Neurobiology of the Hippocampus

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Some Anatomical Comments on the Hippocampus

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A beautiful appearance under the microscope, a striking biochemistry, a miraculous electrophysiological approach as well as a peculiar psychological relevance make the hippocampus the favorite subject for diverse groups of enthusiasts. Each sees the hippocampus from its own angle, a perspective which sometimes excludes facts that are quite apparent from other points of observation. Our own point of view is that of the casual observer of Golgi- and other preparations which are made for other purposes but often contain the hippocampus as an irresistible eye catcher. Our comments will be sporadic, disconnected and mainly centered around a small number of anatomical pictures.

I. Morphological Considerations

Figure 1, a, b and c, shows us the hippocampus as an integral part of the cerebral cortex. The axono-dendritic feltwork of the hippocampus is continuous with that of the rest of the cortex and must therefore be considered as belonging to the same organ, or at least to the same piece of grey substance, whatever that means. (In contrast, the cerebellar grey substance is nowhere continuous with that of the cortex, nor is the tectum or the thalamus.) The hippocampus shares with the cortex the system of intrinsic coordinates in which the histological elements are arranged. In spite of all the bending and folding, there is a well-defined plane everywhere in the cortex (including the hippocampus) which we may call the horizontal (or, perhaps better, tangential) plane. At the transition between the hippocampus and the cortex, the hippocampal "plane" is continuous with the "plane" of the rest of the cortex (Fig. 2). Note that this is not true for the transition from the hippocampus proper to the dentate gyrus, where again a

tangential plane is defined, but it is at right angles (except for the bending) to the plane of the hippocampus. In a way, the hippocampus and the rest of the cortex are one piece, and the dentate gyrus another.

Figure 1a is a planar map of the mouse cortex. Since the shape of the hemisphere in this animal is not very different from that of a cone, with its tip near the olfactory bulb, it is possible to unroll the surface of the cortex without too much distortion. Only the two pole-regions (frontal and occipital) resist smooth flattening out. The resulting map is roughly

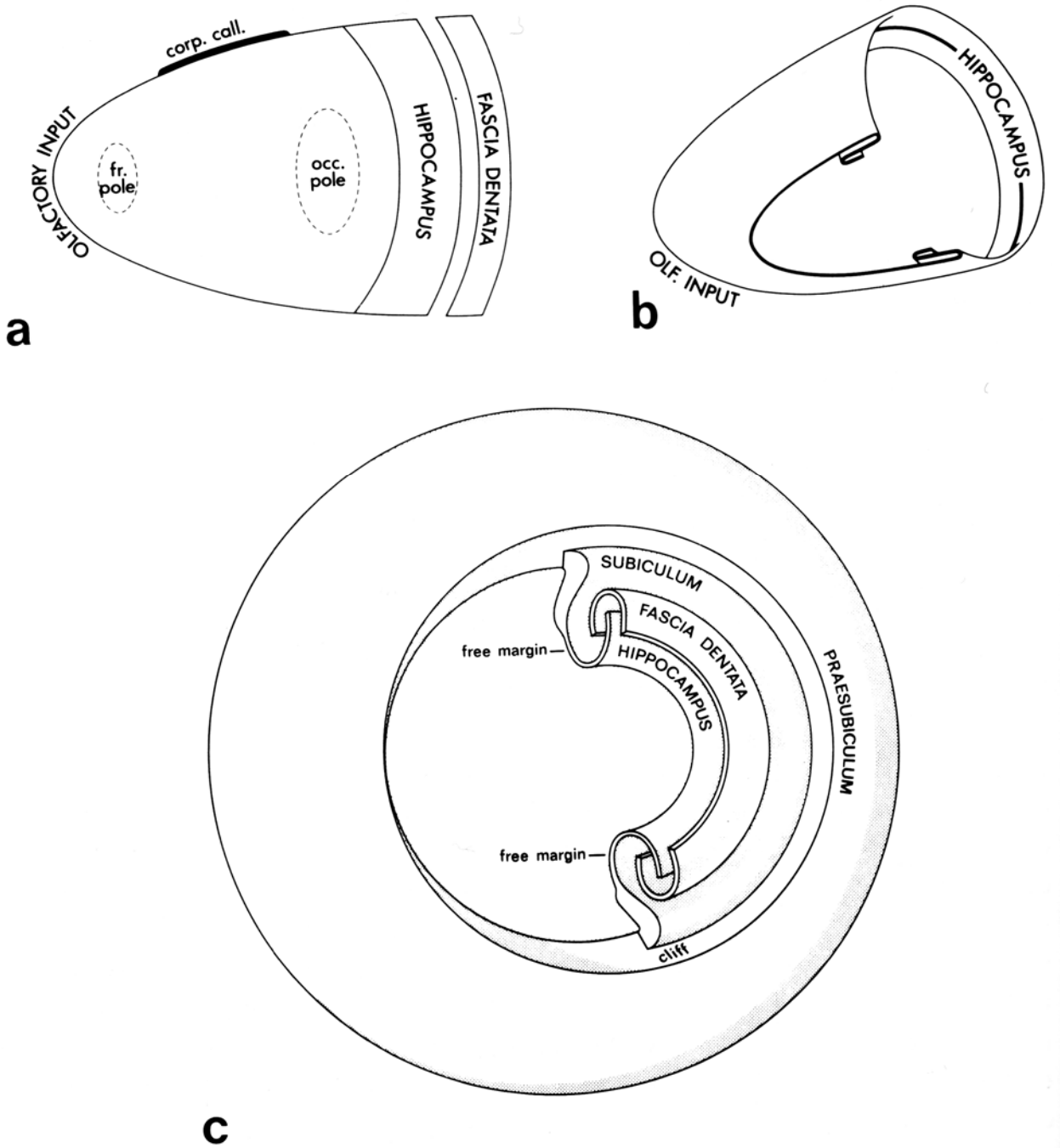

FIG. 1. (a) A planar map of the mouse cortex. (b) To show how the hippocampus is folded in mammals and how the whole pallium is rolled into a cerebral "hemisphere". (c) Schematic view of the right cerebral hemisphere, seen from the medial side, with the hippocampus and dentate gyrus as a protrusion of the inner cortical layers.

triangular, with the hippocampus occupying the entire side opposite the olfactory vertex.

