# A QUANTITATIVE ANALYSIS OF THE STRUCTURE OF THE CEREBRAL CORTEX

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(WITH 3 PLATES AND 31 TEXTFIGURES)

VERHANDELINGEN DER KONINKLIJKE AKADEMIE
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# I. INTRODUCTION.

The accepted division of the cerebral cortex into 6 layers is based on quantitative differences mainly : at different distances from the pia the average size and the number of the ganglion cells and the density of the horizontal and vertical myelinated nerve fibres are different.

The division of the cortex in cytoarchitectonic fields is based on the same quantitative properties. Even those few characteristics of some of these fields that seem to have a more qualitative character — the BETZ cells, the stellate cells of MEYNERT, the „Umfassungszellen" of DE CRINIS, the stria of GENNARI etc. — by a further analysis prove to be of a quantitative nature as well.

Yet consequent measurings of these properties and an attempt to base the description of the layers and fields on measurements are never made. All descriptions in literature are given in this form : at this place the ganglion cells are markably larger than on that, or : here the number of horizontal myelin-fibres is increased or : the main dendrites of these cells are branching at a lower level than the others.

A more accurate description of the cortical layers and fields claims measuring.

Moreover, it is possible that measurements may reveal laws, indicating unknown properties of the cortex which could scarcely be found without them.

Difference in cortical function is always combined with morphological differences of the architectonic fields, that means it is combined with the quantitative differences mentioned above. A more accurate knowledge of the laws, determining these differences, may include valuable indications about the relation between structure and function of the nervous apparatus.

As a third motive for measuring these differences I may add my conviction, that measuring, which is so little done in microscopic anatomy, will be a fruitful method of research in this branch of science. In astronomy, physics and chemistry measuring of the relations in space and in time has brought an unexpectedly deeper insight into the phenomena of dead nature. Why should not they do the same in the relations in space, that is in the form, of the bodies of the living nature?

The attempt to analyse the structure of the cerebral cortex by measurements, therefore, is done with the intention of indicating by the aid of an example the probability that measuring of microscopic anatomical material may be a fruitful method in the study of microscopic anatomy in general.

The great length of time needed to complete the research, has induced

me to publish the results so far obtained. Although these first results are not as extensive as I would like them to be, they are sufficient to show that there is a regularity in the phenomena indicating laws of an exact nature. And the existence of laws in the results of measuring is even the condition, this method will be usefull in the objects of microscopic anatomy.

The conviction of most biologists, that such regular laws do not exist in the structure of living bodies, has lead to the neglect of the measuring method. Even the limited first results given in this paper seem to me to form a convincing proof of the error of this conviction.

## II. METHOD OF MEASURING.

The shape of the nerve cells being fairly irregular, it would be a very laborious task to define their size by means of numbers in an exact degree. The size of the nerve cells in the studied territory varying widely (the volume of the largest cell body is nearly 1000 times the volume of the smallest one) a relatively rough approximation of the individual sizes may suffice for a first analysis and so no attempt was made to reach the highest possible accuracy.

In a previous paper [1]) I could demonstrate, that the size of the nuclei is a measure for the size of the nerve cells, the volume of their perikaryon being proportional to the square of the volume of their nucleus. Therefore, in the analysis of the cortex structure discussed in this paper, the size of the ganglion cells was measured by the volume of their nuclei.

This was not measured with the greatest possible accuracy. From the image of the nucleus, seen in the microscope, only the length and the breadth were measured, namely in the first place the longest diameter and in the second place the largest diameter found in the direction perpendicular to the first. From these values the volume of a rotation ellipsoid with the same longest and smallest diameter was calculated.

These calculated volumes are not exactly the same as the real volumes of the nuclei. In the paper mentioned above, the differences between the two were discussed in detail, the nucleus volumes referred to there being calculated in the same way. From the results of the measurements it could be concluded that they vary according to the laws of probability. So the errors, made in this manner of measuring the nucleus volumes, show the same character as the errors, made in most other measurings. The calculated volumes of the rotation bodies, therefore, will be called here the measured nucleus volumes.

Measuring with the aid of an ocular micrometer was not exact enough : the formation of the real image in the microscope is disturbed by the stripes of the micrometer (a scaled glass placed at the height of the image). Moreover the distance between the stripes — the unity of measuring — is too large.

Therefore a measuring apparatus was constructed, by which the microscopic image of the nucleus was seen together — with the aid of a drawing prism placed on the microscope — with two small light points, that were placed outside the microscope and the

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[1]) S. T. BOK, A quadratic relation between the volumes of the nucleus and body of ganglion cells of different sizes, Psychiatrische en Neurologische Bladen (1934).

distance between which was variable and measurable. If these lightpoints are seen together with two points of the nucleus membrane, the distance between these two points of the nucleus is proportional to the distance between the two light points (their distance from the drawing prism and the objective, the oculare and the tube length of the microscope being kept constant). A scale, giving the distance of the light points can be made in such a way that the distance of the nuclear points in microns can be read from it.

### Construction of measuring apparatus.

At a distance of about 33 cm behind the twice reflecting drawing prism placed on the microscope two vertical glass plates — parallel to each other and about 0.1 mm from each other — are mounted each in a metal ring. These rings can be rotated round a common axis, that runs perpendicular to the glass plates (the prism is situated in the neighbourhood of its elongation). Both glass plates are diapositives, their gelatinated sides are turned towards each other. Both are blackened within a circle of about 2½ cm radius, the centre of which falls in the rotation axis. In the black field of both plates a figure of white lines is present. On the posterior plate this figure consists of two straight lines that meet under a right angle exactly in the centre (fig. 1). In the black field of the anterior plate a white point

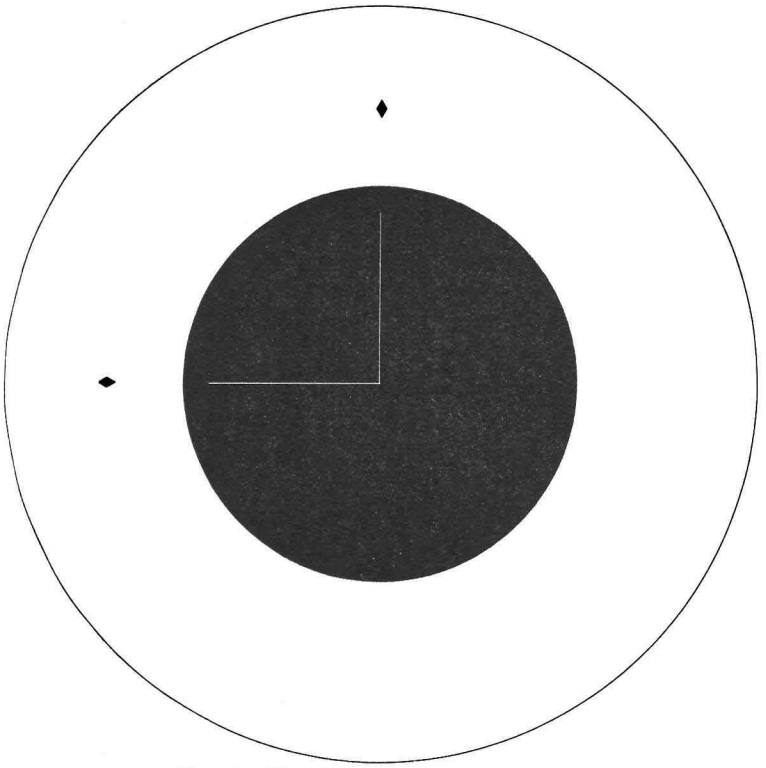

Fig. 1. The posterior measuring plate.

is marked exactly in the centre and a white spiral is drawn around it (fig. 2).

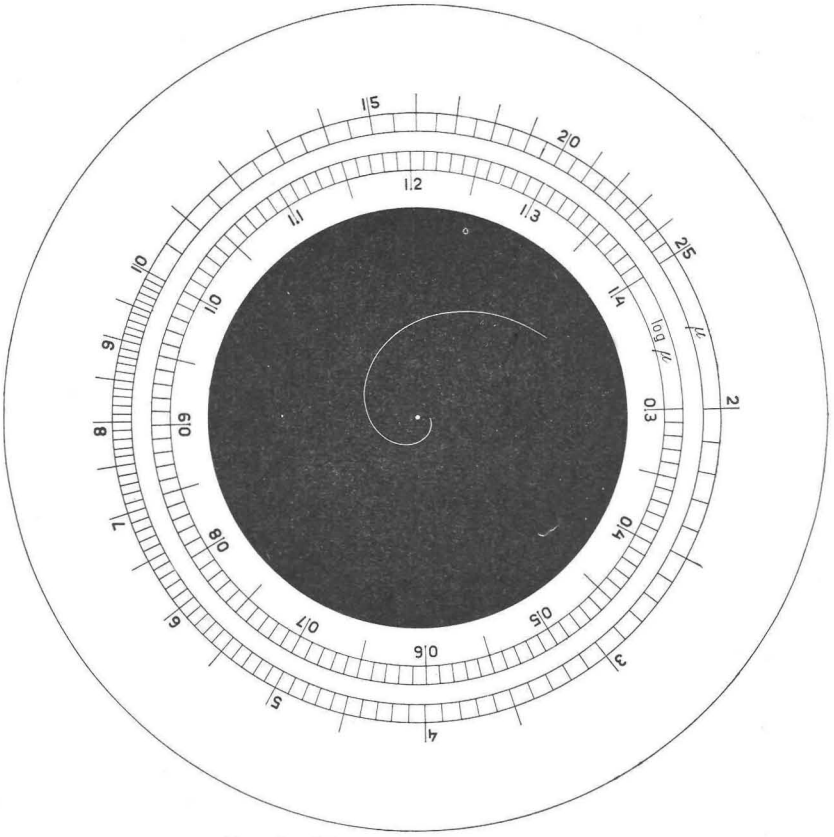


Fig. 2. The anterior measuring plate.

The light, coming from a lamp placed behind the plates, only passes through them at the three points where both plates are not blackened :

1°. in the axis (in the posterior plate here the two white lines meet, in the anterior plate the white point),

2°. at the crossing of one of the white radii of the posterior plate and the white spiral of the anterior plate,

3°. at the crossing of the other radius and the spiral.

Seen through the prism together with the microscopic section these three light points are remarkably delicate.

When the anterior plate is rotated by the aid of its metal ring, the light point in the axis keeps its place, but the two other lights move along straight lines in directions to or from the invariable light point, the white radii of the posterior plate being unmoved and now crossing other parts of the moved spiral. The measure of the rotation is a measure of the movement of the variable light points.

To read the distance of each variable light point from the invariable one on the posterior plate a black mark is drawn in the elongation of each white radius and on the anterior plate a round scale outside the black field is drawn. The place of each mark in the scale thus gives the distance of the corresponding variable light point to the fixed light point and in consequence the distance in the section that was to be measured. The scale runs from 2 to 25 $\mu$.

In order to facilitate the calculations a second scale is drawn, giving the logarithms of these distances. The spiral being chosen as a logarithmic one, this second scale shows an equal division : over the total length of the scale the smallest lines, giving the second decimal of the logarithm, being separated by equal intervals of about 1,7 mm. This logarithmic scale runs from 0,30 to 1,40 and is about 18,5 cm long.

By rotation of the posterior metal ring both glass plates rotate, so that the variable points come in different directions relative to the fixed point, that keeps its place. Thus measuring in any direction is possible.

On the posterior plate two radii are drawn perpendicular to each other in order to facilitate measuring in two directions, exactly perpendicular to each other. By rotation of the posterior ring one of the variable light points is brought in the right direction in regard to the fixed one in order to measure the longest diameter of the nucleus. The breadth can then be measured perpendicular to the length with the aid of the other variable light point, if the posterior metal ring is not rotated after the length was measured.

In order to bring the "fixed" light point accurately on the desired point the whole mechanism can be moved in the plane of the plates by two screws of a cross table on which it is mounted.

The microscope and the measuring apparatus are placed on a rail, the right distance between them being found in the following manner.

The anterior ring is rotated till a mark indicates 20 $\mu$. In the microscope an object micrometer is placed (a glass with a scale, divided in 0.01 mm = 10 $\mu$). Then the distance of the measuring apparatus is changed till the two light points, seen in the drawing prism, coincide with two lines of the object micrometer, the distance of which is 20 $\mu$. After the apparatus is fixed in this position it can be used for measuring.

The light for the microscope was obtained from an electric sodium lamp. In the Nissl sections used the yellow light give a good contrast between the blue details and the uncoloured back ground. And the monochromacy increases the sharpness of the image.

The calculations of the nucleus volumes were made as follows.

Only the logarithms of length and breadth were read. The logarithm of the length was written under the number 0,72 — 1, the logarithm of the breadth was twice written under it. Summarizing of these four values gave the logarithm of the nucleus volume.

The nucleus volume, namely, was reckoned to be the volume of a rotation

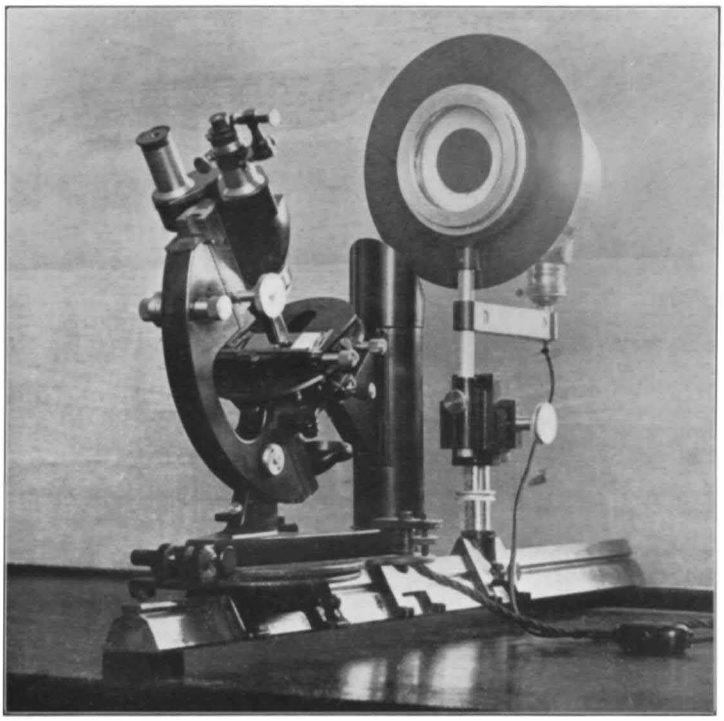

Fig. 3. The measuring apparatus.

ellipsoid the diameters of which are the length ($l$) and the breadth ($b$) of the nucleus. The volume of this ellipsoid is given by the formula :

$$N = \frac{1}{6} \pi l b^2$$

or

$$\log N = 0{,}72 - 1 + \log l + 2 \log b,$$

$\log \frac{1}{6} \pi$ being $0{,}72 - 1$.

A photograph of the apparatus, ready for use, is given in fig. 3.

## III. NUCLEUS VOLUME AND DISTANCE FROM THE PIA.

From different architectonic fields in the left hemisphere of a human cerebrum, sections, 30 $\mu$ thick, were made perpendicular to the pial surface. They were stained by NISSL's method.

Most of the measurements discussed in this paper are taken from a section made in the area temporalis superior posterior (VON ECONOMO). Of each of the ganglion cells in a definite part of this cortex the volume of its nucleus and its distance from the pia were measured.

To obtain correct measurements of the distances from the pia it is highly important to choose parts of the cortex that are not curved, because flexion — e.g. at the borders of a gyrus and at the bottom of a sulcus — influences the height of the different layers in different ways, as I described previously [1]). So the relation between the pia distances of different cells is altered by each flexion of the cortex. To exclude such a flexion, it is not sufficient to choose a part of the cortex that seems to be uncurved when observed in the microscopic section : a flexion perpendicular to that section will also effect the proportions of the layers though it does not curve any line in that section. Therefore the measurements are done at a place, where the cortex was found to be uncurved in all directions over a pretty large area.

From such an uncurved part of the cortex a microphotograph was made, showing a linear enlargement of 300 $\times$. On this photograph two parallel right lines were drawn through the total height of the cortex, 12 c.m. from each other and perpendicular to the pial surface. From each of the 1546 ganglion cells, situated between these two lines, the nucleus volume was measured in the way described above.

If less than the half of a nucleus was lying within this field, its cell was not measured. This rule was followed at the borders, formed by the two said lines as well as at the two surfaces of the section.

The distance of the basis of the perikaryon from the pial surface was measured in the photograph (divided by 300, being its linear enlargement). This distance from the pia will be called the depth of the cell, it being the depth at which the cell is situated in the cortex under the pia.

The results of these two ways of measuring are shown in fig. 5. In this scheme each point indicates of one ganglion cell the nucleus volume and the depth (distance from the pia), the volume of the nucleus being its

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[1]) S. T. BOK, Der Einfluss der in den Furchen und Windungen auftretenden Krümmungen der Grosshirnrinde auf die Rindenarchitektur. Zeitschr. f. d. ges. Neurol. u. Psychiatrie, Bd 121, (1929).

