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Prof. Dr. Ennio Pannese
Università degli Studi di Milano
Istituto di Istologia, Embriologia e Neurocitologia
Via Mangiagalli, 14
Milano 20133
Italy

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Contents

1 Introduction

The earliest mention of a cell sheath enveloping the body of the neurons in sensory ganglia is probably the following description by Valentin: „Sowohl die Kugeln der Belegungsformation[1], als die Primitivfasern, werden von eigenthümlichen, sie isolirenden Scheiden umgeben, welche alle Stufen der Dicke von einer fast gar nicht mehr wahrnehmbaren Zartheit bis zu einer ziemlich bedeutenden Stärke durchlaufen. Diese Hüllen sind aber immer zellgewebeartiger Natur" (1836, p 162). In some illustrations of the above mentioned paper the nuclei of the satellite cells adjacent to the surface of the nerve cell body, both in the trigeminal ganglion and in the ganglia of the vegetative nervous system, are clearly shown (Fig. 1A). The author, however, misinterpreted these nuclei as pigment granules (*Pigmentkörperchen*). A little later, Remak (1838) denied the existence of the perineuronal cell sheath. This prompted a ready reply from Valentin (1839), who offered a more detailed description of the perineuronal cell sheath, illustrated it with new drawings (Fig. 1B), and gave a correct interpretation of the nuclei. In fact, he wrote:

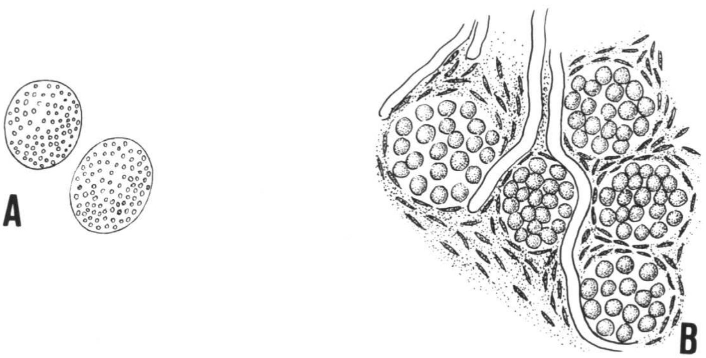


Fig. 1A–B. Nerve cell bodies of sympathetic ganglia with the nuclei of the satellite cells on the neuronal surface. Redrawn from Valentin; *A*, 1836; *B*, 1839. In his 1836 paper *A* Valentin misinterpreted these nuclei as pigment granules (*Pigmentkörperchen*), but in his 1839 paper *B* he gave a correct interpretation of the same nuclei

„Was nun die Scheiden der Ganglienkugeln betrifft, so besitzen sie auf ihrer äußersten Oberfläche eine dünne Schicht runder körniger Pflasterkugeln, in Gestalt, Farbe, Aussehen, nur nicht in Grösse den Exsudatkörperchen sehr ähnlich, welche dicht bei einander liegen, nicht aber polyedrisch, sondern rund sind und in ihrem Innern einen oder mehrere kleinere Nucleoli enthalten. Ob sie Zellenkernen oder Zellen selbst entsprechen, dürfte kaum zu entscheiden sein, da sie zwar durch ein sehr durchsichtiges, in geringer Menge vorhandenes Bindemittel zusammengehalten werden, dieses mir aber eine Abtheilung in Zellen noch nicht zeigte; doch ist es aus Gründen, die an einem anderen Or-

[1] Valentin used the term *Kugel* to indicate the nerve cell body and *Belegungsformation* to indicate the ganglion.

te erörtert werden sollen, wahrscheinlicher, dass sie bloss die Bedeutung von Nucleis haben" (1839, pp 144–145).

Small perineuronal cells (or nuclei) were then described in both sensory and autonomic ganglia by many authors under a variety of names, such as *Polarkerne* (Courvoisier 1868), *Mantelzellen* and *Amphicyten* (Lenhossék 1897), *intrakapsuläre Zellen* (Holmgren 1901, 1902), *Randzellen* and *Scheidenzellen* (Kohn 1907), *Satellitenkörperchen* (Cajal 1907) or *corpuscules ou cellules satellites* (Cajal 1909), *Trophozyten* (Nemiloff 1908), *gliocitos* (De Castro 1921, 1946), *Hüllzellen, Hüllplasmodium,* and *Nebenzellenplasmodium* (Stöhr 1928, 1939, 1941, 1943), subcapsular cells (Penfield 1932), *Scheidenplasmodium* (Riegele 1932), capsular cells (Quade 1939), *ganglionar neuroglia* (Rio Hortega and Prado 1942; Rio Hortega et al. 1942), capsule cells (Kuntz and Sulkin 1947a), and *periphere Glia* (Herzog 1954).

As will be shown in Sect. 20, the term satellite cells, the most frequently used in the current literature, seems to be preferable to the many others, and so will be used hereafter to indicate the cells which in sensory ganglia envelop the perikaryon and the initial segment of the axon. The boundary between the satellite cell envelope and the Schwann cell sheath is demarcated in the typical pseudo-unipolar neurons by the heminode where the myelin sheath begins, and in the sensory neurons encircled by a perikaryal myelin sheath by the first node of Ranvier located along the axon.

