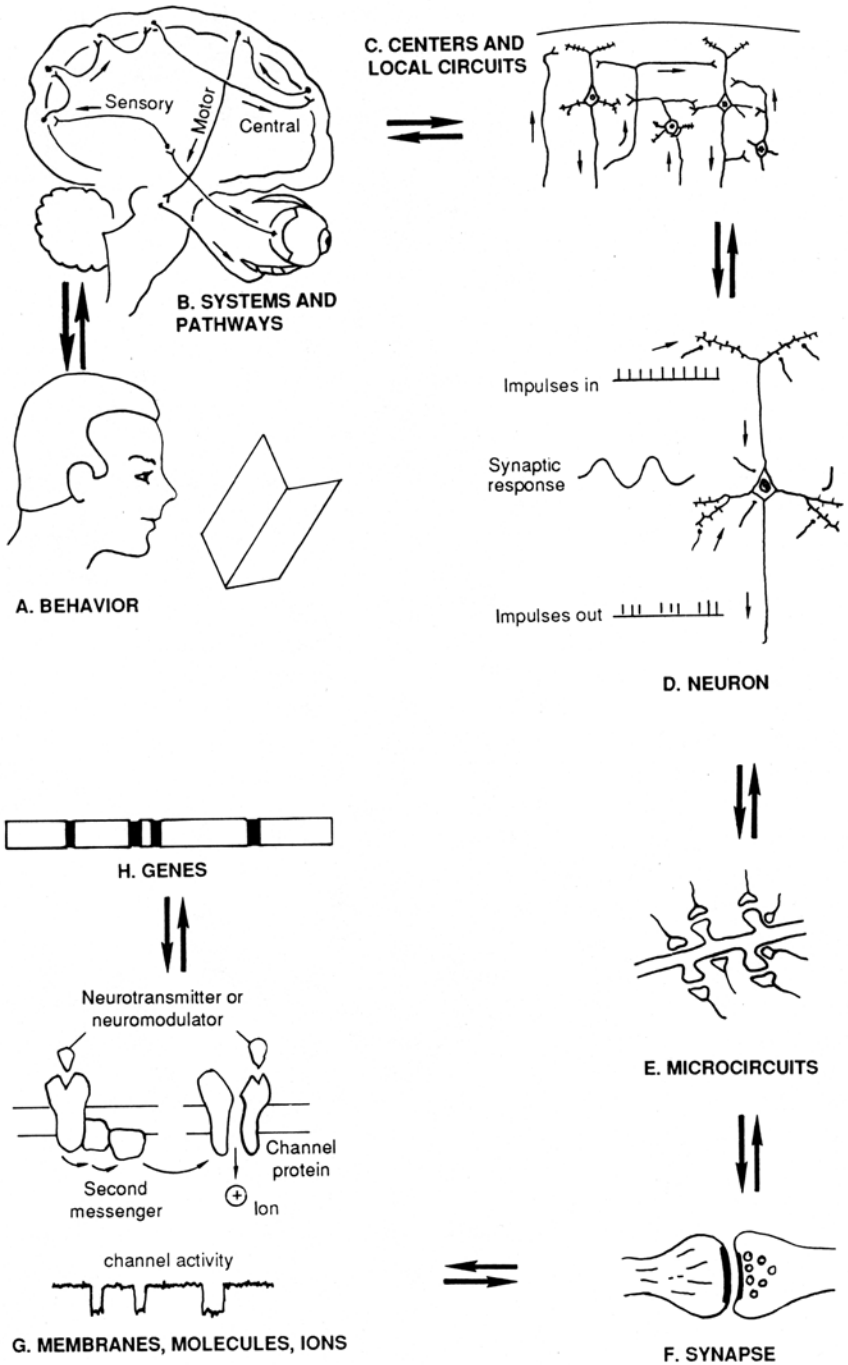

Sensory
Motor
Central
B. SYSTEMS AND PATHWAYS
A. BEHAVIOR
C. CENTERS AND LOCAL CIRCUITS
Impulses in
Synaptic response
Impulses out
D. NEURON
E. MICROCIRCUITS
F. SYNAPSE
H. GENES
Neurotransmitter or neuromodulator
Channel protein
Second messenger
Ion
channel activity
G. MEMBRANES, MOLECULES, IONS

BERNHARD VON GUDDEN (1824-1866)

FACED WITH AN ANATOMICAL FACT PROVEN BEYOND DOUBT, ANY PHYSIOLOGICAL RESULT THAT STANDS IN CONTRADICTION TO IT LOSES ALL ITS MEANING….

SO, FIRST ANATOMY AND THEN PHYSIOLOGY; BUT IF FIRST PHYSIOLOGY, THEN NOT WITHOUT ANATOMY

EDELMAN GM, TONONO, G:

IF SOMEONE POINTED A GUN AT US AND THREATENED

OBLIVION IF WE DID NOT SAY THE SINGLE WORD MOST SIGNIFICANT FOR UNDERSTANDING THE BRAIN, WE

WOULD SAY NEUROANATOMY

IN: A Universe of Consciousness. How Matter Becomes Imagination. Basic Books, 200

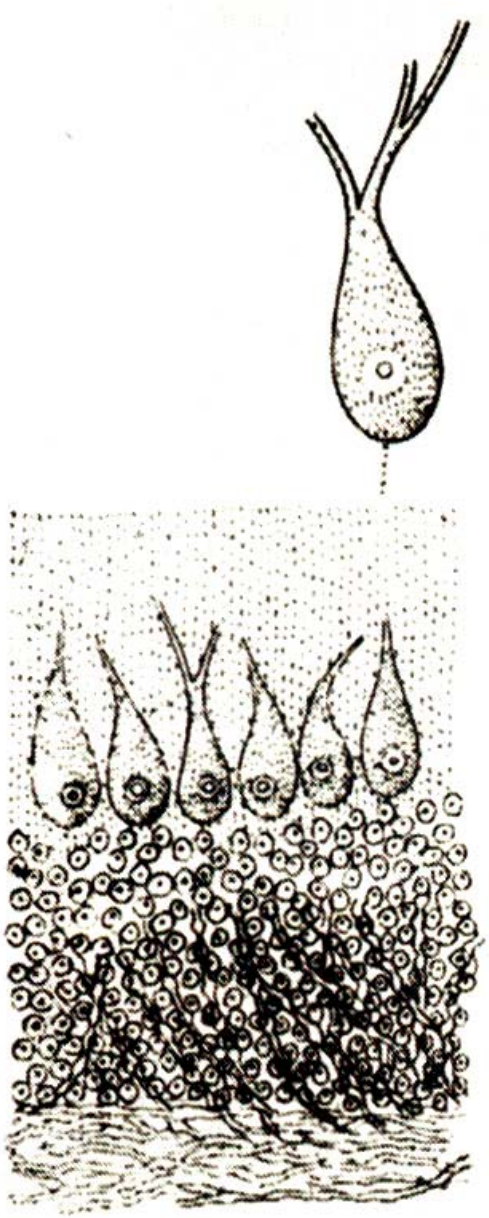
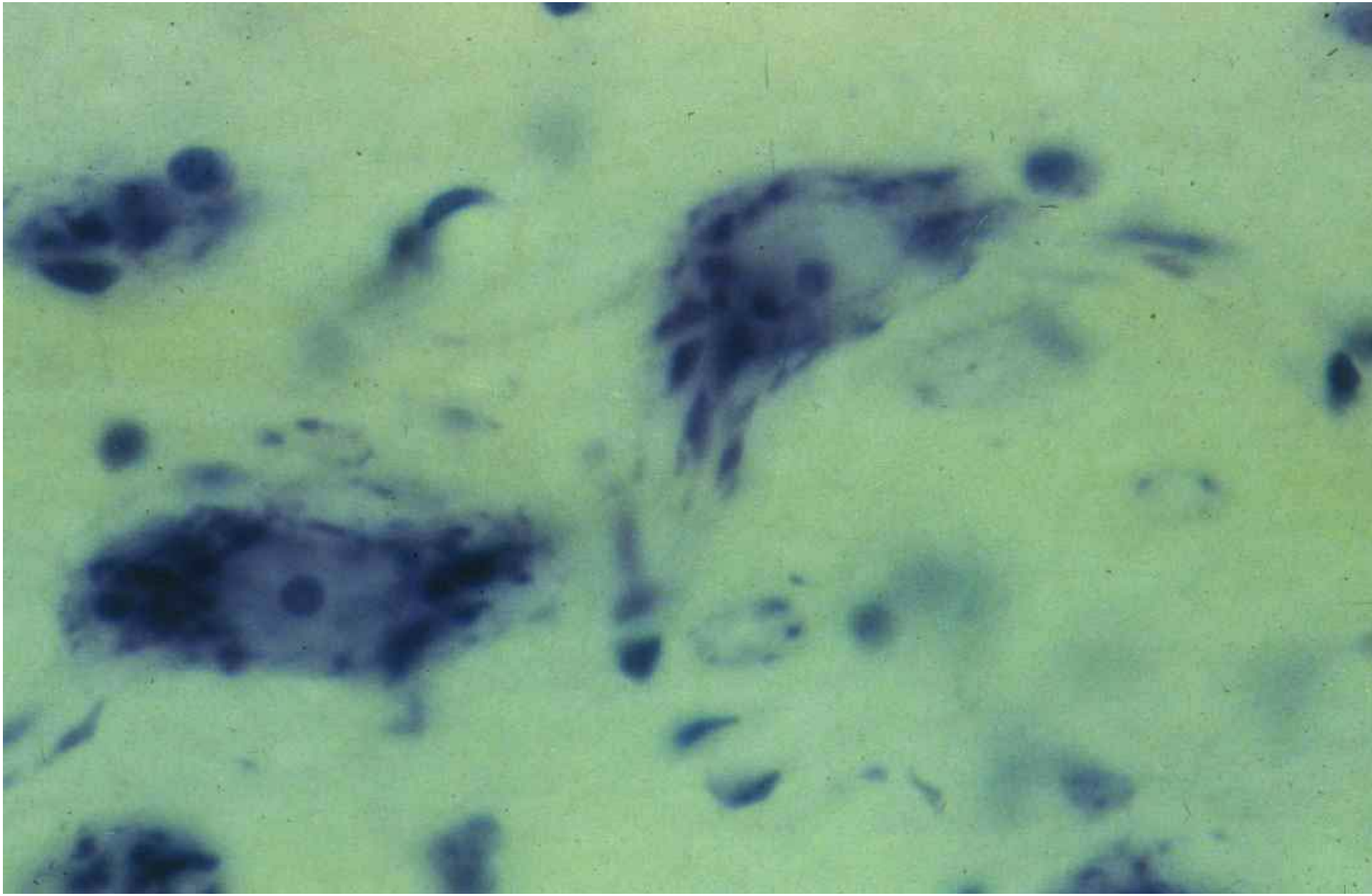


Fig. 2. The first identified nerve cell in the nervous system: the large corpuscles of the cerebellum, which became known as Purkinje cells after their discoverer. This was also the first published view of the cellular composition of the histological layers within a brain region. From below: fibers, granules, large corpuscles (Purkinje cells), molecular layer. (Purkinje, 1837)



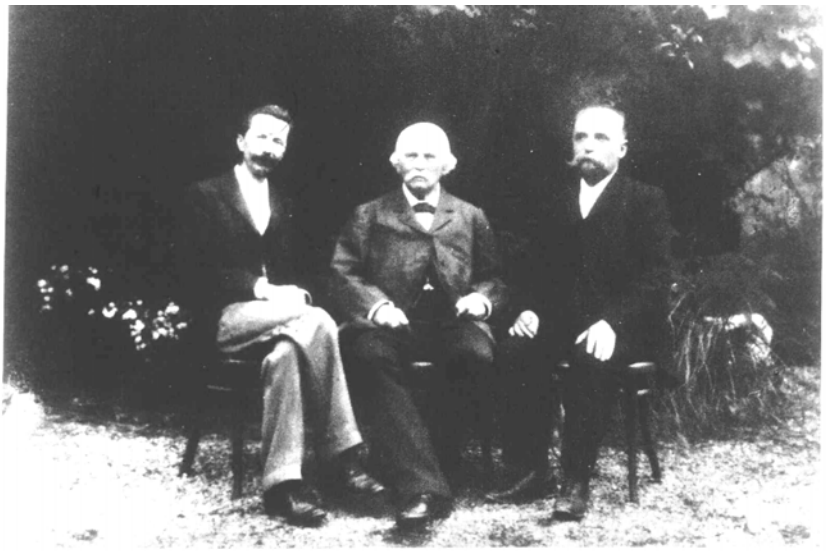


Fig. 21. Portrait of Guilio Bizzozero, Albrecht Kölliker, and Camillo Golgi, at Golgi's home in Pavia, during Kölliker's visit to Golgi in 1887 to learn about the Golgi technique first-hand. Bizzozero was a schoolmate and long-time friend and colleague of Golgi. (Kindly supplied by Professor P. P. C. Graziadei)

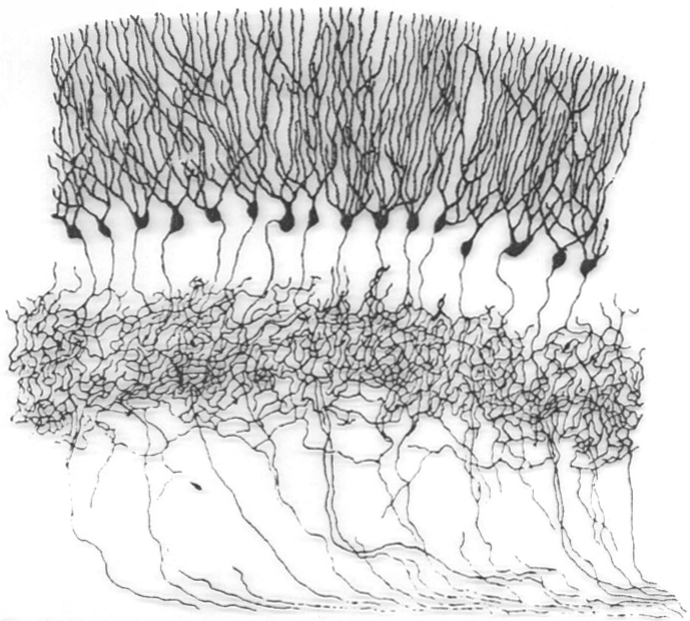


Fig. 38. Golgi's depiction of the reticulum formed by axon collaterals in the dentate gyrus. (Golgi, 1967)

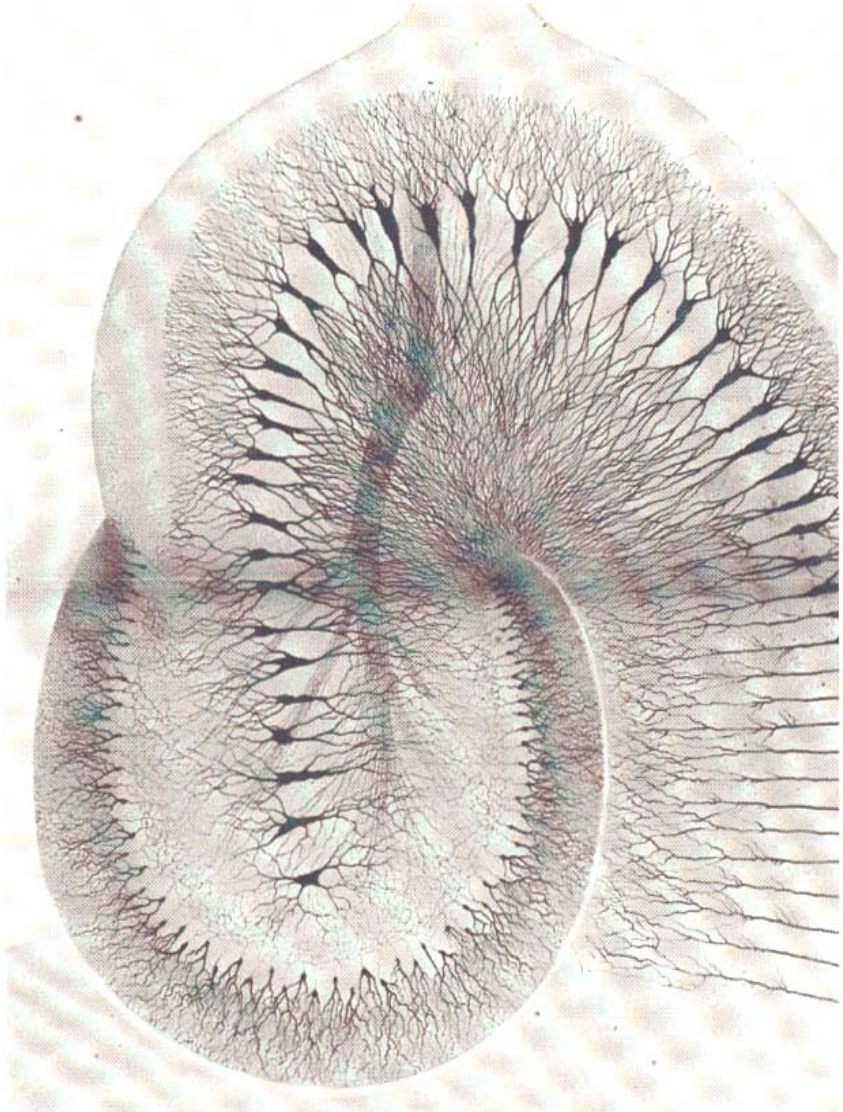


Fig. 13. A diagram by Golgi of the nervous elements of the hippocampus and fascia dentata.

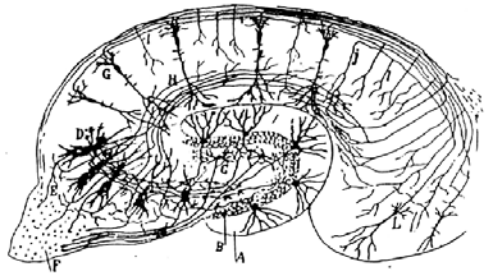
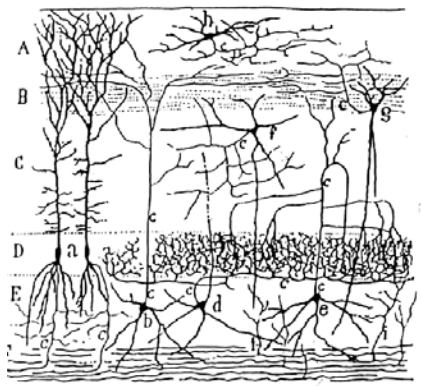


Figure 22
A diagram of Ammon's horn and the fascia dentata to show the relationship between large pyramidal cells of the regio inferior of Ammon's horn and the mossy fibers of granule cells.
A: molecular layer of the fascia dentata; B: granule cell layer; C: molecular layer of the terminal part of Ammon's horn; D: longitudinal bundle of mossy fibers, the axons of granule cells; E: axons of the large pyramidal cells coursing toward the fimbria; F: fimbria; G: small or superior pyramidal cell; H: bundle of large ascending axon collaterals; I: collaterals from the white matter; J: fiber terminals from the subiculum; L: pyramidal cells in the subiculum with an axon that enters Ammon's horn.



igure 20
ection through Ammon's horn of an eight-day-old rabbit.
A: stratum moleculare; B: stratum lacunosum; C: stratum radiatum; D: pyramidal cell layer; E: polymorph cell layer; F: white matter or *alveus*; : pyramidal cell; *b*: cell with an ascending axon; *d*: cell with a horizontal axon hat ramifies between pyramidal cell perikarya; *e*: cell with an arching axon hat ends in the interpyramidal plexus; *f*: short-axoned cell in the stratum adiatum; *g*: cell in the stratum lacunosum; *h*: cell in the stratum moleculare. Axonal processes are indicated by a *c*.