The cortex in this representation appears as that part which is interposed between the olfactory input and the hippocampus, or if we wish, between the olfactory input and the dentate fascia. If we look at the whole telencephalic arrangement as a piece of machinery, we gain the impression that the role of the hippocampus must be as basic to it as that of the olfactory representation, from which we are told it originally arose. In a sweeping generalization we may suppose that, just as the forerunner of the olfactory cortex was the original input to the telencephalic vesicle, perhaps the forerunner of the hippocampus was its original output. All the newcomers, the visual, acoustic, tactile inputs as well as their short-cut outputs to the spinal cord and brain stem, are later additions which make the interposed cortex grow bigger and bigger in phylogeny. Correspondingly, the conditions between the original

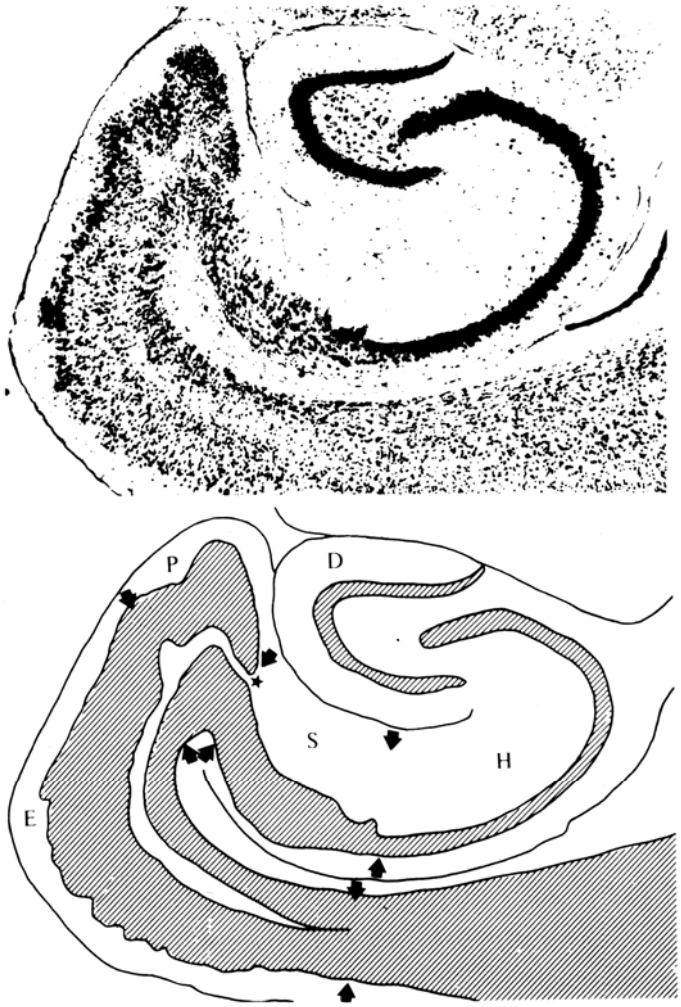

FIG. 2. Hippocampus and adjoining cortex in a Nissl preparation, horizontal section, of the mouse. Pairs of arrows indicate the borders between regions: hippocampus proper (H), subiculum (S), presubiculum (P) and entorhinal cortex (E). The star marks the presubicular cliff. D: dentate gyrus.

input and output become more and more devious. You do not go directly from olfaction to the hippocampus, hypothalamus and septum any more: you interpose loops through the sensory representations and, via pyramidal output and sensory feedback, even loops through the environment.

Figure 1c is clearer, if metrically less correct, than the preceding one. It was designed to aid the beginner in the interpretation of frontal, sagittal, horizontal and oblique sections through the hemisphere in which the hippocampal formation appears in a variety of bizarre ways. In such sections it is quite difficult to mentally reconstruct the connectivity of the various pieces shown, because of the folding of the hippocampal cortex into a roll with a curl, the whole roll and curl being again bent so that the opposite ends of the long axis of the roll are at an angle of about 90° (in the mouse). The schematic drawing shows the right telencephalic "hemisphere" from the medial aspect, stylized as a bubble with an opening. The margin of the opening for some of its circumference is decorated by an extension of the cortex which is folded back and fits into a bent trough easily identified as the dentate gyrus. The main varieties of the sections through the hippocampal system can be gathered from this diagram. Figure 1b is intended to show the relation between Figs 1a and 1c.

This didactic effort may be wasted on the specialists, but we do want to make another point on Fig. 1c. Note that on the drawing only the lower part of the cortex, and not the entire thickness, is continued into the hippocampal extension. This corresponds to an observation which can be best made on Nissl sections that cut the hippocampus across its long axis (Fig. 2). At the level of the presubiculum the upper half (roughly) of the cell population comes to an abrupt end. The adjoining subiculum is continuous only with the lower main layer of the presubiculum and hence of the entorhinal area and of the rest of the cortex. The presubicular "cliff" is particularly striking in the lower-lateral part of the hippocampus (Fig. 2), but even at its upper-medial end, where the subiculum no longer has as its neighbour the entorhinal area but the very different retrosplenial cortex, careful inspection shows that the upper tiers of the retrosplenial cortex do not go over into the cell layer of the subiculum.