For the similarities between satellite and Schwann cells, see Sect. 20, in which other problems of terminology regarding such cells will also be considered.

2 General Characteristics of the Satellite Cell Sheath in the Adult Animal

Suggestions that satellite cells might be absent in certain sensory ganglia or around some sensory neurons were advanced in the past (e.g., Schultze 1871; Lenhossék 1907; Levi 1907; Truex 1939). However, the presence of satellite cells has been demonstrated in all the sensory ganglia which have been studied so far with the electron microscope.

In sensory ganglia of adult animals usually each nerve cell body with the initial segment of its axon is enveloped by an individual satellite cell sheath, sharply separated from the sheaths encircling the adjacent neurons by intervening connective tissue (Fig. 2). Each nerve cell body together with its satellite cell sheath constitutes, therefore, a discrete unit. However, two nerve cell bodies can occasionally be found within a common satellite cell sheath with their plasma membranes in direct contact, to a greater or lesser extent.

In general, satellite cells are particularly numerous around the initial segment of the axon, in cases where the latter forms the glomerulus (Schaffer 1910). The sheath enveloping the nerve cell body may show a variously complicated pattern of organization; it may consist of one single layer of flattened cells (Figs. 3B, 4A, B, 12A) or of several layers of cells which overlap in a complex fashion (Figs. 3A, 15, 20). Both the arrangement of the satellite cells and the thickness of the sheath may vary from area to area within the same sheath. In spinal ganglia of *Xenopus laevis,* fowl, guinea pig, and rab-

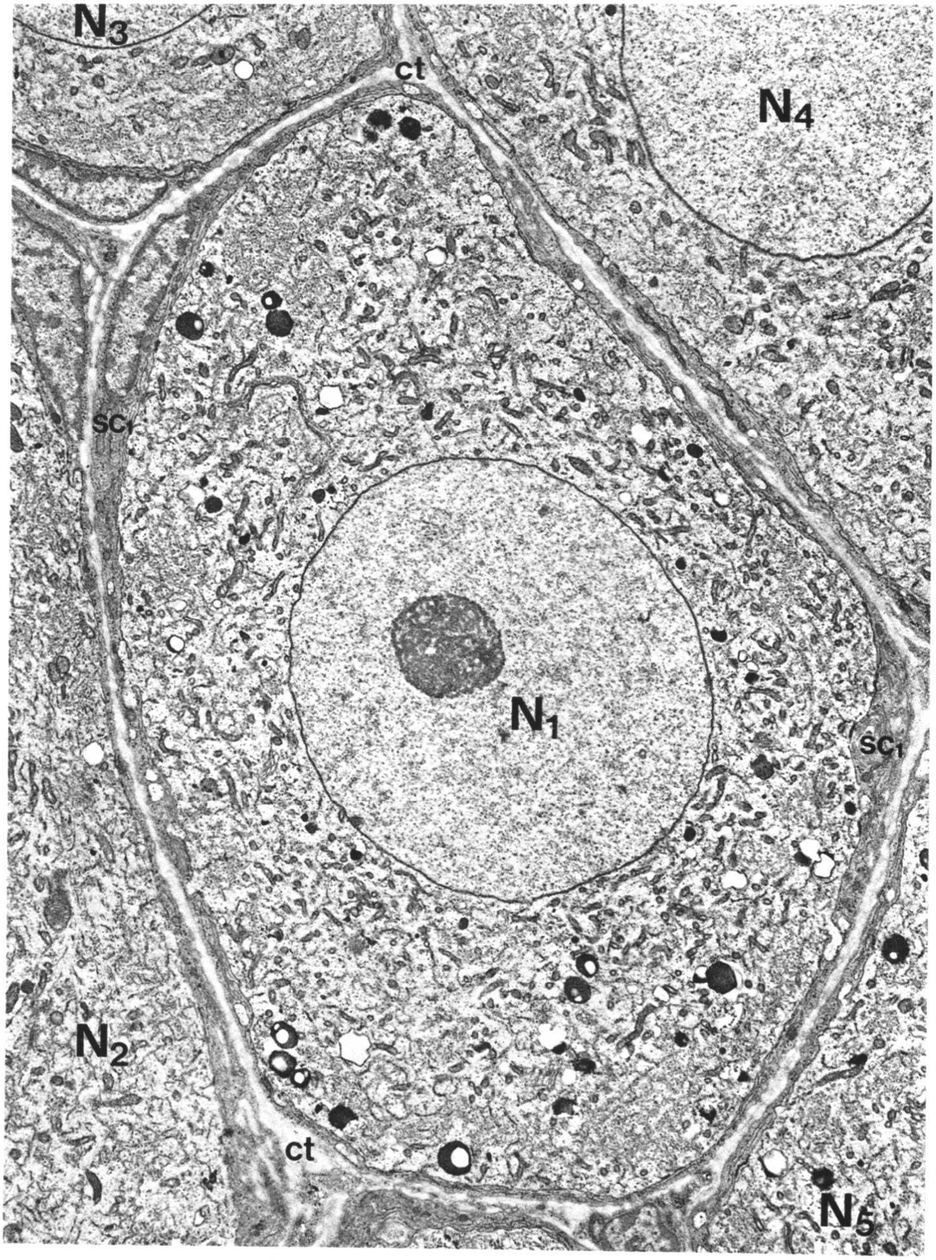


Fig. 2. Unit consisting of a nerve cell body (N_1) and its satellite cell (sc_1) sheath (spinal ganglion of a gecko). The satellite cell sheath belonging to this unit is sharply separated from those encircling the adjacent nerve cell bodies (N_2 - N_5) by the connective tissue space (*ct*). Note that the chromatin is distributed differently in the nuclei of the satellite cells and in those of the neurons. × 7100

