Researches on the origin and development of the epiblastic trabeculae and the pial sheath of the optic nerve of the frog : with illustrations of variations met with in other vertebrates, and some observations on the lymphatics of the optic nerves / by J. T. Gradon.

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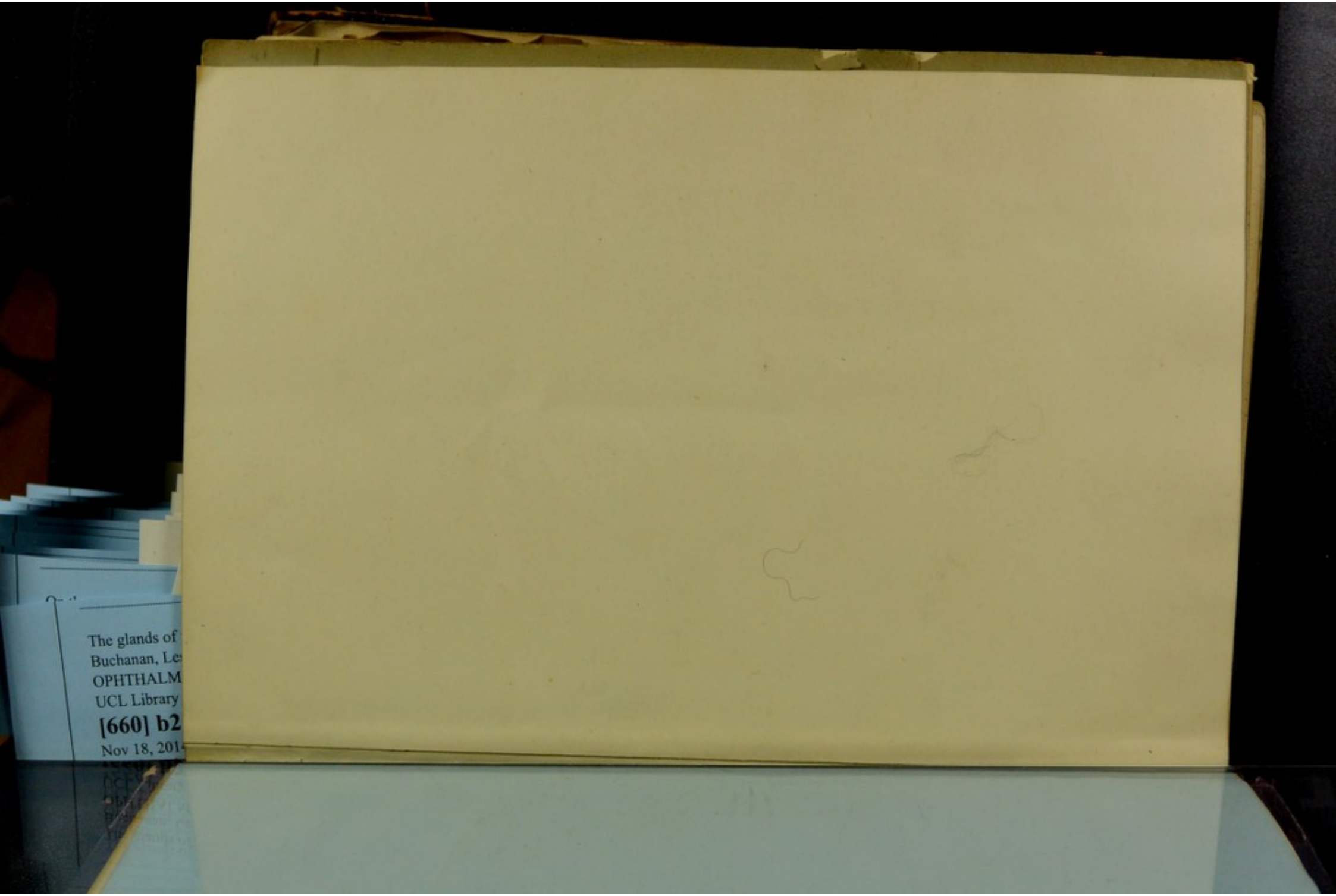
RESEARCHES ON THE ORIGIN AND DEVELOPMENT OF THE EPIBLASTIC TRABECULÆ AND THE PIAL SHEATH OF THE OPTIC NERVE OF THE FROG,

With Illustrations of Variations met with in other Vertebrates, and some Observations on the Lymphatics of the Optic Nerve.

By J. T. GRADON, M.A.

Reprinted from 'The Quarterly Journal of Microscopical Science,' Vol. 50, Part 3, August, 1906.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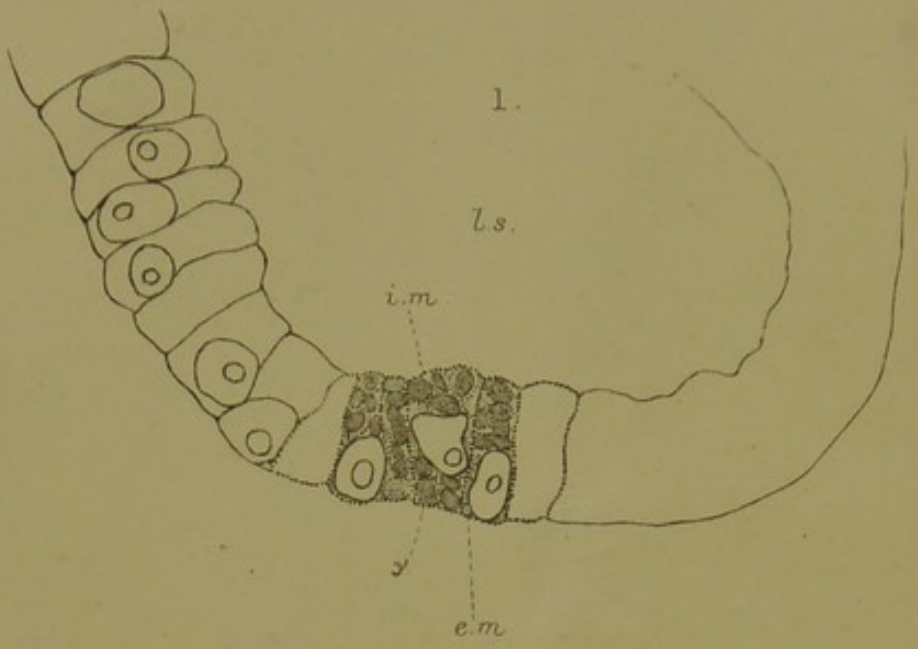

