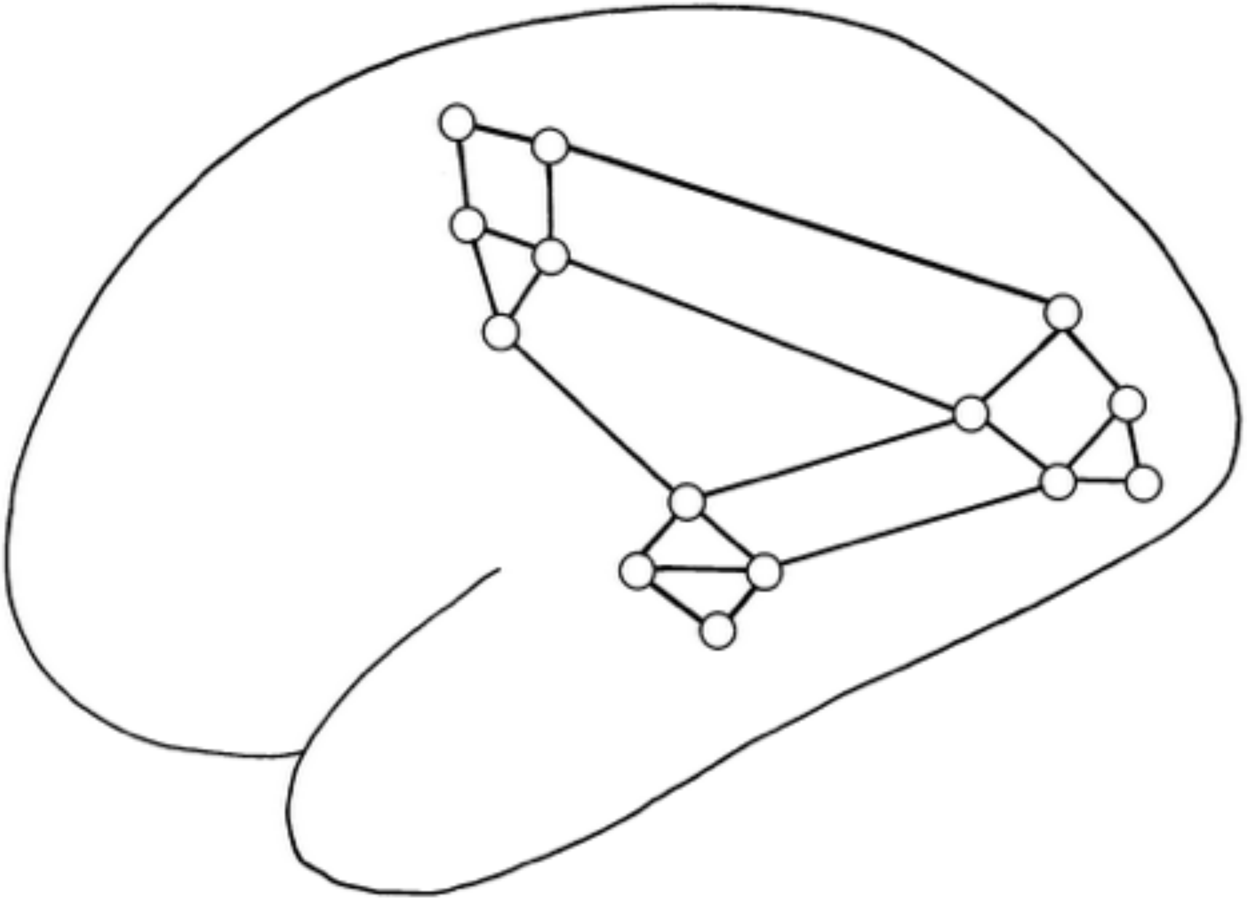
Learning

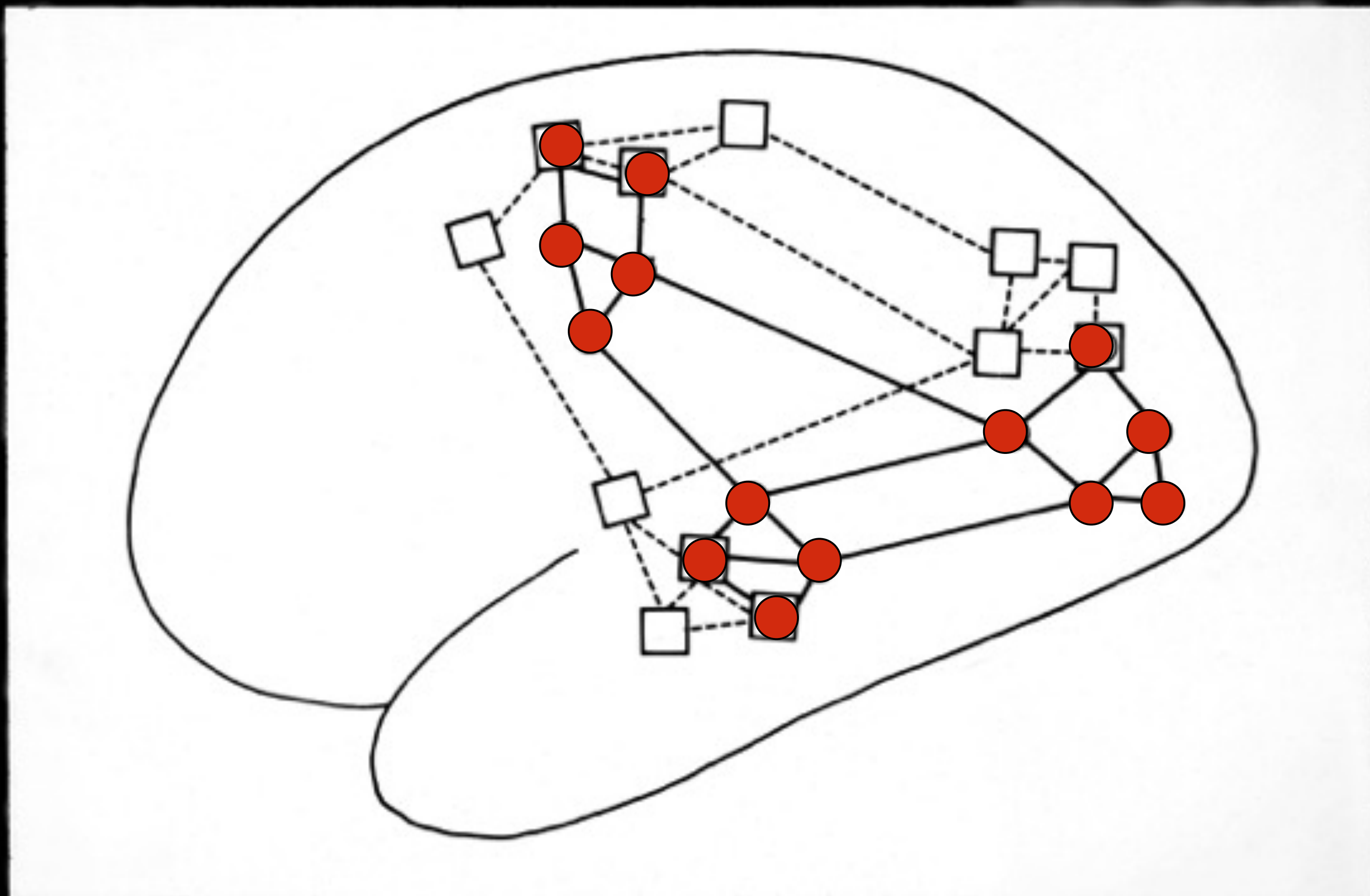
by association

i.e. by bringing together correlated activity

i.e. by forming „cell assemblies“

Hebb (1949)





Requirements for cell assemblies