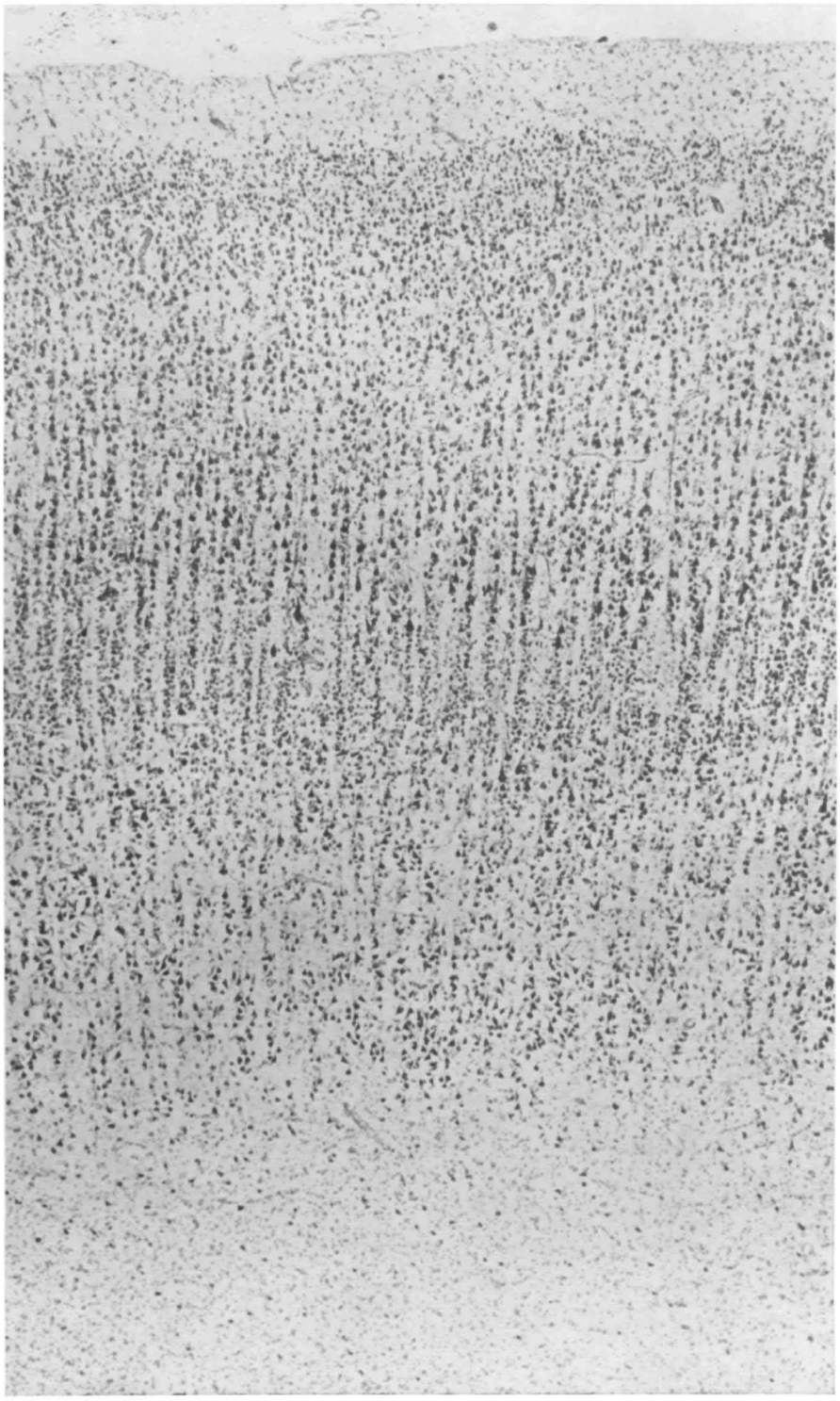

Fig. 4. Photograph of the measured left area temporalis superior posterior of a human cerebral cortex, stained by NISSL's method.

absciss and the depth being its ordinate. The zero of the depth is chosen at the top of the figure; in consequence a cell that is situated lower in the

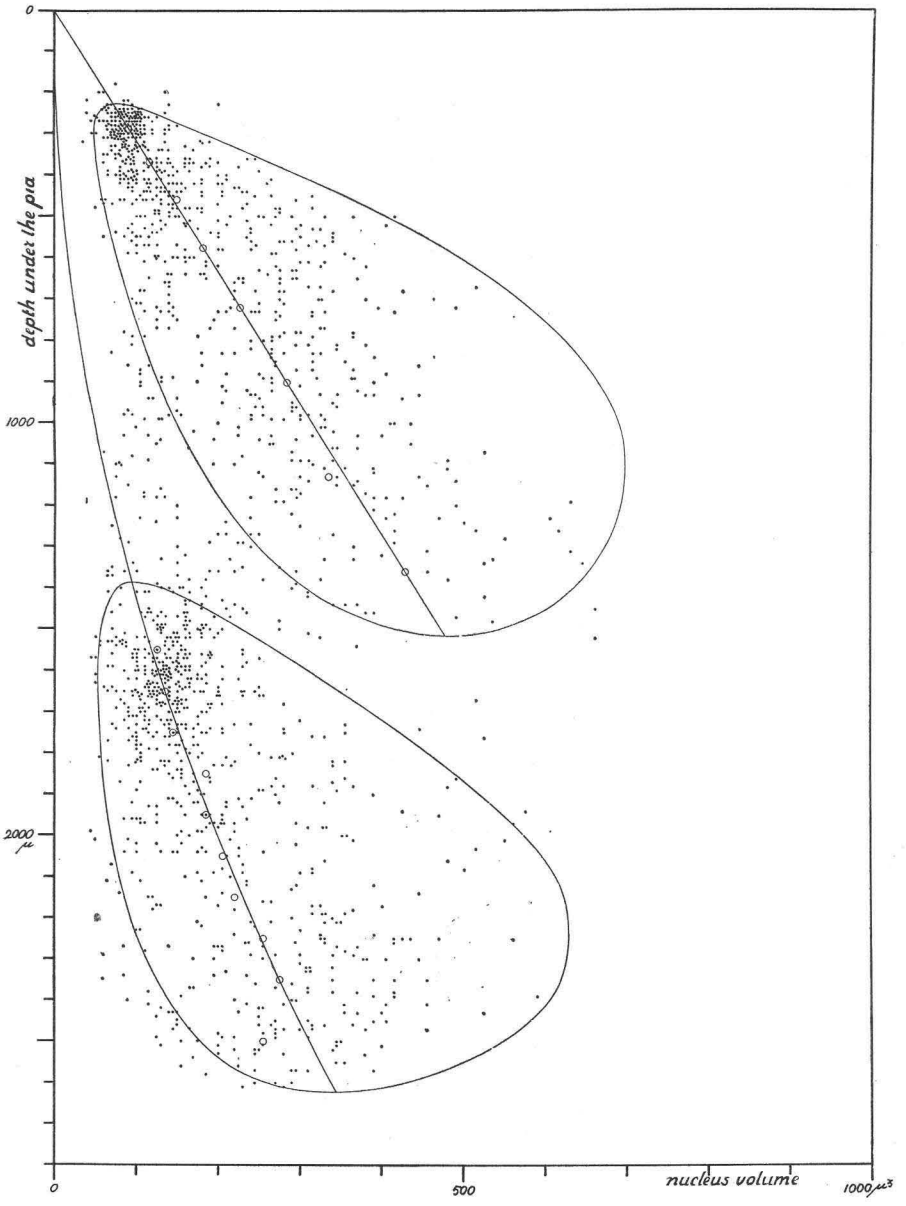


Fig. 5. Diagram of the nucleus volumes and depths of the ganglion cells in the area temporalis superior posterior.

cortex than another cell is represented by a point, that is situated lower in the figure as well. Cells with larger nuclei are represented by points, situated more to the right in the figure. (The different lines, drawn in this figure, will be discussed later on.)

If we examine this figure from the top to the bottom we first meet the points, representing the ganglion cells of the outer corner layer (layer II). They are numerous and situated to the left: their nuclei are small. From here downwards the nucleus volumes increase gradually (the points lying more to the right) and are situated at larger distances from each other: this part of the figure represents the outer pyramid layer (III). At a depth of about 1500 $\mu$ a second group of numerous points appears to the left: the numerous small ganglion cells of the inner corner layer (IV). This group gradually passes into a region in which the points are distributed less densily and are situated more and more to the right: the lager cells of the inner pyramid and of the multiform layer (V and VI).

Another example of such a scheme was published in 1934 [1]). In that paper I came to the conclusion, that by measuring the ganglion cells only a limit between an upper zone of the cortex (the layers II and III) and a lower zone (the layers IV, V and VI) could be recognized. In regard to the size of the ganglion cells the IInd layer only gradually passes over into the IIIrd layer without any clearly marked limit. And so do the three layers of the lower zone. In the new measurements of 1546 ganglion cells, given here, the same unity of each of the two main zones is evident. A subdivision of these two zones into 5 limited layers cannot be based upon differences in the sizes of the ganglion cells. Nor can it be based on their frequencies (fig. 17).

The limit between the upper and the lower zone is not a sharp one, at a certain distance from the pia ganglion cells of both zones seem to be present.

In the following pages it will be shown that the values measured tend to geometrical progression more than to arythmetical progression. In consequence their relations will be demonstrated more clearly in diagrams bringing the logarithms of the measured values, than in diagrams of the values themselves (than in numerical diagrams).

The logarithm diagram of fig. 6 shows the same values as were shown in the numerical scheme of fig. 5. It differs from that of fig. 5 by the fact only that instead of the nucleus volumes and the depths the logarithms of these values are used as abcisses and as ordinates.

This logarithm diagram also suggests the idea, that the cells of the cortex are to be divided into two main groups.

This idea is supported when we calculate the average nucleus volume in each level of the cortex. Of the ganglion cells lying at depths, the logarithm of which varies between 2,4 and 2,5, between 2,5 and 2,6 etc., the geometrical average nucleus volume was calculated by adding the

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[1]) S. T. BOK, Messungen an den Ganglienzellen der Grosshirnrinde, I. Die Einheitlichkeit der einzelnen Hauptzonen. Zeitschr. f. mikrosk. anat. Forschung, Bd **36**, S. 645—650, (1934).

logarithms of their different nucleus volumes and by dividing this sum by their number.

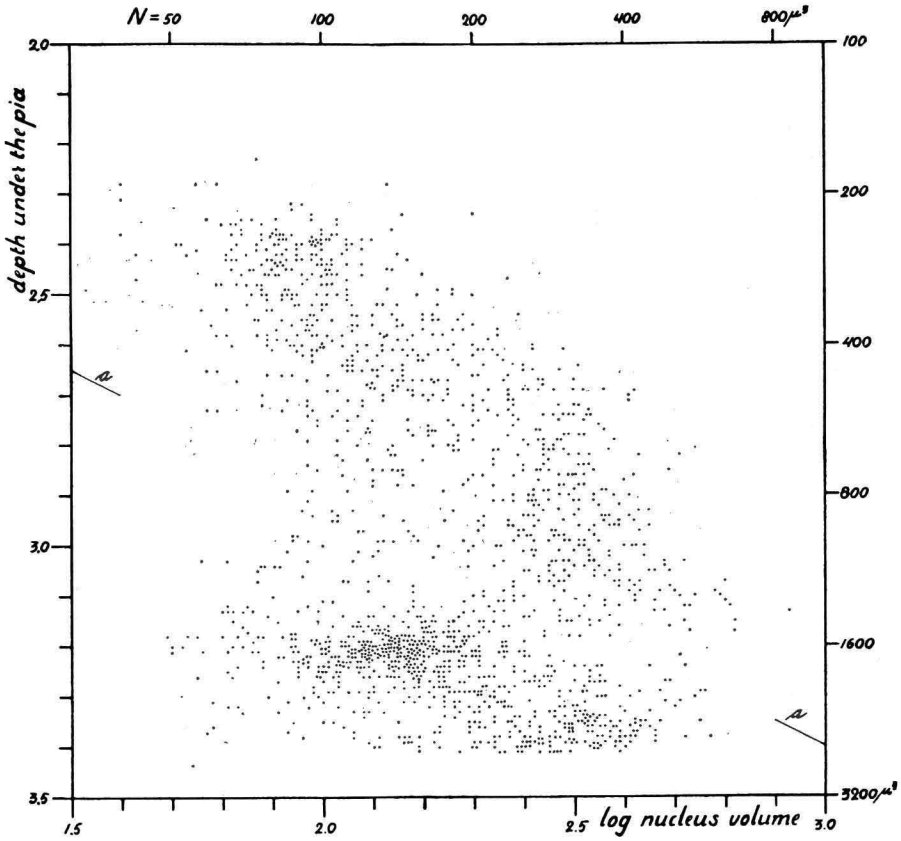


Fig. 6. Logarithmic diagram of the nucleus volumes and depths.

In fig. 7 these average volumes are shown. The points are situated along a line that begins and ends as a straight line. The upper straight part makes an angle of 45° with the vertical line (tangent = 1). The lower straight part, however, makes an angle with the vertical line showing a tangent = 2. Between these two straight parts the line is curved backwards.

This curious form of the line suggests that it may result from two straight lines, the curved middle part being the effect of a mixing up of two groups of cells each with an average value that possibly lies on one of the straight lines.

In fact such a division into two groups of points can be made by drawing in the diagram of fig. 6 a straight line, indicated by the two small lines *a*—*a* and passing through that part of the field in which the points are distributed less densily. In fig. 8 each of this groups shows a simple relation between the average nucleus volume and the distance from the pia.

In the upper group each average nucleus volume is represented by a

small circle, situated in — or quite near to — the above mentioned straight line, the direction of which is given by the tangent = 1. And most of the circles, indicating the average nucleus volume in the lower group, are situated in the neighbourhood of the second straight line with its tangent

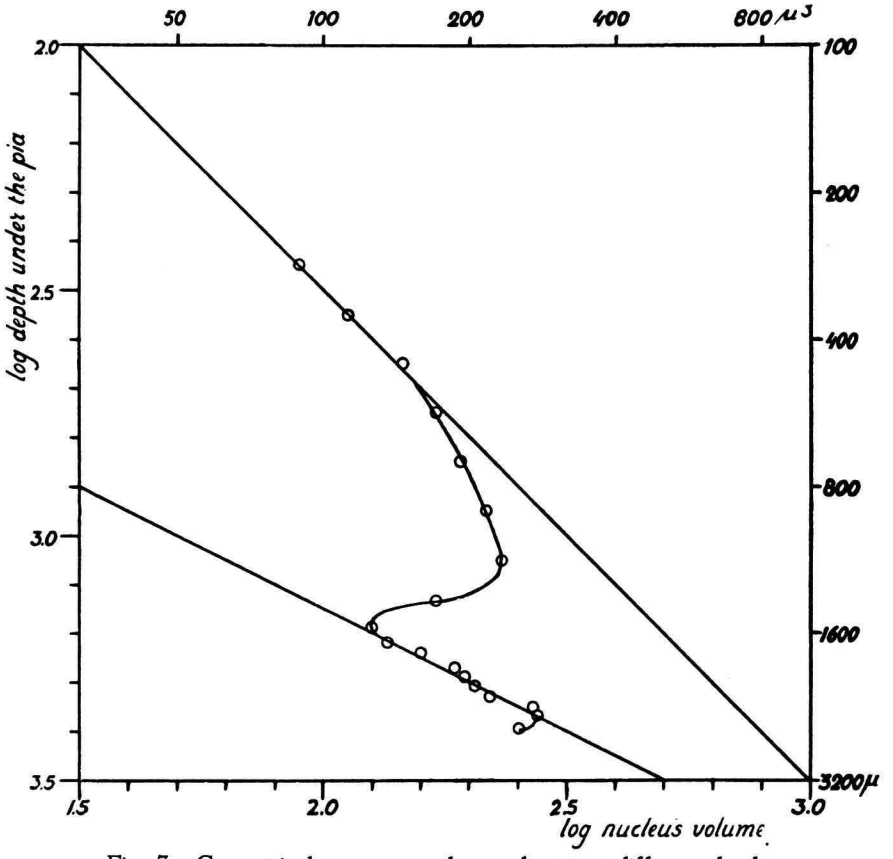


Fig. 7. Geometrical average nucleus volumes at different depths.

= 2. Only the points at the extremities of this group show a greater distance from the line: they represent however a relatively small number of cells and therefore these deviations at the borders of this group are not of so much importance as the fact, that the other points, representing large numbers of cells, lie in the neighbourhood of the second straight line.

Points situated along a line that makes an angle of 45° with the ordinate of a logarithm diagram indicate values that are proportional to each other. In the upper group the points indicating the average nucleus volume at different depth lie on — or very close to — such a line : *in the different levels of the upper group the average volume of the nuclei increases proportionally to the depth.*

This relation is an accurate one : the largest deviation is found between

1000 and 1260 $\mu$ under the pia (log $D$ between 3,0 and 3,1) where the average logarithm of nucleus volume differs 0,02 from the exact pro-

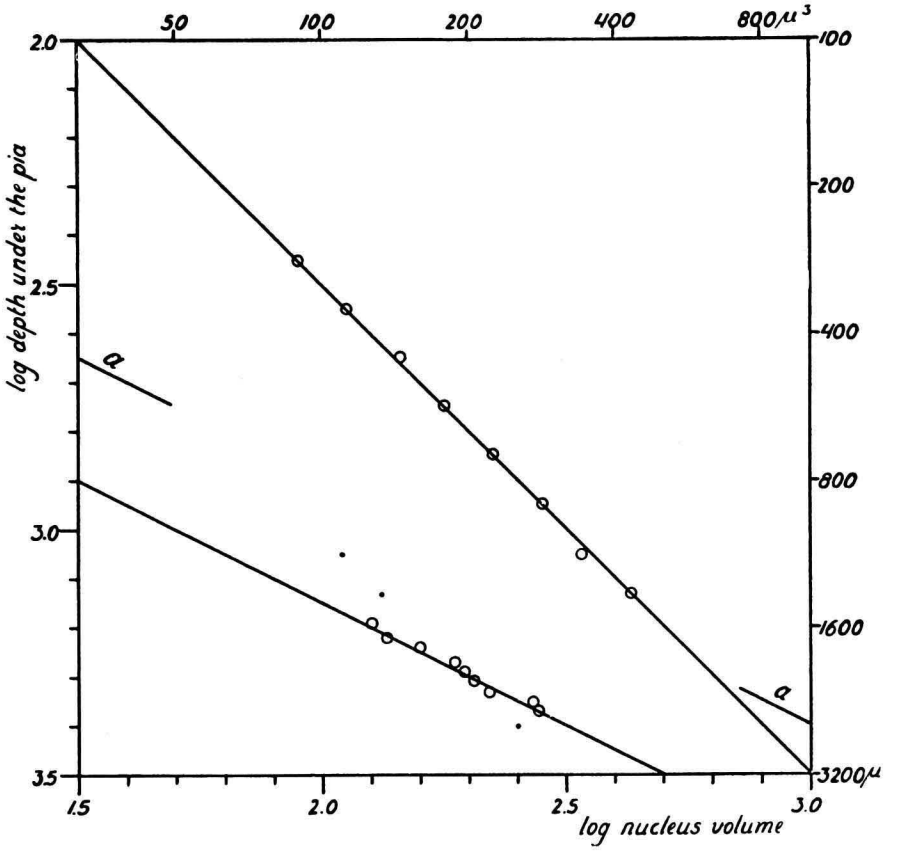


Fig. 8. Geometrical avarage nucleus volumes in each of the two groups of ganglion cells.

portion. So the largest disproportionality amounts to 5 %. This is only a small deviation if we regard the fact, that the largest value of average nucleus volume and pial distance is 5 times the smallest value (500 %).

Moreover this relation is found to be present in all the architectonic fields measured as far in uncurved parts of the cortex. (Even the smallest flexion must disturb this relation, according to the laws of cortical flexion. In the example given in my paper of 1929 it is absent: the studied cortex was curved in a direction, perpendicular to the section, which I did not realize until after the paper was published.)

In the non-logarithmic diagram of figure 5 the average nucleus volumes are indicated by small circles. The proportionality between these volumes and the depths is demonstrated by the fact, that in the upper group they lie in — or very close to — a straight line that passes through the zero (the left upper edge of the diagram, the point of contact between the coordinates of nucleus volume and depth).

It should be noted, that this proportionality between depth and average nucleus volume in the upper group of ganglion cells was stated here, using the geometrical average values: the logarithms of the nucleus volumes were added and then divided by their number, the result being the logarithm of the geometrical average value ($\sqrt[n]{a \times b \times c \times \ldots\ldots \times n}$). The arithmetical average nucleus volumes $\left(\frac{a+b+c+\ldots+n}{n}\right)$ also show this proportionality, but the deviations are larger. This already is an example of the fact, that the nucleus volumes show more relations to geometrical progression than to arithmetical.