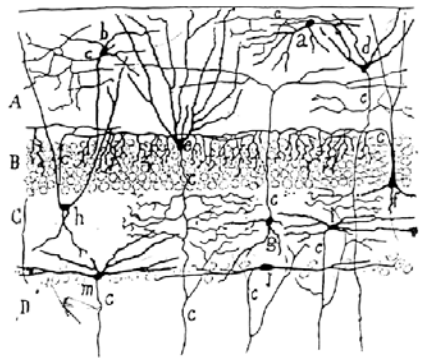
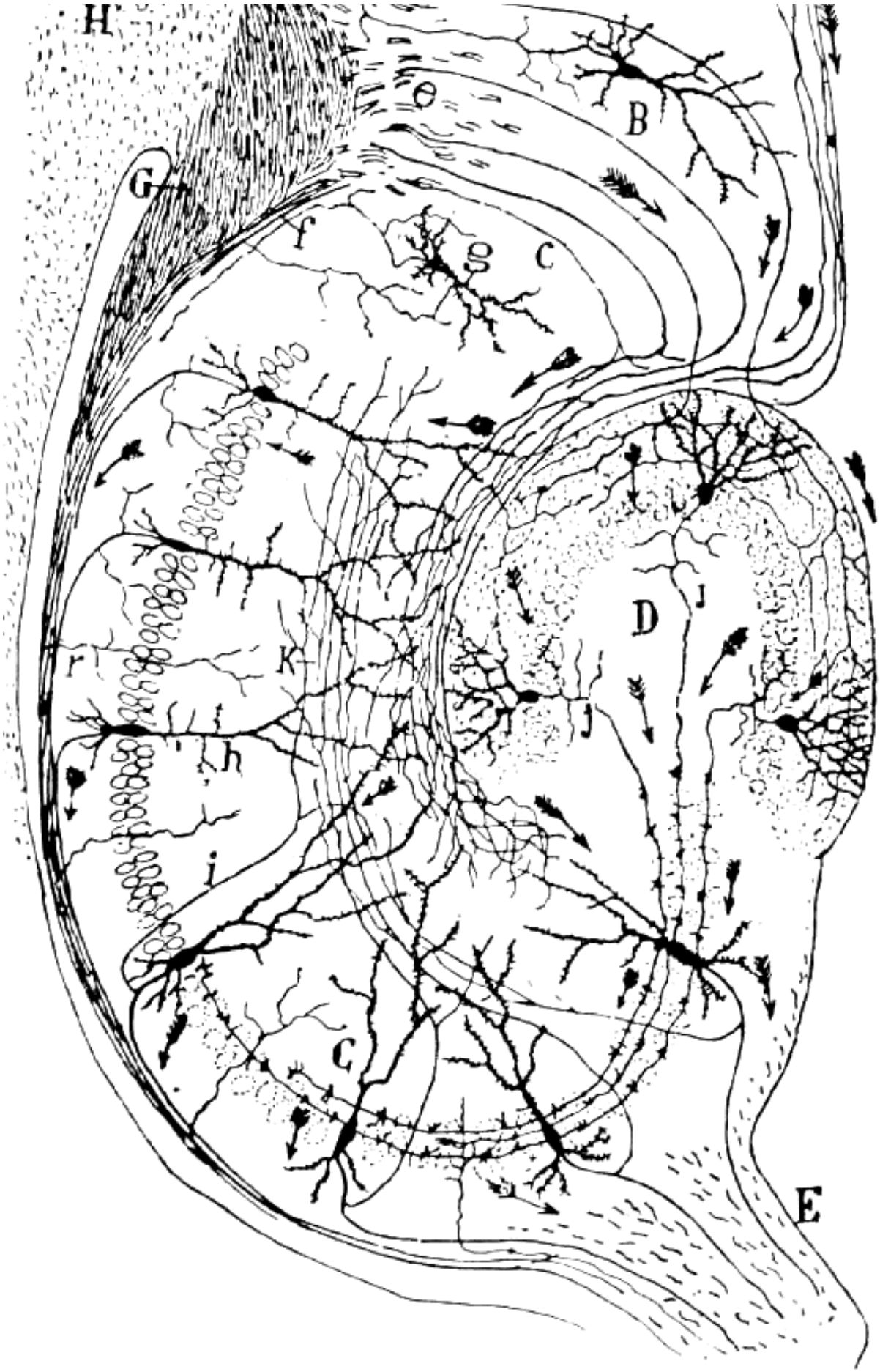


Figure 21
The layers of the fascia dentata in the eight-day-old rabbit.
A: molecular layer; B: granule cell layer; C: polymorph cell layer; D: molecular layer of Ammon's horn; *a*, *b*: cells of the molecular layer; *d*: displaced granule cell; *e*: granule cell; *f*: pyramidal cell with an ascending axon; *h*: cell with an ascending axon that contributes to the supra- and intergranular neural plexus; *g*: cell with an ascending axon that ramifies in the molecular layer; *i*, *j*, *m*: cells with a descending axon that enters the alveus. These axonal processes are indicated by *c*.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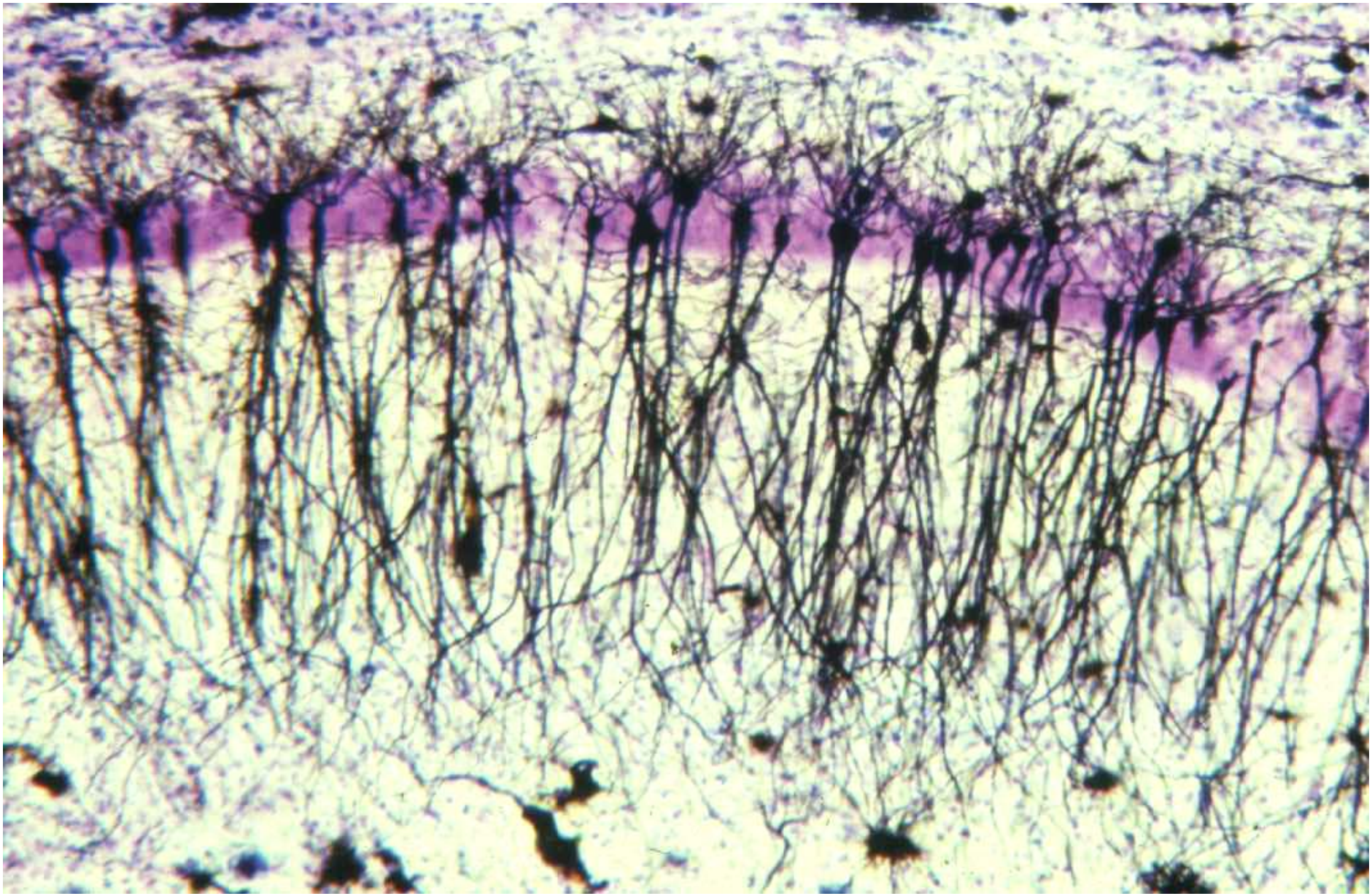


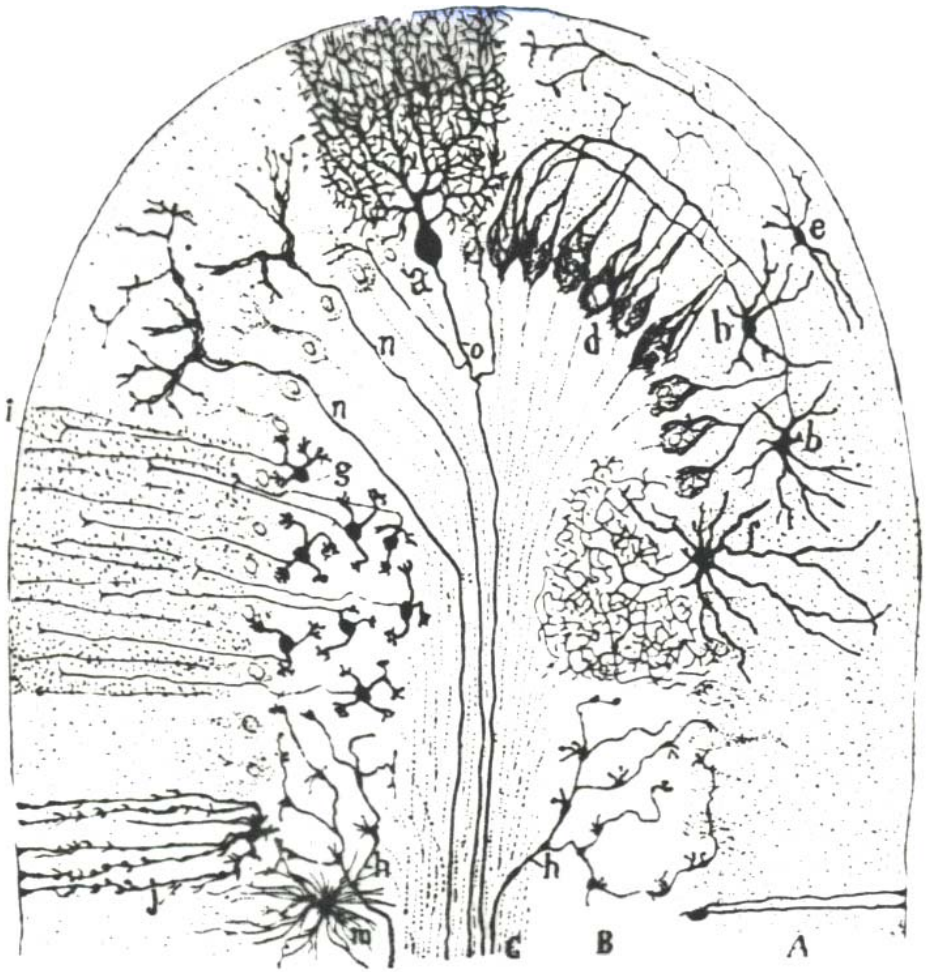


Figure 8
Semidiagrammatic transverse section through a mammalian cerebellar folium. A: molecular zone; B: granular zone; C: white matter; *a*: Purkinje cell, front view; *b*: small stellate cells of the molecular zone; *d*: descending terminal arborizations that surround Purkinje cells; *e*: superficial stellate cells; *f*: large stellate cells of the granular zone; *g*: granule cells with their long ascending axons that bifurcate at *i*. *h*: mossy fibers; *i*: neuroglial cell with its plume; *m*: neuroglial cell of the granular zone; *n*: climbing fibers; *o*: ascending collateral of a Purkinje cell axon.

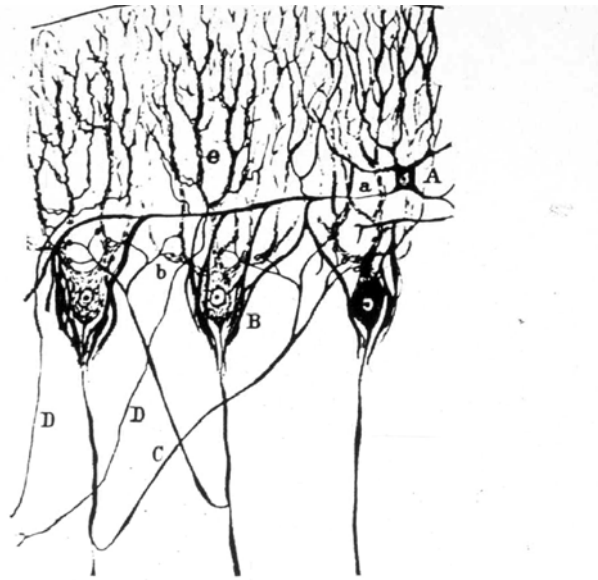
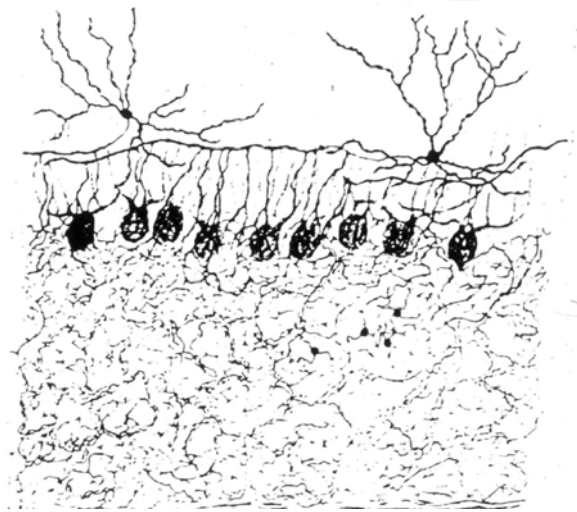


Fig. 4. Semi-schematic reproduction of the Purkinje cell connexions of the cerebellum. Reduced silver method. *A*, star-shaped cell of the molecular layer; *a*, initial narrowed portion of its axon; *B*, terminal baskets; *C*, recurrent collaterals; *b*, final fibrillae of these collaterals, terminating in rings leaning against the large trunks of the Purkinje cells.



- **THE NEURON DOCTRINE**

- **ANATOMY**

- **1. The Neuron is an Anatomical Uni.**
- **2. The Law of Dynamic Polarization.**
- **3. The Neuron is an Embryological (Developmental) Unit.**
- **4. The Neuron is a Metabolic (trophic) Unit.**
- **5. The Neuron is a Basic Information Processing Unit.**

- **CELL BIOLOGY**
- Describing the Axonal Transport Mechanisms. Understanding the protein synthetic machinery and the subcellular organization of cells.

- **PHYSIOLOGY**
- The physiological concept of spinal reflexes.

- **PHARMACOLOGY**
- **The chemical hypothesis of synapse**

- **Intracellular Electrophysiology**
- 1. Generation of impulses by sequential movements of Na and K ions through channels across the membrane in the squid giant axon (Hudgkin-Huxley).

- 2. Intracellular recording of end-plate potentials giving rise to muscle action.

- 3. Intracellular recording of EPSPs giving rise to action potentials in cat spinal motorneurons.

- 4. Intracellular recordings of small quantal deflections (miniature end-plate potentilas) at the muscle end-plate region.