Many neurons of the same kind

Connected with each other

Via excitatory connections

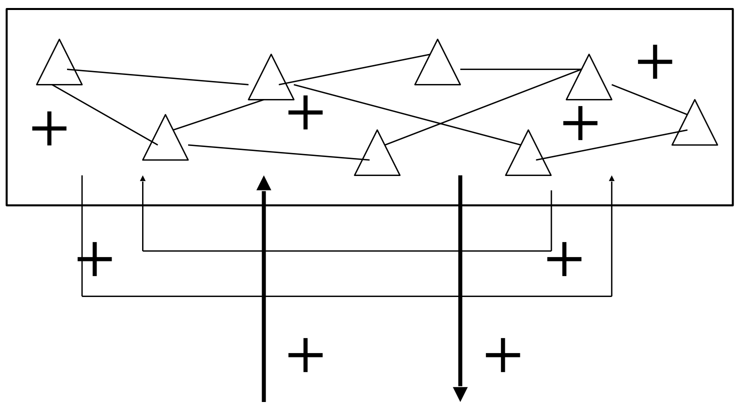
Via modifiable connections

Not only local connections

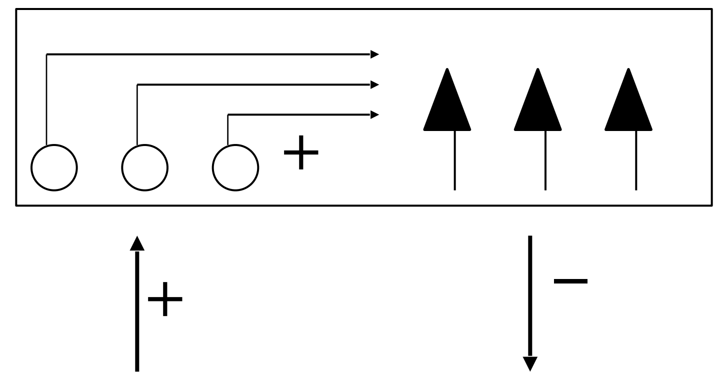
Each neuron should be connected to many others