*In the lower group of ganglion cells the average nucleus volume increases proportional to the square of the depth,* the line of their points in the logarithmic diagram making an angle with the vertical line, the tangent of which is 2.

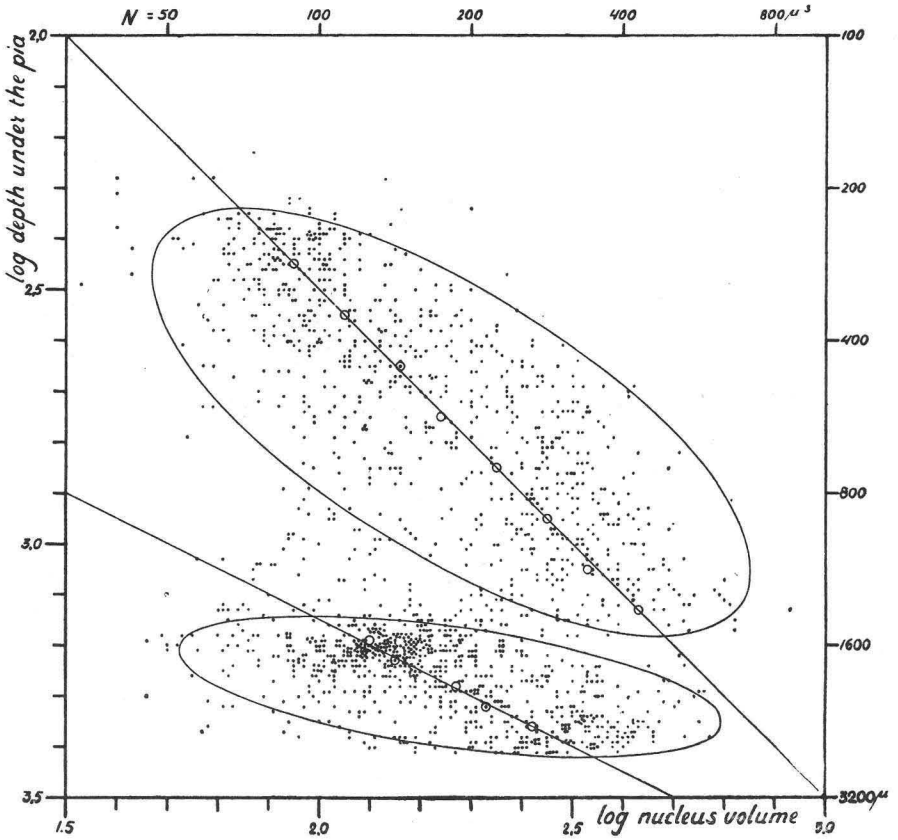


Fig. 9. Logarithmic diagram of the nucleus volumes and depths. The geometrical average volumes are given by the small circles.

In the numerical diagram of fig. 5 this proportionality is demonstrated by the fact, that the small circles of the lower group are situated along

the parabole (the transformation of the second straight line in the logarithmic diagram of fig. 8 and 9 with its tangent = 2).

This proportionality in the lower cell group between the average nucleus volume and the second power of the depth is found to be less accurately demonstrated by the measured values as was the direct proportionality in the upper group.

The greater deviations must be partly caused by the phenomenon, that in the lower group the direction of ganglion cells is less accurately perpendicular to the pial surface than in the upper zone. Consequently the nucleus volume calculated from the measurements differs more from the real nucleus volume than in the upper zone.

To analyse the correlations found between nucleus volume and depth in the two zones of the cortex, we cannot use the usual method of calculating the correlation index because the frequency of these values does not vary in accordance with the laws of probability, especially not in accordance with the GAUSSian formula, as is shown in the frequency diagrams of the figures 18 and 23.

For those, who object that no material totally obeys these laws and who therefore calculate the correlation index even in material that shows marked deviations from the GAUSSian type of frequency-variation it can be said, that in the upper group the correlation index, calculated in the usual way, is found to be 0.73, that is to say a high one, indicating a large correlation.

To analyse the correlation independent of the deviations of the GAUSSian type another method was followed.

At the different levels of the upper group of ganglion cells the average nucleus volume is proportional to the depth. In other words: if the cortex were divided into a number of thin layers, each parallel to the pia, the nucleus volume of the average ganglion cell in each layer would be proportional to the depth, its nucleus volume divided by the depth would give the same value in all these layers:

$$\frac{\text{nucleus volume}}{\text{depth}} = \text{constant}$$

or

$$\frac{N}{D} = K$$

($N$ = the nucleus volume, $D$ = the depth, i.e. the distance of the basis of the ganglion cell from the pia mater).

This constancy only holds good for the average cells. In order to see how this relation varies in the other cells, the value $\frac{N}{D}$ is put in the diagram of figure 10. This diagram is logarithmic, the abcissa of each

point being $log \frac{N}{D}$ of a ganglion cell and the ordinate being $log\ D$ of this cell.

The average values are indicated by small circles. In the upper group they are situated on — or very close to — a straight vertical line, demon-

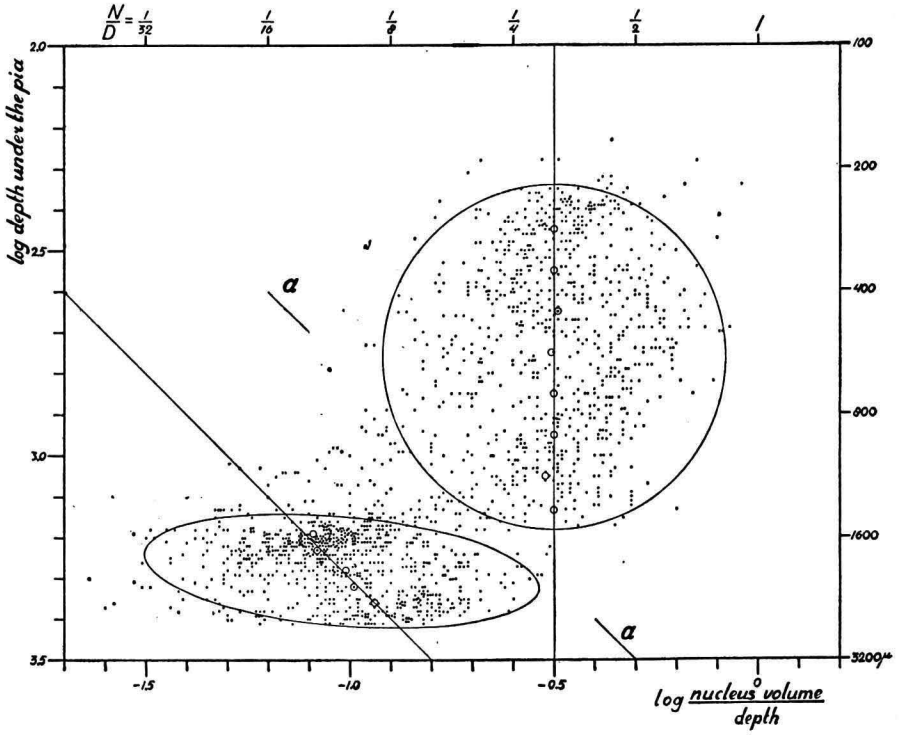


Fig. 10. Logarithmic diagram of the value: nucleus volume divided by depth.

strating the fact that the average nucleus volume divided by the depth is the same value at all distances from the pia.

The other points of the upper group are distributed to the left and to the right of the vertical line: in the other cells the nuclei are smaller or larger than the average value.

In order to study the distribution on either side of the vertical line a frequency diagram of the value $\frac{N}{D}$ was made. It is shown in the thick broken line of figure 11. This line shows two summits, the one to the right caused by the upper group of cells, the other to the left caused by the lower group. The absence of clear distinction between the upper and lower groups makes this diagram rather difficult to read. The dividing line *a—a* in figure 6 is drawn somewhat arbitrarily. Fortunately only in a part of the values $\frac{N}{D}$ both groups are represented. In the frequency diagram a comparatively large part is built up by cells of the upper group

only. The confusion of points belonging to the two groups is restricted to the area between the two summits. The right summit itself and the

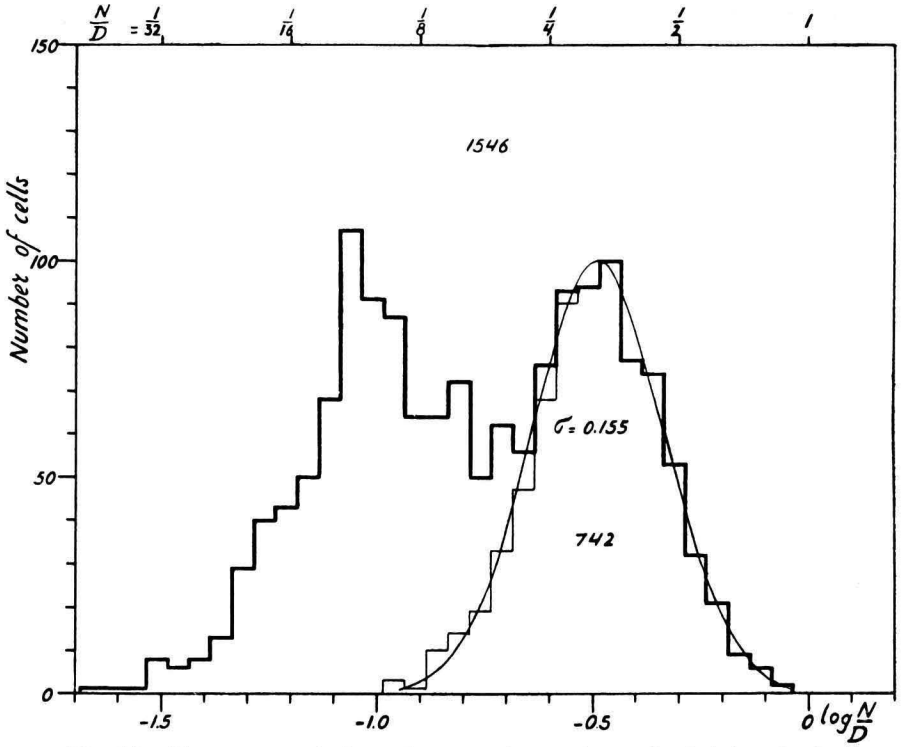


Fig. 11. Frequencies of the value: nucleus volume divided by depth.

whole part of the line to the right of that summit is built up by cells of the upper group only.

The GAUSSian curve that fits best for this part of the frequency diagram is calculated and drawn in the figure (curved line). It corresponds accurately with the frequencies found (with the thick broken line).

By dividing the field of points into two groups by the straight line *a a* (the same as in fig. 6) the frequency of the points belonging to the upper group (limited in this way) can be counted in the part between the two summits also. The result is shown in the thin broken line. This line corresponds accurately with the left part of the GAUSSian curve. The thin part of the frequency line, however, is not as convincing as the thick part, the division between the two groups being somewhat arbitrary.

Still the correspondence to the GAUSSian curve in general is evident. For the larger part of the curve it is obtained without any arbitrary process.

How nearly this curve coincides with the GAUSSian curve can be tested by KAPTEYN's method [1]). In the ideal case the "$z$ points" would be

[1]) J. C. KAPTEYN, Skew frequency curves in biology and statistics (1916). M. DE Waal, Groningen.

situated on a straight line. The $z$ points calculated from the value $log \frac{N}{D}$ of the cells of the upper group are given in fig. 12. They show only small deviations from the straight line (especially small in the right part, being the part which was not influenced by the artificial division into two cell

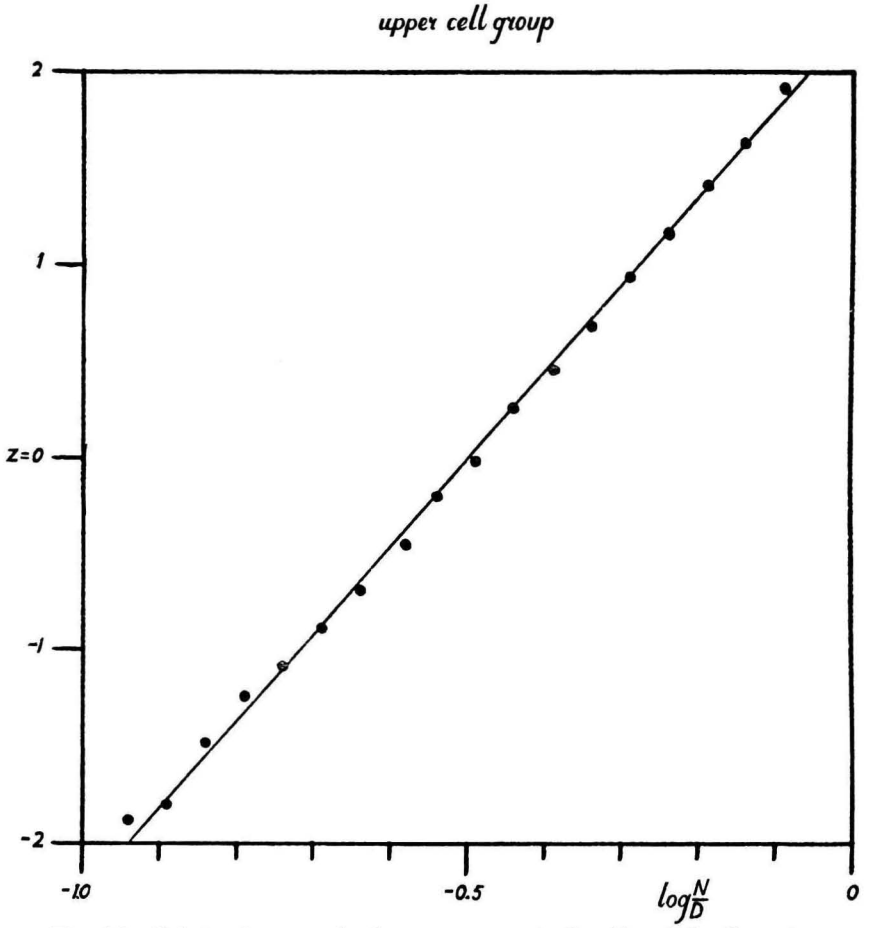


Fig. 12. Relation between the frequency curve in fig. 11 and the GAUSSian curve as shown by KAPTEYN's method. In the ideal case ten $z$ points would be situated on a straight line. Their deviations from that line are small.

groups!). Thus the GAUSSian curve fits fairly accurately. A still sharper test is given by plotting the value $\frac{1}{z'}$ in the upper diagram of fig. 16. The $\frac{1}{z'}$ points being situated along a horizontal line, the distribution is a symmetric one. In both tests the deviations are not larger than in KAPTEYN's example (the measurings of the length of 8585 men).

So the conclusion can be drawn that *in the upper group, the value* $\log \frac{N}{D}$ *is normally distributed on both sides of the average value.*

Special attention may be given to the fact, that this correspondence with the normal GAUSSian line is present in the *logarithms* of the nucleus volumes and of the depths. The nucleus volumes and depths themselves are distributed very asymmetrically. Here we have a second example of how the nucleus volumes and the depths show more relation to a geometrical progression than to an arithmetical one.

In this way the nature of the correlation between the nucleus volumes and the depths in the upper group could be determined. This correlation is found in the proportionality between the depth and the corresponding average nucleus volume. In figure 10 this proportionality in a certain sense is excluded by using the value $\frac{N}{D}$ instead of the value $N$. With this exclusion the correlation has disappeared. For those who calculate correlation indices even in material that shows marked deviations from the GAUSSian type it can be said that the correlation index calculated in the ordinary way for the points in this diagram is found to be 0.09, that is a low value indicating the absence of a perceptable correlation. Even the marked deviations from the GAUSSian type, that increase the result of this calculation, have not made it higher than this small value.

In the lower group of ganglion cells a similar distribution according to the GAUSSian formula can be found.

Here the average nucleus volume increases proportionally to the 2nd power of the depth. In the average cells of this group thus the value $\frac{N}{D}$ is not constant, but the value $\frac{N}{D^2}$ is.

In consequence the average values of $\log \frac{N}{D}$ do not follow a vertical line in figure 10 but a line that makes an angle of 45° with the vertical line (tangent = 1). And the frequency curve of the values $\log \frac{N}{D}$ (left summit of the thick line in figure 11) does not correspond to a GAUSSIAN curve.

In this lower group we thus have to put the value $\frac{N}{D^2}$ in a diagram. This is done in figure 13. In this logarithmic diagram (abscissa = $\log \frac{N}{D^2}$, ordinates = $\log D^2$) the avarage values (small circles) of the lower group are situated along a vertical line $\left(\log \frac{N}{D^2} \text{ is constant}\right)$.

The frequency diagram of this value $\log \frac{N}{D^2}$ is represented in fig. 14.

It also shows two summits, the left caused by the lower group and the right caused by the upper group. In this diagram the overlapping of the

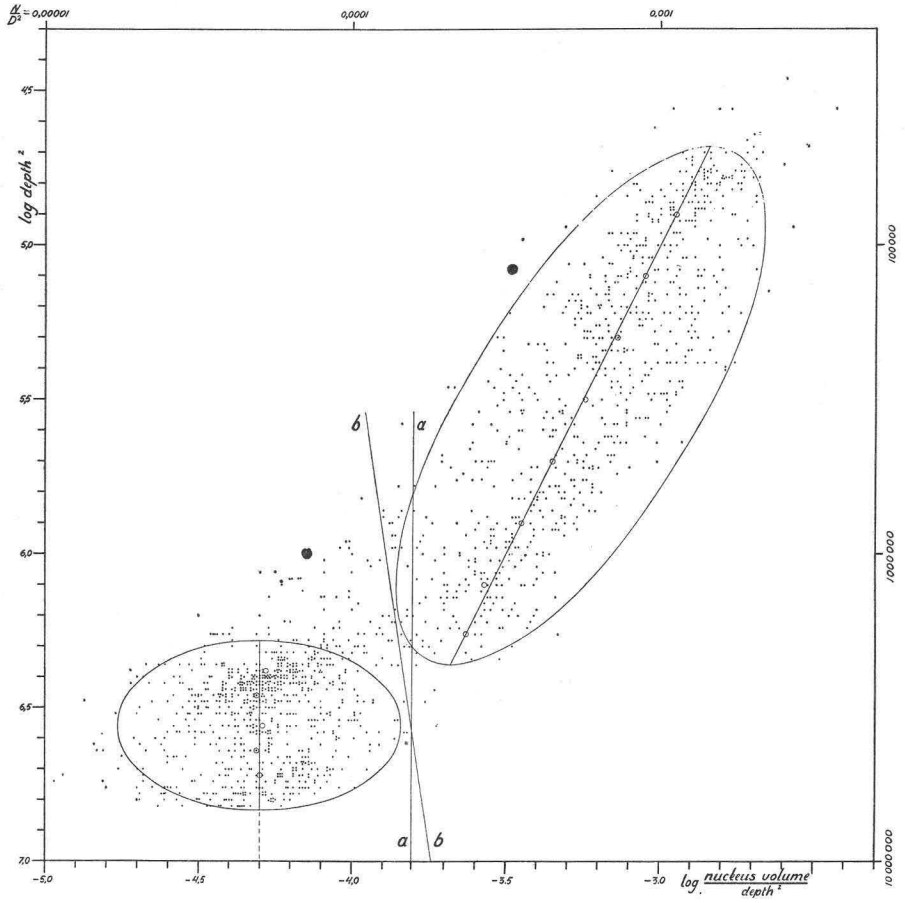


Fig. 13. Logarithmic diagram of the value: nucleus volume divided by the square of the depth.

