threshold θ; the impulse resets the integral to zero, and so on. In this interpretation, the threshold is a random function; I' represents, up to a proportionality factor, the distribution of the amplitude of the threshold sampled at the time of firing. The invariance of I' shows that this distribution is independent of the stimulus acting on the cell.

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Probabilistic Analysis of Dendritic Branching Patterns of Cortical Neurons

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Summary It is argued that the usual method of characterizing dendritic fields of nerve cells by enumerating the number of bifurcations and end points at various distances from the perikaryon, and the number of intersections of dendrites by virtual spheres around the centre is of limited value for an adequate description. Although these parameters give a reliable indication as to the spatial density of the dendritic material, one shortcoming is that the structural content of the plexus remains rather obscure because the topological and metrical aspects are represented in an intermingled way. A statistical theory is put forward that separates the two factors. As to the first factor, many experimental data can be described by assuming that the probability of bifurcation of a segment decreases geometrically with the order of that segment. As to the second factor, it is deduced that in most instances the terminal segments are, on the average, several times longer than the intermediary situated segments.

Upon elaboration of the theory, in comparison with experimental findings reported in the literature, it seems profitable to evaluate these factors separately by measuring the distribution of the number of segments per order or generation, and the distribution of the lengths of the segments for each order. Emphasis is laid on the dynamic aspects of dendritic growth by analyzing data on changes in dendritic ramification patterns of cells in brains of animals of various ages, and reared under either normal or experimental conditions.

Introduction

Treatment of the mode of functioning of the central nervous system lays emphasis on the pattern of connectivity between axons, perikarya and dendrites of nerve cells. Especially the latter category of processes has received rather intensive attention from neurohistologists in the last fifteen years, and a considerable amount of quantitated information has become available on the mode of branching of dendrites.

In some detail, Bok (1936) has described the dendritic ramification for eight cells in the outer layer of an unspecified part of the cat's brain. Common features in the branching pattern of the neurons, as well as certain differences, were noticed. It was tentatively concluded that dendrites of a neuron first bifurcate at an equal distance from the cell body, while their branches tend to bifurcate or end at points that are twice this distance farther from the cell. The said author admitted that not all cells measured showed the relation quite as clearly; in the largest neurons it was even impossible to distinguish groups of related distances.

Sholl (1953) has studied extensively the size and arrangement of the dendrites of 30 neurons in the visual and motor areas of the cerebral cortex of the adult cat, and doubted of a deterministicall mode of branching with preferred sites of bifurcation or ending. He found it impossible to establish a simple rule, for instance for the length of branches. In addition, the use of statistical measures was stressed to exclude irrelevant information and allow pertinent features to be expressed concisely.

Several studies have since been published which were concerned not solely with brains of normal and adult animals, but also with brains of young animals, and animals grown up under abnormal experimental conditions. To our knowledge, no attempt has yet been undertaken to unify in analytic terms the diversity of published material on dendritic arborizations, which is widely diffused through the literature. It is the aim of the present communication to do so by means of a relatively simple theoretical framework; it allows generalizations and suggests improvements with regard to future procedures for data collection. Such an undertaking would seem opportune in the light of the search for the interrelationship between electrical activity recorded by micro-electrodes and gross electrodes, which requires knowledge about the geometry of the "cell territory" of individual neurons expressed in terms of packing density of the perikarya and the extent of their associated dendritic field.

Furthermore, in view of the current interest (cf. Scherrer, 1967) in connections between the onset of electrical functioning of the nerve centres on the one hand, and the anatomical maturation of the brain or the behaviour of the animal during postnatal life on the other, we thought it opportune to focus attention primarily on the dynamic aspects of growth as disclosed in the course of ontogenetic development. We are prompted through good reports on this matter from Peters and Bademan (1963), Eayrs and Goodhead (1959), and Schadé and Van Groeningen (1961); these we shall (re)analyse in some detail and they are, in fact, the main constituent of the present communication. In addition we shall discuss, against the background of theoretical deductions, the outcome of investigations on distortion or retardation of growth of dendritic organization of neocortical neurons, following X-irradiation during foetal life of rats (Berry and Eayrs, 1966), or during early life of monkeys (Caveness *et al.*, 1965), after experimental cretinism in rats (Eayrs, 1955), after sensory deprivation in rats (Holloway, 1966) and cats (Coleman and Riesen, 1968) and surgical deafferentation in the cat (Jones and Thomas, 1962).

Experimental Methods

It was noticed by Sholl (1953) that the dendritic branches of stellate cells and the basal dendrites of pyramids form a reasonably symmetrical field around the perikaryon. This permits a convenient characterization of each dendritic tree by imagining that the perikaryon is surrounded by a set of concentric spheres. Their radii increase with a constant amount, i.e. 20 μ, denoted by Δr hereafter. After supposition of spherical symmetry, the 3-dimensional picture can be condensed to a function of one variable, viz. the distance r to the perikaryon. The number of dendrites intersecting the hypothetical spheres with radius r has been counted and will subsequently be called $c(r)$. By analogy, the number of dendritic segments attached to the cell body, primary or basilar dendrites, is denoted by $c(0)$. If Δr is not too large, the set of numbers $c(0)$, $c(\Delta r)$, $c(2\Delta r)$, etc. gives a good description of the density of dendrites around the centre of the cell body.

One should realize, however, that the characterization of a tree by $c(r)$ is by no means unique. It follows from the definition that $c(r)$ can be found also by counting the number of bifurcations within a sphere of radius r, $P(r)$, adding the number of primary dendrites, $c(0)$, and subtracting the number of endings within that sphere, $Q(r)$, or in symbols $c(r) = c(0) + P(r) - Q(r)$. The method has been utilized by Van der Loos (1959). For large r, larger than the maximum extent of the tree, quantities $P(r)$ and $Q(r)$ converge to the total number of bifurcations and endings per cell, respectively denoted by P and Q. Because $c(r)$ equals zero for large r, it follows $c(0) = Q - P$.

It is easily checked that various combinations of $P(r)$ and $Q(r)$ exist which have the same difference for any particular r, and which, consequently, amount to one and the same $c(r)$. The point is illustrated in the first figure. Fig. 1a gives $c(r)$ with $\Delta r = 18\ \mu$, redrawn from Fig. 7C of Eayrs and Goodhead (1959). Fig. 1b shows the corresponding functions $c(0) + P(r)$ and $Q(r)$, reconstructed from Figs. 7A and B of the said paper. The algebraic difference between the two sets of points for each r is identical to $c(r)$. To these data we shall return in Fig. 4. At the moment it suffices to add that these are averages of counts on 10 cells. The number of primary dendrites is estimated as $c(0) = 5.2$ while the number of bifurcations P equals 23.1. Therefore, in Fig. 1b the circles start at 5.2 and zero respectively, and will both ultimately converge to the value $5.2 + 23.1 = 28.3$. The course is known up to $r = 180\ \mu$. In Fig. 1c a hypothetical case is sketched such that $c(r)$ is exactly equal to that in Fig. 1a. This example has as a peculiarity in that all bifurcations have occurred before any ending has been present. Again $c(0) = 5.2$, but $P = 12.1$, so that the maximum value equals 17.3. Even if the number of bifurcations is equal to $P = 23.1$, shapes of $P(r)$ and $Q(r)$ are imaginable, cf. Fig. 1d, such that the difference equals $c(r)$ of Fig. 1a.

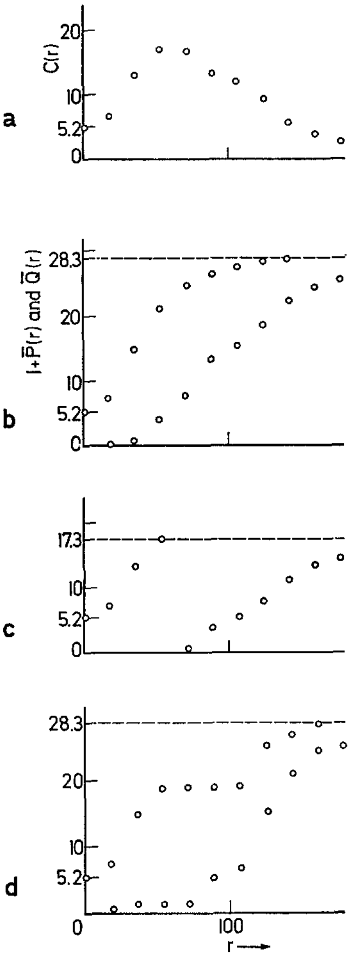

Fig. 1. (a) Mean number of dendrites per cell, $c(r)$, present at a distance r from perkaryon. (b) Mean number of bifurcations added to the number of primary dendrites, $P(r) + c(0)$, and mean number of endings, $Q(r)$, within a distance r from perikaryon. Data reconstructed from Eayrs and Goodhead (1959) for pyramidal cells in adult rat sensori-motor cortex. (c) and (d) As (b) for a hypothetical distribution of bifurcations and endings such that in both cases $c(r)$ as in (a) results. In this and subsequent figures the abscissa is given in μ

It follows that the statistical properties of a dendritic tree are covered largely when giving, in addition to $c(r)$, also $P(r)$ or $Q(r)$ as did Schadé and Van Groeningen (1961), and Coleman and Riesen (1968). Properly speaking, Eayrs and Goodhead (1959) report redundant information when listing all three functions. Actually, the trouble arises from two facts: $c(r)$ is mostly measured with too large a value of Δr, and the data are averaged over several cells. If Δr is small enough then the shape of $c(r)$ reveals accurately at what distances a bifurcation or ending has occurred in the form of unit increments or decrements. However, demanding small values of Δr, makes the compiling work still more painstaking than it is already.