- 5. Central synaptic pathway mediating recurrent inhibition of motorneurons

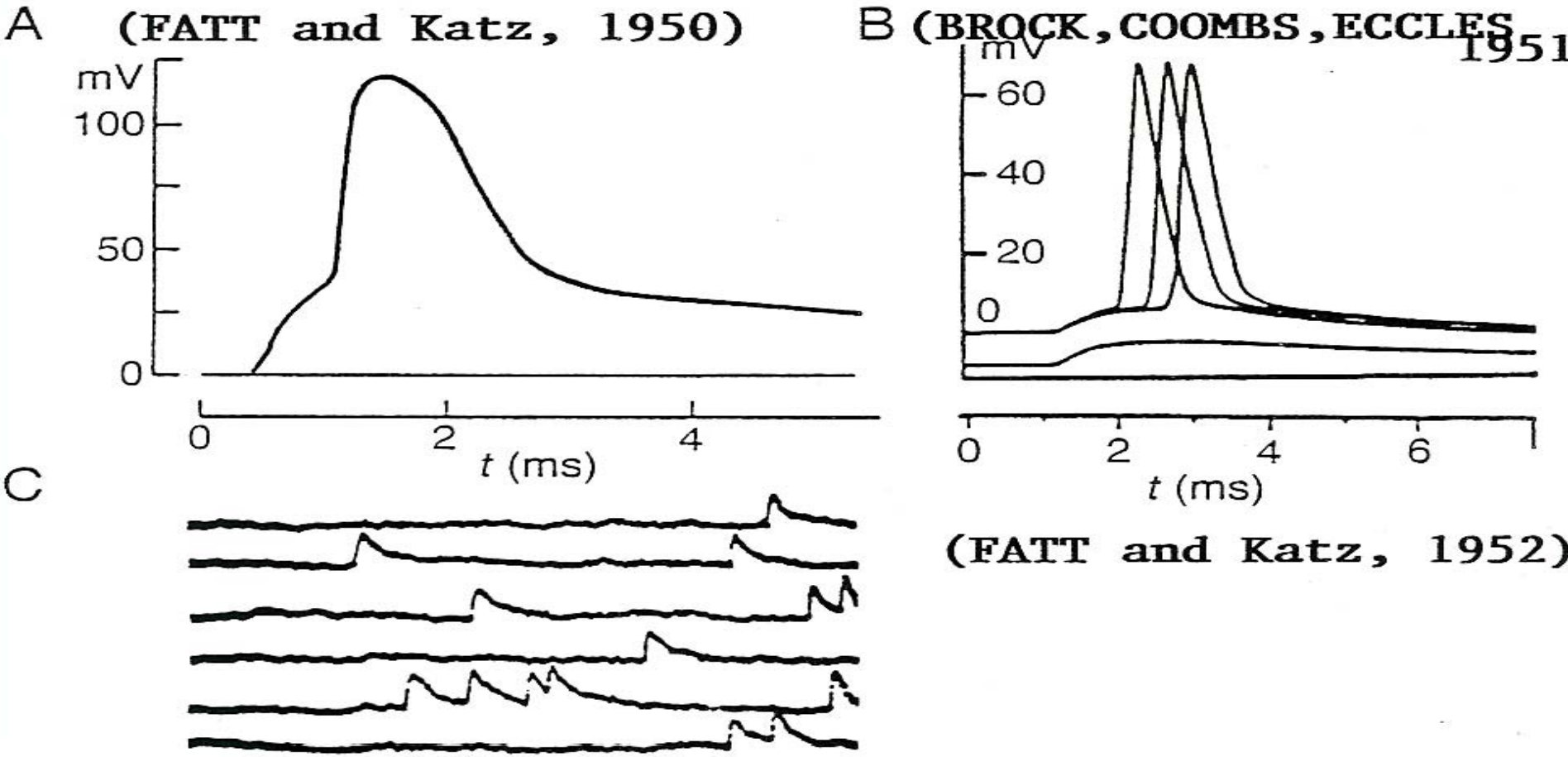
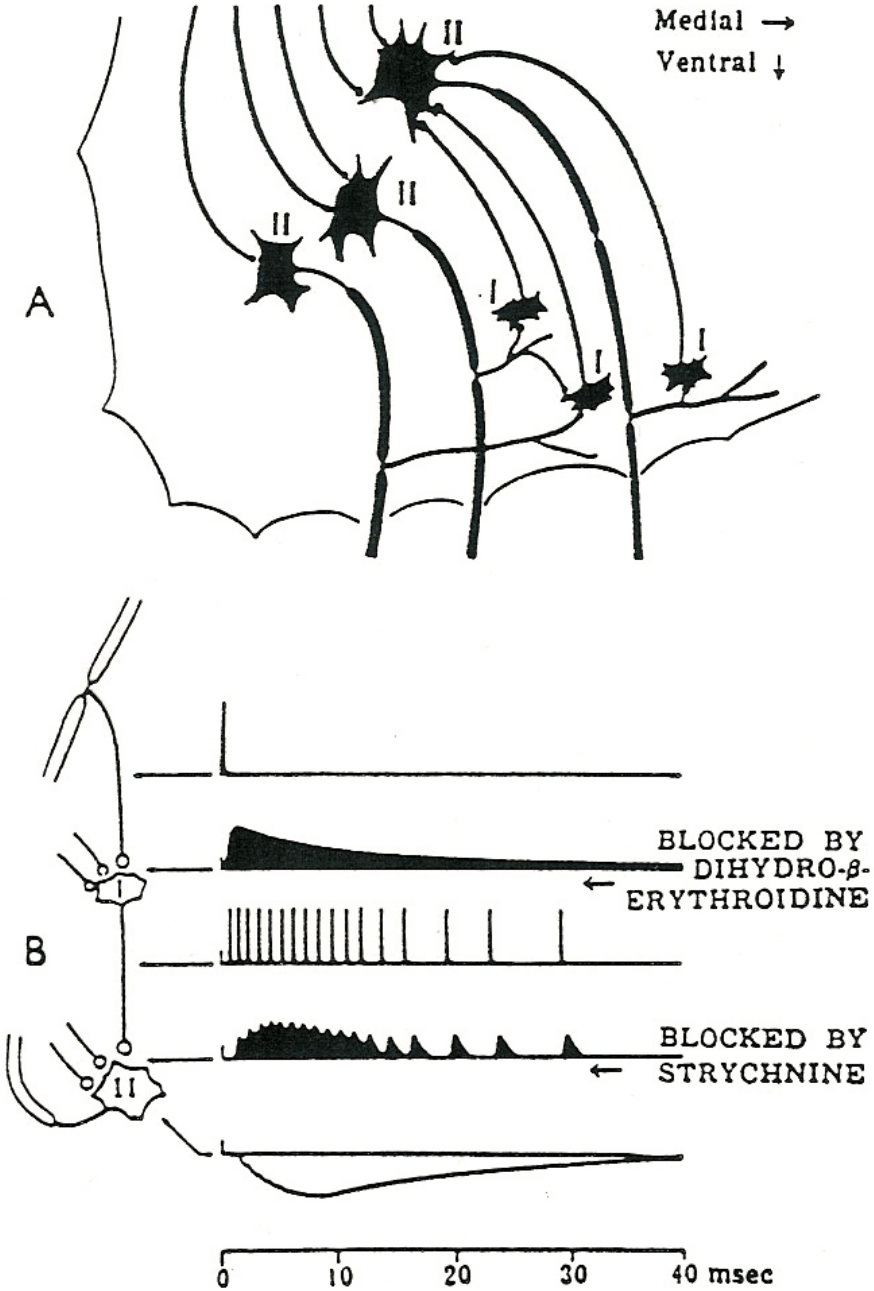
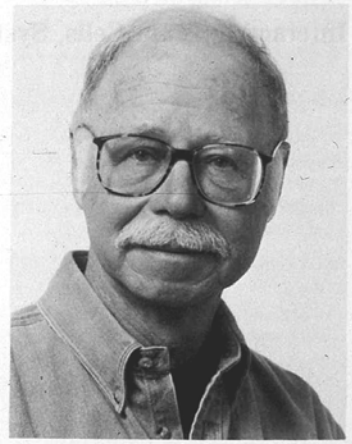


Fig. 3. *Intracellular recordings of end-plate and excitatory postsynaptic potentials (EPPs and EPSPs).* (A) *First reported intracellular recording of the EPP giving rise to the muscle action potential*[29]. (B) *First reported intracellular recordings of EPSPs, shown giving rise to action potentials in cat spinal motoneurons*[33]. (C) *First reported intracellular recordings of small quantal deflections (miniature end-plate potentials) at the muscle end-plate region*[34].


A
Medial →
Ventral ↓
II
II
II
I
I
I
B
BLOCKED BY
DIHYDRO-β-
ERYTHROIDINE
BLOCKED BY
STRYCHNINE
I
II
0
10
20
30
40 msec

SANFORD L. PALAY

Neuroanatomist, educator, editor, and art connoisseur, "Sandy" Palay was born in Cleveland, Ohio, in 1918. The first to visualize the synapse by electron microscopy, Dr. Palay is noted for his technical innovations in the application of electron microscopy to the study of biological material and his meticulous studies of the ultrastructure of the nervous system. His scholarly approach to the study of the neuron and its subcellular constituents has set a standard for the field.



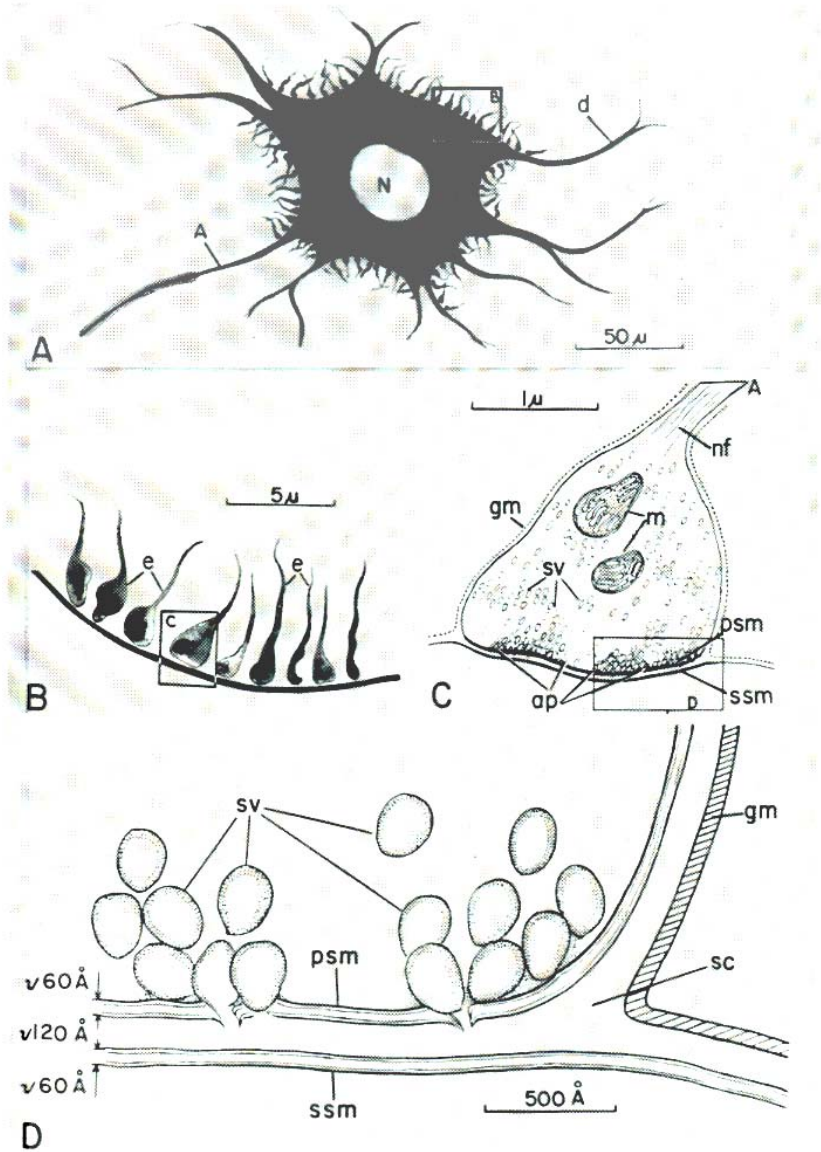
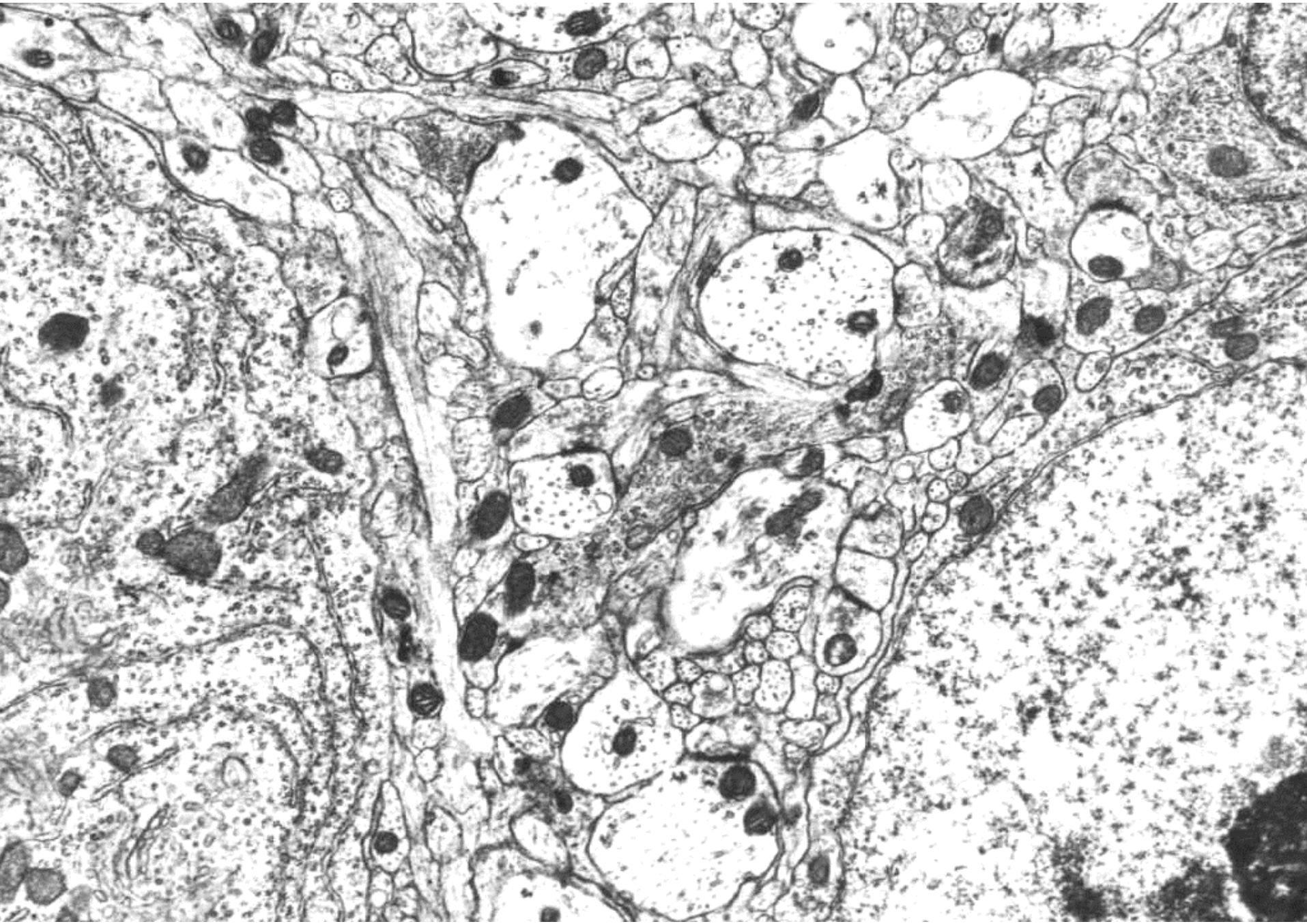


Fig. 39. "Diagram showing bouton-like synaptic junctions at different magnifications with the optical and electron microscope. (A) Illustrates a motoneuron as seen at medium power of the optical microscope. The nucleus (*N*), the axon (*A*), and the dendrites (*d*) are indicated. Numerous bouton-like endings make synaptic contact



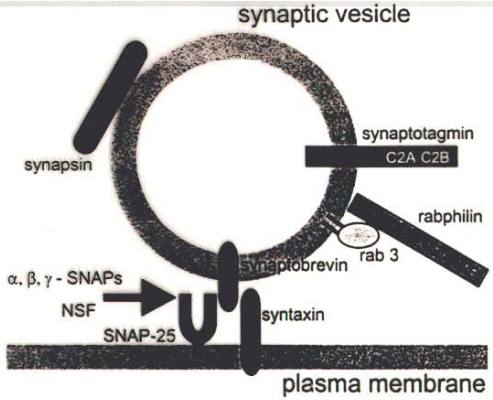
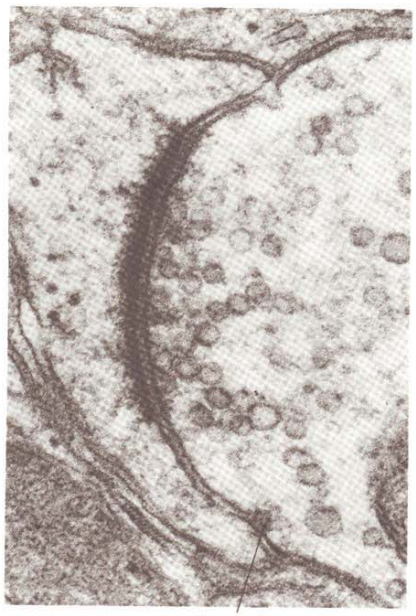
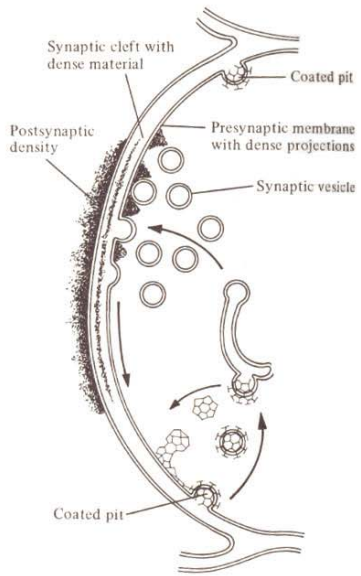


Fig. 3. Cartoon depicting proteins with a putative role in clustering, docking and fusion of synaptic vesicles discussed in the text. Other well-characterized synaptic vesicle proteins not shown in the picture include: the proton pump, synaptophysin, cysteine string proteins, SV2 and some neurotransmitter transporters. Additional proteins which interact with the SNARE complex or with its subunits include the complexins, Sec1, plasma membrane Ca^{2+} channels. Many of these proteins exist as protein families with differential expression in different classes of neurons. For detailed reviews see Südhof (1995) and Calakos and Scheller (1996).



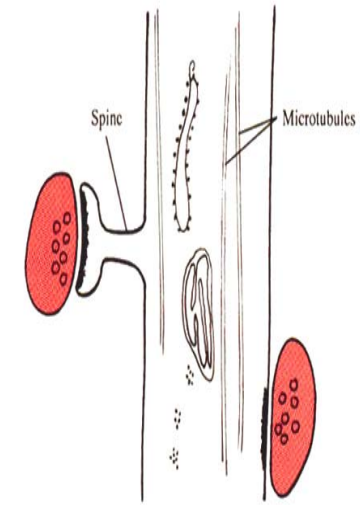
A

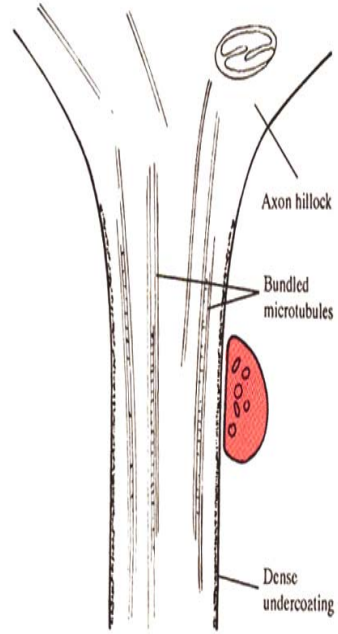


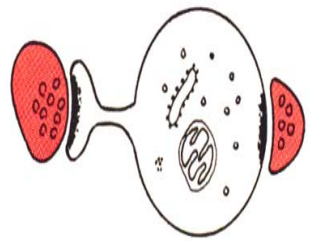
B

Fig. 6–8. The Synapse and the Synaptic Vesicles
A. The synapse consists of a presynaptic component, a synaptic left, and a postsynaptic component. The presynaptic component is characterized mainly by the accumulation of synaptic vesicles that contain the neurotransmitter.