This sounds like a piece of descriptive neuroanatomy but it may in fact contain a lesson. Modern methods, principally HRP transport, have confirmed an old suspicion according to which the cortex is made up of two main tiers, an upper one which subserves association, and a lower one, whose business is projection. More precisely, in most parts of the cortex layers I to III are devoted to the corticocortical traffic, layer VI to projection into the diencephalon, while the interposed layers IV and V receive outside information and relay commands to the motor system respectively. Thus, from its relatedness to the lowermost layer, the hippocampus (including the sub-

iculum) would appear to be a somewhat specialized output station to the diencephalon, and sure enough, its subcortical white substance, the fimbria-fornix, mostly ends up there.

The interesting question then is where does this lonely VIth layer get its input from, if in the ordinary cortical scheme the lowermost layer is mainly fed information which filters down from the topmost layer where the associations come in and from the middle layers where the outside reality is represented, all of which are missing in the hippocampus. They are not entirely missing, of course, since the entorhinal cortex sends off a sizeable stream of fibers, the perforant path, which originate in its top layers (Steward and Scoville, 1976) and terminate, directly or indirectly, over the whole extent of the hippocampus. Thus, we end up with a bizarre view of the hippocampal formation: the entorhinal strip of cortex endowed with a sixth layer of such enormous dimensions that it protrudes like a tongue, carrying with it the fibers from the upper layers.

But this view is very wrong in one respect. The flow of information (through the perforant fibers, mossy fibers and Schaffer collaterals) from the upper layers of the entorhinal cortex toward its extended sixth layer (the subiculum-hippocampus) does not follow the direction one would expect, but skips to the extreme ranges of the protruding tongue and then proceeds backward again in the direction of the entorhinal cortex. The strange discontinuity in this connection seems to be all-pervasive in the comparative anatomy of the mammalian hippocampus and is certainly related to the striking macroscopical form of the hippocampal formation, doubled over to bring the dentate gyrus into convenient proximity with the entorhinal cortex (although this is not too convincing: one might have preferred a simple curl, rather than an s-shaped one, in order to spare the entorhinal fibers the crossing of the subiculum on their way to the dentate gyrus). The re-entrant connectivity is so characteristic that one is tempted to solve the old controversy on the identification of the hippocampus in non-mammalian vertebrates in a very simple way: where there is no fiber system which is topologically identical to the perforant path, there is no hippocampus. I am sure that many of the regions that are at present labelled Hippocampus in textbooks of comparative neuroanatomy would fall by the wayside if this definition were applied.

It is imperative to speculate on the special role which a piece of cortex with such unidirectional re-entrant connectivity might play. We agree with Dr Swanson (1983) that the hippocampus is essentially cortex, and we are quite convinced by his arguments that it should be considered as associational cortex. We are prepared to forget that the hippocampus proper seems to be derived just from those layers that are projectional rather than associational in the conventional scheme: in any case it would be wrong to consider


