VIII. *A Contribution to our Knowledge of the Enteric Plexuses.*

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Contents.

Introduction.

The constitution of the enteric plexuses (the plexus myentericus or plexus of Auerbach and the plexus submucosus or plexus of Meissner) and their rôle in the initiation and regulation of the gut-movements are problems which have been discussed by numerous investigators, and the literature relating to them is voluminous. Nevertheless, it can hardly be said that there is even to-day any general consensus of opinion in regard to them.

The work detailed in the present paper arose out of an endeavour to provide demonstration preparations of the gut-plexuses for teaching purposes. Eventually, with the

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generous and unstinted help of the late Prof. N. KULCHITSKY, a method of partially isolating the plexuses and of staining them with a modified Bielchowsky silver technique was evolved, which yielded preparations of such excellence that I was induced to make the attempt to work out their histological constitution. I propose to give first of all a very brief summary of the purely histological results obtained by previous workers in this field, and later, when setting forth my own observations, to deal more in detail with the related literature.

I desire to express my grateful thanks to Prof. J. P. HILL for his advice and criticism, to Prof. G. ELLIOT SMITH for reading the manuscript, to Dr. H. H. WOOLLARD for his help with the methylene blue injections, and to Mr. A. K. MAXWELL for the care and skill he has taken in retouching my figures and for the originals of figs. 1–4 and text-fig. 1.

PREVIOUS WORK.

DOGIEL (**25**), using the intra-vitam methylene blue technique, studied the gut-plexuses in great detail and came to the conclusion that the intestinal ganglia contain cells of three distinct morphological types. It is not too much to say that the accuracy and detail of his figures have scarcely been equalled by the work of later investigators. The cells designated Type I by DOGIEL are described by him as being multipolar in form and provided with short branching dendrites which anastomose with processes of similar cells in the ganglia to form a network, whilst their axones terminate in the musculature. He accordingly regarded these cells as motor in function. Cells of Type II are described as sensory and as giving off long dendrites which terminate in the mucosa. The precise mode of termination is not described by DOGIEL, whilst the axone itself is said to be indistinguishable in appearance from the dendrites. Type III is similar in form to Type I, but the dendrites are longer and do not anastomose. As to the significance of this type, DOGIEL makes no definite suggestion, and in his general discussion practically ignores it. He believes that on these enteric neurones two kinds of extrinsic fibres terminate, viz., (*a*) fibres from the sympathetic inflow ; (*b*) fibres from the vagus. The sympathetic fibres take part in the formation of an intra-ganglionic plexus and end in relation to the neurones in the form of diffuse varicose endings. Such terminations have been described by KUNTZ (**34**), CARPENTER (**16**), CAJAL (**11**), and SAKUSSEFF (**58**), in the gut-plexuses of various Vertebrates and in ordinary sympathetic ganglia by VON LENHOSSÉK (**45**) and HUBER (**29**). The vagal fibres, after running in the mesentery as finely medullated fibres, lose their medullary sheaths on entering the gut-wall. These fibres are described as breaking up into a number of thread-like fibrils which enclose the cell-bodies of the enteric neurones in the form of pericellular networks. DOGIEL suggests that these pericellular arborizations, which are similar to the intra-capsular pericellular endings of the pre-ganglionic fibres in the sympathetic ganglia, are to be found on cells of Type I, but leaves the question undecided, since in his preparations, the pericellular network was often coloured intensely, whilst the cell-body remained unstained. Similar endings have also been described by HUBER (**29**), DE WITT (**22**), and KUNTZ (**36**).

CAJAL (**10**) at first described the cells of the enteric plexuses as being all of one type, but later (**11**) described, in his ' Histologie du Système Nerveux,' cells of two types, similar to those of DOGIEL's Types I and II, although he does not accept DOGIEL's interpretation of their significance. He believes that the processes of the cells of DOGIEL's Type II are all similar (axonic), and that accordingly the cells cannot subserve a sensory function. He describes both types as occurring in the myenteric plexus, but in the sub-mucous plexus, he maintains that the cells are all of DOGIEL's type II with long processes. His view has received corroboration in the work of L. R. MÜLLER (**52**), who states that the cells forming the sub-mucous plexus possess dendrites similar in form to the axone. In the myenteric plexus, MÜLLER describes two types of cells distinct from those forming the sub-mucous plexus. Both these types of cells possess short dendrites which end either on the neurones in the ganglion of origin or in club-like expansions on the muscle fibres. From these facts, MÜLLER suggests that the intrinsic fibres forming the fibre-tracts in the myenteric plexus are axonic, whereas in the sub-mucous plexus they are chiefly dendritic.

ERIK MÜLLER (**51**) also supported the view that the neurones of the myenteric and sub-mucous plexuses conform to two morphological types and described cells similar to two of the types of DOGIEL. He believed that cells of Type I are vagal in origin, those of Type II (and in this category he included the " interstitial cells of CAJAL "), sympathetic. He did not, however, accept DOGIEL's interpretation of the functional relationships of the neurones of these types, and believed that there exists in the gut-wall a primitive type of nerve-net.

But the view that the enteric ganglia are made up of cells of two types is not uniformly held. KÖLLIKER (**32**), in 1894, expressed the view that the cells were all of one type, and he described the mechanism of the ganglia as purely motor, the sensory impressions for the reflex actions of the intestine reaching the motor mechanism through the cerebro-spinal inflow. KÖLLIKER's point of view has been supported in recent years by the work of CARPENTER and CONEL (**18**) on the superior cervical ganglion of the cat. In this ganglion, these workers found cells, not only answering to DOGIEL's two types, but representing all gradations between them, and they were convinced that such cells did not represent distinct types ; similar intergradations were described by KUNTZ (**36**) in the intestinal ganglia. Still more recently, JOHNSON (**31**) has again expressed the view that the nerve cells forming the enteric ganglia are all of one type. He considers that the visceral vagal fibres, which according to LANGLEY (**40**) are pre-ganglionic, end on the enteric neurones. These cells thus form the second neurone in the vagal path, whilst the fibres of the visceral splanchnic nerves, whose second cell-station is in the cœliac or other visceral ganglia, are necessarily post-ganglionic and end directly in the musculature or glandular tissue of the intestinal wall without coming in contact with the enteric neurones.

Another view of the structure of the enteric plexuses has recently been put forward by LAWRENTJEW (**43**). This observer concludes that the enteric plexuses are in reality

formed of anastomosing protoplasmic strands, a syncytium, in which run bundles of what are ordinarily called neurofibrillæ. The ganglia of the plexuses he designates as "Kreuzungspunkten," and apparently he would deny the existence of discrete ganglion cells in them. He holds, further, that the so-called "interstitial cells of CAJAL" constitute the direct continuations of this syncytial system, and that through them and their processes the neurofibrillæ run to their motor endings in the smooth muscle cells.

From this brief survey of the literature, it is evident that further investigations are necessary to clear up the problem of the histological constitution of the gut-plexuses.

TECHNIQUE.

For this investigation I used in the first instance a silver method suggested to me by the late Prof. N. KULCHITSKY, which is based on DUSTIN'S rapid Bielchowsky method. The method, the details of which are given below, yielded results that were particularly useful for the study of the general arrangement of the plexuses and for the structure of the cells forming their ganglia. The more intimate relations, however, between the fibres and cells of the plexuses could not be made out in these preparations, and for this part of the investigation I had to rely exclusively on material stained with methylene blue. My material came chiefly from rabbit and guinea-pig, since for the silver method it was necessary to use an intestine the thin wall of which was easily separable into its different layers. For this purpose these animals proved ideal; for the methylene blue method, dogs and cats were used in addition to rabbits and guinea-pigs.

The details of the silver method are as follows:—

(1) The intestine, after being washed out with an isotonic saline solution, is cut into pieces about 6 to 12 inches long and distended with a solution of—

60 per cent. alcohol	90 c.c.
40 per cent. neutral formalin	10 c.c.

The pieces are then immersed in the fixing fluid and left for 1 to 20 days. The best results are usually obtained after three days' fixation, but I have had quite good results with material left for several months in the fixative.

(2) The material is next washed in running tap-water for 6 to 12 hours and then left for 24 to 36 hours in several changes of glass-distilled water.

(3) The intestine is cut up into small pieces 1 to 2 cm. in length and the mucous membrane is removed by scraping with a sharp scalpel. It is then quite easy with fine forceps to separate off the sub-mucous layer containing the sub-mucous plexus from the conjoined muscle layers. The latter are then gently torn apart, the best preparations of the myenteric plexus being obtained when the plexus happens to be left on the longitudinal muscle coat.

(4) These strips of intestinal wall are next transferred from distilled water to 20 per cent. $AgNO_3$ at 37° C., where they are left for 5 to 10 minutes in the dark.

(5) After the silver bath they are rinsed rapidly in distilled water ($\frac{1}{2}$ to 1 minute) and placed in a solution of 1·5 grams of hydro-quinone in 100 c.c. of 3 per cent. neutral formalin until yellowish brown.

(6) They are again rinsed in glass-distilled water and transferred to a solution of 3 per cent. ammonium sulphocyanide, to which a few drops of 1 per cent. gold chloride are added just before using. The colour of the pieces changes from brown to bluish-black.

If the strips are overstained, as is usually the case and is to be preferred, the best differentiating agent is a mixture of—

20 per cent. hyposulphite of soda	.. ..	10 c.c.
10 per cent. potassium ferricyanide	.. ..	7 drops.

This solution requires to be changed frequently, as it rapidly becomes inactive.

After differentiation, the strips must be washed in distilled water for 30 to 60 minutes before grading up through the alcohols. Dehydrate in absolute alcohol, clear in oil of cloves or xylol, and mount in Canada balsam.

General Structure of the Enteric Plexuses.

The general appearance of the enteric plexuses after silver impregnation is shown in figs. 1 and 2 (Plate 26). In their gross structure, the myenteric and sub-mucous plexuses agree in the fact that they consist of groups of nerve cells connected together by fibre-bundles, the fibres of which are both intrinsic and extrinsic in origin. The extrinsic (vagal) fibres which run in the fibre bundles end in relation to the nerve cells, and the processes of these latter, either as axones, convey the impulses to the muscle and glands, or as dendrites, terminate as receptive endings in relation to nerve cells in other ganglia of the plexus.

The two plexuses differ, however, in their detailed characters and more particularly in the form of their ganglia and in the variety and size of their constituent neurones. In Meissner's plexus, the ganglia are thin and flattened (fig. 4, Plate 26) and the cells are closely grouped together in a single layer; in Auerbach's plexus, the ganglia (fig. 3, Plate 26) are thicker and more massive and the cells lie superimposed on each other.

Types of Cells present in the Enteric Ganglia.

A comparison of figs. 3 and 4 shows that, whereas the cells in the ganglia of Auerbach's plexus are of two varieties, corresponding in form to the cells designated by Dogiel (**24**) as Types I and II, in those of Meissner's plexus, the cells are all similar and correspond to Type II (fig. 4). Cajal (**10**) and Müller, L. R. (**52**), have also regarded the ganglia of this plexus as being formed of only one type of cell, whereas Dogiel considered that both types of cells were present as in the ganglia of Auerbach's plexus.

In certain mammals, the cells of Meissner's plexus are much smaller than those of the

myenteric plexus; measurements I have made in preparations of the small intestine of the rabbit and dog, show that the cells of the myenteric plexus are two or three times as large as those of MEISSNER'S plexus. In the small intestine of the guinea-pig, the cells of the two plexuses are more or less comparable in size. In the vermiform appendix and cæcum of the rabbit, however, the cells of MEISSNER'S plexus are very large, equalling in size those of the myenteric plexus of the small intestine. Moreover, the ganglia are frequently formed of only three to five cells, whilst isolated cells occur in the fibre-tracts. The cells of AUERBACH'S plexus in the same region, on the other hand, are small and in size are more or less comparable with those of MEISSNER'S plexus in the small intestine.

According to DOGIEL (**25**), definite nucleated pericellular capsules are present round the individual ganglion cells of the enteric plexuses, but I have never been able to observe such capsules in silver or methylene blue preparations, or in sections stained with iron-hæmatoxylin, and in this respect I am in agreement with L. R. MÜLLER (**52**) and KUNTZ (**34**), who also failed to find them.

(*a*) *Cells with Short Dendrites.—Type I* (figs. 3, 5, 6, 7, and 8, Plates 26 and 27).

The cells which we have first to consider are those of DOGIEL'S Type I. These cells are seen in fig. 3, and under greater magnification in figs. 5, 6 and 7. In silver preparations, they are easily recognizable, not only on account of their staining properties—for they stain more darkly than the other cells—but also because of the superficial position they frequently occupy in the ganglia.

The cells have flattened more or less elongated bodies, varying in greatest diameter from 0·02 to 0·06 mm. The cell-body is prolonged out into numerous short dendrites, which form brush-like arborizations on the cells situated deeper and more centrally in the ganglionic masses (figs. 5 and 6). The dendrites show considerable variation in form; frequently they are short and thick and, without branching, end directly in a brush-like arborization (fig. 5, *ad*), or they may originate as thick processes as in figs. 6 and 7, which divide into several fine thread-like branches, each of which terminates in a fine brush-like arborization.

In other rarer cases, they appear as somewhat longer and more delicate processes, generally varicose in character, which run a considerable distance through the ganglion, often giving off slender collaterals before they terminate in a knob-like swelling (fig. 8). These processes ramify either around the more centrally situated cells or they pass into the spaces between the latter, and there they intermingle with the fibres of the intra-ganglionic plexus. Cells with this particular variety of process are only distinguishable in methylene blue preparations, since by this method they stain of a violet colour in contrast with the other and more numerous cells of this type, which stain blue. Their cytoplasm is more granular than that of these latter, and they are larger, resembling in this respect cells of Type II rather than those of Type I.

It seems probable that these violet-staining cells are identical with DOGIEL'S Type III, but since they show the characteristic features of Type I, viz., numerous dendrites of

no great length which ramify in the ganglion of origin, and since they are not distinguishable from the more usual Type I cell in silver preparations, we have included them in this group.

According to DOGIEL (**25**), many of the dendrites of these cells do not end in simple brush-like terminations on adjacent cells, but interlace with the corresponding dendrites of other cells to form a dense network. In his own words: "Auf allen Präparaten, wo die Endverästelungen der Dendriten sich intensiv gefärbt haben, treten sie mit solcher Deutlichkeit hervor, dass eine Feststellung ihrer gegenseitigen Beziehungen zu einander möglich wird. Unter solchen Bedingungen bemerkt man gewöhnlich, wie die kurzen und dünnen Endfäden, mit welchen alle Dendriten jeder Zelle besetzt sind, sich direct mit ebensolchen Verzweigungen von Dendriten anderer Zellen von demselben Typus verbinden, und auf diese Weise gemeinschaftlich ein ausserordentlich dichtes Netzwerk bilden (Taf. V und VI, figg. 2, 5 und 12)."

LA VILLA (**37**), however, also using a methylene blue technique, was unable to find any trace of such networks, and expressed the opinion that they do not occur. DOGIEL, in reply to this criticism, emphasized his previous statement: "Auf Grund dieses Bildes und des Studiums ihres gegenseitigen Verhaltens, meine früher ausgesprochene Ansicht, zwischen ihnen bestehe eine directe Verbindung, nicht nur aufrecht erhalte, sondern noch bestimmter in dieser Ansicht bestärkt werde." More recent observers have also failed to confirm DOGIEL'S statements, and I am in agreement with KUNTZ (**36**), JOHNSON (**31**) and others that such dendritic networks do not exist. The cells frequently lie closely packed together, and thus their processes intermingle, but, in the preparations I have studied, this only occurs to a very slight extent.

The axone arises either directly from the cell-body as a thick process, which generally gives rise to one or more short thorn-like collaterals before passing into an inter-ganglionic fibre-bundle (figs. 5 and 6), or, as is perhaps more usual, it takes origin from a flattened prolongation of the cell-body from which also numbers of dendrites arise (figs. 7 and 8). In the fibre-bundle, the axones appear as fine non-medullated fibres of uniform thickness, rarely varicose. They can be traced for a considerable distance through the neighbouring ganglia and fibre-tracts, but I have failed to observe their actual terminations.

They generally disappear among the fibres of the intra-ganglionic plexus and probably end in relation to a ganglionic cell. DOGIEL, however, describes these axones as running out to terminate in the muscle coats, and accordingly suggests that these cells represent the motor cells of the myenteric ganglia. I have never been able to trace axones of these cells into the musculature, nor, indeed, outside the meshes of the myenteric plexus, so that I find it difficult to accept DOGIEL'S suggestion. Moreover, it has to be remembered that cells of this type do not occur in the sub-mucous plexus, and that the endings of the extrinsic fibres (*i.e.*, those conveying impulses to the gut), as I shall show later, are only found on cells of Type II.

These facts demonstrate that the function of the cells in question is not motor, and

I suggest from the disposition of their processes that they are associative. On the one hand, they are capable of receiving impulses by way of their dendrites, which form receptive terminations on cells of Type II; and, on the other, they can transmit impulses through their axones to neurones of Type II situated in other ganglia.

(*b*) *Cells with Long Dendrites.—Type II.*

Cells of DOGIEL'S Type II are most easily studied in methylene blue preparations, especially those in which only a few of the cells in the ganglia have taken up the stain.

The cells of Type II are more varied in form and are larger than those of Type I. They vary in their long diameter from 0·05 to 0·07 mm., and in transverse diameter from 0·02 to 0·078 mm. The cell cytoplasm stains uniformly with methylene blue, but frequently shows in silver preparations a darkly staining mass situated on one side of the nucleus. This mass occupies the same position as the centrosphere described by N. VAN DER STRICHT (**65**), and is probably identical with that (figs. 5 and 6, Plate 27).

The cells are of three different varieties, multipolar, bipolar and unipolar cells.

(i) *Multipolar Cells* (figs. 9, 10 and 11, Plates 27 and 28).

These cells have long branching processes varying in number from three to six (figs. 9, 10 and 11). Cells of this type with fifteen or more processes have been described by DOGIEL (**25**) and L. R. MÜLLER (**52**) in rabbit, cat and dog, but I have not seen such cells in my preparations. The processes arise as uniform, non-varicose fibres, all usually of about the same thickness. They pass out of the ganglion of origin into one of the related fibre-bundles, where they can frequently be followed for a very long distance, and it is only by their terminations that they can be identified as axones or dendrites. In the fibre-tracts, the fibres become finely varicose, though there is much variation in this respect in different fibres and in different parts of the same fibre (fig. 29, Plate 33).

The fibres may branch dichotomously either before leaving the ganglion of origin or at the points of intersection of the interganglionic fibre-tracts, when each branch takes a separate course in one of the latter. In other cases (*e.g.*, fig. 10) they may pass to their destination without previous branching. The determination of these processes as axones or dendrites is only possible when they can be followed to their endings. The dendrites run to other ganglia more or less adjacent to their seat of origin. There they form a delicate varicose plexus, the fibres of which terminate in minute knob-like swellings either on the surfaces of the bodies of other nerve cells or in an apparently diffuse fashion in the intercellular spaces (fig. 21, Plate 31), though it may be that this latter appearance is simply due to the fact that the related cell-bodies are unstained. The axone, on the other hand, usually enters a fibre-bundle and may run in that for a long distance, even passing through other ganglia. In its course it may divide, and eventually

it passes out to the muscle coat, where it terminates in relation to the muscle fibres. If we take the cell in fig. 9 as an example, we find that the cell has three processes. Of these process I (axonic), after entering one of the related fibre-bundles, divides and the branches, after pursuing a separate course, run out to terminate in the muscle coat; process II (dendritic) is almost immediately lost to view in the fibre-tract; whilst process III (dendritic) breaks up into three branches in the ganglion of origin and these pass into the fibre-tracts and terminate in relation to nerve cells in other ganglia. Another example is the cell shown in fig. 11. Of the four processes of this cell, it is possible to trace *da* and *dd* (dendrites) to their terminations on ganglion cells, *axb* (the axone) to the muscle coat, while process *dc* (dendritic) is lost to view before leaving the ganglion of origin.

I have never succeeded in tracing all the processes of a particular cell to their ultimate destinations. The reasons for this are threefold: (1) The fibres stain very faintly towards their endings, with the result that it is frequently impossible to trace them through the entanglement of fibres in the ganglia and fibre-tracts. In MEISSNER'S plexus it is particularly difficult to trace the processes, since the fibres form a dense network around the cell-bodies. (2) The fibres run for a considerable distance, and are frequently torn across in making the preparations. (3) The axonic end-ramifications occur at various levels in the musculature.

Nevertheless, such observations as I have been able to make indicate that in cells of this type one process, presumably the axone, passes out into the musculature, whilst the other dendritic processes terminate in relation to nerve cells, generally in ganglia of the myenteric or more rarely in those of the sub-mucous plexus, and this, I believe, holds true also in the case of the bipolar cells, and probably for the unipolar cells as well. These observations, taken in conjunction with the fact (*vide* p. 366) that the extrinsic vagal fibres end in relation to these cells, render it probable that they represent the motor cells of the enteric plexuses and are not sensory, as DOGIEL suggested.

(ii) *Bipolar Cells* (figs. 12 and 13, Plate 28).

These cells give rise to two processes which become varicose in the fibre-tracts. One fibre, presumably the axone, after running for some distance in a fibre-tract, passes out generally without previous division to the muscle coat, where it runs as a thick varicose fibre among the muscle cells. Ultimately it becomes extremely delicate, and running parallel with the muscle fibres terminates on or actually in the muscle cells. The other process, presumably dendritic, frequently divides dichotomously in the ganglion of origin and the branches so formed run a considerable distance through several ganglia before terminating in diffuse, receptive endings in relation to nerve cells of Types I and II. Occasionally I have been able to trace processes of these cells into a fibre-bundle broken in making the preparation. Such a bundle was probably passing up through the circular muscle coat to join MEISSNER'S plexus in the sub-mucous coat. A typical bipolar cell is seen in fig. 13. In this cell, process *axb* is the axone and passes out to terminate in the

musculature. The other (dendritic) process, labelled *da*, divides dichotomously into two branches a_1 and a_2. These redivide and the branchlets so formed terminate in the following manner: those originating from a_2 end in adjacent ganglia, those from a_1 have been broken across along with numerous other fibres in making the preparation and are probably fibres passing up to MEISSNER'S plexus.

(iii) *Unipolar Cells* (figs. 14, and 15 *a* and *b*, Plates 28 and 29).

These cells are more numerous than cells of the bipolar type. They are large pear-shaped cells each with a small spherical nucleus, placed eccentrically in the widest part of the cell-body (figs. 5, 6, 14 and 15). From the tapering end of the cell a single process arises which divides dichotomously into two branches, either almost immediately or after running a short distance (figs. 14 and 15*b*). Sometimes these branches may redivide (figs. 14 and 15*b*), or they may pass to their destination without further division. They invariably become varicose: one branch (the axone) passes out to the muscularis, where it becomes extremely delicate and eventually disappears among the muscle fibres. In case of division, the branchlets so formed also, I think, pass out to the muscularis (fig. 14, process *ax*). The other main branch (the dendrite) divides into two or more branchlets, but although many of these can be followed for some distance, I have never been able to trace them to their terminations. It is thus difficult to decide whether these cells differ functionally from the multipolar and bipolar cells, but it seems very probable that, like other cells of Type II, they have a motor function, since they are provided with the typical pericellular endings of the extrinsic vagal fibres (fig. 15*a*).

INTERSTITIAL CELLS.

In addition to the typical nerve cells of AUERBACH'S and MEISSNER'S plexuses, there is present in the gut-wall a complex feltwork formed by the interlacing of peculiar cells now generally spoken of as the "interstitial cells of CAJAL," that observer having been the first to describe them.

This feltwork is present in all organs innervated by the "autonomic system" and has been described in connection with the ganglia of the gut-wall, the heart, bladder, diaphragm and blood-vessels, as well as in the pancreas and salivary glands of various mammals. In the gut-wall these cells are found in constant relationship with the enteric plexuses. In relation to AUERBACH'S plexus, they form a dense feltwork lying between the circular and longitudinal muscle layers, and their processes penetrate between the muscle cells. The interstitial cells, so far as I have observed, do not themselves penetrate in between the fibres of the muscle layers, though their processes penetrate to some extent. In the sub-mucosa, these cells are not so closely related to the nerve plexus and lie scattered throughout this layer and in the interior of the villi.

Fig. 18 (Plate 30), taken from a methylene blue preparation, shows a low-power view of a small portion of the feltwork formed by these "interstitial cells" and lying in relation to

AUERBACH'S plexus, from which it is clear that the cells are quite separate units. The cells are very variable in form, the cell-body varying in shape from oblong or triangular to elongated fusiform and possessing a relatively small amount of protoplasm, which frequently presents a vacuolated appearance (fig. 19). The nucleus is usually oval in form, is devoid of a nucleolus, and the chromatin in the form of small granules is scattered diffusely through the reticulum. From the cell-body arise two or more, often numerous, varicose processes, which interlace with other processes to form an irregular feltwork. The processes of the cells related to AUERBACH'S plexus usually end among the smooth muscle cells. Fig. 19 shows one of these cells under greater magnification. The cytoplasm of the cell is finely vacuolar, and the processes which branch frequently are beset with large spherical or oval varicosities. Many of the delicate processes end without any obvious end-swellings, whilst others form minute brush-like endings. It has not been possible in my silver and methylene blue preparations to distinguish either a neurofibrillar network in the cells or any connection between the interstitial cells and the nerve fibres.

Much discussion has taken place concerning the nature of these cells since CAJAL described them in 1889, and there are two contradictory views regarding them. CAJAL (**9**) demonstrated the existence of a neurofibrillar network in these cells, and his observations were later confirmed by those of his pupil LA VILLA (**37**). This network was in silver preparations frequently better impregnated than a similar network in the neurones of AUERBACH'S and MEISSNER'S plexuses. The existence of these fibrillæ, the varicose form of the processes, and the fact that they stain deeply with methylene blue, claimed to be specific for nerve cells, were held by CAJAL and LA VILLA to demonstrate their nervous character. But it must be noted that neither CAJAL nor LA VILLA succeeded in tracing a connection between them and the neurones and extrinsic fibres of the enteric plexuses, although they state they were able to trace their processes to the smooth muscle fibres and to the crypts of LIEBERKÜHN, in relation to which they describe them as terminating.

In 1895, P. SCHULTZ (**59**) gave a description of these cells and definitely stated that they are of a nervous nature, and in 1920 E. MÜLLER (**50**), from his observations on embryos of chick and *Squalus acanthias*, claimed that the interstitial cells and the neurones of Type II are derived from the sympathetic primordium, whilst the nerve cells of Type I migrate along the vagus primordium. MÜLLER believed that the interstitial cells become united by their processes to form in the adult a syncytium, enclosing a neurofibrillar network.

Recently TIEGS (**63**) has described in the gut-wall a nerve-net, distinct from the enteric plexuses, which he believes is the seat of origin of the so-called myogenic contractions of the gut-wall. This nerve-net appears to be identical with the system of interstitial cells described by CAJAL, E. MÜLLER and others, although the author makes no statement to this effect.

Finally, LAWRENTJEW (**43**), in a preliminary note on the structure of these cells,

states that they form a protoplasmic syncytium in which a system of neurofibrillæ lies embedded. According to him, the interstitial cells form a closed and continuous covering to the neurofibrillæ up to their terminations in the smooth muscle cells, and are found everywhere in relation to the endings of the autonomic system. "Die interstitiellen Zellen sind das letzte Glied dieser Leitungsbahn; ihre Fortsätze begleiten die Neurofibrillen bis zu den Endverzweigungen und Endigungen in den glatten Muskelfasern." In this view he upholds HELD'S conception that the neurofibrillæ of the spinal nerves passing to their terminations grow into lemmoblastic (sheath) cells, which form a complete covering to them.

The view that these interstitial cells are of the nature of nervous elements is not, however, universally held. DOGIEL in 1899 concluded that they were of connective tissue origin, since he was unable to observe neurofibrillæ in them or to trace any connection between them and the nerve-fibres of the plexuses. HUBER (**29**), HEIDENHAIN (**28**), KUNTZ (**36**) and TELLO (**60**), all failed to find neurofibrillæ in these cells, and accordingly support DOGIEL'S view that they are a peculiar variety of connective tissue cell.

In some respects, notably in their association with nervous elements and in the form of their processes, these cells call to mind the microglia of the central nervous system.