Perhaps changing over from the classical morphologist's instrumentation to modern scanning and pattern recognition systems (Glaser and Van der Loos, 1965; Ledley *et al.*, 1966), in combination with stereophotograms (Mannen, 1965), opens new perspectives towards rapid acquisition of sizable amounts of numerical information on stereometric properties of dendritic arborizations.

The quantifications enumerated so far give an idea about the spatial extent of a dendritic plexus, but the structural constitution remains obscure. That aspect has been introduced by Jones and Thomas (1962); they pay attention to the number of generations that sprout from one primary dendrite, and they count the number of segments that belong to each generation. Unfortunately, these authors do not list the metrical data. As far as we have been able to trace, only Peters and Bademan (1963) have touched upon both the topological as well as upon the metrical properties, when they tabulate the number of segments per order or generation and the mean lengths of the segments of each order. Both types of information are pertinent to a probabilistic description of arborization of nervous processes. We intend to use these, in the next Section, as a basis for an attempt to generalize dendritic branching patterns.

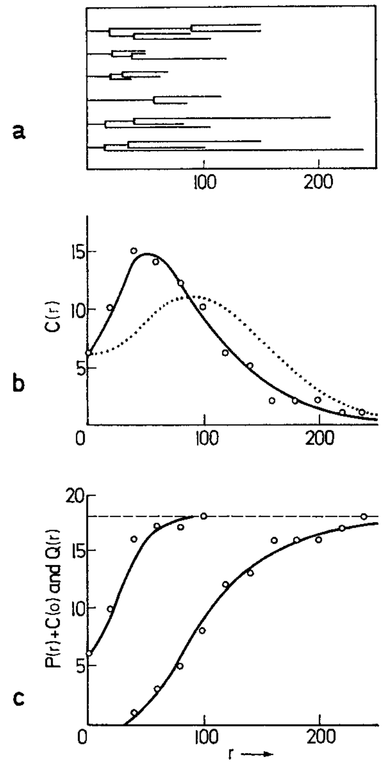

Fig. 2. (a) Schematic representation of mode of dendritic branching; redrawn from Sholl (1953). (b) Number of dendrites per cell, $c(r)$, present at a distance r from the perikaryon. (c) Number of bifurcations added to the number of primary dendrites, $P(r)+c(0)$, and endings, $Q(r)$, within a distance r from perikaryon. Circles reconstructed from (a). In this and subsequent figures curves are from theory

Theoretical Methods

In order to introduce the ingredients for a theoretical concept, we have used a clear-cut example of Sholl (1953). His material is otherwise not considered, mainly because, as amply explained, the condensation of the data is not so complete as it might have been.

Fig. 2a is redrawn from Fig. 1 of Sholl (1953). In diagrams of this kind the directions of the branches are ignored but the lengths are plotted to scale, after being corrected, in case of dendrites which do not run parallel to the plane of section, for an error due to the fact that the observed lengths are projections of the true lengths and due to the refractory index of the mountant. The lengths of the short vertical lines have no meaning: these merely indicate positions of bifurcations. Counting the number of intersections at distances of $\Delta r = 20\ \mu$ furnishes $c(r)$, drawn in Fig. 2b as circles and starting with $c(0)=6$. The total number of bifurcations up to r, $P(r)$, added to $c(0)$, and the total number of endings up to r, $Q(r)$, are given as circles in Fig. 2c. With regard to the total length of the tree (amounting to 1,650 μ) and the total number of bifurcations (12) this specimen is allotted to the category of the smaller cells among the thirty investigated by Sholl (1953). The cell has a simple branching rule and forms, for this reason, a convenient starting point to explain the model. Six primary or first order segments all bifurcate and make up twelve secondary segments. Half of these are terminal segments, the others branch once again, so that the total number of terminal segments amounts to 18, and the total number of segments to 30. Knowing the pattern of branching and the total length of the tree, obtained by adding the lengths of all segments, one may ask what distribution of segment lengths will account for the found $c(r)$, $P(r)$ and $Q(r)$.

The simplest assumption, along the lines of reasoning of Bok (1936), is that all segments are of equal length, viz. equal to $1{,}650\ \mu/30 = 55\ \mu$. Then, $c(r)$ would be equal to 6 from 0—55 μ, abruptly changing to the value 12 from 55—110 μ, and also from 110 to 165 μ. From 165 μ on $c(r)$ would remain equal to zero. Obviously this is not so, $c(r)$ being more smoothly and having a more pronounced peak value for $r = 40\ \mu$. Indeed, inspection of Fig. 2a shows a great variety in segment lengths, ranging from 5—226 μ. In view of this, the next simplest assumption would be that the segment lengths are exponentially distributed with a mean of 55 μ. Computation learns that the variation of this distribution is too large, $c(r)$ being too flat of shape, flatter than for instance the dotted curve in Fig. 2b. In accordance with the actually found distribution of lengths, we have next assumed a gamma distribution of the segment lengths, which is intermediary to the two functions just tried and which, analytically, is fairly well treatable. Even then the fit is far from ideal (dotted curve in Fig. 2b).

The clue seems to be that the distribution of intermediary segment lengths differs from that of the terminal segments, the latter being more variable in length and possessing an additional length. Let $\phi(x)$ denote the probability distribution of the intermediary segment lengths with mean m_ϕ and standard deviation σ_ϕ; let $\psi(y)$ denote the probability density function of the additional length y of the terminal segments with mean m_ψ and standard deviation σ_ψ. The mean of the terminal segments is thus equal to $m_\phi + m_\psi$ and the standard deviation to the square root of $(\sigma_\phi^2 + \sigma_\psi^2)$. If it is assumed that all intermediary segment lengths are distributed according to a gamma distribution, and the terminal segments have an extra length that is exponential distributed, a good agreement between experimental data and theory is found, cf curves in Figs. 2b and c. The way these have been computed is discussed in the Appendix.

We wish to state that the assumption of the intermediary segments having another mean length than the terminal segments is not a mere artifice. It has been assessed accurately by Peters and Bademan (1963), and by Mungai (1967). However this may be, we have been led to use that item throughout this paper.

Table 1. *Distribution of mean number of segments per primary dendrite by order*

	Order 1	Order 2	Order 3, etc.	Sum
Intermediary segments	p_1	$2p_1p_2$	$2^2p_1p_2p_3$	$\bar{P}$
Terminal segments	$1\text{-}p_1$	$2p_1(1\text{-}p_2)$	$2^2p_1p_2(1\text{-}p_3)$	$\bar{Q}$
Total	1	$2p_1$	$2^2p_1p_2$	$\bar{P}+\bar{Q}$

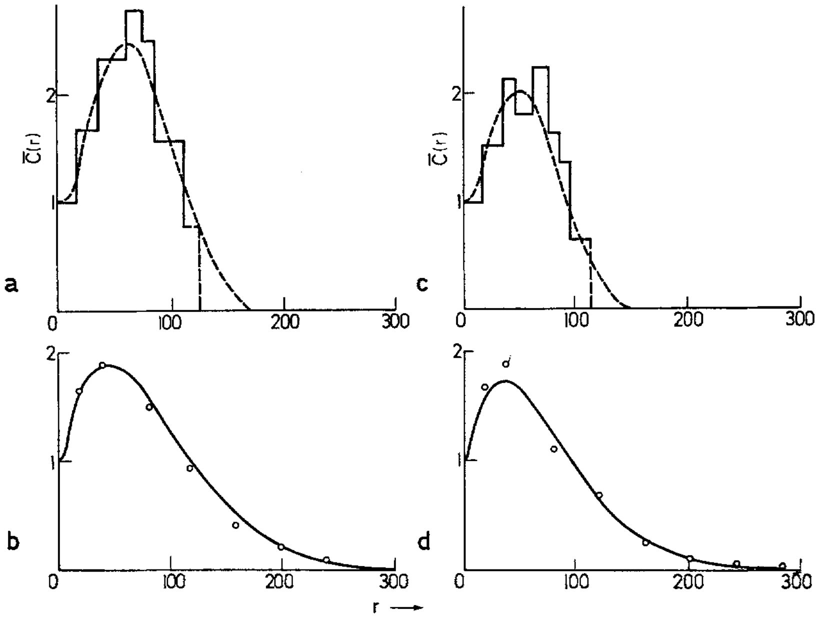

Fig. 3. Number of dendrites per partial tree, $c(r)/c(0) = \bar{c}(r)$, present at a distance r from perikaryon. Circles in (b) and (d) after data from Peters and Bademan (1963) for stellate cells in cortex of adult and newborn guinea pigs respectively. Curves for different distributions of segment lengths

Elaboration of these outlines for trees with higher order segments, and when the occurrence of bifurcations is of a probabilistic nature, leads to formulae for $c(r)$, $P(r)$ and $Q(r)$ which are listed in the Appendix, and which then refer to average values. It is sometimes opportune to express the said functions per primary dendrite, and not per cell; a dash is then added, viz. $\bar{c}(r)$, $\bar{P}(r)$ and $\bar{Q}(r)$. Because $c(0)+P=Q$, it holds that $1+\bar{P}=\bar{Q}$.