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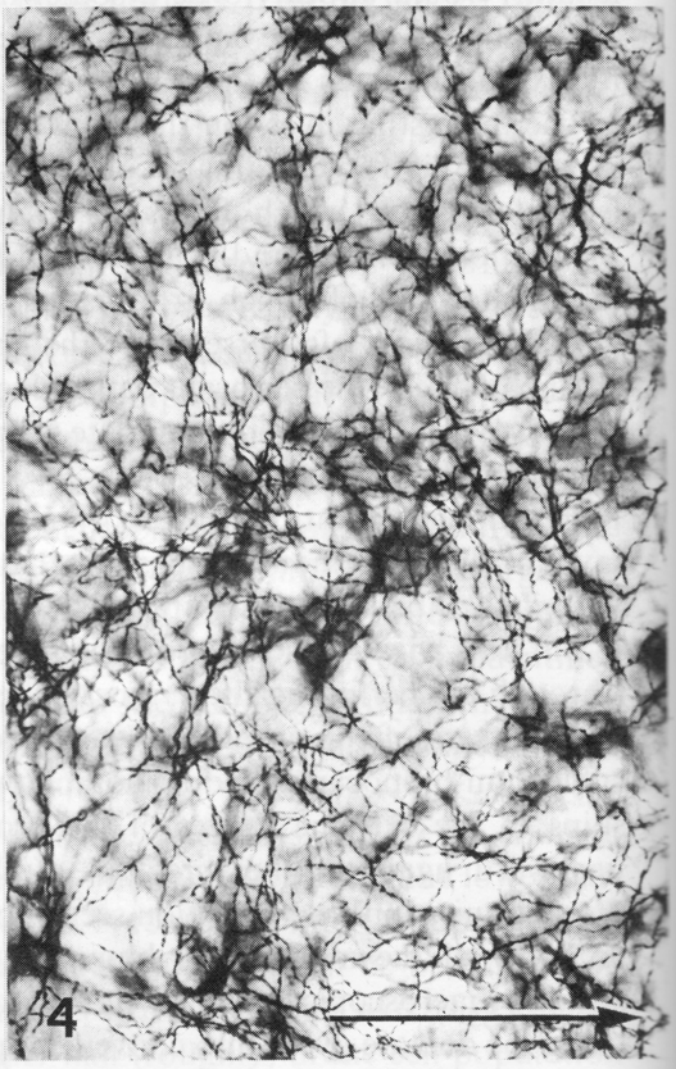
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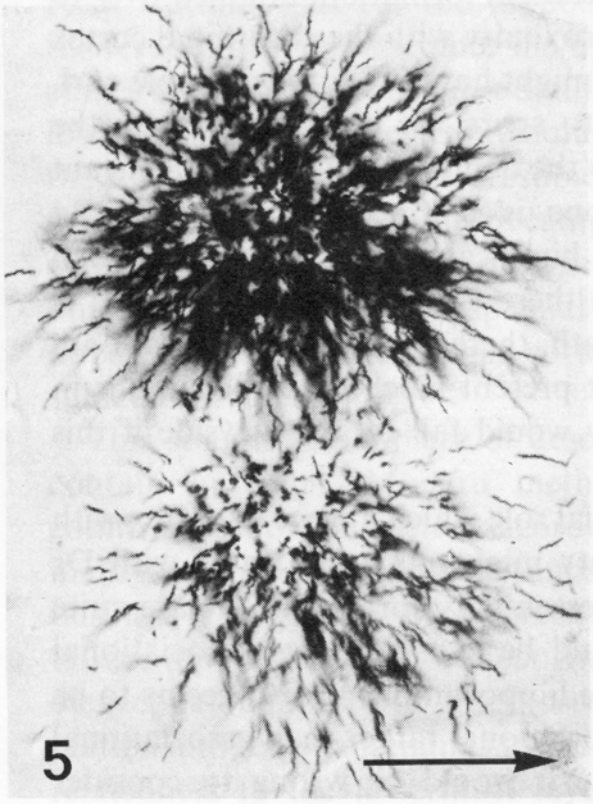
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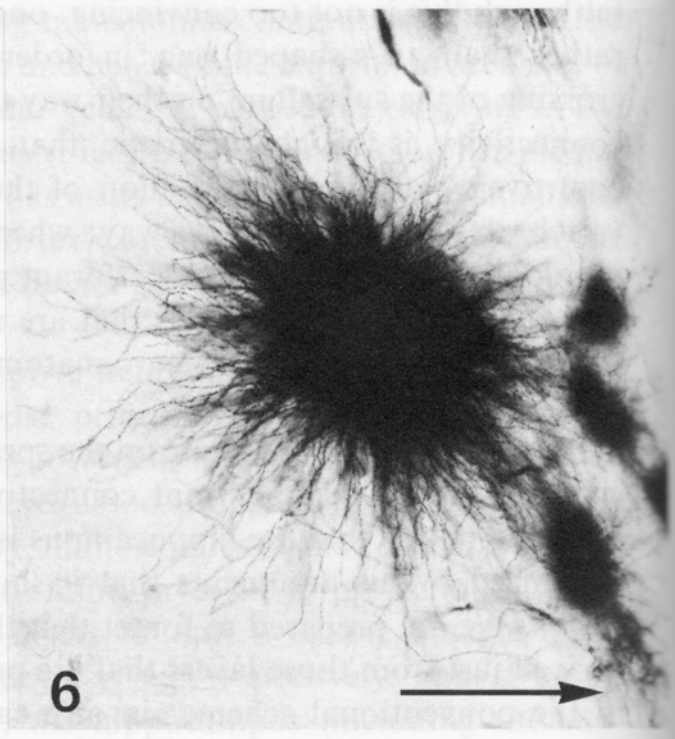
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Ammon's horn in isolation instead of the whole entorhinal–hippocampus complex, with its upper layers plus extended lower layers. Putting together the two concepts of hippocampus as associational cortex and hippocampus as characterized by re-entrant unidirectional connectivity, it is tempting to see the hippocampus as the place where sequential aspects of associations are dealt with. Since the perception of space in moving animals is largely based on sequential perception, besides the more obvious parallel perception typified by vision, this may give us a lead to the role of the hippocampus in orientation.

Our next point takes us away again from the slice-like view that overemphasizes the unidirectional connectivity. Figures 3 to 6 represent flat sections through the hippocampus, as tangential as possible to the layers. There are, of course, two curvatures that limit the extent of such quasi-horizontal sections: the double narrow bend which reminded the old neuroanatomists of the sea-horses' tail, and the slower bend of the whole hippocampal formation around the medial opening of the hemisphere (Fig. 1c). The purpose of our tangential sections is to provide evidence for an homogeneous, massive connectivity without any preferential direction which puts neighbouring elements in relation to each other in all layers of the hippocampal formation, very much in the same fashion as in the rest of the cortex. Our point is that the famous unidirectional pathway (perforant fibers, mossy fibers, Schaffer collaterals) may be quantitatively less significant, e.g. in terms of the number of synapses which it subserves, compared to the overall scheme of undirected connections.

Figure 3 is a tangential section through a Golgi preparation at the level of the stratum radiatum. The region is CA3. Some axons are stained, presumably an unsystematic selection of the total (much denser) axon population. We may assume that these are mostly axon collaterals of hippocampus pyramidal cells. No preferential direction can be seen.

FIGS 3–6 *Fig. 3*. Tangential section through the hippocampus of the mouse, CA3, at the level of the stratum radiatum. Golgi preparation. Axons are stained which run in all directions. The arrow points in the direction CA3 to CA1. The length of the arrow corresponds too 100 μm. *Fig. 4*. Tangential section through the stratum oriens. Golgi preparation, mouse. The axons again have no preferential orientation. Arrow: as in Fig. 3. *Fig. 5*. Tangential section through the stratum moleculare of the hippocampus of the mouse. Golgi preparation. Two clusters of pyramidal cells are stained, the apical dendrites of which branch in all directions of the hippocampal plane. Arrow: same direction and length as in Figs 3 and 4. *Fig. 6*. Tangential section through the stratum oriens, Golgi preparation, mouse. Presumably all the axons running through a center of precipitation of the Golgi reaction product are stained. This provides a pictorial view of the isotropy of the axonal network. Arrow: same meaning as in Figs 3 to 5.

Similarly in the stratum oriens (Fig. 4). Again the fibers roughly running in a tangential plane seem non-oriented. They run at all angles to the direction of the hippocampal slice, which is horizontal in the picture (left to right corresponds to the direction CA3 to CA1, the direction of the mossy fiber–Schaffer collateral pathway).