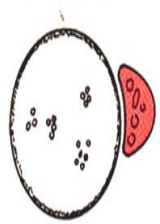
B. Idealized drawing of the synapse in **A** illustrating the recycling of synaptic vesicle membrane. (Modified from The Journal of Cell Biology, 1973, 57:315–344 by copyright permission of The Rockefeller University Press.)





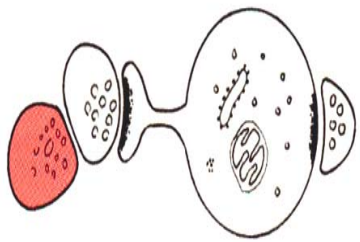


A Axodendritic synapses

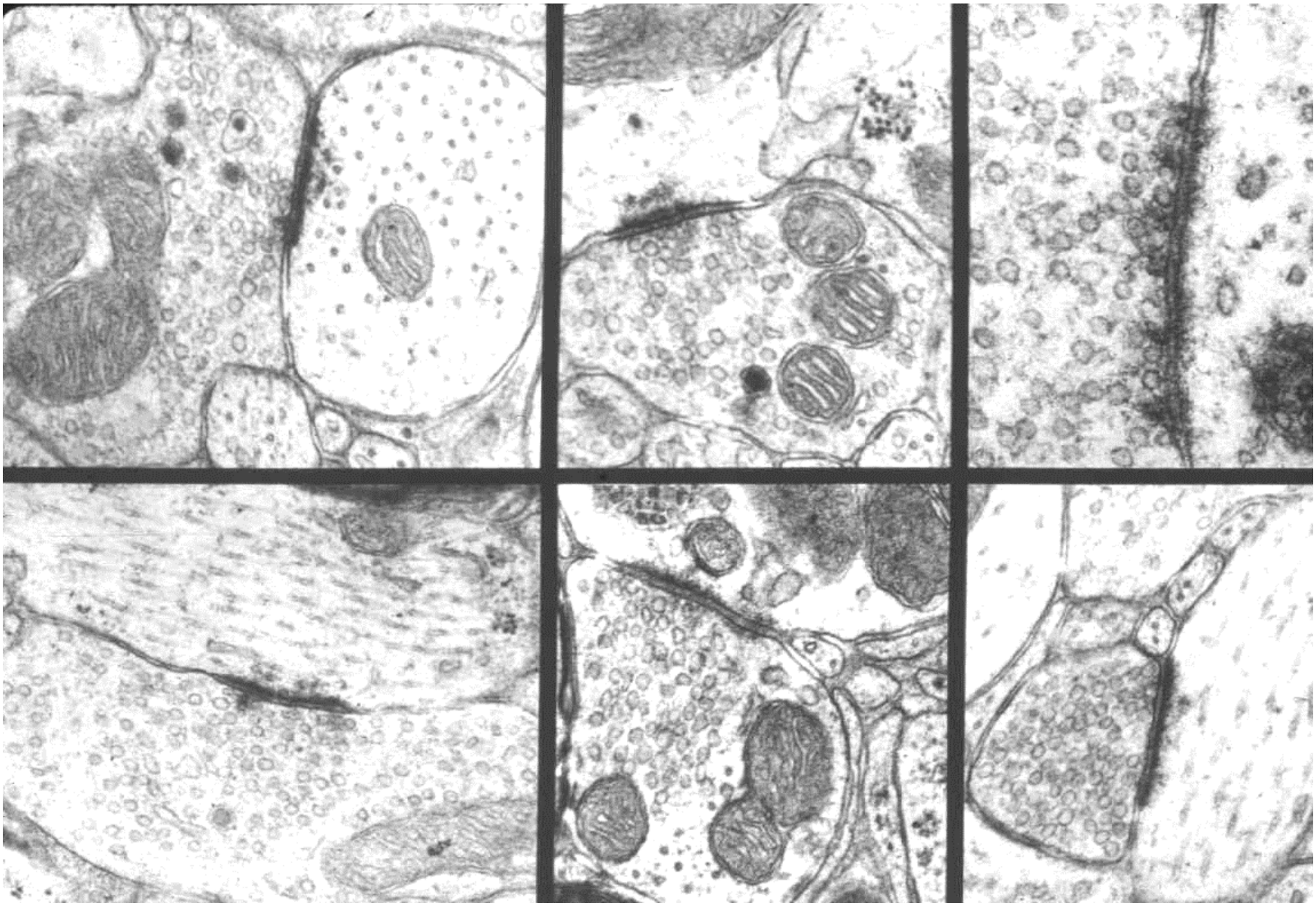


B Bouton on initial axon segment

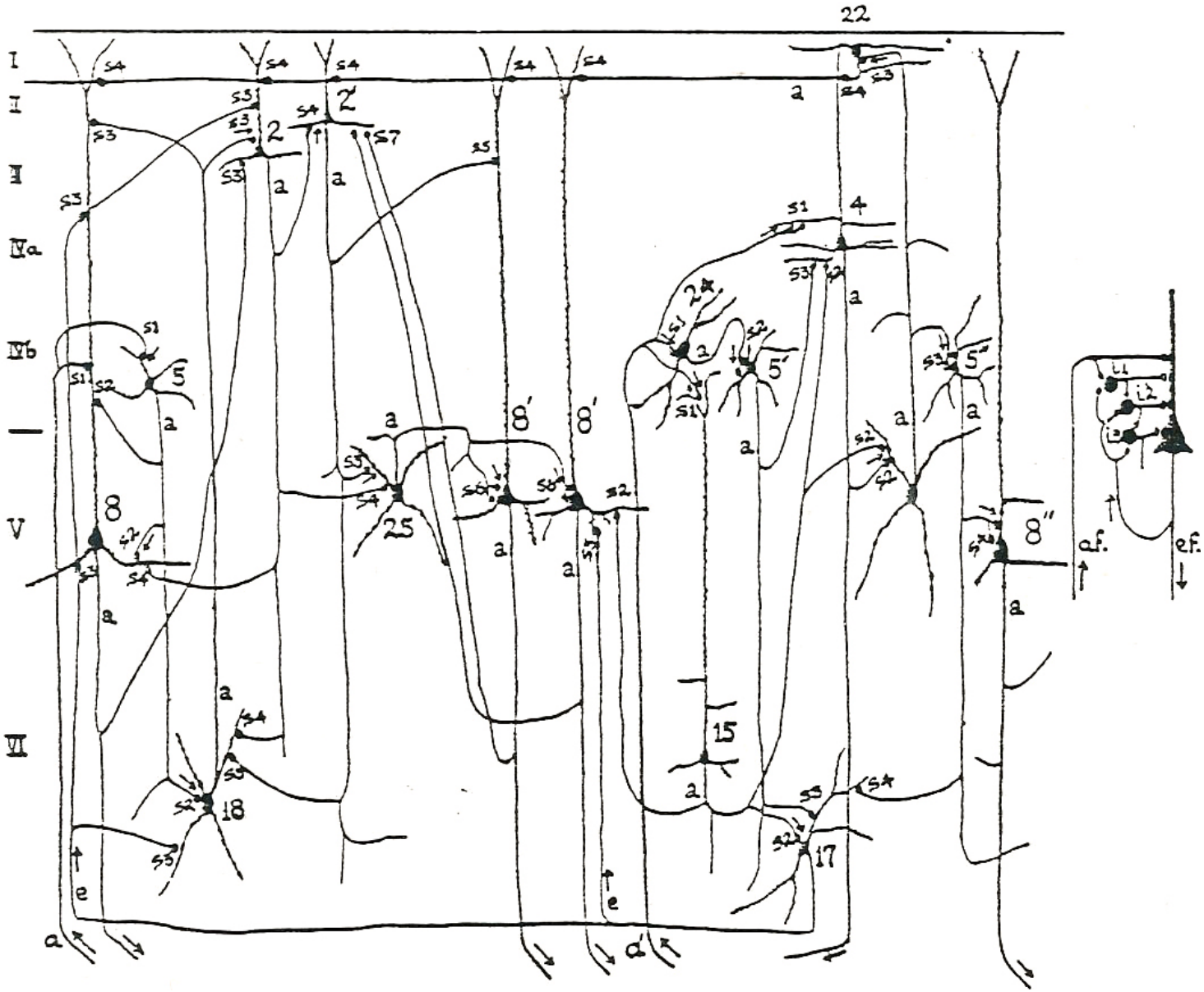
Fig. 6–11. Axodendritic and Axoaxonic Synapses
A. The postsynaptic element of an axodendritic synapse can be either a spine or a dendritic shaft.
B,C. The postsynaptic component of an axoaxonic synapse is usually the initial segment (**B**) or another bouton (**C**). The initial segment of an axon can usually be distinguished from a dendrite by a characteristic undercoating, or dense layer, beneath the cell membrane and the presence of microtubules that are bundled together into fascicles.



C Axoaxonic synapses



LORENTE de NO, 1938



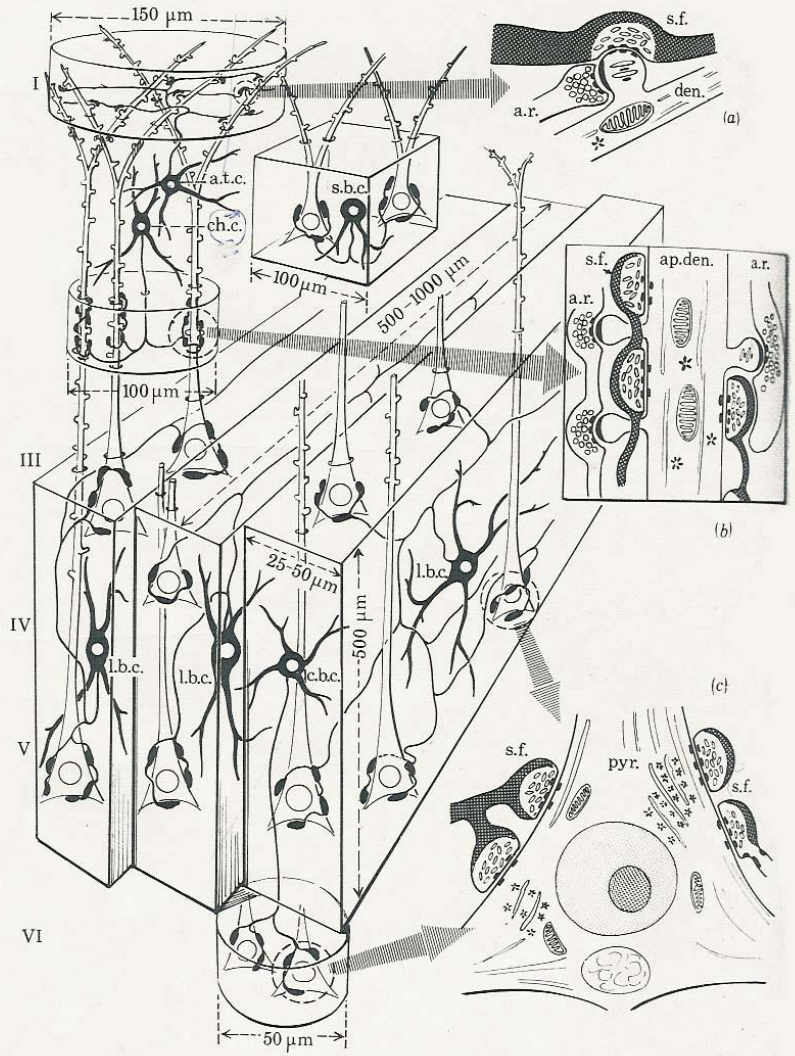
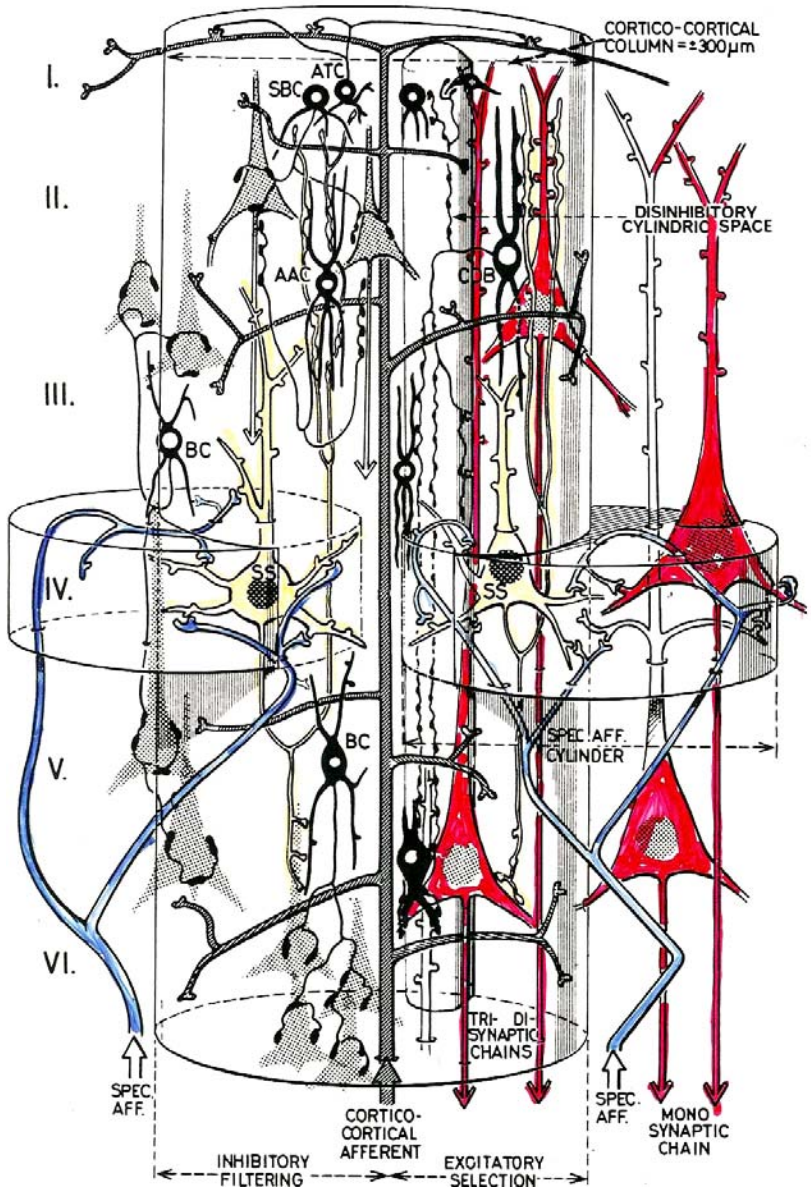
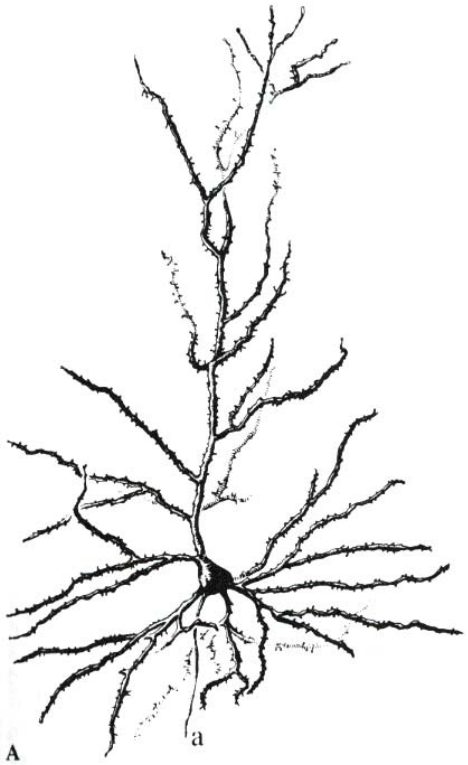
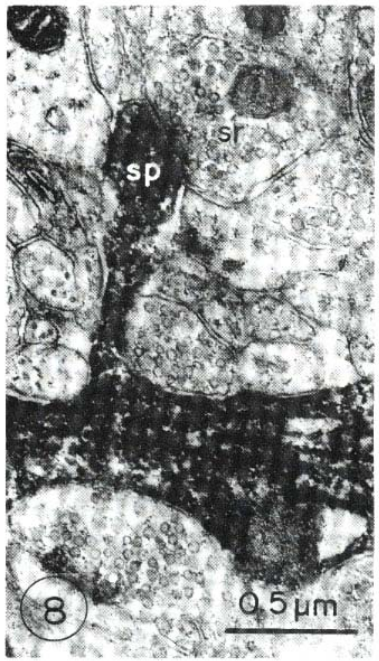
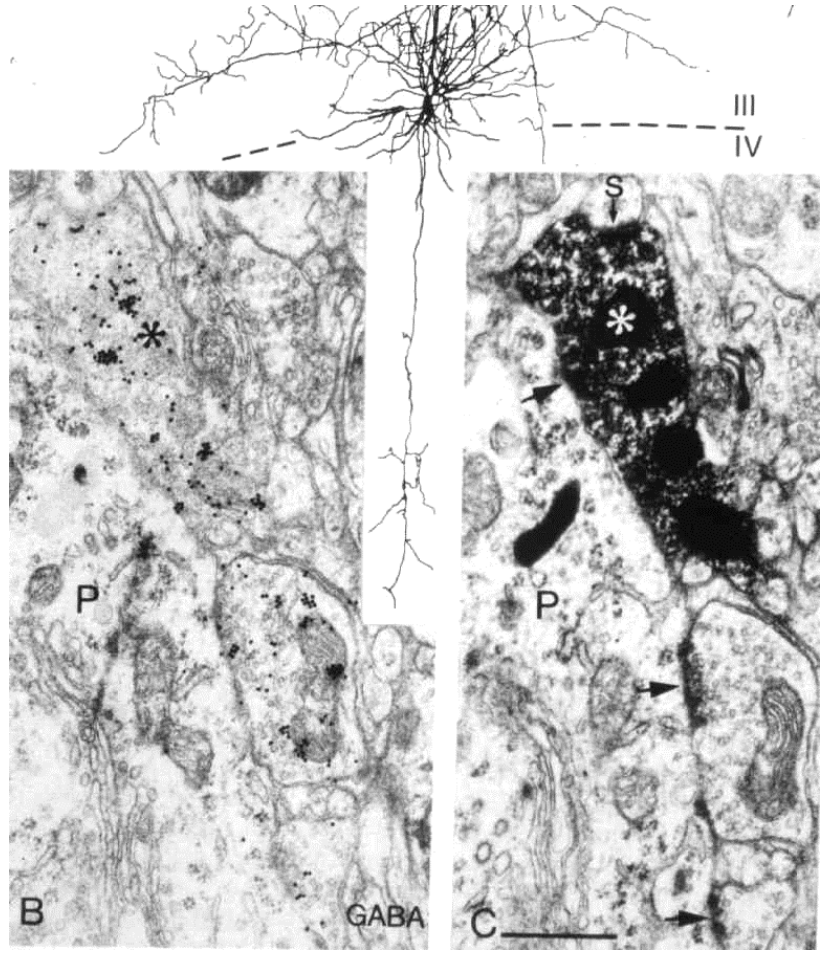


FIGURE 6. For description see opposite.