bit (Fig. 3), the satellite cell sheath may vary in thickness from 40–50 nm to 4–6 μm; in the gecko it may vary from about 30 nm to about 3 μm and in the lizard (Figs. 4, 18), from about 30 nm to about 1.5 μm. The sheath can in some places be as thin as 18 nm in the eighth cranial nerve ganglion of the goldfish (Rosenbluth and Palay 1961). In the autonomic ganglia, also, the sheath can in some places be as thin as tens of nanometers (Yamamoto 1963, Forssmann 1964, Unsicker 1967). This shows that in some areas the thickness of the satellite cell sheath may fall below the limit of resolution of the light microscope (Figs. 4A, 5) and therefore explains why the sheath may have appeared discontinuous to some optical microscopists (e.g., Holmgren 1901, Penta 1934).

In electron microscopic preparations the satellite cell sheath appears in general as a continuous structure. Gaps (Fig. 4B) of varying width may rarely leave the surface of the neuron exposed directly to the basal lamina[2]. Small gaps in the sheath were occasionally observed in the spinal ganglia of the rat (Cervos-Navarro 1960, Andres 1961), bovine (McCracken and Dow 1973a), fowl, guinea pig, and rabbit (Pannese, unpublished observations), as well as in the spiral ganglion of the cat (Adamo and Daigneault 1973b); in these species the gaps are generally no wider than 0.5 μm. Less exceptional and larger than in the animals quoted above are these gaps in the spinal ganglia of the gecko and lizard, in which they can sometimes reach a linear length of 5 μm (Pannese, unpublished observations).

Of course, the possibility cannot be ruled out that the smallest gaps observed in the sheath are due to artifactual retraction of the thin cytoplasmic expansions of the satellite cells. It is difficult, however, to admit an artifactual origin of the gaps when they are extensive, and the adjacent satellite cells do not show retractions, increased cytoplasmic density, or other signs of alteration. So it seems reasonable to conclude that gaps in the satellite cell sheath can preexist in vivo, although exceptionally.

Small satellite cell-free areas of the perikaryal surface of the neurons have also been described in the autonomic ganglia (Elfvin 1963, Pick 1963, Dixon 1966, Colborn and Adamo 1969, Olivieri Sangiacomo 1969, Watanabe and Burnstock 1978). Such areas are more common in these ganglia than in sensory ganglia.

It was long debated whether the sheath is built of discrete cells or has a syncytial structure. While Lenhossék (1907) merely noted that the limits between satellite cells are not quite distinct, other authors regarded the perineuronal sheath as mainly syncytial in structure (Palumbi 1944) or partly (Cajal 1909; Penta 1934; Kubota and Hioki 1943; Ortiz-Picón 1949, 1955). According to Rio Hortega et al. (1942), it is built of discrete cells, a view supported by electron microscopic observations. In fact, Wyburn (1958) noticed in spinal ganglia of the adult rabbit that each cell of the sheath

[2] To avoid confusion, this layer will be indicated with the term basal lamina, proposed by Fawcett (1966), instead of the term basement membrane. The latter was originally employed by light microscopists to indicate a much thicker structure, including collagen fibrils.

Fig. 3A–B. Different thicknesses and patterns of organization of the satellite cell sheath (spinal ganglion of a rabbit). In *A* the sheath consists of several layers of overlapped cells and appears thick, whereas in *B* it consists of one or two layers of cells and appear thinner. *Arrows* point to coated pinocytotic vesicles; *double arrows* point to close membrane appositions between satellite cells; the *crossed arrow* points to a subsurface cisterna; * indicates cross sections of projections which arise from the neuronal perikaryon at other levels; and ▫ indicates primitive hemidesmosomes. *bl*, basal lamina; *ct*, connective tissue space; *N*, neuronal perikaryon. *A* and *B*, × 40 000

