

ASPECTS OF THE ELECTRICAL ACTIVITY
IN THE CEREBRAL CORTEX
OF VARIOUS MAMMALS

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by
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1.

ABSTRACT

The first Section of this work concerns the origin of the potential waves evoked at the cerebral cortex of the cat by contralateral forepaw stimulation. Initially positive deflexions have been recorded in somatic Area I and initially negative waves in the region medial to this. It is suggested that there is one region, in the upper limb of the cortex at the base of the coronal sulcus, which receives an afferent projection from the dorsal tips of the contralateral digits.

The current and voltage fields generated by the depolarisation of pyramidal cells in this region have been calculated from volume conductor theory and account for the different waves recorded from the cortical surface. Depth records of both unitary and mass extracellular potentials support this hypothesis.

Work has also been undertaken on the species variation in the response evoked by contralateral forepaw stimulation. Those species with a flat cortical surface (rat, rabbit and coypu) yield similar evoked potentials,

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which are usually initially positive.

This is in contrast with the responses observed on the convoluted cortex of the cat. These results suggest that cortical architecture is an important factor in the variety of responses observed in the cat.

Some components of both mass and unitary potentials evoked at the cerebral cortex, by contralateral cortical stimulation are affected by the absence of spontaneous cortical activity at the instant of arrival of the afferent volley. In the absence of spontaneous activity the response is a pure positive wave, whilst in periods of activity there is a small positive deflexion followed by a large negativity. Evidence is put forward that this large surface negativity is the reflection of a superficial pocket of negativity, within the cortex, which is observed only during cortical activity.

CHAPTER I

HISTORICAL INTRODUCTION

3.

In 1929 Berger recorded from electrodes placed on the scalp of a human, electrical oscillations which were attributed to the spontaneous activity of the brain. Prior to this, Caton (1874) had recorded electrical activity in the brains of living animals; he related this to central nervous function. Bartley & Bishop (1933) recorded, from electrodes lying on the surface of the exposed cerebral cortex of an anaesthetised animal, electrical activity evoked by stimulation of the optic nerve. These potentials were obtained using recording electrodes which were much larger than the size of the cells in the brain and hence the potentials recorded represented the summed activity of elements in a large mass of nervous tissue underlying the electrode. For this reason this type of record is termed a "mass potential".

More recently, with the advent of micro-electrodes and advances in electronics, records have been made of the activity of individual cells. Thus Brooks & Eccles (1947), recorded the activity of a group of anterior horn cells within a motonucleus, by the use of an extra-cellular micro-electrode. Micro-electrodes record mass

activity but, additionally, if the electrode tip is close to a cell, the record yields action potentials from the cell; such all-or-none activity is referred to as unitary activity. There has been much speculation about the relationship between mass and unitary activity; the present work provides some new information about the correlation between these two types of activity.

The origin of mass cortical potentials

In the present work the cortical potential evoked, by stimulation of the contralateral forepaw of an experimental animal, has been used as a means of obtaining a fairly reproducible wave of electrical activity in a circumscribed area of the brain. The mass potentials probably reflect changes in the degree and sign of polarisation of nerve cells and their processes in the brain matter underlying the recording electrode. Little is known, however, of the site of these polarity changes.

In the species studied (rat, rabbit, coypu and cat), the potential evoked at the cortical surface by contralateral forepaw stimulation usually consists of a positive wave or series of positive waves, sometimes followed by

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a negative wave (Holmes & Short, 1970 in the rat; Angel (1967) in the rabbit; Adrian (1940) in the cat). Forbes & Morrison (1939) and Adrian (1941), considered the early positive wave to be closely associated with the afferent discharge, because records taken from the surface of the exposed white matter were indistinguishable from those taken on the surface of the cortex. Eccles (1951), however, attributed the positivity recorded on the exposed white matter to the injury current as a volley approached the cut end of a nerve. He considered it more likely that the initial positivity recorded at the cortical surface was due to the synaptic excitatory action of an afferent volley on the dendrites of cortical neurons (Eccles, 1951).