Expressions for frequently used additional measures are listed below. The probability that a primary or first order dendrite bifurcates is called p_1, that it does not bifurcate $1-p_1$. For segments of order n, one has the probabilities p_n and $1-p_n$. The mean number of intermediary segments per order per primary dendrite and their sum $\bar{P}$, and the mean number of terminal segments and their sum $\bar{Q}$, stated in terms of p_1, p_2, etc. are given in Table 1. Reversely, given the number of segments per order and per primary dendrite, one can estimate the bifurcation probabilities p_n.

If the intermediary segments have a mean length of m_ϕ and the terminal segments $m_\phi+m_\psi$ the mean length per primary segment is given by $\bar{L}= \bar{P} m_\phi + \bar{Q}(m_\phi+m_\psi)$ which is also equal to $\int_0^\infty \bar{c}(r)\,dr$. The average length of a segment is obtained by dividing $\bar{L}$ by the mean number of segments, $\bar{P}+\bar{Q}$.

The mean length of segments of order n equals:

$$p_n m_\phi + (1-p_n)(m_\phi+m_\psi).$$

The mean distance of an ending relative to the centre of the cell, a measure used by Eayrs (1955) and referred to in our Table 3, can be shown to be:

$$(\bar{L}+m_\phi \cdot \varrho)/\bar{Q}$$

where

$$\varrho = p_1 + 2\times 2 p_1 p_2 + 3\times 2^2 p_1 p_2 p_3 + \cdots.$$

Results

Peters and Bademan (1963), investigating form and growth of stellate cells in the prepiriform cortex of newborn and adult (6 month) guinea-pig, have reported very useful data on the mean of 36 cells for each age. The mean number of primary dendrites per cell were calculated and found to be closely similar (6.62 and 6.94), as were the number of segments per cell (33.80) and 35.68). Also the mean lengths of intermediary segments were about the same (22 μ) for both ages and irrespective of the order of the segments. In addition, the probability of bifurcation of a segment decreased roughly geometrically with the order of the segment (as far as enumerated); thus $p_n = p_1^n$ for n up to four, higher order segments being small in number.

For both sets of measurements p_1 was about 0.7; it means that primary segments bifurcated with a probability of 70%, secundary segments with $0.7^2 = 49\%$, etc.

The essential difference between newborn and adult resided in the mean length of the terminal segments. Those of the newborn were roughly two times, those of the adult were three times larger than the intermediary segments. Trying to reconstruct $c(r)$ with the help of these facts, one is faced with the difficulty of being ignorant about the variability in length of the segments.

Table 2. *Data relating to Fig. 5 and 6*

Age	Adult	30 days	24 days	18 days	12 days
$c(0)$ = mean number of primary dendrites	5.2	5.3	5.3	5.2	5.4
P = mean number of bifurcations	23.1	19.4	18.0	8.3	4.7
Mean number of segments	51.4	44.1	41.3	21.8	14.8
L = mean length of dendritic tree (μ)	1,880	1,560	1,113	511	224
Mean segment length (μ) (experimental)	36.6	35.4	27.0	23.6	15.1
$\bar{P}$ = mean number of bifurcations per primary dendrite	4.5	3.7	3.4	1.6	0.9
p_1 = bifurcation probability	0.797	0.772	0.763	0.646	0.514
$m_\phi(\mu)$; $\sigma_\phi/m_\phi = 0.6$	12.5	same	same	same	same
$m_\psi(\mu)$; $\sigma_\psi/m_\psi = 1.0$	42.8	40.6	29.0	22.1	7.9
Mean segment length (μ) (theoretical)	36.0	35.2	28.9	26.2	17.9

If there exists no variation and all segments are exactly equal to the mean, one finds for the adult case, by using the data of Table 2 of the cited publication, a discontinuous $\bar{c}(r)$ as drawn in Fig. 3a. The last part is dotted because no data are available for segments of order five or higher. For moderate values of variation in the mean length, one may try a normally distributed $\phi(x)$ and $\psi(y)$. For $m_\phi = 20\,\mu$,

$$\sigma_\phi/m_\phi = 4/20, \quad m_\psi = 42\,\mu \quad \text{and} \quad \sigma_\psi/m_\psi = 8/42$$

one has the smooth curve in Fig. 3a. In Fig. 3b, experimentally found values are given as circles, redrawn from Fig. 2 of Peters and Bademan (1963). The maximum is lower and the points extend over a greater distance. However, if the lengths of intermediary and terminal segments are assumed to possess both a considerably larger spread in length, a good fit is obtained. The proof is given by the curve in Fig. 3b, where $\phi(x)$ and $\psi(y)$ are taken exponential, and $m_\phi = 20\,\mu$ and $m_\psi = 42\,\mu$. For the newborn animal similar considerations hold (cf. Fig. 3c and d). The curves are computed for the same parameter values with the exception that $m_\psi = 25\,\mu$. Again, a reasonable fit is found if the distributions $\phi(x)$ and $\psi(y)$ are exponential.

In a study on the development of the cerebral cortex in the rat, Eayrs and Goodhead (1959) have supplied a thoroughly documented and extensive amount of quantitative information, which besides to the axon network and the cell/gray coefficient, related to the basal dendritic field of pyramidal cells in the sensory motor cortex. The dendrites were measured on coronal sections and in sections cut tangentially to the cortical surface for newborns and adults as well as for animals of 6, 12, 18, 24 and 30 days of age.

We shall first compare the theory and experimental data for the adult rats. Being ignorant of the distribution of segment lengths and the bifurcation probabilities p_n, we cannot reconstruct $c(r)$, $P(r)$ and $Q(r)$ directly. From observation of dendritic trees, as seen in Fig. 2 of Eayrs and Goodhead (1959) which are redrawings of magnified pictures, it would seem that the bifurcation probabilities p_n decrease with n. In analogy with the findings of Peters and Bademan (1963), we start from the assumption that p_n decreases geometrically with order n, which proves to fulfil the purpose for a good deal. From their Table 1 it can be deduced that $\bar{P} = 4.5$ so that, with $p_n = p_1^n$, it follows that $p_1 = 0.797$. One gains further the impression that the terminal segments are longer than the intermediary ones, but in terms of the model m_ϕ and m_ψ are not known. Only the mean length of the total tree per cell can be approximately computed from $c(r)$, and is estimated as $L = 1,880\,\mu$. We have tried several ratios of m_ϕ and m_ψ such that $P m_\phi + Q(m_\phi + m_\psi) = 1,880\,\mu$. The full drawn curve in Fig. 4, giving $\bar{c}(r)$, and the curves in Fig. 6a representing $1 + \bar{P}(r)$ and $\bar{Q}(r)$, are computed with $\phi(x)$ and $\psi(y)$ Gaussian, $m_\phi = 12.5\,\mu$ and $m_\psi = 42.8$ while σ_ϕ/m_ϕ and σ_ψ/m_ψ are rather arbitrarily set equal to respectively 7.5/12.5 and 1. These values imply that the terminal segments are about five times as long as the intermediary segments, on the average. For comparison two other combinations are drawn in Fig. 4, namely $m_\phi = 20.0\,\mu$ and $m_\psi = 29.1\,\mu$ (curve *b*), and $m_\phi = 36\,\mu$ and $m_\psi = 0$ (curve *c*), thus all segments having the same mean length; σ_ϕ/m_ϕ and σ_ψ/m_ψ are kept as before.

It is tempting to ask ourselves how the configuration of the dendritic plexus in the adult cortex might have developed during the various stages of maturation. In doing so, we start from the parameters known for the adult cells and try to modify their values as minimally as possible. With regard to the structural aspects we are tied, without comment, to the total number of bifurcations which are the smaller the younger is the animal. In contrast, the number of primary dendrites remains nearly unchanged from 12 days old animals onwards. There is no indication that the law of geometrically decreasing p_n is not obeyed, and we have assumed this to be so. For animals at birth and 6 days old no useful quantitative data are available as neurons were not impregnated or because the dendrites extended but a negligible distance from the perikaryon.