In our Golgi preparations clusters of neurons frequently receive the stain, probably initiated by an amorphous lump of silver dichromate precipitation which infects all axons and all dendrites that pass through it (sometimes more axons, at other times more dendrites). Such a cluster provides a pictorial view of the statistics of orientations in a random network. In Fig. 6 axons are seen emanating from the center of precipitation in all directions, without any obvious bias. The section is tangentially oriented in the stratum oriens.

Two more such clusters provide evidence of an equally diffuse, non-oriented growth of dendrites (Fig. 5). The section is tangential through the molecular layer of the hippocampus. The two roses of dendrites are formed by the apical ramifications of two groups of neighbouring pyramidal cells. Again there is no tendency for the dendrites to respect the direction parallel, or at right angles to that of the "slice".

II. Quantitative Relationships

The number of pyramidal cells in the hippocampus of the mouse is about 3×10^5 according to our own estimate. We arrived at this number in the following way. The density of nuclei in the pyramidal layer of CA1 and CA3, calculated from the average distance of nearest neighbours as well as from the number of nuclei in a region of known volume, is $3 \times 10^5/\text{mm}^3$. The volume of the pyramidal layer, which is 6.5 mm long, 2 mm wide and 0.07 mm thick, is 0.91 mm^3. This makes 2.7×10^5 neurons in CA1 to CA3. Add to this 10% for the neurons in CA4, and you have a total of 3×10^5. The density of cell bodies in the pyramidal layer can be checked against the upper limit of closest packing of spheres with a diameter of 14 μ which is $5.2 \times 10^5/\text{mm}^3$, and against an absurdly loose spacing, equal to that in the rest of the cortex, of 20 μ between the centers of the cell bodies which is $1.7 \times 10^5/\text{mm}^3$.

Our estimate should be compared to the figures given by Schwartzkroin *et al.* (1982) for the rabbit and by Gaarskjaer (1978) for the rat. The rat seems to have more hippocampal pyramidal cells than the mouse (2×10^5 in CA3 plus CA4, which makes about twice as much for the whole hippocampus). For the rabbit the authors report a surprisingly high density of neurons in the pyramidal cell layer, compatible only with cell bodies much smaller than those in the mouse.

There are about 7×10^5 granular cells in the dentate gyrus of the mouse (West and Andersen, 1980). They make synaptic contacts with the apical dendrites of about 1.5×10^5 hippocampal pyramids, under the assumption that about half of the pyramids are in the regions CA3 and CA4* and hence are recipients of mossy fiber endings. Thus from the dentate granules to the hippocampal pyramids there is a convergence of at least 4 to 1. In reality, each mossy fiber carries about 10 pieces of "moss" (our estimate is in excess of that given by Blackstad and Kjaerheim, 1961, for the rat) and therefore contacts at least 10 different pyramidal cells. In fact the mossy terminals of one fiber are spaced at such distances that two consecutive ones could hardly reach the same target neuron.

Actually, the divergence factor is probably even higher, since it has been shown (M. Frotscher, personal communication) that one mossy bouton may (or perhaps always does) contact more than one pyramidal cell. Since the number of spines invaginating one bouton is about 5 (Amaral and Dent, 1981), if they all belong to different pyramidal cells, each granular cell may reach a maximum of 50 hippocampal pyramidal cells.

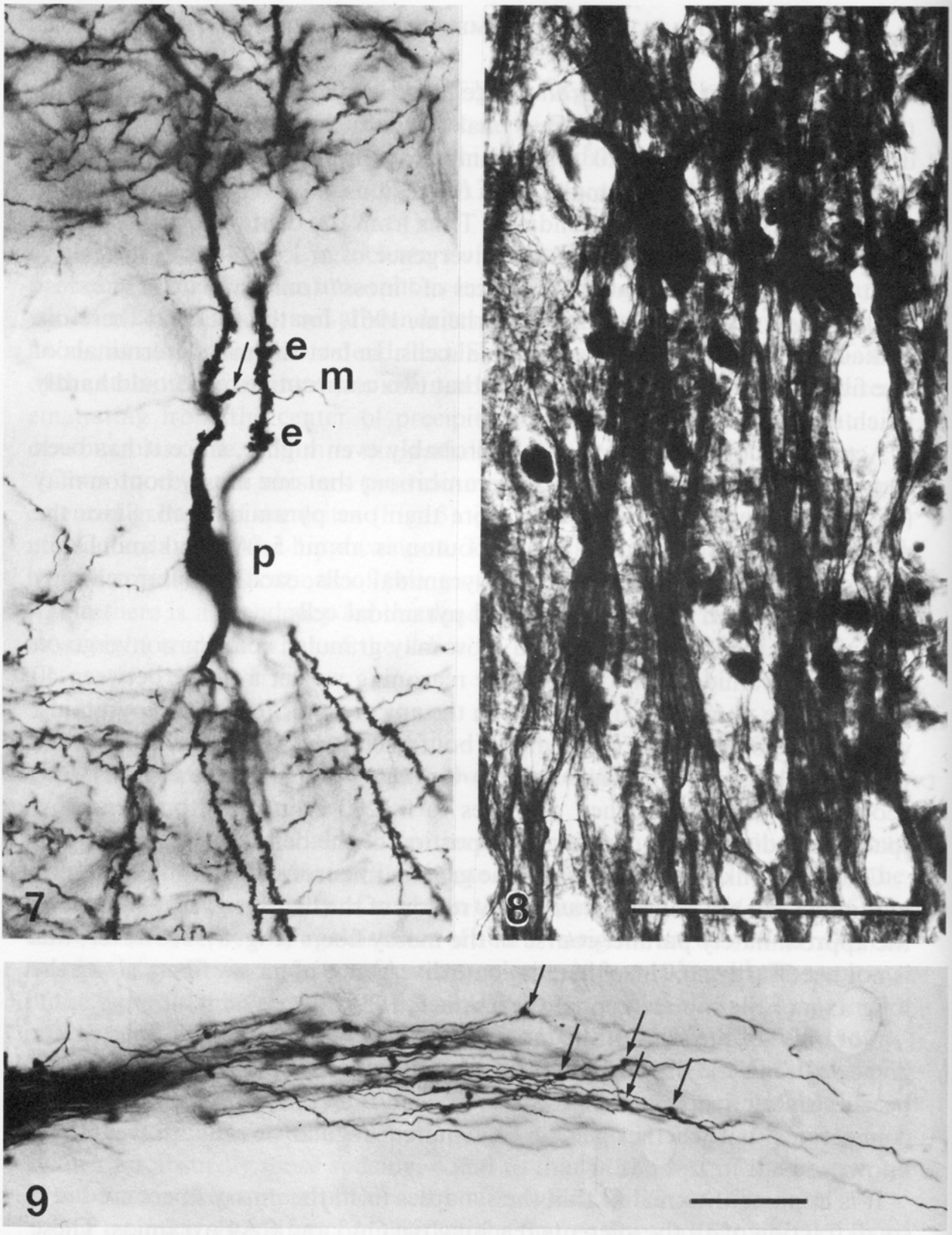
If we ask, the other way around, how may granular neurons converge on the same pyramidal cell, by the same reasoning we get a figure between 40 and 200. The number of tiny spines on the apical dendrites of CA3 pyramids, which are known to receive the mossy bouton contacts (Fig. 7), is compatible with this large convergence factor. On the other hand one runs into geometrical difficulties when one tries to fit 200 boutons into the narrow space immediately surrounding that portion of the dendrite.

