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

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 Giulio Bizzozero, Albrecht Kolliker, and Camillo Golgi, at Golgi's home in Pavia, during Kolliker'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. F. C. Graziani)

Fig. 38. Golgi's depiction of the reticulum formed by axon collaterals in the dentate gyrus. (Golgi, 1904)

Fig. 13. A diagram by Golgi of the nervous elements of the hippocampus and fascia dentata.
Figure 21
A diagram of Ammon’s horn and the fascia dentata to show the relationship between large pyramidal cells of the region interior of Ammon’s horn and the efferent 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 efferent fibers; E: soma of granule cells; F: axons of the large pyramidal cells running toward the hippocampus; G: fimbriae; H: small or superior pyramidal cell; I: bundle of large ascending mossy fibers; J: collaterals from the white matter; K: fiber terminals from the subiculum; L: pyramidal cells in the subiculum with an axon that inactivates Ammon’s horn.

Figure 22
Section through Ammon’s horn of an eight-day-old rabbit.

1. stratum moleculare; 2. stratum lucidum; 3. stratum radiatum; 4. pyramidal cell layer; 5. polymorph cell layer; 6. white matter or alien; 7. pyramidal cell; 8. cell with an ascending axon; 9. cell with a horizontal axon; 10. cell with an ascending axon that ends in the interpyramidal plexus; 11. short-axon cell in the stratum lucidum; 12. cell in the stratum moleculare. Proximal processes are indicated by a.

Figure 23
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; E: fimbriae; F: cells of the molecular layer; G: displaced granule cell; H: granule cell; I: pyramidal cell with an ascending axon; J: cell with an ascending axon that terminates in the subiculum; K: cells with a descending axon that enters the subiculum. These axonal processes are indicated by a.
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 connections of the cerebellum. Reduced silver method. A, star-shaped cell of the molecular layer; b, initial narrowed portion of its axon; B, terminal baskets; C, recurrent collaterals; h, final filaments 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 Unit.
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 potentials) 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\(^{34}\).
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, SNARE complexes or with its subunits include the complexes, Sec1, plasma membrane Ca\(^{2+}\) channels. Many of these proteins exhibit with differential expression in different classes of neurons. For detailed reviews see Südhof (1995) and Calakos and Scheller (1996).

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 pre-synaptic 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.)

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 axodendritic 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 undereacting, or dense layer, beneath the cell membrane and the presence of microtubules that are bundled together into fascicles.
Figure 6. For description see opposite.
C. Photomontage of a single dendrite of a spiny stria
tel projection neuron intracellularly stained with HRP.
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. (From Wilson, C.Y. and
With permission of Wiley-Liss, a division of John Wiley,
New York.)
Fig. 6-12. Neuroglia
Schematic drawings and photographs of histologic preparations showing the different types of glial cells (drawings from Jenkins, T. N., 1970. Functional Mammalian Neuroanatomy. 2nd ed. With permission of the author and Lea and Febiger, Philadelphia. Photographs courtesy of Dr. Enrico Mugnaini.)
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

EXPERIMENTAL NEUROANATOMICAL DEGENERATION TECHNIQUES

ANTEROGRADE CHANGES  RETROGRADE CHANGES

A

WALLERIAN CHANGES
METHODS
NAUTA
FINK-HEIMER
ELECTRON MICROSCOPY

CHROMATOLYTIC CYCLE
METHODS
NISSEI STAINS
U.V. ABSORPTION
PHOSPHATASES
ELECTRON MICROSCOPY

NO EFFECTIVE REGROWTH
WITHIN THE MAMMALIAN
CENTRAL NERVOUS SYSTEM

_recovery

RECOVERY

OR

ATROPHY

METHODS
MARCHI
GLEES
NAUTA
NISSEI STAINS
LOSS OF CELL NUMBERS
FINK-HEIMER
ELECTRON MICROSCOPY

B

C

ANTEROGRADE TRANSNEURONAL DEGENERATION

AS B ABOVE

RECOVERY

OR

ATROPHY

RETROGRADE TRANSNEURONAL DEGENERATION

AS B ABOVE

RECOVERY

OR

ATROPHY
Anterograde transport from uptake sites in neuronal soma, e.g., rhodamine, isotopically labelled amino acids, etc.

Retrograde transport from terminal uptake sites, e.g., horse radish peroxidase (HRP), cobalt chloride, HRP-lectin, isotopically labelled amino acids, etc.

Retrograde transport from injured axon site. e.g. HRP

Anterograde transport from intracellular injection site. e.g. HRP, fluorochrome dyes, etc.

Anterograde and retrograde labelling of membranes by externally applied lipophilic dyes. e.g. Dil, DiO.
1. Rabbit anti-Ag IgG
2. Goat anti-rabbit IgG
3. Rabbit anti-HRP
4. HRP

1. Rabbit anti-Ag IgG
2. Goat anti-rabbit IgG
   (Biotin conjugated)
3. Avidin-Biotin Comple

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