I have not, however, made a special study of these cells and am not in a position to express a definite opinion as to their nature and significance. I would only remark à propos of LAWRENTJEW'S conclusions that I have frequently been able to trace the processes of the neurones of the enteric ganglia directly to their terminations in the smooth musculature, and not in a single instance have I been able to observe such fibres coursing through the bodies of the interstitial cells.

SYNAPTIC RELATIONS BETWEEN THE FIBRES AND NERVE CELLS.

Synapses have been described by many workers (CAJAL (**11**), DOGIEL (**25**), KUNTZ (**36**), CARPENTER (**16**) and JOHNSON (**31**)) in the enteric plexuses and their existence is generally accepted, but in the most recent work which has come to my notice on this subject, viz., that of JOHNSON (**31**), the author, whilst admitting that synapses occur between the extrinsic fibres and the ganglionic neurones, denies the occurrence of synapses between the local nerve cells themselves.

In the course of my investigations, I found that fibres terminated in relation to the enteric neurones in two different ways, viz., as terminal axonic endings derived from the extrinsic vagal fibres and as receptive endings formed by the dendrites of the intrinsic neurones.

The extrinsic fibres end in the form of pericellular arborizations on cells of Type II in both the myenteric and sub-mucous plexuses. The fibres giving rise to these endings are, as I have already stated, preganglionic fibres of vagal origin, and enter the gut-wall as smooth non-medullated fibres of uniform diameter. After running for some distance in the fibre-tracts, they become varicose, and on reaching their terminations

break up into a number of delicate fibrils which anastomose together, forming a delicate network with characteristic nodal thickenings closely adherent to the cell-body. In figs. 9 and 10 these endings are seen on multipolar cells and in fig. 15*a* on a unipolar cell, all from the myenteric plexus, whilst in fig. 17 a similar ending is seen on a unipolar cell from the sub-mucous plexus. The endings on the cells of the sub-mucous plexus are coarser and not so closely adherent to the cell-body as in those of the myenteric plexus (compare figs. 9 and 17).

The dendritic components of the intrinsic fibres, namely, the dendrites of cells of Types I and II, terminate in the form of more or less branched and diffuse endings, variable as to their precise form in different cases and clearly distinguishable from the above-described pericellular endings. In figs. 5, 6, and 7 are shown multipolar cells of Type I from AUERBACH'S plexus, with what is, perhaps, the simplest type of ending. The dendrites of the multipolar cell have the form of simple or slightly branched processes, each of which terminates in a small brush-like arborization, situated on the cell-body of an adjacent neurone of Type II. Figs. 8, 11 and 12 illustrate another variety of termination of the intrinsic processes. Here the dendrites, usually after previous branching, terminate in delicate varicose fibrils, provided with end-knobs and situated on the bodies of cells of Types I and II. Endings of this diffuse type are not very closely applied to the surfaces of the cells and frequently endings of several processes occur on the same cell (fig. 11). It may be emphasized that the two types of ending described above are perfectly distinct, both morphologically and physiologically. The pericellular arborizations of the vagal fibres represent true terminal axonic endings, while the diffuse endings derived from the dendrites of the local neurones are purely receptive.

The impulses which are transmitted to the muscle fibres through the axones of Type II neurones may accordingly be regarded as compounded of extrinsic vagal impulses directly affecting the neurones and of accessory or intrinsic impulses conveyed to the latter by their dendrites and induced by vagal impulses to cells situated at different levels of the intestinal wall.

DOGIEL in 1899 was the first to describe pericellular and diffuse synapses in the enteric plexuses. He regarded the pericellular endings as of cerebro-spinal (? vagal) origin, the diffuse as sympathetic. More recently KUNTZ (**36**), in a paper on the reflex arcs in the enteric plexuses, states that the synapses he observed " are all similar in character " and have the form of " a more or less complex pericellular arborization." These pericellular synapses, he holds, are both extrinsic (preganglionic) and intrinsic in origin, the synapses of intrinsic origin conditioning the occurrence of local reflexes. CARPENTER (**16**), accepting DOGIEL'S view of the existence of two distinct types of synapses, respectively vagal and sympathetic, is led to suggest that certain differences in the reaction of the vagus and splanchnic nerves under the influence of nicotine applied to the gut-wall might be thereby explained. BAYLISS and STARLING (**3**) showed that whereas the action of the vagus can be entirely suppressed by this drug, the action of the splanchnic is, on the other hand, almost unaffected.

LARSELL (**41**) and LARSELL and MASON (**42**) have shown by direct observation and degeneration experiments that in the rabbit's lung the vagal fibres end in typical pericellular arborizations on the nerve-cells situated therein, and, as I have shown above, the preganglionic fibres which form the visceral component of the vagus (LANGLEY (**40**)) end in similar arborizations on the enteric neurones. Nicotine, as is well known, paralyses the pericellular arborizations of the preganglionic fibres in sympathetic ganglia. In view, therefore, of the experimental and histological evidence, the conclusion appears justified that the effect of nicotine on the synapses between the vagal fibres and the enteric neurones is comparable to that of the drug on the ordinary sympathetic ganglia.

CARPENTER (**16**), following DOGIEL, believes that the more diffuse endings belong to the splanchnic fibres which enter the gut-wall from the cœliac and other ganglia, but the evidence I have been able to bring forward shows that these endings are not axonal, as CARPENTER suggests, but are receptive in function, and originate exclusively from the local neurones. Moreover, the splanchnic fibres are post-ganglionic fibres having their second cell-station in the cœliac and other ganglia, and it is difficult to understand why a third neurone should be interpolated in their pathway contrary to all accepted views of the morphology of the sympathetic system. In my opinion, the splanchnic fibres never enter into relationship with the enteric nerve-cells, but pass out directly to the musculature, where they terminate. Thus, if there are no sympathetic synapses, the experimental results obtained by BAYLISS and STARLING would receive in this way a ready explanation.

FIBRE-TRACTS.

The fibre-tracts which form the connecting strands between the ganglia are composed entirely of non-medullated fibres. These fibres are either intrinsic in origin when they arise as processes of local neurones or they enter the gut-wall from the vago-sympathetic complex and are therefore extrinsic in origin.

The extrinsic fibres of the small intestine come from two sources and are either pre- or post-ganglionic fibres. The fibres forming the splanchnic nerve and representing the sympathetic inflow have their second cell-station in the cœliac and other ganglia, so that the fibres which enter the intestinal wall from this system are post-ganglionic. The fibres of the vagal component, on the other hand, are preganglionic and pass through the cœliac plexus to terminate in relation to the cells of the enteric ganglia. The two sets of fibres can be distinguished from each other by their distribution in the gut-wall and by differences in their form ; those of the vagus are smooth and of uniform diameter, while those of the sympathetic are varicose and thinner than the vagal fibres (figs. 20 and 22, Plates 30 and 32).

The vagal fibres, as just mentioned, are preganglionic fibres which terminate as pericellular arborizations on cells of Type II in the ganglia. They form bundles of smooth non-varicose fibres which, after leaving the cœliac plexus, run either free in the mesentery or alongside the larger blood-vessels and generally enter the intestinal wall with the latter (fig. 20). These fibre-bundles do not appear to have much, if any,

connection with the vessel walls, although they run parallel to them for considerable distances (fig. 20). After penetrating the sub-serous coat, the bundles of vagal fibres run up through the longitudinal muscle layer and enter the myenteric plexus itself. The vagal fibres can be recognized as such in the fibre-tracts for a considerable distance (fig. 21), but they eventually become varicose and so are indistinguishable at first sight from the other fibres forming the connecting bundles. It is possible, however, to trace them continuously from their entry into the myenteric plexus to the ganglia, where they terminate in the form of pericellular arborizations on cells of Type II. The second neurone in the vagal path would thus seem to be the cells of Type II in the myenteric or sub-mucous ganglia, and the processes originating from these cells are accordingly to be interpreted as post-ganglionic vagal fibres.

The extrinsic fibres of vagal origin and the intrinsic fibres originating from cells of the ganglia constitute the main, if not the exclusive, components of the connecting or interganglionic fibre-bundles (fig. 29, Plate 33). If sympathetic fibres are present (as they probably are in the plexuses of the small intestine), they are indistinguishable as such from the other fibres, and in any case, so far as my observations go, they do not enter into synaptic relationship with the nerve cells of the ganglia.

From the myenteric plexus the axones of the nerve cells run out as small bundles to the muscle layers. They form in the longitudinal coat a fine-meshed secondary fibre-plexus (fig. 23, Plate 32). Fibres from this latter in the longitudinal coat and directly from the bundles leaving the myenteric plexus in the circular coat form delicate bundles which run between and parallel to the muscle fibres. The fibres of these bundles eventually terminate on the latter.

Besides fibre-bundles passing out to terminate in the muscle coats there are also given off from AUERBACH'S plexus fine fibre-bundles which pass up through the circular muscle to MEISSNER'S plexus (fig. 4). In the ganglion figured, the bundle was torn in making the preparation. These bundles are formed partly by fibres originating in one or other of the plexuses and partly by vagal fibres which end in relation to the neurones in the sub-mucous plexus.

In the corium of the villi and round the crypts of LIEBERKÜHN is a complex network of anastomosing fibres, which form a dense sub-epithelial plexus. The fibres forming this plexus originate partly as axones of cells in MEISSNER'S plexus and partly from extrinsic fibres of vagal or sympathetic origin (probably from both these latter sources). The fact that stimulation of the vagus causes increased secretion of the gastric glands (ANREP and SUBBA RAU, unpublished observations) suggests that processes of neurones in either the myenteric or sub-mucous plexus are involved in the production of this secretory reaction. Fibres from the sub-mucous plexus certainly pass up to terminate in relation to the musculature of the villi (fig. 28), and it seems probable that fibres from this plexus also provide the efferent innervation of the glandular crypts.

Fine fibrils from the just-mentioned sub-epithelial plexus penetrate the epithelium of the villi and terminate around and between the epithelial cells (fig. 27, Plate 33),

just as has been described by KUNTZ (**36**) in the gut of mammals and by SAKUSSEFF (**58**) in that of fishes. These fibrils are, we suggest, of a sensory character, probably vagal in origin. In the region of the crypts, the fibres seem to terminate in the form of knob-like endings just underneath the epithelium, but this appearance may possibly be due to incomplete silver impregnation, the fine fibrils remaining unimpregnated.

The muscularis mucosæ is richly innervated by fibres which originate from the submucous plexus and ramify between and terminate on the muscle cells just as in the circular and longitudinal muscle layers.

My observations on the relations of the extrinsic fibres to the neurones of the enteric plexuses are in general agreement with the views set forth by S. E. JOHNSON (**31**) in a paper published since this investigation was undertaken. He states " that the extrinsic fibres which enter the gut-wall and form part of the intercellular plexus are of vagal origin. The vagal neurone thus represents the preganglionic link, whereas the post-ganglionic links are the local neurones whose cell-bodies compose the myenteric ganglia. The cell-bodies of the post-ganglionic neurones associated with the splanchnic nerves are situated in the cœliac, or other extra-intestinal, sympathetic ganglia." JOHNSON, however, assumes that almost the entire intraganglionic (his " intercellular ") plexus is derived from vagal fibres, whereas, in my view, only a very small proportion of the fibres forming this plexus are vagal, the majority being the processes of the local ganglion cells. Moreover, the experiment which he quotes in support of the view that the sympathetic fibres have no relation to the enteric nerve cells does not elucidate the problem. His account of the experiment is as follows :—" The splanchnic nerves were divided just proximal to the cœliac plexus. Sections of the gut after degeneration of the nerves show no appreciable change in the appearance of the myenteric plexus, and there is no evidence to indicate that the splanchnics take any part in the formation of the intercellular plexus." JOHNSON seems to have overlooked the fact that in dividing the splanchnic nerves proximal to the cœliac ganglion, he was cutting out only the preganglionic fibres of the sympathetic system, and that the post-ganglionic fibres, being still in connection with their cells of origin, would show no sign of degeneration.

According to my observations, the sympathetic inflow has little or no connection with the ganglia of the enteric plexuses. The fibres enter the gut-wall in close connection with the adventitia of the larger vessels in which many of them terminate (fig. 20), others form a plexus with free endings in the sub-serous coat and are probably chiefly sensory in function. Still other fibres penetrate the longitudinal muscle coat and form a delicate varicose plexus, immediately internal to the myenteric plexus (*i.e.*, on the outer surface of the circular muscle coat). Fibres from this plexus join the " intramuscular plexus," formed by processes of the cells in the myenteric plexus, and probably terminate like the latter in relation to the muscle fibres, but I found it impossible to distinguish between the two sets of fibres. So far as I am aware, no previous investigator has observed the sympathetic plexuses herein described and figured.

The general relations of these sympathetic plexuses can be seen in fig. 21 (Plate 31),

taken from a preparation of the stomach wall of the cat, and under greater magnification in fig. 22 (Plate 32), from the colon of the same animal. In these regions the sympathetic plexus is extremely well developed. Curiously enough, in my preparations of the small intestine, I have so far not been able to observe a separate sympathetic plexus on the outer surface of the circular muscle coat, and in this region of the intestine I think it is possible that the sympathetic fibres actually run in the fibre-bundles of the myenteric and sub-mucous plexuses.

Nerve Endings in Smooth Muscle.

(1) *Motor Endings.*

The nature of the endings of efferent nerve fibres in smooth muscle has been much investigated. Apart from the early view that the efferent fibres terminated actually inside the nucleus (Obregia (**54**)), all observers, and of these I need only mention Kölliker (**32**), Löwit (**46**), Retzius (**57**), E. Müller (**49**), Dogiel (**25**), Huber and de Witt (**30**), Boeke (**6** and **7**), Agababow (**1**) and Lawrentjew (**44**), agree that the motor fibres, after forming complicated plexuses between the smooth muscle fibres, eventually terminate in close relationship to the muscle cells themselves, either on the surface of the cell or actually in its substance.

It would be out of place to attempt to discuss here the observations made by the numerous workers on this problem, and I need only briefly refer to the work of the more recent investigators, Agababow (**1**), Boeke (**6** and **7**) and Lawrentjew (**44**), with whose conclusions my own observations are in general agreement.

Agababow (**1**) found, in Golgi and methylene blue preparations of the human eye-muscles, that the smooth muscle cells were enclosed in a net of very fine nerve fibres, which wound round the cell but never penetrated into its substance. These endings, according to Agababow, originated from motor nerve fibres. The technique used by Agababow, namely, intra-vitam methylene blue and Golgi methods, was not sufficient to show the actual relationship between the nerve fibres and the muscle cells, since, according to Boeke, the final terminations are unstained by these methods, or take such a light stain as to render it impossible to draw any conclusions as to the real relations between nervous and muscular elements.

Boeke (**6**), using a Bielchowsky technique, has shown that, in addition to fine varicose fibres which run between the muscle cells and encircle them in a network of extremely fine fibrils with more or less thickened points of junction (the terminal network of Agababow), there are present even finer fibrillæ which branch off from the network and penetrate into the substance of the muscle cell, where they terminate in the form of end-rings or loops. These fine fibrillæ form a reticulum in the protoplasm of the muscle cells, often enclosing the nucleus.

The nature of the relations between the terminal fibrillæ and the nucleus is discussed by Boeke (**7**) in a recent paper. He shows in figures from tangential sections of the

human ciliary muscle that, in almost every case, one of the terminal fibrillæ lies in close proximity to the nucleus, often indenting it, so close is the relation. LAWRENTJEW (**43**), working on the musculature of the cat's stomach, has found similar appearances.

The preparations I have studied were stained with methylene blue, and my observations, so far as they go, are in general agreement with those of BOEKE. The fibres forming what I have termed the " intramuscular plexus " (*ante*, p. 369) and which lie in parallel bundles between the smooth muscle cells, eventually terminate round the latter in the characteristic networks shown in figs. 24, 25 and 26 (Plate 32).

In fig. 25 a single fibre is seen to break up, on the surface of a muscle cell, into a number of fine fibrils, which are beset with small varicosities and which anastomose together to form a delicate network closely encircling its entire surface (figs. 24 and 25). My observations lead me to conclude that the varicose swellings of the fibrils lie on the surfaces of the muscle cells and that extremely delicate fibrillæ take origin from these swellings and actually penetrate into the substance of the muscle fibres, just as BOEKE describes. In my preparations I have not been able to follow these fibrillæ to their ultimate terminations, though LAWRENTJEW, working on the musculature of the cat's stomach, confirms BOEKE's statements as to their mode of termination.

In fig. 24, the fibrillæ in the region of the nucleus have a very similar disposition to that described by BOEKE (**7**) and LAWRENTJEW (**44**), but in figs. 25 and 26 they do not appear to have any relationship to the nucleus.

In fig. 26 a somewhat different type of termination is depicted. Here a small bundle of fibres from the intramuscular plexus runs parallel to the muscle cell, and from it arise a number of delicate collaterals which end on the surface of the cell in the form of minute varicose swellings. From some of these latter delicate fibrillæ are given off, but I found it impossible to determine whether or not they penetrate into the substance of the cell. The fibre-bundle in these cases was directly traceable to the myenteric plexus, and accordingly is composed of axones of myenteric neurones; but I was not able to observe the relations of the fibres giving rise to the endings shown in figs. 24 and 25. I am consequently unable to decide whether we have to do with two distinct types of ending, related respectively to vagal and sympathetic fibres, or with two varieties of one type. It should be mentioned that the great majority of the endings are of the type shown in figs. 24 and 25. TIEGS (**62**), working on the musculature of the frog's stomach, states that he has observed in methylene blue preparations a double innervation on each muscle fibre, namely, a motor ending similar to that described above and a smaller, more delicate, plate-like ending. This latter type of ending has not, so far as I am aware, been observed by any other investigator, and there is certainly no trace of it in my preparations stained by a similar method.

The muscularis mucosæ and the smooth muscles of the villi are innervated by fibres from the cells of MEISSNER'S plexus which form an " intramuscular " plexus between the muscle cells, just as in the circular and longitudinal coats. My preparations have not enabled me to observe the actual endings on the muscle cells, but I have traced many

fibres from their origin in MEISSNER'S plexus into the smooth muscle of the villi (fig. 28, Plate 33).

(2) *Sensory Endings.*

RANSON (**55**) states that " in spite of the negative character of the histological evidence the existence of sensory fibres in the gastro-intestinal mucosa has been assumed by most physiologists. And indeed receptive endings in the epithelium seem to be required by the fact that responses may be obtained from both chemical and mechanical stimulation of the mucosa. The acid control of the cardia and pylorus (W. B. CANNON (**12**)), the inhibition of hunger contractions by introduction of various fluids into the stomach (A. J. CARLSON (**15**)), variations in the rate of passage of different kinds of food along the intestinal tract (W. B. CANNON (**12**)), and other phenomena, indicate the presence of chemical sensibility in the gastro-intestinal mucosa."

In 1899 DOGIEL (**25**) described a complete reflex arc in the intestinal plexuses, the sensory component being a nerve-cell, situated in an enteric ganglion, whose dendrites terminated in the mucosa. About the same time SAKUSSEFF (**58**), working with DOGIEL, claimed to have traced, in the gut of fishes, fibres from the intestinal plexuses into the mucosa. According to RANSON'S account of SAKUSSEFF'S work, " these [fibres] ramified beneath the epithelium and sent fine varicose threads into the columnar epithelium, where they ran between the epithelial cells and formed a network about the individual cells." Similar terminations were described by R. MÜLLER (**53**) in the gastric epithelium of the frog and by ERIK MÜLLER (**50**) in the epithelium of the digestive tract in *Selachii* and in the chick.

More recently KUNTZ (**36**) has described sensory endings in the gastric and intestinal epithelium of the cat. According to this worker, the fibres which give rise to these endings originate from the intestinal plexuses, although he was unable to demonstrate their actual connection with the latter. He is led to postulate this origin because the fibres " are present in such abundance that they could not be accounted for as visceral afferent fibres contained in the vagus and spinal nerves, even though we should admit of the most profuse branching."

Preparations I have made by the silver method of DE CASTRO (**21**) show appearances in the epithelium of the villi of the small intestine very similar to those described by SAKUSSEFF in the gut of fishes and by KUNTZ in the cat. There is present directly under the epithelium of the villi a richly developed plexus composed of very fine varicose fibres (fig. 27, Plate 33). From this plexus fibres penetrate between the epithelial cells to form a network round their basal halves. The fibres were never seen to penetrate to the striated free border and generally terminate as fine fibrillæ, seldom, if ever, ending in the knob-like swellings with which they are beset. So far I have never been able to trace a connection between the sub-epithelial plexus and the cells of the enteric plexuses, although I have frequently been able to follow axones from the cells of MEISSNER'S plexus to the villi (fig. 28), where they end in relation to the muscle fibres. For this reason,

and also because of the contention of BRUNEMERER and CARLSON (**8**) that chemical and mechanical stimulation of the intestinal mucosa causes an inhibition of tonus and contraction of the empty stomach, primarily at any rate, through a central reflex path, I suggest that the intra-epithelial endings are those of extrinsic sensory fibres.

As already described, sensory fibres are also present in the sub-serous coat, where fibres of sympathetic origin form a diffuse wide-meshed plexus, the terminal fibres of which end freely in the connective tissue (fig. 20). Sensory endings, such as have been described by CARPENTER (**17**) in the longitudinal muscle coat and by BERKLEY (**4**) in the muscularis mucosæ of the dog's intestine, were not observed by me in either silver or methylene blue preparations. I am accordingly of the opinion that the sensitivity of the intestinal wall is located in the mucosa and sub-serosa and not in the muscularis.

DISCUSSION.

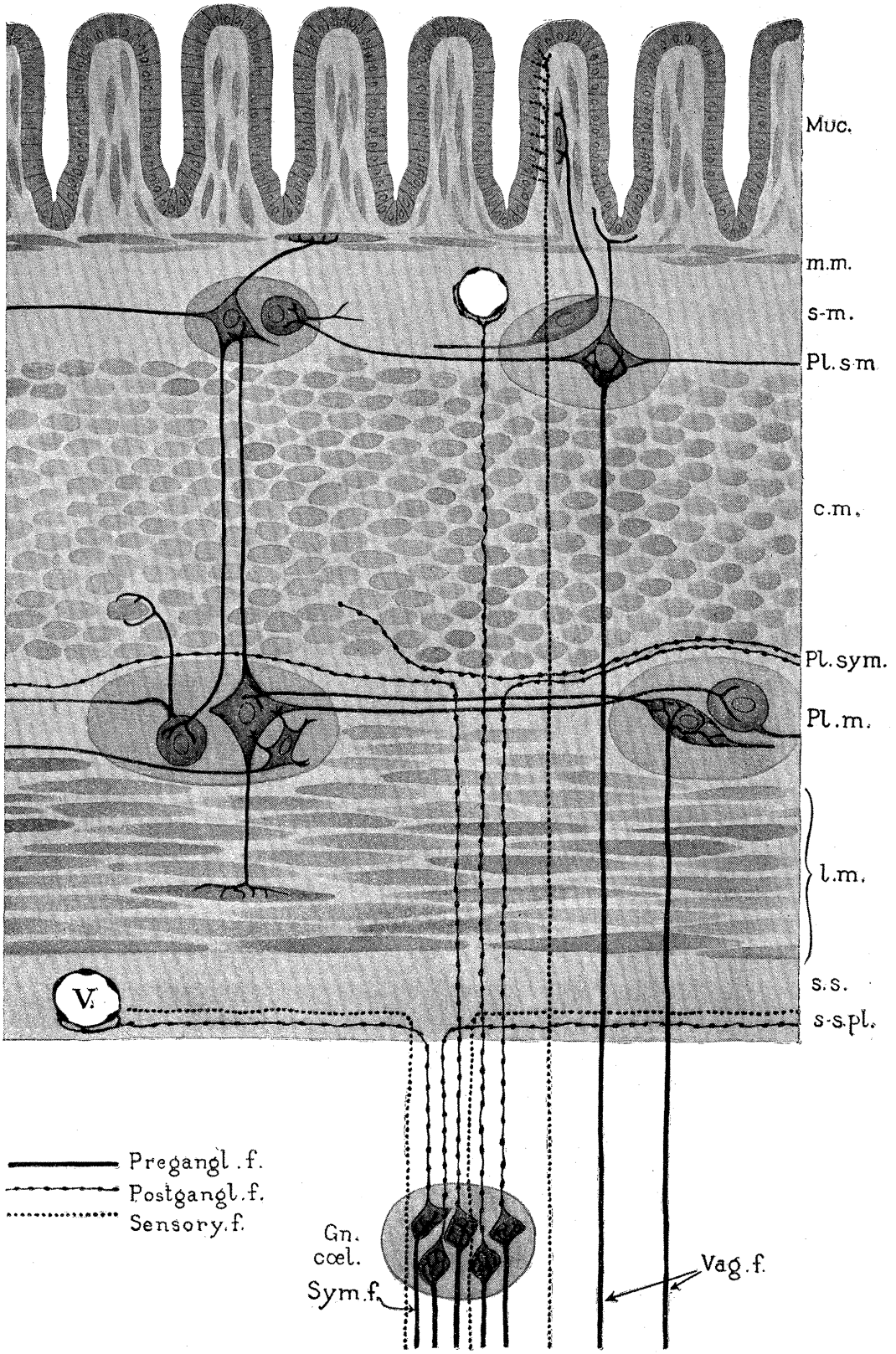
The accompanying text-fig. 1 summarizes in pictorial form the chief conclusions I have arrived at concerning the structure and relations of the elements entering into the formation of the enteric plexuses.

There are two opposing views as to the constitution of the enteric plexuses : (*a*) That they are essentially composed of neurones and the processes of neurones in synaptic relationship with each other; and (*b*) that they are not neuronic but really of the nature of a continuous syncytial nerve-net.

DOGIEL (**25**) held that the enteric neurones are in true synaptic relationship with each other and that they comprise cells of at least two distinct types. Cells of Type I, according to him, are motor in function and are intimately connected together by the interlacement of their dendritic processes, whilst their axones terminate in the muscularis. Cells of Type II he regarded as sensory in function, since he believed their dendrites terminated in the mucosa, but he was unable to determine the mode of termination of their axones. DOGIEL further believed that the extrinsic fibres ended in relation to the enteric neurones, the vagal fibres forming pericellular arborizations around them, whilst the sympathetic fibres also terminated on them but in more diffuse endings.

Other workers, KUNTZ (**34**), CARPENTER (**16**), and JOHNSON (**31**), found it impossible to classify the enteric neurones into DOGIEL'S two main types, since they considered that all possible gradations exist between them. I am unable to accept the conclusions of these authors, since in silver and methylene blue preparations of the myenteric plexuses from various mammals I have been able, without any great difficulty, to distinguish the enteric neurones into types corresponding to those of DOGIEL. Cells of Type II are far more numerous than those of Type I and can be classified as multipolar, bipolar and unipolar. Of these three varieties, the multipolar cells are the most numerous ; next in order of abundance come the unipolar cells, which are present in much greater number than the bipolars.

DOGIEL'S views regarding the relation of the enteric ganglion cells to each other and to the extrinsic fibres entering the gut-wall are not universally accepted. KUNTZ (**36**)



TEXT-FIG. 1.—Diagrammatic representation of the relations of the elements of the gut-plexuses as seen in longitudinal section of the gut-wall. *Muc.*, mucosa. *m.m.*, muscularis mucosæ. *s-m.*, sub-mucosa. *Pl. s-m.*, sub-mucous plexus. *c.m.*, circular muscle. *Pl. sym.*, sympathetic plexus. *Pl. m.*, myenteric plexus. *l.m.*, longitudinal muscle. *ss.pl.*, sub-serous plexus. *s.s.*, sub-serosa. *Gn. cœl.*, cœliac ganglion. *Sym. f.*, sympathetic fibres. *vag. f.*, vagal fibres. *V.*, vessel.

believes that processes of the enteric neurones, as well as the extrinsic fibres, form pericellular arborizations around the other neurones in the plexuses, and that these arborizations are the only form of synapse met with in the ganglia. CARPENTER (**16**), on the other hand, believes that the pericellular arborizations are the endings of vagal fibres, whilst a more diffuse type of ending present in the ganglia represents the endings of splanchnic or sympathetic fibres. More recently JOHNSON (**31**) states that the cells forming the ganglia are all of one type, viz., DOGIEL'S Type II, and on these cells the vagal fibres end in pericellular arborizations. He is, however, unable to find any synapses between the enteric neurones themselves.

