segments successifs et des lames latérales, constatation en accord avec O'CONNOR et VAN GEERTRUYDEN, mais en opposition avec VAN DETH. Les résultats de VAN DETH ayant été communiqués sous forme d'un résumé, il n'est pas possible d'élucider la cause de cette contradiction. D'autre part, il apparaît que l'uretère primaire peut abandonner son trajet normal en présence d'un transplantat contenant un proctodæum secondaire et du matériel somitique et se trouvant à une certaine distance du parcours normal, mais *seulement* au cas où le transplantat était placé sur l'endroit (marque d'un astérique) de la fig. 1 ou dans les environs de cet endroit.

Quoiqu'on ne puisse encore exclure toute intervention du matériel somitique, les indications actuelles sont nettement en faveur de la notion que le proctodæum greffé exerce une action attractive sur l'uretère primaire. Rien ne paraît s'opposer à ce que cette notion soit transposée à l'étirement normal de ce canal vers la région cloacale. C'est ce que les expériences en cours s'efforceront d'examiner.

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Summary

A transplant consisting of the rudiment of a cloaca with some somatic material implanted at a certain distance ventral from the normal route taken by the pronephric duct can be the cause of a deviation of the duct from its normal course. The pronephric duct grows towards the secondary proctodæum, whereas the duct is lacking in the part of the body behind the secondary proctodæum. It seems that the proctodæum exercises an attractive effect on the growing pronephric duct.

The results of the experiments, at any rate, are in favour of the conception of O'CONNOR (1938) and VAN GEERTRUYDEN (1942), who found that the pronephric duct develops by its own independent growth. I cannot agree with VAN DETH'S opinion (1946), according to which the pronephric duct develops *in situ* out of the dorsal parts of the lateral plate.

Some further Data concerning the Determination of the Mesonephros

(a) *Introduction*

In this communication some new data will be given to show the great complexity of the relations between the mesonephros on the one hand and the Wolffian duct and pronephros on the other.

The investigation of VAN GEERTRUYDEN[1], 1947, on *Rana fusca* induced me to reinvestigate my experiments on extirpation and transplantation of the pronephros and Wolffian duct rudiment in *Amblystoma* made in the course of my study on the origin of the germ cells in the Urodeles (NIEUWKOOP[2], 1947).

(b) *Normal development*

Axolotl larvæ, reared for about 4 weeks, show well-differentiated mesonephros blastemata. The degree of differentiation in successive regions of the trunk, however, markedly decreases in a cranio-caudal direction. Five successive degrees of differentiation may be distinguished.

The most cranial units contain a well-differentiated, much coiled tubule with a nephrostome and an open communication with the Wolffian duct (stage V). In the following rudiment(s) the mesonephros tubule is only beginning to stretch and coil. Communications with the Wolffian duct and the cœlomic cavity are not yet present (stage IV). The next rudiments are only beginning to differentiate; they are oblong, and the cells are regularly arranged around a central lumen (stage III). The more caudal parts of the mesonephros show only a rather regular arrangement of the cells in a still massive blastema (stage II) or a first concentration of the presumptive cell-material only (stage I)[1].

In normal and experimental animals irregularities in the distribution of the mesonephros rudiments along the longitudinal axis of the trunk can often be observed.

Some experimental animals suggest an explanation. On the operated (*R*) side of animal 190/1, Fig. 2*a*, where a rather rudimentary Wolffian duct is present, the degree of differentiation of the successive rudiments alternates *regularly*. Between the highly differentiated units smaller, less differentiated ones are present. They form the "primary" and the "secondary" generations of mesonephros rudiments respectively (cf. HALL[2], 1904). Irregularities in the localization of the mesonephros rudiments may be caused by relatively late, individual differentiation of mesonephros blastemata, *and* even by the complete failure of one or more "primary" (e.g. No. 178/9, Fig. 1*d*, and No. 165/8/9, *R* side, Fig. 2*d*) or "secondary" (e.g. No. 192/5/6, Fig. 1*c*) rudiments to differentiate. In that event, the open space is secondarily filled, wholly or partly, by the adjacent rudiments.

The original "segmental" arrangement of the successive blastemata[3] has therefore been more or less disturbed by a secondary shifting in their localization.

(c) *Correlations between the differentiation of the mesonephros rudiments and the presence of the Wolffian duct; dependent* (i) *and independent* (ii) *differentiation of the mesonephros blastemata, and the relation of their rate of differentiation to the functional state of the Wolffian duct* (iii)

In the operated animals, in which the pronephros and Wolffian duct rudiments had been wholly or partly extirpated at the early neurula stage[4], the differentiation of the mesonephros blastemata on the operated side of the trunk varies greatly in individual cases.