One would like to think that all the granular neurons converging onto one pyramidal cell are housed in a narrow region of the dentate gyrus, because of the approximately parallel course of the mossy fibers (Fig. 8). However, this is not necessarily so, since there is some divergence of mossy fibers along the long axis of the hippocampus (Gaarskjaer, 1981).

Not only do the sizes of the mossy excrescences of one mossy fiber vary a great deal, but the distances between them vary as well (Fig. 9). There must be some selective process at work to determine the specificity of these connections, but whether genetic or acquired, regular or random we do not know.

It is important to realize that the synapses from the mossy fibers are but a small fraction of all the afferents reaching the CA3 and CA4 pyramids. These are covered by a multitude of spines, several thousands of each neuron which presumably receive intrinsic as well as extrinsic afferents. We may actually suppose, by analogy with the rest of the cortex (Braitenberg, 1981),

* We include the spiny hilus cells among the pyramids.



FIGS 7–9. *Fig. 7.* A pyramidal cell of CA3 of the mouse, Golgi preparation. p: perikaryon, e: thorny excrescences which are postsynaptic to the mossy fibers (m). Arrow: synaptic swelling of the mossy fiber ("moss"). Bar: 50 μm. *Fig. 8.* Tangential section through the layer of mossy fibers in CA3 of the mouse. Bielschowski stain, modified by Staiger. The mossy fibers run fairly parallel to each other in a vertical direction of the picture. The moss is not shown in Bielschowski preparations. Bar: 50 μm. *Fig. 9.* Oblique section through the layer of mossy fibers in CA3 of the mouse, Golgi preparation. Arrows: "moss". Bar: 50 μm.

that a large part of the synapses in the hippocampal tissue are synapses between axon collaterals of pyramidal cells and dendrites of other pyramidal cells. The fiber felt, which is partially stained in the Golgi preparations of Figs 3, 4, 5 and 6, may be largely composed of axons and dendrites pertaining to this system. One of the reasons for this supposition is the lack of directionality in this fiber felt, which is more compatible with a system of short range connections than with orderly systems of external afferents.

We have not ourselves made counts of synapses on electron micrographs of the hippocampus, but we may safely assume that their density is the same as that in the rest of the cortex, i.e. 10^9 synapses/mm^3. (The figure given by Schwartzkroin *et al.* for the stratum radiatum in CA1 of the rabbit is 5×10^9/mm^3.) Figure 10 gives a realistic impression of the density of the synapses in the hippocampal tissue. For the whole hippocampus of the mouse, which has a volume of about 6.5 mm^3, we get 6.5×10^9 synapses. If we identify each moss with a (admittedly very special) synapse, the number of synapses along the unidirectional mossy fiber pathway is only a small fraction of the total number of synapses. Even if we assume that each moss is the site of five synaptic contacts (Amaral and Dent, 1981), the estimated number of mossy fiber synapses would only be 3.5×10^7 and thus less than one hundredth of the total number of synapses in the hippocampus.

From the total number of synapses in the hippocampus and the number of neurons in the same region (we suppose that the non-pyramidal neurons add another 20% to the number of pyramidal cells given above), we can compute the number of synapses on each individual cell. This turns out to be higher than in the rest of the cortex, 18 000 synapses per neuron as compared to an average of 5000 per neuron in the non-hippocampal mouse cortex. We arrived at a similar figure by computing the density of dendritic spines and then adding 20% for the synapses residing on cell bodies and on dendritic shafts (total dendritic length of a hippocampal pyramidal cell: 5000 μm; density of spines: 2.5 spines per micron of dendritic length, making 12 500 spines, plus 2500 other synapses making 15 000 synapses per pyramidal cell).

Thus we may conclude that whatever happens in the striking unidirectional entorhino-hippocampal pathway does so on a background of very rich, diffuse, non-oriented connections with a very large divergence–convergence factor. In fact, by arguments of sheer geometry we are led to suppose that multiple contacts between any two pyramidal cells are the exception rather than the rule in the hippocampus as well as in the rest of the cortex (Braitenberg, 1981). Thus, if each neuron partakes in 18 000 synapses on the receiving as well as on the giving end, it is likely to receive signals from (and to pass signals on to) not much less than 18 000 other neurons. Such convergence/divergence is of course most welcome in any system destined to serve as an associative memory.