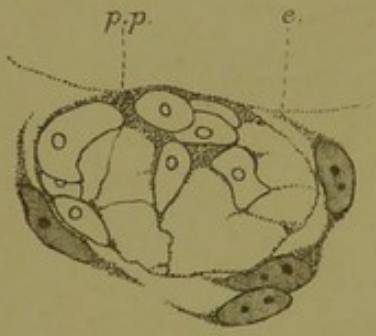

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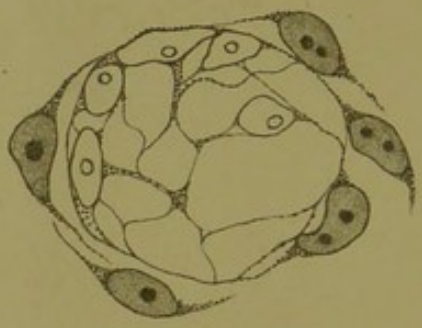

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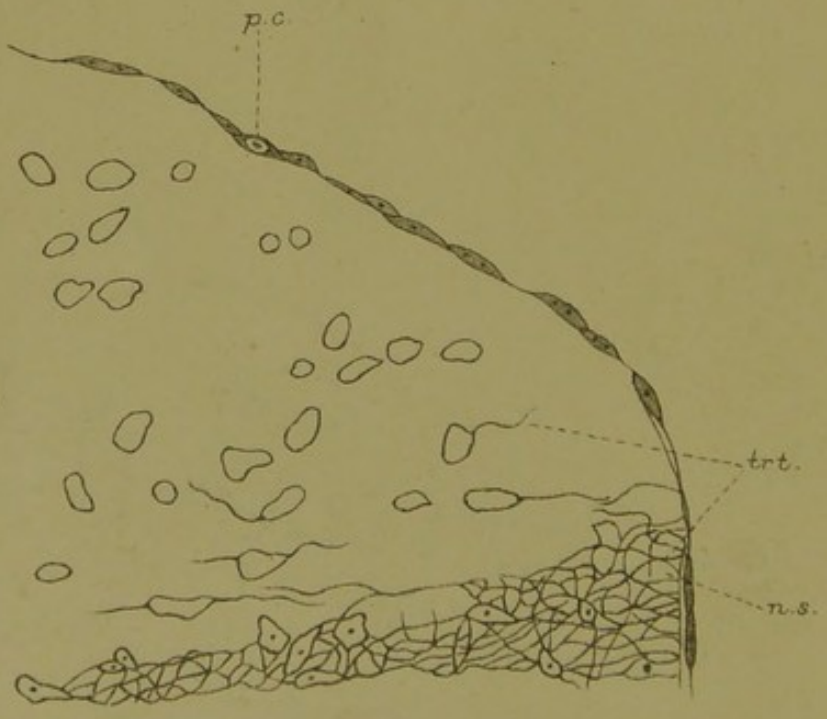

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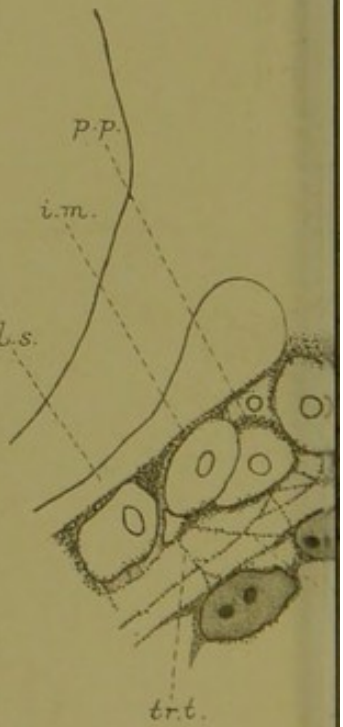

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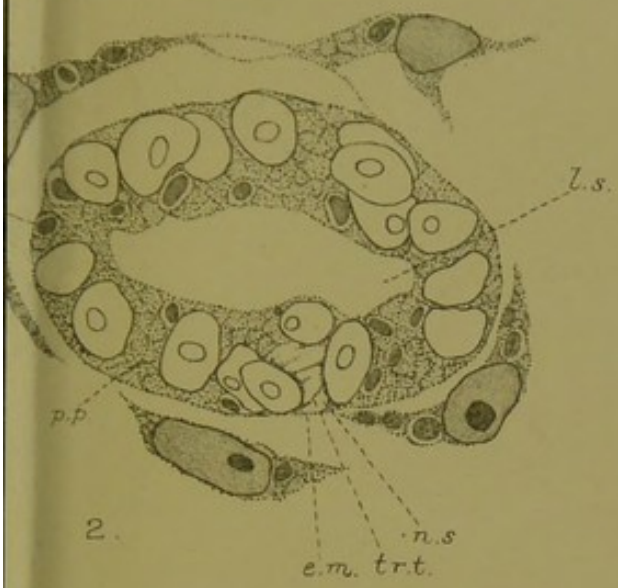

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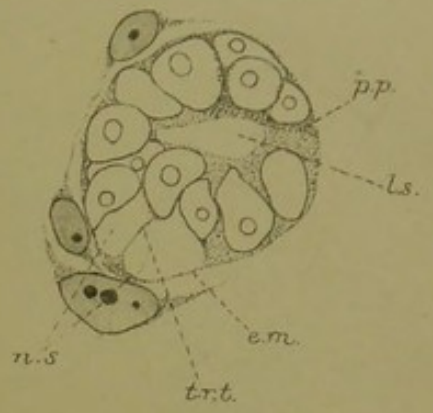

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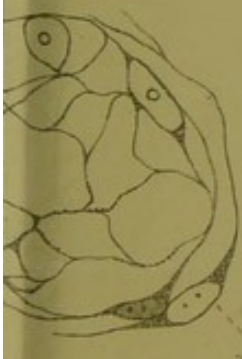

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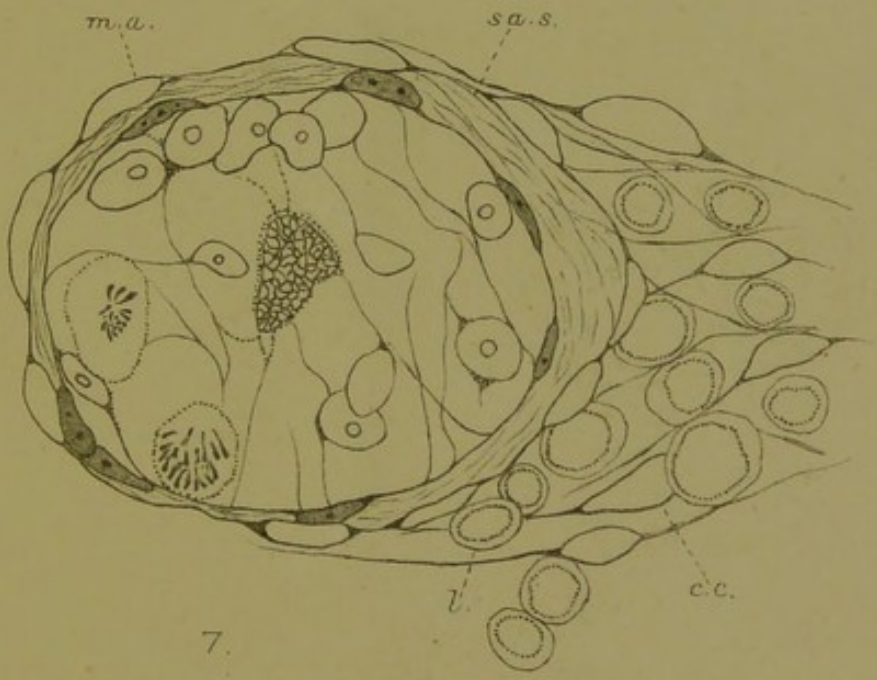