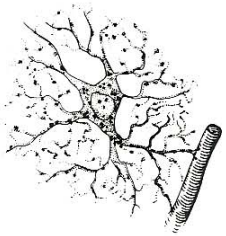




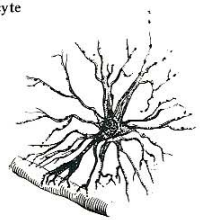


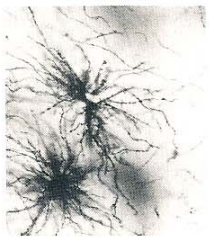
C. Photomontage of a single dendrite of a spiny striatel projection neuron intracellularly stained with HRP. (Ffrom Wilson, C.J. et al., 1983. J. Neuroscience, 3:383-398. With permission of Elsevier Sciene Publishers, New York.)

D. Electron micrograph of a dendritic spine (SP) from the dendrite shown in **C**. The spine is contacted by a containing small round synaptic vesicles. This kind of synapse is formed by most axons originating in cerebral cortex and thalamus. (Ffrom Wilson, C.Y. and Groves. P.M., 1980. J. Comp. Neurol. 194:599-615. With permission of Wiley-LIss, a division of John Wiley, New York.)

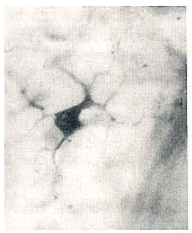


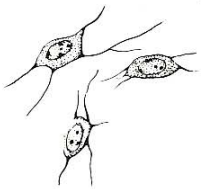
A. Protoplasmic astrocyte



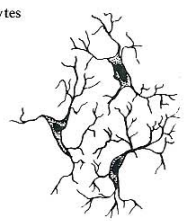


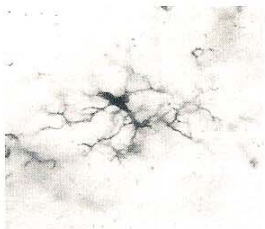
B. Fibrous astrocyte





C. Oligodendrocytes

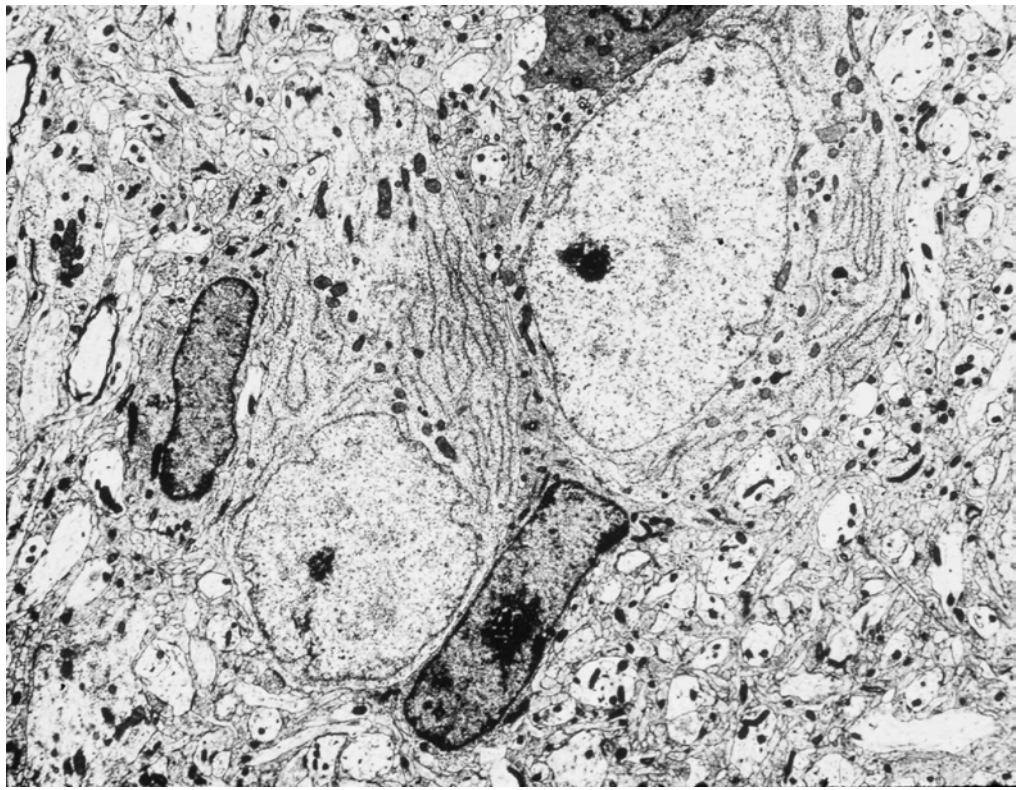


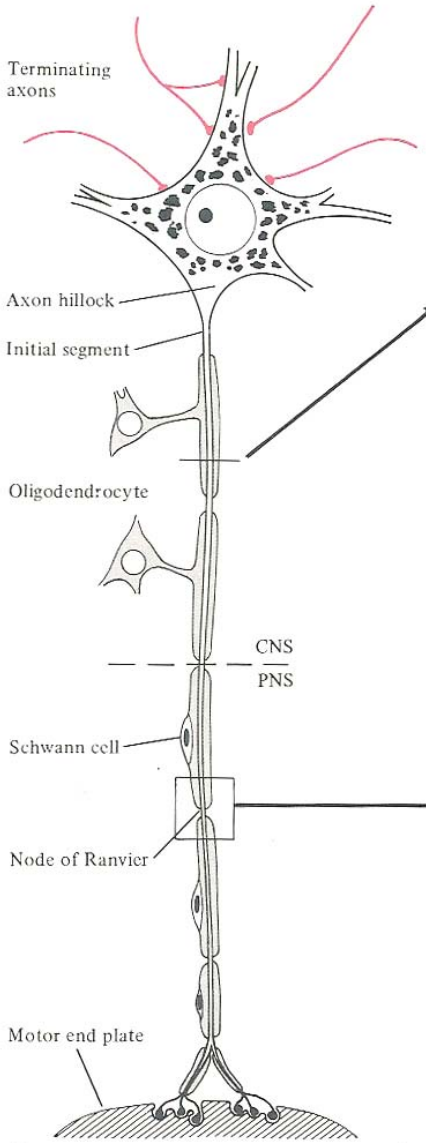


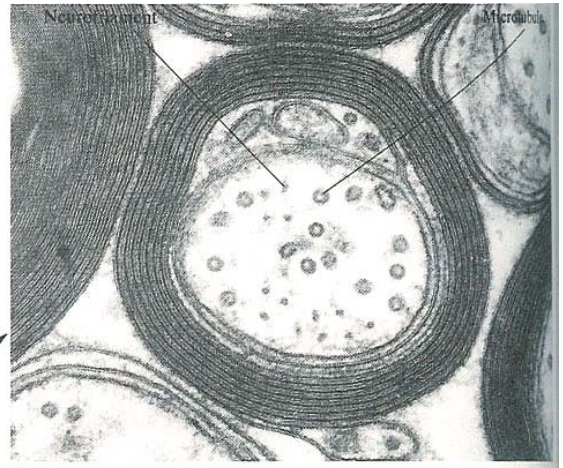
D. Microglia

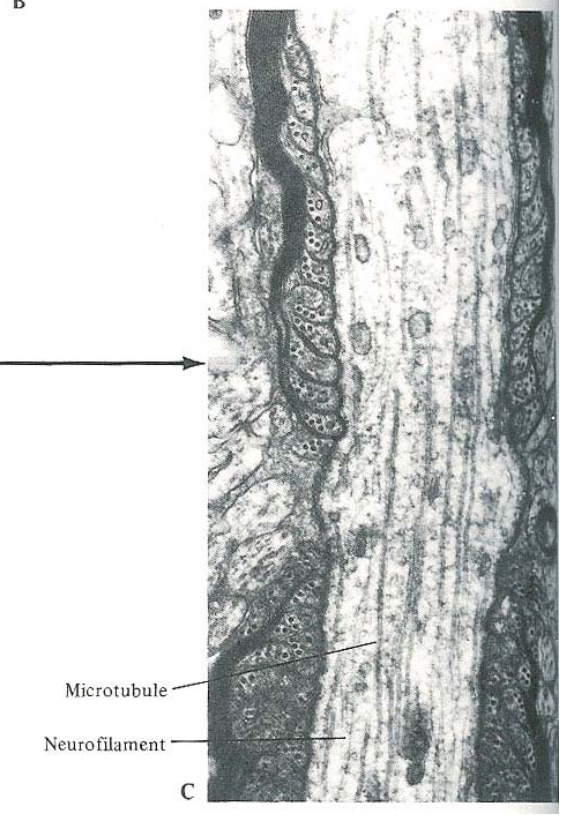
E. Ependyma

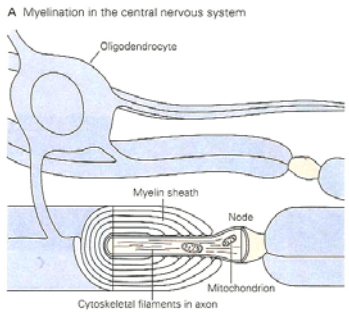
Fig. 6–12. Neuroglia
Schematic drawings and photographs of histologic preparations showing the different types of glial cells. (Drawings from Jenkins, T. N., 1978. Functional Mammalian Neuroanatomy, 2nd ed. With permission of the author and Lea and Febiger, Philadelphia. Photographs; courtesy of Dr. Enrico Mugnaini.)

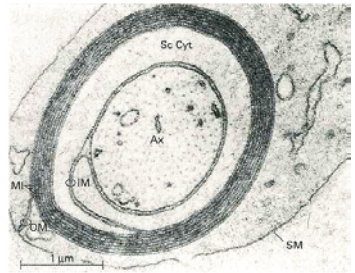


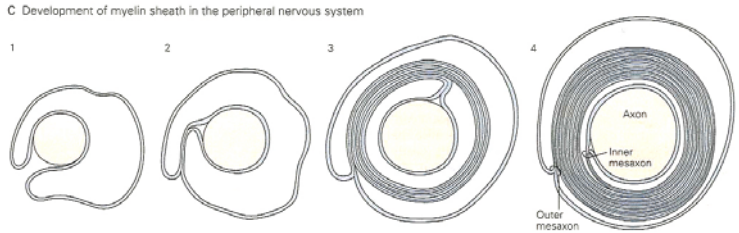

Terminating axons
Axon hillock
Initial segment
Oligodendrocyte
CNS
PNS
Schwann cell
Node of Ranvier
Motor end plate
A

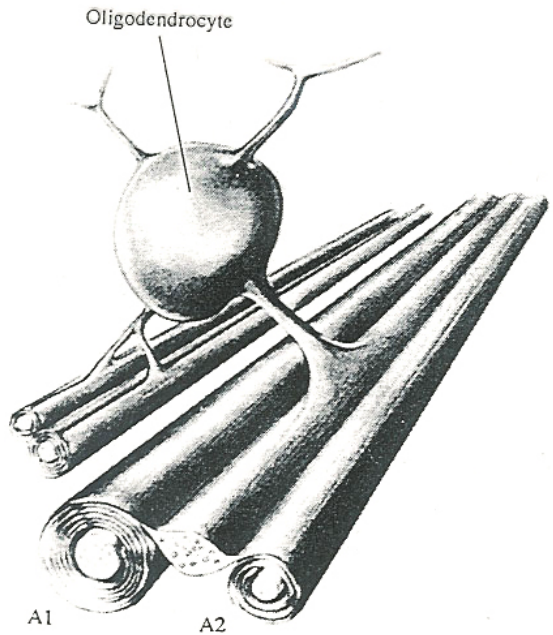

Neurofilament
Microtubule
B

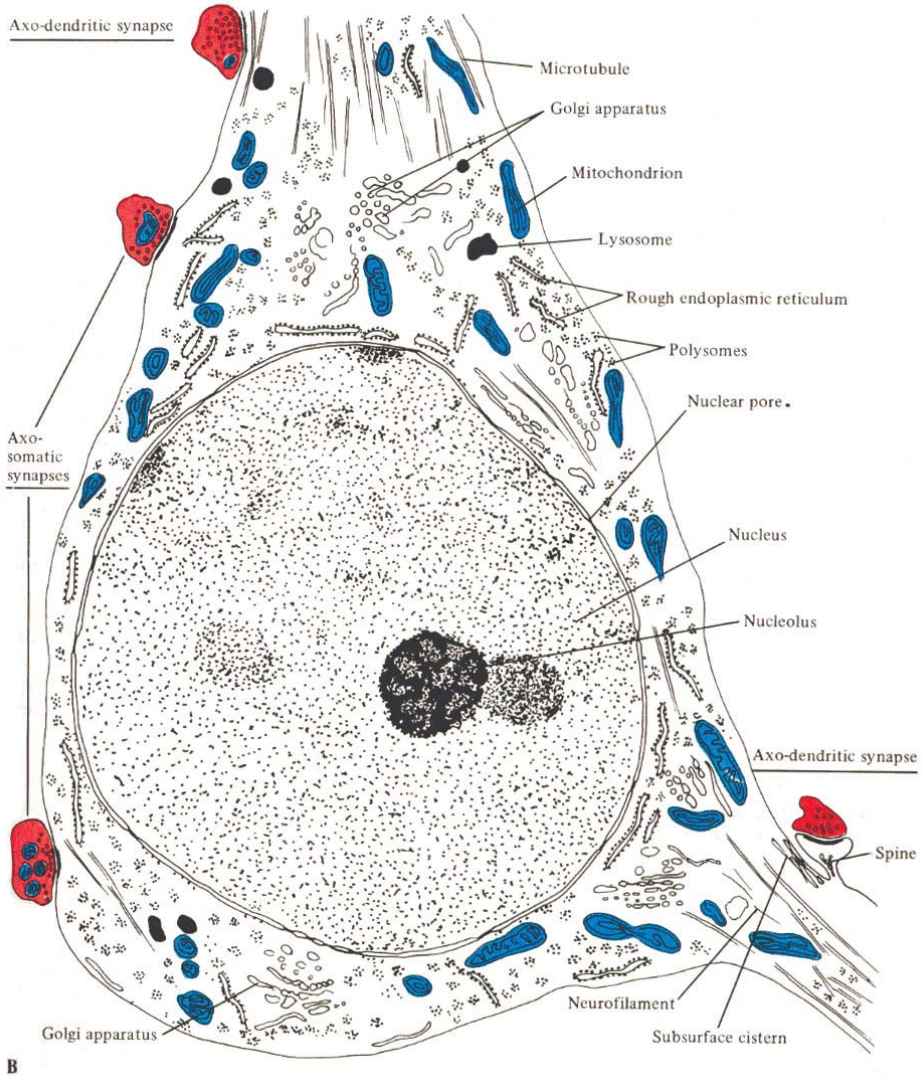

Microtubule
Neurofilament
C


A Myelination in the central nervous system
Oligodendrocyte
Myelin sheath
Node
Mitochondrion
Cytoskeletal filaments in axon


B Myelination in the peripheral nervous system
Sc Cyt
Ax
IM
OM
SM
1 μm


C Development of myelin sheath in the peripheral nervous system
1
2
3
4
Axon
Inner mesaxon
Outer mesaxon


Oligodendrocyte
A1
A2



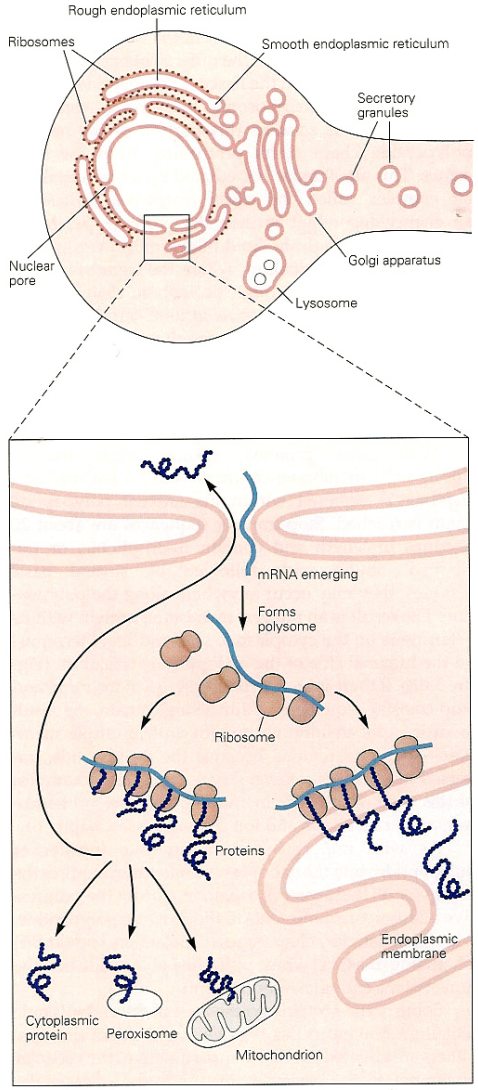
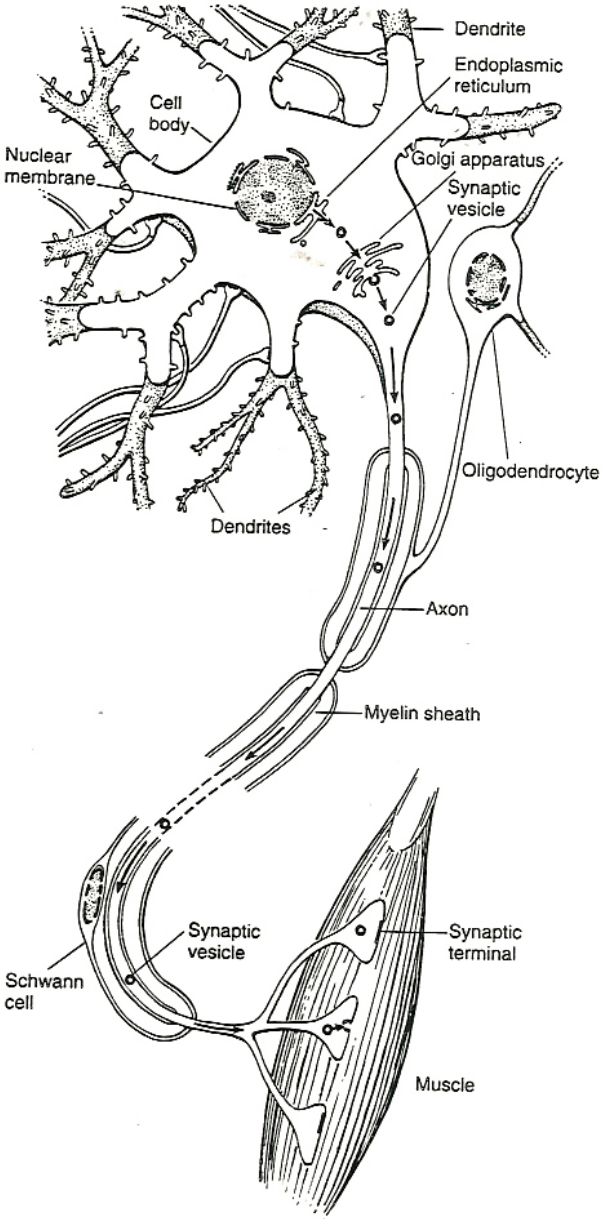


Figure 5-5 Free and membrane-bound polysomes translate mRNAs that encode proteins with a variety of destinations. Messenger RNAs, transcribed from genomic DNA in the neuron's nucleus, emerge through nuclear pores (enlargement) to form polysomes by attaching to ribosomes.