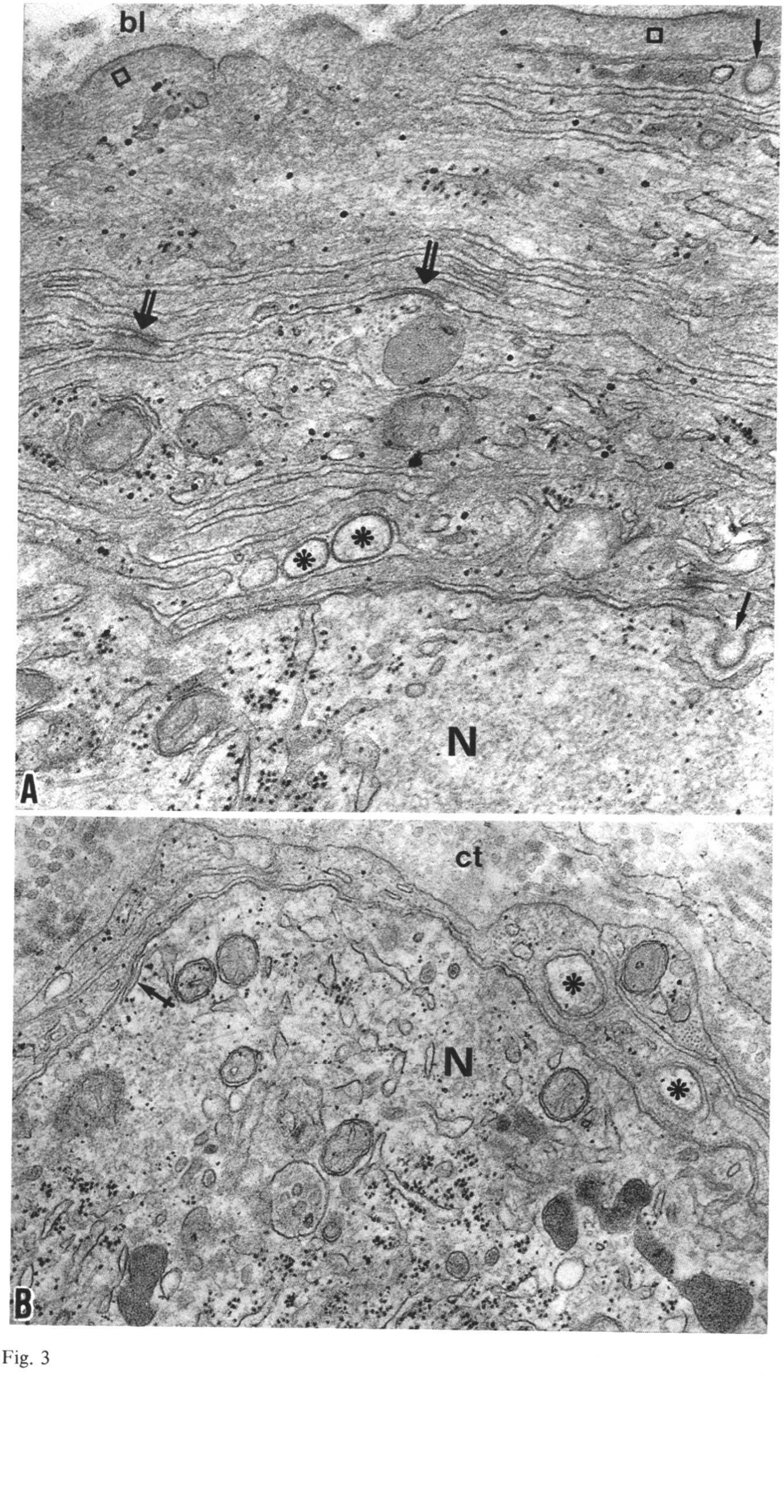


Fig. 3

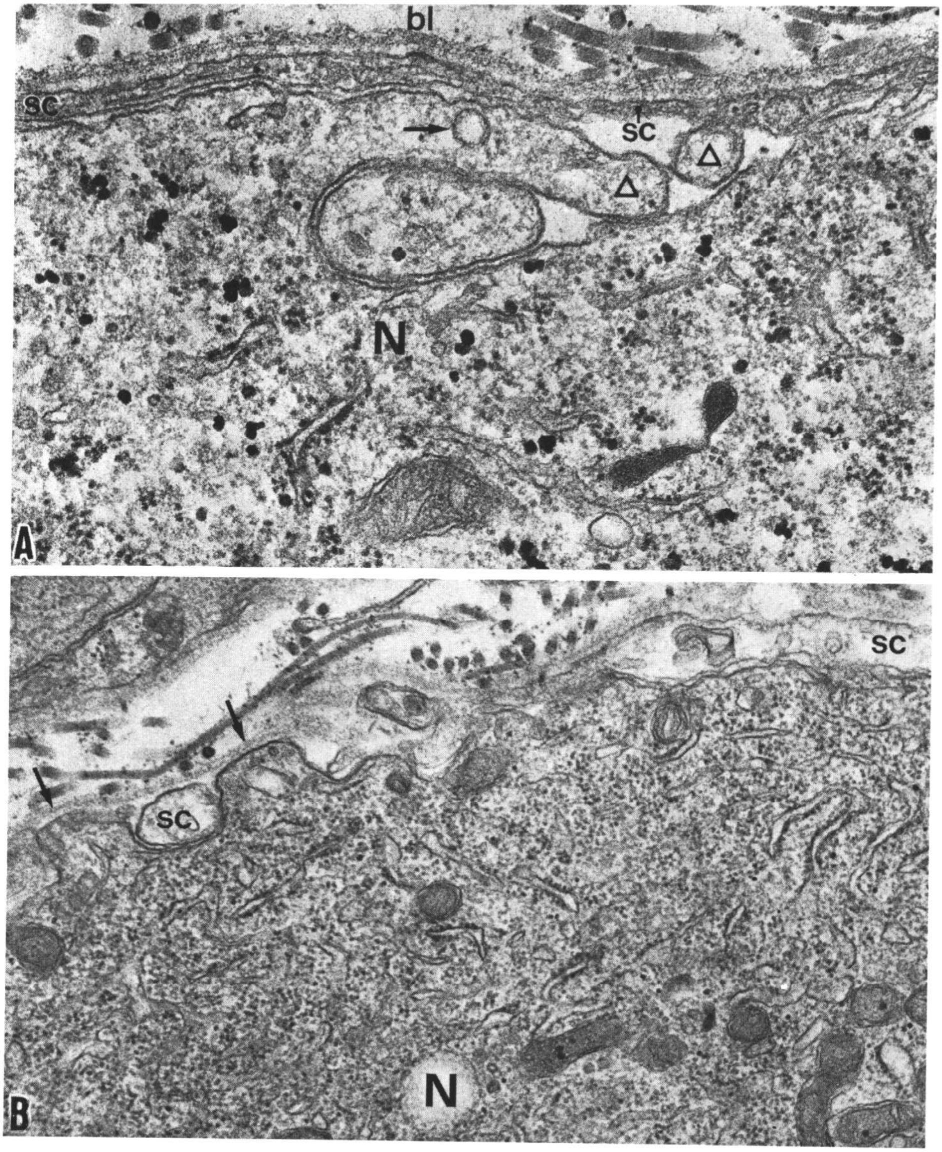


Fig. 4. *A* Satellite cell sheath (*sc*) which in this region consists of one single flattened cell and falls below the limit of resolution of the light microscope (spinal ganglion of a lizard). The *arrow* points to a vesicle free in the satellite cell cytoplasm; △ indicates neuronal projections which extend between the neuronal perikaryon (*N*) and the satellite cell sheath (*sc*). *bl*, basal lamina. *B* In the satellite cell sheath (*sc*) small gaps (*arrows*) leave the surface of the neuron exposed directly to the basal lamina (spinal ganglion of a lizard) *N*, neuronal perikaryon. *A*, × 44 500; *B*, × 32 500

Fig. 5. Nerve cell bodies with their satellite cells (spinal ganglion of a rabbit; 1μm plastic section stained with toluidine blue). The nuclei of the satellite cells are evident, while their cytoplasm can be identified only in certain places; consequently some portions of the neuronal surface seem to be without a satellite cell covering. *Arrows* point to axonal glomeruli; *v*, blood vessels. × 610