Many observations support the hypothesis that the initial positive wave is cortical in origin. Thus Chang (1953b) and Perl & Whitlock (1955) have reported that responses elicited by stimulation of the contralateral cortex reduced the surface positive wave recorded in response to contralateral forepaw stimulation in the cat. This interaction occurs in the cortex (Chang, 1953b).

Adrian (1941) and Chang (1955) observed that cortical anoxia affected the later negative wave before it affected the early positive wave, and these authors suggested that the surface positivity was presynaptic and the surface negativity was postsynaptic in origin. Curtis (1940b) also observed that the positive and negative components of the response to contralateral cortical stimulation were separate; the surface application of nembutal obliterated the negative wave but left the positive wave unchanged.

There is conflicting evidence on the relative contributions of action potentials and postsynaptic potentials to the evoked potential. Adrian & Matthews (1934) considered action potentials to form the basis of the evoked potential. Likewise Amassian (1953) found that the surface positive wave was associated with bursts of unitary activity deep in the cortex. Holmes & Short (1970) have also observed units, deep in the cortex, which responded with a latent period similar to that of the surface positive wave. This unitary activity has been shown, by histological identification, to originate in pyramidal cells. The simultaneous stimulation of points on the

7.

contralateral cortex and forepaw of an anaesthetised rat evoked a surface positive cortical wave, which was smaller in amplitude than the sum of the individual responses; the deficit was confined to the second, larger positive wave (Carter, Holmes & Short, 1969b). Holmes & Short (1969a) have found a similar occlusion at the unitary level, suggesting that action potentials may play an important part in the production of surface positive waves.

The observations just cited all suggest action potentials as the origin of mass potentials. However, some authors consider action potentials to be an unlikely source. They argue that action potentials of 1 msec duration could not produce evoked potentials of 10-100 msec duration. Humphrey (1968) considered that the antidromically evoked discharge of a pyramidal tract neuron contributed little to the surface deflexions, most of which came from postsynaptic potentials. The evidence for this came from the calculated extracellular voltages resulting from a spike and an inhibitory postsynaptic potential, which were separable in time, in a model pyramidal cell.

Humphrey concluded that extracellular potentials resulting from an IPSP were larger, at a distance from the soma, than the corresponding potentials from a spike.

The most numerous cells in the cerebral cortex are the pyramidal, stellate and glial cells. Both glial and stellate cells are irregularly orientated within the cortex (Jones & Powell, 1970a), and when several of these cells are excited, their electric fields are likely to cancel. On the other hand, apical dendrites and axons of pyramidal cells lie on a straight line parallel with each other (Scholl, 1956; Jones & Powell, 1970a). Hence similar electrical changes in neighbouring cells produce extracellular currents which will sum.

Holmes & Houchin (1967) constructed the voltage and current fields which would be anticipated when a pyramidal cell body was depolarised. At rest the net current flow across the membrane of a neuron is zero and no extracellular current field is generated. When a portion of the membrane is depolarised e.g. by the arrival of an afferent volley, then extracellular current flows. The geometrical configuration of a neuron has a profound effect on the extracellular current which flows. Fig. 1 shows the extracellular

Fig. 1. The theoretically calculated extracellular field generated by the depolarisation of a pyramidal cell body and its basal dendrites in layer 4 of the rat cortex. Arrows indicate the flow of positive current (continuous lines). Each dashed line joins points of equal voltage numbered on an arbitrary scale. The density of the flow lines indicates the density of the field. Close to the neurone itself the field is very dense and for the sake of clarity the electric field in this region is omitted.