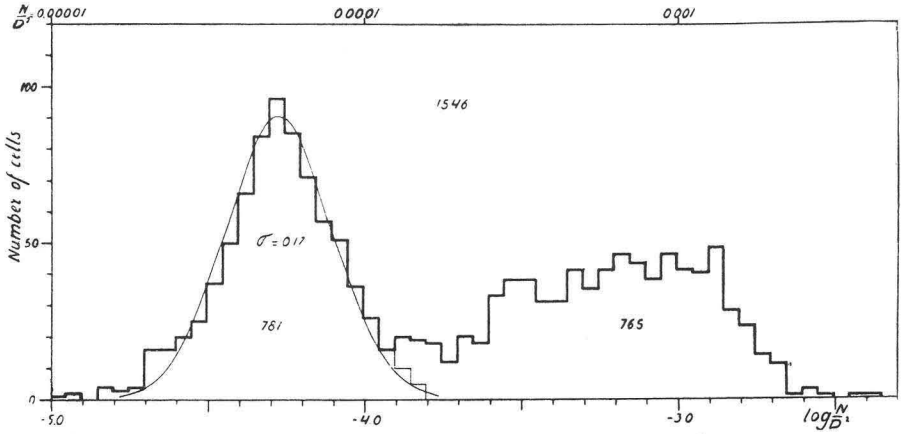


Fig. 14. Frequencies of the value: nucleus volume divided by the square of the depth.

two groups is so small, that it clearly suggests that the cortex is built up by two separate groups of ganglion cells.

In consequence of the small area of overlapping nearly the whole frequency curve of the lower area can be read from the thick line. The GAUSSian curve, calculated for this group, is drawn in the figure (curved line). It corresponds fairly well with the frequencies found (thick broken line). This correspondence was tested by KAPTEYN's method. The $z$ points (fig. 15) are situated in the neighbourhood of the straight line, though

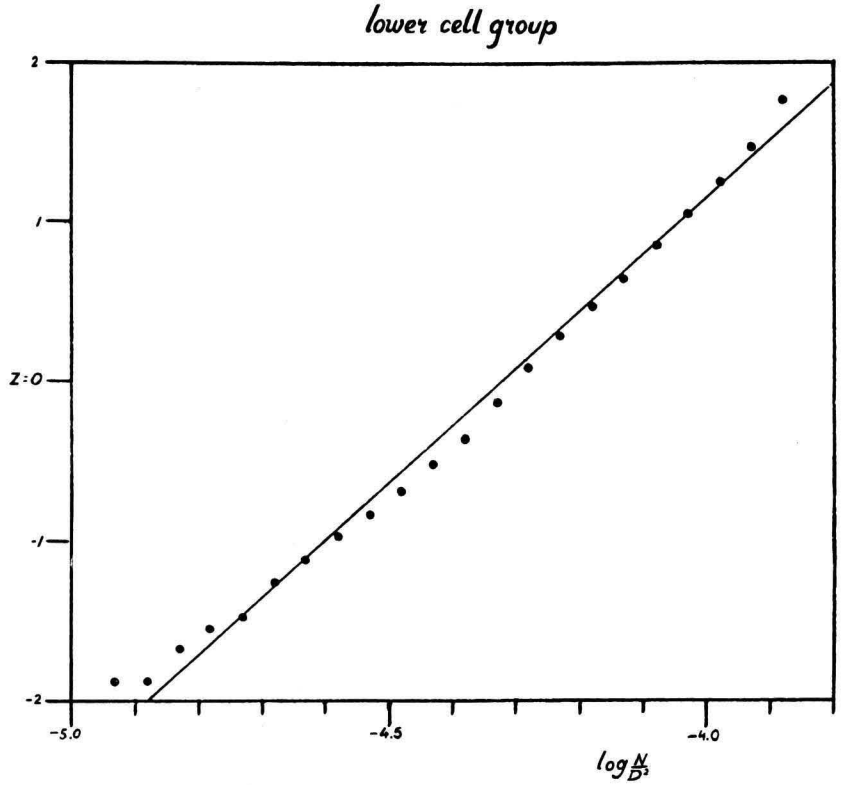


Fig. 15. Relation between the frequency curve of fig. 14 and the GAUSSian curve, as shown by KAPTEYN's method. In the ideal case the $z$ points would be situated on a straight line. Their deviations from that line are relatively small.

their deviations are not as small as in the upper group. The $\frac{1}{z'}$ points in the lower diagram of fig. 16 reveal a small asymmetry of the distribution by the fact that in the left part they are lying a bit higher than to the right. Still it may be concluded that the GAUSSian curve fits fairly well.

*In the lower group of ganglion cells the value log* $\frac{N}{D^2}$ *is distributed according to the formula of* GAUSS.

In the diagram of fig. 13 we can try to make a division between the two groups of cells so that the frequencies of the lower group in the area

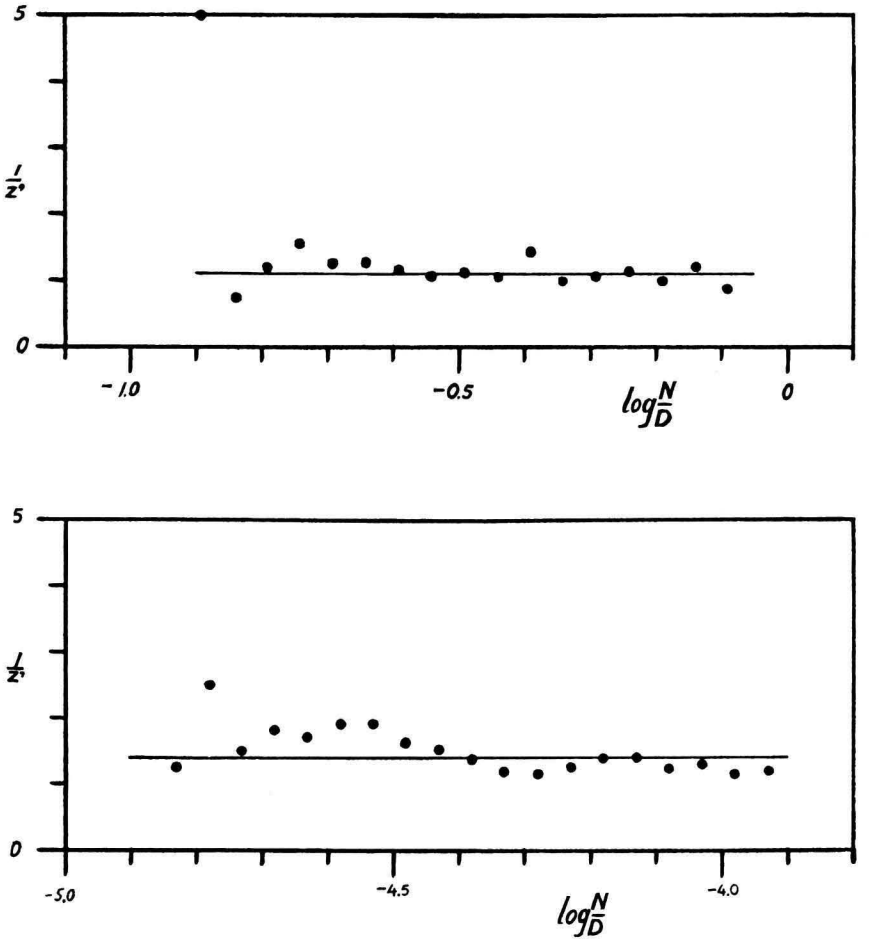


Fig. 16. Relation between the curves in fig. 11 and 14 and the GAUSSian curve as shown by KAPTEYN's method. If the distribution is a symmetric one, the $\frac{1}{z'}$ points are situated along a horizontal line. In the upper group (upper figure) the distribution is symmetric, in the lower group it is nearly symmetric.

of overlapping correspond with the GAUSSian formula. This line of division is drawn in the fig. 13 as the line *b*—*b*. Limiting the lower group by this line the frequencies are found, that are given by the thin broken line in the frequency diagram of fig. 14. The correspondance with the theoretical GAUSSian curve is evident.

The line *b*—*b* however is not identical with the line *a*—*a* used until now to limit the upper group of ganglion cells. The line *a*—*a* is shown in

fig. 13 as well. It there runs vertically. The line *b*—*b* makes a sharp angle with the vertical line.

So the limit of the upper group is not quite identical with the limit of the lower group when we take the frequency diagrams as the basis for this division.

The difference is not great, only 23 cells out of the 1546 (1½ %) lying between the two limits. In consequence a conclusion can scarcely be made. It seems possible that a small number of cells builds up a very small third group between the two main groups. It also seems possible that small errors of measurement or a too small number of measured cells should be responsible for this slight difference.

In other words the attempt to draw an ideal limit for each of the two main cell groups with the aid of frequency diagrams results into two limits that are nearly identical: they differ for 1½ % of the cells only. Formulated in that way this fact leads us to the conclusion that a division of the cortex into two main groups of ganglion cells is justified by the measurements.

The curious fact that these two groups contain about the same number of cells confirms this conclusion: the upper group of the measured part of the cortex containing 742 cells and the lower group 781.

By the two rules stated ($log \frac{N}{D}$ in the upper group and $log \frac{N}{D^2}$ in the lower group varying according to the GAUSSian formula of "normal" variation) the distribution in the horizontal direction of our diagrams is characterized. What is the distribution in the vertical direction?

In the vertical direction of all the logarithmic diagrams the distances from the pia are given. The frequencies of these depths at different levels in the cortex (i.e., the frequencies of the ganglion cells in these different

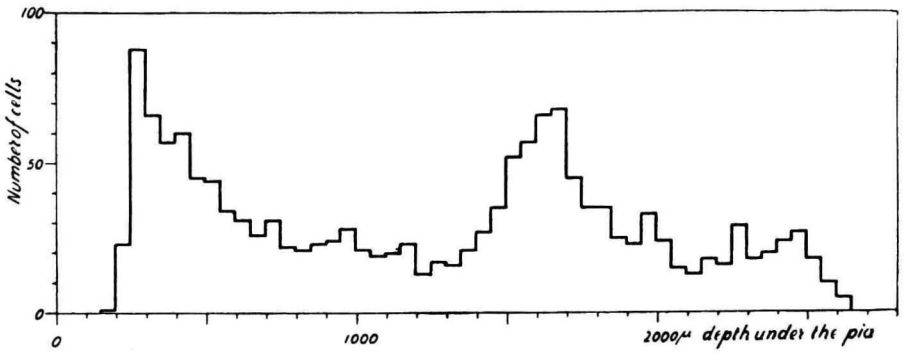


Fig. 17. Frequencies of the depths.

levels) are shown in fig. 17, the frequencies of the logarithms of these depths are given in fig. 18.

These diagrams do not resemble the GAUSSian curves. Thus these

frequencies must depend upon other factors. What factors determine the number of ganglion cells at each distance from the pia?

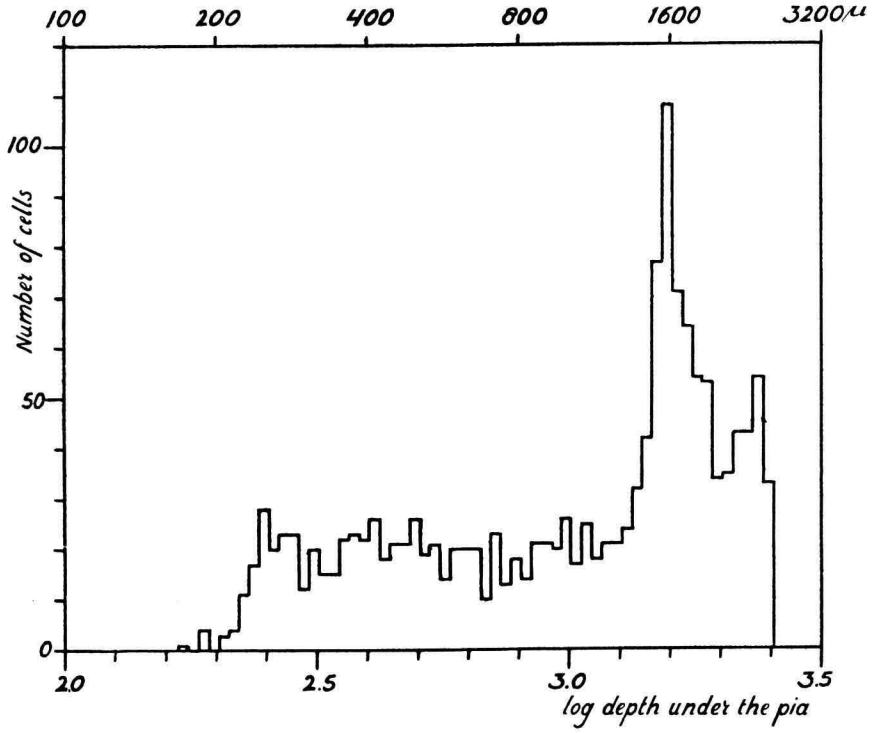


Fig. 18. Frequencies of the logarithms of the depths.

In the non logarithmic (the numerical) diagram of fig. 17 it is evident that the cells are more numerous at those depths where the cells are smaller. The diagram shows that if the studied part of the cortex were divided in layers parallel to pia and each 100 $\mu$ thick, in each layer the number of cells are found that is indicated by the ordinate. These parts have all the same volume of $100 \times 30 \times 400 = 1200000\ \mu^3$, their height being 100 $\mu$, their thickness 30 $\mu$ (the thickness of the microscopic section) and their breadth $120000 : 300 = 400\ \mu$ (given by the distance of 12 cm between the two vertical lines on the photograph, that limit the field of research and by the enlargement of the photograph $= 300 \times$).

The parts of the cortex, limited in this way and having the same volume, contain more nerve cells if their nerve cells are small and fewer nerve cells if they are large. Or in other words : if the cortex were divided in territories, each containing one ganglion cell, the territories containing a small cell would be smaller than the territories containing a large cell. So the question arises if the size of the nerve cell shows a definite relation to the size of its "territory". Are these "nerve cell territories" proportional to some quality of their nerve cell?

If this were so, the sum of these qualities would be the same in all parts of the cortex with the same volume. In consequence their sum would be a constant value in the parts of 100 $\mu$ height, referred to above. Our question now takes this form : can any quality of the nerve cell be found, the sum of which in these parts of 100 $\mu$ height is approximately a constant value?

If such a quality were to be found, each nerve cell would claim for itself and for the surrounding elements an area that measured a constant times a definite measure of that nerve cell itself and in each part of the cortex all the ganglion cells together would claim the whole volume of that part. In each part of the cortex the number of its nerve cells would be then determined by their sizes. And in this case the distribution in the vertical direction of our diagrams would be determined by the laws ruling their size.

Until now the answer to this question cannot be given as accurately as it was done for the distribution in the horizontal direction of the diagrams. Still there is evidence that the volume of the "nerve cell territory" is proportional to the volume of the perikaryon of its nerve cell.

The volume of the perikaryon increases proportionally to the square of the nucleus volume. If the territories were proportional to the perikaryons, the sum of the squares of the nucleus volumes should be constant in the above mentioned parts of the cortex of 100 $\mu$ height.

In fig. 19 these sums are shown. If the line in this figure had been

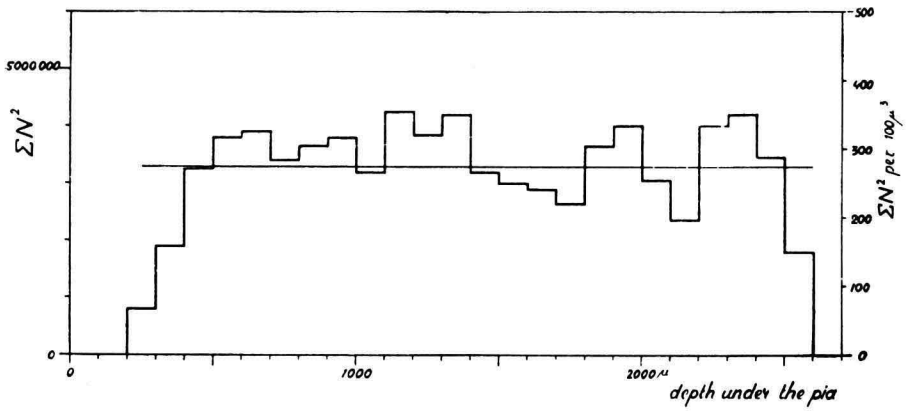


Fig. 19. Sum of the squares of the nucleus volumes at different depths in the temporal cortex.

a horizontal straight one, the sum of the perikaryons accurately had been the same in all these parts of the cortex. As a matter of fact the line tends to the horizontal, in a rough manner thus demonstrating the proportionality between territory and perikaryon volume. But it shows marked deviations from the straight line.

A complete analysis of these deviations has not been made yet.

It is possible that special structures at special distances from the pia cause these deviations, e.g., the varying number of myelin sheats.

Therefore a similar research was made in the area gigantopyramidalis, in which area the myelinated fibres are more equally distributed over the depth of the cortex. Fig. 20 brings the sums of the squares of the nucleus volumes of this cortex at different distances from the pia. The sum is more constant than in the area temporalis.

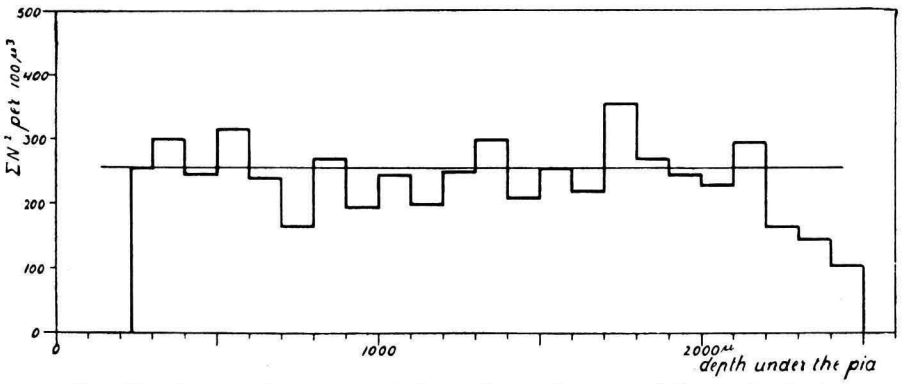


Fig. 20. Sum of the squares of the nucleus volumes at different depths in the area gigantopyramidalis.