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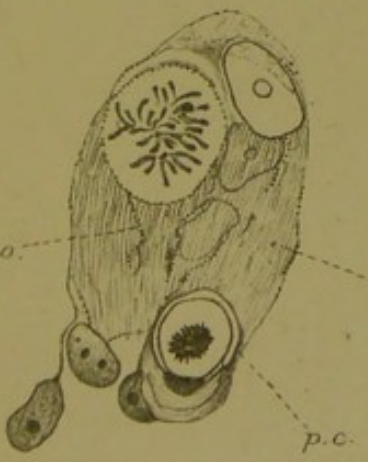

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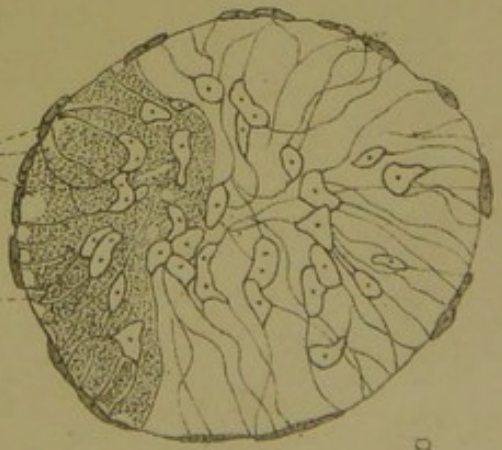

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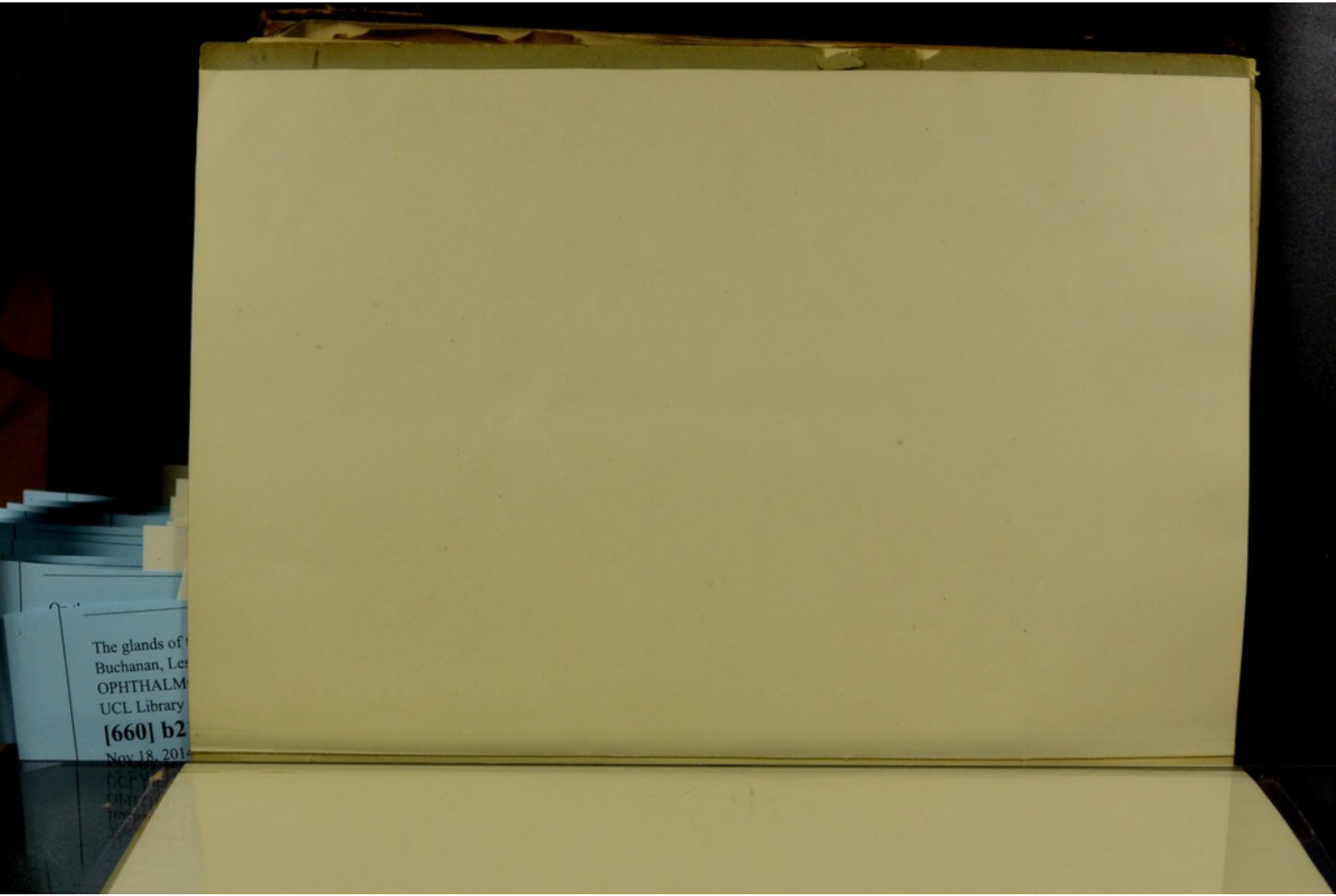
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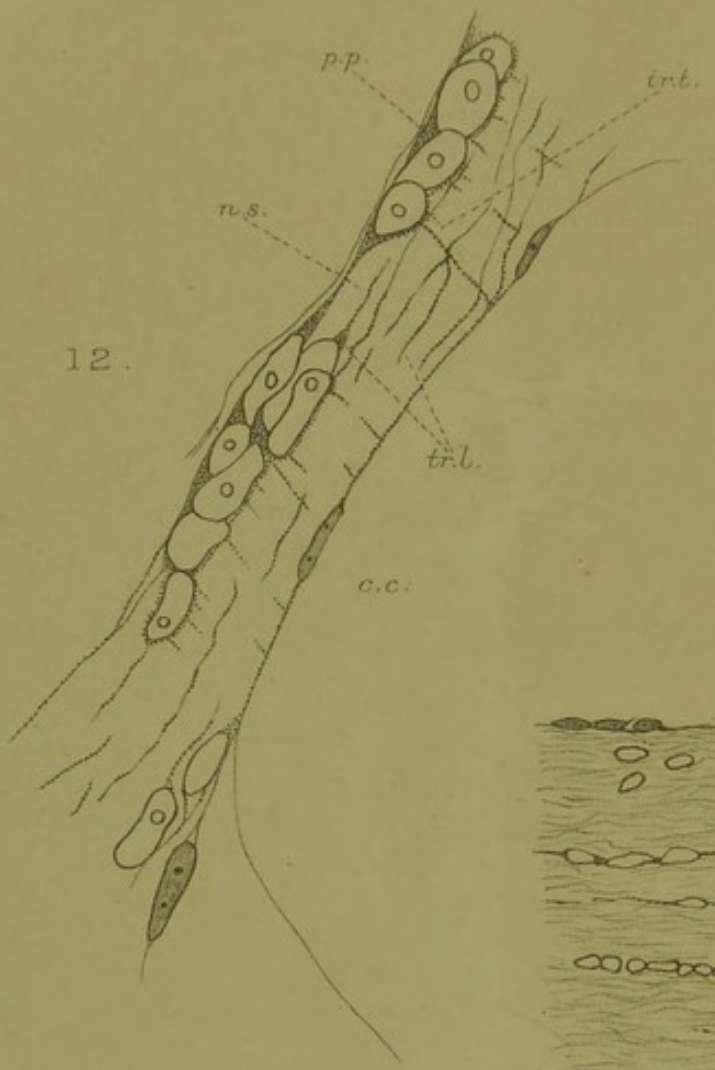