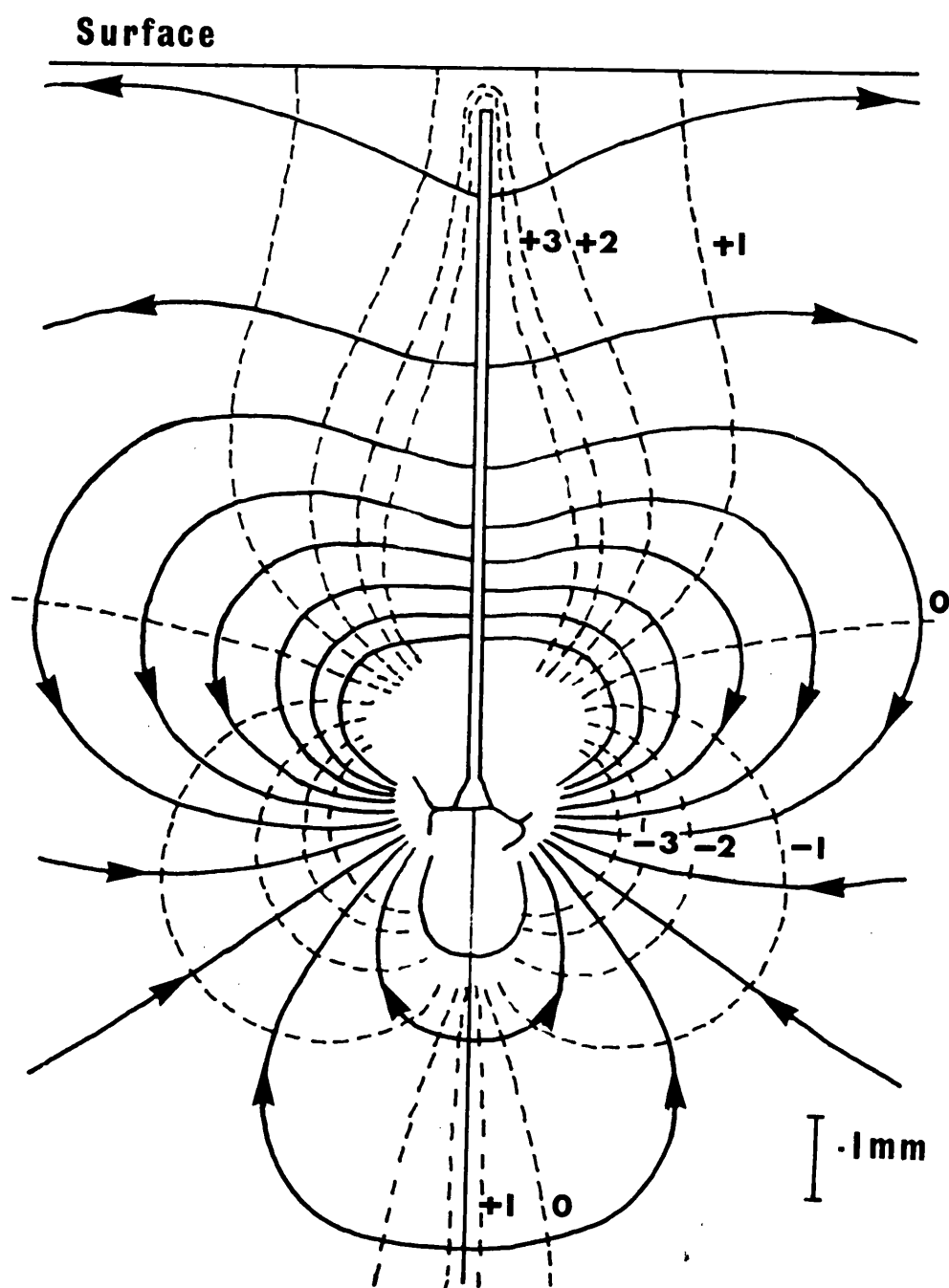


Fig. 1

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voltage and current fields generated by the depolarisation of the cell body of a pyramidal cell in layer 4 of the cortex (from Holmes & Houchin, 1967). The arrows, in this and subsequent field diagrams, indicate the flow of positive current and each dashed line joins points of equal voltage; these voltage contour lines are numbered on an arbitrary scale. The depolarisation produces a negativity which is greatest close to the depolarised region and a positive potential, of smaller amplitude, at the cortical surface. A small positivity is also seen deep to the region of depolarisation.