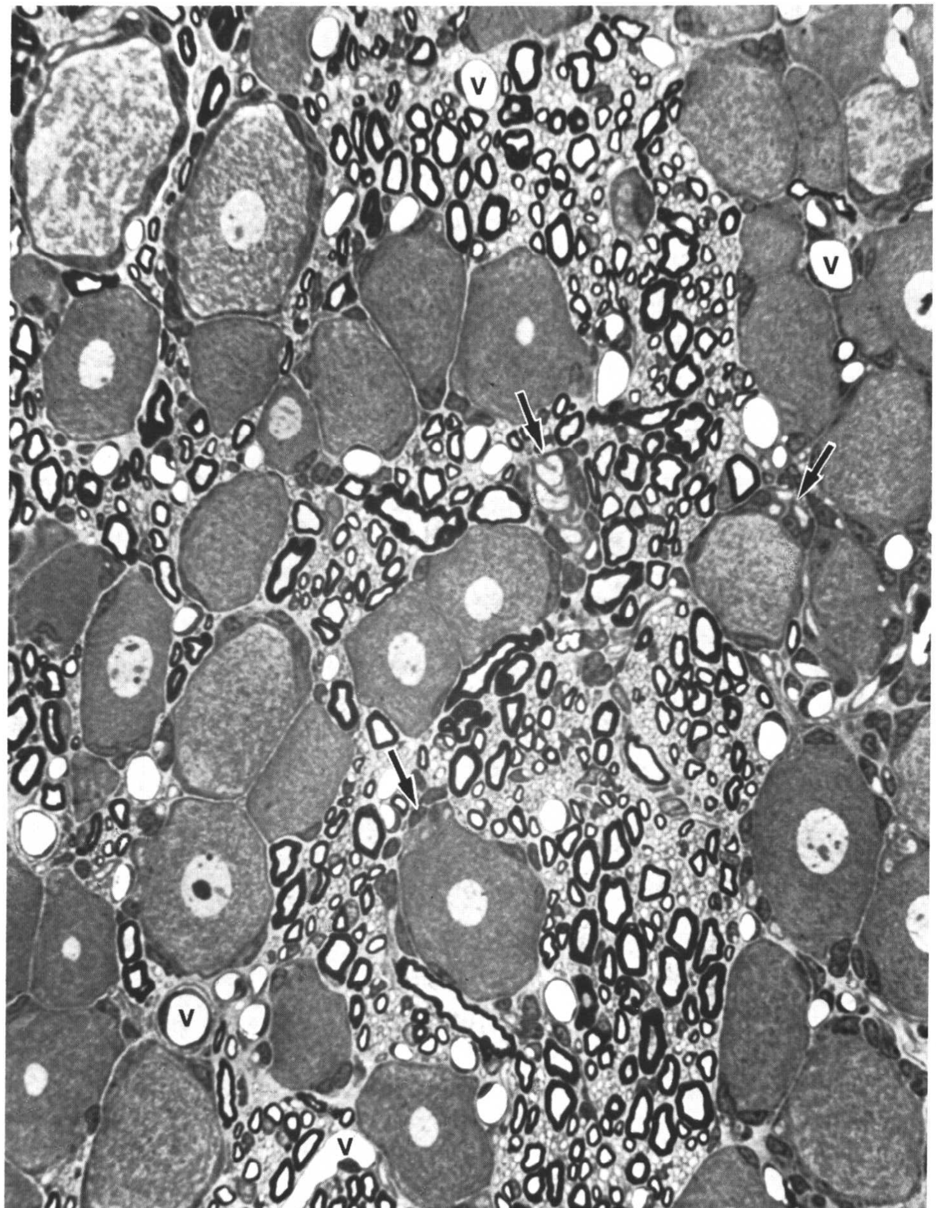


Fig. 5

is bounded by its own plasma membrane. This finding was confirmed in the spinal ganglia of the rabbit (Pannese 1960) and of several other species (rat: Cervós-Navarro 1960, Pannese 1960, Andres 1961; guinea pig and cat: Pannese 1960; toad: Rosenbluth 1963; lizard: Pannese 1964), in the eighth cranial nerve ganglia (goldfish: Rosenbluth and Palay 1961; rat: Rosenbluth 1962b), and in the trigeminal ganglion (guinea pig and rabbit: Moses et al. 1965; monkey: Moses et al. 1965, Pineda et al. 1967; man: Beaver et al. 1965; cat: Pineda et al. 1967). In autonomic ganglia, also, the perineuronal sheath is built of discrete elements (Cravioto and Merker 1963, Forssmann 1964).

3 Shape of Satellite Cells

The various opinions which have been held on the shape of the satellite cells can be summarized as follows:

1. Satellite cells are laminar elements (Fig. 6) lacking processes (Hannover 1844, Fraentzel 1867, Key and Retzius 1873, Penta 1934, Palumbi 1944), with a regular (Hannover 1844, Penta 1934) or irregular (Fraentzel 1867) polygonal shape.

2. Satellite cells bear variously long and branching processes (sensory ganglia: Holmgren 1901, 1902; Ortiz-Picón 1932, 1949, 1955; Bertrand and Guillain 1933; Della Pietra 1937; Rio Hortega et al. 1942; Scharenberg 1952; Stramignoni 1953; autonomic ganglia: Rio Hortega and Prado 1942; Herzog 1954). According to Rio Hortega et al. (1942), to whom we are indebted for a detailed description, the satellite cells associated with the neuronal perikaryon (Fig. 7B) bear branching processes which intertwine with those of the adjacent cells, thus building an intricate network. The satellite cells associated with the axon (Fig. 7A) appear more variously shaped; they can enwrap the axon with one spiral-shaped process only (*espirocitos*), a pair of pincer-like processes, some branching processes, or finally with the whole flattened cytoplasm, if lacking processes.

3. Star-like and spindle-shaped satellite cells bearing processes lie close to the neuron, while sheet-like cells lacking processes form an outer sheath (Cajal and Oloriz

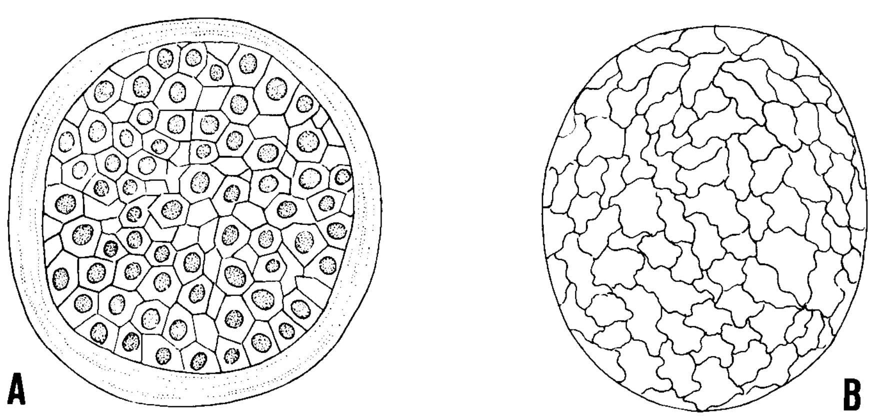


Fig. 6A–B. The satellite cells are shown as laminar elements with an irregular polygonal shape. Redrawn and slightly modified from Fraentzel (1867). In *A* the satellite cells are shown with their nuclei; in *B* only the outline of the same cells is evident

1897, Cajal 1909). The sheet-like cells, called capsule cells, were regarded by Cajal (1909) as endothelial elements.