It is possible too, that the deviations are the effect of a too small number of measured cells in each 100 $\mu$ depth.

To exclude both probable influences the same question was studied by comparing the total thickness of the cortex in different architectonic fields. In the area gigantopyramidalis and in the area striata (the field with the largest and the field with the smallest ganglion cells) the nucleus volumes were measured in the same way as described above for the area temporalis superior posterior. In these three fields, the average sum of the square volumes of the nuclei per 100 $\mu^3$ cortex was calculated by dividing 100 $\times$ the sum of the square of the nuclei of all the nerve cells present in the total depth of the cortex by the volume of the field studied. It was found to be exactly the same: in the area striata, area temporalis and area gigantopyramidalis resp. 254, 257 and 256 $\mu^3$ (see fig. 21). These values differing less than 1 % furnish strong evidence that the cell territories are proportional in volume to their perikaryon. (In the said architectonic fields the average perikaryon takes 2.81 %, 2.85 % and 2.84 % of the cortex volume, the sum of the $N^2$ per 100 $\mu^3$ being 254, 257 and 256 and the perikaryon volume being $\frac{1}{90} \times N^2$).

Further evidence was supplied by Miss J. A. VAN SWET, who in my laboratory measured the nucleus volumes in the hippocampal region. In both main parts of the hippocampus large cells lie close together, in the

fascia dentata even closer than in the region of the hippocampal pyramid cells. If only those parts are considered in which the cell bodies are present,

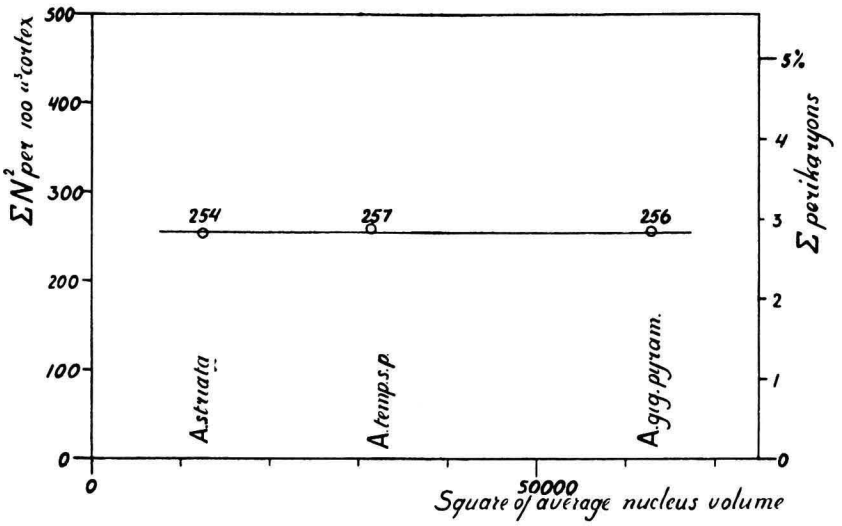


Fig. 21. Sum of the squares of the nucleus volumes in 100 $\mu^3$ cortex volume in different architectonic fields.

the relation between the perikaryon and its "territory" would be quite different to that in the neocortex, the average perikaryon taking a much higher percentage of the given space.

It is known, however, that the dendrites of these hippocampal cells lie outside the area in which the cell bodies are found. So the extention of the field in which both body and dendrites are present is much larger.

From the measured volume of the nuclei the volume was calculated, which this field would have if the perikaryons of these ganglion cells occupied the same percentage of that field as in the neocortex. The borders of this calculated field exactly coincide with the known real borders of the field, in which the dendrites are stretched out at both sides of the cell band. And it is seen in fig. 22 that the calculated fields — drawn in the photograph — just meet each other in those parts of the hippocampus where the different cortices are folded over each other. (Miss VAN SWET's research has not yet been published).

So the same quantitative relation between perikaryon and territory exists in parts of the brain that differ greatly in the size of their neurones and in the structure of their neuronal apparatus.

The conditions found in the hippocampal region point to a possible cause of the deviations, found in the $\Sigma N^2$ of the temporal cortex. Calculated from the whole cortex the perikaryon volumes occupy exactly the same percentage of the cortex as elsewhere, in some of the layers only the perikaryons seem to be somewhat larger and in other layers somewhat smaller in volume. Possibly, in the different layers the cell bodies may be

not situated at quite the same height within their dendrite fields. In the hippocampus the cell bodies are shifted so to speak out of their dendrite fields. So it is not at all necessary that in the different layers of the neocortex the cell bodies occupy equivalent points within the field of their own dendrites. And only when all the ganglion cell bodies occupy equivalent spots within their dendrite fields the sum of their perikaryons would be the same in all the parts of the cortex. [1])

The strong evidence yielded by the comparison of different architectonic fields for an accurate proportionality between perikaryon and territory (accurate within 1 %), the smallness of the deviations at different distances from the pia within each architectonic field and the possibility of giving a rational — though still unproved — possible explanation of these deviations justify the provisional conclusion, that *each ganglion cell occupies a part of the cortex (its territory) the volume of which is a constant times (35 ×) the volume of its perikaryon.*

The average nucleus volume being given by the law that this volume in the upper group of cortex cells increases proportionally to the distance from the pia and in the lower group proportionally to the square of that distance, the number of ganglion cells at each definite distance from the pia is determined by the law, stated just now : in each part of the cortex so many cells of the prescribed average size are present, that their territories just fill up this part of the cortex.

The number of the ganglion cells in each part of the cortex being determined by the laws governing their size and by the rule that their territories together just fill that part of the cortex, it is evident that their frequencies at different distances from the pia do not follow the GAUSSian type of normal distribution.

The question remains, how much do the extreme values of distribution differ? Which factors determine the limits of the groups? To find the answer to this, the distribution in both the horizontal and vertical direction must be examined.

In the horizontal direction the distribution can be characterized easily, as it agrees the GAUSSian formula.

In the upper group this distribution was found to be represented by the value $log \frac{N}{D}$ (the logarithm of the relation between nucleus volume and depth). The distribution of this value can be characterized by the standard deviation of the GAUSSian curve, it being 0.155.

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[1]) The irregularities in the curve of the temporal cortex are the cause, that the power of the nucleus volume, which in this field is proportional to the territory volume, is not measurable with great accuracy. Different powers are summarised in the same way as it was discussed for the 2 d power. It is possible that an exponent somewhat lower than 2 gives a better horizontal line, the irregularities, however, being too large to give certainty. In the other architectonic fields measured the second power fits the best.

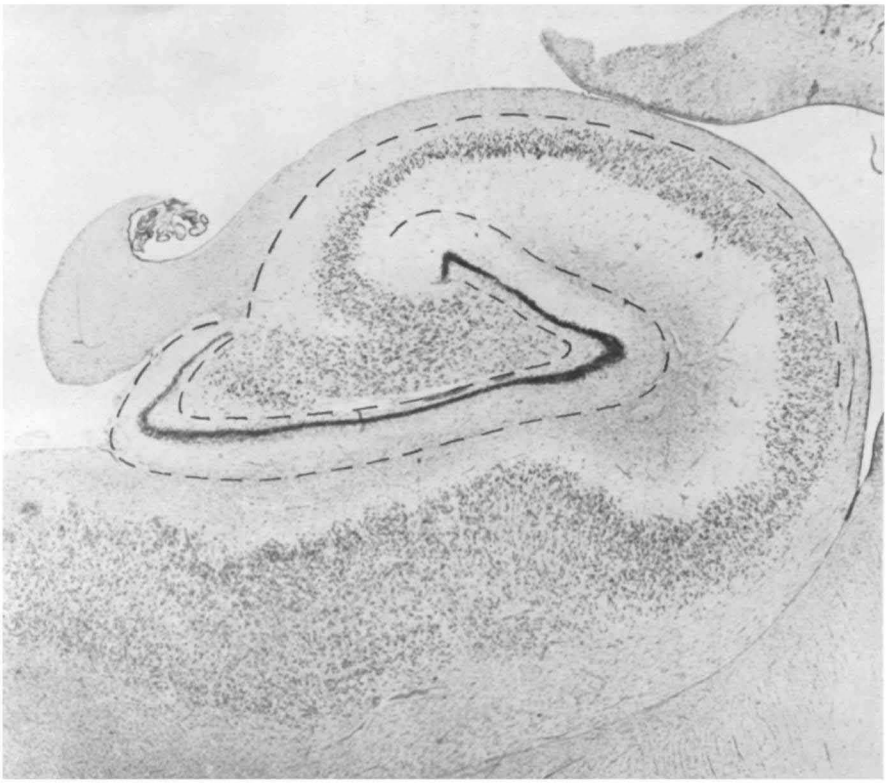

Fig. 22. Calculated dendrite fields in the hippocampal region (calculated from its measured nucleus volumes and the relations, found in the temporal cortex, that $^1/_{35}$ of the space is occupied by perikaryons and that the perikaryon volume is $^1/_{90}$ of the square of the nucleus volume in $\mu^3$).

In the lower group the value $log \frac{N}{D^2}$ shows a GAUSSian distribution. Its standard deviation is 0,17.

So the distribution in the two groups is of the same order. In the lower group it is 10 % larger only than in the upper group. As I have said, the errors of measurement were larger in this lower group than in the upper group. It is probable, therefore, that the calculated standard deviation of 0,17 in the lower group is somewhat too high. This diminishes the meaning of the small difference in the standard deviation of the two groups: *the standard deviation in the horizontal direction of our diagrams is found to be nearly the same in the two main groups of ganglion cells.*

In the vertical direction the distribution does not follow the GAUSSian law and so it is difficult to compare it with the horizontal one.

It seems to me useless to characterize the amount of the variation in vertical direction by the common formula $\sigma = a^2 : n$. Another way must be followed.

In the diagram of fig. 10 the field occupied by the upper group seems to have the same vertical and horizontal diameter. This fact cannot be illustrated by numbers, the borders of the field not being sharply determinable. But it is evident a circle can be drawn that in a rough manner coincides with the limits of the field.

When this circle is drawn around the upper group of points in the diagram of fig. 9 and of fig. 5, it takes another form owing to the different ordinates used in these diagrams; it is transformed in the same way as all relations are transformed. In all these diagrams this circle or its transformations characterizes the upper field of points.

*Thus the pial distances (D) in the upper group vary as much as the value* $\frac{N}{D}$ *varies.*

According to this peculiarity the nucleus volumes and the pial distances of the upper group can be described in another and more simple way.

The centre of the circle drawn in fig. 11 is a point, the abscissa of which is the average value of $\frac{N}{D}$ in this group and the ordinate is the mean value of the depths. A nerve cell showing these values may be called *the central cell* of the upper group. All the other cells differ from this central cell in nucleus volume and in depth in such a way, that the variation in the depth is as large as the variation of the value $\frac{N}{D}$. The manner in which the value $\frac{N}{D}$ varies from the central value is given by the rule that their logarithms obey the GAUSSian formula of normal distribution. The manner in which the depths are distributed is given by

the rule that each part of the cortex is "filled up" by cell territories (each proportional in volume to the perikaryon of its cell, i.e., with the square of its nucleus).

Given the nucleus volume of the central cell, its distance from the pia and the standard deviation of $log\ \frac{N}{D}$ the whole field is determined. *Thus the whole upper group of nerve cells can be described quantitatively by the two measures of its central cell and by its standard deviation.*

In order to study these relations in the lower group we must use the diagram of fig. 13. The vertical dimension of the field, occupied by the lower group, is more difficult to indicate than it was with the upper group. The upper limit especially is vague. It seems to be somewhat smaller than the horizontal diameter. If it were as large as the horizontal one the variation of the square of the pial distance ($D^2$) would be the same as the variation of the value $\frac{N}{D^2}$. *So it seems that the variation of $D^2$ is somewhat smaller than the variation of $\frac{N}{D^2}$ in the lower group of ganglion cells.* It is not possible to give exact values for this relatively small difference.

So this field seems to be characterized by an ellipse more than by a circle. The excentricity of this ellipse cannot be measured exactly. In the figure an ellipse is drawn, the longest diameter of which is 10 % larger than the diameter of the circle of the upper group. Its height is $\frac{2}{3}$ of that circle. Its transformations are drawn in the diagrams of the figures 10, 9 and 5. They characterize the extension of the points belonging to the lower group, though somewhat less sharply than the transformed circle characterizes the upper group.

In this lower group too we can imagine a central cell having the mean value of the depths and the geometrical average of the value $\frac{N}{D^2}$. In the diagram of fig. 13 this cell would correspond with the centre of the ellipse.

This lower group too can be described by giving the two measures of its central cell and the dispersion. This is true with the restriction, that the (relatively small) difference in extension along which the values $D^2$ and $\frac{N}{D^2}$ vary is not known exactly so far.

Two of these values that characterize the lower group happen to be identical or nearly identical with the analogous values of the upper group.

As already stated above the standard deviation in both groups is nearly the same. They differ less than 10 %.

The nucleus volume of both central cells is the same, 182 $\mu^3$ (given by its logarithm = 2,26).

*Thus the two central cells have the same size, they differ in their distance from the pia only.*

In all architectonic fields, measured up till now the two groups have almost equal standard deviations and nearly equal sizes of their central cell. The differences found are so small that they may easily be caused by errors in the measurements. The three values which characterize the upper group being given, two of the three characterizing values of the lower group are known also.

The third and last value that characterizes the lower group is the depth of its central cell. In the cortex described here this is 3,3 times the depth of the upper central cell.

Further measuring of more cytoarchitectonic fields must show, whether this relation in the depths of the two central cells is a constant value. In the fields studied already it differs only slightly from 3,3, somewhat more, however, than the other factors that may be considered as being constant.

Thus the size and the number of all the ganglion cells at all the depths of the measured cortex can be described by some general rules of distribution and by four values only :

1. the standard deviation,
2. the volume of the nucleus of the upper central cell,
3. the distance of that central cell to the pia,
4. the distance of the lower central cell to the pia.

Further measurements of the architectonic fields must prove if these 4 values that characterize this cortex field, depend upon each other. So it may be that the relation : the lower central cell lying 3,3 times farther from the pia than the upper central cell, turns out to be a general rule in all architectonic fields ($\pi \times ?$). And it may be that the two measures of the upper central cell (nucleus volume and depth) depend upon the measure of the standard deviation. In that case the whole type of an architectonic field would be characterized by one number only : its standard deviation.

These questions can be answered only by comparing the measurements of several architectonic fields.

Until this has been done we have to content ourselves with the result that the one part of the cortex, the measurements of which are discussed in this paper, can be quantitatively described by four values only.

There is one irregularity in the diagrams that has not been discussed yet: in the centre of the field of points of each group an area is present in which the points are less dense than in the higher and in the lower parts of that field.

This fact is partly due to the relations stated above.

The sum of a group of numbers, the logarithms of which are distributed according to the GAUSSian formula, depends not only on their quantity and their average value but on their dispersion also. When this is larger the sum will be found larger too (according to the formula $N_a = N_g e^{\frac{1}{2}\sigma^2}$, in which $N_a$ represents the arithmetical average value and $N_g$ the geometrical average value, $\sigma$ the standard deviation of the natural logarithms. I owe this formula to Professor Dr. J. DROSTE to whom I here express my

hearty thanks for his kind assistance). The dispersion is largest in the middle of each field (the broadest part of the circle or ellipse). In the geometrical centre of the height of each group therefore fewer cells will "fill" the room and at these heights the points must be found less dense.

If the field of lesser density was caused by this factor only, it would show a horizontal extension in the diagrams. This is not the case, however. In both groups it runs upwards

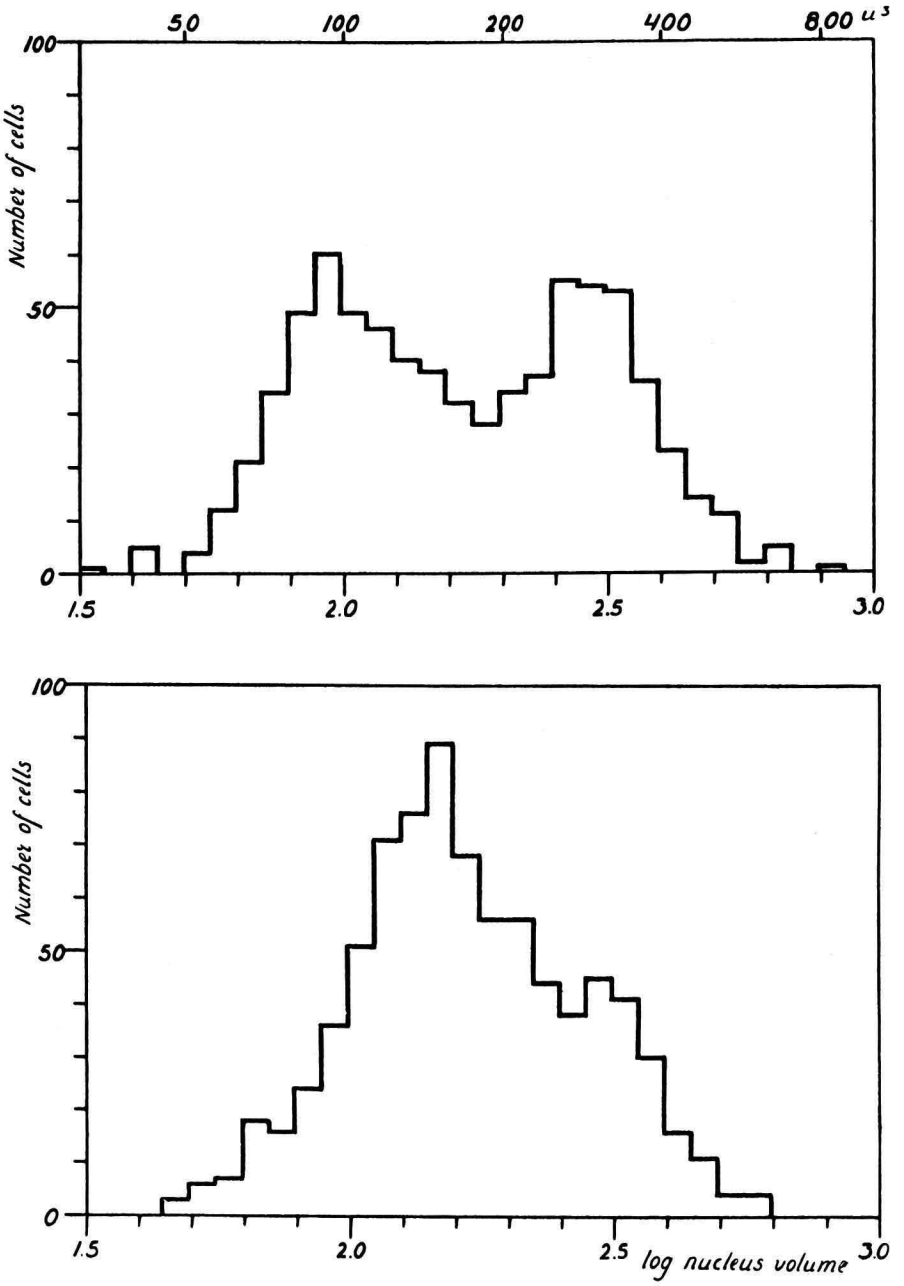


Fig. 23. Frequencies of the nucleus volumes in the upper and lower cell groups (logarithmic).

from the left to the right (see the upper group in fig. 10 and the lower group in fig. 13). In the fig. 6 and 9, in which the logarithms of the nuclear volumes themselves are used, they tend to take a vertical position.