Since depolarisation in the region of the cell body of a pyramidal cell produces a widespread extracellular voltage field and since similar changes in neighbouring cells produce extracellular currents which sum, the arrangement of pyramidal cells in the cortex is favourable for the generation of mass cortical potentials.

From a consideration of the effects of membrane current in a pyramidal cell, it is also to be expected that hyperpolarisation of a superficial region of the neuron membrane would produce a surface positivity (Fig. 2).

Fig. 2. The extracellular field generated by the hyperpolarisation of a superficial region of the apical dendrite of a pyramidal cell. The symbols used are the same as in Fig. 1.

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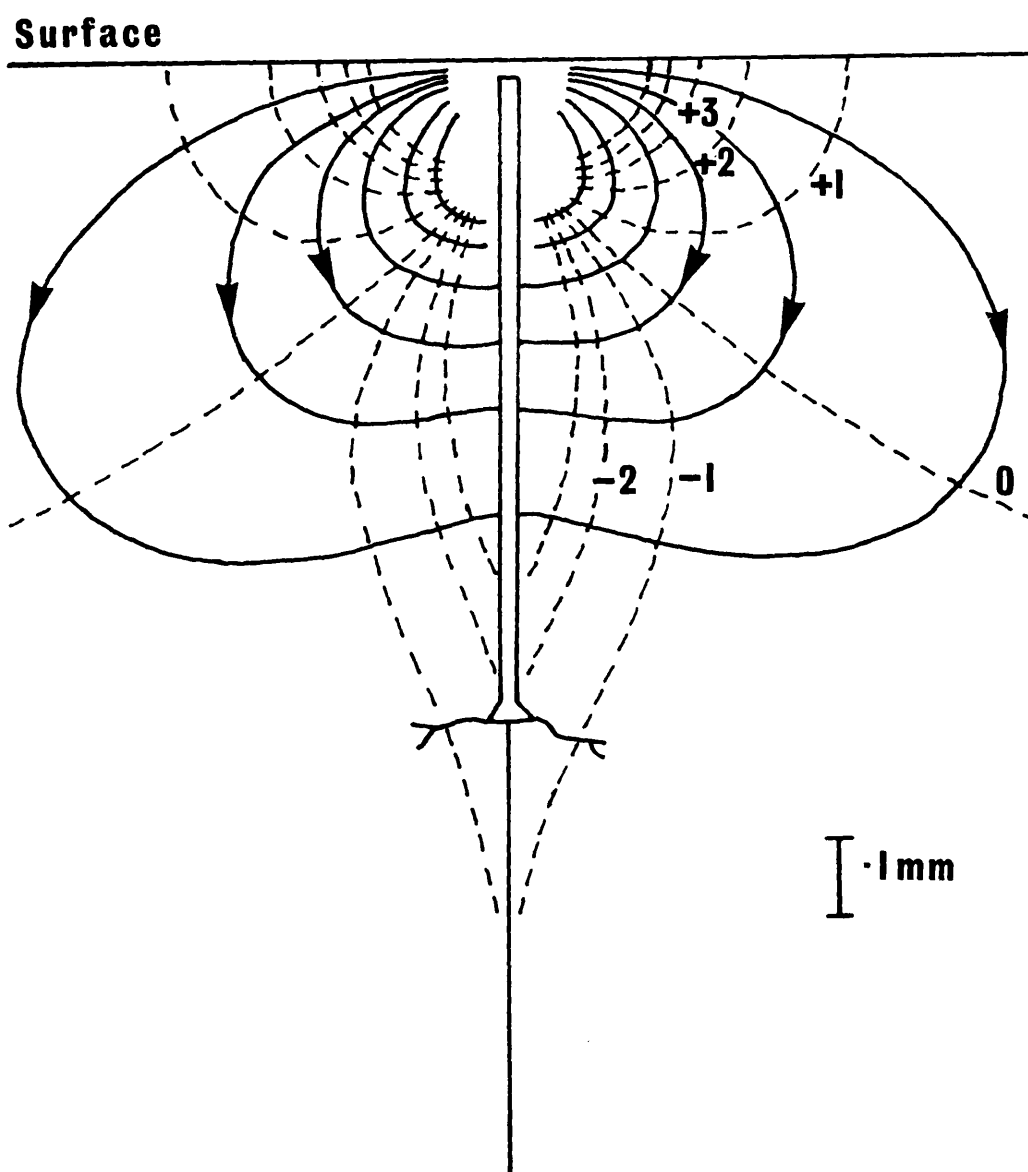