Requirements for cell assemblies	Structure of the cortex
Many neurons of the same kind	85 % pyramidal cells
Connected with each other	Mainly connected with each other
Via excitatory connections	Via excitatory synapses
Via modifiable connections	Via modifiable synapses (spines)
Not only local connections	Both local and distant connections
Each neuron should be connected to many others	Each pyramidal cell is connected to thousands of others

Cerebral cortex

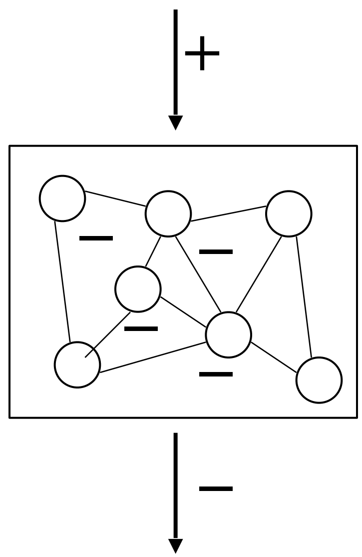


Cerebellar cortex



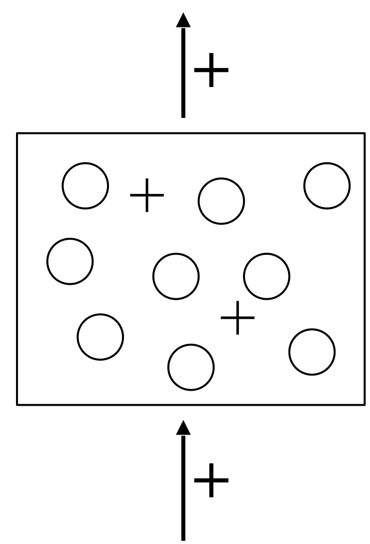
(V. Braitenberg)

Basal ganglia



J. Wickens,
R. Miller

Thalamus



E.G.Jones
R. Miller

Basic function of the cortex:

Dealing with correlations:

Detect, incorporate and handle correlations

<u>Basic function of the cortex:</u>

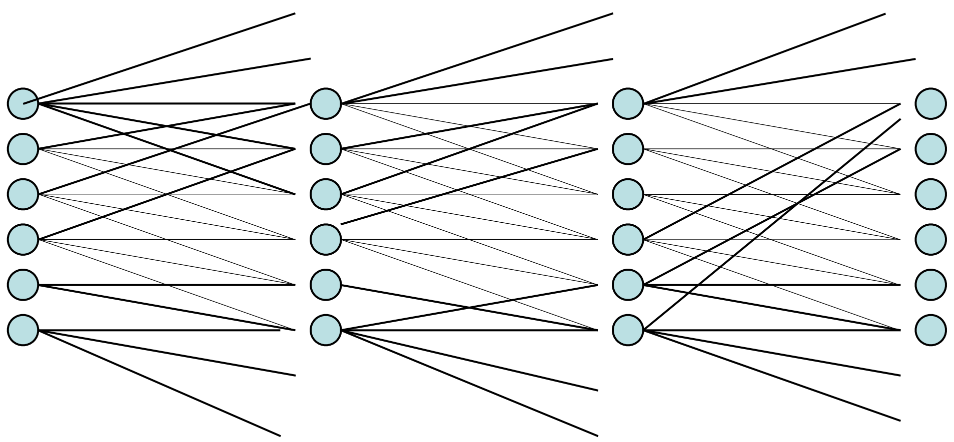
Dealing with correlations:

Detect, incorporate and handle correlations

i.e. Learning, Associating, Thinking

Synfire chain theory (M. Abeles, 1982; 1991)

How can sequences of activity be organized?



Cell assemblies – result of coincident correlations

Synfire chains – result of timeshifted correlations

Moshe Abeles (1991)

Statistical connectivity

- Number of cell types or subtypes

- Patterns of ramification

e.g. Binzegger, Douglas and Martin (2004) A quantitative map of the circuit of cat primary visual cortex. The Journal of Neuroscience 24 (39):8441-8453

Deviations from the expected probability:

-Possibly different times of maturation of layers or subtypes

-Learning

-Cell type specificity (chandelier cells)

Dantzker and Callaway (2000) Laminar sources of synaptic input to cortical inhibitory interneurons and pyramidal neurons

Potjans and Diesmann (2012) The cell-type specific cortical microcircuit: Relating structure and activity in a full-scale spiking network model