All these observers are in agreement concerning the endings of the vagal fibres on the enteric neurones in the form of pericellular arborizations, but in regard to the origin of the more diffuse type of ending there is considerable difference of opinion. In my own preparations, where the fibres are coloured intensely, it is possible to trace processes of cells of Type II for a considerable distance through the fibre-tracts into other enteric ganglia. There they terminate in relation to other neurones in the diffuse endings in question. Moreover, the endings of processes of the cells of Type I on cells of Type II are so clearly visible in silver preparations that it is impossible to accept JOHNSON'S view as to the non-existence of synapses between the local neurones. CARPENTER'S suggestion that these diffuse endings might be derived from the sympathetic or splanchnic fibres has never been confirmed, and the facts put forward earlier in this paper (*ante* p. 370) show that these fibres have no connection whatever with the enteric neurones.

The view that the enteric nervous system is composed, at least in part, of a syncytial nerve-net is held by a number of investigators. BETHÉ (**5**) and R. MÜLLER (**53**) described the enteric plexuses in the frog as composed of anastomosing cells in the form of nerve-nets, and COLE (**19**) has also stated that he has found isolated groups of anastomosing nerve-cells in the myenteric plexus of the same animal. ERIK MÜLLER (**51**), whilst he believed the enteric plexuses in the Elasmobranch fishes were true nerve-nets, described those of birds and mammals as consisting partly of nerve-nets and partly of free neurones. He believed, however, that the non-synaptic nerve-net possessed a definite polarity in the higher vertebrates, whilst the reflex actions which take place through the mediation of the myenteric plexus he regarded as of the nature of axone reflexes. His conception of the structure of the enteric plexuses was largely influenced by his studies on their development (**50**). He believed that the neurones of Type I are vagal in origin, whilst those of Type II, and in this category he included the "interstitial cells of CAJAL," are derived from the sympathetic primordium. He maintained further that the myenteric plexus contains only vagal elements in the stomach, but both vagal and sympathetic elements in the intestine, whilst the sub-mucous plexus is sympathetic throughout its extent. MÜLLER'S views, apart from that of a vagal contribution to the plexuses, have not, however, met with general acceptance. KUNTZ (**35**), who has also investigated the early development of these plexuses, affirms that the cells which form the enteric ganglia migrate along the primitive vagus before the sympathetic path is laid

down, and this, he states, holds true for the sub-mucous as well as for the myenteric plexus. On the other hand, TELLO (**61**), more recently, has come to the conclusion that the nerve cells constituting the myenteric plexuses originate *in situ* before either vagal or sympathetic pathways are laid down, and that only later does the cellular plexus become transformed into a fibro-cellular plexus through the ingrowth of fibres derived from the vagus and sympathetic.

My observations lead me to believe that the neurones in the enteric plexuses are vagal in origin, as suggested by E. MÜLLER and KUNTZ. This conclusion is supported by the recent work of WOOLLARD (**66**) on the innervation of the heart, and by that of DE CASTRO (**20**) on the nerve supply of the pancreas. WOOLLARD has shown that, in the heart, the vagal fibres end in relation to the neurones of the heart ganglia, and that the axones of these cardiac neurones pass to the musculature. The sympathetic fibres never make connection with the cardiac neurones, but pass directly to form fine plexuses in the epicardium, endocardium, valves and blood-vessels, where they terminate in the muscle fibres, or as fine, probably sensory, endings in the connective tissue. DE CASTRO (**20**), using a silver technique, has shown that the vagal fibres to the pancreas similarly terminate on the neurones in the extra-pancreatic ganglia, and that the axones of these neurones pass out to the acini and the islet cells in relation to which they terminate. The fibres from the sympathetic, just as in the heart, have no connection with the ganglia, and according to DE CASTRO innervate the blood-vessels. The innervation of the gut-wall in its general features is similar to that described for these two organs. Vagal fibres end round the enteric neurones in pericellular arborizations, as DOGIEL (**25**), KUNTZ (**36**), CARPENTER (**16**), JOHNSON (**31**), and DE WITT (**22**) have described. The axones of these cells terminate in the muscularis and around the glands in the stomach and intestine. Confirmation of the histological findings is afforded by the unpublished observations of Drs. ANREP and SUBBA RAU, that stimulation of the vagus causes increased secretion of the gastric glands.

Still another view of the structure of the gut-plexuses has been put forward by LAWRENTJEW (**44**), who states that the plexuses of non-medullated fibres in the smooth muscle, mucosa and sub-mucosa of the gut and bladder in mammals consist of "ein System von untereinander anastomosierenden Protoplasma-strängen—ein Synzytium, in dessen Protoplasma Komplexe von Neurofibrillen verlaufen," and he further states that the interstitial cells are "die Endglieder des Synzytiums—eigentümliche Lemmoblasten, denen Fortsätze die Neurofibrillen bis zu den motorischen Endigungen in den glatten Muskelzellen bringen." Without venturing to call in question LAWRENTJEW'S conclusions as to the lemmoblastic nature of these "interstitial cells," I would point out that he has in my opinion completely misinterpreted the structure of the ganglia, which he speaks of as "Kreuzungspunkten." These ganglia, and, indeed, the plexuses as a whole, are neither of the nature of a syncytium nor of nerve-nets, but are essentially composed of neurones and the processes of neurones, which are in synaptic relationship with each other.

In a recent paper RANSON (**55**) has reviewed our knowledge of the physiological nature of the intestinal reflexes, and accepts the view that whilst many of the reflexes are controlled by the extrinsic nerves, others such as the myenteric reflex are carried out entirely by the intrinsic nervous mechanism, and persist after all extrinsic nerves to the gut have been severed (BAYLISS and STARLING (**3**)). The question then arises as to the mechanism of these movements of the digestive tract. How are they initiated, and by what means are they carried out ? The experimental data available indicate that the rhythmical movements of smooth muscle are myogenic in origin, and this fact, originally demonstrated by ENGELMANN, has received confirmation from many workers. BAYLISS and STARLING found that a solution of nicotine of sufficient strength to paralyse the ganglia abolished the myenteric reflex and left the rhythmical contractions unaffected. FLETCHER (**26**) confirmed this statement when he showed that the retractor penis muscle of the dog and cat, which is said to contain no nerve cells, undergoes rhythmical movements when removed from the animal, and further confirmation is afforded by the investigations of GUNN and UNDERHILL (**27**), ALVAREZ and MAHONEY (**2**). MAGNUS (**47**) at one time believed that these contractions were neurogenic in origin, and claimed that by removing all traces of AUERBACH'S plexus the rhythmical movements were abolished. Later (**48**), however, he satisfied himself as to the myogenic nature of the contractions.

More recently VAN ESVELD (**64**) has shown that, although there are isolated nerve cells present in the circular muscle layer, they are located specially near the attachment of the mesentery, and are present in such small numbers that it is possible to obtain a strip of muscle quite free from true ganglion cells. Such a preparation has been shown by GASSER (quoted by VAN ESVELD) to contract rhythmically.

There are, however, other elements which must be taken into consideration in any discussion of the origin of the rhythmical contractions of smooth muscle, viz., the so-called "interstitial cells of CAJAL." These cells, LAWRENTJEW maintains, form a network in which run the neurofibrillæ which terminate in the smooth muscle fibres. The nerve-net in the muscularis described by TIEGS (**62**), which he believes initiates the rhythmical movements of the gut-wall, appears to be composed of interstitial cells, though the author makes no mention of such. If the interstitial cells merely conduct the neuro-fibrillæ, as LAWRENTJEW maintains, it is difficult to see how they can play any direct part in originating these movements.

The myenteric reflex is even more difficult to explain. Apart from the view of CAREY (**14**), that these movements are myogenic in nature and due to the helicoidal arrangement of the muscle coats, the general belief is that this reflex is neurogenic and conditioned by a definite reflex mechanism, located in the enteric plexuses, since it persists after section of the extrinsic nerves (BAYLISS and STARLING). Accordingly, various workers have attempted to find the sensory constituents of the reflex arc and have described sensory endings in different parts of the intestinal wall. DOGIEL believed that in his cells of Types I and II he had a reflex mechanism of the usual type. Cells of Type I he

believed to be motor in function, receiving the pericellular arborizations of the vagal fibres, whilst cells of Type II, whose dendrites passed up to the mucosa, represent the sensory element of his reflex arc. SAKUSSEFF (**58**) and, more recently, KUNTZ (**36**) have described sensory endings in the intestinal mucosa in the form of fine fibrils which ramify between the epithelial cells of the crypts and the villi, whilst CARPENTER (**17**) believes that he has found " intramuscular " sensory endings in the longitudinal muscle coat of the dog's intestine, originating from fibres of the myenteric plexus. But, as RANSON (**55**) points out, apart from DOGIEL'S description of a sensory type of sympathetic cell in the enteric plexuses and the observations of KUNTZ and CARPENTER, which might be interpreted as favouring DOGIEL'S theory, the bulk of the evidence seems against this view of a local reflex mechanism, and "indicates that all visceral afferent fibres have their cells of origin in the cerebro-spinal ganglia." With the views of this author I am in agreement, since I hold that the cells forming the enteric ganglia constitute a purely motor system.

I have shown (*ante*, p. 373, and fig. 27) that endings similar to those described by DOGIEL (**25**) and KUNTZ (**36**) are present in the epithelium of the villi of the small intestine, but in no case was it possible to trace the fibres giving rise to these endings to the neurones of the sub-mucous or myenteric plexuses, although the axones of these cells could frequently be traced in serial sections to their terminations in the smooth muscle of the villi. KUNTZ (**36**) states that these fibres " are present in such abundance that they could not be accounted for as visceral afferent fibres contained in the vagus and spinal nerves, even though we should admit of the most profuse branching." Whilst not wishing to call in question KUNTZ'S statement regarding the number of visceral afferent fibres contained in the extrinsic nerves to the intestine, it seems to me, in view of the fact that chemical or mechanical stimulation of the intestinal mucosa causes an inhibition of tonus and a contraction of the empty stomach, primarily, at any rate, through a central reflex path (BRUNEMERER and CARLSON (**8**)), that some at least of these endings in the epithelium of the mucosa are those of extrinsic fibres.

The facts that the neurones of Type II (DOGIEL'S sensory Type II) receive the pericellular arborizations of the vagal fibres and that these cells probably constitute the second neurone in the vagal path and are therefore motor in function, render it difficult to see how a reflex arc can exist in the intestinal wall. It seems more probable that the myenteric reflex is, as suggested by E. MÜLLER, of the nature of an axone reflex, such as has been described in the bladder and skin of the cat by LANGLEY and ANDERSON (**38**) and more recently by KROGH (**33**) in blood-vessels and capillaries. Although such an assumption in the case of the myenteric reflex appears to be impossible of direct experimental proof, elements which may well be the seat of such reflexes, viz., the unipolar cells, are present in considerable numbers, and, indeed, this seems to be the only means of explaining the localized reflex acts of the intestinal wall when all connections with the higher centres have been removed.

SUMMARY.

The observations recorded above justify the following conclusions:—

(1) Cells of two types are present in the enteric ganglia. (*a*) Multipolar cells with short dendrites, present only in the myenteric plexus (Type I of DOGIEL). (*b*) Cells with long dendrites present in both myenteric and sub-mucous plexuses (Type II of DOGIEL).

It is suggested that cells of Type II are the motor cells of the enteric plexuses, whilst those of Type I are intercalary or associative.

(2) Cells of Type II may be unipolar, bipolar or multipolar in form, the latter being the most numerous.

(3) The size of the cell varies in the two plexuses, cells of the myenteric plexus of the small intestine being two or three times as large as those of the sub-mucous plexus in the dog, cat, and rabbit.

(4) The "interstitial cells of CAJAL" form an interlacing system in the meshes of the fibro-cellular plexuses, and are specially aggregated round the ganglia. Only their gross form and relations are dealt with.

(5) The plexuses are essentially composed of neurones and the processes of neurones which are in synaptic relation with each other. In the mammals studied there is no evidence of the existence of a nerve-net in either of the gut-plexuses.

(6) Synapses of two morphologically distinct types are present in the ganglia, viz.: (*a*) pericellular terminal networks, which are derived from preganglionic axones of the vagal inflow and which are found on the cell-bodies of neurones of Type II; (*b*) more diffuse receptive endings, derived from dendrites of local ganglion cells and found on neurones of both types.

(7) The intraganglionic fibres are constituted in at least two-thirds of their entirety by the processes of the enteric neurones, whilst processes of these latter also form a large proportion of the fibres in the interganglionic fibre-tracts.

(8) The plexuses of AUERBACH (myenteric) and MEISSNER (sub-mucous) are connected by bundles of fibres which run up at irregular intervals through the circular muscle layer.

(9) Fibres from the sub-mucous plexus pass up to the muscularis mucosæ and to the smooth muscles in the villi, to terminate in relation to the muscle cells.

(10) Immediately below the epithelium of the villi is a rich fibre-plexus, the fibres of which penetrate between the epithelial cells and ramify round their basal halves. These endings are probably sensory, and it is suggested that they are derived from extrinsic fibres.

(11) The fibres which ramify round the crypts of LIEBERKÜHN do not penetrate between the glandular epithelial cells, but appear to terminate under the epithelium in the form of minute knob-like swellings. This latter appearance, however, may be due to incomplete impregnation of the terminal fibrillæ.

(12) The extrinsic fibres enter the gut-wall along the larger blood-vessels and comprise : (*a*) vagal fibres in the form of bundles of smooth fibres which have little or no connection with the blood-vessels and pass directly to the enteric plexuses ; (*b*) sympathetic fibres, which are more closely bound up with the vessel-walls, many of the fibres terminating in the same. Those sympathetic fibres which penetrate the gut-wall form a fine plexus on the outer surface of the circular muscle coat (*i.e.*, just internal to AUERBACH'S plexus). This sympathetic plexus is well marked in the stomach and colon, but was not observed as a separate entity in the small intestine. In this region, it is suggested, the sympathetic fibres run in the fibre-bundles of the myenteric plexus.

(13) Fibres from the sympathetic inflow and the axones of the motor cells of the myenteric plexus form an intramuscular plexus, the fibres of which run parallel to the muscle cells. The two sets of fibres are indistinguishable from each other, and probably both terminate around and actually in the latter.

(14) The fibres of the intramuscular plexus, on approaching the muscle cells, break up each into a number of fine fibrils which form a complicated network extending over the surface of the cell. The fibrils are beset with small varicosities, and from these delicate fibrillæ arise which penetrate into the substance of the muscle cell.

(15) Some of the fibres of the sympathetic inflow form a delicate plexus in the sub-serous coat, the fibres of which appear to end freely in the connective tissue and are probably sensory in function.

(16) No sensory endings have been observed in the muscle coats.

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EXPLANATION OF PLATES 26 TO 33.

List of reference letters.

ax., axone.
cap., capillary.
c., collateral.
cm., circular muscle.
d., dendrite.
f. tr., interganglionic fibre-tract.
gn., ganglion.
gf. tr., intraganglionic fibres.
im. pl., intramuscular plexus.
lm., longitudinal muscle.
N_{I}, neurones of Type I.
N_{II}, neurones of Type II.
p.n., pericellular network.
s.f., sympathetic fibre.
ss. pl., subserous plexus.
S. pl., sympathetic plexus.
sm., smooth muscle.
v.f., vagal fibre.

PLATE 26.

FIG. 1.—General view of the myenteric plexus from the small intestine of Cavia. Silver nitrate. *gn.*, ganglion. *f. tr.*, interganglionic fibre-tract. *lm.*, longitudinal muscle coat. × about 40.

FIG. 2.—General view of the sub-mucous plexus from the small intestine of Cavia. Silver nitrate. *gn.*, ganglion. *cap.*, capillary. *f. tr.*, interganglionic fibre-tract. × about 75.

FIG. 3.—Ganglion of the myenteric plexus from the small intestine of Cavia. Silver nitrate. N_{I}, neurone of Type I. N_{II}., neurone of Type II. *f. tr.*, interganglionic fibre-tract. *lm.*, longitudinal muscle coat. *gf. tr.*, intraganglionic fibres. × about 335.

FIG. 4.—Ganglion of sub-mucous plexus from the small intestine of Rabbit. Silver nitrate. N_{II}., neurone of Type II. *f. tr.*, interganglionic fibre-tract. *c. tr.*, fibre-tract connecting sub-mucous and myenteric plexuses (in this case broken in making the preparation). *cm.*, circular muscle. × about 335.

PLATE 27.

FIG. 5.—Nerve cells from a myenteric ganglion. Small intestine, Cavia. Silver nitrate. N_{I}., neurone of Type I. uN_{II}., unipolar cell of Type II. *ax.*, axone. *c.s.*, centrosphere. *n.f.*, neurofibrillæ. *gf. tr.*, intraganglionic fibres. *ad.*, dendrite terminating in a brush-like ending without previous branching. × about 450.

FIG. 6.—Cells from another myenteric ganglion. Small intestine, Cavia. Silver nitrate. N_{I}., cell of Type I. mN_{II}., multipolar cell of Type II. uN_{II}., unipolar cell. *ax.*, axone. *c.*, collateral. *d.*, dendrite. *gf. tr.*, intraganglionic fibres. *c.s.*, centrosphere. *f. tr.*, interganglionic fibre-tract. × about 410.

FIG. 7.—Multipolar cell of Type I (0·025 × 0·03 mm. in diam.) from the myenteric plexus of the small intestine, Dog. Methylene blue. *d.*, dendrite. *ax.*, axone, originating in this case from the tip of a broad flattened dendrite. *c.*, collateral. Note the vacuolated appearance of the cell cytoplasm. × about 800.

FIG. 8.—Multipolar cell of Type I (probably corresponding to Type III of DOGIEL) from the myenteric plexus of the small intestine, Dog. Methylene blue. *d.*, branching dendrite ending in varicose enlargements. *ax.*, axone originating from one of the broad flattened dendrites. Note the granular cytoplasm of the cell body. × about 600.

FIG. 9.—Multipolar cell of Type II (0·054 × 0·028 mm. in diam.) from the myenteric plexus of the small intestine, Dog. Methylene blue. *p.n.*, pericellular arborization round body of cell. *v.f.*, vagal fibre giving rise to arborization. ax_{I}., axone passing out to terminate in the musculature. d_{II}., dendrite which is lost to sight in the fibre-tract. d_{III}., dendrite, the branches of which terminate on the ganglion cells. × about 800.

PLATE 28.

FIG. 10.—Multipolar cell of Type II (0·053 × 0·04 mm. in diam.) from the myenteric plexus of the small intestine, Dog. Methylene blue. *p.n.*, pericellular network, incompletely impregnated. *v.f.*, vagal fibre ending in pericellular network. *da.* and *db.*, dendrites which are lost to view in fibre-tracts. *axc.*, axone passing out to terminate in the musculature. × about 900.

FIG. 11.—Multipolar cell of Type II from the myenteric plexus of the small intestine, Dog. Methylene blue. *da.* and *dd.*, dendrites terminating on ganglion cells in adjacent ganglia. *axb.*, axone terminating in the smooth muscle. *dc.*, dendrite which is lost in fibre-tract. Note the numerous diffuse endings, *d.e.*, on the cell body. × about 800.

FIG. 12.—Bipolar cell of Type II from the myenteric plexus. Small intestine, Dog. Methylene blue. In this particular cell it was impossible to trace the processes to their terminations. *d.e.*, diffuse endings on the cell body. × about 900.

FIG. 13.—Bipolar cell of Type II from the myenteric plexus. Small intestine, Dog. Methylene blue. *axb.*, axone terminating in the muscularis. *da.*, dendrite which divides into two branches da_1, and da_2. da_1 joins a bundle passing to MEISSNER'S plexus and is broken across in making the preparation; da_2 ends on a cell in an adjacent ganglion. × about 495.

FIG. 14.—Unipolar cell of Type II from the myenteric plexus. Small intestine, Dog. Methylene blue. *p.n.*, pericellular arborization. *pr.*, undivided process of unipolar cell. *ax.* (axone) passes out to the muscularis. *d.* (dendrite) lost to sight in the fibre-tract. × about 900.

PLATE 29.

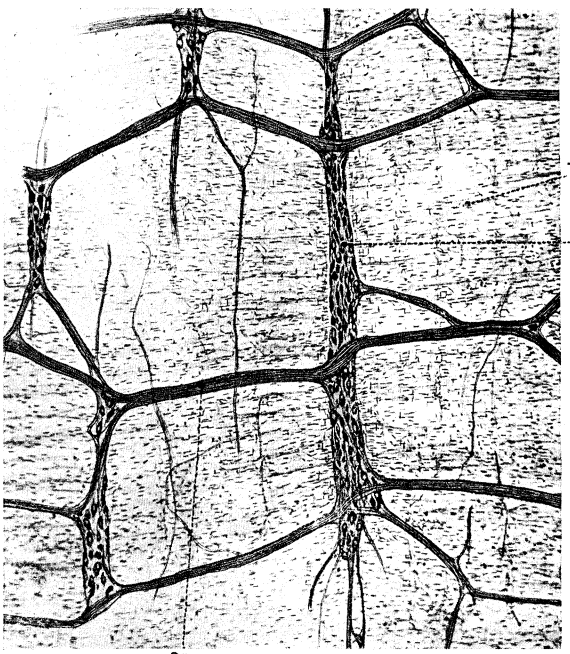
FIG. 15 *a* and *b*.—Unipolar cells of Type II from the myenteric plexus. Small intestine, Dog. Methylene blue. Cell *a* shows a well-impregnated pericellular network (*p.n.*), but the process (*pr.*) could not be traced beyond the ganglion of origin. Cell *b* has a process (*pr.*) which divides into an axone, *ax.*, the divisions of which pass out to the musculature, and a dendrite *d*, the divisions of which are lost to view before leaving the fibre-tracts. × about 1500.

FIG. 16.—Cells from the sub-mucous plexus of the small intestine, Dog. Methylene blue. N_{II}, neurone of Type II, stained very faintly with well-marked pericellular network, *p.n.*, *nuc.*, nucleus of N_{II}. bN_{II}, bipolar cell of type II. *gf. tr.*, intraganglionic fibres. Measurements, N_{II}, 0·027 × 0·042 mm. in diameter; bN_{II}, 0·012 × 0·027 mm. in diameter. × about 1200.

FIG. 17.—Unipolar cell from the sub-mucous plexus. Small intestine, Dog. Methylene blue. Note the small size of the cell as compared with those represented under the same magnification in figs. 9, 10, 12 and 14. *p.n.*, incompletely impregnated pericellular network. The process "*pr.*" could not be traced. × about 1200.

PLATE 30.

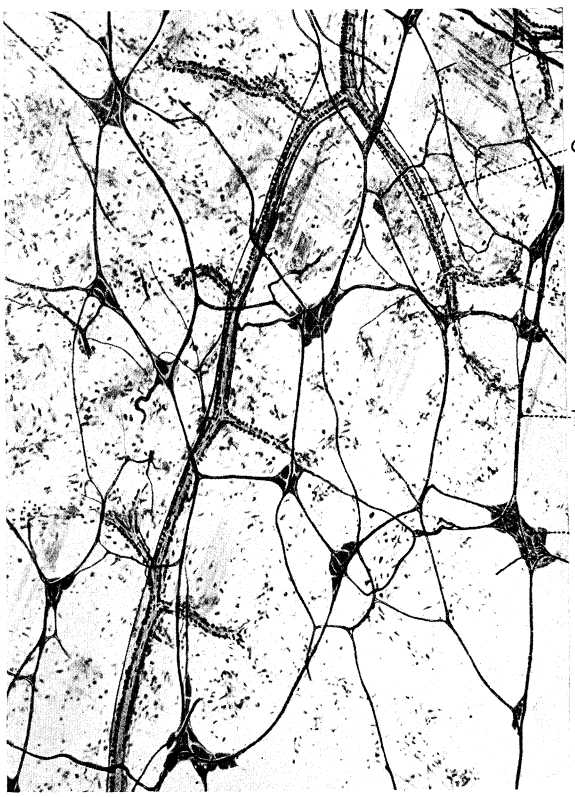
FIG. 18.—Low-power view of the feltwork of interstitial cells lying in relation to the myenteric plexus. Small intestine, Dog. Methylene blue. Measurements of cells (approx.), 0·014 × 0·16 mm. × about 500.


lm.
gn.
f.tr.

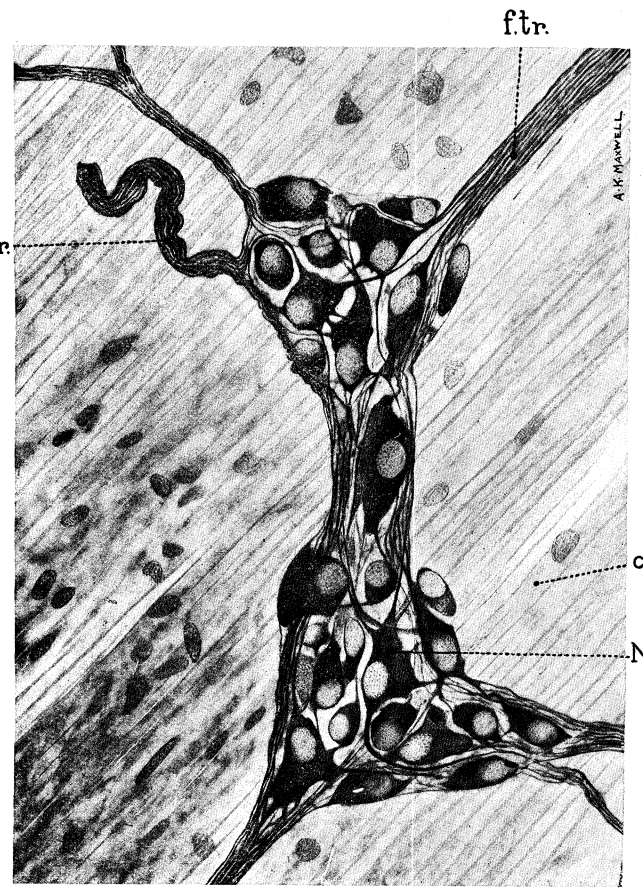
1


N_II
g.f.tr.
N_I
lm.
f.tr.
A.K. MAXWELL

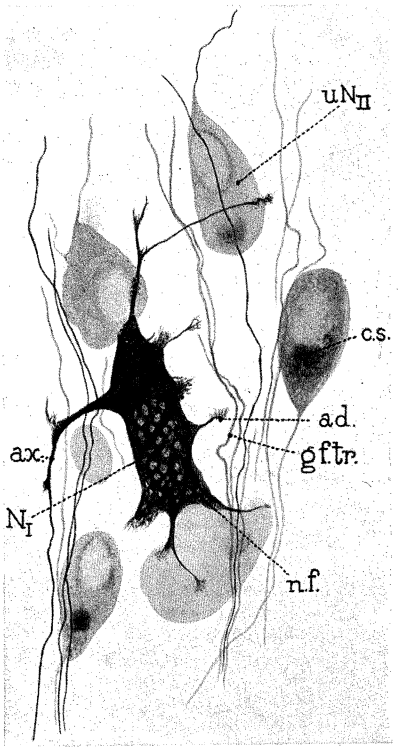
3


cap.
f.tr.
gn.

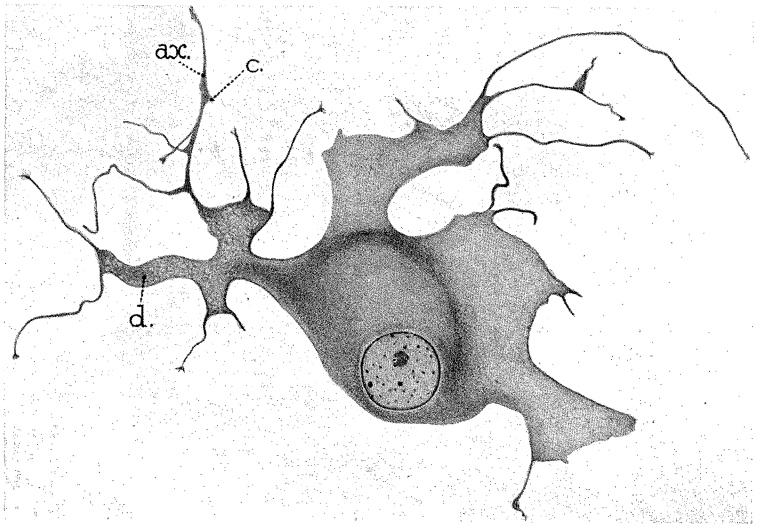
2


f.tr.
c.tr.
A.K. MAXWELL
cm.
N_II

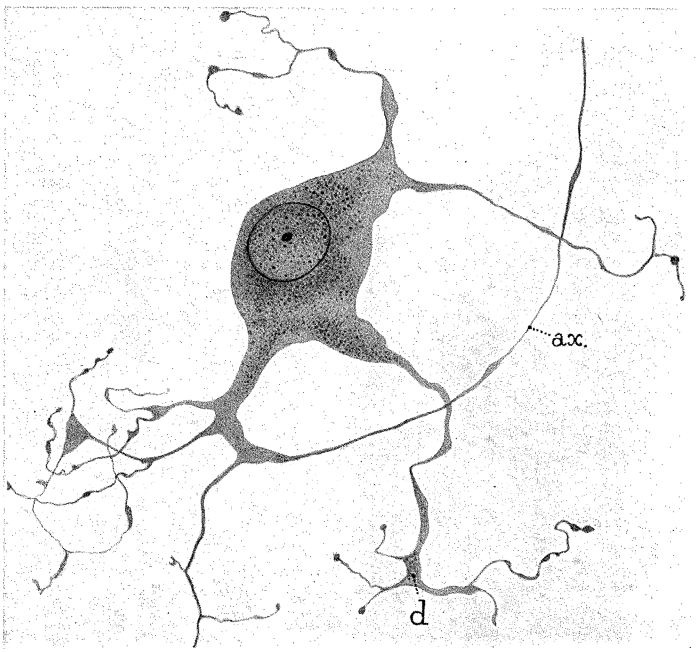
4


uN$_{II}$
c.s.
a.d.
ax.
g.f.tr.
N$_I$
n.f.