(*i*) A more extensive investigation has brought to light that in half of the cases (6 mesonephros segments in 5 animals) in which, after successful removal of the Wolffian duct rudiment, differentiation of a mesonephros blastema has taken place on the operated side of the trunk, a small part of the Wolffian duct could still be found in the immediate neighbourhood of this blastema (dependent differentiation). Cf. Figs. 1*b* and *d*, and 2*b* and c. In several animals the second or following mesonephros rudiments have differentiated in the presence of a part of the Wolffian duct, whereas the preceding blastema(ta) show(s) no signs of differentiation. Cf. Figs. 1*c* and *d*. This shows that the Wolffian duct cells, when they were only in a temporary contact with the presumptive mesonephric cell-material along which they migrated, did not evoke the differentiation of these blastemata. The influence of the Wolffian duct on the

[1] J. VAN GEERTRUYDEN, Arch. Biol. *57*, 2, 145 (1947).

[2] P. D. NIEUWKOOP, Arch. Néerl. Zool. *8*, 1 (1947).

[1] Stage V corresponds to the third phase of development distinguished by VAN GEERTRUYDEN, 1947. Similarly, stages III and IV can be compared with his second, and stages I and II with his first phase of differentiation.

[2] R.W. HALL, Bull. Mus. comp. Zool. Harward Coll. *45*, 31 (1904).

[3] The first three or four "primary" mesonephric rudiments show a uniform "segmental" arrangement, the position of the following ones, however, does not completely agree with that of the segments of the trunk. Cf. HALL[2], 1904, and GRAY[5], 1932.

[4] The operation has been performed on 18 animals; normally on the *left* side with the exception of two animals marked (*R*).

[5] P. GRAY, Quart. J. Micr. Sci. *75*, 425 (1932).