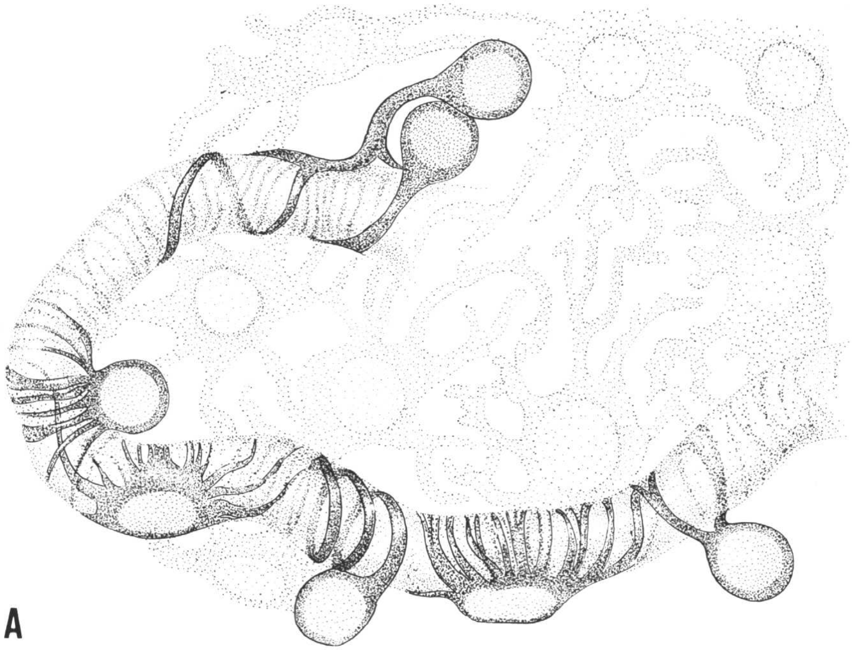
If the techniques employed by the above-mentioned authors are taken into consideration, the impression gained is that the variety of the results might well depend on the different methods applied to the same material. Experiments carried out on spinal ganglia by using different fixatives (Pannese 1960) seem to support this assumption.

In the ganglia fixed in formaldehyde, bromurated formaldehyde, or Bouin's fluid (Fig. 8A, C, E), a cleft is nearly always apparent under the light microscope between the nerve cell and the perineuronal connective tissue. In this cleft, already noticed by Lenhossék (1886) and interpreted as a lymphatic space, lie variously shaped, scattered satellite cells. The satellite cells associated with the perikaryon can appear as polygonal cells with short processes, or as star- and spindle-shaped cells bearing branching processes (Fig. 8A, C); the length and thickness of the processes may vary considerably, much as the appearance of the surface, which can be smooth or granular. The satellite cells associated with the axon (Fig. 8E) may bear one or two long spiral processes coiled around the former, or numerous, thin processes enwrapping it.

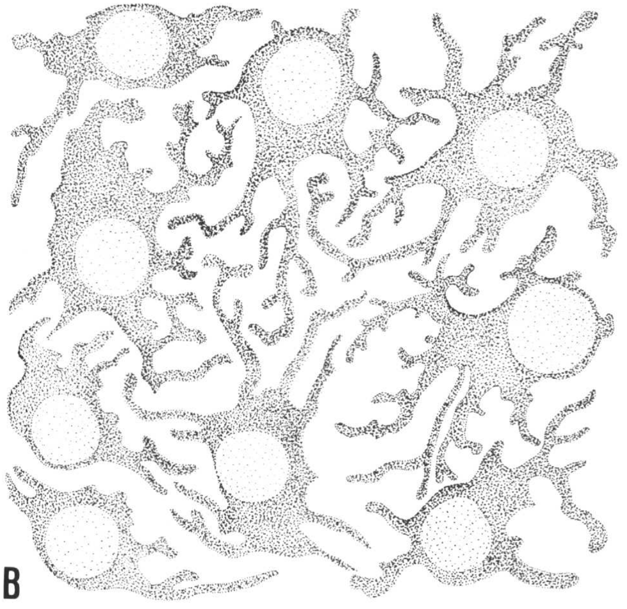
In osmium-fixed preparations (Fig. 8B, D, F) the ganglionic structure is definitely better preserved, and satellite cells lie in close contact with the neuron and the connective tissue, so that no cleft can be seen around the neuron. The shape of the satellite cells is rather uniform. They appear laminar (Fig. 8B, D), with an irregular outline as described by Fraentzel (Fig. 6) in 1867 („die Kapsel der spinalen Ganglienzellen ist von einem unregelmässig polygonalen, grosskernigen, einschichtigen Plattenepithel ausgekleidet." p 554). Some of the satellite cells associated with the axon look like long and narrow sheets which wind spirally around it, thus forming a short, continuous sleeve (Fig. 8F).

The images of satellite cells bearing long, branching processes seem, therefore, to be the result of artifacts due to distortion of the cell shape during fixation. According to Pomerat (1952), the addition of formalin to the culture medium determines a shrinkage in the thin laminar cytoplasm of neuroglial cells and the formation of thread-like processes. The distortion of the cell shape is particularly marked in the thin, flattened elements, such as most cells cultured in vitro and satellite cells both in vitro and in vivo. Stöhr (1941) noted that the perineuronal sheath of the autonomic ganglia is highly susceptible to the action of fixatives. The fixative probably distorts the shape of the satellite cell, by directly shrinking not only its delicate cytoplasm, but also the adjacent neuron. The portions of the satellite cell cytoplasm which stick more firmly to the neuronal surface would be stretched as a consequence of the neuron shrinkage and so take the appearance of cytoplasmic processes. The sites of firmer attachment of satellite cells to neurons perhaps correspond to the adhering junctions which have been recently demonstrated under the electron microscope (see Sect. 7). In this connection it can be noted that in 1873, Key and Retzius suggested that satellite cell processes could be artifactual formations due to shrinkage of the ganglionic neuron.