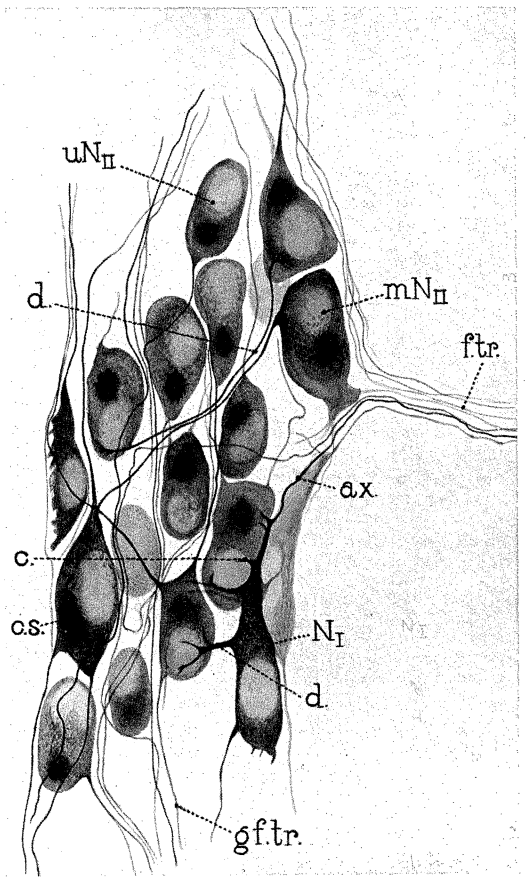
5


ax.
c.
d.

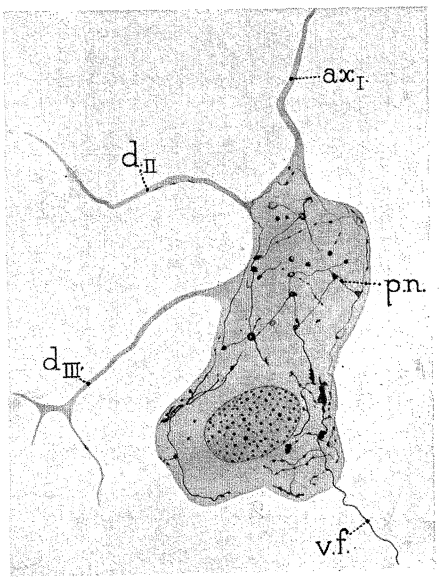
7


ax.
d

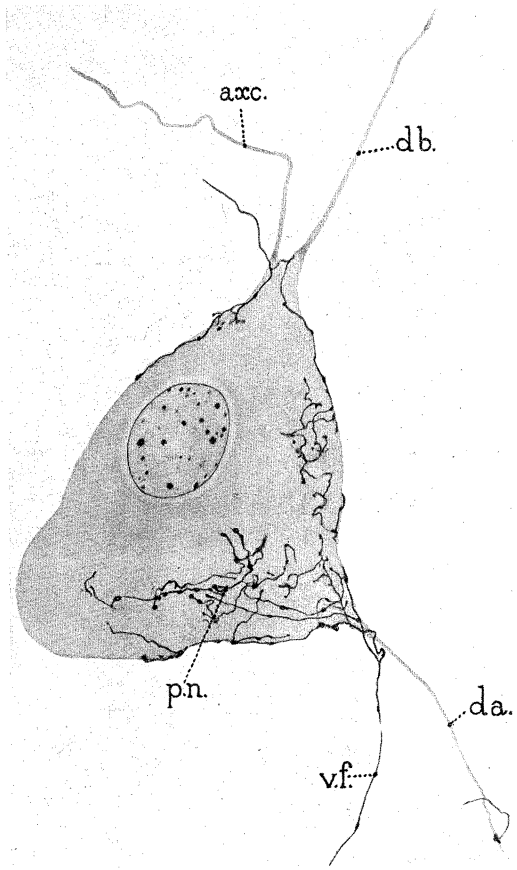
8


uN$_{II}$
d.
mN$_{II}$
f.tr.
ax.
c.
c.s.
N$_I$
d.
g.f.tr.

6


ax$_I$.
d$_{II}$
p.n.
d$_{III}$.
v.f.

9



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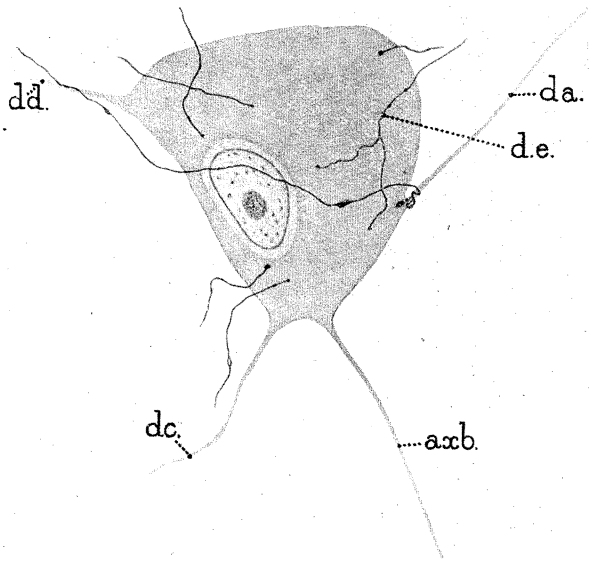

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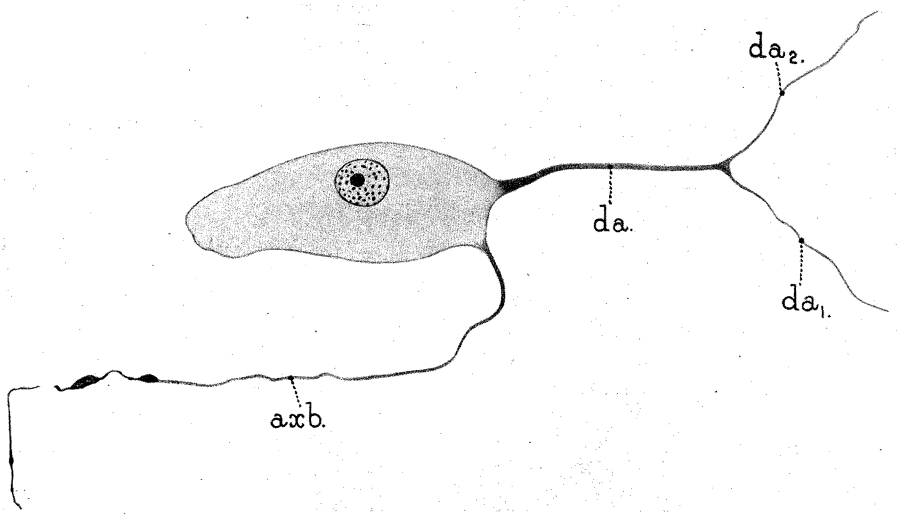

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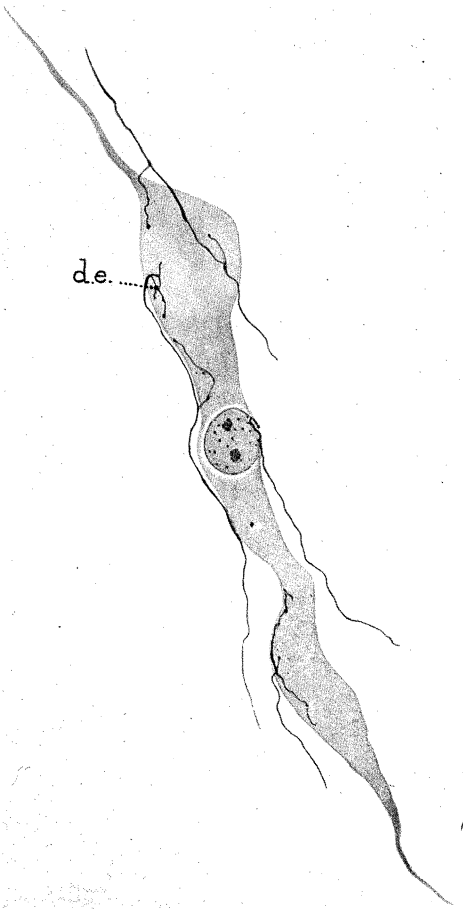

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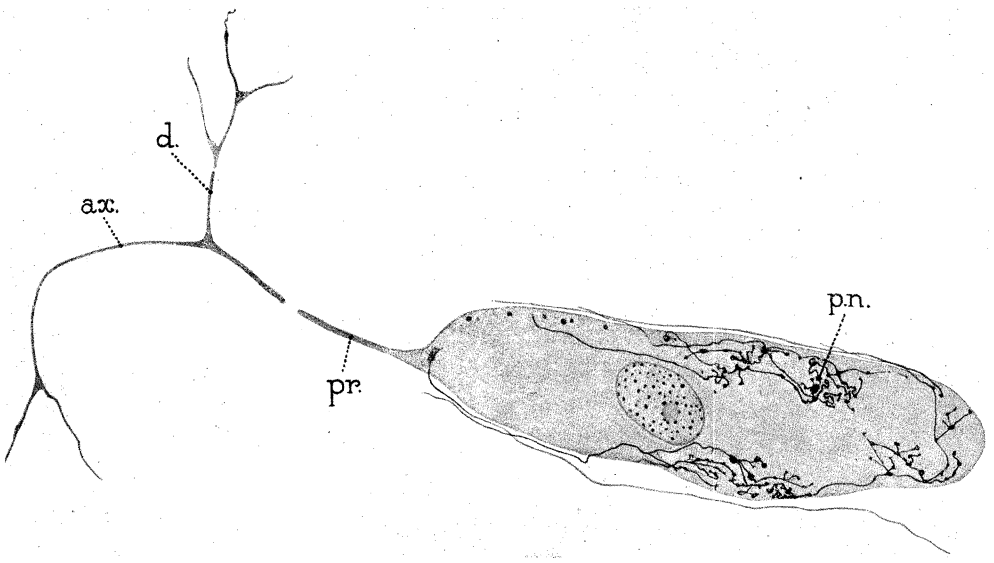

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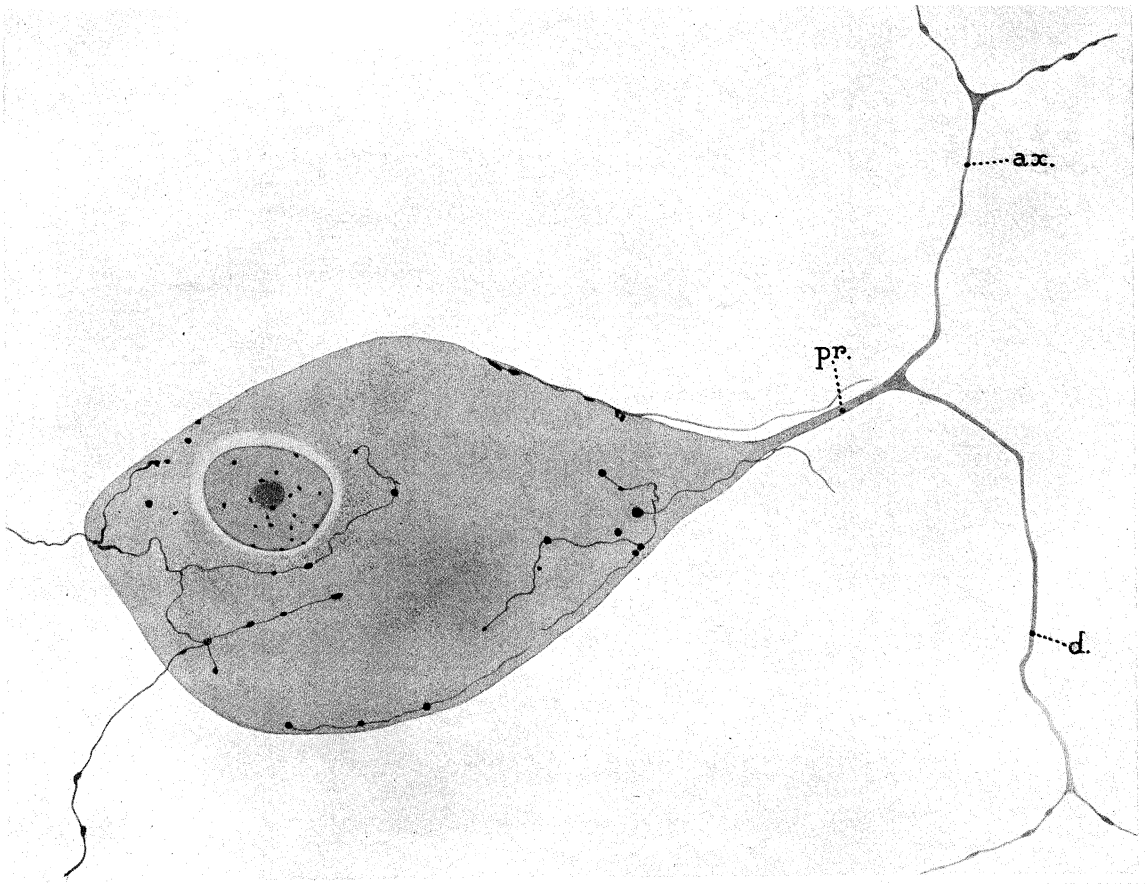

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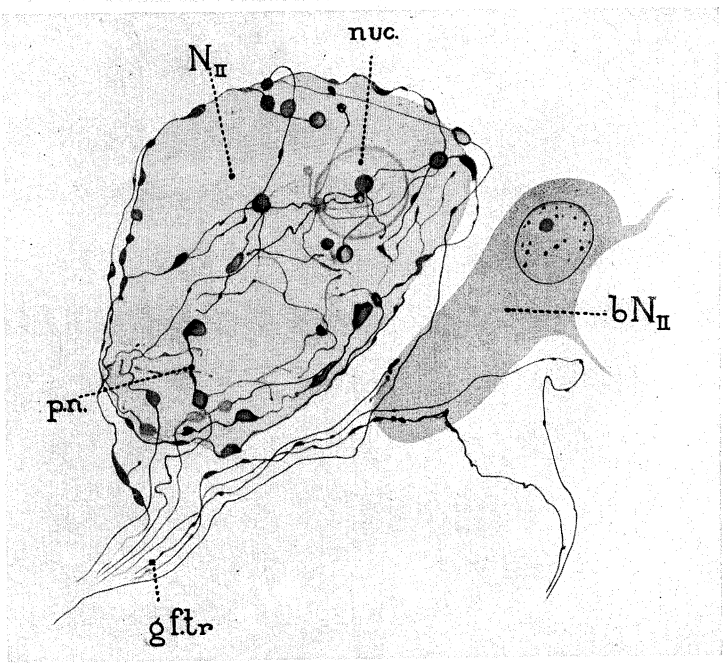

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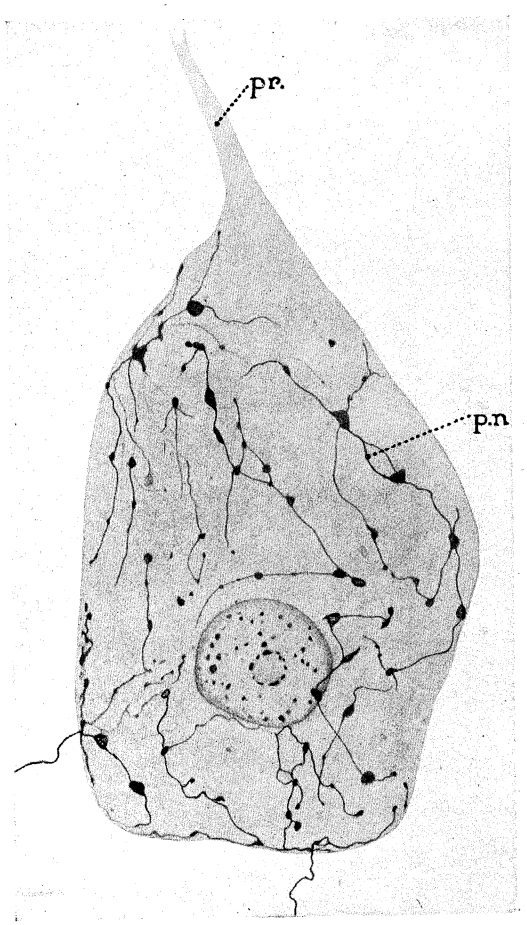

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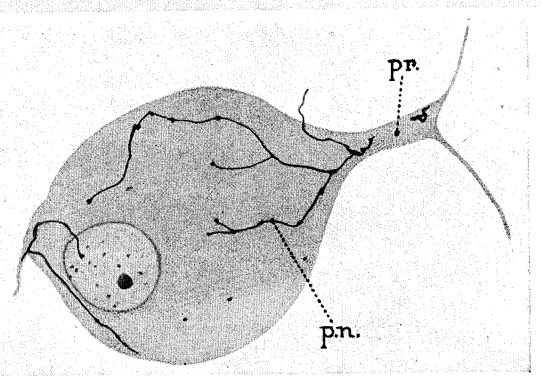

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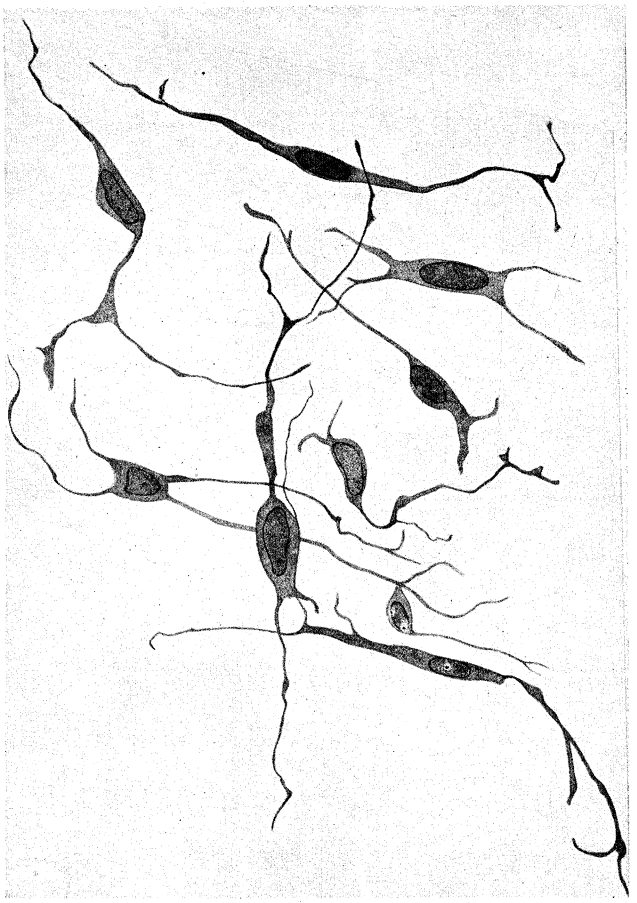

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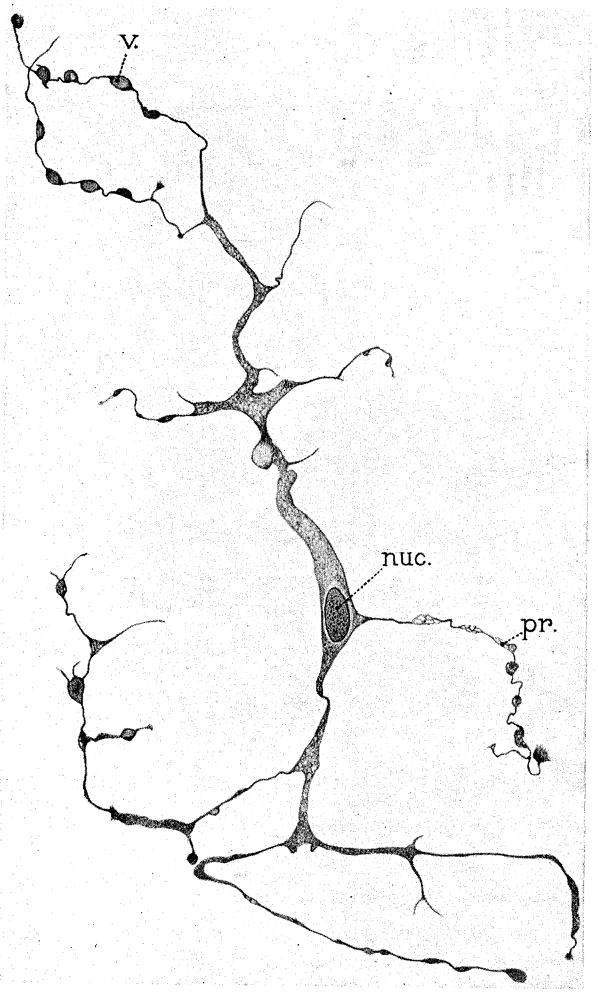

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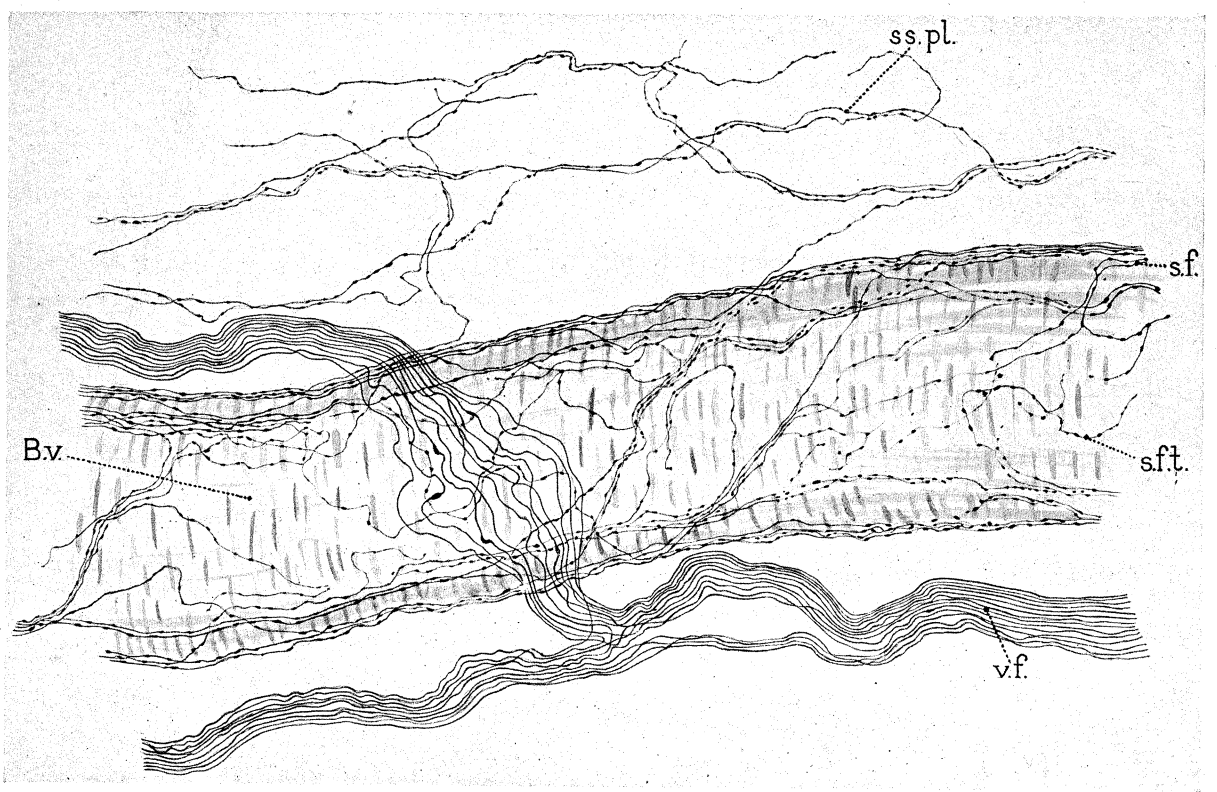

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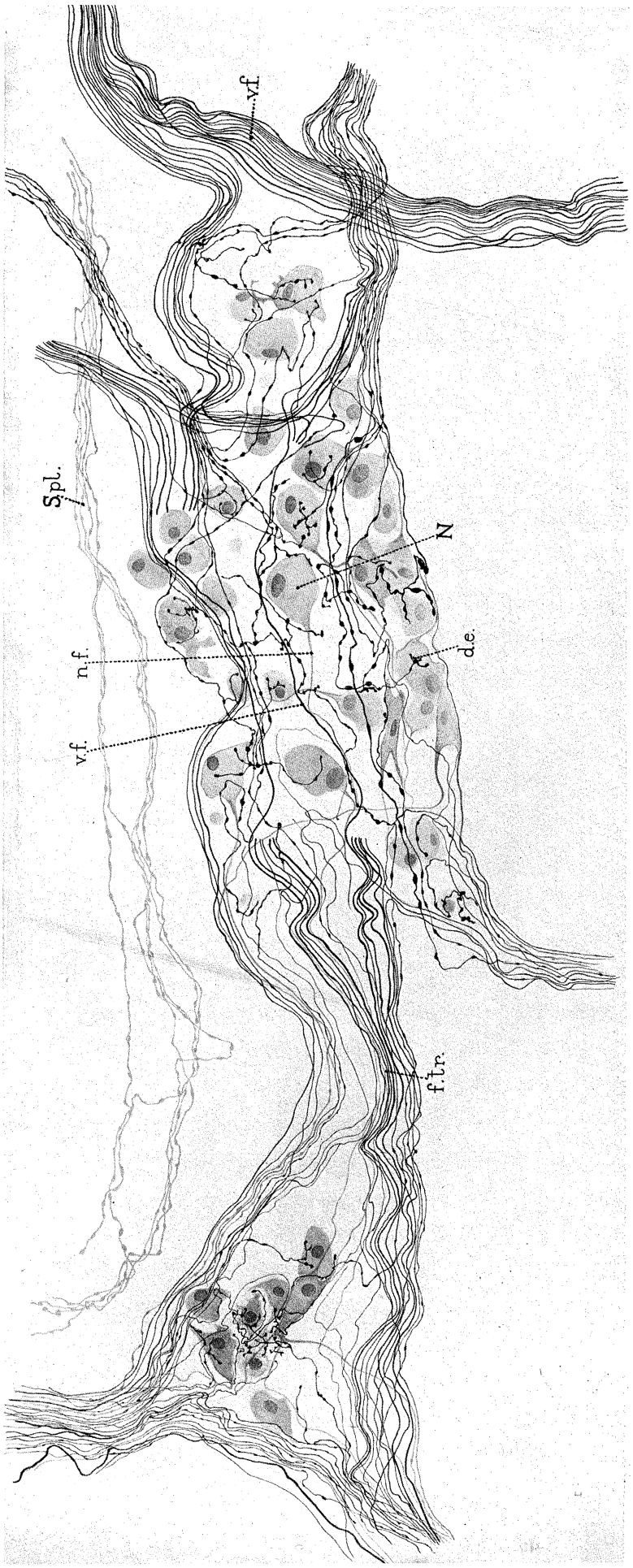