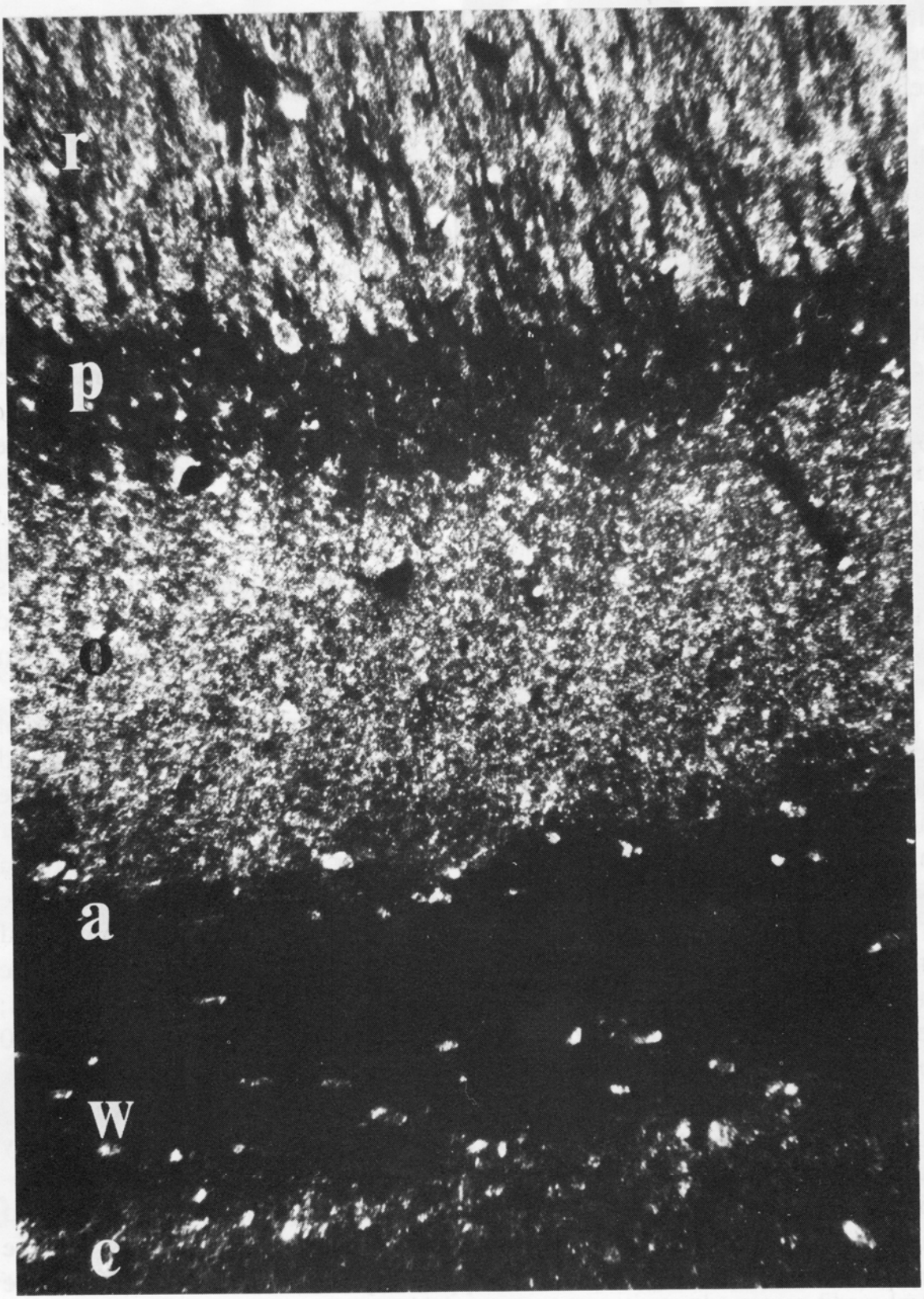


FIG. 10. Dark field light micrograph of a 2μm section stained for synapses with the phosphotungstic acid method of Bloom and Aghajanian (1966). Most of the fine bright dots are synapses, but some nuclei of glia cells and some mitochondria also show. r: stratum radiatum, p: layer of hippocampal pyramidal cells, o: stratum oriens, a: alveus, w: cortical white substance, c: cerebral cortex.

III. Conclusions

We were motivated by the feeling that the hippocampus is an integral part of the cerebral cortex, essentially similar to the rest of the cortex in its basic wiring and not to be understood independently from the general problem of the cortex. Both the hippocampus and the rest of the cortex are characterized by the prevalence of one neuronal type, the pyramidal cells, which receive input and provide output and are connected to each other. The connections between pyramidal cells form the majority of the synapses in the cerebral cortex in general and, we may assume, in the hippocampus as well. The axon collaterals which are responsible for these pyramidal-cell-to-pyramidal-cell connections make most of their synapses en passant, a fact which leads to a very high degree of divergence/convergence in this system (Braitenberg, 1978). It is generally assumed that the synapses between pyramidal cells are excitatory. From the standpoint of brain theory (Palm, 1982) a system of neurons connected by a large number of excitatory synapses subject to some kind of Hebbian plasticity is what is needed for associative memory. To our mind there is little doubt that the whole cerebral cortex, including the hippocampus, serves this purpose.

There are, however, some important traits which distinguish the hippocampus from the rest of the cortex.