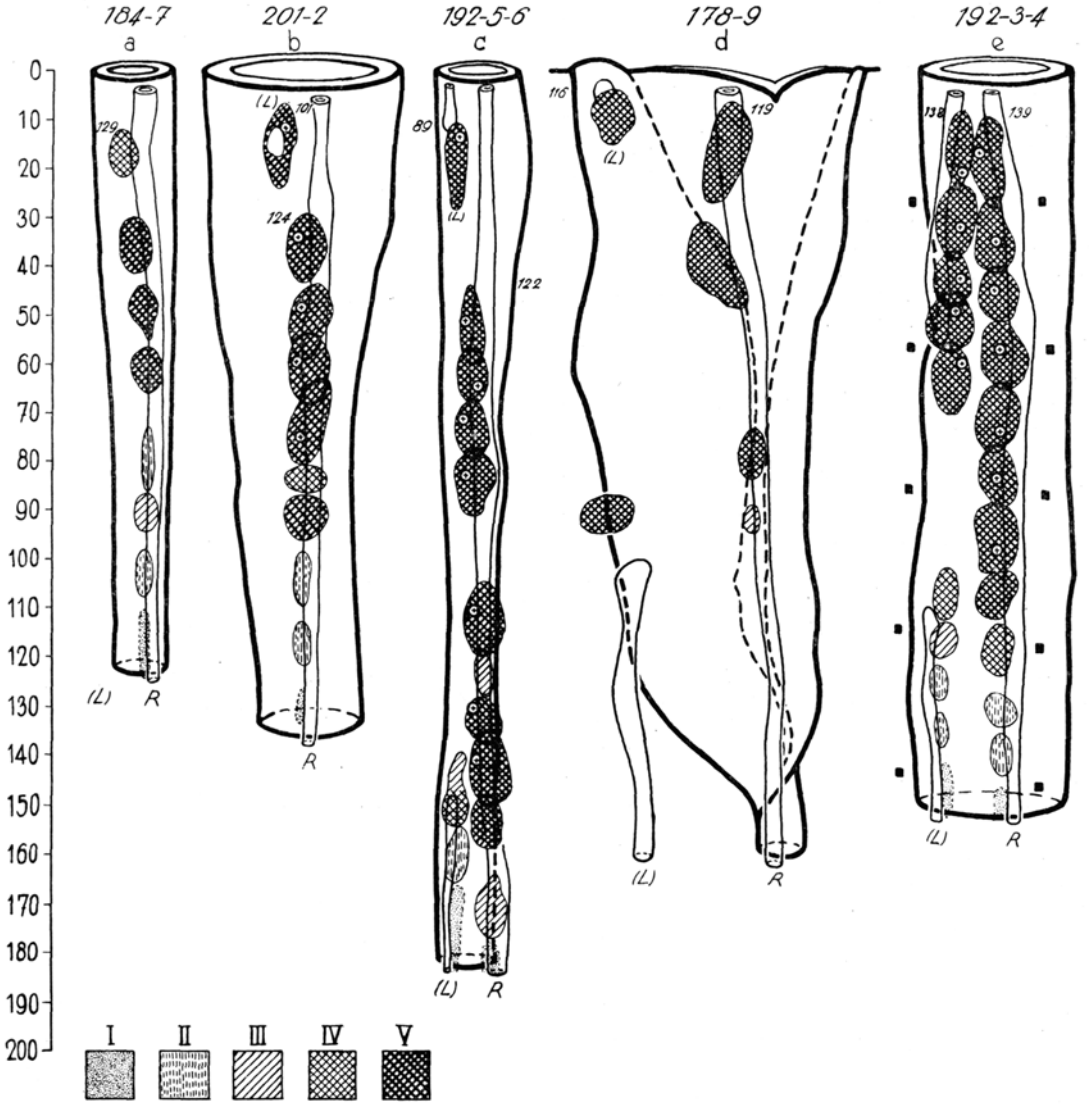

Fig. 1. – Graphic reconstructions of animals 184/7, 201/2, 192/5/6, 178/9, and 192/3/4. Projection of intestinal tube (dark line), Wolffian duct (fine line) and mesonephros blastemata on a frontal plane. Dorsal view. Operated side marked with ( ). Number of sections between end of pronephros and beginning of mesonephros noted in figures. Black cubes: position of spinal ganglia. +: position of nephrostoma. Degrees of differentiation of mesonephros rudiments (I—V) correspond to the description on p. 391. – – – in reconstruction of animal 178/9: outline of intestinal fistula. Medio-lateral enlargement 80×, cranio-caudally 1 section (8μ) = 0,64 mm.

differentiation of the mesonephros blastemata, therefore, takes place at an older stage of development than that at which the Wolffian duct grows out. Cf. Hall[1], 1904, O'Connor[2], 1939, and Van Geertruyden[3], 1947. My experiments further demonstrate that a very small part of the Wolffian duct, consisting of a few cells only, suffices to ensure a normal differentiation of the whole adjacent mesonephros blastema. Cf. Figs. 1*b* and *d*. This fact indicates that the cell-material of a presumptive mesonephros rudiment needs only a very weak inductive stimulus from the Wolffian duct to differentiate normally[4].

(ii) This last supposition is also strongly supported by the observation of *a completely independent differentiation* of mesonephros blastemata in a number of cases (6 mesonephros segments in 5 animals)[1]. Cf. Figs. 2*c*, *d* and *e*, and 3. Evidently, in contrast to *Rana*, the mesonephro sblastemata in *Amblystoma mexicanum* have rather strong self-differentiation potencies. In a number of cases they may differentiate completely autonomously. Cf. Humphrey[2], 1928, Machemer[3], 1929, Burns[4], 1938, and Holtfreter[5], 1943. In other cases the threshold is not reached without a stimulating influence from the Wolffian duct. Evidently, the latter

[1] R.W. Hall, Bull. Mus. comp. Zool. Harvard Coll. *45*, 31 (1904).
[2] R. J. O'Connor, J. Anat. *74*, 34, 301 (1939/40); *75*, 95 (1940).
[3] J. Van Geertruyden, Arch. Biol. *57*, 2, 145 (1947).
[4] This fact may help us to explain the interesting observation of Van Geertruyden[3] that the role of the Wolffian duct can be taken over by the spinal cord (a completely abnormal inductor) when it has direct contact with the mesonephros blastemata.

[1] In these cases no indications of the presence of possible inductive influences of another kind could be found, while the possibility of overlooking very small parts of the Wolffian duct can be excluded in the rather large number of cases in which an independent development has taken place.
[2] R. R. Humphrey, Anat. Rec. *40*, 67 (1928).
[3] H. Machemer, Roux' Arch. *118*, 200 (1929).
[4] R. K. Burns, Proc. Soc. Exp. Biol. Med. N.Y. *39*, 111 (1938).
[5] J. Holtfreter, Rev. Canad. Biol. *3*, 220 (1944).