Fig. 2

12.

A large positivity would be seen close to the region of hyperpolarisation and a smaller negativity at a deeper level. However, extracellular records of mass responses to forepaw stimulation taken during the course of a micro-electrode penetration into the cortex of a rat have shown a surface positivity and subjacent to this a negativity of greater voltage at a depth of 0.6-1.4 mm (Carter, Holmes & Houchin, 1969a). This observation supports the hypothesis that the surface positive wave is a reflection of depolarisation at depth and not of hyperpolarisation near the surface. Histology adds further evidence, for the cortical afferent fibres from the thalamus end in layers 3 and 4 of the cortex (Lorente de Nó, 1943; Jones & Powell, 1970b). Impulses in such fibres would synaptically affect cells and basal dendrites in these layers; synaptic depolarisation would give a sink at relatively deep levels of the cortex and inactive apical dendrites would constitute the source.

The same hypothesis can be applied to the surface positive wave recorded after stimulation of the contralateral cortex. Thus Perl & Whitlock (1955) recorded a

large negativity, in response to contra-cortical stimulation in the cat, at a depth of 1.8 mm in the cortex; on the surface, they recorded a pure positivity. Nauta (1954) observed that after a contra-cortical lesion in the cat, degeneration occurred at a depth of 1.8 mm, suggesting that the callosal afferent fibres terminate there. A section of the present work is devoted to elucidating further the mechanisms involved in the surface response to contra-cortical stimulation.

Unlike the rat, in the cat there is a region of cerebral cortex in which an initially negative surface wave is consistently found in response to stimulation of the contralateral forepaw (Malcolm & Darian-Smith, 1958; Whitehorn, Morse & Towe, 1969). On theoretical grounds it may be postulated that this wave is the reflection of either a hyperpolarisation of deep cortical elements or a depolarisation of superficial elements. In the first case one would expect to find a region of positivity deep in the cortex during a micro-electrode penetration; in the second case a superficial pocket of negativity should be observed. Another possibility for the appearance of

a surface negative wave is the effect that the convolutions of the cat's cortex may exert. It is the intention of this work to attempt to provide an explanation for the initial negativity observed at certain surface regions of the cat cerebral cortex, in response to contralateral forepaw stimulation.

The physiological information at present available is insufficient to decide on the relative importance of the nature of the cellular activity which generates mass potentials. Emphasis is therefore laid on the site, rather than the nature, of the cellular activity responsible for mass potentials.

Potential evoked from cortex by peripheral stimulation: cat

Adrian (1940) observed that, when the periphery of an animal was stimulated, an electrical deflexion could be recorded from the surface of the contralateral cerebral cortex. He also observed that stimulation of different points on the periphery gave responses at different points on the cortex. In addition, he noted that tactile stimuli applied to the forepaw of the cat, anaesthetised with dial or chloralose, evoked electrical responses on the

15.

surface of the contralateral cortex in two discrete areas. The main sensory receiving area for the forepaw was found around the coronal sulcus and the second region was situated in the anterior part of the ectosylvian gyrus. The two were separated by the region for the face; this region was situated in the anterior part of the suprasylvian gyrus. Figure 3 shows a lateral view of the left cerebral hemisphere of the cat, with the sulci drawn and named. Adrian (1941) did not observe this double representation in the dog or monkey and he considered that it may be related to the special importance of the claws in cats.