There is a marked two-dimensional connectivity in the hippocampus which is not so evident elsewhere in the cerebral cortex. There, the cortical sheet has a third dimension, the cortical thickness, in which the neurons are dispersed. In addition to the more symmetrical synaptic relations in the "horizontal" plane, there are more assymetrical synaptic relations between neurons situated in different cortical layers. This is not so in the hippocampus where the vast majority of pyramidal cells are all aligned on one level (Fig. 2), thus eliminating any bias which may come with their different position in the cortical thickness. Thus the probability, or intensity, of their connection must be simply a function of their distance in the cortical plane. True, there are some long axon collaterals running along the long axis of the hippocampus (Lorente de No, 1934) and perhaps in other directions as well, but the majority of the axon collaterals remain local (Knowles and Schwartzkroin, 1981) and make the connectivity of the network essentially two-dimensional. It is certainly also significant in this connection that the hippocampus has only a very limited amount of subcortical white substance associated with it. In the rest of the cortex the subcortical white matter contains a large number of axons mediating long distance corticocortical connections. These abolish in part the metrics imposed by the two-dimensional connectivity of the cortex. The subcortical fibers of the hippocampus are mostly collected in the relatively narrow bundle of the fimbria-fornix, and thus seem to be input and

output, rather than associational connections. Some collaterals of descending fibers of pyramidal cells, however, have also been described in the alveus, from where they appear to enter again into the hippocampal tissue (Knowles and Schwartzkroin, 1981).

This is the place for a rather daring speculation. If the hippocampus contains a map of external space, as some would like us to believe (O'Keefe and Nadel, 1978), it should be two-dimensional space such as the surface of the earth in order to conform to the connectivity of hippocampal pyramids. And sure enough, there is no markedly two-dimensional hippocampal tissue in fishes which live in three-dimensional space, nor in birds, or in amphibia whose life is at least undecided between the two-dimensional surface of the earth and the three-dimensional water. Interestingly enough, as an exception among the mammals, the dolphin has a surprisingly small hippocampus (Haug, 1970; Morgane *et al.*, 1980). We realize that the failure to detect a clear isomorphism between the location of "place neurons" in the hippocampus and the external space to which they refer works against this idea, but such an isomorphism may still be found.

The other peculiarity of the hippocampus is the system of unidirectional connections in the entorhino-hippocampal loop. As far as anybody knows, there is no such striking exception to the prevailing isotropy of connections anywhere else in the cortex. The synapses in this system are not numerically prevalent, as we have already seen, but they must have a very strong influence on hippocampal pyramidal cells especially in the dentate to CA3 connection because of their placement on a crucial part of the dendritic tree,* perhaps made more sensitive still by special, complex spiny "excrescences". Speculation on this pathway has suggested three routes.

First of all, some of the synapses in this system seem to be very special in their chemistry. This might imply that here the neurological elaboration of signals is under the influence of other, more humoral systems. This is not surprising, since both from the standpoint of "limbic lobe" philosophy and from that of hippocampus as a selective learning device such humoral control is to be expected.

Then we may speculate on the fact that the pathway is re-entrant. We may of course suppose that signals originating in the entorhinal cortex after travelling through perforant path, mossy fibers and Schaffer collaterals come back to the entorhinal area through the subiculum (Swanson *et al.*, 1978). Loops have been greatly in fashion since the early days of neural net theory (e.g. McCulloch and Pitts, 1943) as the possible substrate of intermediate memory.

There is little we can add to this charming supposition, except that it is

* See however, Andersen *et al.* (1980) for evidence against a strong weighting of different sections of the dendritic tree.

difficult to imagine the details. Do the messages themselves whirl around the entorhino-hippocampal loop until they are definitively inscribed into permanent memory, or is each re-entrant signal just one element of a more complex message which is coded in a distributed fashion over the whole extent of the hippocampus? And if we think of spike patterns looping around, at what phase of their trajectory does the inscription take place? And where? In the hippocampus, or in the rest of the cortex, and how do they get there?

There is another aspect of the entorhinal-hippocampal pathway which leads to the third speculation. The pathway is directional, one way, not matched by a similar pathway going in the opposite direction (Hjorth-Simonsen, 1973). Unidirectionality is an important property of time. Could it be that temporal sequences are imposed onto the hippocampal tissue by the sequential activation of the powerful mossy fiber synapses distributed along the direction of the fibers? The delays generated by spike conduction along the mossy fibers are quite small, of the order of one millisecond, probably too small to be meaningful in the context of sensory or motor sequences. However, there is use for such a sequencing in connection with the theory of cell assemblies, to which we subscribe (Braitenberg, 1978; Palm, 1982). A cell assembly (Hebb, 1949) is a set of neurons, connected by excitatory synapses, whose explosive ignition constitutes a meaningful event in the brain. Once ignited, the cell assembly will "hold" for a while, i.e. the neurons of the assembly keep each other in a state of activity because of reverberation of excitatory stimuli. This reverberation must have a certain spatio-temporal structure since it is not likely that all the neurons will fire in synchrony. More likely, depending on the part of the assembly that was initially excited, various modes of oscillation can occur. If it is important to let each cell assembly become active in one predetermined mode of oscillation, one might ignite part of the cell assembly in a certain sequence. That part may be housed in the hippocampus, the sequence being imposed by the mossy fiber pathway. Thus the role of the hippocampus in memory may be ultimately its role in igniting cell assemblies. This may be particularly important in the early phase of the inscription of cell assemblies, and thus be compatible with the survival of long term memory (= of well established cell assemblies) after hippocampal destruction.

One last point. The hippocampus is sometimes considered as an auxiliary mechanism of the memory store, not as part of that store itself. This may be misleading. If the memory store is diffusely located in the synapses of the pyramidal cell system, and particularly in the synapses between axon collaterals of pyramidal cells and dendritic spines of other pyramidal cells, at least in the mouse we gain the impression that a considerable part of these synapses are in the hippocampus. In particular, there are more spines and synapses in the mouse hippocampus than in those very debatable regions of the cortex that could be truly classified as "associational".

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