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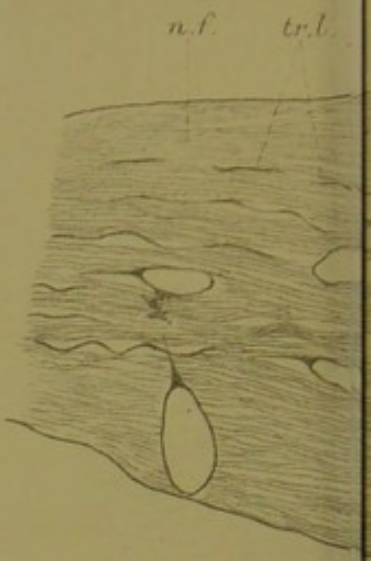

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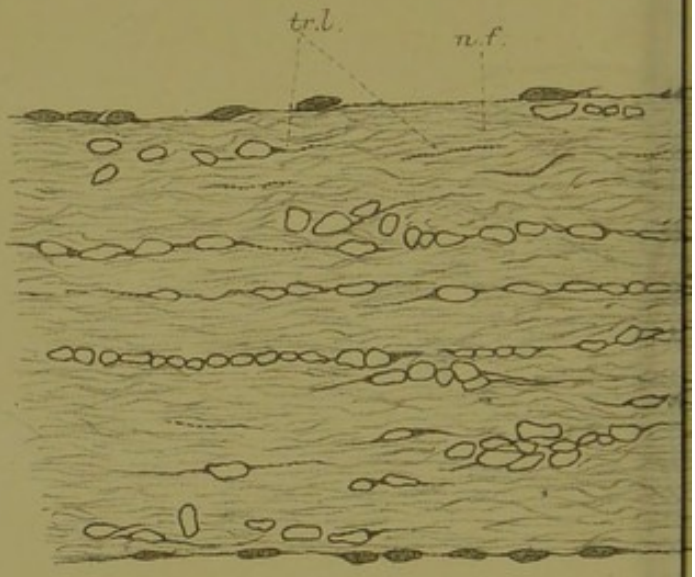

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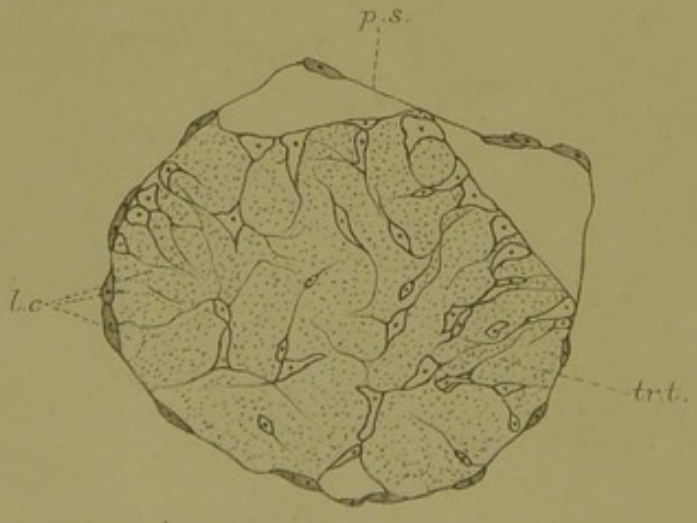

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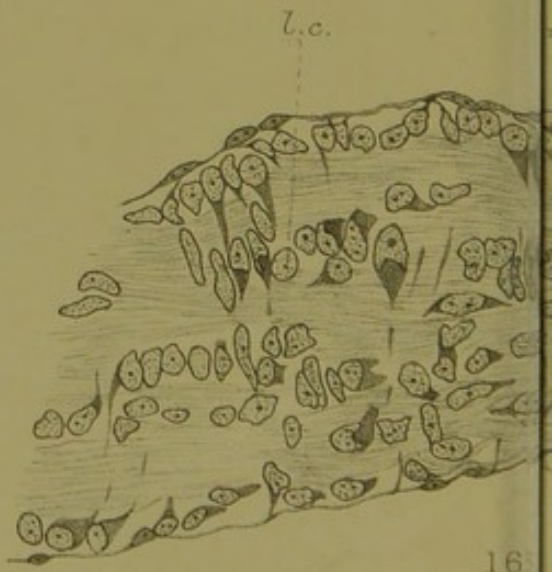

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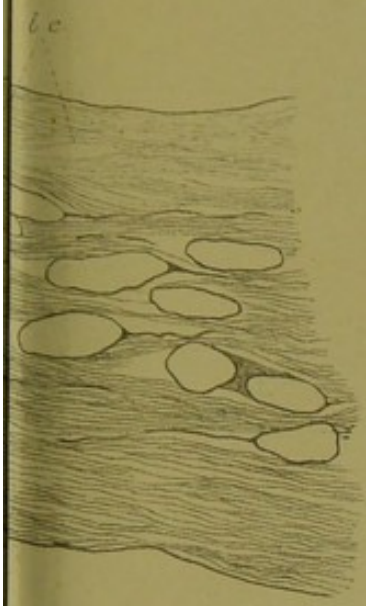