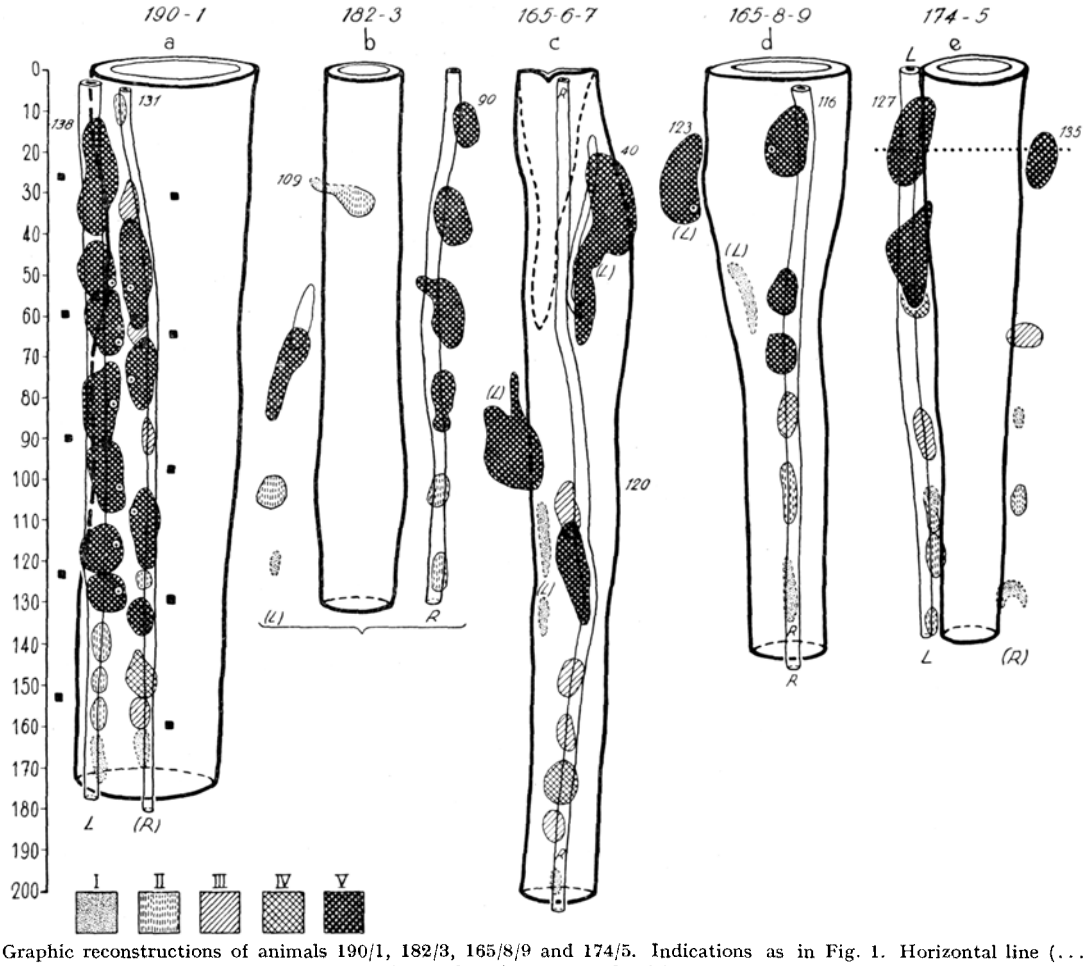

Fig. 2. – Graphic reconstructions of animals 190/1, 182/3, 165/8/9 and 174/5. Indications as in Fig. 1. Horizontal line (.....) in graphic reconstruction of animal 174/5 corresponds with cross section given in Fig. 3.

is of only little importance in *Amblystoma*. My conclusion that the intensity of the self-differentiation tendencies of the mesonephros blastemata on the one hand and the necessary strength of the inductive action from the Wolffian duct on the other may vary in different species, agrees with that of O'CONNOR[1], 1939 and 1940. I prefer, however, to speak of a necessary complement of the two phenomena rather than of double insurance.

(iii) In 5 cases I observed that the mesonephros rudiments showed a somewhat lower degree of differentiation on the side of the rudimentary Wolffian duct than on the normal side[2]. Cf. Fig. 1*c* and *e*, and 2*a*, in which latter on the normal side *primary* and *secondary* units have completely differentiated, whereas on the operated side the *secondary* rudiments show a lower degree of differentiation. Evidently, a normal, functioning Wolffian duct influences the *rate* of differentiation of the mesonephros blastemata. Here, another difference between *Amblystoma* and *Rana* becomes manifest; in *Rana* the differentiation of the mesonephros rudiments

[1] R. J. O'CONNOR, J. Anat. *74*, 34, 301 (1939/40); *75*, 95 (1940).