For animals of other ages the values of P and p_1 are tabulated in Table 2. As to the spatial factor, an

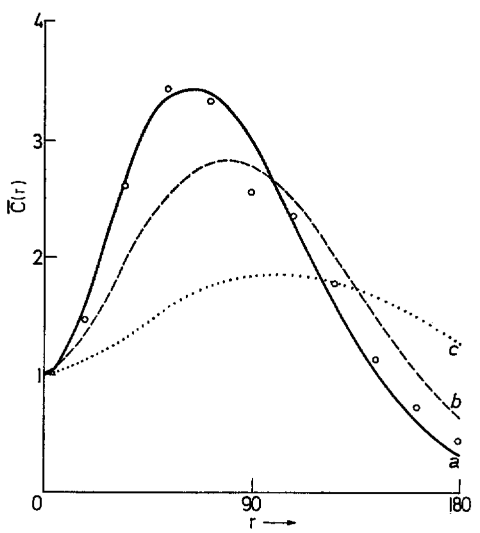

Fig. 4. Number of dendrites per tree, $\bar{c}(r)$, present at a distance r from perikaryon. Circles reconstructed from Eayrs and Goodhead (1959) for pyramidal cells in adult rat sensori-motor cortex. Curves for different distributions of segment lengths

important starting-point is formed by the total length of a tree L, which may be calculated from the graph of $c(r)$ or by a method indicated in the discussion, or by the mean segment length which is equal to L divided by the number of segments. One finds a considerable decrease in mean segment length in comparison with the adult, cf. Table 2. It is possible that a change in the mean segment length is due to a change in length of both intermediary and terminal segments, possibly in different ratios, or, in our nomenclature, to a change in m_ϕ as well as to one in m_ψ. A change in the length of the intermediary segments is not a very plausible assumption to make, as it implies that the sites of bifurcation would have migrated relative to the perikaryon during the maturation process. Moreover, if a change in m_ϕ is allowed within the scope of a prescribed mean segment length, a quantitative agreement between theory and experiment with regard to functions in Fig. 4 is difficult to achieve, as computation has shown us. More probably and in accordance with the findings of Peters and Bademan (1963), the intermediary segments remain constant in length during development, once these have been established as intermediary through the appearance of a bifurcation.

We have investigated this possibility further by changing, besides p_1, only m_ψ. The result for $\bar{c}(r)$ is shown in Fig. 5 and that for $1+\bar{P}(r)$ and $\bar{Q}(r)$ in Fig. 6, where m_ψ has diminished as given in Table 3 and such that the mean segment length equals the estimated values; σ_ϕ/m_ϕ and σ_ψ/m_ψ are kept as before. In its overall appearance the fit in Figs. 5 and 6 would seem acceptable. Undoubtedly a better agreement between theory and experiment is obtainable by allowing small deviations from the law $p_n = p_1^n$.

Table 3. *Data relating to Fig. 8*

	Layer Vb		Layer IIIc	
	normal	abnormal	normal	abnormal
$\bar{Q}=1+\bar{P}=$ branching index	2.47	1.79	1.95	1.55
Mean extension (μ) (experimental)	82.6	61.0	63.5	46.6
p_1 = bifurcation probability	0.629	0.490	0.535	0.400
$m_\phi(\mu)$; $\sigma_\phi/m_\phi=0.6$	17.5	same	22.5	same
$m_\psi(\mu)$; $\sigma_\psi/m_\psi=1.0$	34.8	21.8	11.8	7.5
Mean extension (μ) (theoretical)	82.3	58.3	63.1	48.2

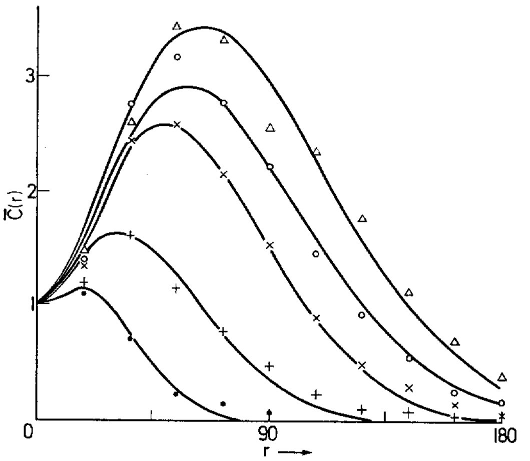

Fig. 5. Number of dendrites per tree, $\bar{c}(r)$, present at a distance r from perikaryon. Data reconstructed from Eayrs and Goodhead (1959) for pyramidal cells in sensori-motor cortex of adult rats (△), rats of 30 days (○), of 24 days (×), of 18 days (+) and of 12 days (●)

Analogous data are available from Schadé and Van Groeningen (1961) for histological parameters in the middle frontal gyrus of human cerebral cortices of newborns, infants of 3, 6, 15 and 24 months and adults. We restrict ourselves to the basal dendrites of pyramidal cells in layer III. Pyramidal cells in other layers (IV and V) and stellate cells were reported to exhibit similar changes in regard to development. It can be taken from their Table 2 that the mean segment length increases from 16 μ for newborns to 63 μ for 6 months, thereafter not much changing, namely from 79 μ for 24 months to 77 μ for adults. For 3 and 15 months no data were given. The number of bifurcations per primary dendrite increases over a larger lifespan: $\bar{P}$ equals 0.46 for newborns, 2.44 for 6 months, 2.11 for 24 months and 5.37 for adults.

As before we have assumed $\phi(x)$ and $\psi(y)$ Gaussian, and $p_n = p_1^n$ so that for the adult case $p_1 = 0.812$. Changing the ratio of m_ϕ and m_ψ by trial and error a fairly good fit is obtained with $m_\phi = 25\ \mu$, $\sigma_\phi/m_\phi = 8/25$, $m_\psi = 55.2$ and $\sigma_\psi/m_\psi = 1$ as seen in Fig. 7a, $\bar{c}(r)$ and in Fig. 7b, $1+\bar{P}(r)$ and $\bar{Q}(r)$. The circles are reconstructed from Figs. 8 and 9 of Schadé and Van Groeningen (1961) and refer to the corrected data of 12 cells for each age. The correction relates to the fact that in 75 μ sections only a part of the neuron is preserved, because dendrites of an adult pyramidal cell extend in all directions as far as 400—500 μ from the perikaryon. The experimental $\bar{c}(r)$ seems to possess a second maximum for $r = 200\ \mu$, an item that is not incorporated in the model at least as long as we stick to a geometrically decreasing probability of bifurcation.

Adjustment of parameter values to the 24 month experimental data is effected as previously, by letting m_ψ decrease to 52.6 μ and p_1 to 0.695 in accordance with $\bar{P} = 2.11$: curves belonging to (◒) in Fig. 7. When passing on to the newborn case, by further decreasing p_1 to 0.360 corresponding to $\bar{P} = 0.46$ and letting m_ψ approach to zero, one has the dashed curve in Fig. 7a. Obviously $m_\psi = 0$ is not sufficient and also m_Φ diminishes. Shortening m_Φ from 25 μ to 16 μ and $m_\psi = 0$ gives a good fit, cf. curves belonging to the points (●). The mean segment length amounts to $(0.46 \times 16 + 1.46 \times 16)/1.92$ which is very close to the experimentally found value of 16 μ. Unfortunately, only two points per curve are known due to the fact that $\Delta r = 25\ \mu$ is large relative to the short extension of these trees.

Alternatively, one may suggest that the intermediary segments remain equal to $m_\Phi = 25\ \mu$, but that the terminal segments are shorter than these, or m_ψ negative. Inserting $m_\psi = -11.8\ \mu$, again corresponding to a mean segment length of 16 μ, can be shown to give a bad fit.

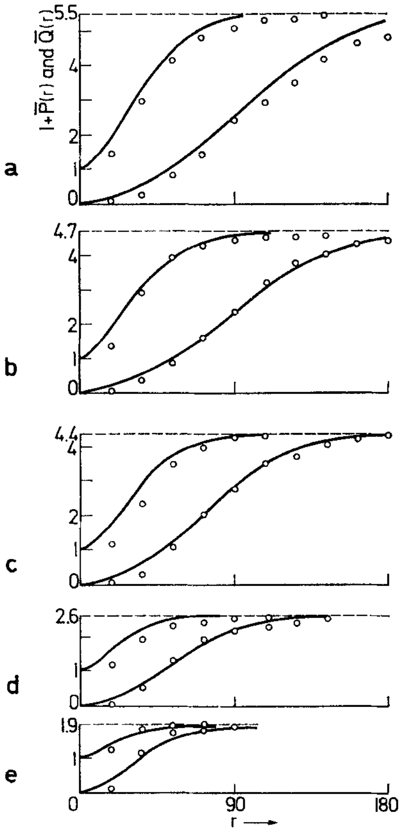

Fig. 6a—e. Numbers of bifurcations added to the numbers of primary dendrites per partial tree, $[c(0) + P(r)]/c(0) = 1 + \bar{P}(r)$, and endings, $Q(r)/c(0) = \bar{Q}(r)$, within a distance r from perikaryon. Circles reconstructed from Eayrs and Goodhead (1959) for pyramidal cells in sensori-motor cortex of adult rats (a), rats of 30 days (b), of 24 days (c), of 18 days (d) and of 12 days (e)

In studies designed to correlate the histological abnormalities arising as a result of experimental cretinism with changes in adaptive behaviour, Eayrs (1955) has determined, among other things, the properties of the dendritic plexus of pyramidal cells in different parts of the cortex. In comparison with normal rats of the same age, it was found that, after daily treatment from the day of birth on during a period of 24 days, the number of primary dendrites does not change significantly, but that the dendrites extend over a shorter distance and bifurcate less.