Similar observations on the subject were made by Marshall, Woolsey & Bard (1941) who used small discrete tactile stimulation (hair displacement by means of a brush). Working on cats under nembutal anaesthesia they stimulated the dorsum of the contralateral forepaw and found that positive-going responses of large amplitude (0.1 mV) were evoked at three separate areas on the surface of the cortex. Two of these areas corresponded with those originally observed by Adrian (1940); the third area was situated at the anterior end of the lateral sulcus.

Fig. 3. Lateral view of cat left cerebral hemisphere showing sulci. Cr.-cruciate; Co.- coronal; A.- ansate; L.- lateral; Ss.- suprasylvian; E.- ectosylvian sulci respectively.

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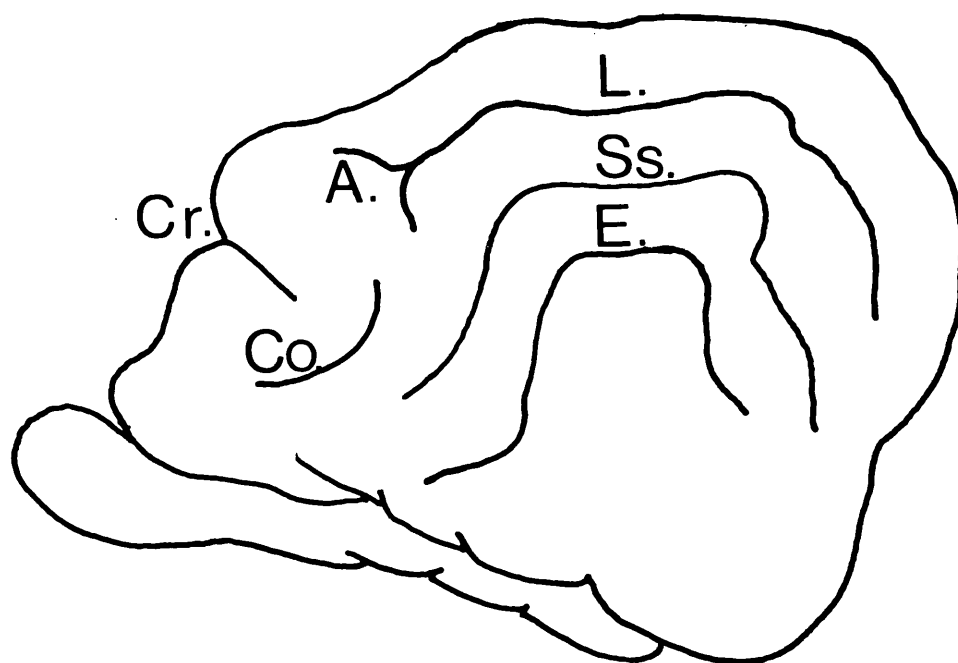


Fig. 3

17.

Adrian (1941) however, could not find this triple cortical representation of the forepaw and thought it doubtful if a single receptor sent impulses to more than one region in the cortex. When he stimulated very small regions of the forepaw he found that each stimulus elicited a response at a single point on the cortex. For instance he found that stimulating the dorsal side of the digits evoked a response near the coronal sulcus whereas stimulation of the ventral side evoked a response in the anterior end of the ectosylvian gyrus approximately 5 mm away. Impulses reached both regions, however, when the claws were tapped; in this circumstance toe pads, hairs and joints may be stimulated.

Woolsey and his co-workers produced corroborative evidence for the existence of dual somato-sensory, visual and auditory cortical areas in primates (Woolsey, 1944), cats (Woolsey, 1947) and rabbits (Woolsey & Wang, 1945). In his review of the subject, Woolsey (1947) used the terms somatic areas I and II (SI & SII) to describe the main and second regions of Adrian (1940).