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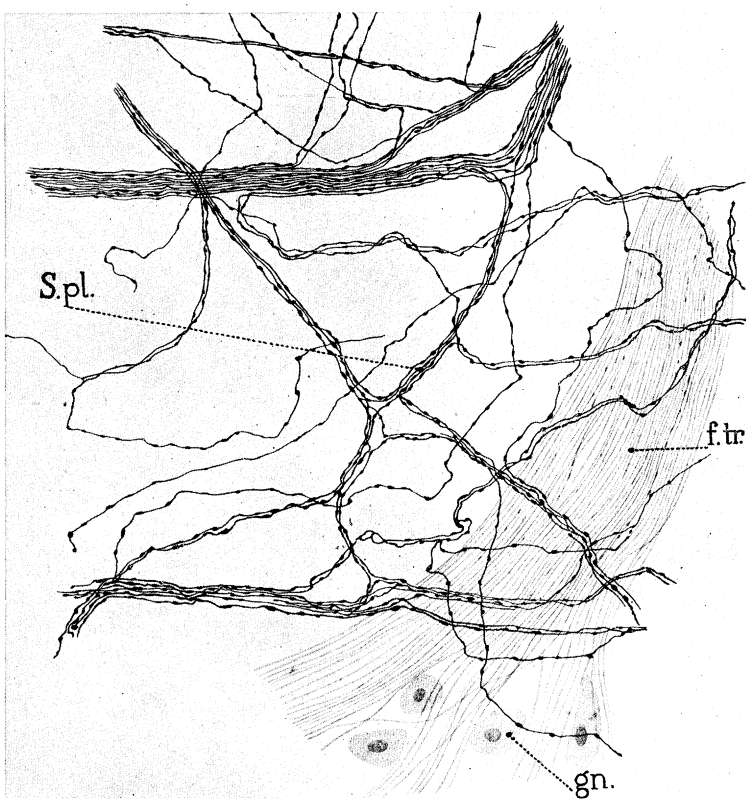

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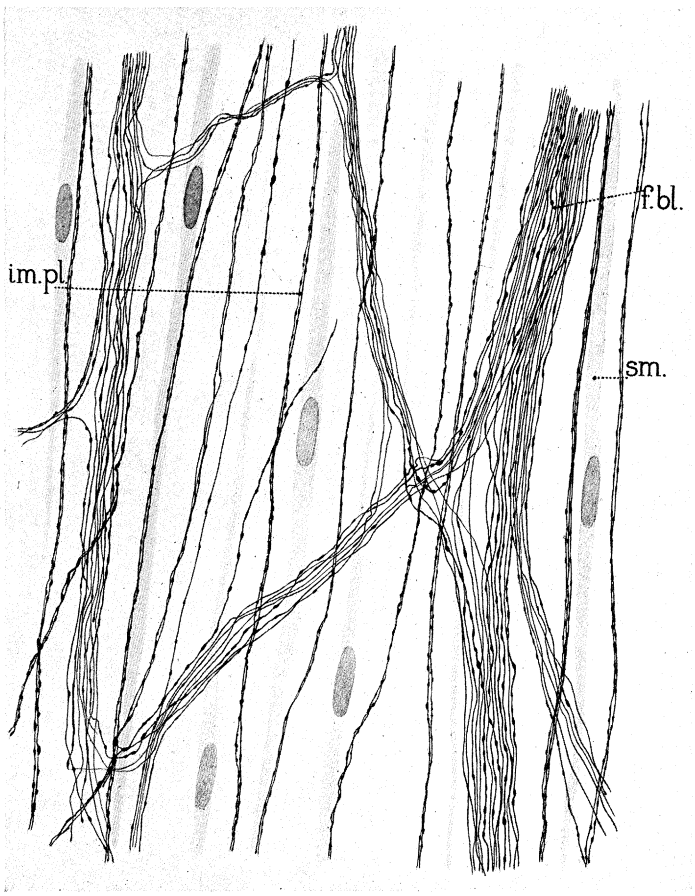

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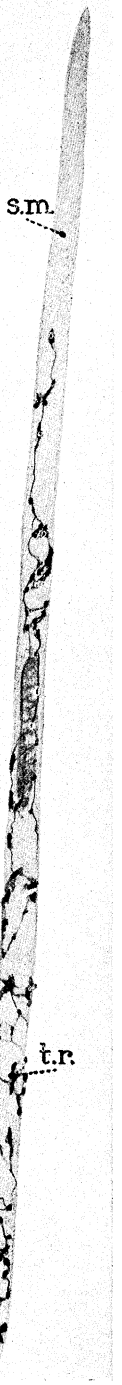

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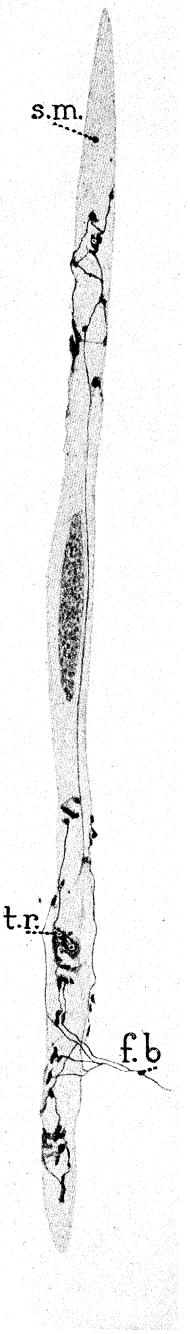

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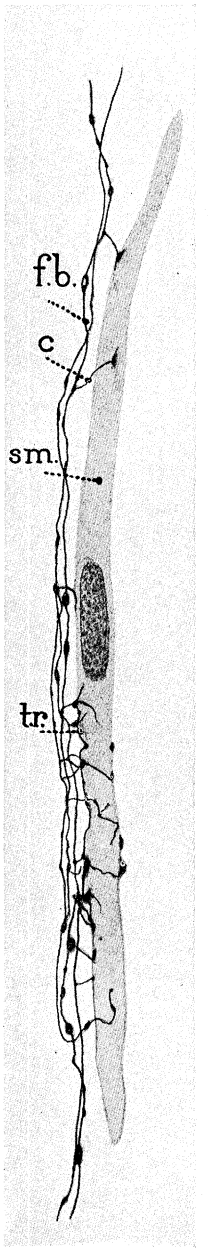

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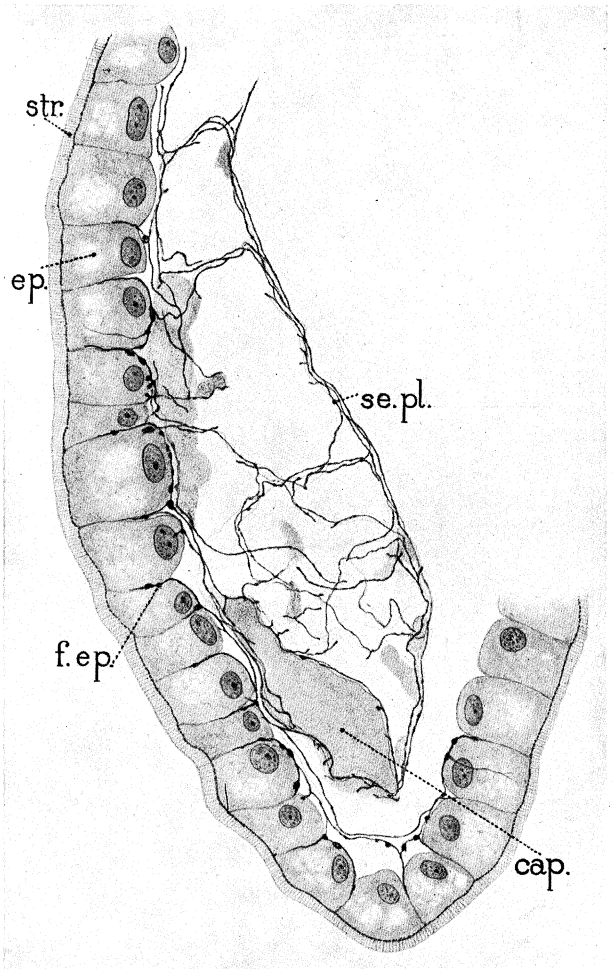

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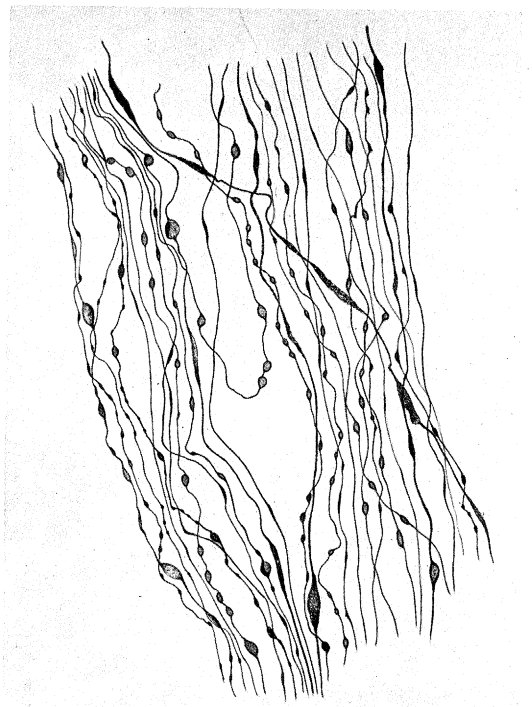

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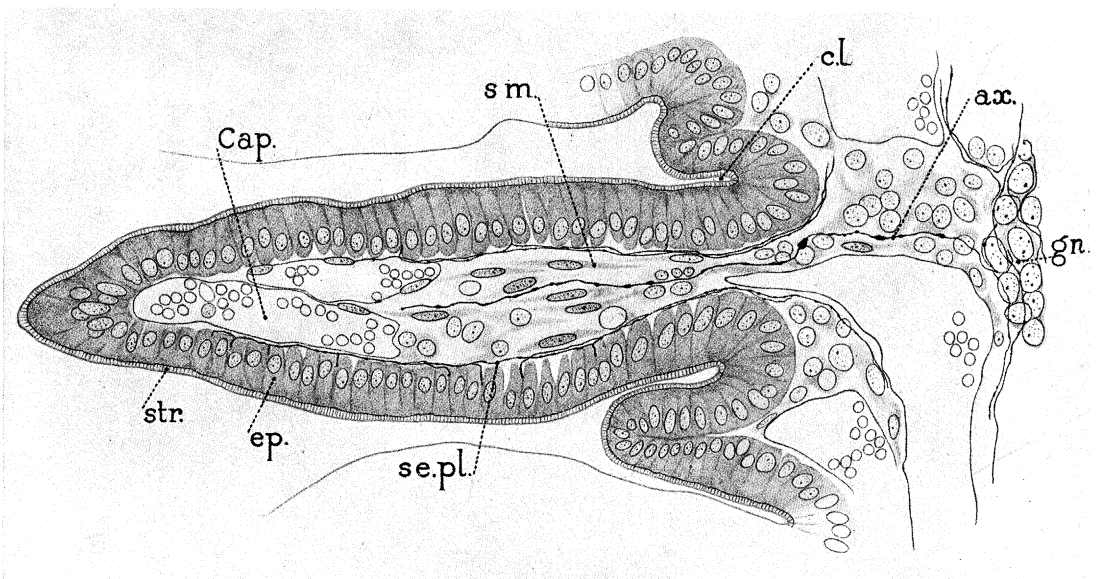


28

FIG. 19.—High-power view of interstitial cell (0·005 × 0·201 mm. in diam.) in relation to the myenteric plexus. Small intestine, Dog. This cell is larger than the majority of interstitial cells. Note the varicosities *v.* and the vacuolated appearance of the cytoplasm. *nuc.*, nucleus. *pr.*, process. × about 600.

FIG. 20.—Portion of the sub-serous coat of the small intestine, Dog. Methylene blue. *B.v.*, blood-vessel. *ss. pl.*, sub-serous plexus formed of sympathetic fibres. *s.f.*, sympathetic fibres. *v.f.*, vagal fibres. *s.f.t.*, sympathetic fibres terminating in the vessel wall. × about 330.

PLATE 31.

FIG. 21.—Part of the myenteric plexus. Stomach, Dog. Methylene blue. *N.*, a nerve cell of the myenteric ganglion. *n.f.*, processes of cells of ganglia. *d.e.*, diffuse endings of intrinsic fibres on cells of ganglia. *f.tr.*, interganglionic fibre tracts. *v.f.*, vagal fibres. *S.pl.*, sympathetic plexus which is distinct from the myenteric plexus. × about 310.

PLATE 32.

FIG. 22.—Fine plexus of sympathetic fibres lying internal to the myenteric plexus between the circular and longitudinal muscle coats. Colon, Dog. Methylene blue. *S.pl.*, sympathetic plexus. *f.tr.*, fibre tract of myenteric plexus. *gn.*, ganglion of myenteric plexus. × about 300.

FIG. 23.—Plexus of fibres in the longitudinal muscle coat. Small intestine, Dog. Methylene blue. *sm.*, smooth muscle cells. *f.bl.*, fibre-bundles from the myenteric plexus. *im.pl.*, intramuscular plexus, × about 450.

FIGS. 24 AND 25.—Endings of the fibres of the intramuscular plexus on smooth muscle cells in the circular muscle coat. Small intestine, Rabbit. Methylene blue. *sm.*, smooth muscle cell. *f.b.*, fibre giving rise to ending. *t.r.*, terminal ramification of fibre on the smooth muscle cell. × about 750.

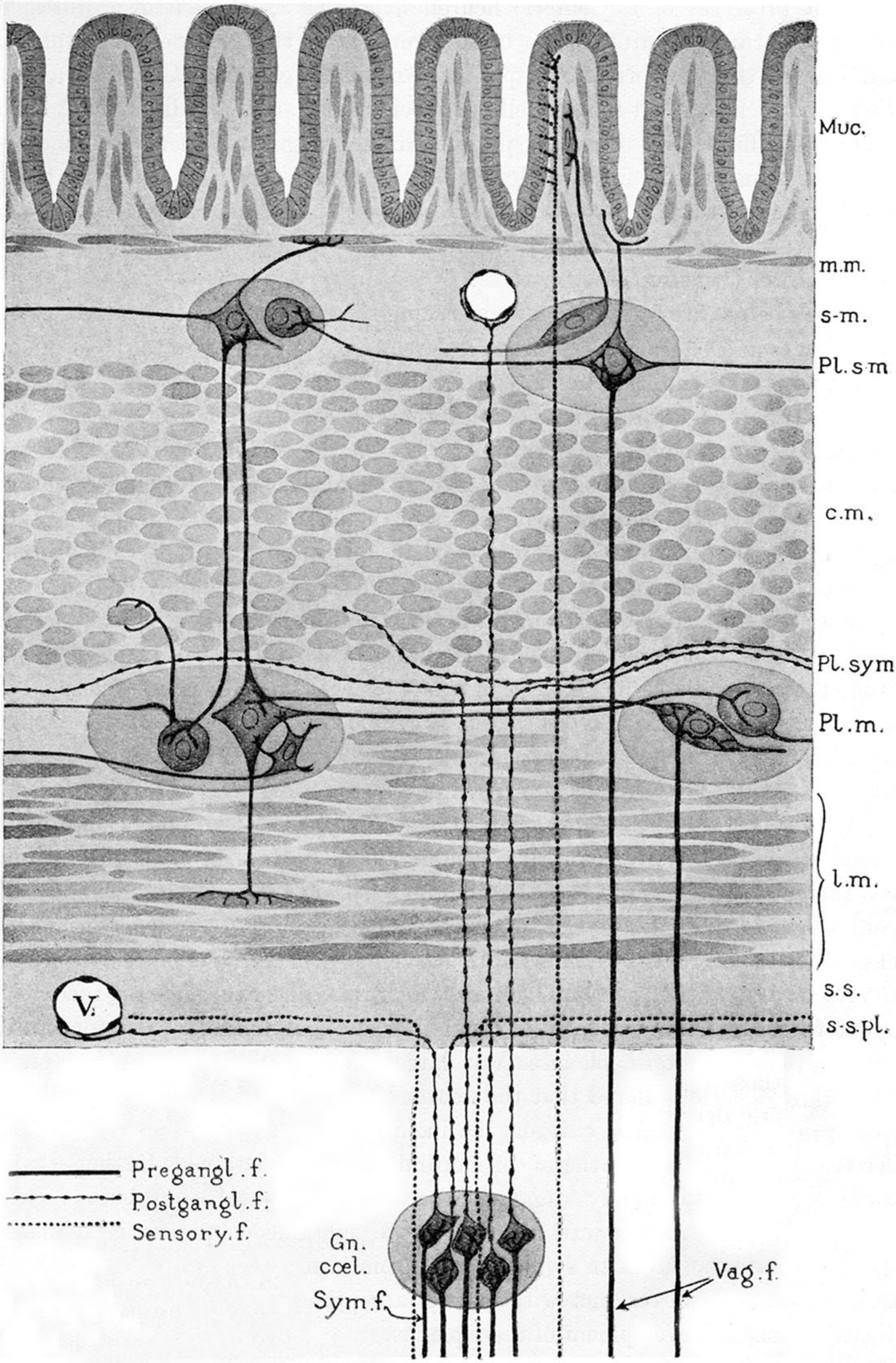
FIG. 26.—Ending on smooth muscle cell, of a different form to those in figs. 24 and 25. Circular muscle coat. Small intestine, Rabbit. Methylene blue. *f.b.*, fibre of intramuscular plexus. *c.*, collaterals given off by fibres and forming a ramification, *t.r.*, on the muscle cell, *sm.* × about 750.

PLATE 33.

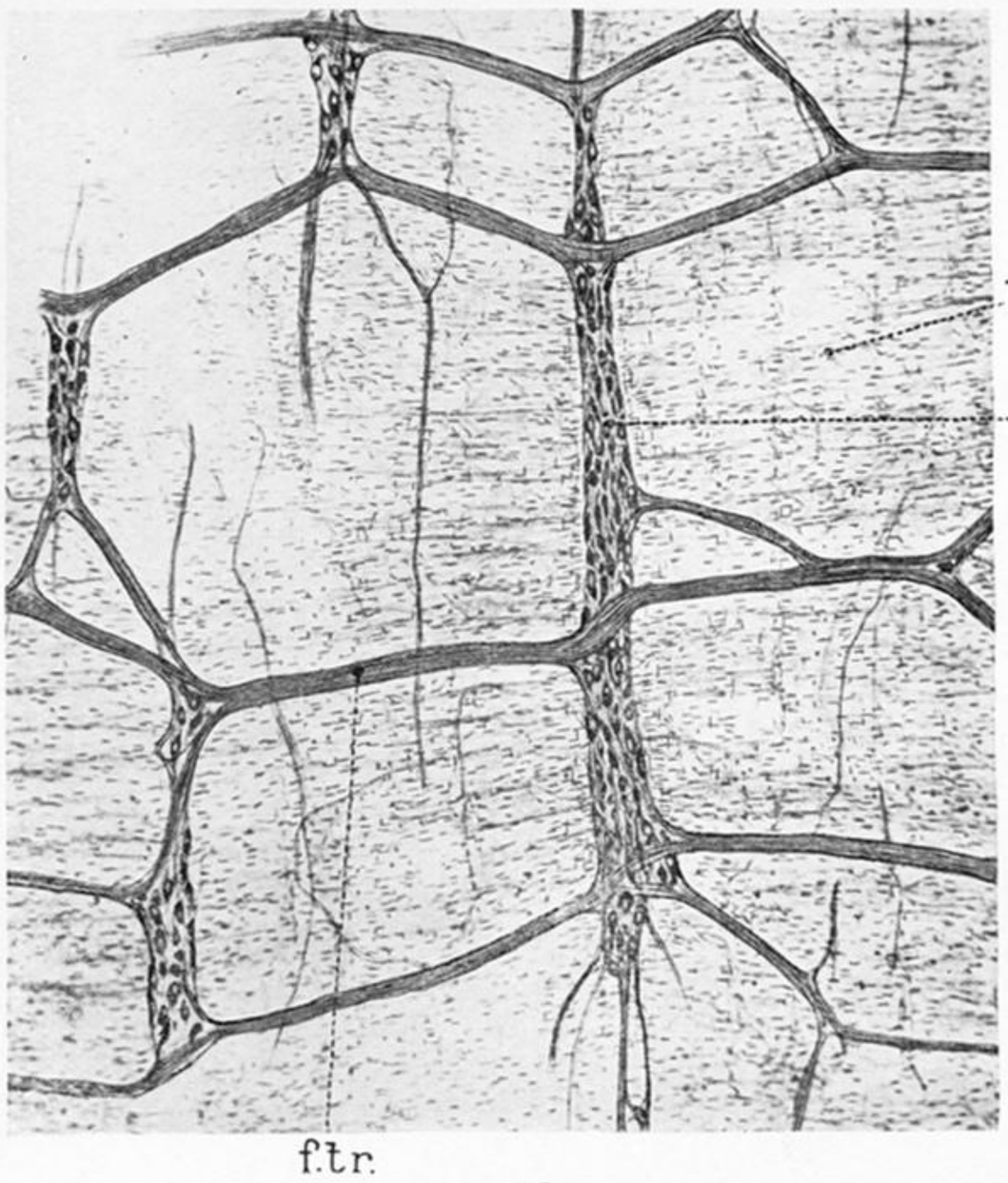
FIG. 27.—Terminations of sensory fibres between the epithelial cells of a villus. Small intestine, new-born Rabbit. Silver method of DE CASTRO. *ep.*, epithelium of villus. *str.*, striated free border. *se.pl.*, sub-epithelial plexus. *f.ep.*, fibrils which penetrate between the epithelial cells. *cap.*, capillary. × about 560.

FIG. 28.—Section through the mucosa, small intestine, new-born Rabbit, showing a fibre from the sub-mucous plexus running up to terminate in relation to the smooth muscle fibres of the villus. Silver method of DE CASTRO. *ep.*, epithelium. *str.*, striated free border. *cap.*, capillary. *sm.*, smooth muscle cells. *c.L.*, crypt of LIEBERKÜHN. *gn.*, ganglion of the sub-mucous plexus. *ax.*, axone of ganglion cell. *se.pl.*, sub-epithelial plexus. × about 260.

FIG. 29.—Portion of interganglionic fibre-tract, from the myenteric plexus, small intestine, Cat, to show the variations in the form of the fibres. Methylene blue. × about 600.



TEXT-FIG. 1.—Diagrammatic representation of the relations of the elements of the gut-plexuses as seen in longitudinal section of the gut-wall. *Muc.*, mucosa. *m.m.*, muscularis mucosæ. *s-m.*, sub-mucosa. *Pl. s-m.*, sub-mucous plexus. *c.m.*, circular muscle. *Pl. sym.*, sympathetic plexus. *Pl. m.*, myenteric plexus. *l.m.*, longitudinal muscle. *ss.pl.*, sub-serous plexus. *s.s.*, sub-serosa. *Gn. cœl.*, cœliac ganglion. *Sym. f.*, sympathetic fibres. *vag. f.*, vagal fibres. *V.*, vessel.



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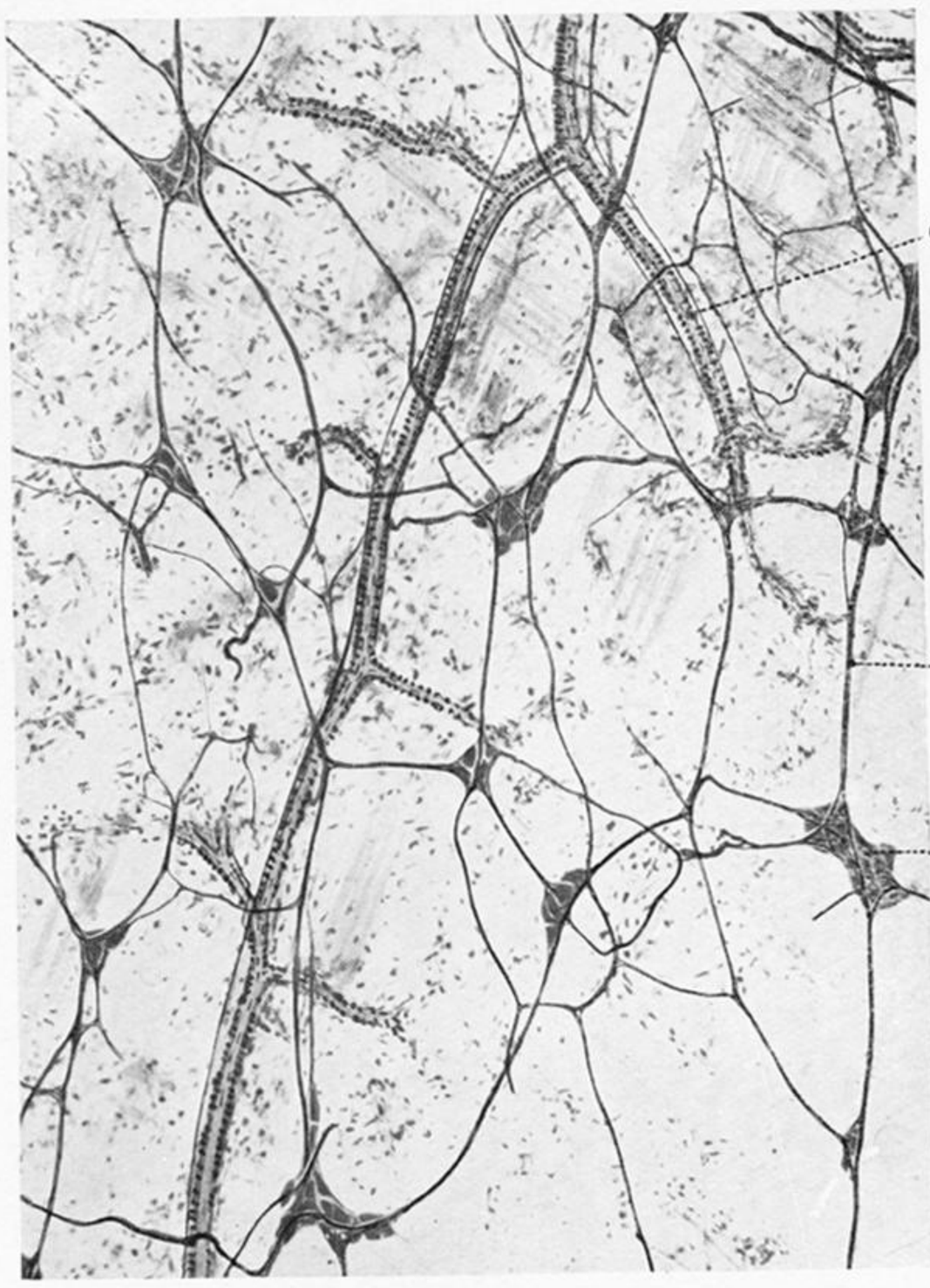

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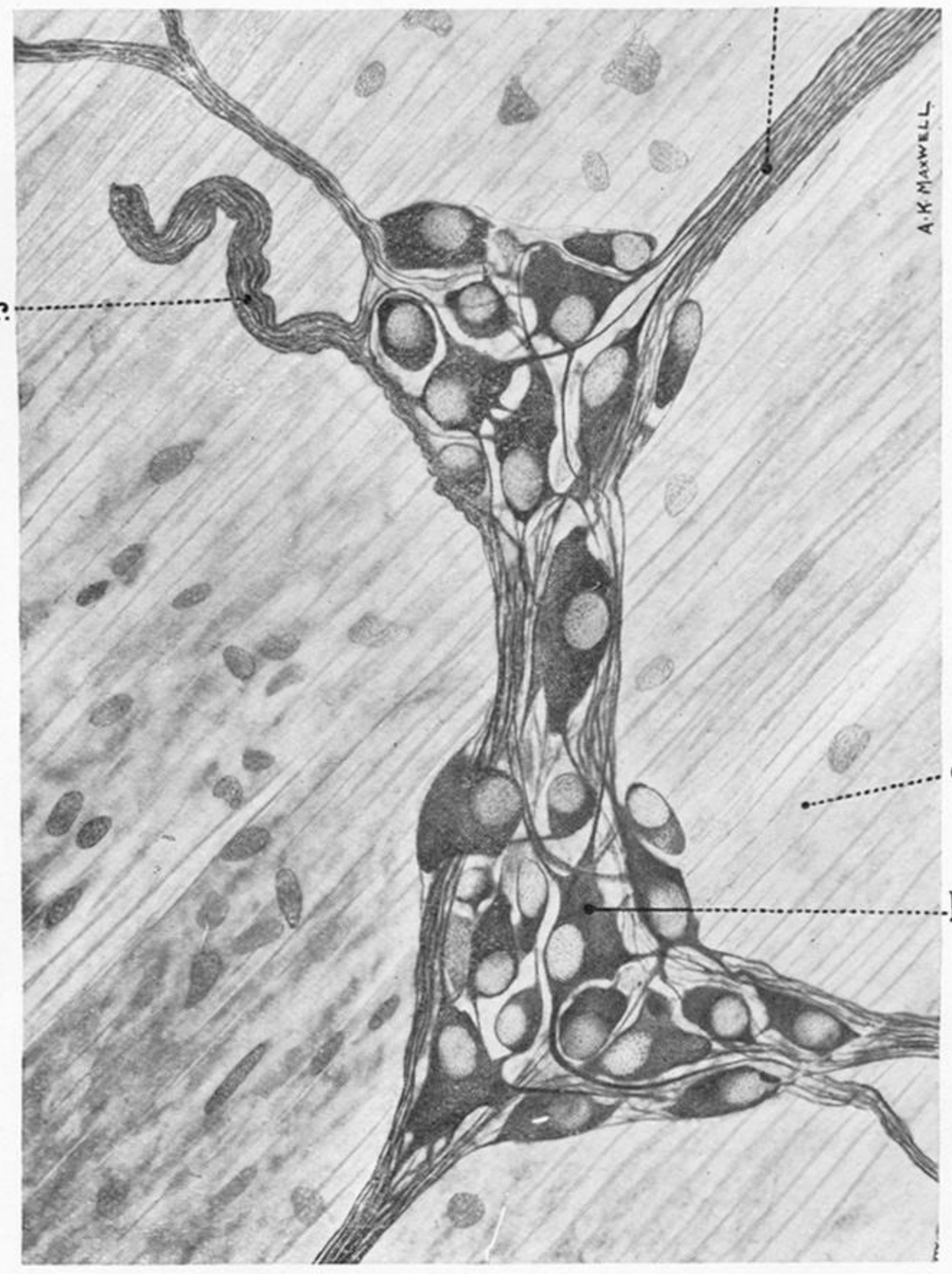

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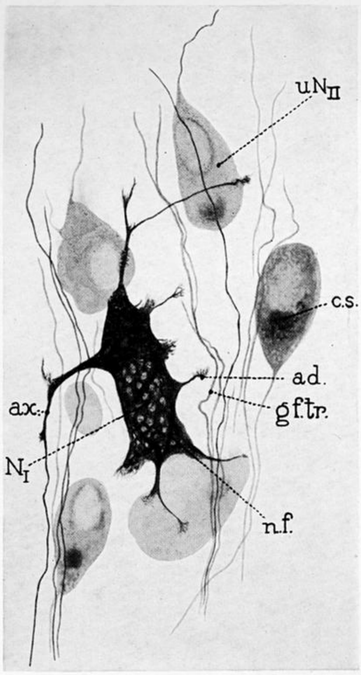
Plate 26.