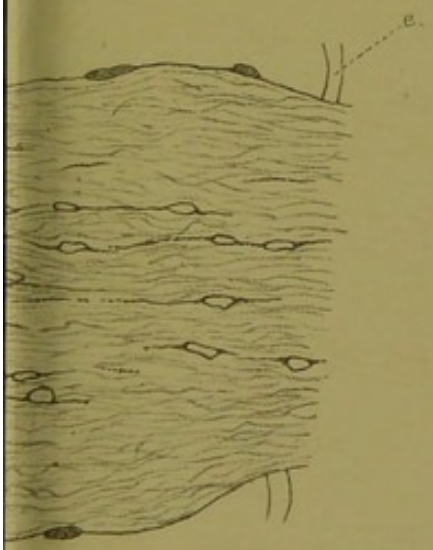

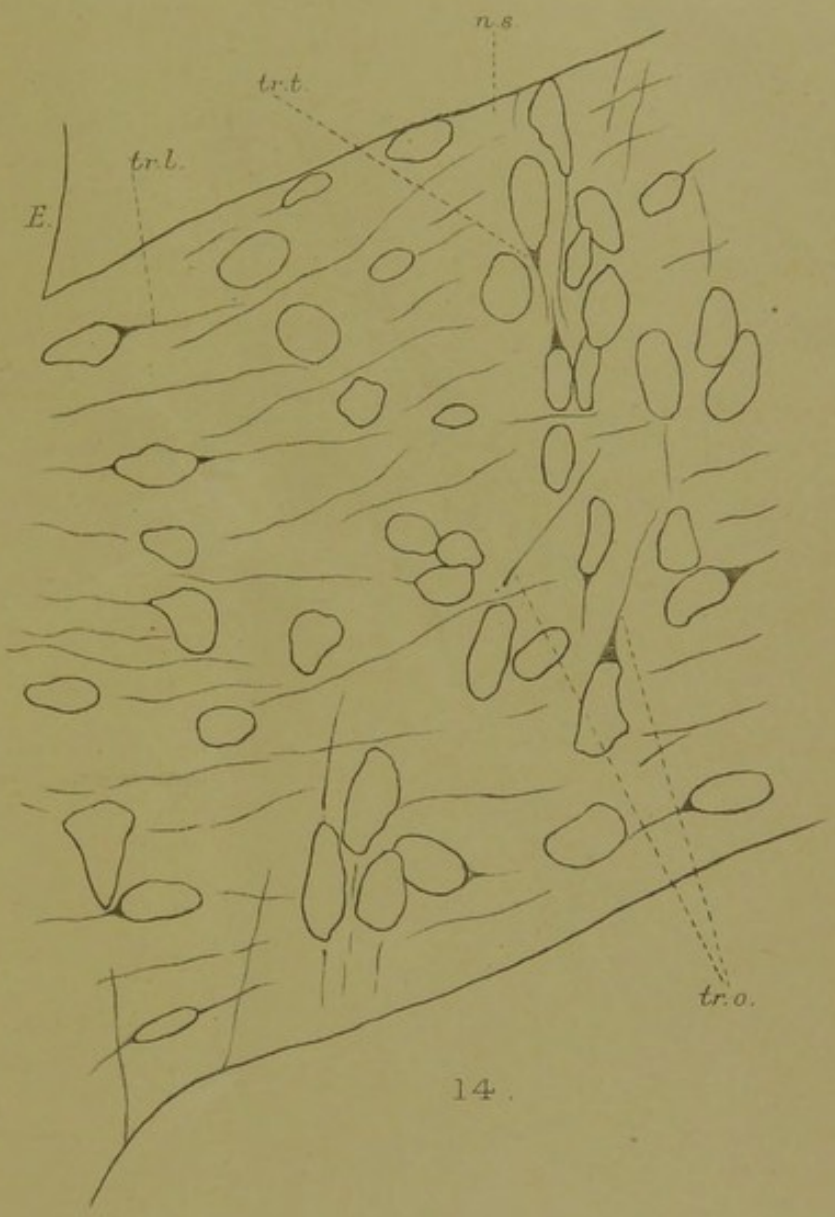

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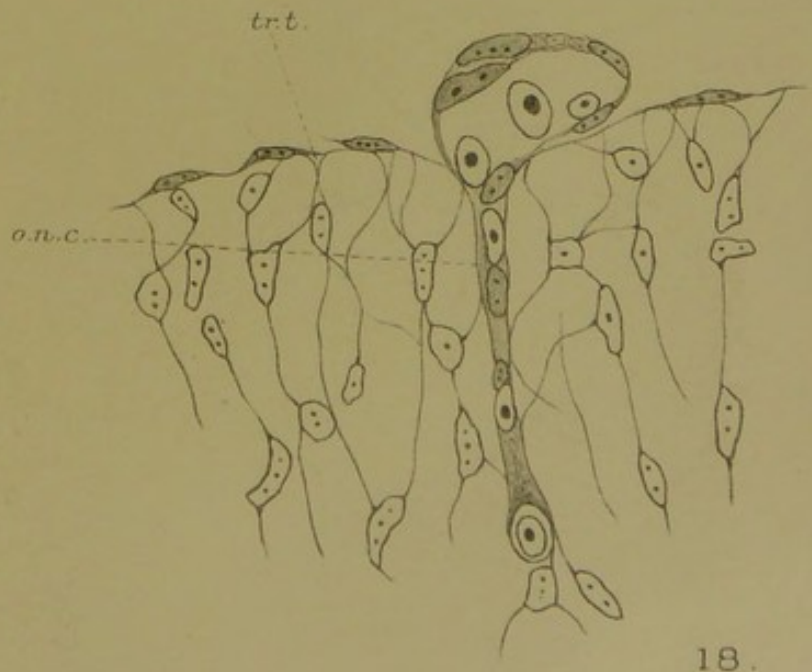

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Researches on the Origin and Development of the Epiblastic Trabeculæ and the Pial Sheath of the Optic Nerve of the Frog, with illustrations of Variations met with in other Vertebrates, and some Observations on the Lymphatics of the Optic Nerve.

By

J. T. Gradon, M.A.,
St. John's College, Oxford.

With Plates 26, 27.

Introduction.

Just over a year ago I began to feel dissatisfied with Assheton's (1) conclusion that the cells of the optic stalk do nothing more than serve as a conductor for the fibres of the optic nerve.