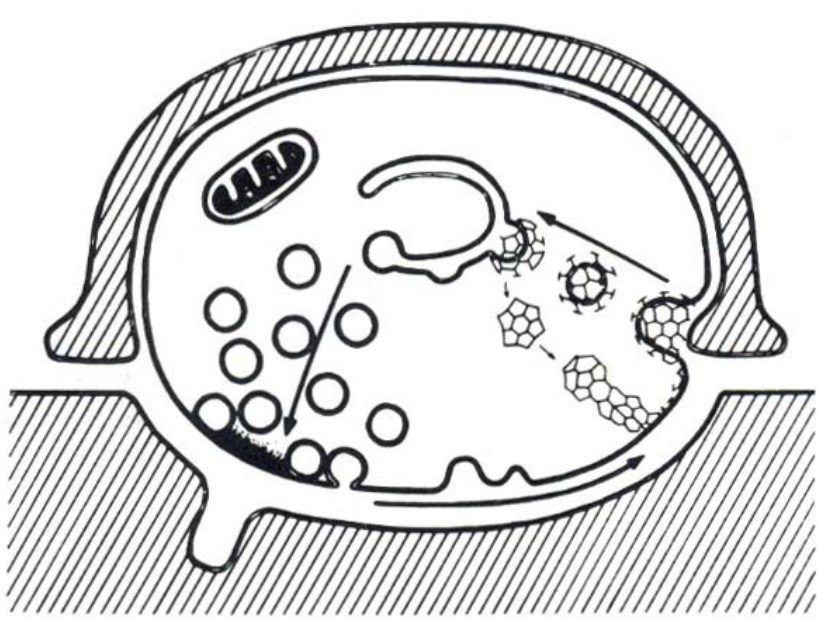


Fig. 40. Modern view of the neuromuscular junction, representing the main structures and sequence of events that take place at a typical synapse during release of vesicles and recycling of vesicle membranes. (From Heuser and Reese, 1973)

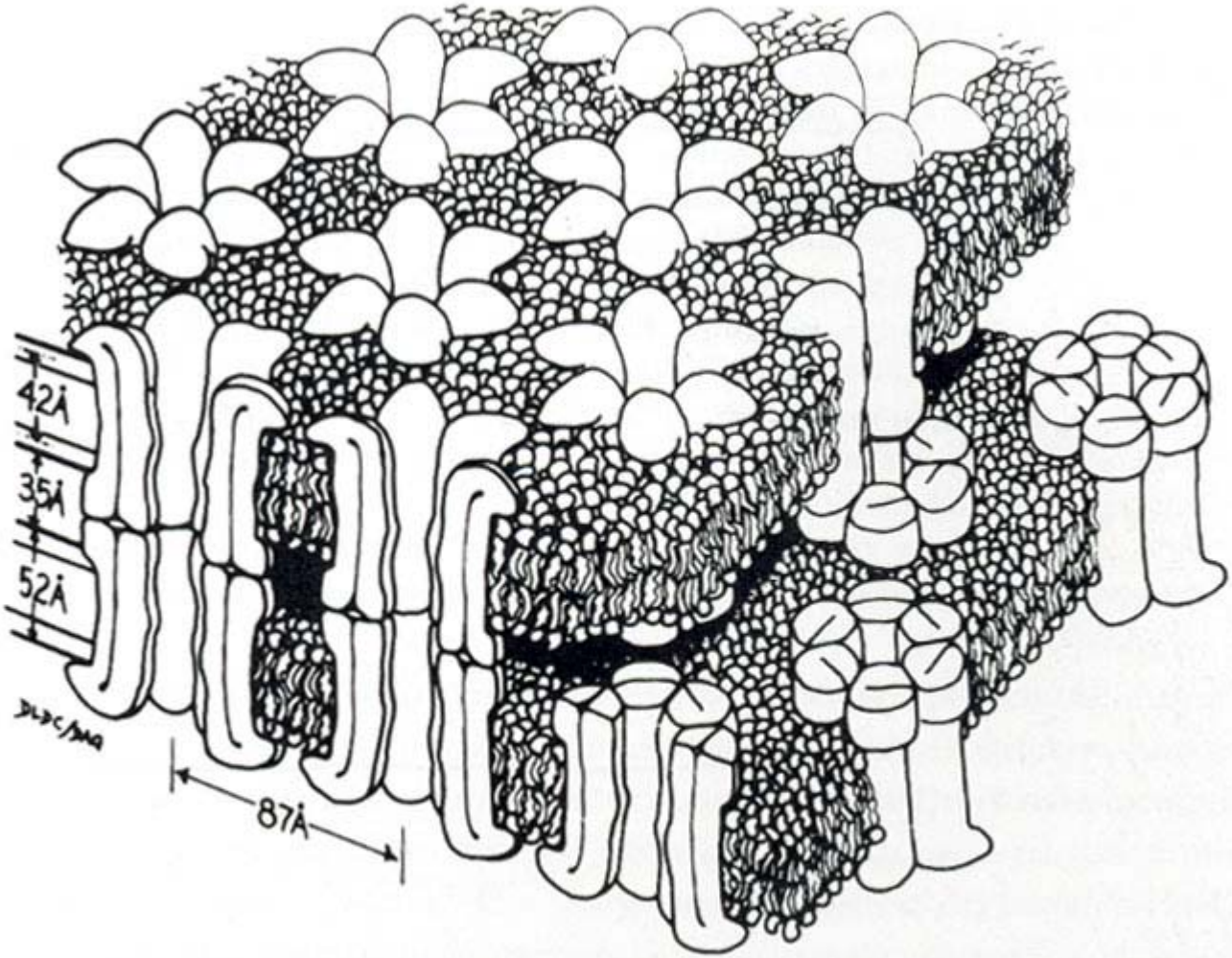
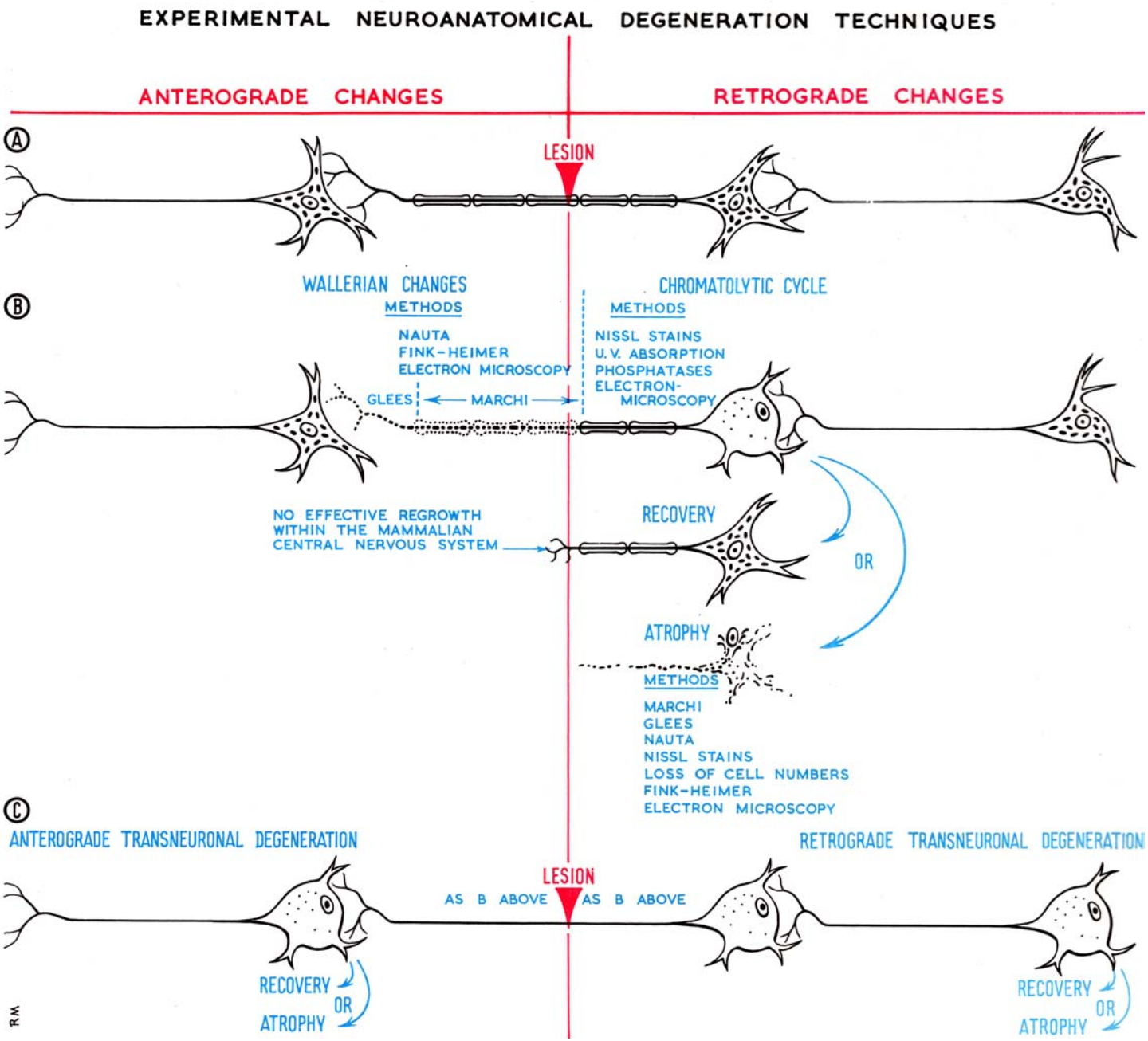


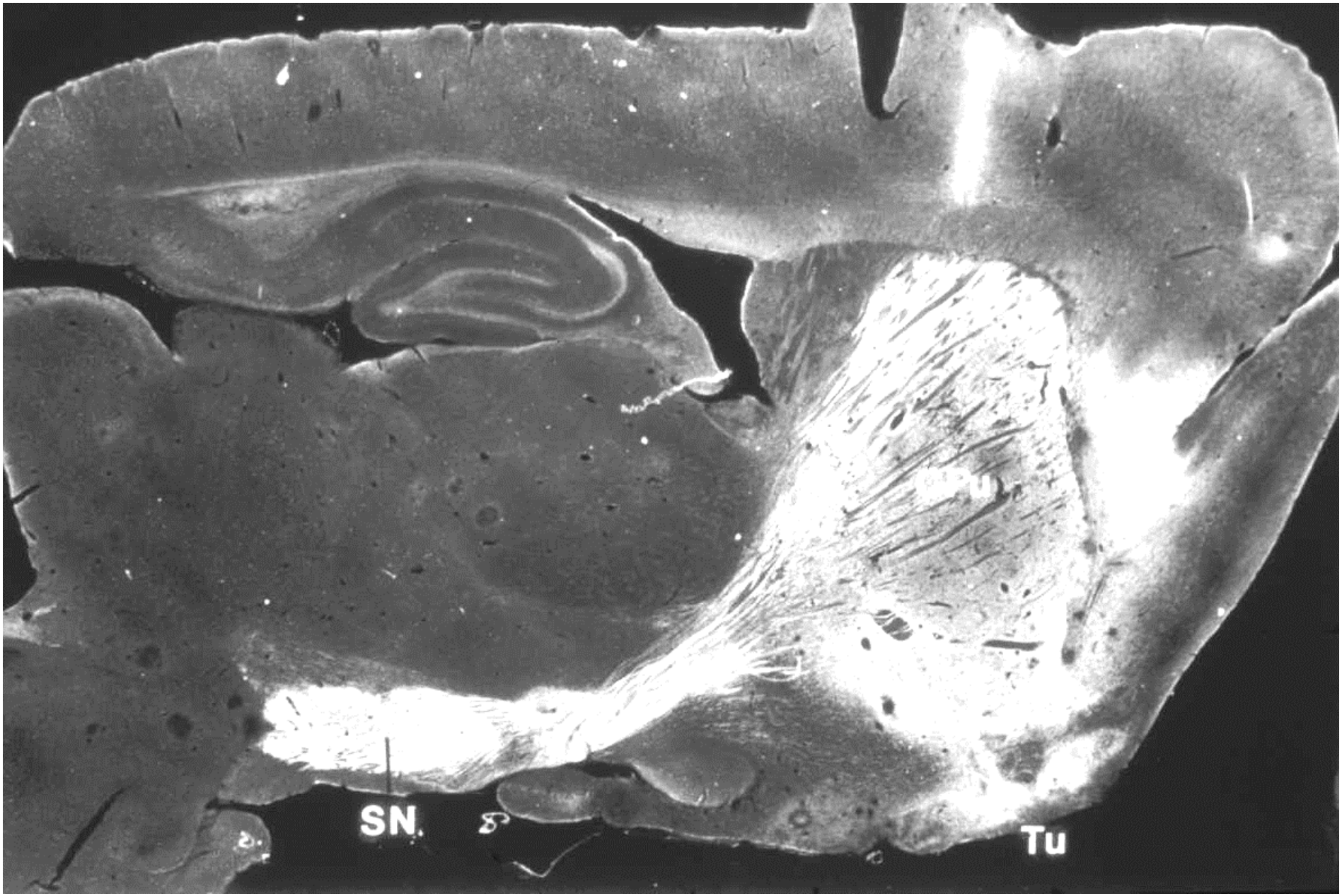
Fig. 41. Diagram summarizing the fine structural organization of a gap (electrical) junction. The two apposed membranes are shown, with channel proteins composed of six circularly arranged subunits forming bridges across them that allow for the passage of ions, small molecules, and electric current. (From Mackowski et al., 1977)

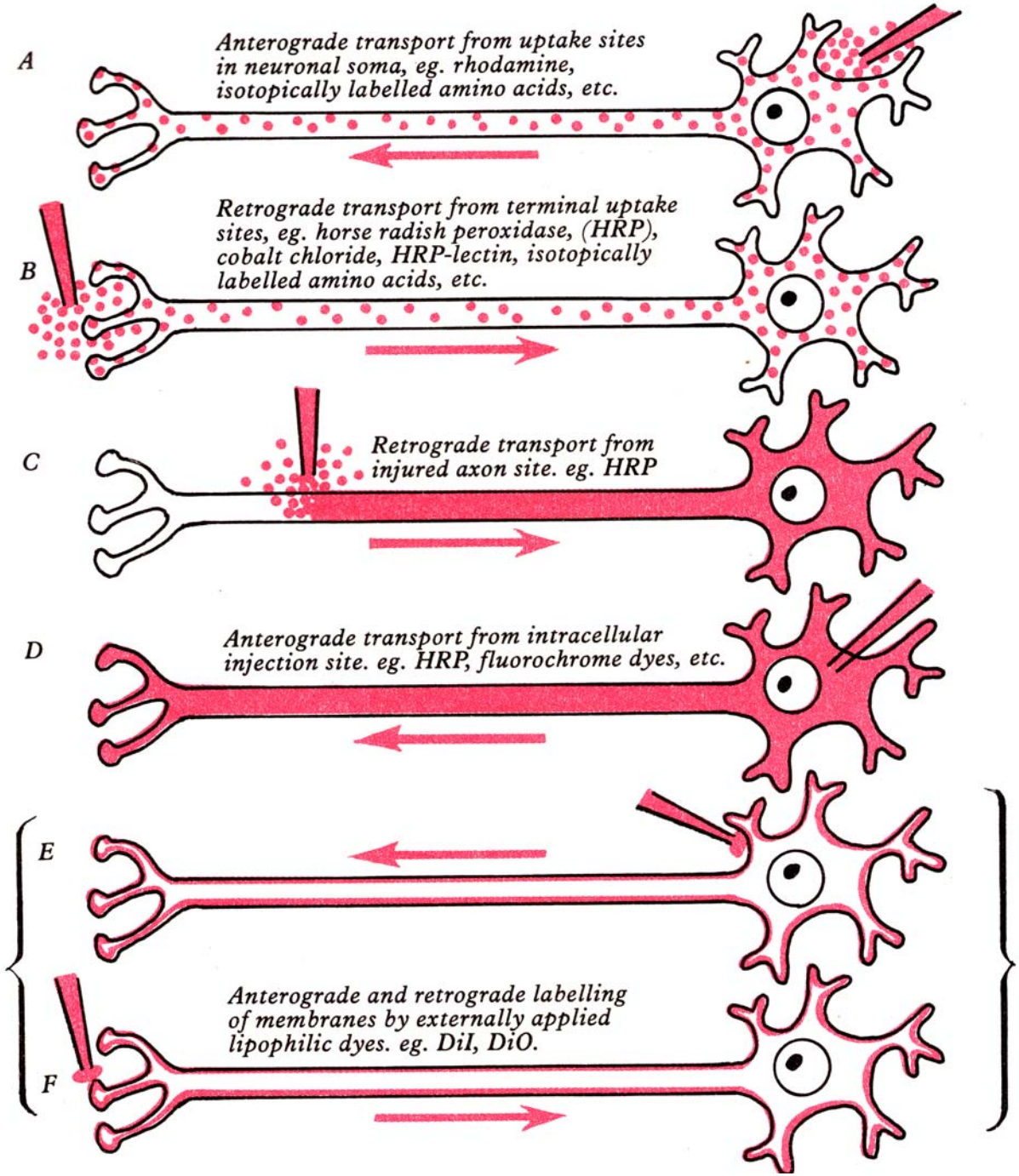
- **REVISIONS of the NEURON DOCTRINE**

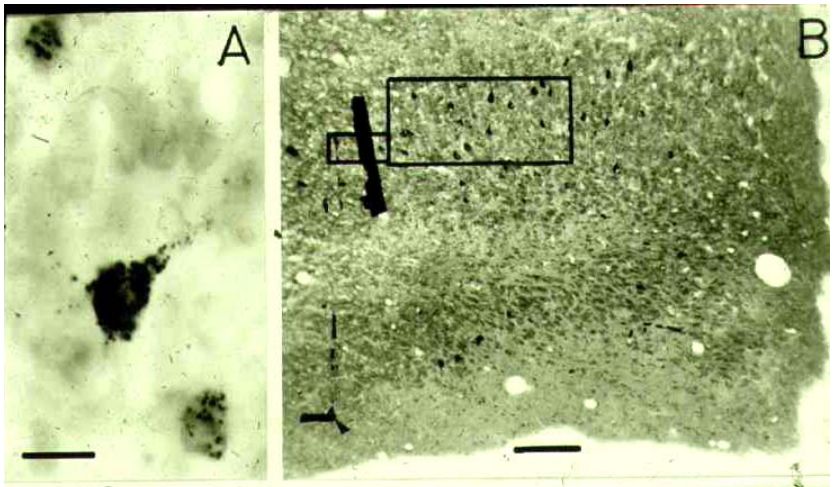
- 1. The presence of electrical synapses – gap junctions
- 2. Axo-axonic synapses
- 3. Dendro-dendritic synapses (e.g. amacrine cells of the retina; granule cells of the olfactory bulb
- 4. Transynaptic regulation of transmitters, enzymes; transynaptic transport of amino acids, viruses
- 5. Metabolic subunits within the neuron (e.g. spines as microcompartments)
- 6. Backpropogation of action potentials from the soma to the dendrites