Fig. 1.—General view of the myenteric plexus from the small intestine of Cavia. Silver nitrate. *gn.*, ganglion. *f. tr.*, interganglionic fibre-tract. *lm.*, longitudinal muscle coat. × about 40.

Fig. 2.—General view of the sub-mucous plexus from the small intestine of Cavia. Silver nitrate. *gn.*, ganglion. *cap.*, capillary. *f. tr.*, interganglionic fibre-tract. × about 75.

Fig. 3.—Ganglion of the myenteric plexus from the small intestine of Cavia. Silver nitrate. N_I, neurone of Type I. N_{II}., neurone of Type II. *f. tr.*, interganglionic fibre-tract. *lm.*, longitudinal muscle coat. *gf. tr.*, intraganglionic fibres. × about 335.

Fig. 4.—Ganglion of sub-mucous plexus from the small intestine of Rabbit. Silver nitrate. N_{II}., neurone of Type II. *f. tr.*, interganglionic fibre-tract. *c. tr.*, fibre-tract connecting sub-mucous and myenteric plexuses (in this case broken in making the preparation). *cm.*, circular muscle. × about 335.



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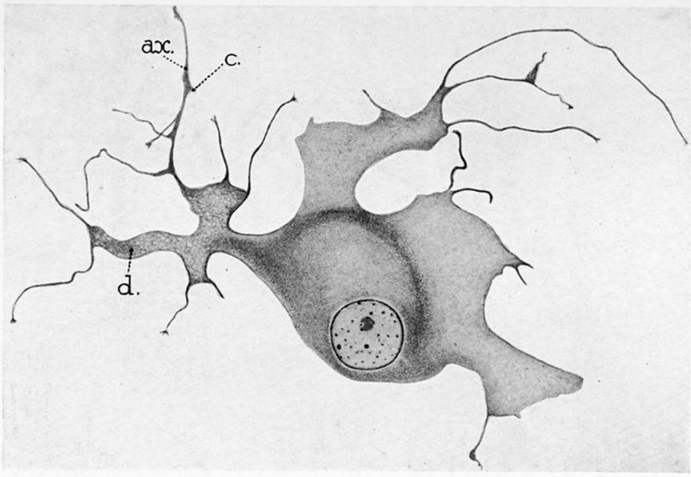

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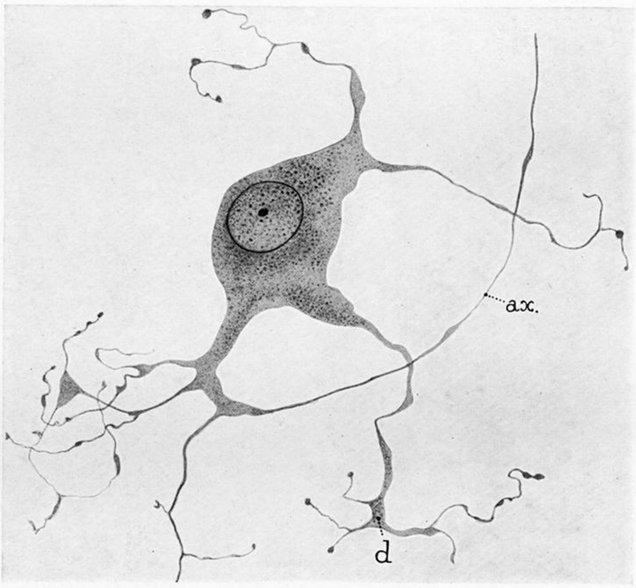

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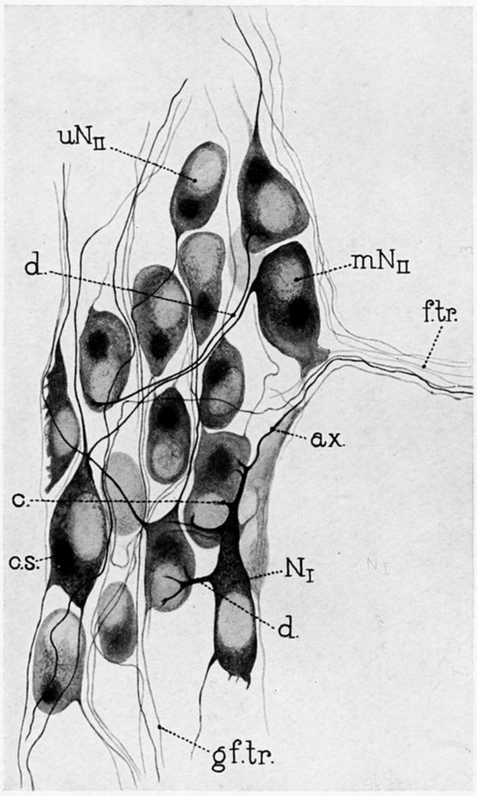

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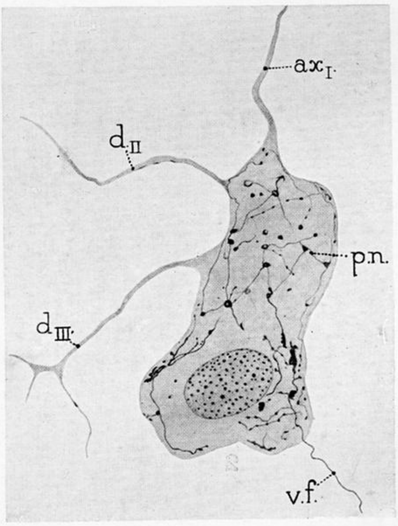

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Plate 27.

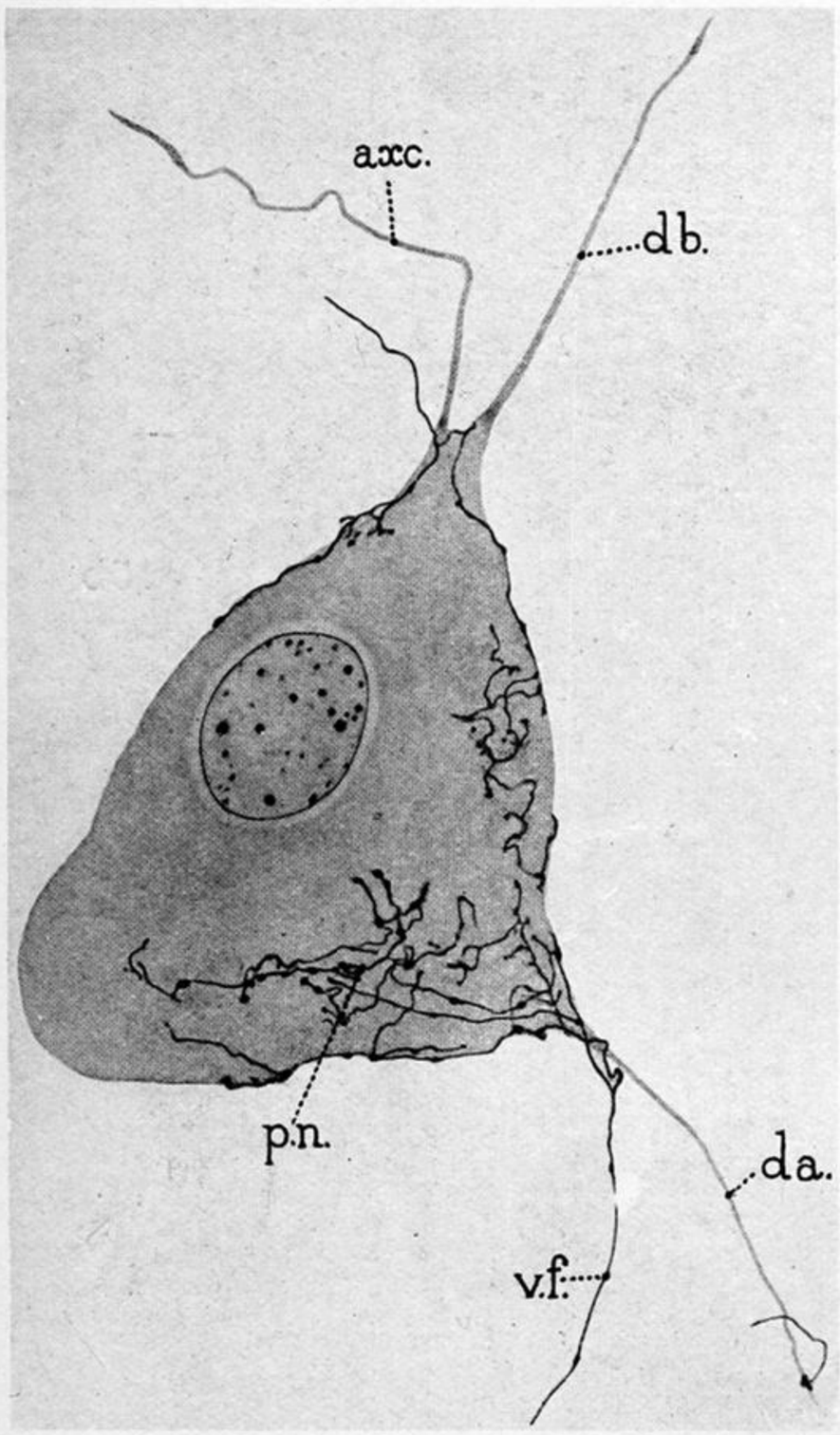
Fig. 5.—Nerve cells from a myenteric ganglion. Small intestine, Cavia. Silver nitrate. N_I., neurone of Type I. uN_{II}., unipolar cell of Type II. *ax.*, axone. *c.s.*, centrosphere. *n.f.*, neurofibrillæ. *gf. tr.*, intraganglionic fibres. *ad.*, dendrite terminating in a brush-like ending without previous branching. × about 450.

Fig. 6.—Cells from another myenteric ganglion. Small intestine, Cavia. Silver nitrate. N_I., cell of Type I. mN_{II}., multipolar cell of Type II. uN_{II}., unipolar cell. *ax.*, axone. *c.*, collateral. *d.*, dendrite. *gf. tr.*, intraganglionic fibres. *c.s.*, centrosphere. *f. tr.*, interganglionic fibre-tract. × about 410.

Fig. 7.—Multipolar cell of Type I (0·025 × 0·03 mm. in diam.) from the myenteric plexus of the small intestine, Dog. Methylene blue. *d.*, dendrite. *ax.*, axone, originating in this case from the tip of a broad flattened dendrite. *c.*, collateral. Note the vacuolated appearance of the cell cytoplasm. × about 800.

Fig. 8.—Multipolar cell of Type I (probably corresponding to Type III of Dogiel) from the myenteric plexus of the small intestine, Dog. Methylene blue. *d.*, branching dendrite ending in varicose enlargements. *ax.*, axone originating from one of the broad flattened dendrites. Note the granular cytoplasm of the cell body. × about 600.

Fig. 9.—Multipolar cell of Type II (0·054 × 0·028 mm. in diam.) from the myenteric plexus of the small intestine, Dog. Methylene blue. *p.n.*, pericellular arborization round body of cell. *v.f.*, vagal fibre giving rise to arborization. ax_I., axone passing out to terminate in the musculature. d_{II}., dendrite which is lost to sight in the fibre-tract. d_{III}., dendrite, the branches of which terminate on the ganglion cells. × about 800.



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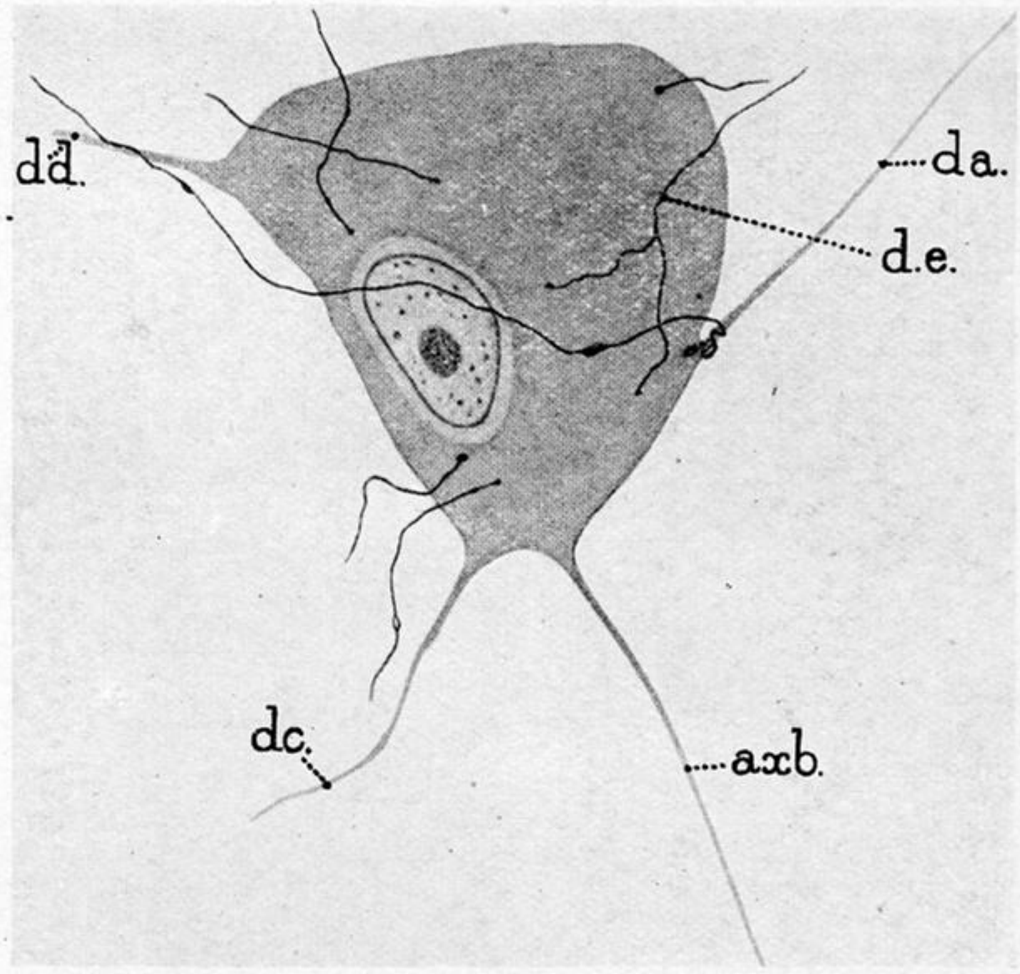

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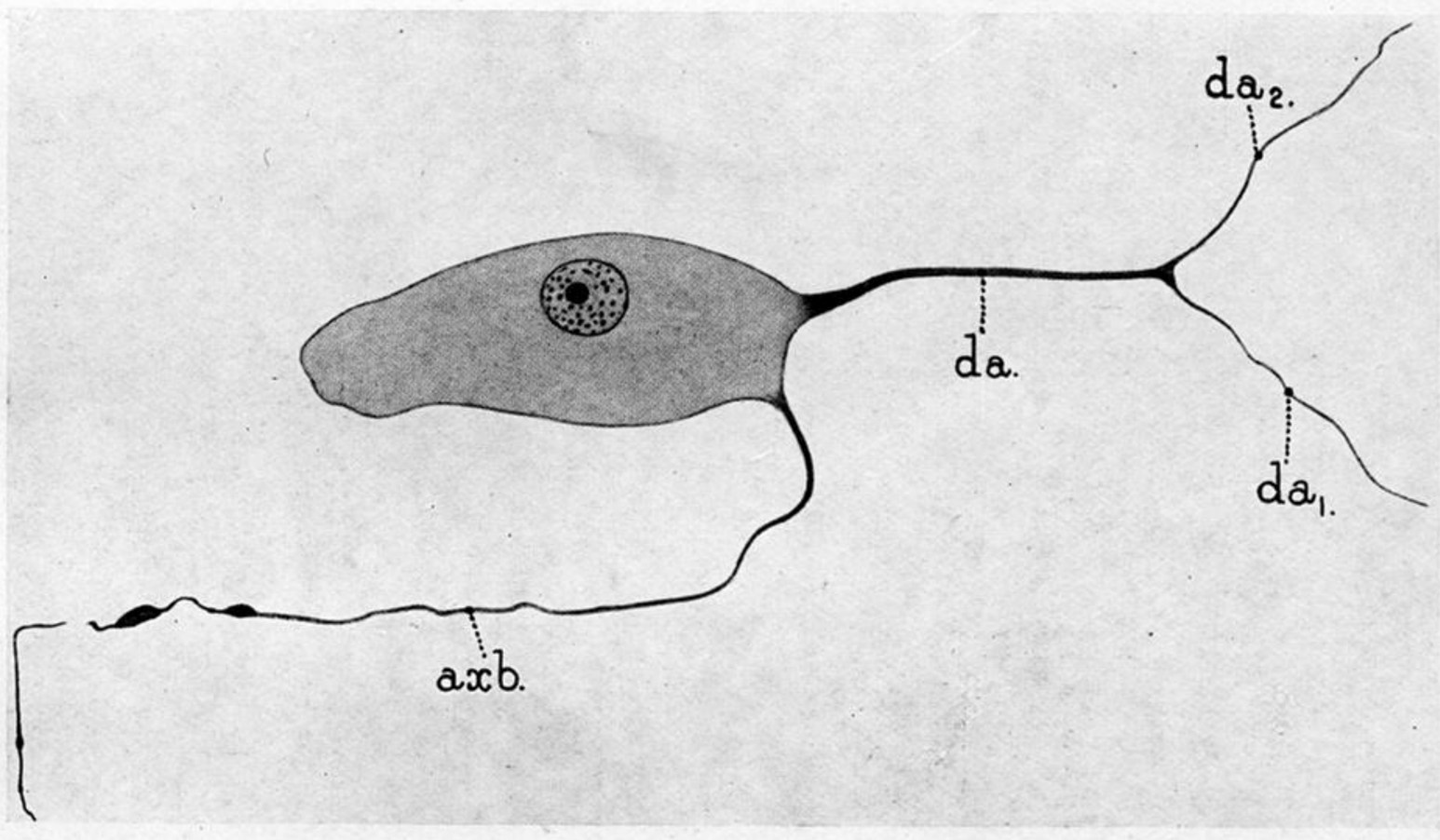

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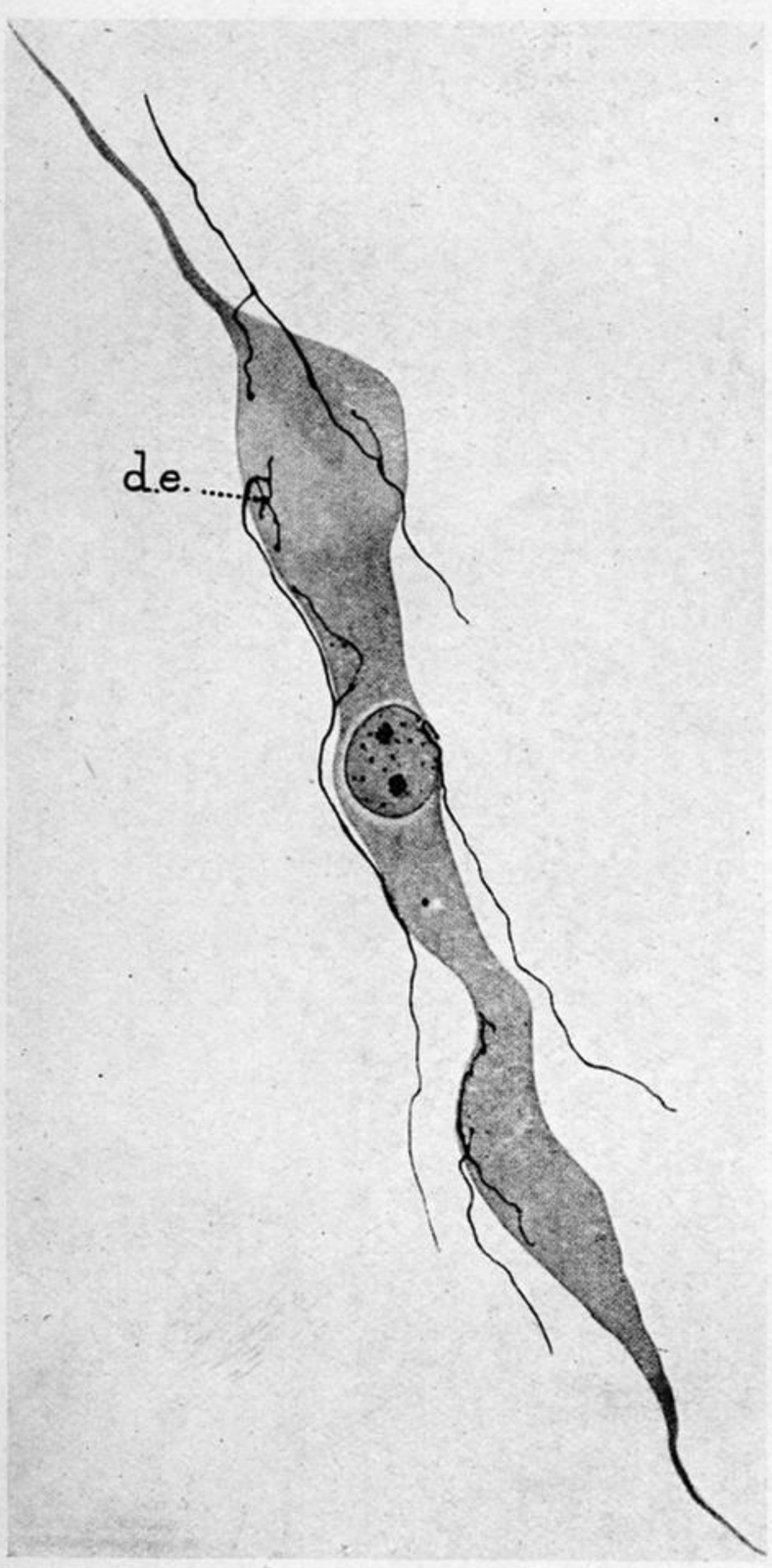

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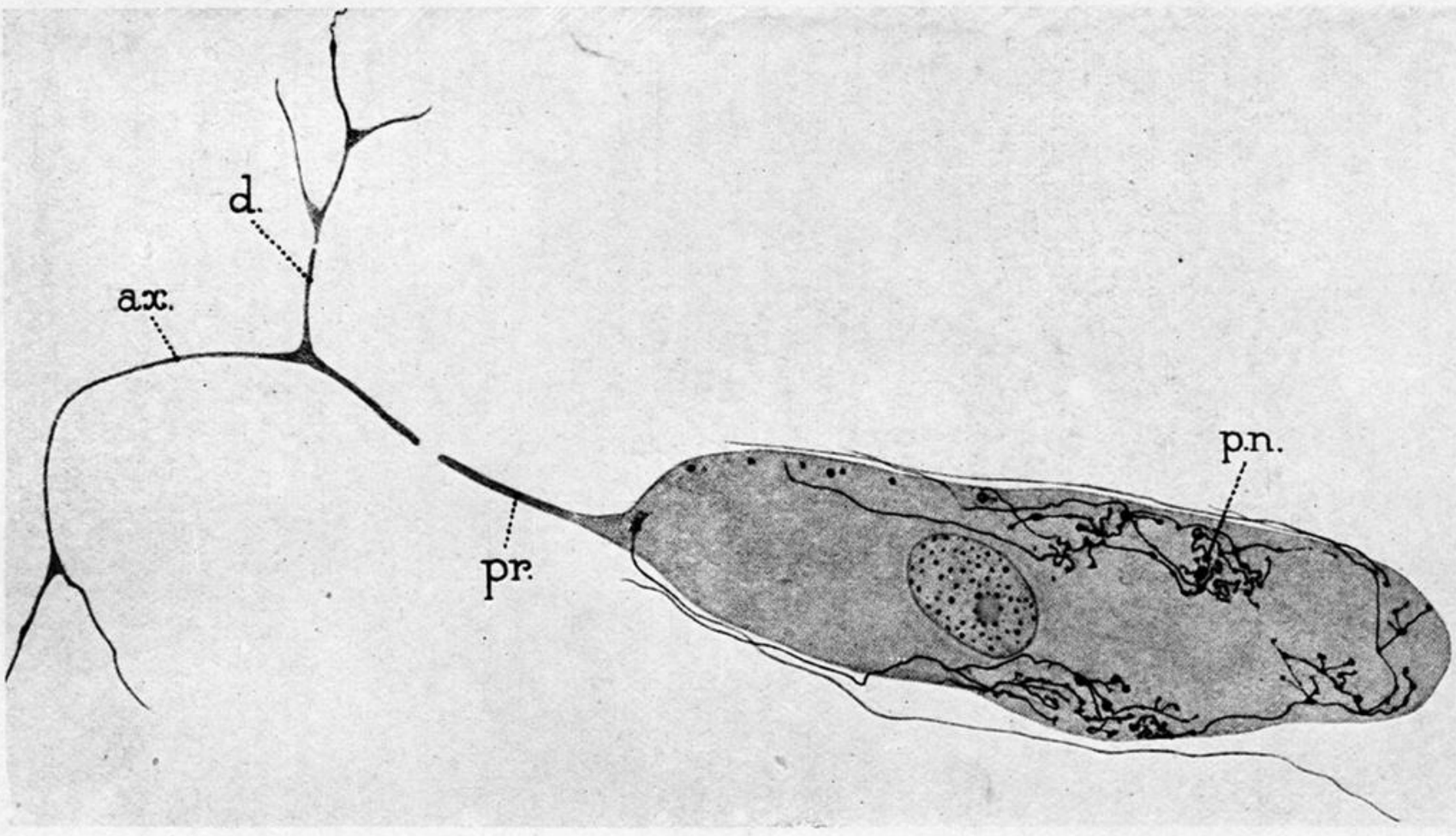

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Plate 28.