In consequence the frequency diagram of the nucleus volumes of the upper group in the logarithmic diagram of fig. 23 shows two distinct summits. They differ nearly 0,6 in a horizontal direction. This being the logarithm of 4, the nuclei of the upper group show two groups of high frequency, the volume of the largest being 4 times the volume of the smallest. The two summits of the lower group differ 0.3, the larger nuclei having a volume twice as large as the smaller ones.

The main summit of the lower group lies just in the middle between the summits of the upper group thus representing a nucleus volume twice as large as that of the smaller cells of the upper group.

Thus the regular increase of the nucleus volume, that would be expected by the laws discussed above, to a certain degree is distorted by the fact, that volumes twice and four times as large as a definite volume are more frequent than volumes between these

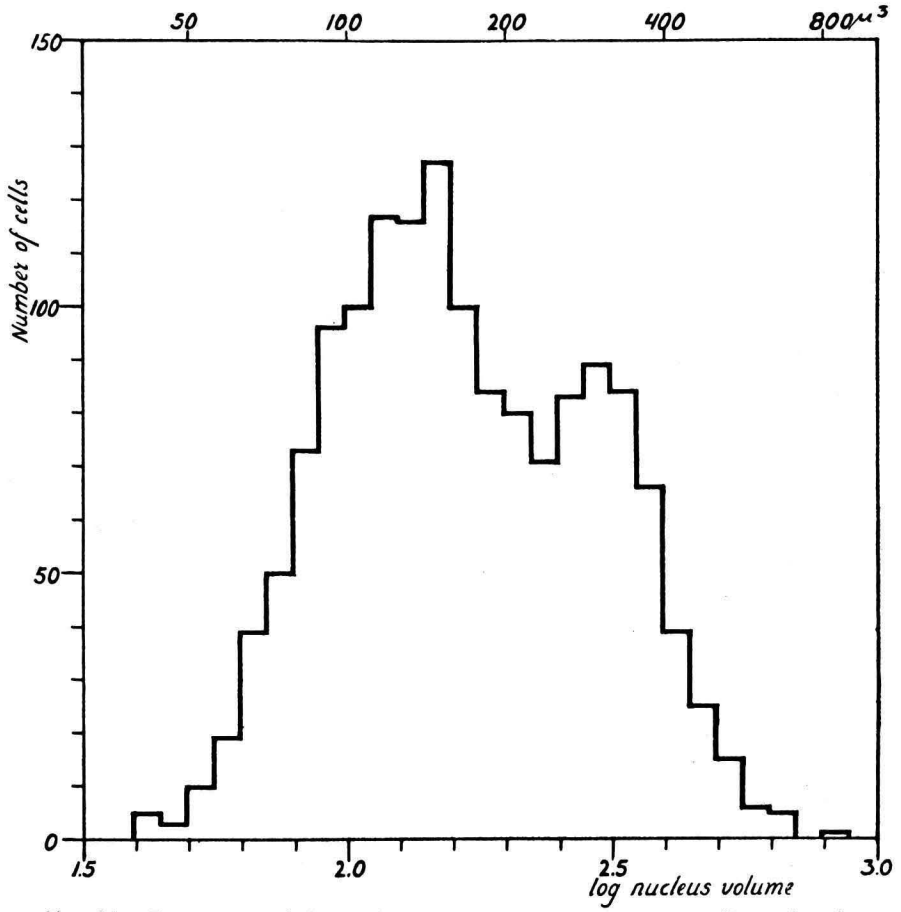


Fig. 24. Frequencies of the nucleus volumes in the whole cortex (logarithmic).

values. This peculiarity has been found in several types of cells by JACOBJ already and it is noted in ganglion cells by HERTWIG, though less convincingly as in other types of cells. In the Leyden laboratory of histology it has been demonstrated by Mej. A. B. J. DE VRIES (not yet published). So it may be that the tendency of the cells to increase their

nucleus volume with jumps to volumes twice as large is responsible for the fields of lower density in our diagrams.

More measurements are necessary to ascertain whether the lower density is due to this, or to some other cause.

## Summary of the relations found in the nucleus volumes and distances from the pia (depths).

The measurements of the volumes of the nuclei and of the depths of the ganglion cells in the cortex of the area temporalis superior posterior yield strong evidence that this cortex is built up of two groups of ganglion cells, an upper and a lower one, each containing approximately the same number of cells.

At the different levels of the upper group the average volume of the nuclei is proportional to the depth. In the lower group it is proportional to the square of the depth. Or formulated in another way: in the average cells at the different levels of the upper group the value: nucleus volume divided by depth $\left(\frac{N}{D}\right)$ is constant and in the lower group the value $\frac{N}{D^2}$ is the same at all distances from the pia.

In the upper group the value $\frac{N}{D}$ of each of the cells varies in such a way, that the frequences of their logarithms correspond exactly to the GAUSSian formula of "normal" distribution. The depths vary in the same extension.

In the lower group the value $\frac{N}{D^2}$ varies in the same manner and to the same extent. The squares of the depths ($D^2$) vary somewhat less.

The size of the nuclei thus being determined at each distance from the pia, the number of the cells in each part of the cortex is given by the rule that a constant percentage (2,83 %) of its volume is occupied by perikaryons of nerve cells.

*According to these rules the upper group can be described quantitatively by giving the two measures of its "central" cell (its nucleus volume = 182 $\mu^3$ and its distance from the pia = 575 $\mu$) and the measure of its standard deviation ($\sigma$ = 0.155). The lower group has the same standard deviation and its central cell has the same nucleus volume as the upper central cell, it lies 3,3 times farther from the pia.*

So the size and the place of all the ganglion cells in this architectonic field are characterized by 4 values only.

The measurements of several architectonic fields must be compared to decide whether these four values depend upon each other. If so, each architectonic field could be described by giving one value only.

## IV. THE PROBABLE SIGNIFICANCE OF THE RELATIONS, FOUND IN THE NUCLEUS VOLUMES AND DEPTHS.

What is the significance of the results, discussed in the previous chapter?

Most of the cortical nerve cells send a large dendrite to the pial surface, called the main dendrite. In the upper zone much more than 90 % of the cells do so, in the lower zone the percentage of the cells without such a main dendrite is somewhat higher, but still they are much less frequent than the cells with one.

The main dendrites run pretty straight upwards till they arrive near the cortex surface, where they split up into a number of branches that end in the pia glia membrane limiting the cortex. Thus the length of a main dendrite is identical with the distance between the cell and the pia, that is, identical with the depth of the cell [1]). And the law, found in the previous chapter, that in the upper group the average nucleus volume at each level is proportional to the depth of that level, can be expressed in this form : *in the upper group the average nucleus volume at each level is proportional to the length of the main dendrites.* Or alternatively : in the average sized ganglion cells of each level of the upper group the volume of its nucleus is proportional to the length of its main dendrite.

Here a relation is found between the nucleus volume and a special type of dendrites. It turns out to be a proportionality of the nucleus volume with the *length* of that dendrite.

Is this relation present in the other dendrites also?

In the section, stained by NISSL's method in which the measurements were made, the dendrites are not visible. And sections, in which the dendrites are impregnated by GOLGI's method, do not show the nuclei. In consequence a direct measurement was not possible yet and we have to search for indirect indications.

In a number of drawings, made by CAJAL from GOLGI preparations of the cerebral cortex, I measured the horizontal diameter of different dendrite fields (this can be done roughly only, the dendrite fields not being sharply limited) and the distance of their cells from the pia. These measurements are shown in fig. 25. The points are distributed along a straight line passing through the zero : the average length of the local dendrites is proportional to the length of the main dendrites, and therefore proportional to the nucleus volumes also.

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[1]) Exactly expressed the depth of the cell, being measured as the distance of the cell basis from the pial surface, is identical with the length of the main dendrite + the length of the cell body.

This can be demonstrated in a second way. In the drawings of CAJAL I drew circles around different ganglion cells, the radius of these circles being $\frac{1}{4}$ of the distance of the cell body to the pia. Some of these drawings are reproduced in fig. 26, 27 and 28. It is evident that these circles coincide roughly with the fields of the local dendrites. Some of the local dendrite fields are rather smaller and some rather larger than their circle, but this is the same in small and in large circles.

Thus the average diameter of the local dendrite fields seems to be proportional to the length of the main dendrite, the radii of the circles being proportional to it $\left(\frac{1}{4} \text{ of the depth}\right)$. And in the average ganglion cells of the different levels the diameter of their local dendrite field, consequently, will be proportional to the length of their main dendrite. By this proportionality the dendrite fields of these average cells are of the same

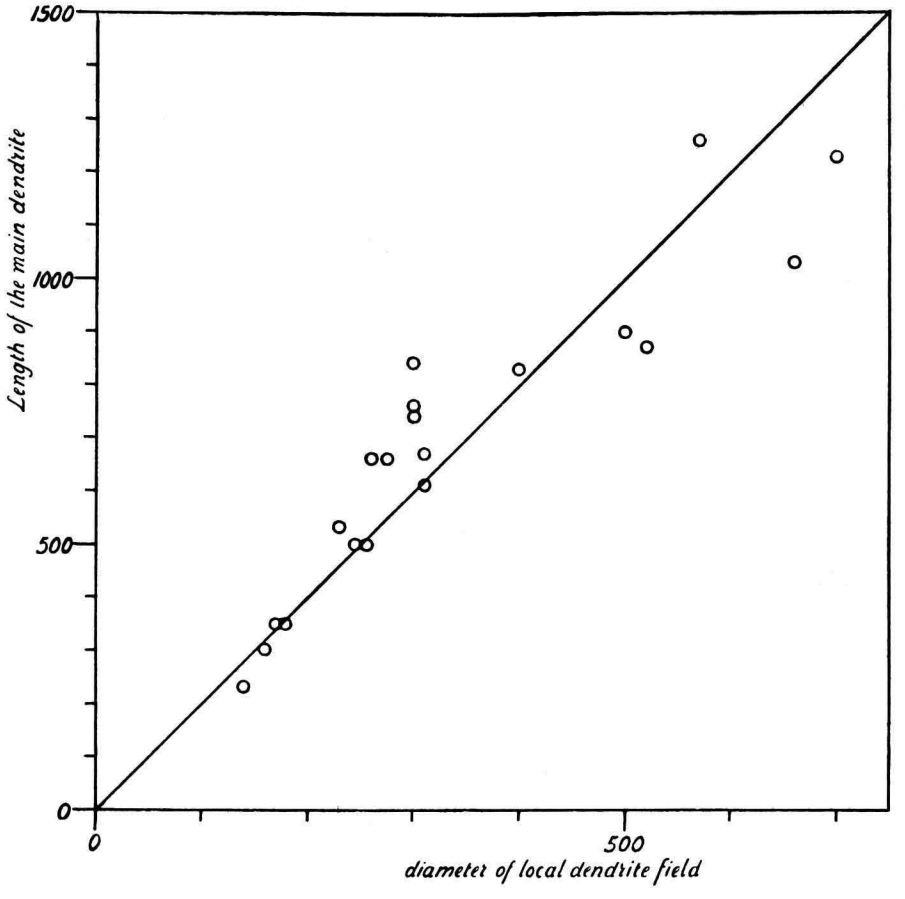


Fig. 25. The diameter of the fields of local dendrites (measured in drawings of the cerebral cortex by CAJAL) as a function of the length of the main dendrite.

shape: their height and their breadth show the same mutual relation in different sized cells. Consequently the avarage neurones of the different levels of the upper group differ in their size only, not in the main form of their dendrite complexes (here "main form" does not stand for the details of the dendrite complex, e.g. not for the shape and the branching up of the individual dendrites themselves).

As the average cells of the different levels have similar dendrite fields, the other fields cannot be similar, because the length of their main dendrite is the same as in the average cells of their level and the length of their local dendrites is different from, and can be larger or smaller than in these average cells. The question now is, how do these dendrite fields differ from the average ones?

The average diameter of the local dendrite fields are found to be proportional to the depth. And the average nucleus volume in the upper group of ganglion cells being exactly proportional to that depth also, the average diameter of the local dendrite fields are proportional to the average nucleus volume.

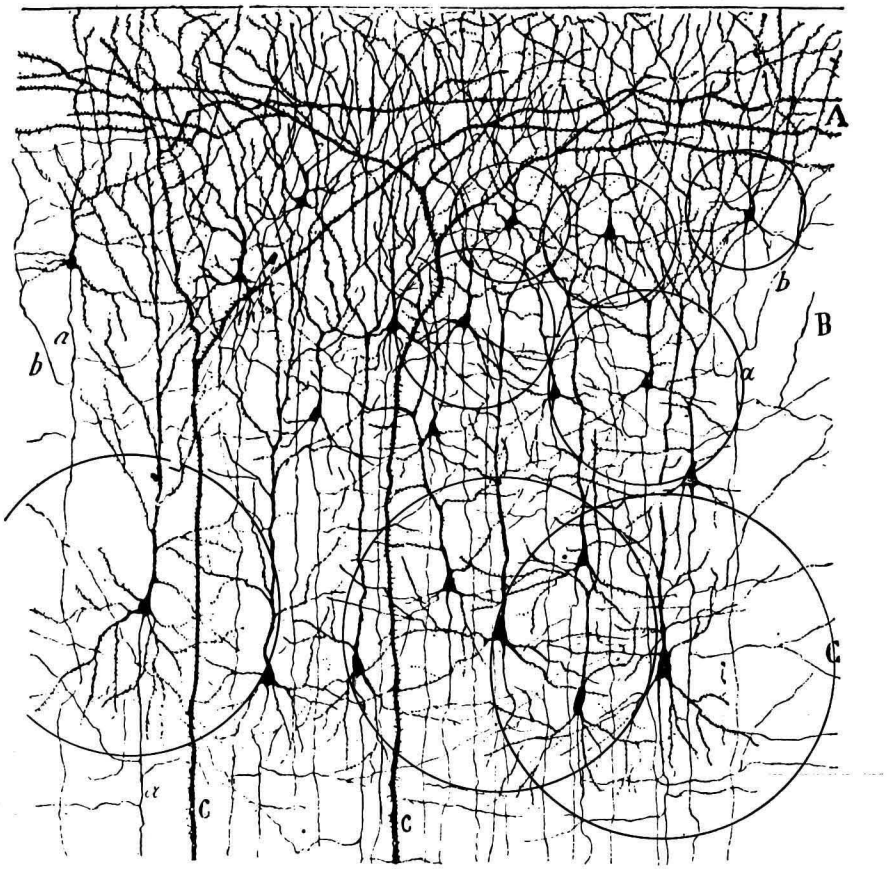


Fig. 26. A figure by CAJAL of the visual cortex in which circles are drawn with a radius equal to ¼ of the depth of their centre.

The mean diameter of the local dendrite fields at the different levels being proportional to the average nucleus volume and both the diameters and the nucleus volumes at each level varying in both directions from the average values of that level, *it is probable that the individual diameter of the local dendrite field is proportional to the individual nucleus volume.* [1])

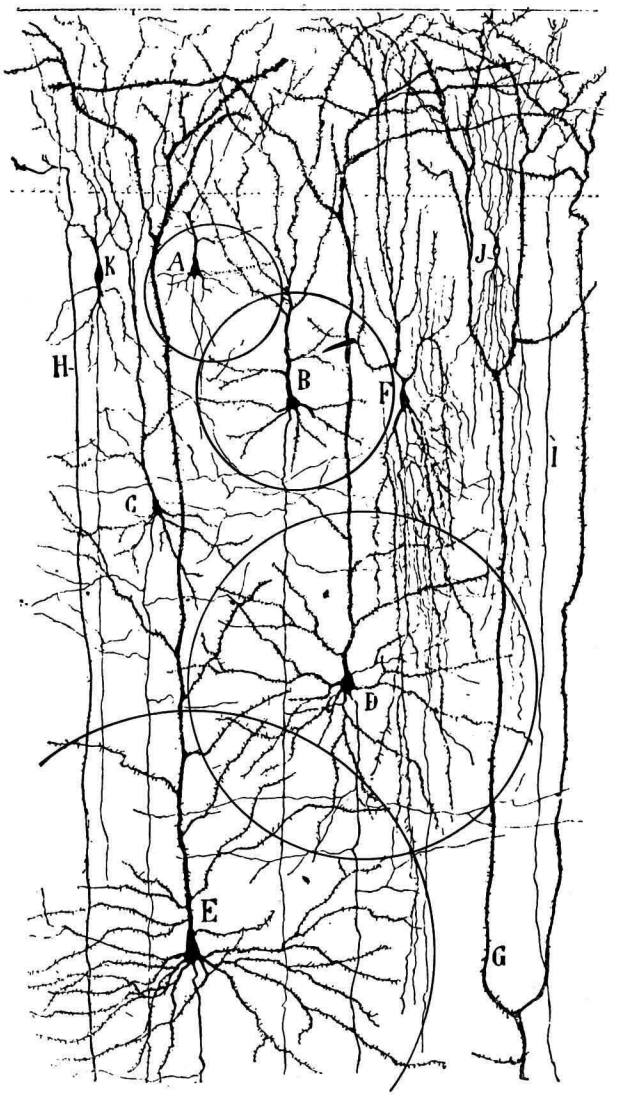


Fig. 27. A figure by CAJAL of the motor cortex area in which circles are drawn with a radius equal to ¼ of the depth of their centre.

[1]) This proportionality between the nucleus volume and the diameter of the dendrite field runs remarkedly parallel to the conclusion of TAKAGI and his collaborators, that the size of a nerve cell is determined by the size of the field innervated by its neurite (motoric and sensible neurones of the spinal cord and ganglia). For literature see JAPAN. J. of Med. Sc. I, Anat. Vol. 5 no 3 (1935).

If this be true — as is very probable — the structure of the cortex could easily be understood from the relations found in the previous chapter and it would prove to be a structure of a very simple character.