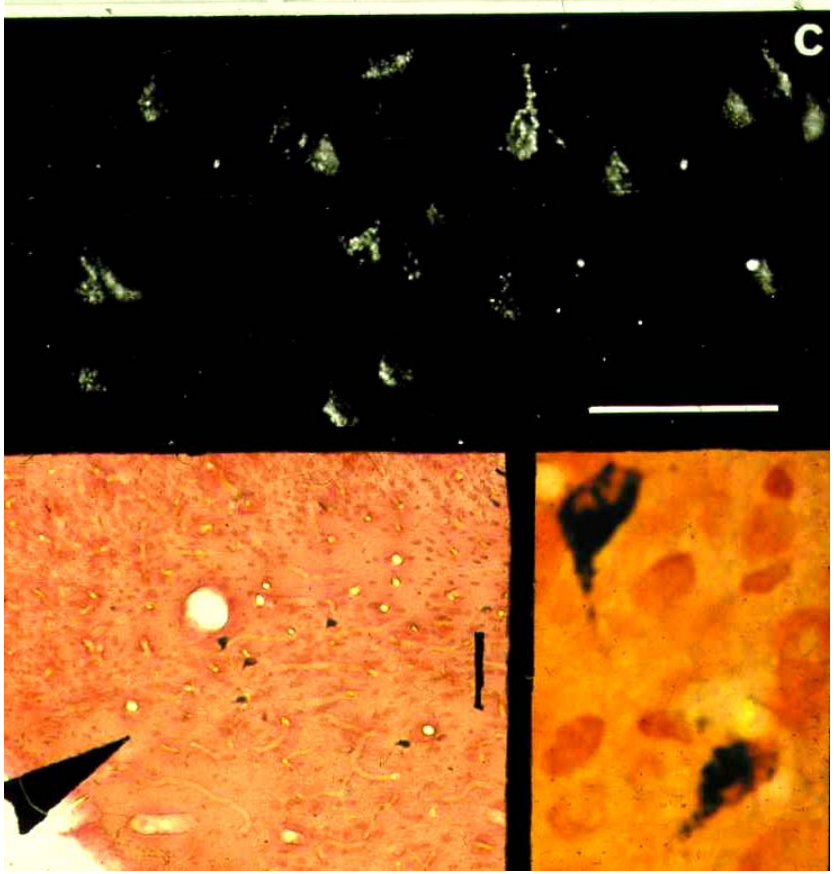
NEURON TRACING TECHNIQUES

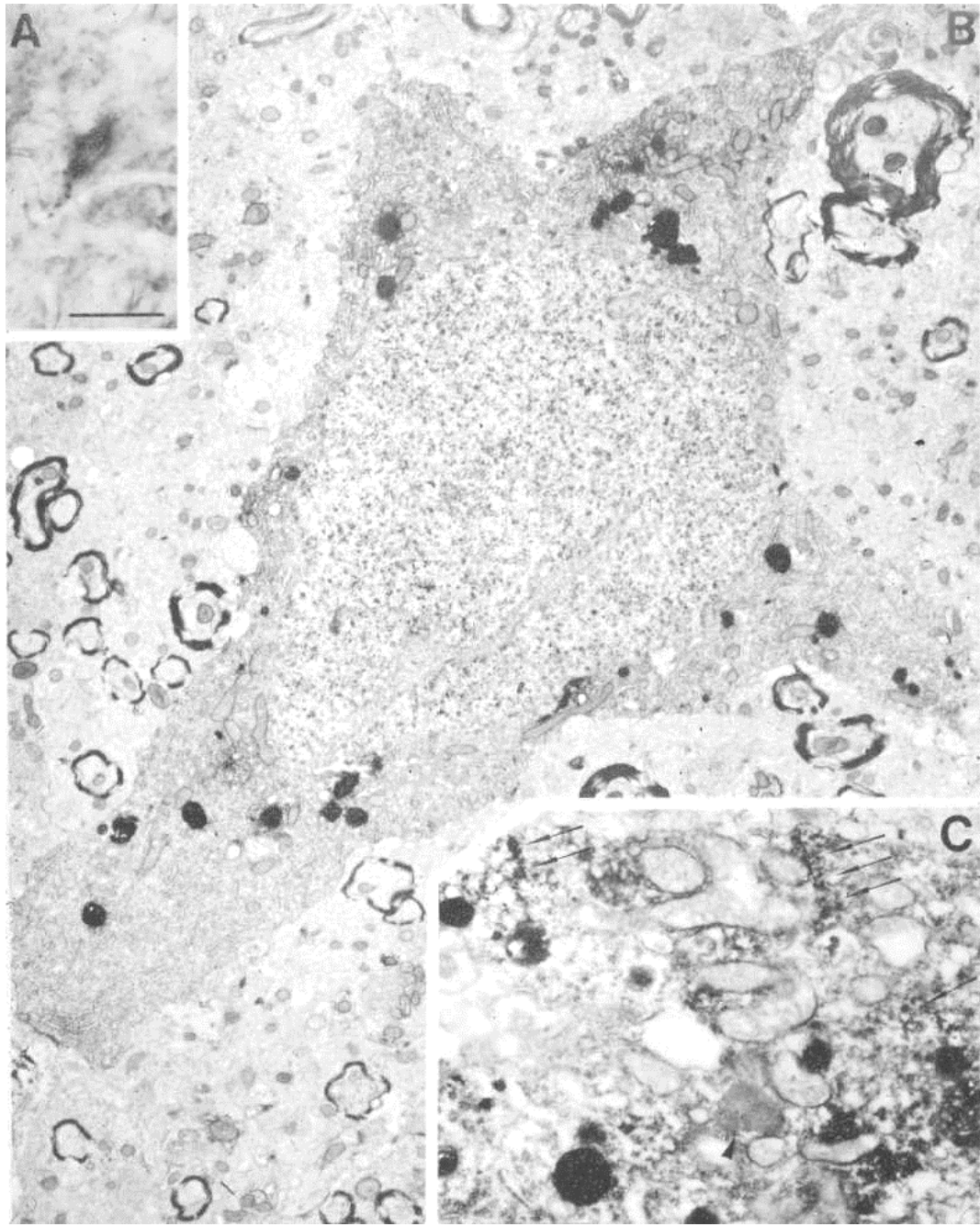



SN
Tu

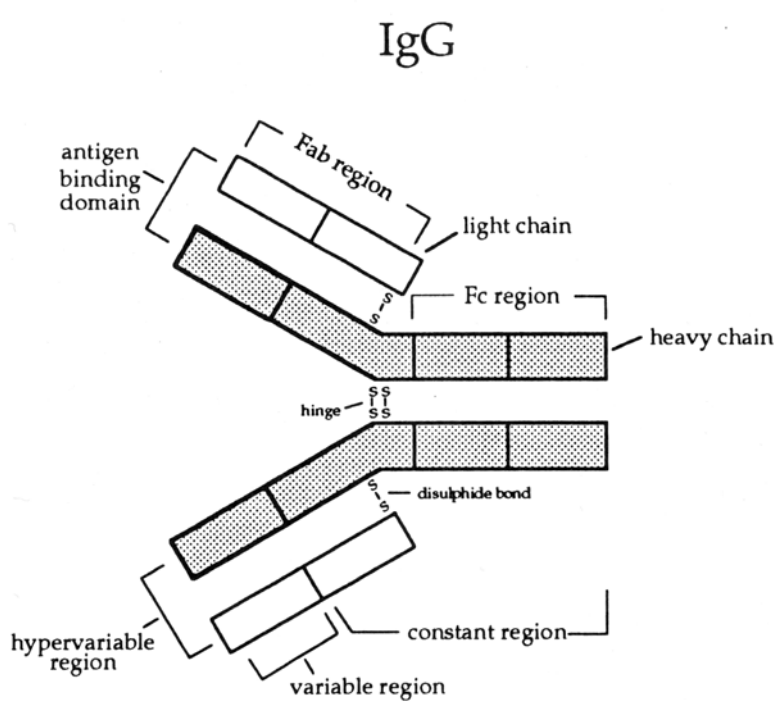

A
Anterograde transport from uptake sites in neuronal soma, eg. rhodamine, isotopically labelled amino acids, etc.
B
Retrograde transport from terminal uptake sites, eg. horse radish peroxidase, (HRP), cobalt chloride, HRP-lectin, isotopically labelled amino acids, etc.
C
Retrograde transport from injured axon site. eg. HRP
D
Anterograde transport from intracellular injection site. eg. HRP, fluorochrome dyes, etc.
E
F
Anterograde and retrograde labelling of membranes by externally applied lipophilic dyes. eg. DiI, DiO.


A
B

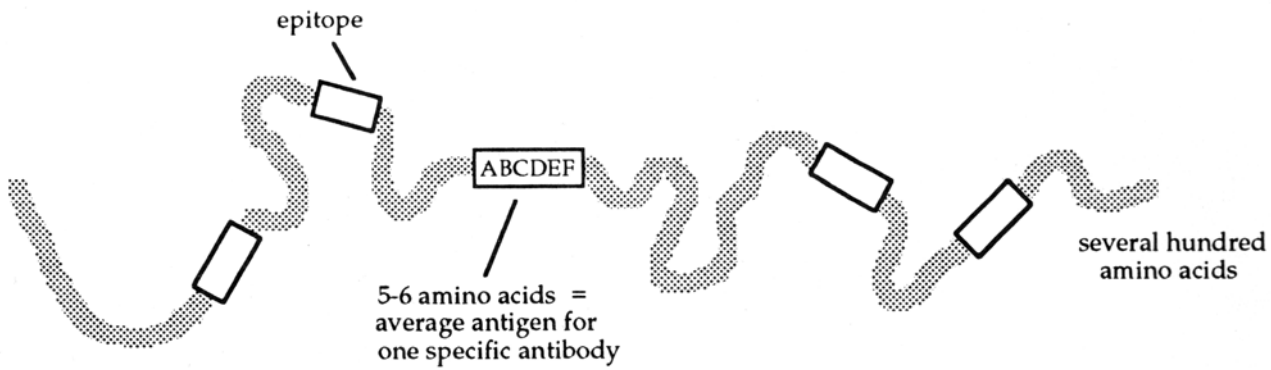

C

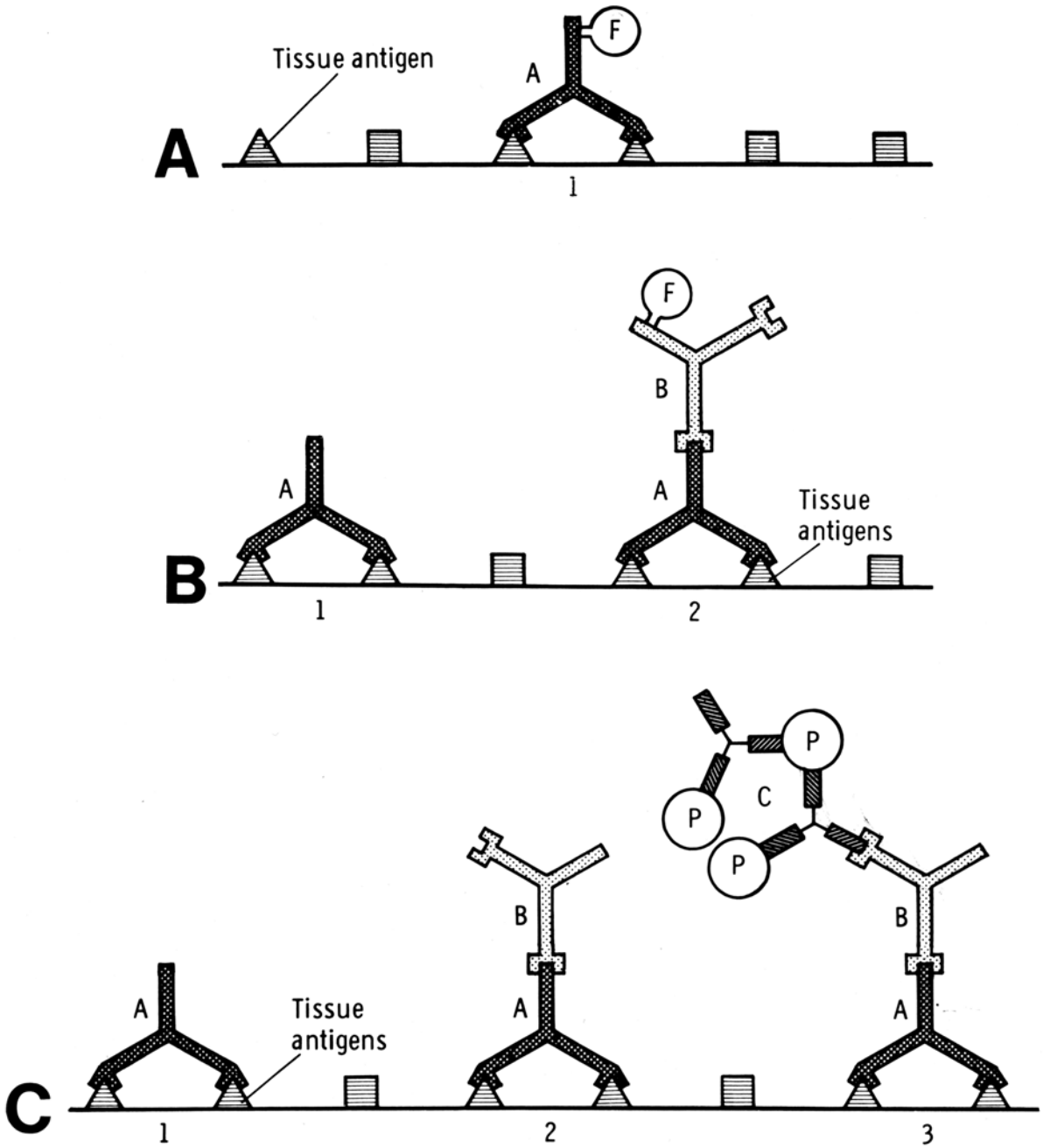

A
B
C

A


IgG
antigen binding domain
Fab region
light chain
Fc region
heavy chain
hinge
disulphide bond
hypervariable region
constant region
variable region

B


epitope
ABCDEF
5-6 amino acids = average antigen for one specific antibody
several hundred amino acids


A
Tissue antigen
A
F
1
B
A
F
B
A
Tissue
antigens
1
2
C
P
P
P
C
B
B
A
A
A
Tissue
antigens
1
2
3