[2] A difference in the rate of differentiation between both sides, normally present in *Rana* (VAN GEERTRUYDEN, 1947[8]) is unknown in *Amblystoma*.

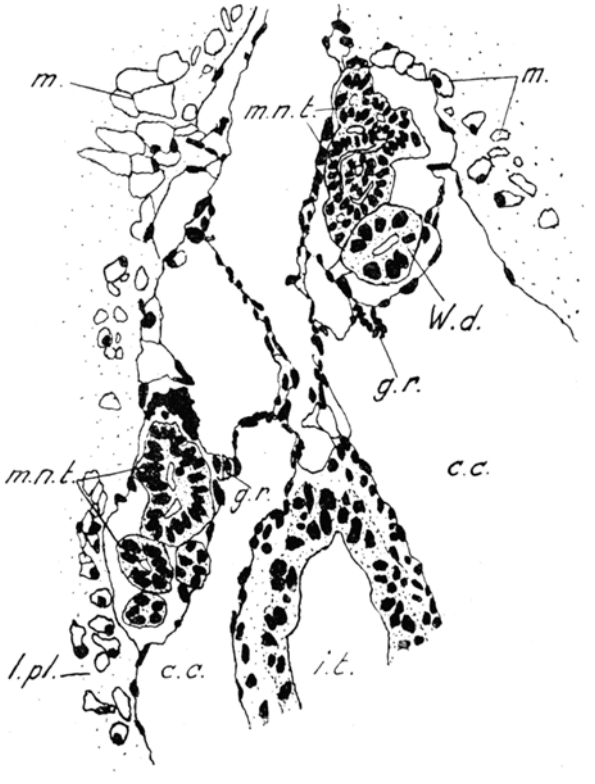

Fig. 3. – Part of cross section through trunk of animal 174/5, showing independent differentiation of mesonephros rudiment on operated side (*R*). *C.c.* cœlomic cavity, *g.r.* genital ridge, *i.t.* intestinal tube, *l.pl.* lateral plate, *m.* myotome, *m.n.t.* mesonephros tubules and *W. d.* Wolffian duct.

is probably entirely independent of the functional state of the Wolffian duct. Cf. MIURA[1], 1930, and VAN GEERTRUYDEN[2].

(d) *Correlations between the regional differentiation of the mesonephros and the presence of the pronephros*

In the animals 201/2, 192/5/6, and 165/6/7 the mesonephros rudiments begin at *a much more cranial level* on the operated than on the normal side of the trunk[3]. This phenomenon may be explained in two ways: (*a*) It may have been caused by a secondary displacement of the mesonephros blastemata by a regulation of the original defect in the lateral mesoderm (removal of the presumptive pronephros rudiment), and by the secondary formation of intestinal fistulæ. The course of the spinal nerves, however, does not point to an extensive cranial displacement in the lateral mesoderm. (*b*) The removal of the pronephros rudiment has directly or indirectly influenced the normal cranio-caudal regional localization of the mesonephros on this side of the trunk. This may be caused directly by a possible interfering influence of the pronephros on the differentiation of the mesonephros over several segments of the trunk, or indirectly by a disturbance in the regional structure of the trunk itself. In these cases, in which any influence of the pronephros has been experimentally reduced, the mesonephros rudiments should be able to differentiate also at a more cranial level in the trunk.

(e) *Conclusion*

Although some new data have been added to our knowledge of the development and determination of the mesonephros, many important questions are still to be solved. For example, what are the causes of the differentiation of the mesonephros blastemata in a distinct part of the nephrogenic cord only? Does the determination process of the nephrogenic cell-material take place step by step, i.e., is the first step a general activation of a rather narrow longitudinal strip of the lateral mesoderm of the neurula to form a still homogeneous nephrogenic cord, and is this step followed by later ones, by which the regional subdivision into pro-, meso- (and meta-)nephros is finally determined.

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May, 1, 1948.