If we suggest the nucleus volume to be proportional to the diameter of the local dendrite field, the value $\frac{N}{D}$ would be a measure of the relation between the length of the local dendrites (being proportional to the nucleus

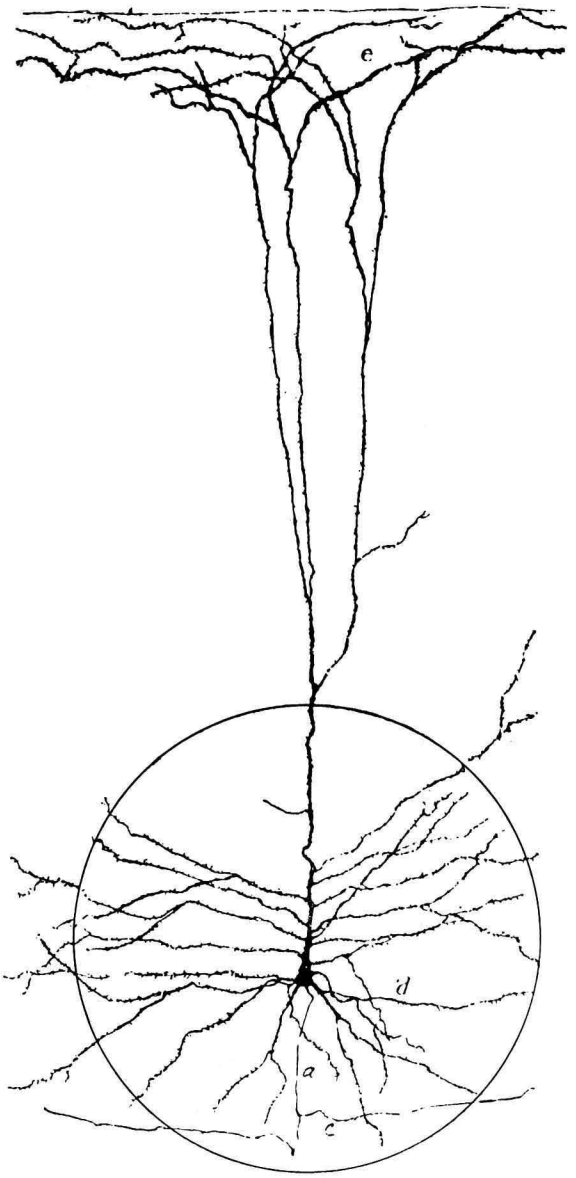


Fig. 28. A figure by CAJAL of a giant motor cell in which a circle is drawn with a radius equal to ¼ of the depth of its centre.

volume $N$) and the length of the main dendrite ($D$) in each neurone, it would be a measure of the shape of its dendrite field. In the upper group of cells this value $\frac{N}{D}$ varies normally (more exactly expressed the logarithm of this value varies according to the GAUSSian formula of normal distribution). *Thus the form of the dendrite fields in the upper zone would vary normally.*

The value $\frac{N}{D}$ varies to the same extent as the value $D$. So the "form" of the dendrite complexes varies as much as the length of the main dendrites, and as much as the size of the average cells.

*If our hypothesis be correct (the nucleus volume being proportional to the diameter of the local dendrite field), the relations found in the previous chapter would mean that the upper group is built up of neurones, varying as much size as in form. The variation in form is "normally" distributed and independent of the frequencies in size, which are given by the "filling up" of the cortex.*

Here "size" stands for the volume of the nucleus of the *average* cells. It also stands for the length of the main dendrite of every cell. And "form' stands for the relation between height and breadth of the dendrite field, for the relation between the length of the main dendrite and the length of the local dendrites (not for the details of the form, such as the shape of the dendrites themselves). Thus the conclusion can be formulated more exactly — though less concisely — as follows: *the upper zone is a group of neurones in which the relation between the lengths of the main and the local dendrites varies as much as the length of the main dendrites and independently of it.*

That the mean type of the ganglion cells in the higher levels of the upper zone is small (the outer corner layer!) and the mean type in its lower levels is larger (the outer pyramid layer!) is a consequence of the variations in shape of the dendrite fields being independent of the variations in their size. The ganglion cells of the lower levels have longer main dendrites than the cells, situated higher in the cortex, the distance of a ganglion cell from the pia being the length of its main dendrite. In consequence of the rules discussed above, the mean length of their local dendrites will be larger, too, and their cell body and nucleus, consequently, will have a larger average size than in the higher levels.

An example may elucidate this simple relation. If we imagine a group of men standing on a horizontal ground and varying in shape and in size, the variations in their shape being independent of the variations in their size, most of the larger bodies will be found farther from the ground than the smaller bodies, the average length of the legs of the larger bodies being larger than those of the smaller bodies.

Our hypothesis, that the length of the local dendrites is proportional

to the nucleus volume, is made highly probable by the fact, that the average length of these dendrites is proportional to the average nucleus volumes. That this hypothesis leads to so simple a conception of the structure of the cortex, is very much in its favour and increases its probability.

An analoguous reasoning can be made for the lower group, the conditions seeming more complex, however, by the law, that the average nucleus volumes in this group are proportional to the *square* of the depth. If the diameter of the local dendrite fields of these cells also would be proportional to the nucleus volume, the length of the local dendrites of the average cells would increase with the square of the length of the main dendrites.

I could not find drawings of the dendrite fields of the lower zone showing the pia also and which were accurate enough to measure the local dendrites. In my own COX preparations they are not sufficiently impregnated, I have the impression, however, that in these preparations the length of the local dendrites does not vary with the square of the depth but proportionally to the depth itself.

More investigations are necessary to know if I am right. If so the lower group of cells also would be built up in a very simple way.

The length of the local dendrites of the average cells varying proportionally to the depth and their nucleus volume varying with the square of the depth, their number will vary with the depth also. In that case the "form" of the average dendrite complexes would be the same, namely the relation between the lengths of the main and the local dendrites, it would be neurones of the same shape also, with this restriction only that in the lower group the number of the local dendrites increases with the size of the cells (or by an increasing branching of these dendrites). It can be demonstrated easily that in that case in the lower group the form of the neurones varies as much as in the upper group of cells and the size varies in same order but perhaps somewhat less.

This suggestion is given only to show, that a simple structure can be imagined as hidden behind the quantitative laws found. In no way is it proved to be right. Other views are possible. They might be based upon the possibility that the proportionality between the nucleus volume and the square of the depth is accidental and caused by a proportionality between the nucleus volume and the depth minus a definite value.

Too little is known about the dendrites of this lower zone to know the direction in which the real relations should be sought.

What may be the significance of the "filling up of the cortex by the neurones"? To what cause is it to be attributed that each ganglion cell occupies a part of the cortex, the volume of which depends upon the volume of the nucleus of that cell?

This portion of the cortex, containing one ganglion cell and called the cell territory, consists only for a small part of the cell itself. The rest is built up of all the other elements that lie between the cell bodies : dendrites, neurites, blood vessels and glia. First the relation of the cell body to the nucleus volume will be discussed and than the relation between its intercellular part and the nucleus volume.

A relation between the perikaryon volume and the nucleus volume is discussed in my paper : "a quadratic relation between the volumes of the nucleus and body of ganglion cells of different sizes" (1934). In that

paper I described how in 247 ganglion cells of the 2d and 3d layer of the human cerebral cortex (area temporalis superior posterior) the volume of the nucleus and the volume of the cell were measured by drawing the outlines of the body and of the nucleus and by calculating the volume of the rotation bodies with the same outlines. (The results of these measurements demonstrated that the differences between their volumes and those of the real cells and nuclei are distributed according to the laws of probability.) The volume of the perikaryon was calculated as being the difference between the measured cell volume and the measured nucleus volume of each ganglion cell. These volumes of the perikaryon were found to be proportional to the square of the nucleus volumes after the formula $P = \frac{1}{90} N^{2.0096 \pm 0.05}$.

This is a relation between one of the measured values (the volume of the nucleus) and the difference of the two measured values (cell volume — nucleus volume = perikaryon volume).

Between the measured values themselves (nucleus volume and cell volume) too a special relation was found later on.

In the diagram of fig. 29 the logarithms of the nucleus volumes are the abcisses and the logarithms of the cell volumes are the ordinates. The points are situated in a narrow band along the straight line drawn. The angle between this line and the horizontal line has a tangent $= \frac{3}{2}$. The tangent of this angle in a logarithmic scheme being the exponent of the proportionality between the measured values, the volume of these nerve cells increase proportionally to the $\frac{3}{2}$ power of the nucleus volume:

$$C \sim N^{\frac{3}{2}}$$

($C$ = cell volume, $N$ = nucleus volume).

By calculation according to the method of the smallest squares this exponent is found to be $1.55 \pm 0.008$. The exactitude of the measuring is a high one (the probable fault being ½ %), but the calculated value of the exponent turns out not to be exactly 1.5, but 1.55. It can easily be demonstrated that a difference in the measure of shrinking between the nuclei and the protoplasm, that has no influence upon the exponent of the relation between nucleus and protoplasm, must have a small influence upon the exponent of the relation between nucleus and cell, the cell being an addition of a nuclear component and a protoplasm component. So the exponent in the relation $P \sim N^2$ could be found exactly $= 2$ ($2.0096 \pm 0.05$) but the exponent in the relation $C \sim N^{\frac{3}{2}}$ cannot be expected to be

found exactly $= \frac{3}{2}$ even in the case that in the living cells this relation would be found exactly.

In my laboratory, P. J. ALLAART measured the nucleus volumes and the

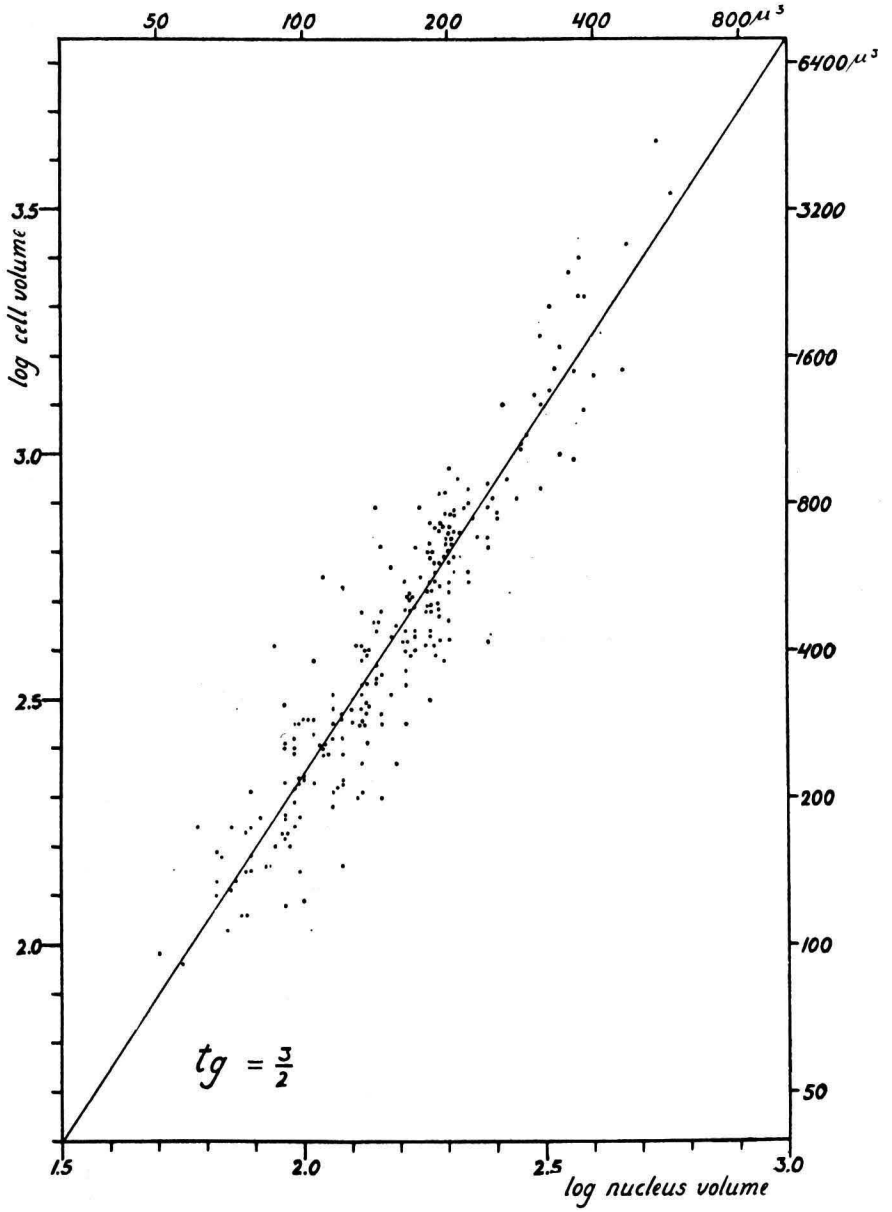


Fig. 29. Logarithmic diagram of the cell volumes and the nucleus volumes.

cell volumes of the neurones in both main zones and in different architectonic fields of the cortex and in the spinal ganglia of men and apes and found the same relation $C \sim N^{\frac{3}{2}}$, the exactly calculated exponent of

this relation differing in all these cases from 1.50 in a small degree and in different directions (not published yet). Thus the conclusion can be drawn that in the unshrunk cells the relation $C \sim N^{\frac{3}{2}}$ is present in a fairly exact degree.

The cell bodies of the measured ganglion cells do not differ much in form. The linear dimensions of similar bodies vary proportionally to the $\frac{1}{3}$ power of their volumes. Their surfaces, varying proportionally to the 2d. power of their linear dimensies, vary to the $\frac{2}{3}$ power of their volumes. If we take the ganglion cells as all of one form and we put $c$ for their surfaces, this can be read as $c \sim C^{\frac{2}{3}}$. The measurements have shown that:

$$C \sim N^{\frac{3}{2}};$$

so $c \sim C^{\frac{2}{3}}$ can be written as

$$c \sim N^{\frac{3}{2} \times \frac{2}{3}}$$

or $$c \sim N.$$

*Thus the surface of these ganglion cells proves to be proportional to the volume of their nucleus.*

This proportionality can be demonstrated in another way.

The surfaces of these cells can be measured in a similar way as their volumes. In the same drawings the length of the outline of the cell was measured and also the distance of the centre of gravity of the half of that line from the longest (= rotation) axis as was described in the paper of 1934. According to the GULDIN law (surface of a rotation body = length of the rotating line × path of its centre of gravity) from these measurements the surfaces of the cells were calculated. They are shown in fig. 30, where the logarithms of these surfaces are the ordinates and the logarithms of the nucleus volumes are the abscisses. The points are situated along a line making an angle of 45° with the coordinates, the tangent being = 1. So these direct measurements of the cell surfaces show that they increase proportionally to the nucleus volumes (in the same way as in my paper of 1934 on the perikaryon volumes it can be argued, that the deviations of the points from the drawn median line will be caused by errors of measurements).

Thus the *surface* of these ganglion cells is proportional to the volume of their nuclei.

In other cells of the body not the surface but the *volume* of the cell

is found to be proportional to the nucleus volume. This was found in secretory cells by HERTWIG. A biological interpretation of this peculiar

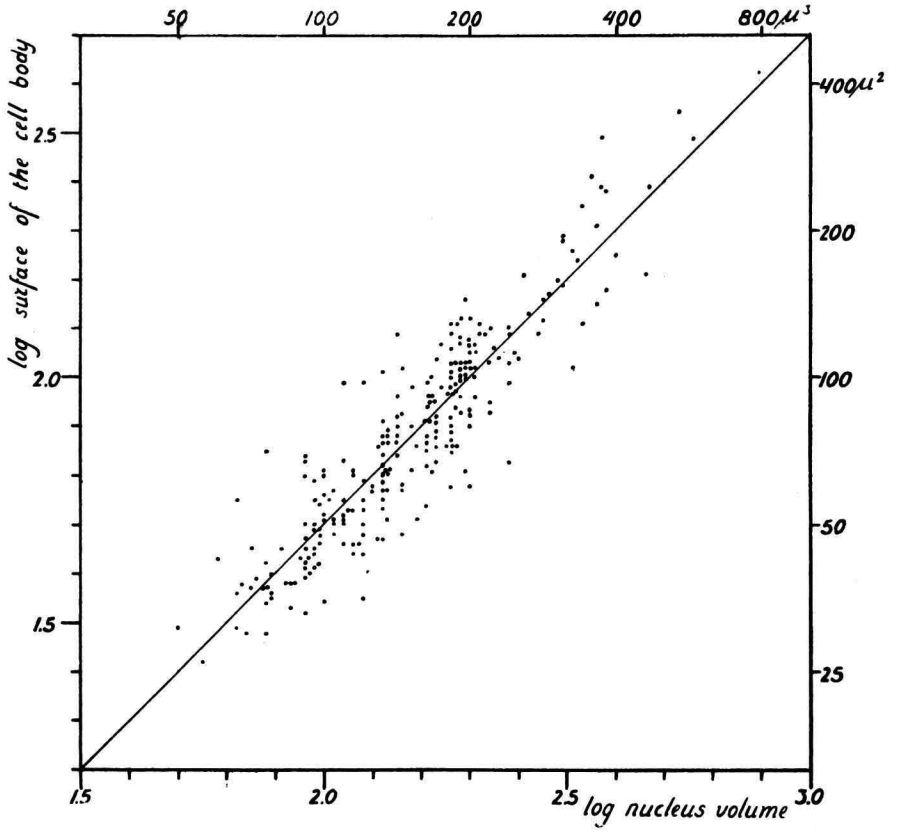


Fig. 30. Logarithmic diagram of the cell surfaces and the nucleus volumes.

difference between ganglion cells and secretory cells is found in the fact, that it is the surface of a ganglion cell that has an important function. It may be covered by end eyes of neurites that bring stimuli to the cell as is seen in cells of the brain stem and spinal cord (figs. 31 and 32), or it may be surrounded by a dense network of afferent neurites as is seen in cortical cells in fig. 33. The surface of the cell body is a receiver of stimuli and so the volume of the nucleus is proportional to the size of this receiver, it is proportional to a distinct function of the cell.

In a secretory cell the capacity of function is given by the amount of protoplasm, i.e. by the volume of the cell body. Thus in both types of cell the nucleus volume may be said to be proportional to a capacity of function.