In Fig. 8, $\bar{c}(r)$, $1 + \bar{P}(r)$ and $\bar{Q}(r)$ are drawn, valid for the mean of 10 cells in layers Vb and IIIc (reconstructed from Fig. 8 of Eayrs, 1955) for normal (0) and abnormal (●) cells. As the normal case refers to the same sort of cells in the same cortical area as those treated in our Fig. 4, the data should be describable by assuming the segment lengths to be Gaussian distributed and $p_n = p_1^n$. From the parameter values listed in Table 3, result the curves corresponding to (0) in Fig. 8.

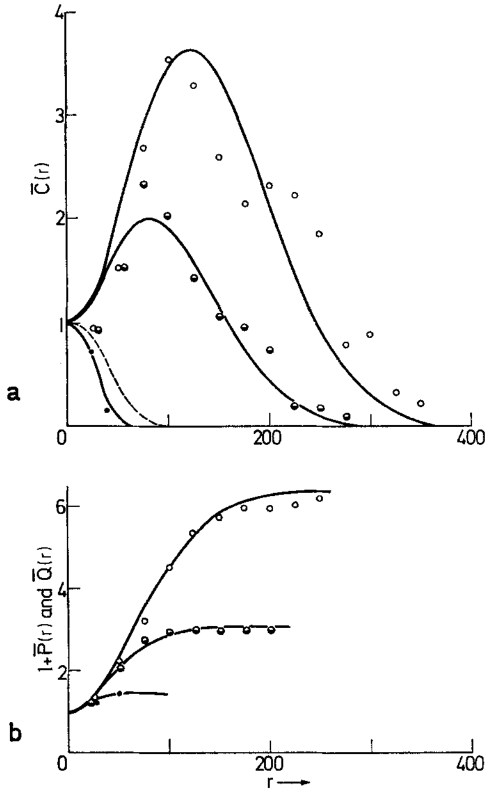

Fig. 7. (a) Number of dendrites per tree, $\bar{c}(r)$, present at a distance r from the perikaryon. (b) Number of bifurcations added to the number of primary dendrites, $1 + \bar{P}(r)$, and endings, $\bar{Q}(r)$, within a distance r from perikaryon. Data reconstructed from Schadé and Van Groeningen (1961) for pyramidal cells in cerebral cortex of adults (○), infants of 24 months (◒) and newborns (●)

If the hypothyroid condition may be interpreted as a form of retarted growth, it should be possible to relate the data for the normal and abnormal animals, besides by an appropriate change in p_1 (due to another value for $\bar{P}$), by taking m_Φ the same while m_ψ has a smaller value. For the parameter values of Table 3 one finds the other set of curves in Fig. 8, belonging to (●). Especially the tail of the curve for $\bar{c}(r)$ does not cover very well the experimental findings. If p_n is taken slightly differing from a geometric law a better fit can be obtained. The mean distance over which the

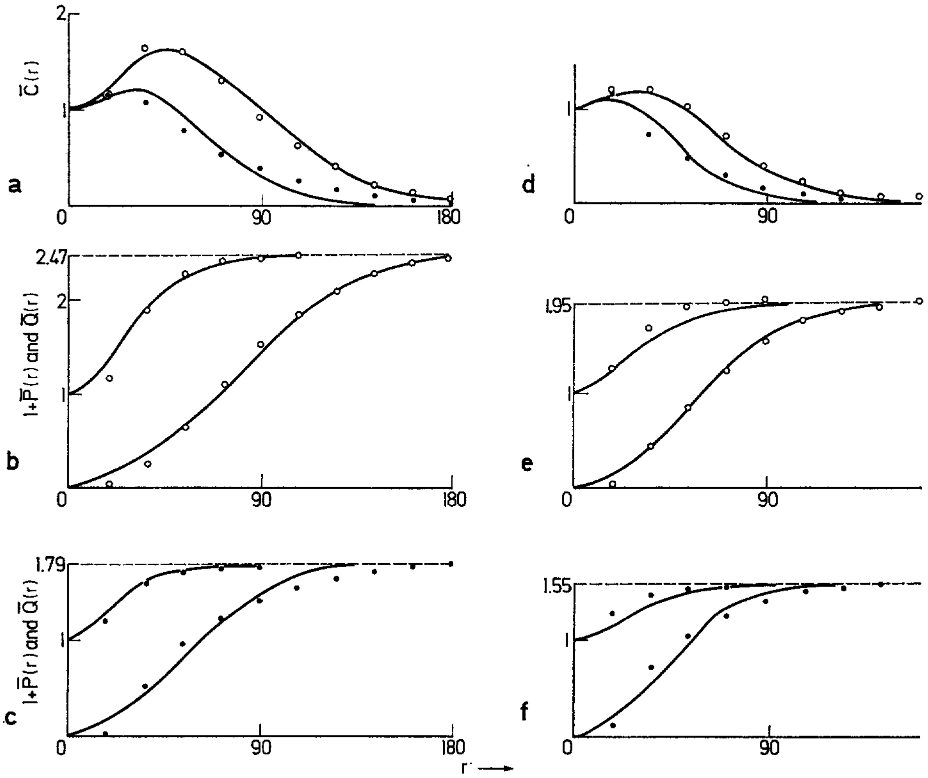

Fig. 8. (a) Number of dendrites per tree, $\bar{c}(r)$, at a distance r from perikaryon. (b) and (c) Number of bifurcations added to the number of primary dendrites, $1+\bar{P}(r)$, and endings, $\bar{Q}(r)$, within a distance r from the perikaryon. Data reconstructed from Eayrs (1955) for pyramidal cells in layer V b of sensorimotor cortex of normal rats (○) and for hypothyroid animals (●). (d), (e) and (f) As (a), (b) and (c) for cells in layer III c

dendrites extend, or the mean distance of the endings relative to the perikaryon, are, as the table reveals, well in accordance with each other.

It is generally accepted that components of an intact nervous system may fail to develop in a normal fashion as a consequence of disuse or decreased input. In contrast to earlier studies, Coleman and Riesen (1968) found that in cat the effect of dark-rearing from birth to about six months are rather pronounced on visual cortex, and result in a reduction in length of dendritic tree and in a smaller number of bifurcations for layer IV stellate cells. Functions $\bar{c}(r)$, $1+\bar{P}(r)$ and $\bar{Q}(r)$ in Fig. 9 (circles) are reconstructed from Fig. 1 of the said publication. The curves are computed with $m_\phi = 18.0\ \mu$ and $m_\psi = 53.2\ \mu$ while inserting p_n as deduced from the number of segments of each order. The reduction in length of the dendritic tree by 78% compared with normal litters must be attributed nearly entirely to a decrease in the number of bifurcations ($\bar{P}$ decreases from 1.73 to 1.51, cf. Figs. 9b and d), as may be checked from these values. It follows that, contrary to the previous example concerning hypothyroid rats, the mean segment length hardly differs for the two cases.

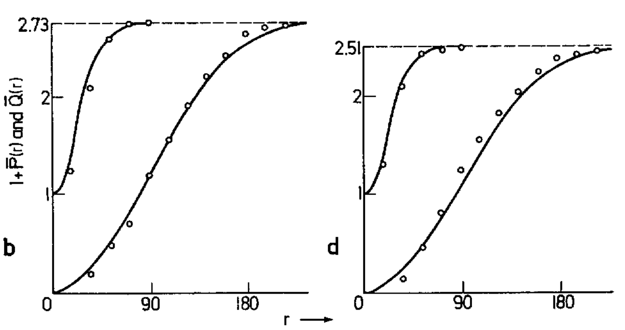

Fig. 9. (a) and (b) Number of dendrites per tree, $\bar{c}(r)$, present at a distance r from perikaryon. (c) and (d) Number of bifurcations added to the number of primary dendrites, $1+\bar{P}(r)$, and endings, $\bar{Q}(r)$, within a distance r from perkaryon. Circles reconstructed from Coleman and Riesen (1968) for striate cortex stellate cells in normal rats, (a) and (b), and in animals reared in the dark, (c) and (d)

Discussion

It has been argued (Globus and Scheibel, 1967) that the approach of Bok and Sholl to characterize the dendritic plexus of neurons had been directed away from the organization of the individual synaptic connections in favour of a statistical approach to cortical organization. We would consider the information gained from submicroscopic observation of fine structures as spines and synaptic sites of a few nerve cells, rather than being of diverging nature, to form a supplementum to the knowledge of gross parameters like cell packing density, concentration of dendritic and axonal fields, etc., obtained from averaging over many cells.