As I was aware that Assheton's (1) opinion had been fully endorsed by Professor Ryder (8) in the embryological section of Norris and Oliver's 'System of Diseases of the Eye,' I thought it unnecessary to go any further into the literature of the subject before beginning the present researches, and unfortunately I had finished them before I found that the part of the epiblastic trabeculæ that I shall speak of as transverse, had been dealt with by W. Müller (6), Kölliker (5), Robinson (7), Studnička (9), and Froriep (3 a). But, as all of these well-known investigators have dealt with the transverse fibrils as though they were the whole epiblastic trabeculæ of the optic nerve, instead of being only a part of

its complex framework, it will be my aim in the present paper to describe its origin and development as a whole.

The subject will be dealt with under the following heads:

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I. The Relation of the Optic Stalk to the Nerve-fibres.

In discussing Assheton's (1) contention that the first nerve-fibres, though lying along the posterior border of the stalk, are at first entirely outside it and separate from it, Robinson (7), after showing that this conclusion is altogether at variance with the observations of W. Müller (6) upon the lamprey, of Kölliker (5) upon rabbits, pigs, and calves, of Keibel (4) upon reptiles, and of Froriep (3) upon cartilaginous fishes, makes the following very important statement:—"If the condition which Assheton (1) found in the frog is present in mammals also, then it follows that the sustentacular framework of the optic nerve of man may consist, for the most part, like the framework of an ordinary cerebro-spinal nerve, of mesoblastic tissue surrounding and embedding the epiblastic nerve-fibres, but if Müller's and Kölliker's statements are well founded, then the sustentacular tissue of the optic nerve in man and mammals must consist chiefly of epiblastic tissue derived from the primitive epithelial cells of the optic

stalk; . . . this is a matter of some morphological, and certainly of pathological, importance."

All my specimens undoubtedly confirm the observations of the authorities quoted by Robinson (**7**), and his own statements, which are based upon observations made on human embryos, cats, ferrets, sheep, rabbits, rats, and mice, viz. that the ingrowing nerve-fibres lie within the membrana limitans externa, throughout the whole of their course in the optic stalk, and that they enter the stalk along the ventral wall; though Froriep (**3 a**) has lately stated that, in his specimens of rabbit embryos, the earliest bundles of nerve-fibres grow in higher up on each side of the ventral wall, and that the nuclei that lie above the ingrowing nerve-fibres are pushed up towards the lumen of the stalk, whilst those that lie below are pushed still further down, as the number of nerve-fibres increases.

In tadpoles of 6 mm. in length I have invariably found the earliest bundles of nerve-fibres, as they issue from the optic cup, occupying a central position just within the membrana limitans externa of the ventral wall of the stalk, and, as they approach the brain, getting more and more towards the posterior side of it, though in 8·5 mm. tadpoles they seem first of all to travel a little anteriorly for a very short distance, just after leaving the optic cup. These observations are in agreement with Froriep's (**3 a**), figs. 237—239, taken from tadpoles.

II. Cellular Segmentation.

Robinson (**7**) has referred to the difficulty of obtaining indications of definite cell-territories in the early stages of the embryonic optic stalk of the rat.

In tadpoles of 4·5 mm. in length cell limits are certainly recognisable (fig. 1), but in those of 6 mm. in length they can rarely be distinguished from the pigmented fibrils of the protoplasm that encircles the granules of food-yolk, or

takes up the position lately occupied by those that have been assimilated.

An inspection of fig. 2 will show that the entrance of the nerve-fibres along the ventral wall of the stalk produces a confluence and stretching of these delicate protoplasmic fibrils, and, at the same time, brings into prominence the connections subsisting between nucleus and nucleus.

Further ingrowth of the nerve-fibres resolves these fibrils into a complex framework of supporting elements which, from transverse, longitudinal, and horizontal sections, may be seen to radiate in every direction from the border of each nucleus of the stalk.

This intermediate arrangement of the condensed protoplasmic fibrils finally becomes differentiated with the multiplication of the nuclei of the stalk into a transverse, oblique, and longitudinal framework which, as we shall afterwards see, also provides a complete system of lymph channels throughout the interior of the optic nerve.

III. Obliteration of the Lumen of the Optic Stalk.

The obliteration of the lumen of the stalk has received considerable attention from previous observers. Assheton (1) ascribes it to pressure from the cartilaginous walls of the cranium, whilst Robinson (7) considers that this cannot be looked upon as an important agent, and concludes that the obliteration "is brought about by developmental changes in growth and relationship of the constituent parts of the stalk," and that "with these is associated the invasion of the optic nerve-fibres."

In fig. 12 we can see that pressure is exerted on the stalk by the cartilaginous walls of the cranium, and it is also certain that pressure produced by contact with the back of the eye is the cause of the very decided oval shape of the stalk at this point; in an 11 mm. tadpole (fig. 4), its shape, when free, is almost round. But there are probably several causes at

work—both within the stalk itself and outside it—in bringing about the obliteration of the lumen.

The pressure everywhere outside the stalk is evidently greater than that within its lumen for, although the first nerve-fibres lie just within the external membrane, the presence of the smallest bundle is enough to produce a certain amount of bulging of the upper border of the ventral wall into the lumen without in the slightest degree altering the regularity of the outline of the external membrane underneath it (fig. 2).

It is true that further ingrowth of nerve-fibres produces a considerable change in the outline of the stalk, as shown in fig. 3, but by this time, the lumen has almost been closed, and still further ingrowth of nerve-fibres at the sides, completes its obliteration, and, at the same time, restores the slightly longer axis of the stalk to the horizontal position (figs. 4 and 5).

IV. Period of Slow Growth, followed by one of Great Activity, consequent on the Formation of the Arachnoid Sheath and the Enclosure of the Subarachnoidal Lymph Space.

Between the stages shown in figs. 4—6, representing tadpoles from 11 mm. to 21 mm. in length, the diameter of the stalk increases only very slightly. This is due to the fact that there is scarcely any karyokinesis going on within the stalk, and the protoplasmic framework, which is now binding the nerve-fibres together, seems unable to accommodate itself to further expansion.

Meanwhile, the stalk is being continually more and more stretched between the eye and the brain, so that it is possible to obtain transverse sections of a 21 mm. tadpole that do not contain a single nucleus, only the protoplasmic fibrils proceeding from nuclei that lie in the preceding and succeeding sections.

As there are no blood-vessels inside the optic nerve of the frog, and very few capillaries on the pial sheath, it will be evident that, up to this stage, the nutrition of the stalk is at a very low ebb; there are, however, no indications of degeneration; in fact, it is possible to show a solitary instance of cell-division now and again where the fibrils of the trabeculæ are in contact with the delicate capillaries that have crept up the pial sheath from the pia mater of the brain (fig. 9).