If the density of the nerve fibres everywhere in the cortex was the same (if they had the same distance from each other) this "capacity of receiving function" could be formulated more exactly: in that case a cell surface twice

as large as another would receive its stimuli from twice as many fibres passing in its direct neighbourhood, in other words the nucleus volume

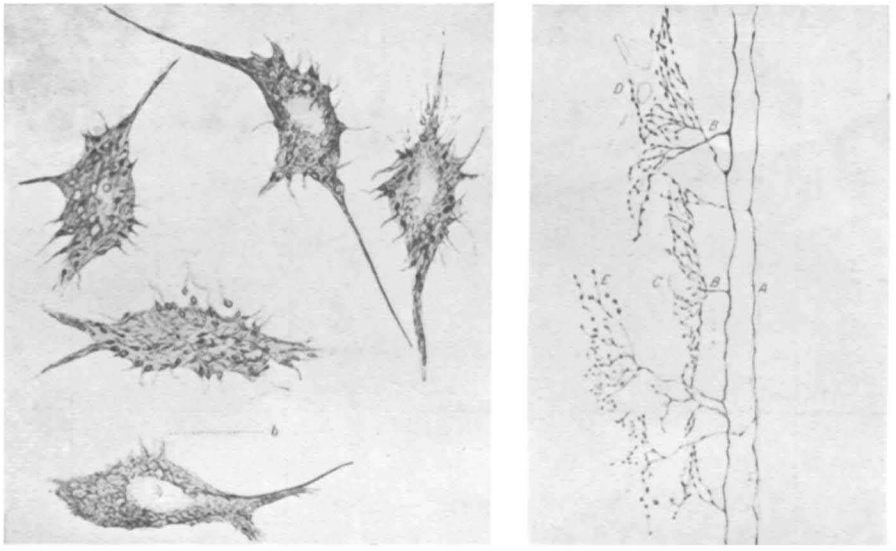

Fig. 31 and 32. Axonic endings on the surface of nerve cells in the olive and in CLARK's column (after CAJAL).

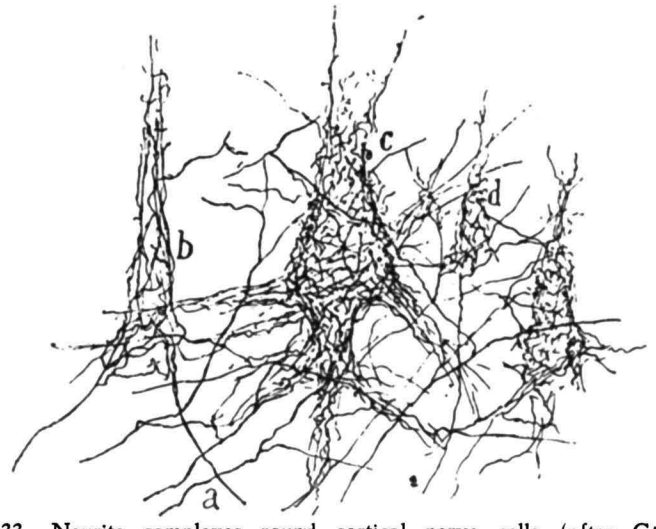


Fig. 33. Neurite complexes round cortical nerve cells (after CAJAL).

would be proportional to the number of fibres, from which the cell body receives its stimuli.

That the density of the nerve fibres in the cortex is constant is demonstrated by R. C. RENES, who in my laboratory has measured the total fibre length per unit of volume in different layers and in different architectonic fields of the human cerebral cortex.

These measurements were made in sections, the nerve fibres in which were impregnated by BIELSCHOWSKY's method. All the fibres present in a small field between the nerve cells were drawn with the aid of a drawing prism placed on the microscope. In the drawing the length of each line was measured and the length of the fibre was calculated by considering the enlargement and the angle, the fibre made with the plane of the drawing.

Some of the results are demonstrated in fig. 34. The ordinates of the small circles in the thick line are the total lengths of the nerve fibres per 1000 $\mu^3$ space measured at different depths of the cortex in one section, taken from the area frontalis granularis magnocellularis (VON ECONOMO). The 5th layer excepted they differ only slightly. Moreover the differences are independent of the average size of the nerve cells, as is shown

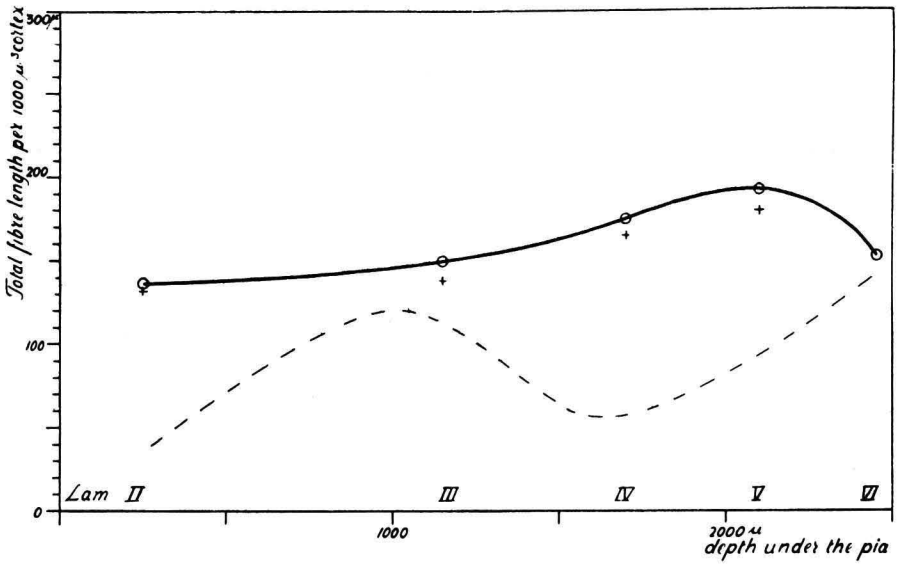


Fig. 34. The small circles in the thick line show the total length of the nerve fibres in 1000 $\mu^3$ space in different layers of the frontal cortex, measured by R. C. RENES. The variations of the nucleus volumes are shown by the dotted line. The figures + give the fibre lengths in the corresponding layers of the area striata.

by the dotted line, giving the average nucleus volumes at these depths. The curves of this dotted line do not coincide with the one smooth curve in the thick line of the fibre distances.

The figures + give the total fibre length per 1000 $\mu^3$ space in the corresponding layers of the area striata in the same cerebrum. These fibre lengths agree with those in the frontal cortex. And in the 5th layer of the area striata, area temporalis and area praecentralis of another human cerebrum the total fibre length was measured 202, 202 and 197 $\mu$ per 1000 $\mu^3$ space.

*Thus the total length of the nerve fibres per unit of volume is fairly constant in the cerebral cortex.*

It is a remarkable fact, that in each part of the cortex the total length of the nerve fibres per unit of volume is almost the same. Possibly this is due to the distance between these fibres being constant.

If the nerve fibres do not approach each other nearer than a given minimum distance, their total length would be almost constant in parts of the cortex with equal volumes. Differences in their arrangement would cause differences in their total length, but these differences would be relatively small.

If the minimum fibre distances were constant, cylinders, imagined around each fibre with a radius measuring the half of that distance, would not overlap each other: if they overlapped the distance between their axisses would be less than twice the radius, i.e., less than the minimum fibre distance. At several spots or lines these cylinders would touch each other, namely at the points of minimum fibre distance. The total volume of these cylinders would measure $\frac{1}{4} \pi l d^2$ ($l$ = the total length of the fibres $d$ = the minimum fibre distance). This volume differs from the total volume of the part in which the fibres are measured by the volume of the space between the touching cylinders.

If the volume of the space between the touching cylinders were a constant percentage of the volume of the cylinders themselves, the volume of the cylinders would be equal in parts of the cortex with equal volumes and, according to the formula given above, in which $d$ is constant, the total length of the fibres ($l$) would be the same. It would be different, however, if the cylinders are arranged differently.

In the arrangement of the cortical fibres the "wasted" space certainly will be relatively small, smaller in volume than the cylinders. Moreover the arrangements of the fibres in the measured parts of the cortex are so like each other that in most of the measured fields no differences in these arrangements could be seen. In consequence the space between the cylinders probably will differ only relatively little in comparison with the total volume and thus the constancy of the total length of the nerve fibres found in the unit of cortex volume probably is caused by a constant minimum distance between the cortex fibres.

This is made more probable still by the fact, that in one of the fields the arrangement of the fibres differs from that in the others: in the measured field of the Vth layer many more fibres than in the other fields have a direction parallel or transverse to the pia. If the minimum fibre distance were the same as in the other fields less space would be "wasted" here by the many parallel fibres and in consequence the unit of cortex volume would contain a larger total length of fibres. As a matter of fact the total fibre length found in this 5th layer is markedly higher than in the other layers.

If the cortical nerve fibres never approached eachother nearer than a constant minimum distance, the stimuli, passing from one neurone to

another, would be conducted over this distance by protoplasm not differentiated into nerve fibres, and everywhere in the cortex this synaps bridge would be of the same length.

A simple calculation shows, that this distance would be somewhat smaller than 2,4 $\mu$. If all the fibres were lying parallel to each other and each at equal distances from all the surrounding ones — the latter passing a transverse section at the edgepoints of a regular hexagonal round the first — a fibre distance of 2,4 $\mu$ would account for 200 $\mu$ fibre length per 1000 $\mu^3$ cortex. The arrangement of the cortical fibres being more irregular, this distance will be somewhat smaller.

The density of the fibres in the cerebral cortex being practically constant, the number of the fibres, passing the surface of a ganglion cell body (or ending on it) is proportional to that surface and this surface being proportional to the nucleus volume, *the number of the fibres, out of which the surface of a ganglion cell body can receive its stimuli, is proportional to the volume of its nucleus.*

It being possible to see the relation between the surface of the ganglion cell and the size of its nucleus as a quantitative relation between nucleus volume and a special receiving capacity of the cell body, it is interesting to know the quantitative relation between the nucleus and the other receiving apparatus of the neurone, its dendrites.

The perikaryons occupying a small percentage of the space only, it is obvious, that the larger part of what was called the cell territory contains the dendrites. In some way or another the size of the territory must depend upon the size of the dendrite complex.

If the territories would express some reality, they would contain all the dendrites of their cell. We have seen, that the diameter of the local dendrite field is proportional to the nucleus volume, in consequence the diameter of the territories also will be proportional to the nucleus volume. And if the territories of different sized ganglion cells were all of the same shape, their volume would be proportional to the third power of their diameter, i.e. to the 3d. power of the nucleus volume. Their volume is found to be proportional to the 2d. power of the nucleus volume, however, the sum of the 2d. power of the nucleus volumes being the same in all parts of the cortex with equal volumes.

This is a distinct contradiction. The only conclusion possible is, that the territories of different sized ganglion cells cannot be similar in shape.

Two points may be discussed, in which the shapes of different sized territories must differ from each other.

In the first place the larger part of the dendrites are thin fibres with a diameter, many times smaller than the average fibre distance. The space between the fibres being part of the territories (the territories together built up the total space of the cortex) the transverse diameter of those parts of the territories that contain a finer dendrite may depend upon the fibre

distance more than upon the transverse diameter of the dendrites. Thus it may be almost the same in smaller and in larger neurones, the fibre distance being the same. A territory of a neurone, the dendrites of which are twice as long as those of another neurone, by this peculiarity may have a volume nearly twice as large in stead of $2^3 = 8$ times larger.

In the second place the territories of smaller and larger ganglion cells must differ in shape owing to the dentrites of a larger cell having more branches than those of smaller cells. This is clear in every section of the cortex, impregnated by the method of GOLGI and it is demonstrated by figs 26, 27 and 28 of this paper.

In the drawings of CAJAL I measured the total length of the local dendrites of several cells in the upper zone and I compared this total length with the depth of the cell (with the length of the main dendrite). In the different drawings I got nearly identical results, the total length of the local dendrites growing proportional to the 2d. power of the depth (the power found in the different drawings varied between 1,8 and 2,3). I do not give the details of these measurements and calculations, because this method of measuring, using the drawings only, is not exact and direct measurings in COX preparations are being made in my laboratory. They are not finished and for the present we have to content ourselves with the comparatively rough measurements of the drawings.

A proportionality between the total length of the dendrites and the 2d. power of the depth means a proportionality between the total dendrite length and the volume of the territories (the volumes of the territories too being proportional to the 2d. power of the nucleus volume). *It means, that in parts of the cortex with equal volumes the same length of dendrites is present.*

The measuring of the dendrites in these drawings being a somewhat rough method, the constancy of the dendrite length per unit of space is not at all certain. Yet this result is remarkably simple and therefore I take it as a preliminary answer to our question : what influences regulate the "filling up" of the cortex? Probably so many neurones are present in each unit of cortex volume, that their dendrites have a maximum total length.

This view can be formulated in another way.

The total length of the dendrites in equal cortex volumes being constant, *the average dendrite distance will be constant. Thus the cell territories are parts of the cortex, each containing a nerve cell with its dendrites and exceeding their surfaces over a constant distance.* (We shall see that this distance probably measures about 2 $\mu$.)

The constancy of the total length of the dendrites per unit of space has a second remarkable consequence. RENES found the total length of the nerve fibres per unit of space to be constant. These nerve fibres are neurites as well as dendrites, both being impregnated in the sections used in his measurements. The sum of neurite and dendrite lengths per unit of space

being constant, the constancy of the dendrite length means, that the total length of the neurites per unit of space is constant as well. *Thus everywhere in the neuropilem of the cortex the total length of the dendrites and the total length of the neurites would have a constant relation to each other.*

The exact relation between neurite and dendrite length can be estimated only by measuring the total length of the dendrites in sections, impregnated by GOLGI's method and taken from parts of the cortex, the number of its nerve cells being known.

A preliminary result was obtained by the measurements of the total dendrite length in CAJAL's figures. The thickness of the drawn sections not being noted in his papers, the measuring of the absolute length of all the dendrites of a cell from these drawings is much more uncertain than the measurement of the relative increase of these lengths discussed above. Therefore I only state that these masurements give the impression, that the total length of the dendrites does not differ much from half the length of all nerve fibres. If this is right the neurite-dendrite-relation would be an equality. Certainly the total length of the neurites cannot be many times that of the dendrites.

A remarkable detail of the cortex structure can be concluded from this relation, although it may be arrived at by rather inexact means. It may be concluded that between adjacent dendrites no more than one layer of neurites is present. If each dendrite were surrounded by neurites only, the total length of the neurites would be many times that of the dendrites (3 times at least) and if more than one layer of neurites would be situated between adjacent dendrites the total neurite length would be at least 6 times that of the dendrites. From the roughly found neurite-dendrite-equality it can safely be concluded, that the total length of the neurites will not be 6 or more times that of the dendrites. Consequently only one layer of neurites is present between adjacent dendrites. Each neurite thus passes between dendrites lying at both sides of it.

And the average fibre distance being constant, the neurites must be situated in the surfaces which limit the cell territories from each other. *Thus the territories would express a reality: they would be the cortex fields, each containing a nerve cell with its dendrites and being limited by the adjacent neurites passing between this neurone and the adjacent ones.*

The number of fibres, out of which the cell body receives its stimuli, was found to be proportional to the nucleus volume, this volume being proportional to the cell surface. What is the relation between the nucleus volume and the number of fibres, from which the dendrites receive their stimuli?

The larger part of the dendrites being thin fibres with a diameter far smaller than the average fibre distance, the number of fibres that pass a dendrite will be proportional to the length of that dendrite. And the total length of the dendrites of one neurone probably being proportional to the square of the nucleus volume, the number of the neurites, from which the dendrites of a neurone can receive their stimuli, would be proportional to the 2nd. power of the nucleus volume. Consequently it would be proportional to the volume of the perikaryon.

This result is in accordance with another method of reasoning. An attempt was made above to estimate the number of the neurites passing in the immediate neighbourhood of the surfaces of the dendrites and cell bodies. The number of neurites, that can give stimuli to a neurone may be estimated in a second way. These fibres must pass the dendrite field

of the neurone, i.e. that part of the cortex which is limited by a surface of a fairly simple shape, passing through the ends of the longest dendrites, thus being the space that is traversed by the dendrites of that cell. The diameter of this field we found above to be proportional to the nucleus volume. We come to the conclusion in two ways that the number of the fibres passing through this dendrite field is proportional to the square of its diameter. These fibres must enter it through its surface. Their average distance being constant, their number is proportional to that surface and consequently proportional to the square of its diameter. Or in a second way. If we imagine a part of the cortex in which the neurites run parallel to each other, the number of neurites passing the dendrite field would be proportional to the surface of its section perpendicular to the neurites, that is, proportional to the square of the diameter.

The number of fibres, passing through the dendrite field of a neurone being proportional to the square of its diameter and this diameter being proportional to the nucleus volume, the number of neurites, from which the dendrites of a neurone may receive their stimuli, will be proportional to the square of the nucleus volume.

This relation is the same as was obtained by measuring the total lengths of the dendrites in CAJAL's figures, but it is now found without making use of that rather inexact method.

In the foregoing 5 pages an attempt has been made to give an analysis of the relations between the neurites and dendrites passing each other in the neuropilem of the cerebral cortex. Many of the details of this analysis are based upon the inexact method of measuring the length of the dendrites in the figures of CAJAL and therefore the measurements of the dendrite lengths will be repeated in my laboratory with GOLGI preparations. The results of this more direct method may make it necessary to revise some of the details of our conclusions, but so much will be clear, that the quantitative relation, found in the third chapter, between the sizes of the territories and their cells in no way contradicts the conclusion of the fourth chapter, the cortex being built up of neurones, varying as much in size as in the shape of their dendrite fields.

## V. SUMMARY.

In different architectonic fields of a human cerebral cortex the volume of the nucleus of the ganglion cells and their distance from the pia was measured. Especially one field, the regio temporalis superior posterior, was discussed.

The cells in this region can be divided into two groups. In the upper group the geometrical average nucleus volume increases proportionally to the distance from the pia, in the lower group it increases proportionally to the square of that distance. The variation of the nucleus volumes at each level of the cortex is thus: in the upper group the value: nucleus volume divided by the pia distance varies normally (more exactly expressed: the logarithm of that value varies according to the GAUSSian formula of normal distribution); in the lower group the value: nucleus volume divided by the square of the pia distance varies normally.

In each part of the cortex the perikaryons occupie the same percentage of the space. Their surface is proportional to the volume of their nucleus.

By these rules the size of the ganglion cells at each depth of the cortex can be described quantitatively by giving 4 values: the nucleus volume of the "central" cell of the upper group, the pia distances of the "central" cell of each of the two groups and the standard deviation. Possibly these 4 values depend upon each other.

*The significance of these quantitative rules is this, that the cortex is built up of two groups of neurones varying as much in size as in the shape of their dendrite fields, the shape varying normally and independently of the size.*

In each unit of cortex volume probably so many neurones are present that their dendrites together have a given length, the adjacent dendrites running at a constant minimum distance from each other. The total length of nerve fibres (dendrites and neurites) being nearly constant in each unit of cortex volume (200 $\mu$ nerve fibre per 1000 $\mu^3$ cortex), the relation between the total length of the neurites and that of the dendrites in each part of the neuropilem probably is constant also (after a preliminary rough measurement this relation would be an equality).

The number of fibres, from which the surface of a cell body may receive its stimuli, is proportional to the volume of its nucleus, the number of fibres, out of which its dendrites receive their stimuli, probably is proportional to the square of the nucleus volume and proportional to the perikaryon volume.

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