The method of virtual concentric spheres introduced by Sholl (1953) must be regarded as a first attempt to trace in quantitative-probabilistic terms the distribution of dendritic branches relative to the perikaryon as revealed by the number of perforations $c(r)$ at a distance r from the centre. This measure may, to some extent, provide an anatomical basis for the estimation of neural connectivity as suggested by Sholl and Uttley (1953) and utilized by Eayrs (1955), and by Eayrs and Goodhead (1959). Sholl (1953) proposed an empirically fitted analytical function for $c(r)$ as $c(r)/4\pi r^2 = a\exp(-kr)$. On formal grounds objections must be raised because a discrepancy comes to light if one rewrites $c(r) = 4\pi r^2 a \exp(-kr)$. This expression converges to zero when r approaches zero, whereas it should reach the value $c(0)$, the number of primary dendrites arising from the cell body. Otherwise the approximation seems to give a good description of $c(r)$ for r larger than about 20 μ. Several authors have given numerical values for a and k. It enables one to compute rapidly the mean length of a tree per cell which can be shown to be equal to $L = 8\pi a k^{-3}$. The values of L in Table 2 have been obtained in this way.

If dendrites do not unfold symmetrically in all directions, or if they do but the sections are thin compared with the total extent of the tree, corrections are needed in order to have a correct estimate of $c(r)$. Apart from this disadvantage, we have shown with the help of Fig. 1 that knowledge of $c(r)$ leaves us with ambiguities, because more than one mode of bifurcation and ending may result in one and the same shape of $c(r)$. A minimum requirement is that also the distributions of bifurcations $P(r)$ or endings $Q(r)$ as functions of the radial distance are given.

Even then there remains a shortcoming of said functions, because these intermingle two fundamental properties of any spatial branching process, viz. the topological and metrical aspects. We have explained that for an adequate description of the mode of ramification, the information concerning the two sorts of items can better be listed separately. These are largely covered when one determines the distribution of the number of segments by order on the one hand, and, on the other hand, the distribution of segment lengths of each order. The latter distribution may preferably be specified further for intermediary and terminal segments. From these data, one may compute functions $c(r)$, $P(r)$ and $Q(r)$; the reverse is not possible.

Keeping apart topology and metrics may prove to be a useful tool to express in quantitative terms, the degree of morphological specialization of dendritic fields and the classification of cell populations, for instance into the groups: isodendritic, allodendritic and idiodendritic as proposed by Ramón-Moliner and Nauta (1966). An additional advantage of such a set-up is that the method does not presuppose spherical symmetry of the tree. Possible preferences for a tree to spread out in certain directions relative to the pial surface can better be studied as an independent additional property, as was done by Colonnier (1964) for the visual cortex and by Wong (1967) for the auditory cortex of the cat.

We have made clear in Figs. 2 and 3 that, if all segments are equal in length, $c(r)$ can be computed straightforwardly from the distribution of segment orders and will then show a discontinuous appearance. The shape of $c(r)$ generally being more smoothed, indicates that the lengths differ from segment to segment. In fact, to obtain a fit to the experimental data, large variations in segment lengths have to be assumed. This may be the reason that Sholl (1956, p. 52) was not able to find a simple rule for the lengths of segments.

Still another deviation from the ideal case proves necessary, namely a division in length of intermediary and terminal segments. Not many authors have touched upon this peculiarity explicitly. In our analysis it has played a major role. In order to account for the experimental data, we have to assume without exception that terminal segments are mostly several times longer than intermediary ones, on the average. The finding is confirmed by Peters and Bademan (1963), cf. our Fig. 3, and by Mungai (1967). For instance, from Fig. 7 of the latter publication it can be ascertained that for 12 stellate cells in the cat's somatic sensory cortex about 90% of the intermediary segments are shorter than 50 μ, whereas terminal segment lengths are widely scattered equiprobably up to 250 μ with offshoots as long as 400 μ. Apical and basilar dendrites of pyramids show a similar large difference between the two sorts of branches.

The unequality of the means of intermediary segments (denoted by m_ϕ) and of terminal segments (denoted by $m_\phi + m_\psi$) finds further expression when cells in the same cortical area, but in animals of different age, are compared. Peters and Bademan (1963) find for stellate cells of adult guinea pigs that terminal segments are about three times as long as intermediary segments, while for newborns the factor is two, this constituting the only significant difference between the two groups of cells. It was noticed, from comparison of the number of segments of each order, that the probability of bifurcation p_n decreases geometrically with the order n of the segments, viz. $p_n = p_1^n$ for n up to 4. Less nicely this bifurcation law is present in cells analyzed by Jones and Thomas (1962), and by Coleman and Riesen (1968). The property has been used with resonable success in Figs. 4 through 9.

The data of Eayrs and Goodhead (1959) on cortical neurons have been treated by assuming that the mean length of intermediary segments remains constant and equal to 12.5 μ throughout the maturation process. In young animals (12 days) the terminal segments are slightly longer than intermediary segments but in adults these are about five times as long. The huge change in this factor is partly obscured when the segments of all orders and irrespective of being terminal or not are compared, cf. Table 2. Our suggestion to separate topological and metrical factors is graphically clarified in Fig. 10 for cells in animals of 12 and 24 days and for adults. The picture allows a crucial test of the concepts developed so far.

Similar remarks refer to the measurements of Schadé and Van Groeningen (1961) on neurons in the human brain. From fitting $\bar{c}(r)$ and $\bar{P}(r)$ it is deduced that in newborns all segments have a mean of 16 μ, while about one bifurcation per two primary dendrites occurs ($\bar{P} = 0.46$). At 24 months of age, intermediary segments are estimated as 25 μ and terminal segments three times larger in length. The number of bifurcations has increased by nearly a factor of five ($\bar{P} = 2.11$).

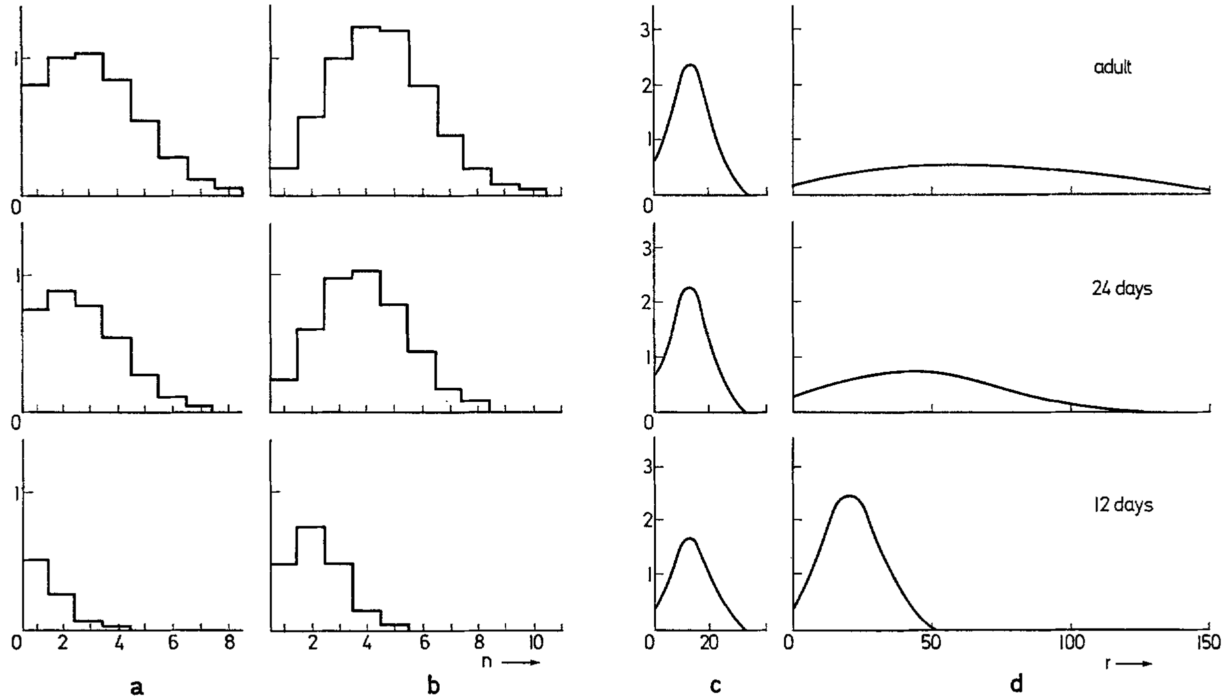

Fig. 10. (a) and (b) Mean number of intermediary and terminal segments of order n per partial tree, as predicted by theory for cells treated in Fig. 5 and 6, downwards for adult rats, rats of 24 days and rats of 12 days. (c) and (d) Distribution of lengths of intermediary and terminal segments. Ordinates in % per μ

The number of bifurcations per cell increases still further ($\bar{P} = 5.37$) towards maturity, but the metrical measures do not change much after 24 months.