But when we turn to a 27 mm. tadpole (fig. 7) it is evident that a remarkable change has taken place; mitosis is everywhere abundant, the number of cells has already greatly increased, and the total diameter of the stalk is considerably greater than it was in the preceding stage.

This sudden change coincides with the more complete enclosure of the subarachnoidal lymph space, which has come about through the formation of the arachnoid sheath. Before the dural sheath has had time to form, the arachnoid itself is directly connected with the ophthalmic artery by a band of connective tissue, by means of which transudation of lymph from the artery doubtless takes place.

The subarachnoidal space, which is evidently not sufficiently enclosed until this stage has been reached, is now filled with nutritive material, which passes through the pial covering, and then reaches every nucleus of the stalk by means of the elaborate system of tiny channels that follow the course of each fibril of the epiblastic trabeculæ (figs. 8 and 13, and *pc.* fig. 17).

Moreover, we may now find, among the meshes of the connective-tissue cells that join the ophthalmic artery and the optic nerve, numbers of lymph-corpuscles, all in various stages of cell-division, though I have only shown them in outline in fig. 7.

Development now proceeds very rapidly, but I have not thought it necessary to publish any drawings of stages between that shown in fig. 8 and the adult stage shown in fig. 10.

In the latter figure we can see the final arrangement of th

epiblastic trabeculæ from the sector that I have filled in with nuclei and fibrils; the other part of the drawing only shows the distribution of the nuclei and some of the thicker fibrils.

It will also be evident from this drawing that the stellate arrangement of the nuclei and the trabeculæ, found in a 32 mm. tadpole, does not persist; it is gradually lost in succeeding stages.

V. Pigmentation.

In the earliest stages of the stalk the fibrils of the protoplasm surrounding each granule of food-yolk, are pigmented, and can be traced perhaps separately.

But, when there has been a confluence of probably several of these, through ingrowth of nerve-fibres, it makes the condensed transverse fibrils, seen in sections transverse to the stalk, stand out in bold relief, and, when one has learnt what to look for by means of these sections, allows the condensed oblique and longitudinal fibrils to be seen, in longitudinal sections, without having recourse to special methods of staining.

But as soon as the increased flow of lymph, that we have ascribed to the enclosure of the subarachnoidal lymph space, takes place throughout the nerve, the trabeculæ, excepting sometimes a very short and thickened piece close to the nucleus, become completely depigmented.

This renders it afterwards very difficult to follow the delicate, oblique and longitudinal fibrils among the nerve-fibres.

But even in the adult state the amount of pigment which the thickened end of the fibril sometimes contains near its nucleus is sufficient to catch the eye when the rest of the fibril would easily escape notice.

I have not thought it necessary to publish drawings of longitudinal sections from stages later than that represented in fig. 14, as there is nothing further to show than a con-

tinual increase of the number of nuclei and fibrils of the trabeculæ, without any apparent increase in the thickness of the latter.

It clearly follows, from what has been said, that the cells of the optic stalk are spongioblasts, and that they, therefore, take no part in the production of optic nerve-fibres, which arise, according to the researches of Ramon y Cajal (2) and other well-known investigators, from neuroblasts, chiefly in the retina.

VI. Supplementary Remarks.

Even when there is not sufficient protoplasm surrounding the resting nuclei of the stalk to be represented in the drawings, it will be understood that there is still an extremely delicate layer of it covering them, and that the fibrils of the trabeculæ form the continuations of it. This thin sheet of protoplasm may, however, be distinctly recognised around the nuclei that are undergoing division (vide especially fig. 9).

The fantastic outlines of the nuclear walls are accounted for by the fact that each fibril of the trabeculæ is being stretched by continual ingrowth of nerve-fibres, and is, therefore, pulling its nucleus towards the point of its attachment.

In this connection it will be interesting to compare the nuclear outlines of the densely-packed optic nerve of the frog (fig. 8), with those of the much less densely packed optic nerve of the dog-fish (fig. 17).

The nerve-fibres contained in the optic nerve of the latter are so comparatively few in number, and the lymph channels so wide and numerous, that, when favourable transverse sections of it are viewed with a very low power, the nuclei themselves appear to form a well-defined framework, through being pulled into mere threads between the nerve-fibres.

In the frog, on the other hand, the lymph channels, though

numerous, are so comparatively narrow, and the nerve-fibres so densely packed around the nuclei, that the pull exerted on a nucleus by each fibril of the trabeculæ, can only result in the production of a short cone.

VII. Formation of the Pial Sheath, and its Relation to the Membrana Limitans Externa.

I have figured the formation of the pial sheath from the earliest stages to show how the mesoblastic cells that enter into the formation of its connective-tissue layer, gradually unite with the external membrane of the stalk or its later representatives—the ends of the epiblastic trabeculæ.

But the union is only apparent, for a regular system of lymph spaces is formed between the ends of the trabeculæ and the layer of connective tissue, which may be separated in sectionising (fig. 17).

I have referred to the scantiness of its vascularity in the frog in a preceding section, p. 484.

In rat embryos of 8 mm. in length Robinson (7) found the peripheral boundary of the stalk clearly defined, but was unable to demonstrate a distinct external limiting membrane.

In the frog there never is any doubt about the external limits of the stalk, though the boundary is naturally more delicate in a 6 mm. tadpole than in those of succeeding stages.

The optic stalk of the chick, containing a very great number of cells, shows a well-defined external limiting membrane, supported by numerous mesoblastic cells, when the nerve-fibres begin to grow in, on the fourth day of incubation.

VIII. Some Variations of Epiblastic Trabeculæ met with in the Developing Optic Nerve of the Mouse, the Trout, the Dog-fish, and the Chick.

Although I have selected the tadpole for tracing the complete development of the epiblastic trabeculæ, still we can

find in other embryos some interesting variations which assist us very materially in gaining a fuller comprehension of the subject.

Fig. 15, which represents a longitudinal section of the optic nerve of an embryo mouse of fourteen days, gives us a better idea of the longitudinal fibrils than we have been able to gain in considering the later stages of these fibrils in the frog, as they lie in the same plane for a much greater distance, and are, at the same time, rather thicker for a greater part of their length than those we have seen in the frog.

On the other hand, in fig. 16, representing a longitudinal section of the optic nerve of a developing trout (length of optic stalk ·5 mm.), we see fibrils that are extraordinarily thick, and consequently very easily seen near their nuclei, but undulating to such an extent that it is only possible to follow them a very short distance away from their nuclei.

In fig. 17 I have shown a transverse section of the optic nerve of a 33 mm. dog-fish, and on p. 486 I have compared the nuclear outlines of the densely packed optic nerve of the frog (fig. 8) with those of the much less densely packed optic nerve of the dog-fish, shown in this figure, so that I need only point to the difference in the arrangement of the nuclei themselves, though, as I have stated on p. 485, the stellate arrangement of the nuclei and the trabeculæ in the optic nerve of the tadpole is lost before the adult stage is reached.