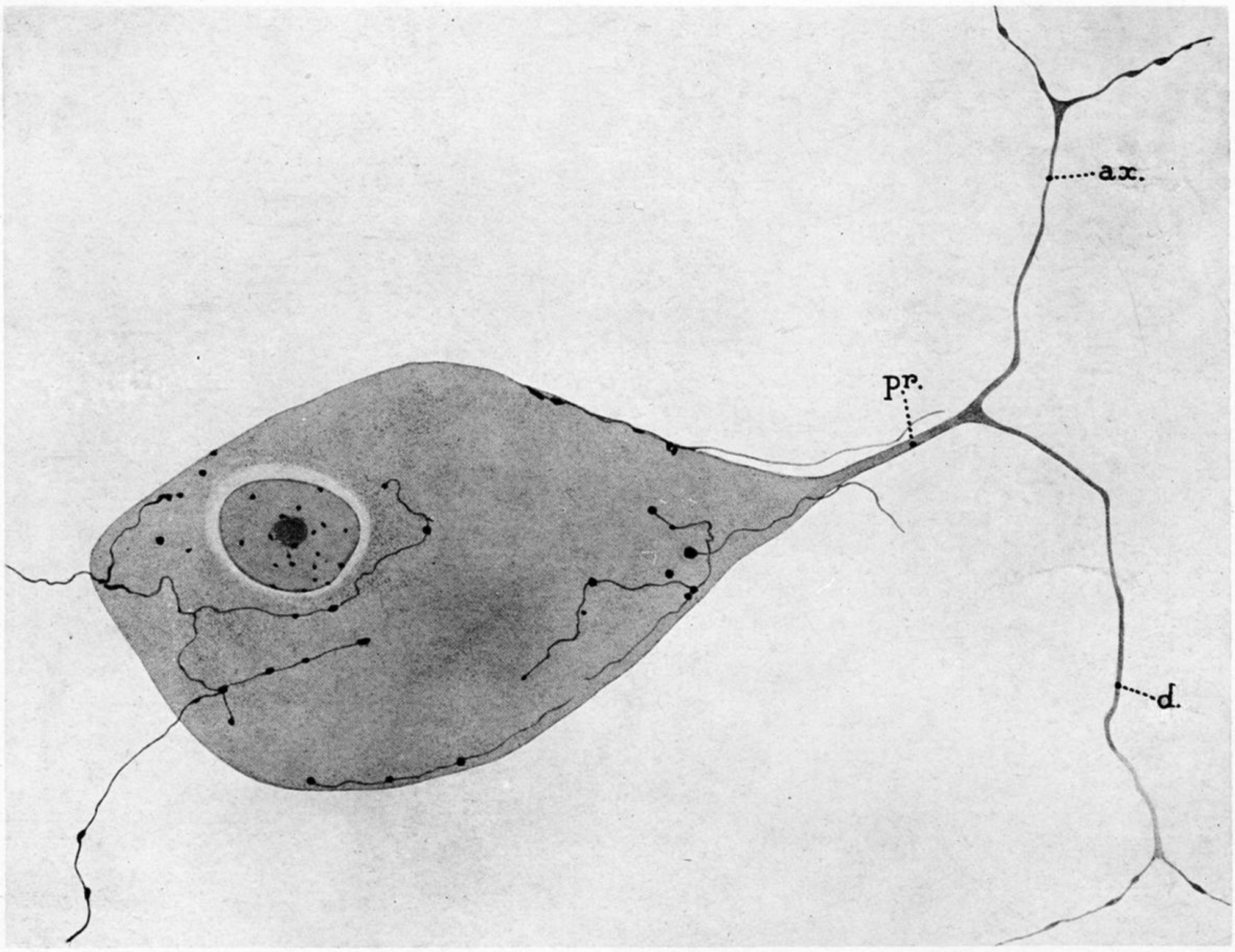
Fig. 10.—Multipolar cell of Type II (0·053 × 0·04 mm. in diam.) from the myenteric plexus of the small intestine, Dog. Methylene blue. *p.n.*, pericellular network, incompletely impregnated. *v.f.*, vagal fibre ending in pericellular network. *da.* and *db.*, dendrites which are lost to view in fibre-tracts. *axc.*, axone passing out to terminate in the musculature. × about 900.

Fig. 11.—Multipolar cell of Type II from the myenteric plexus of the small intestine, Dog. Methylene blue. *da.* and *dd.*, dendrites terminating on ganglion cells in adjacent ganglia. *axb.*, axone terminating in the smooth muscle. *dc.*, dendrite which is lost in fibre-tract. Note the numerous diffuse endings, *d.e.*, on the cell body. × about 800.

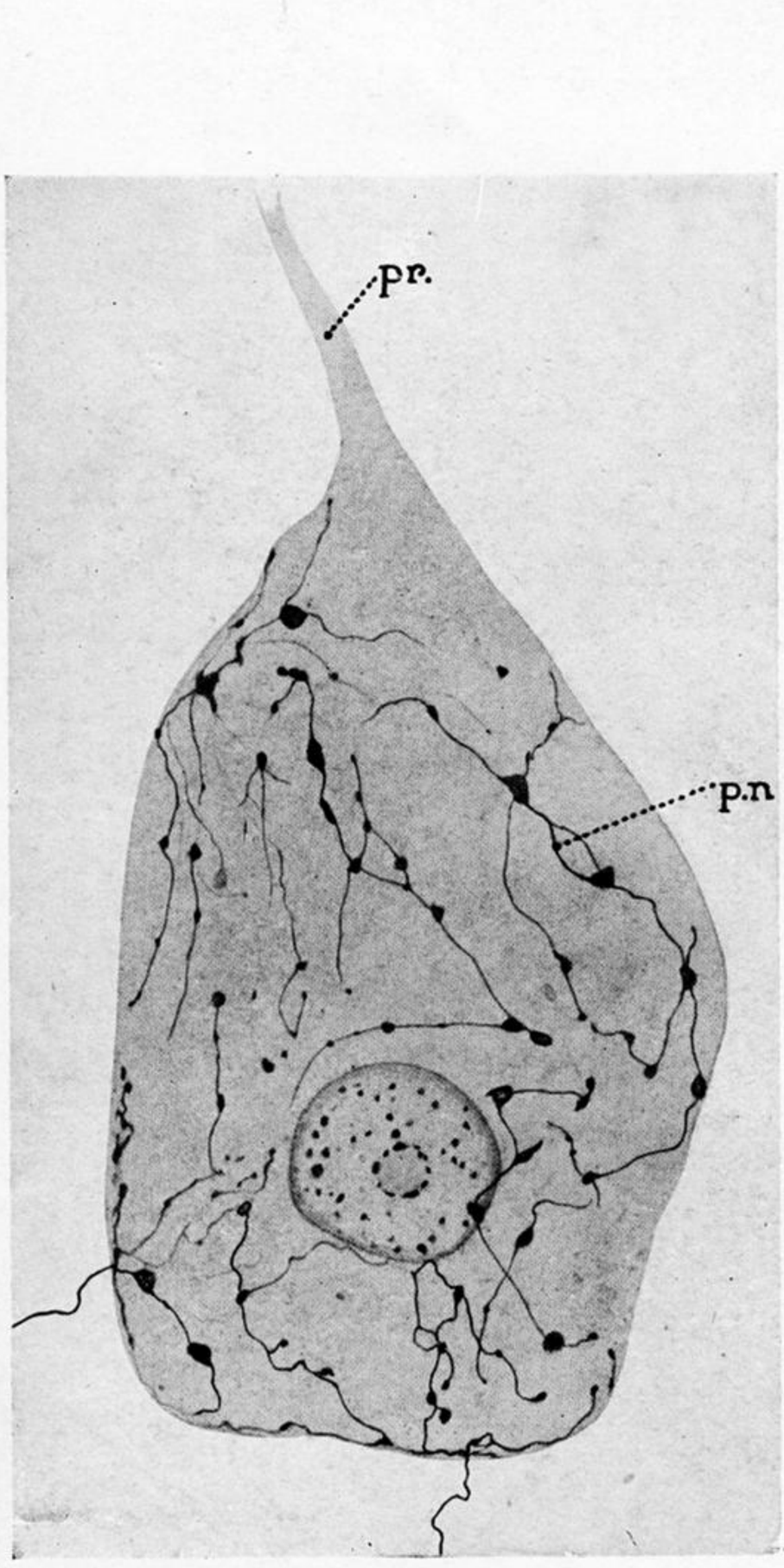
Fig. 12.—Bipolar cell of Type II from the myenteric plexus. Small intestine, Dog. Methylene blue. In this particular cell it was impossible to trace the processes to their terminations. *d.e.*, diffuse endings on the cell body. × about 900.

Fig. 13.—Bipolar cell of Type II from the myenteric plexus. Small intestine, Dog. Methylene blue. *axb.*, axone terminating in the muscularis. *da.*, dendrite which divides into two branches da_1, and da_2. da_1 joins a bundle passing to Meissner's plexus and is broken across in making the preparation; da_2 ends on a cell in an adjacent ganglion. × about 495.

Fig. 14.—Unipolar cell of Type II from the myenteric plexus. Small intestine, Dog. Methylene blue. *p.n.*, pericellular arborization. *pr.*, undivided process of unipolar cell. *ax.* (axone) passes out to the muscularis. *d.* (dendrite) lost to sight in the fibre-tract. × about 900.



15b



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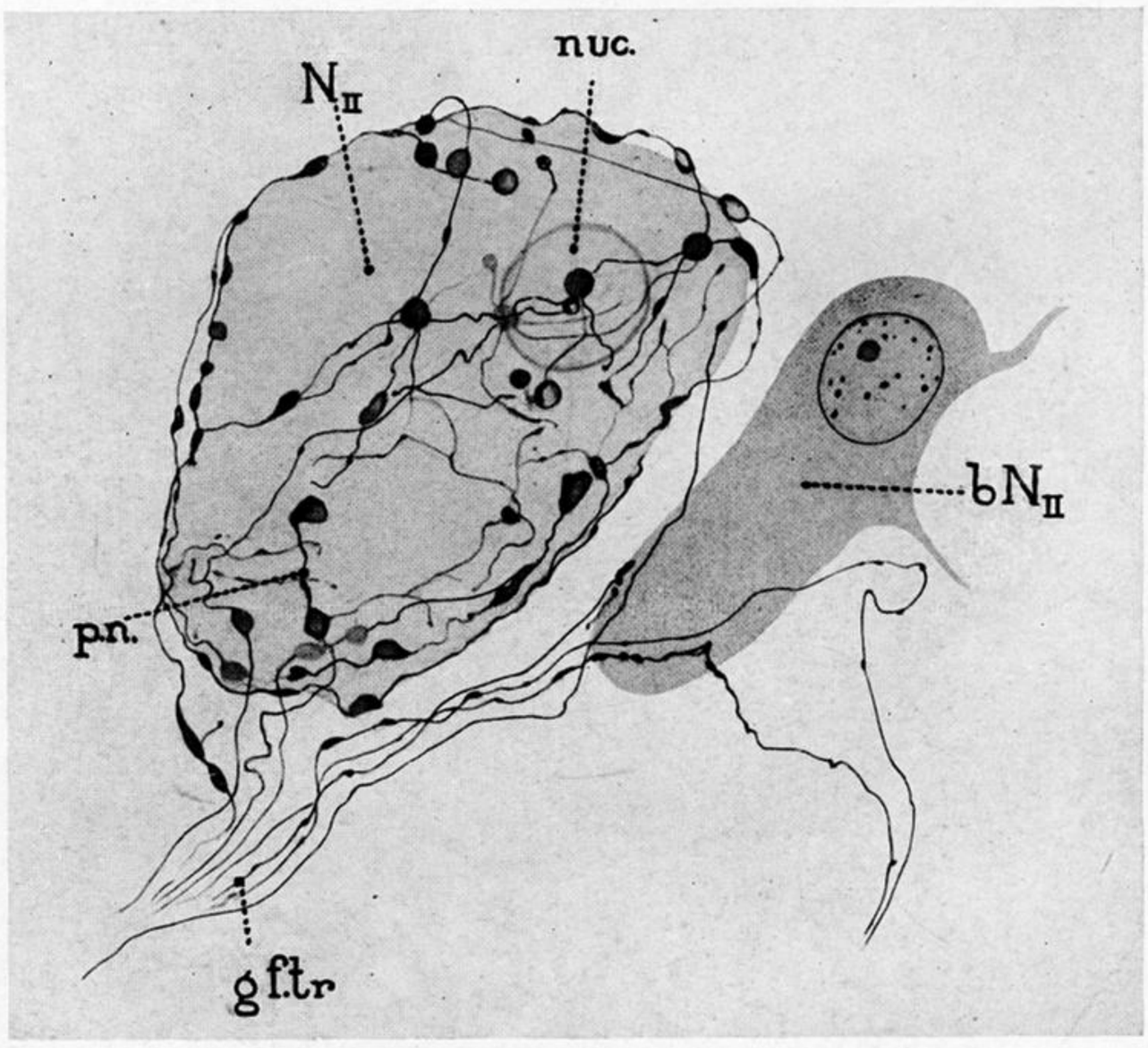

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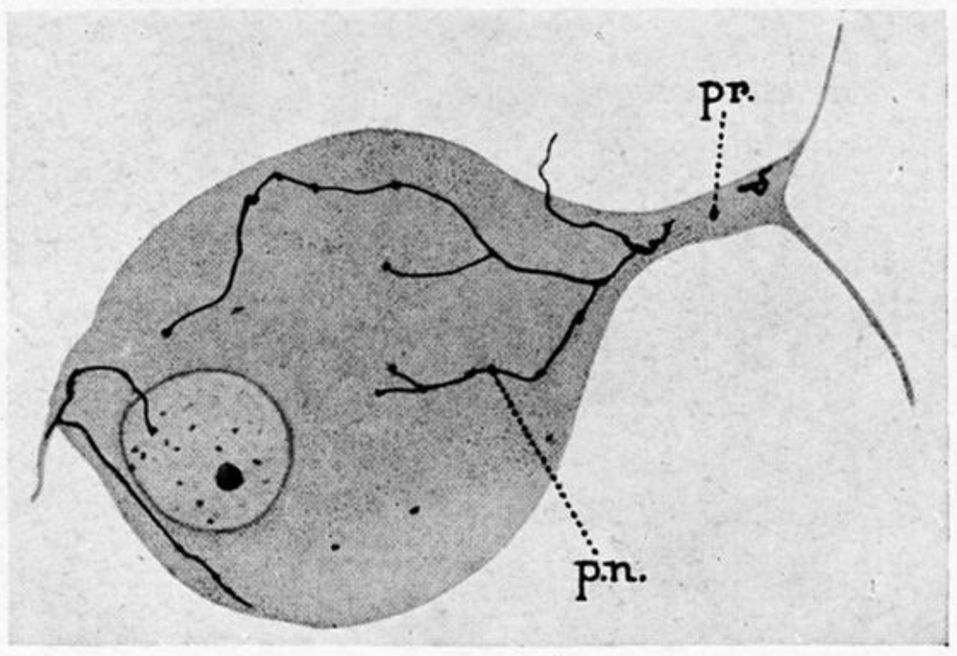

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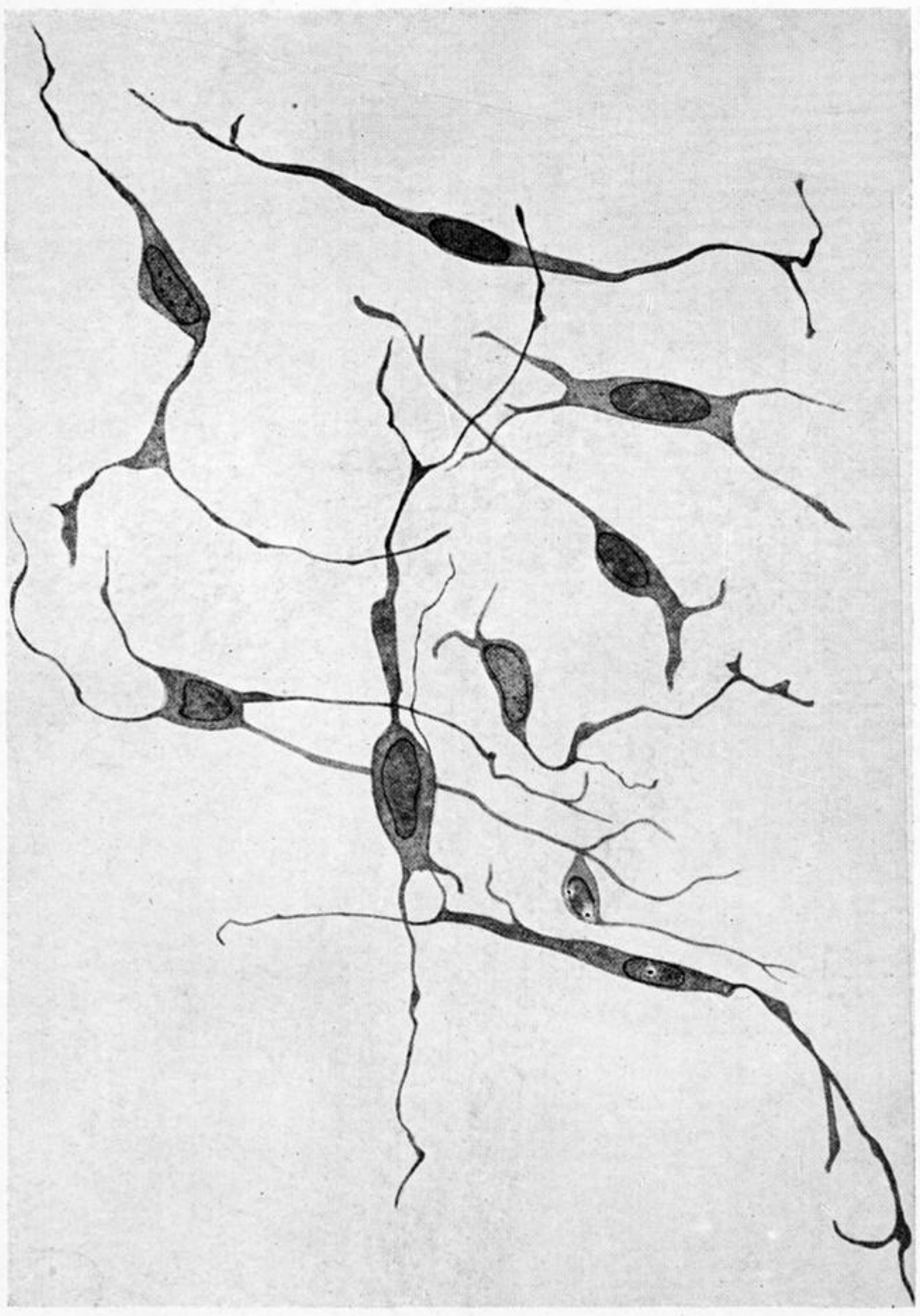
Plate 29.

Fig. 15 *a* and *b*.—Unipolar cells of Type II from the myenteric plexus. Small intestine, Dog. Methylene blue. Cell *a* shows a well-impregnated pericellular network (*p.n.*), but the process (*pr.*) could not be traced beyond the ganglion of origin. Cell *b* has a process (*pr.*) which divides into an axone, *ax.*, the divisions of which pass out to the musculature, and a dendrite *d*, the divisions of which are lost to view before leaving the fibre-tracts. × about 1500.

Fig. 16.—Cells from the sub-mucous plexus of the small intestine, Dog. Methylene blue. N_{II}, neurone of Type II, stained very faintly with well-marked pericellular network, *p.n.*, *nuc.*, nucleus of N_{II}. bN_{II}, bipolar cell of type II. *gf. tr.*, intraganglionic fibres. Measurements, N_{II}, 0·027 × 0·042 mm. in diameter; bN_{II}, 0·012 × 0·027 mm. in diameter. × about 1200.

Fig. 17.—Unipolar cell from the sub-mucous plexus. Small intestine, Dog. Methylene blue. Note the small size of the cell as compared with those represented under the same magnification in figs. 9, 10, 12 and 14. *p.n.*, incompletely impregnated pericellular network. The process "*pr.*" could not be traced. × about 1200.



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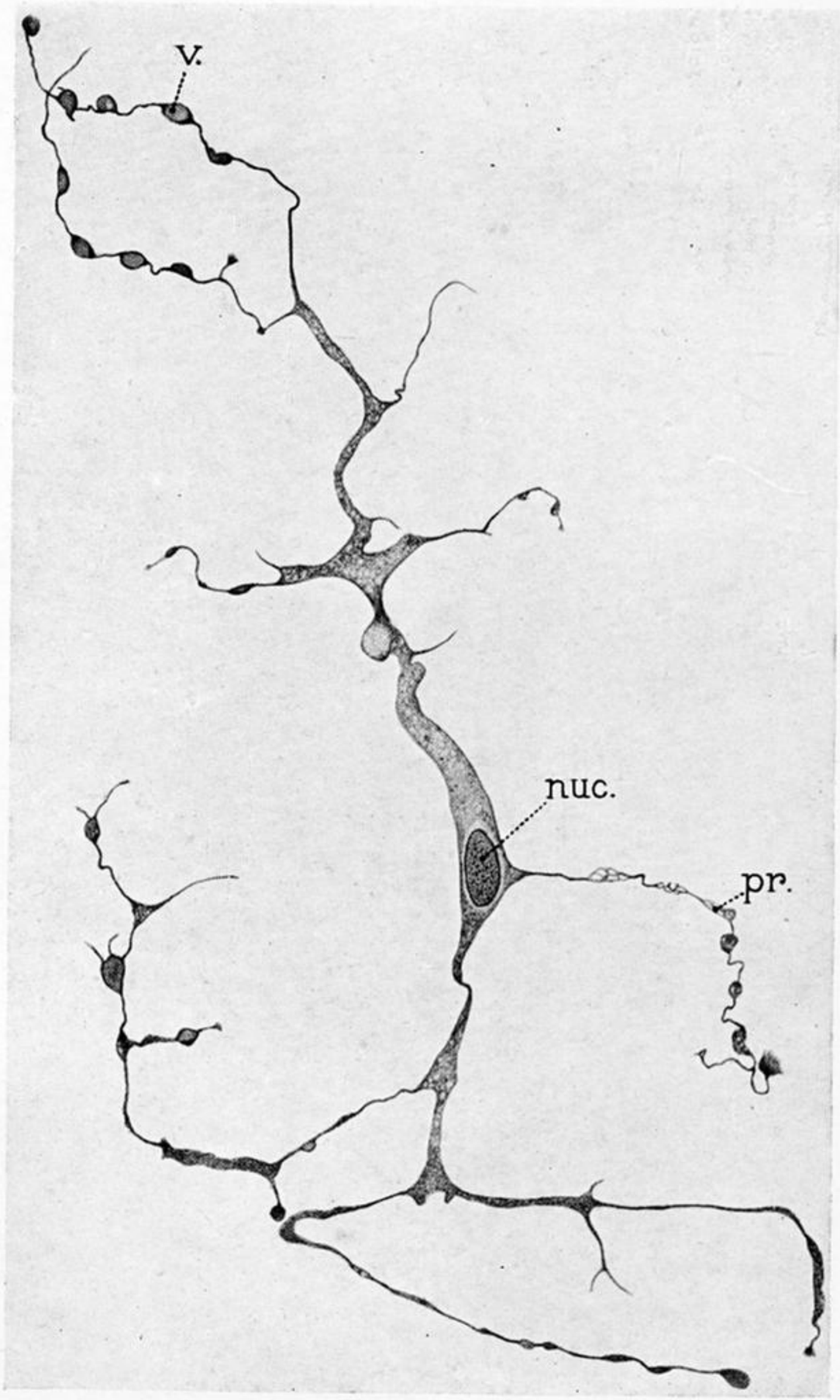

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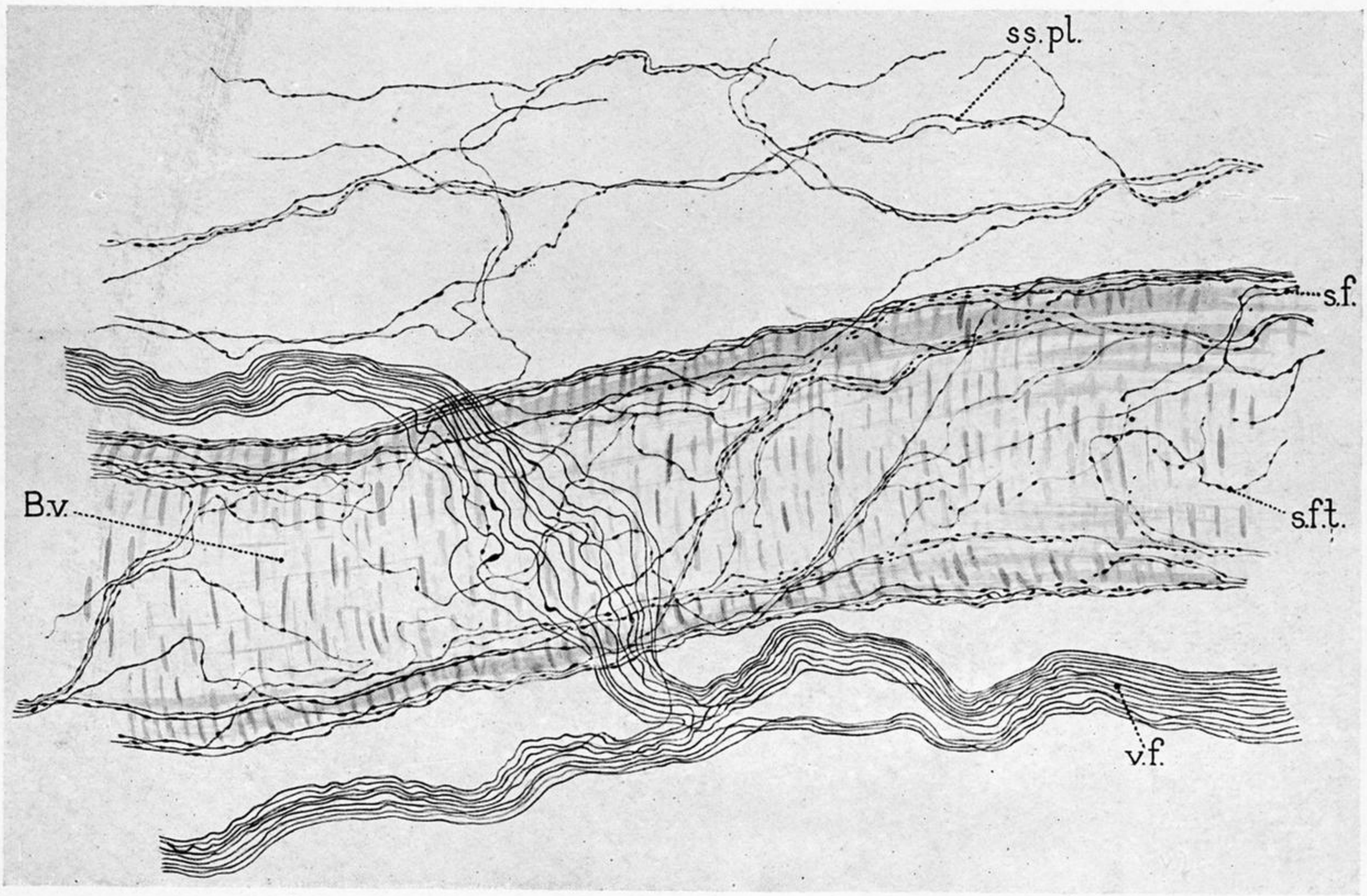

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Plate 30.

Fig. 18.—Low-power view of the feltwork of interstitial cells lying in relation to the myenteric plexus. Small intestine, Dog. Methylene blue. Measurements of cells (approx.), 0·014 × 0·16 mm. × about 500.

Fig. 19.—High-power view of interstitial cell (0·005 × 0·201 mm. in diam.) in relation to the myenteric plexus. Small intestine, Dog. This cell is larger than the majority of interstitial cells. Note the varicosities *v.* and the vacuolated appearance of the cytoplasm. *nuc.*, nucleus. *pr.*, process. × about 600.

Fig. 20.—Portion of the sub-serous coat of the small intestine, Dog. Methylene blue. *B.v.*, blood-vessel. *ss. pl.*, sub-serous plexus formed of sympathetic fibres. *s.f.*, sympathetic fibres. *v.f.*, vagal fibres. *s.f.t.*, sympathetic fibres terminating in the vessel wall. × about 330.