Zusammenfassung

In *Amblystoma* besitzen die präsumtiven Urnierenanlagen starke Tendenzen zur Selbstdifferenzierung, während der induktive Einfluß von seiten des primären Harnleiters eine mehr untergeordnete Rolle spielt. Dieser Einfluß auf die Differenzierung der Urnierenanlagen wird erst nach dem Auswachsen des Harnleiters zur Kloake ausgeübt. Der Differenzierungsgrad der Anlagen zeigt jedoch eine gewisse Abhängigkeit vom funktionellen Zustande des Harnleiters. Nach Entfernung der Vorniere ist die Differenzierungszone der Urnierenanlagen in verschiedenen Fällen ziemlich stark kranialwärts verschoben, was einen hemmenden Einfluß der Vorniere auf die Differenzierung der Urnierenanlagen im kranialen Abschnitt des Rumpfes andeuten könnte.

[1] K. MIURA, Jap. J. Med. Sci. Anat. *2*, 105 and 125 (1930).
[2] J. VAN GEERTRUYDEN, Arch. Biol. *57*, 2, 145 (1947).
[3] This difference lies very probably beyond the normal variability.

La structure de certaines terminaisons nerveuses montre des variations cycliques

De tous les organes ou tissus, le système nerveux paraît être le moins sujet à des modifications durant la vie d'un animal. D'une façon générale, depuis la période embryonnaire jusqu'à la mort, le nombre des neurones ne varie guère, si ce n'est par la dégénérescence de quelques-uns d'entre eux. Il est peu probable, surtout chez les Vertébrés supérieurs, comme les Mammifères, qu'il se trouve encore chez l'adulte, des neuroblastes capables de se différencier et de remplacer les cellules nerveuses disparues. En mettant à part les cas de traumatismes accidentels ou d'ordre expérimental, les voies nerveuses centrales ou périphériques conservent également, pendant toute la vie, une fixité presque absolue. Il ne semble pas qu'il en soit de même pour leurs terminaisons; les aspects de certaines de ces dernières correspondent indiscutablement à de véritables variations cycliques.

La méthode de l'imprégnation argentique, le plus souvent employée, montre que les fibres nerveuses aboutissent à un bouton terminal ou *club*. En améliorant la fixation, il est possible d'entrevoir au delà de ces petits renflements, un *appareil métaterminal*; il est constitué par des filaments extraordinairement fins, à la limite de la visibilité, longs d'environ 0,01 mm et dont le diamètre est voisin de celui des cils vibratiles.

Dans certaines membranes, telle la dure-mère du Rat, tous les boutons terminaux des fibres du nerf trijumeau sont prolongés par ces filaments métaterminaux, pourvus eux-mêmes, à leur extrémité, d'un grain minuscule. Ce granule gonfle, prend l'aspect d'un corpuscule ovoïde ou piriforme, ou bien s'amincit dans sa partie centrale, puis se perfore et se transforme ainsi en une petite rondelle. En même temps, le filament ténu qui relie cette dernière au bouton terminal, s'atrophie et disparaît après s'être réduit en une rangée de grains à peine visibles, ou bien en se rompant par une sorte d'autotomie. Il ne reste plus alors comme trace de cet

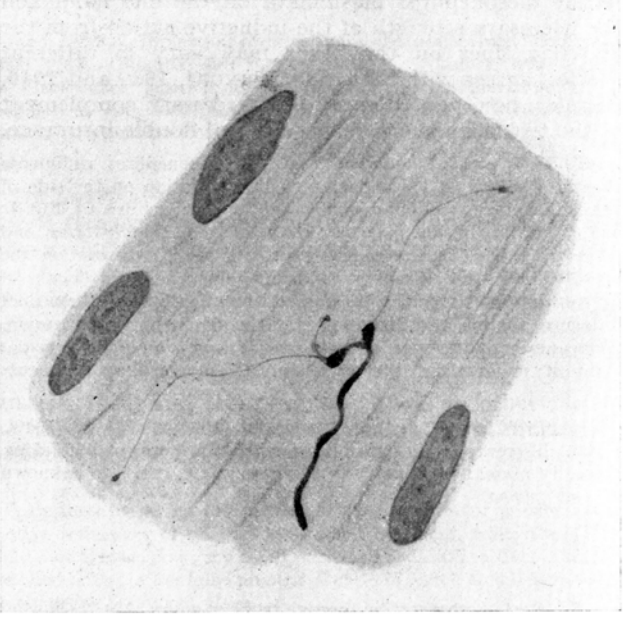

Fig. 1. – Filaments métaterminaux à l'extrémité de boutons terminaux sur une fibre du nerf trijumeau, dans la dure-mère du Rat. Gross.: 2875.