Another point of difference between the frog and the dog-fish lies in the fact that the pial sheath of the latter is richly supplied with blood-vessels, though not represented in the drawing.

A transverse section of the optic nerve of an eight-day chick (fig. 18) shows certain peculiarities of trabecular formation; the arrangement of the nuclei is free, like that of the dog-fish, but the nuclear outlines more closely resemble those of the frog, due, in my opinion, to the same causes as those I have given to account for the peculiarities of these outlines in the frog.

I have shown one of the numerous capillaries that supply

the interior of the optic nerve of the chick with blood and lymph descending into it from the pial sheath which is richly supplied with blood-vessels, and the adjacent fibrils of the epiblastic trabeculæ may be seen in contact with it (fig. 18).

In conclusion, I deeply regret to say that since this article was written, the sudden death of the Linacre Professor of Comparative Anatomy has rendered it impossible for me to publicly express my thanks to him for allowing me to carry on my researches in ocular embryology in the Department of Comparative Anatomy at Oxford, and more especially for the kind interest that he always took in my work. But I gratefully avail myself of this opportunity of thanking Dr. J. W. Jenkinson, Assistant to the Linacre Professor, for kindly providing me with unlimited material and preparations for the purpose of the present article.

Summary.

We have seen that our trabeculæ are entirely epiblastic in origin, for we have shown that the entrance of the nerve-fibres along the ventral wall of the embryonic optic stalk produces a confluence and stretching of the protoplasmic fibrils of the epiblastic cells of the stalk, which result in a complex framework of supporting elements radiating in every direction from the border of each nucleus of the stalk, and that this complex framework afterwards becomes more or less differentiated into a transverse, oblique, and longitudinal trabeculæ with the multiplication of the nuclei of the stalk and without any admixture of mesoblastic cells, for we have also shown that the nerve-fibres lie, throughout the whole of their course, in the optic stalk, within the membrana limitans externa, on the outside of which we have followed the gradual formation of the connective-tissue layer of the pial sheath.

We have noticed the obliteration of the lumen of the stalk, and have ascribed it to various causes operating within the stalk itself and outside it, though chiefly to the ingrowth of nerve-fibres.

We have seen that, in the development of the optic nerve of the frog there is a period of slow growth, followed by one of great activity, and we have felt justified in ascribing this sudden outburst of activity to a greatly increased flow of lymph into it by means of the elaborate system of minute channels that follow the course of each fibril of the epiblastic trabeculæ, and consequent upon the formation of the arachnoid sheath and the enclosure of the subarachnoidal lymph space.

We have therefore shown that the cells of the optic stalk perform the following three functions:

1st. They conduct the nerve-fibres, which, in their turn, resolve the constitution of the cells of the stalk, so that they—

2nd. Provide the nerve-fibres with a supporting framework which—

3rd. Provides the whole interior of the optic nerve with an elaborate system of minute lymph channels.

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EXPLANATION OF PLATES 26 AND 27,

Illustrating Mr. J. T. Gradon's paper, "Researches on the Origin and Development of the Epiblastic Trabeculæ and the Pial Sheath of the Optic Nerve of the Frog."

ALPHABETICAL LIST OF REFERENCE LETTERS FOR ALL THE FIGURES.

Br. Brain. c.c. Cartilage of the cranium. *c.c.* Connective tissue cells between the ophthalmic artery and the optic nerve. E. Eye. *e.* Outline of pigmented epithelium of retina. *e.m.* Membrana limitans externa. *i.m.* Membrana limitans interna. *l.* Lymph-corpuscle. *l.c.* Lymph channel. *l.s.* Lumen of optic stalk. *m.a.* Mesoblast of the arachnoid sheath. *n.f.* Optic nerve fibres. *n.s.* Space occupied by nerve fibres, not represented. *o.n.c.* Interior capillary of optic nerve. *p.c.* Capillary of pial sheath. *p.p.* Pigmented protoplasm. *p.s.* Pial sheath. *sa.s.* Subarachnoid space. *tr.l.* longitudinal, *tr.o.* oblique, *tr.t.* transverse trabeculæ. *y.* Granules of food-yolk.

Fixing agent: Aceto-corr. subl. Stain: Borax carmine + picro-indigo-carm.

All the figures have been drawn with the Abbe camera.

The terms transverse and longitudinal apply to the optic stalk.

Figs. 1 to 8 are transverse sections taken from tadpoles, the lengths of which are given below.

They are all taken from the distal fourth of the stalk, except Fig. 2, which is taken from the proximal fourth.

They show the gradual formation of the transverse trabeculæ and the pial sheath.

The nerve fibres have only been represented in some of the figures, but they will be understood to occupy the spaces between the trabeculæ.

The resting nuclei of the stalk, except in Fig. 16, have been outlined only, and all the nuclei of cells entering into the formation of the pial sheath have been shaded.

The top of the page represents "dorsal."

PLATE 26.

FIG. 1.—4·5 mm. × 800. (See previous page.)

FIG. 2.—6 mm. × 800.

FIG. 3.—8·5 mm. × 800.

FIG. 4.—11 mm. × 800.

FIG. 5.—15 mm. × 800.

FIG. 6.—21 mm. × 800.

FIG. 7.—27 mm. × 800.

FIG. 8.—32 mm. The nerve fibres and lymph channels are shown in part of the drawing only. × 500.

FIG. 9.—Oblique transverse section, from the same series as Fig. 6, taken close to the brain. × 800.

FIG. 10.—From a transverse section of the optic nerve of an adult frog. Taken 160 μ from the eye. Only a sector has been filled in with the transverse trabeculæ. × 500.

FIG. 11.—Horizontal section from an 8·5 mm. tadpole; showing fibrils of the transverse, oblique, and longitudinal trabeculæ. × 800.

PLATE 27.

FIG. 12.—Longitudinal section, from a 15 mm. tadpole. Taken near the brain. × 800.

FIG. 13.—Peripheral longitudinal section, from a 29 mm. tadpole. Taken midway between the eye and the brain. × 800.

FIG. 14.—Longitudinal section, from a 32 mm. tadpole. × 800.

FIG. 15.—Longitudinal section, from a 14 day embryo mouse. × 500.

FIG. 16.—Longitudinal section, from a developing trout. Body length not known; length of stalk ·5 mm. × 500.

FIG. 17.—Transverse section from a 33 mm. dog-fish. The two large spaces between the pial sheath and the membrana limitans externa, here represented by the epiblastic trabeculæ, are due to sectionising, and they show that the pial sheath forms a separate layer around the optic nerve. × 500.

FIG. 18.—From a transverse section of the optic nerve of an 8-day chick. × 800.