More or less parallel to the study of cells in brains of normal and adult animals have run investigations of cells in brains of adults after damage. After surgical deafferentation following olfactory bulb resection of 6 weeks old rats, Jones and Thomas (1962) found that pyramidal cells in the plexiform cortex possess the same number of primary dendrites in comparison with normal cells but that the number of bifurcations per cell has diminished by a factor of four, three months after treatment. Unfortunately, these authors do not comment in quantitative terms on the spatial measures of the trees, but from their microprojector-retracings (their Fig. 3) one may conclude that also the metrical parameters have undergone a notable change.

Damage of nervous structures in adult monkeys has been observed by Caveness *et al.* (1966) after X-ray irradiation applied to one side of the cerebral cortex. The dendritic branching reveals a significant reduction in the number of bifurcations and the tree length per cell on the irradiated side between second and fourth week with a pronounced difference between right and left side being evident thereafter. From their table it can be taken that the tree length per cell L decreases from 2,200 μ to less than 500 μ, while the number of bifurcations P diminishes from roughly 16 to 5. If the number of primary dendrites $c(0)$ is in the usual range of 5 to 10, one can estimate the number of segments per cell and find that the mean segment length reduces by a factor of two. Within the context of the model it would be highly interesting to have additional data at our disposal in order to verify whether the reduction in segment length is due to a diminution in the terminal segment lengths (m_ψ smaller) or to an overall change in length measures.

The effect of X-ray irradiation during foetal life on the histogenesis of the cerebral cortex, and the morphology of its constituent neurons, has been studied by Berry and Eayrs (1966). The basal dendritic plexus of pyramids was investigated after embryos were radiated on the 17-th through 21-st days of gestation. At 30 days post partem $c(r)$ was little affected, though in general $c(0)$ and P were less than normal.

The dynamics of growth of the nervous system during normal ontogenetic development of the rat has been supplemented by investigations of alteration of growth of animals reared under thyroid deficiency conditions by Eayrs (1965). He found that, although the number of primary dendrites of the basal fields of pyramids remains unchanged in comparison with normals, the processes are shorter and branch less in treated individuals. Further, the decay of the dendritic field density with radial distance does not seem to conform to the exponential law, $c(r)/4\pi r^2 = a \exp(-kr)$, which applies to neurons of normally reared animals. We have been able to fit the normal case by again assuming that the bifurcation probabilities are geometrical and that the terminal segments are larger than the intermediary ones. While the latter seem to have the same mean length, irrespective of treatment, the terminal segments are shorter for the hypothyroid rats. For the cells in abnormal milieu, the fit of $\bar{c}(r)$ in the tail is less good than for normals. The dissimilarity corresponds with the remark of Eayrs (1955) that the tail extends longer than expected for the normal development. In terms of our model, the decrease of m_ψ is not the only factor that counts. We agree with the said author that from the changes which take place in the distribution of cell processes between birth and maturity, it is difficult to say whether the configuration seen in tissues of hypothyroid rats represents a retardation or a distortion of the normal pattern of growth. From our analysis it would follow that treatment does not amount to purely a retardation. Next to it, we maintain that discrimination between alternatives can be enhanced if the material is analyzed along the lines suggested above, viz. by evaluating the distribution of segment orders and lengths.

Adjunct to these experiments, Clendinnen and Eayrs (1961) have investigated the effect of administering growth hormones to rats during gestation. A hypertrophy of dendritic fields associated with pyramidal neurons in layer III of the cerebral cortex is found. The data can be described analytically by the model (unpublished results) by assuming again that $p_n = p_1^n$ and that the intermediary segments have the same length equal to $m_\phi = 15\,\mu$ in both situations, whereas P and m_ψ are different, that is to say, the numerical values are now larger for cells in the treated animals than in normals. For the rest similar remarks hold as made in the previous paragraph.

Sensory deprivation has been embraced as another means of setting down the rules that determine the influences of environmental effects on the outgrowth of dendritic ramifications. Holloway (1966) compared stellate cells from the second layer of the visual cortex of two groups of rats, separated after weaning and placed either in normal situations (communal life, etc.) or kept in isolated conditions. The cells in brains of the former group show richer dendritic branching than their litter mates of the other category in 11 out of 15 cases after about 85 days. Unfortunately that author only counts the total number of intersections, thus the sum of $c(0) + c(\Delta r) + \cdots$, not $c(r)$ proper or any other parameter.

The influence of sensory deprivation on dendritic fields of striate cortex stellate cells has been thoroughly investigated by Coleman and Riesen (1968), when rearing cats in the dark from birth to about six months of age. Besides noticing a reduction in length of the dendrites and in the number of bifurcations per neuron, the cited authors comment that the number of intersections with concentric spheres $c(r)$ for distances larger than $36\,\mu$ is less for the experimental animals than for the normals, but that nevertheless the dendrites appeared to extend to an approximately equal distance from the cell body. The phenomenon bears a close resemblance to the results of Eayrs (1955) for hypothyroid rats, cf. Fig. 8. We have been able to fit the data, as shown in Fig. 9, by taking the mean length of intermediary segments equal to $18.0\,\mu$ and of the terminal segments $71.2\,\mu$ $(= 18.0\,\mu + 53.2\,\mu)$ for both the cells of the normal and treated animals. The only difference thus lying in the bifurcation probabilities p_n.

Our finding of the metrical factors being the same in both cases seems to be in accordance with the conclusion of Coleman and Riesen (1968) that the major effect of dark-rearing on the dendritic fields is to decrease the probability of bifurcation. This was deduced by the said authors from the observation of the apparently equal maximal extension of the dendritic field as disclosed by $c(r)$, coupled with the finding that the mean length increases with their order. The latter fact is understandable in terms of the model. For many branching laws for which p_n decreases with n and ultimately tends to zero, as usually happens, segments of low order consist for the greater part of intermediary segments, while for higher order segments the reverse holds and most of them are of the terminal category. The segments of the highest order are, of course, all terminal. If the terminal segments are longer than intermediary ones, on the average, as we have deduced in all cases analyzed so far, it follows that in most instances the segments (taking intermediary and terminal parts together) will increase in length per order. In the underlying case this is true also as computation has shown us. The property, therefore, forms an indirect indication for the correctness of the assumption of different lengths of the two sort of segments.

As to quantitative details we come across a discrepancy between theory and measurements. For lower order segments the mean lengths are in close agreement and equal about $20\,\mu$. For the model, the 5-th order segments have a mean length of $71.2\,\mu$ for both cases. For the normal stellate cells the length of these segments measures more than $90\,\mu$, and for cells in the brain of treated animals, surprisingly, a larger value of $120\,\mu$ is found. Such a property is readily incorporated in the model by assuming that the additional length of the terminal segments (m_ψ) and/or the length of intermediary segments (m_ϕ) depend on their order. The supposition bears some resemblance to the explanation of Coleman and Riesen (1968), viz. that the individual dendrites of each order are longer in the dark-reared individuals because they are les likely to be interrupted by a bifurcation. It is questionable whether these sorts of subtle relationships can be detected reliably with the techniques of analysis now available and the relatively small numbers of neurons usually investigated.

The same remark pertains to another extension of the theory which is represented by the fact that the number of primary dendrites is nearly the same for any sort of cell or species, whatsoever the age of the animal. It might be that part of the primary dendrites remain latent as to growth and bifurcation, but will still start branching successively during maturation until in the adult status the tree is fully grown under normal conditions, whereas in abnormal circumstances the outgrowth of the primary dendrites is inhibited to a certain degree. The hypothesis predicts that for young or damaged cells there exist partial trees of different structure for each cell, or, otherwise stated, that $c(r)$ is made up of different components. Testing requires rather detailed investigation for each primary dendrite and allows no pooling of data per cell, as is done always. Meanwhile it suggests an interesting direction for future research.

Although the present concept, be it in its simplest form or with additional properties, may reflect more or less truthfully the real state of affairs with regard to dendritic growth of cortical neurons, it does so only at discrete times. A draw-back is that the factor time is not present as a continuous parameter. Without further specification it is not possible to recognize how one stage changes into the next stage. One way to account for this, within the scheme set forth so far, is the following. Given the ultimate shape of a tree at the end of the growing phase, and characterized by p_n, m_ϕ and m_ψ one may imagine several modes as to how the predetermined skeleton will be filled up in the course of time. We can exclude the possibility that a tree grows concentrically with the same velocity for each end point, otherwise $c(r)$ per cell would exhibit an abrupt drop to zero for a certain value of r, this discontinuity in $c(r)$ moving onwards with age of the cell. Therefore one must assume that local differences in the rate of growth occur. This idea is now being studied. Preliminary results have revealed that a good fit can be obtained, assuming that the growth rate at each growing end point is a realization of a stationary Gaussian random process with delay.