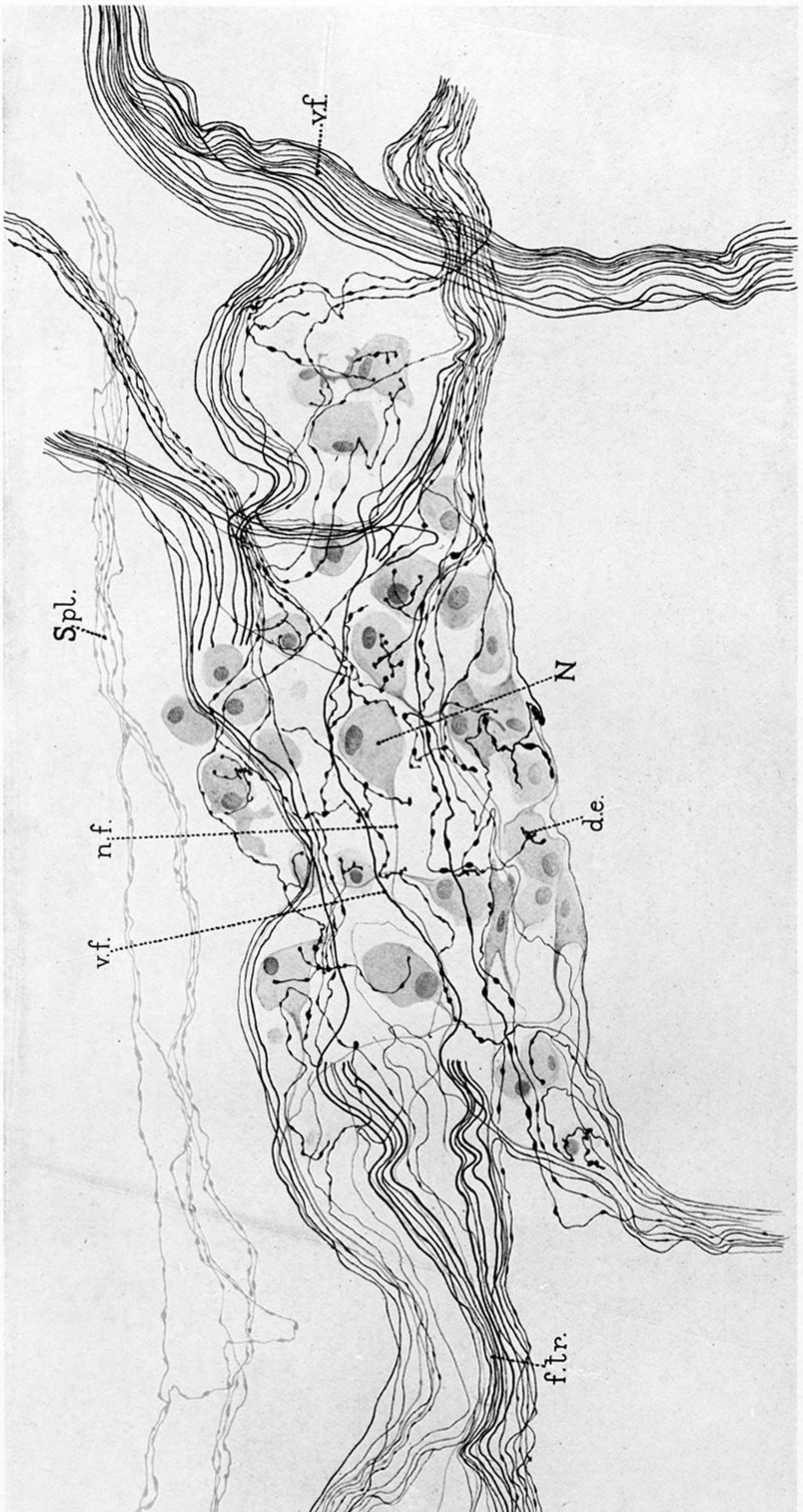
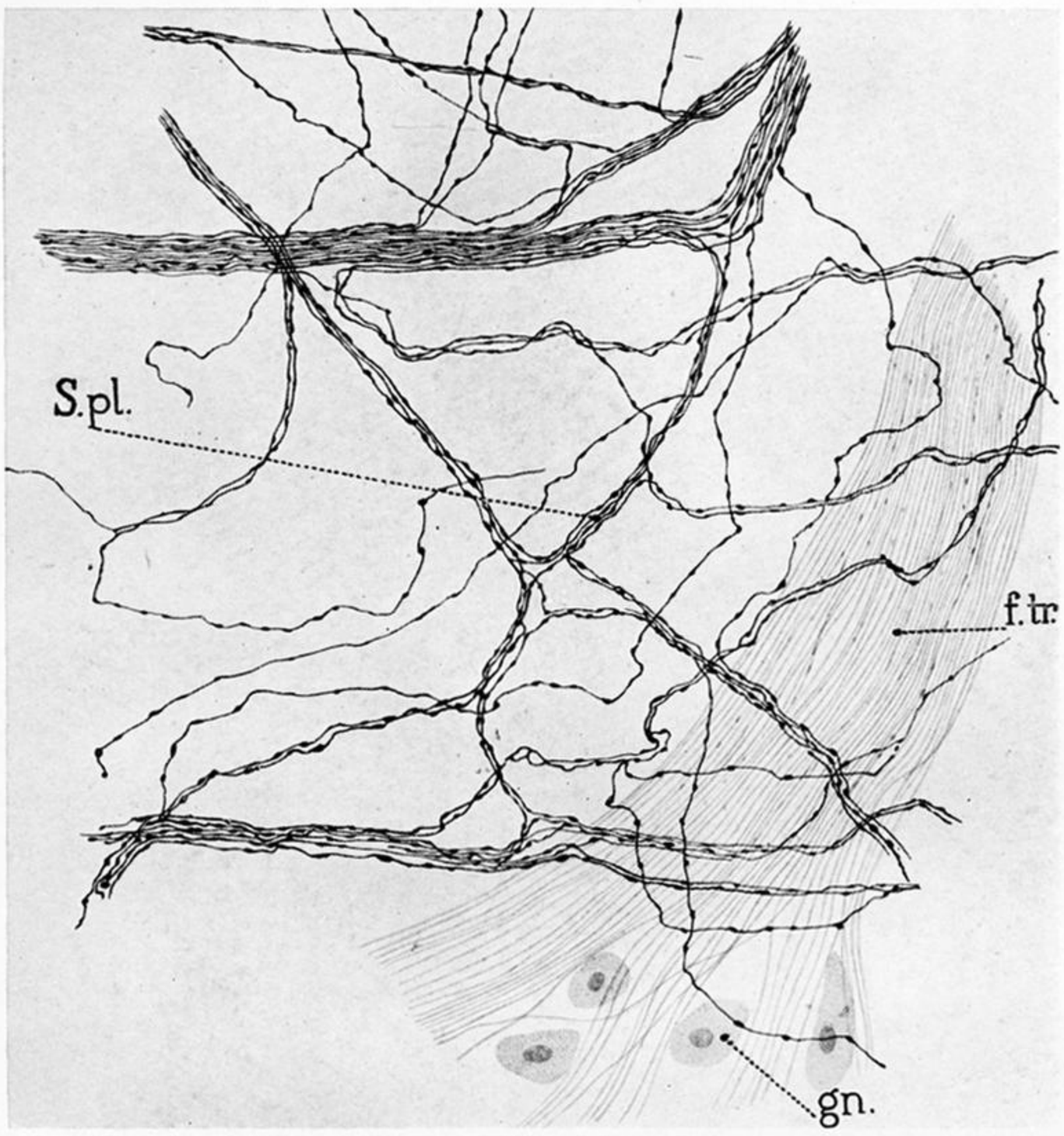


Plate 31.

Fig. 21.—Part of the myenteric plexus. Stomach, Dog. Methylene blue. *N.*, a nerve cell of the myenteric ganglion. *n.f.*, processes of cells of ganglia. *d.e.*, diffuse endings of intrinsic fibres on cells of ganglia. *f.tr.*, interganglionic fibre tracts. *v.f.*, vagal fibres. *S.pl.*, sympathetic plexus which is distinct from the myenteric plexus. × about 310.



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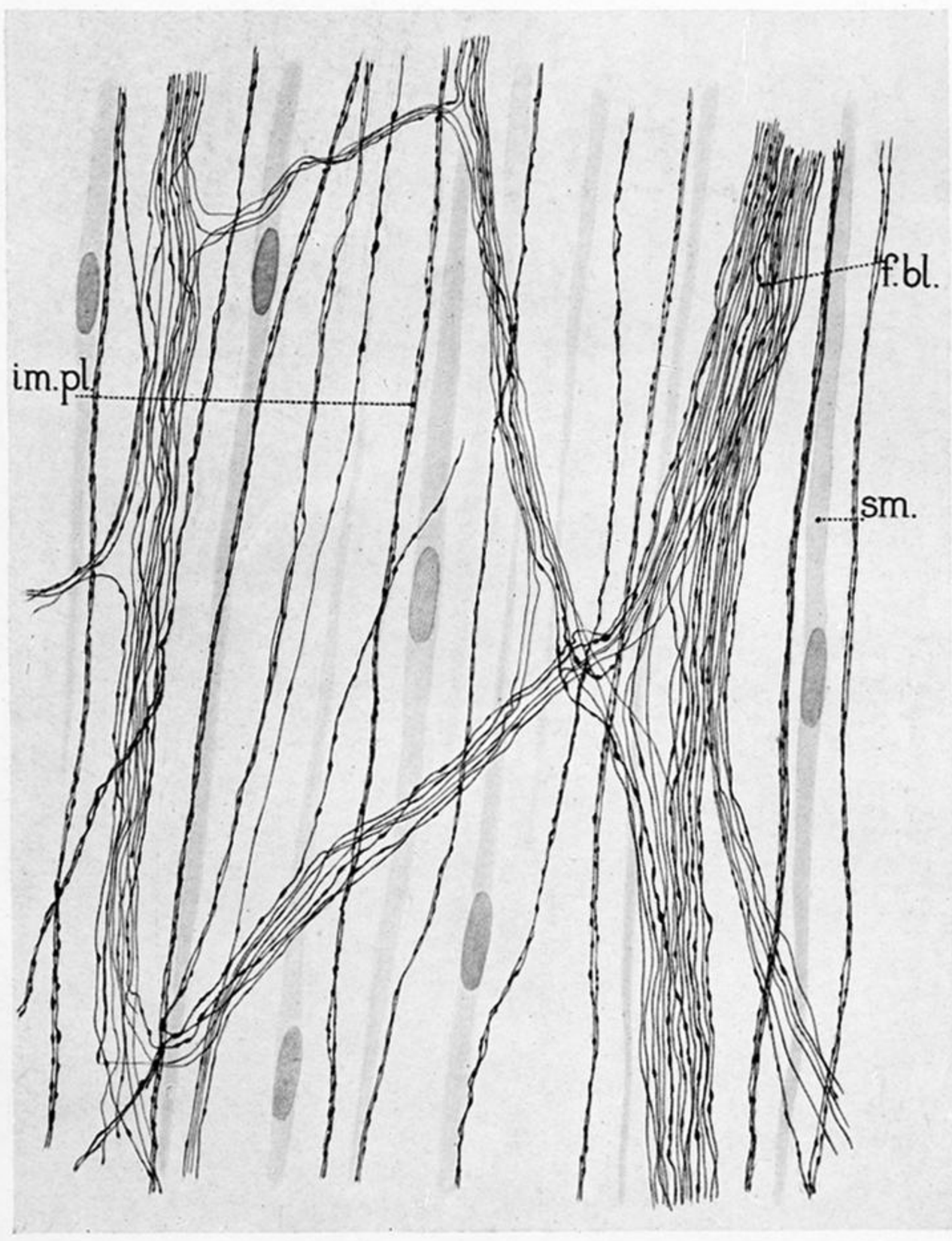

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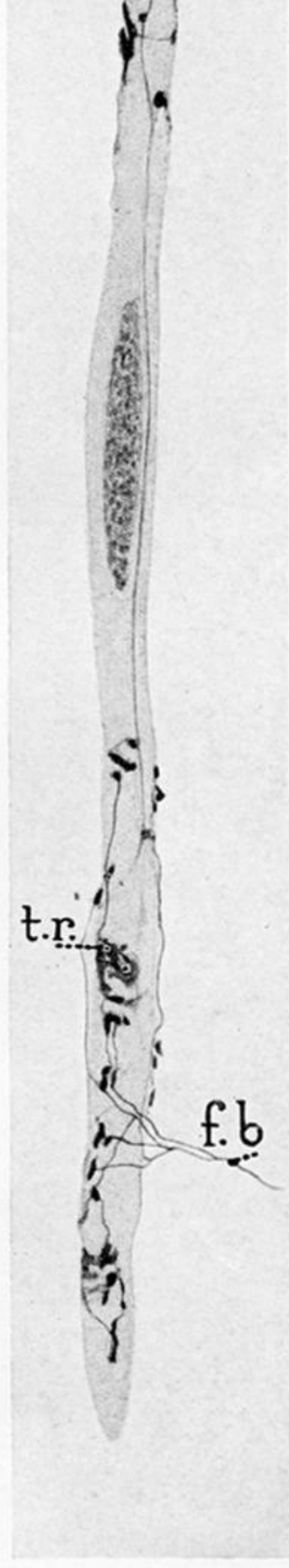

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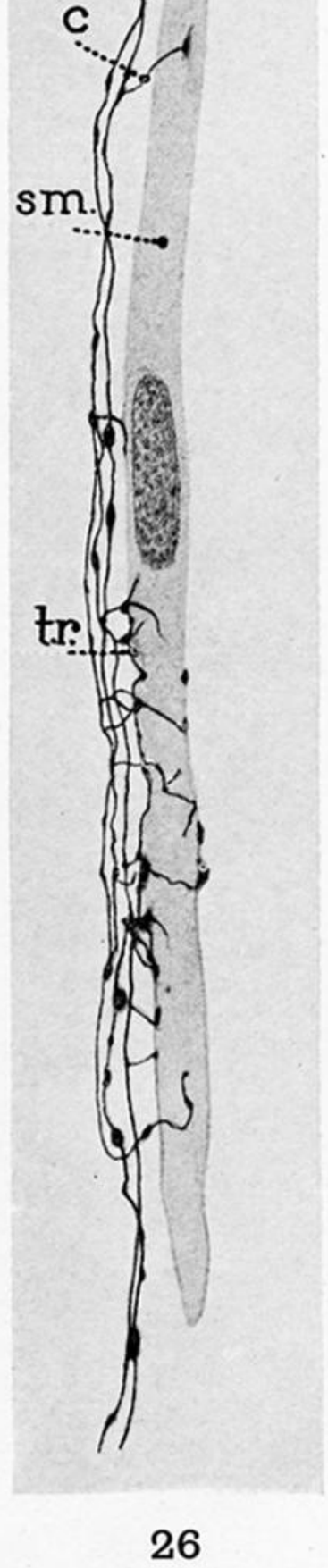

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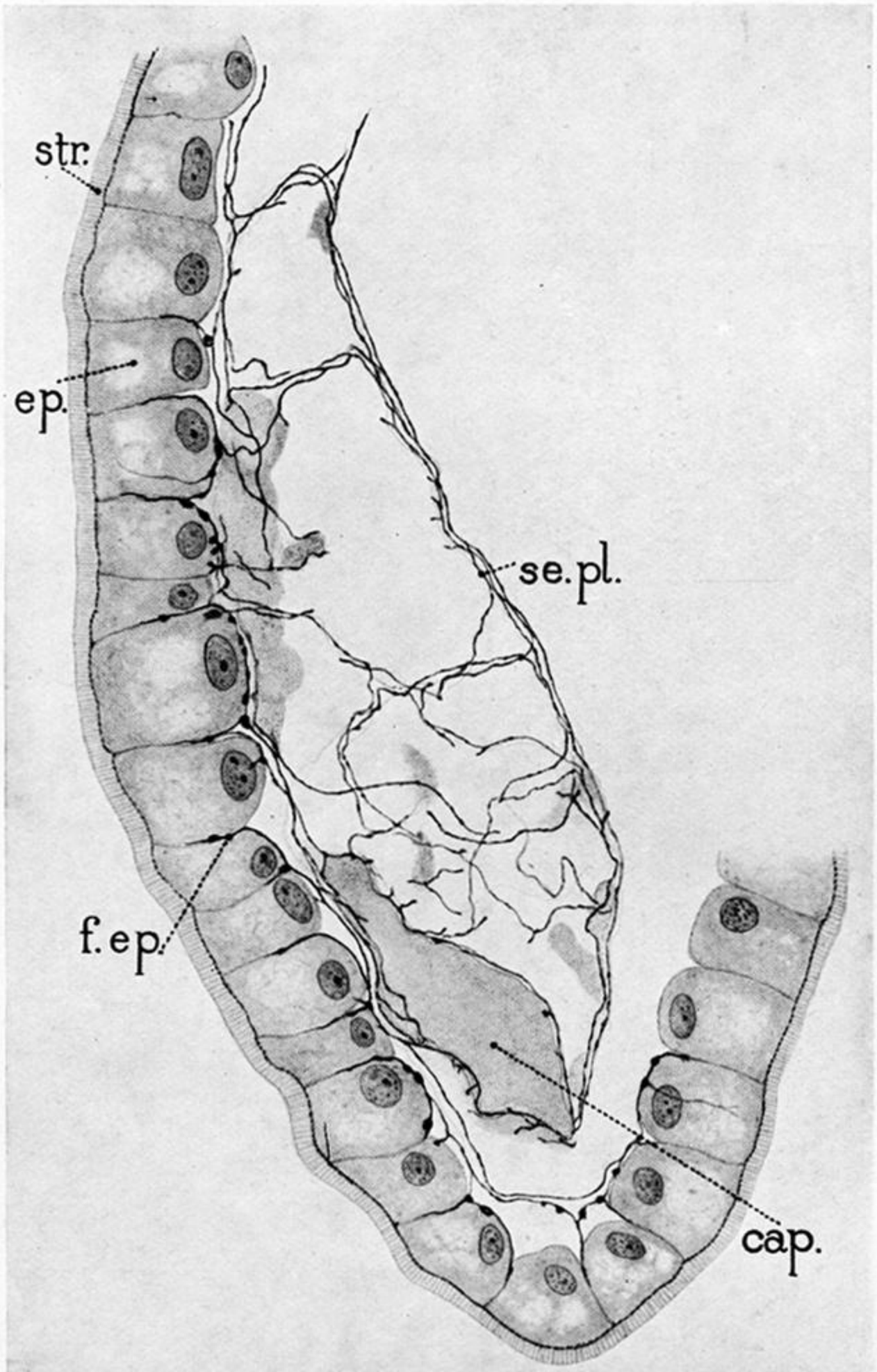
Plate 32.

Fig. 22.—Fine plexus of sympathetic fibres lying internal to the myenteric plexus between the circular and longitudinal muscle coats. Colon, Dog. Methylene blue. *S.pl.*, sympathetic plexus. *f.tr.*, fibre tract of myenteric plexus. *gn.*, ganglion of myenteric plexus. × about 300.

Fig. 23.—Plexus of fibres in the longitudinal muscle coat. Small intestine, Dog. Methylene blue. *sm.*, smooth muscle cells. *f.bl.*, fibre-bundles from the myenteric plexus. *im.pl.*, intramuscular plexus, × about 450.

Figs. 24 and 25.—Endings of the fibres of the intramuscular plexus on smooth muscle cells in the circular muscle coat. Small intestine, Rabbit. Methylene blue. *sm.*, smooth muscle cell. *f.b.*, fibre giving rise to ending. *t.r.*, terminal ramification of fibre on the smooth muscle cell. × about 750.

Fig. 26.—Ending on smooth muscle cell, of a different form to those in figs. 24 and 25. Circular muscle coat. Small intestine, Rabbit. Methylene blue. *f.b.*, fibre of intramuscular plexus. *c.*, collaterals given off by fibres and forming a ramification, *t.r.*, on the muscle cell, *sm.* × about 750.



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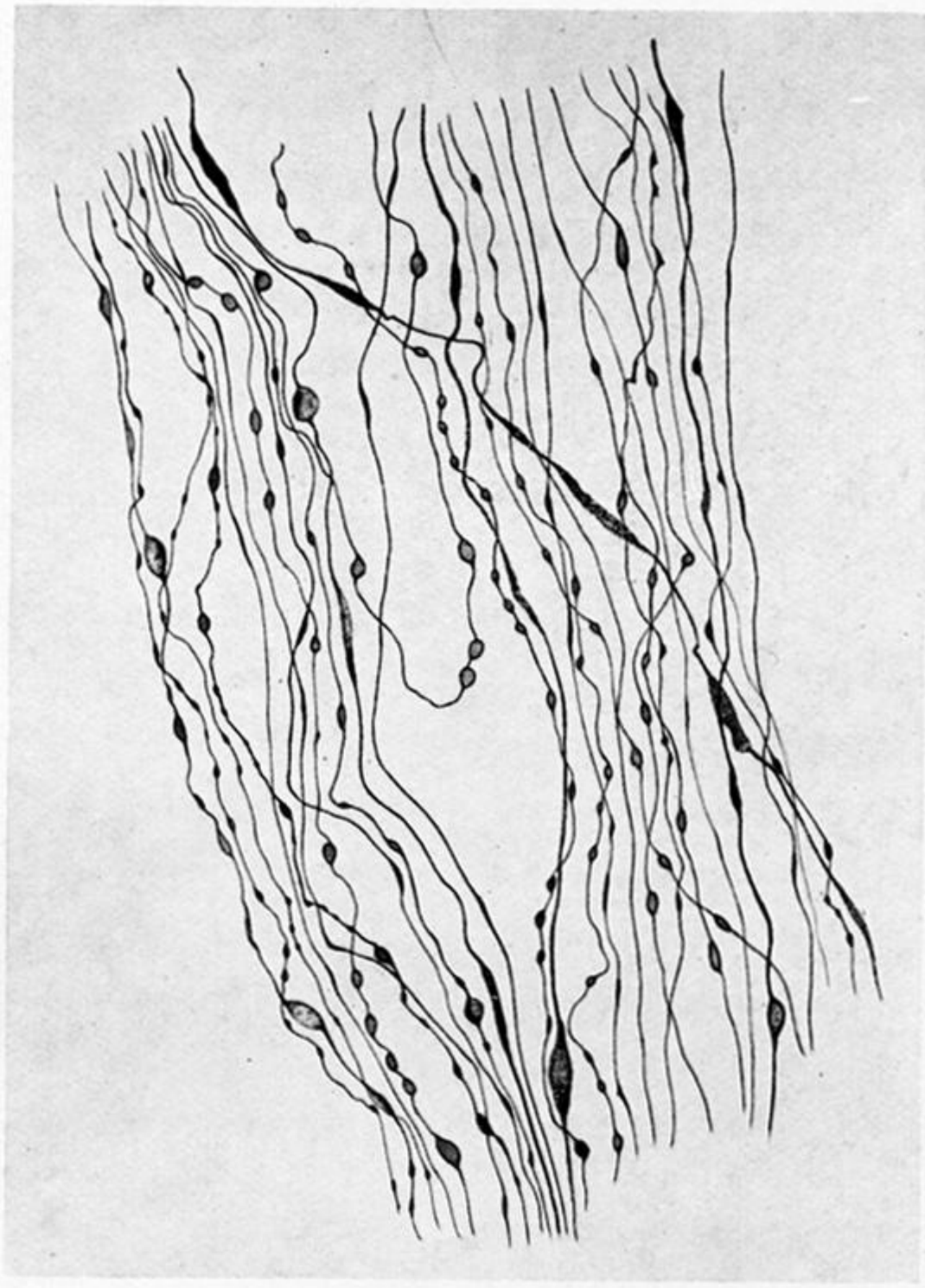

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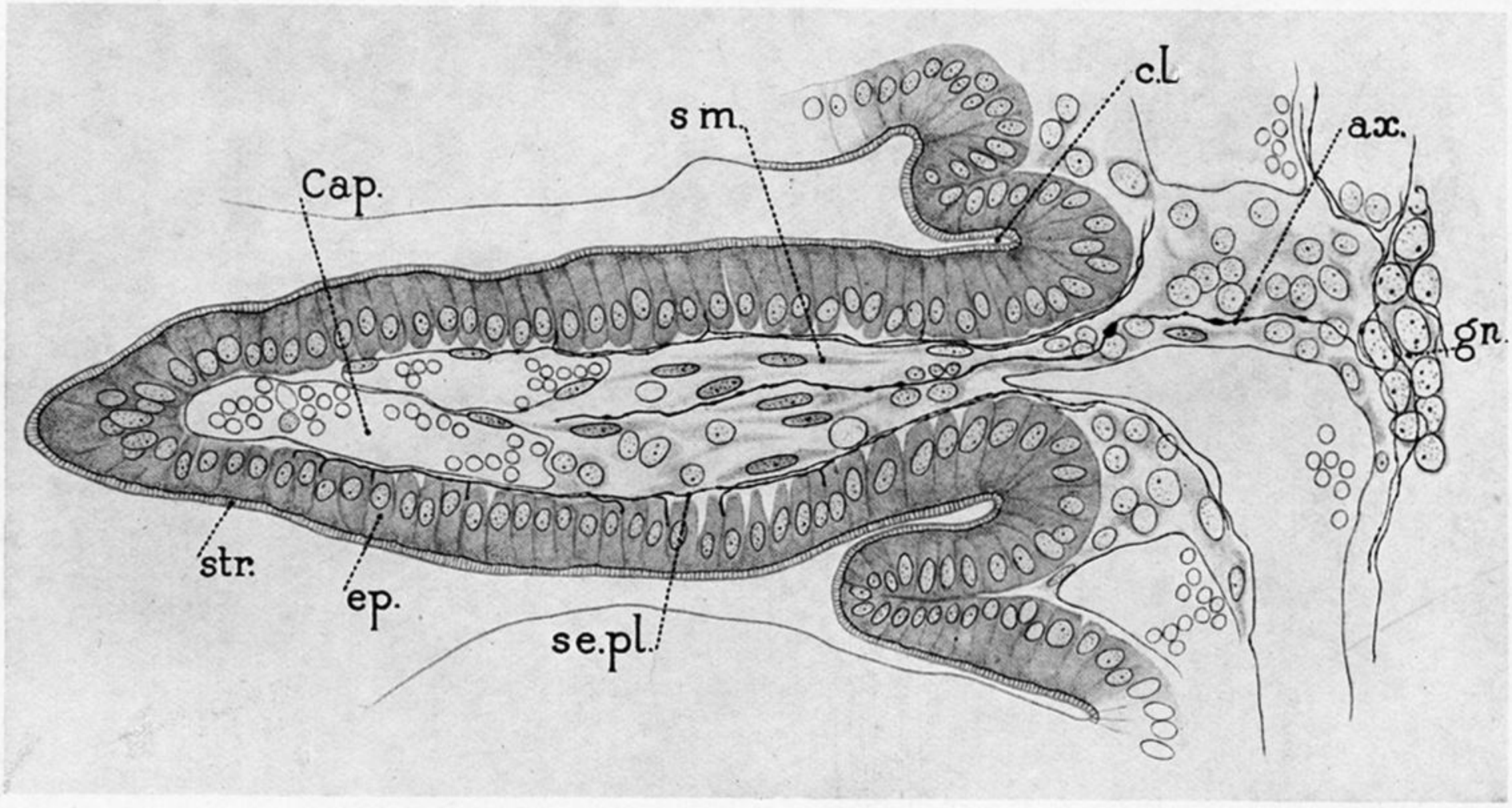

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Plate 33.

Fig. 27.—Terminations of sensory fibres between the epithelial cells of a villus. Small intestine, new-born Rabbit. Silver method of de Castro. *ep.*, epithelium of villus. *str.*, striated free border. *se.pl.*, sub-epithelial plexus. *f.ep.*, fibrils which penetrate between the epithelial cells. *cap.*, capillary. × about 560.

Fig. 28.—Section through the mucosa, small intestine, new-born Rabbit, showing a fibre from the sub-mucous plexus running up to terminate in relation to the smooth muscle fibres of the villus. Silver method of de Castro. *ep.*, epithelium. *str.*, striated free border. *cap.*, capillary. *sm.*, smooth muscle cells. *c.L.*, crypt of Lieberkühn. *gn.*, ganglion of the sub-mucous plexus. *ax.*, axone of ganglion cell. *se.pl.*, sub-epithelial plexus. × about 260.

Fig. 29.—Portion of interganglionic fibre-tract, from the myenteric plexus, small intestine, Cat, to show the variations in the form of the fibres. Methylene blue. × about 600.