The cleft which is sometimes apparent in microscopic preparations between the nerve cell and the perineuronal connective tissue is also the result of an artifactual shrinkage of the neuronal body, as Koneff (1887), Flemming (1895), Schaffer (1896), Lenhossék (1897), Buehler (1897), Nemiloff (1908), and other authors later hypothesized.



A



B

Fig. 7A–B. According to the results of Rio Hortega et al. (1942) both the satellite cells associated with the axon *A* and those associated with the neuronal perikaryon *B* are shown as elements bearing processes

Fig. 8A–F. Shape of satellite cells in spinal ganglia fixed in Bouin's fluid *A* and *C*, formaldehyde *E*, and osmium *B, D*, and *F*. Phase contrast. *A, B*, and *D*, horse; *C*, ox; *E*, rabbit; *F*, guinea pig. Note that in the ganglia fixed in Bouin's fluid *A* and *C* a cleft is apparent around the nerve cell body (*N*) where satellite cells (*sc*) bearing branching processes can be seen. In the osmium-fixed ganglia *B* and *D*, no cleft can be seen around the nerve cell body (*N*), and the satellite cells (*sc*) lie in close contact with the latter and appear as laminar elements. *sp*, spiral processes of satellite cells coiled around axons. *A, B, C*, and *D*, × 1050; *E* and *F*, × 1500

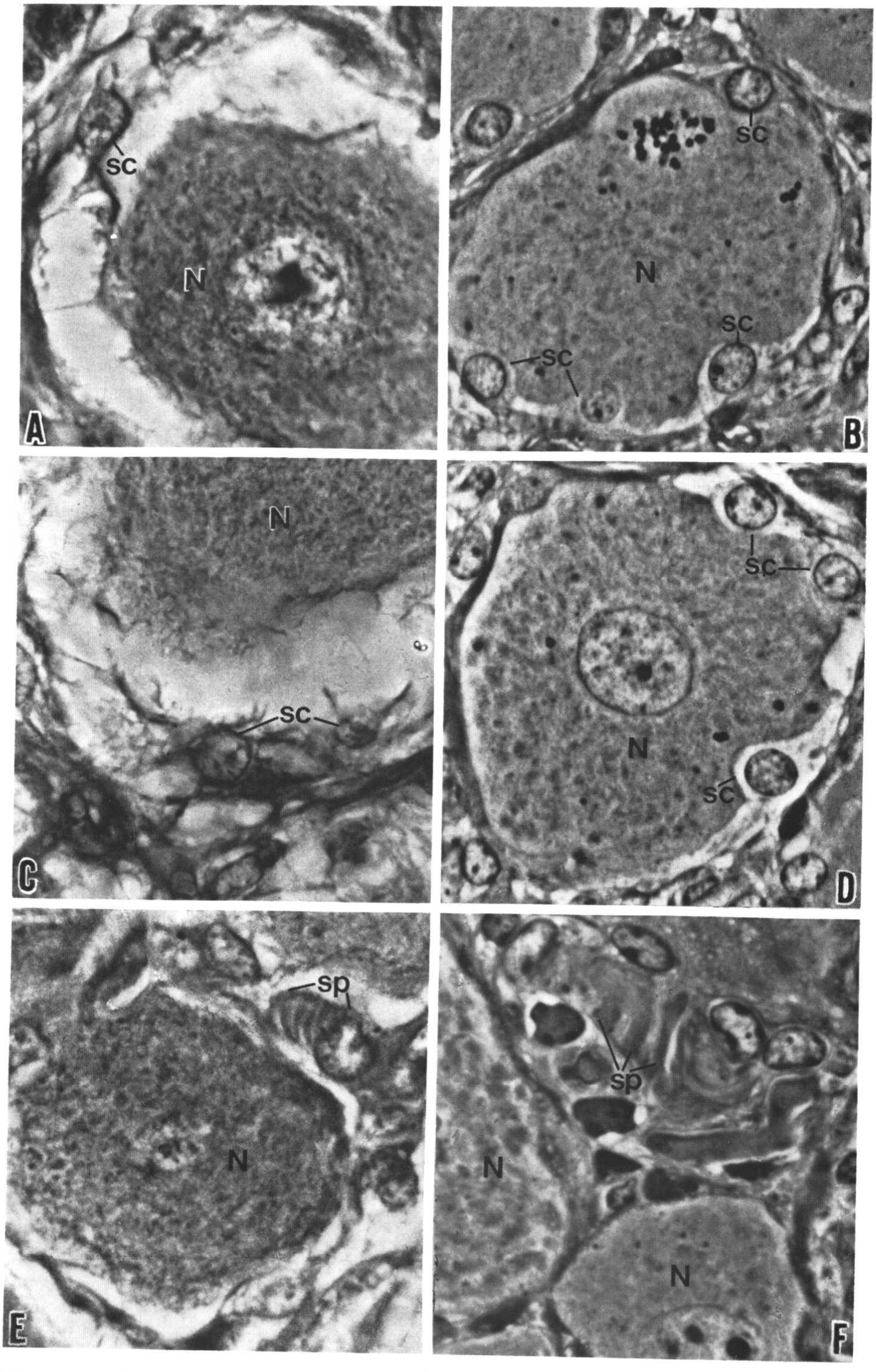


Fig. 8