Appendix

To arrive at the curves of Fig. 2 one reasons as follows. All primary dendrites bifurcating signifies that the mean number of first order bifurcations between 0 and r is given by

$$c(0)\int_0^r \phi(z)\,dz. \qquad (1\text{a})$$

Half of the secundary segments bifurcate and the mean number of second order bifurcations found between 0 and r is given by

$$c(0)\int_0^r \phi_2(z)\,dz, \qquad (1\text{b})$$

where $\phi_2(z)$ stands for the convolution of $\phi(z)$ with itself, or,

$$\phi_2(z)=\int_0^z \phi(\bar{z})\,\phi(z-\bar{z})\,d\bar{z}.$$

If it is assumed that the length of a segment is not influenced by the length of the segment where it originates from, as found by Sholl (1956, p. 52), it follows that the mean number of bifurcations $P(r)$ of whatever order in between 0 and r is equal to the sum of (1a) and (1b). As all primary segments bifurcate, there are no first order terminal segments and first order end points. Half the secundary order segments are terminal segments, they number $c(0)$. The mean number of second order end points in between 0 and r is equal to

$$c(0)\int_0^r \phi_2(z)\,dz. \qquad (2\text{a})$$

The number of remaining, third order, terminal segments is equal to $2c(0)$. The mean number of third order endings in between 0 and r is given by

$$2c(0)\int_0^r \phi_3(z)\,dz, \qquad (2\text{b})$$

where $\phi_3(z)$ is the three-fold convolution of $\phi(z)$, or,

$$\phi_3(z)=\int_0^z \phi_2(\bar{z})\,\phi(z-\bar{z})\,d\bar{z}.$$

It follows that the mean number of end points $Q(r)$ of arbitrary order in between 0 and r is given by the sum of (2a) and (2b).

The mean number of intersections at a distance r from the perikaryon follows from $c(r)=c(0)+P(r)-Q(r)$.

The dotted curve in Fig. 2b holds for $\phi(x)=\nu(\nu x)^{n-1}\cdot\exp(-\nu x)/(n-1)!$ with $n=4$ and $\nu=0.0727\,\mu^{-1}$, so that the mean segment length is $m_\phi=n/\nu=55.0\,\mu$.

The total length of the tree equals $30\times 55.0\,\mu=1{,}650\,\mu$, while the total number of segments equals $6+12+12=30$.

The better fitting, full-drawn, curves in Figs. 2b and c are found by assuming that the additional length for each terminal segment is distributed according to a probability density function $\psi(y)$. The expressions for $P(r)$ are not affected by this.

The mean number of second order endings in between 0 and r is now given by

$$c(0)\int_0^r \overset{*}{\phi}_2(z)\,dz, \qquad (3\text{a})$$

where

$$\overset{*}{\phi}_2(z)=\int_0^z \psi(\bar{z})\,\phi_2(z-\bar{z})\,d\bar{z}.$$

Similarly, the mean number of third order end points in between 0 and r equals

$$2c(0)\int_0^r \overset{*}{\phi}_3(z)\,dz, \qquad (3\text{b})$$

where

$$\overset{*}{\phi}_3(z)=\int_0^z \psi(\bar{z})\,\phi_3(z-\bar{z})\,d\bar{z}.$$

The mean number of endings $Q(r)$ in between 0 and r is the sum of (3a) and (3b).

The full-drawn curves in Figs. 2b and c have been computed for $\phi(x)=\nu(\nu x)^{n-1}\exp(-\nu x)/(n-1)!$ with $n=4$ and $\nu=0.177\,\mu^{-1}$, and $\psi(y)=\lambda\exp(-\lambda y)$ with $\lambda=0.0185\,\mu^{-1}$.

The total length of the tree equals

$$P\,m_\phi+Q(m_\phi+m_\psi)=12\times 22.6\,\mu+18(22.6\,\mu+54.1\,\mu)$$
$$=1{,}650\,\mu.$$

For partial trees with an arbitrary set of p_n one may derive

$$\overline{P}(r)=\sum_{k=1}^{\infty}2^{k-1}\prod_{n=0}^{k}p_n\int_0^r \phi_k(z)\,dz,$$

where $p_0=1$, and

$$\overline{Q}(r)=\sum_{k=1}^{\infty}(1-p_k)\,2^{k-1}\prod_{n=0}^{k-1}p_n\int_0^r\int_0^z \phi_k(\bar{z})\,\psi(z-\bar{z})\,d\bar{z}\,dz,$$

where $\phi_k(z)$ denotes the k-fold convolution of $\phi(z)$.

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Eigenschaften von Nervenimpulsfolgen

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Summary. In the first part of this paper some phenomena in the nervous system are described, concerning the time interval structure of the nervous signals. The characteristics of the neurons are introduced and interpreted. It is shown theoretically and proved by experiments, that the time interval distributions in the axons can be appoximated by gamma-distributions.

In the second part, some experiments with electronic neuron models are described. It is tried to find a correlation between the interval distributions of the output signals and the structure of the systems.

The third part concerns experiments at the cerci of the cockroach periplaneta americana. From the measured transition probabilities for various amplitudes, the entropy, the transinformation rate and the channel capacity of various nervous channels are calculated.

The average transinformation rate results between 1.5 to 30 bit/sec. The channel capacity is about threefold the transinformation rate.

1. *Einleitung*

Im Nervensystem erfolgt die Informationsübertragung und Verarbeitung durch eine analoge elektrische Größe: die mittlere Impulsfrequenz. Diese Codierungsart der Information bedingt besondere Auswertverfahren und Grenzen. Unter Einbeziehung der biologischen Randbedingungen werden nachfolgend theoretisch sowie in Modell- und Tierexperimenten vor allem diejenigen Eigenschaften neuronaler Datenverarbeitung untersucht, die durch die besondere zeitliche Struktur nervöser Signale bedingt sind. Darüber hinaus wird der Transinformationsfluß in Nervennetzen experimentell bestimmt und die Möglichkeit von Funktionsbeschreibungen diskutiert. Die elektrophysiologischen Experimente wurden am Cercus und den sechs Abdominalganglien der Küchenschabe (Periplaneta americana) durchgeführt.

2. *Zur zeitlichen Struktur nervöser Signale*

2.1. Kennlinien von Neuronen

Ein nachrichtentechnisches System läßt sich im allgemeinen mit Hilfe von zeitabhängigen Eingangs-Ausgangsbeziehungen beschreiben. Bei linearen Netzwerken genügt zur Kennzeichnung des Systems die Impulsreaktionsfunktion. Für nichtlineare Nervennetze ist eine das dynamische Verhalten kennzeichnende Beschreibungsfunktion, die eine theoretische Bestimmung sämtlicher Eingangs-Ausgangsbeziehungen gestattet, nicht bekannt. Es werden daher zur Beschreibung von Nervennetzen Kennlinien benutzt die dynamische Vorgänge nicht mit einbeziehen, sondern im allgemeinen den eingeschwungenen Zustand charakterisieren. Ermittelt man Kennlinien abhängig von verschiedenen Reizbedingungen und zeitabhängigen Parametern, so sind Rückschlüsse auf die dynamischen Eigenschaften des Systems zu gewinnen. Darüber hinaus läßt sich abschätzen, in welchen Bereichen Linearisierungen möglich sind.

Aufgrund einer großen Zahl von Messungen sind der Nervenzelle folgende Eigenschaften und Größen zuzuordnen:

1. Das Neuron hat n Eingänge mit den Eingangsgrößen $y_1(t) \ldots y_n(t)$ und eine Ausgangsgröße $z(t)$; beide Größen beschreiben im allgemeinen Pulsfrequenzen.
2. Die Eingangsgrößen $y_j(t)$ werden mit Koppelfaktoren b_j bewichtet, die die synaptischen Kontakte beschreiben, $j = 1,2 \ldots n$.
3. Oberhalb einer Schwelle S ist die Ausgangsgröße $z(t)$ eine Funktion der Summe aller bewichteten Eingangsgrößen.

Aus einer größeren Zahl von Experimenten ergibt sich für die Neurone folgende Beschreibung [1]:

$$z(t) = \begin{cases} k \ln\left(\dfrac{\sum\limits_{j=1}^{n} b_j y_j(t) - S}{k^*} + 1\right) & \text{für } \sum\limits_{j=1}^{n} b_j\, y_j(t) \geqq S \\[2ex] 0 & \text{für } \sum\limits_{j=1}^{n} b_j\, y_j(t) < S, \end{cases} \tag{1}$$

k und k^* sind Konstante.

Außer durch Ein- und Ausgangssignale wird das dynamische Verhalten der Nervenzellen durch die veränderlichen Parameter b_j und S bestimmt. Die Größen b_j sind im allgemeinen durch einen Tiefpaß erster Ordnung mit der Zeitkonstanten τ zu beschreiben [2]; dabei wird angenommen, daß für sämtliche Synapsen die Zeitkonstanten gleich sind. Die Schwelle S schwankt infolge zellinterner Störungsvorgänge stochastisch um einen Mittelwert. Daraus folgt, daß eine genauere Beschreibung der Nervenzellen einer Verteilung der Pulsabstände am Eingang $\varphi(t_e)$ eine Pulsabstandsverteilung am Ausgang $\psi(t_a)$ zuordnen muß, wobei die Information durch die Zahl der Pulse innerhalb der von τ abhängigen Integrationszeit t_i dargestellt wird.