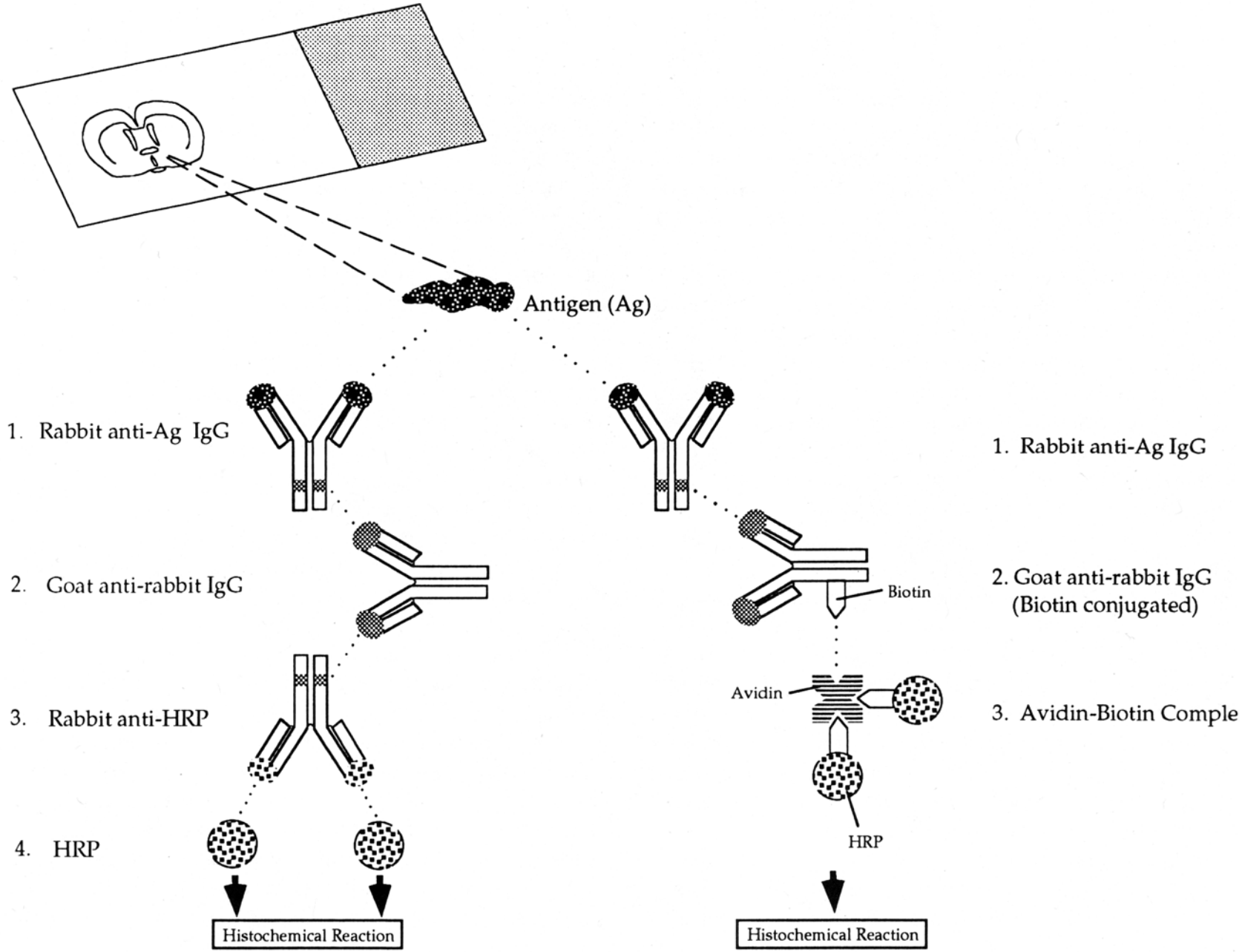
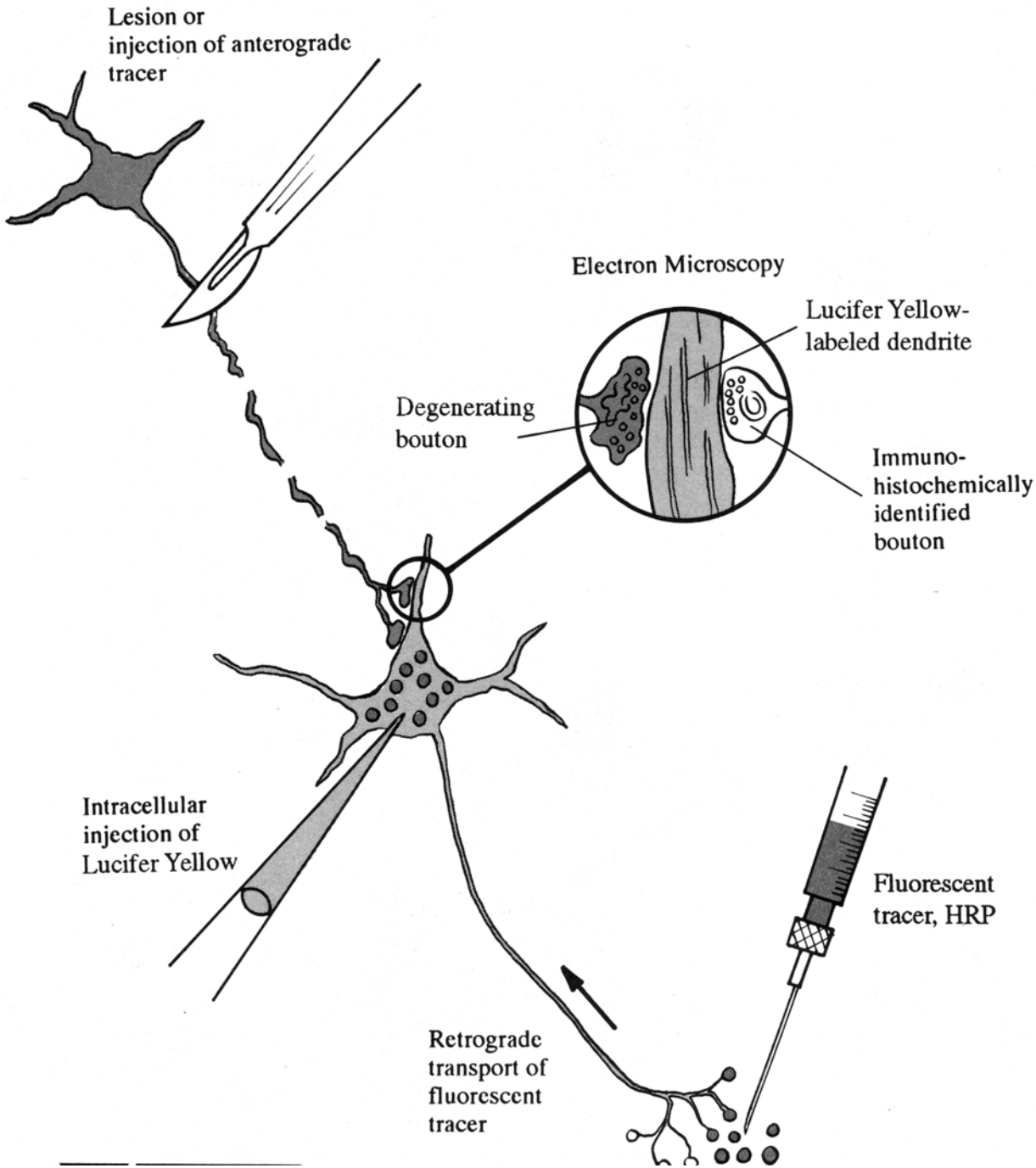
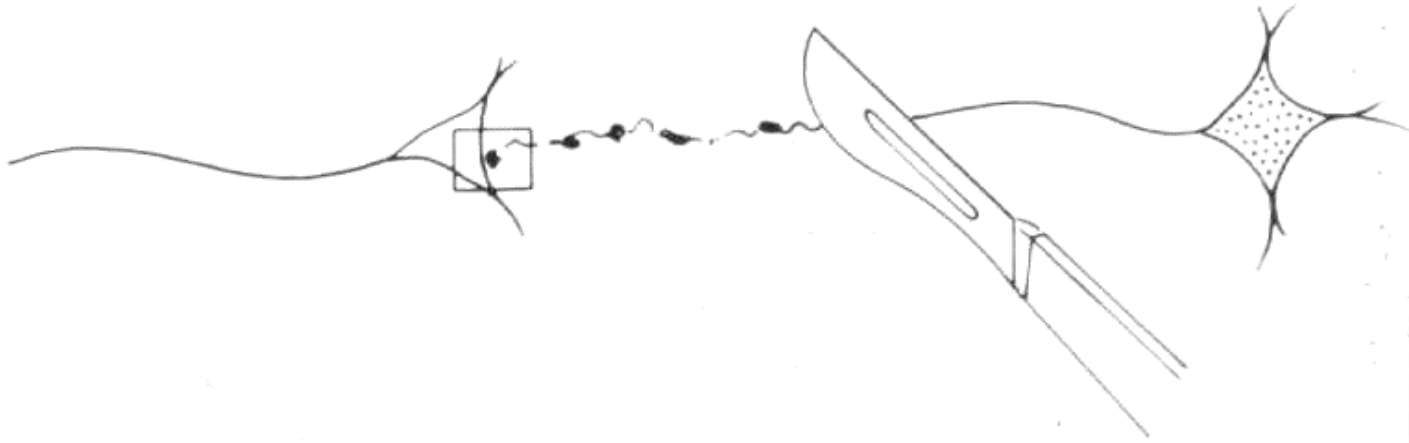


FIG. 5. Schematic diagram illustrating two variations of an immunocytochemical protocol utilizing peroxidase histochemistry.

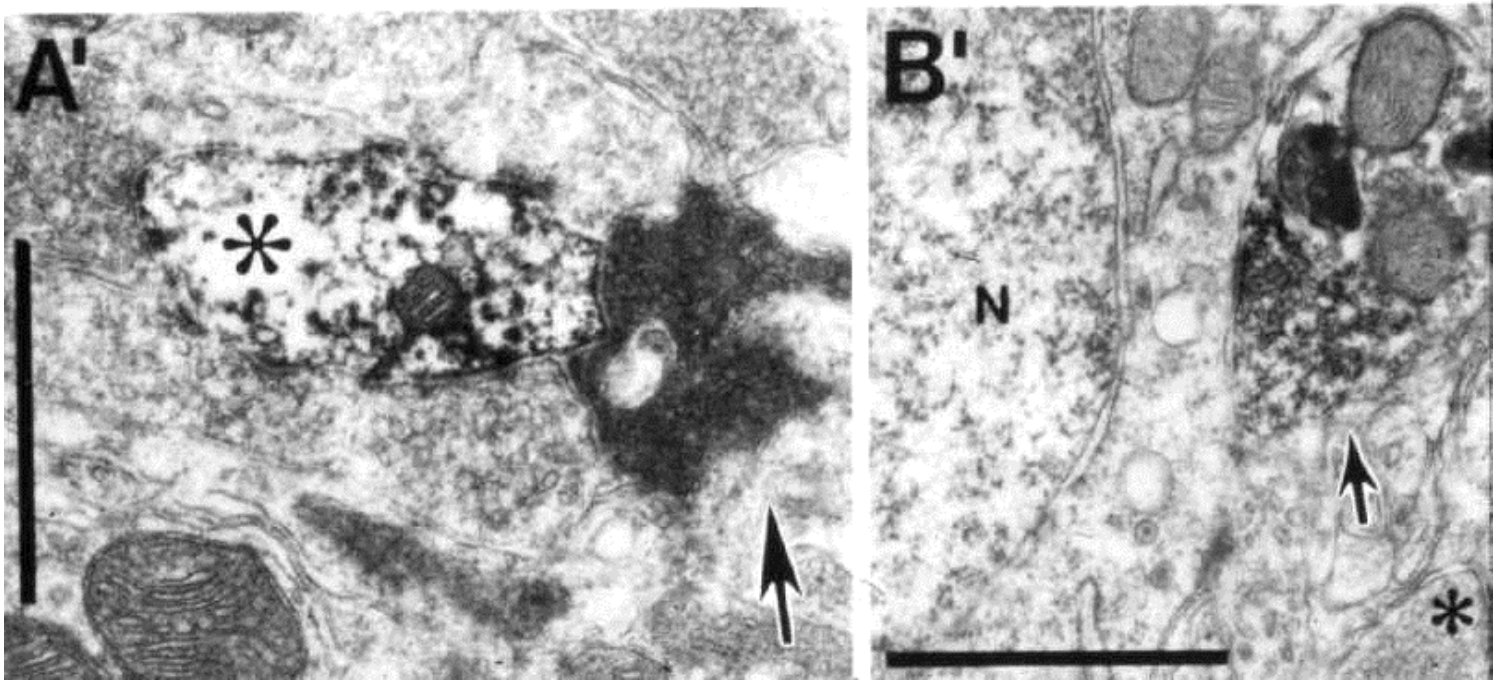

Lesion or
injection of anterograde
tracer
Electron Microscopy
Lucifer Yellow-
labeled dendrite
Degenerating
bouton
Immuno-
histochemically
identified
bouton
Intracellular
injection of
Lucifer Yellow
Fluorescent
tracer, HRP
Retrograde
transport of
fluorescent
tracer

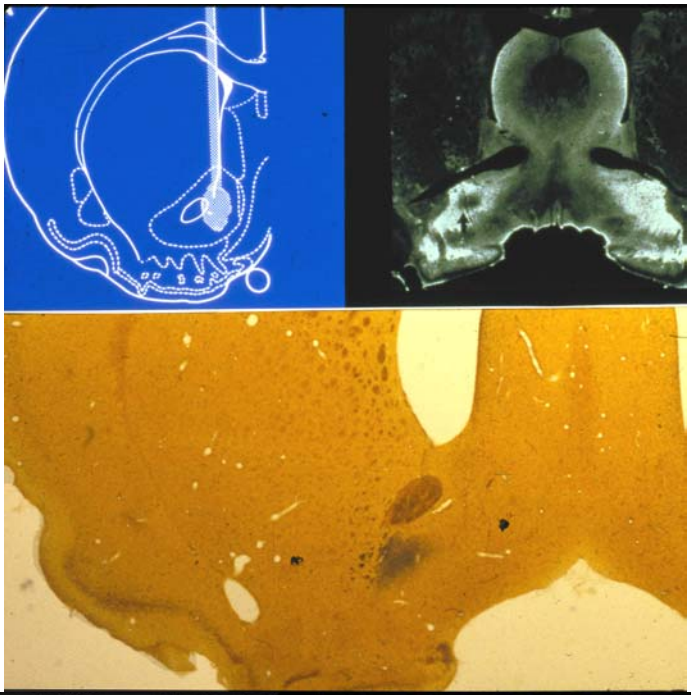
Immunostaining and

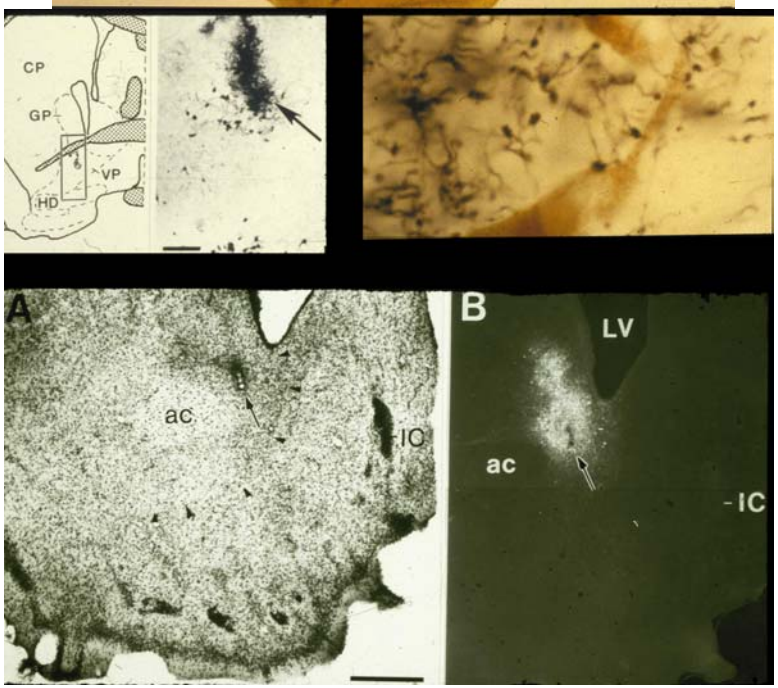
Anterograde deg

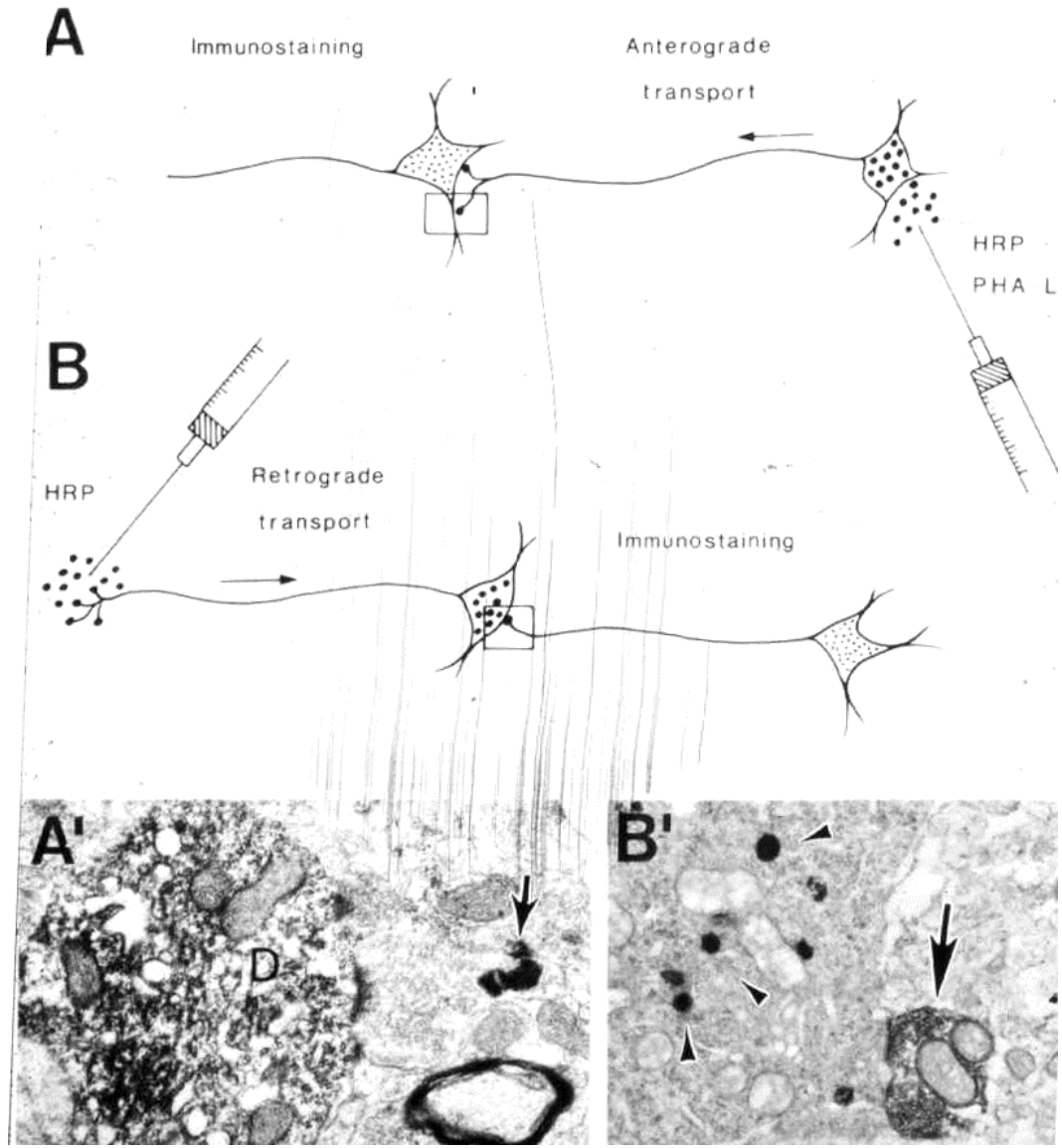


B



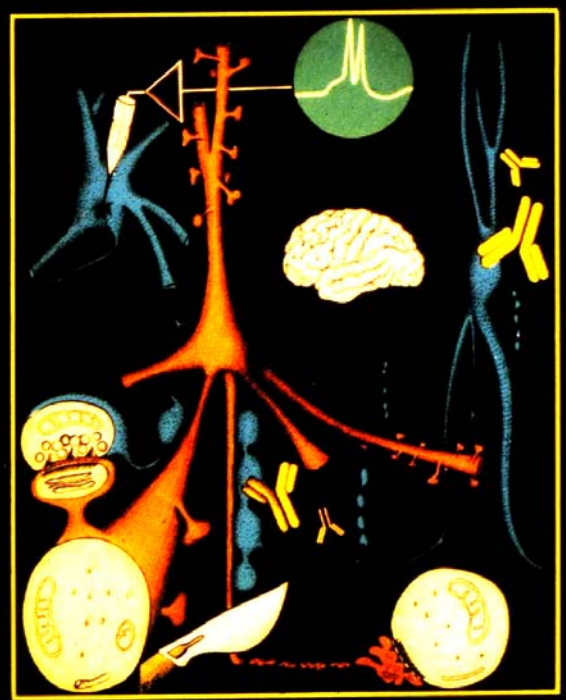



CP
GP
VP
HD
A
ac
IC
B
LV
ac
IC


A
Immunostaining
Anterograde
transport
HRP
PHA L
B
HRP
Retrograde
transport
Immunostaining
A'
D
B'

Neuroanatomical Tract-Tracing Methods 2

Recent Progress



Edited by
Lennart Heimer and László Záborszky