The multiple nature of the cortical receiving area

in the cat was also observed by Malcolm & Darian-Smith (1958) using tactile stimulation of the dorsum of the contralateral forepaw. With cats under pentobarbitone sodium anaesthesia they were able to record positive-going responses confined to the classical areas SI and SII. However with chloralose anaesthesia they noticed that the responses were more widespread. Outside SI and SII, certain regions (in the lateral and suprasylvian gyri and in the medial end of the cruciate sulcus) showed a response which was initially negative. They illustrated the multiple nature of the projection to the cortex by plotting the latent period of the start of the response at different regions on the cortex; minima occurred in the three regions described by Marshall et al. (1941). These observations were confirmed by Darian-Smith, Isbister, Mok & Yokota (1966), also using cats under barbiturate anaesthesia.

The fundamental question still remains, however, as to whether the cerebral cortex has a multiple representation of a single receptor. Marshall et al. (1941), Woolsey and his co-workers and Malcolm & Darian-Smith (1958) consider

that there are multiple sensory projections. However, unless one stimulates a single receptor or a single afferent fibre and records responses in more than one area of the cortex, one cannot discredit Adrian's suggestion (1941), that a single receptor sends impulses to only one point on the cortex.

The response that Adrian (1941) recorded was not significantly affected by the type of anaesthetic used (dial, chloralose and urethane) as long as the animal was under moderately deep anaesthesia. The evoked potential under barbiturate anaesthesia was usually positive-going, but Marshall et al. (1941) noticed, in the lateral gyrus and medial post-cruciate cortex, some waves which were initially negative in cats under chloralose anaesthesia. Other authors have also observed a negative wave in response to peripheral stimulation. Thus stimulation of the superficial radial nerve in the contralateral forepaw gave initially negative responses medial to SI, (Oscarsson, Rosén & Sulg, 1963). Whitehorn et al. (1969) reported an initially negative wave in the post-cruciate area in response to contralateral forepaw stimulation. A widespread

cortical wave of initial negativity was also observed by Mickle & Ades (1953) in response to auditory stimulation.

Amassian (1954) used the term "association" responses for those potentials evoked by peripheral stimulation, but recorded outside the classical areas SI and SII. The areas in which these responses were found he designated "association" areas. In animals under chloralose anaesthesia he found association responses to be variable, often initially negative and to have a longer latent period of onset than the responses evoked in SI and SII. Association responses to somatic stimulation could be elicited in the cat from the anterior lateral gyrus; here responses could be evoked by stimuli applied to any paw (fore or hind).

Albe-Fessard & Rougeul (1958) also described somatic sensory association responses in the cat, with overlapping receptor fields. Subsequently Thompson, Johnson & Hoopes (1963) found four association areas which showed similar responses to all modalities of forepaw stimulation. These were the medial cruciate, anterior lateral and suprasylvian gyri and the pericruciate classical motor area. Thompson et al. (1963) also observed the variability of association

responses and quoted a standard deviation of the amplitude of association responses of 50% or more, in contrast to responses in SI and SII where it is about 10%. They also observed a zero correlation between the responses recorded simultaneously in the association and in the primary somatic sensory areas, for all stimulus modalities.

Morse & Towe (1964) and Thompson et al. (1963), provided evidence which suggested that association responses are not due to cortico-cortical relays from SI and SII, as ablation of SI and SII had no effect on the responses found in the association areas. Similar observations were noted by Darian-Smith et al. (1966) with local cooling of SI and SII.

The latent periods of the response in the somatic sensory areas SI, SII and the third region at the anterior end of the lateral sulcus have been measured by various experimenters. Malcolm & Darian-Smith (1958) observed that the latent period was different for the three regions of the cortex. In cats under chloralose anaesthesia, they quoted latent periods of SI = 10.1 msec; SII = 8.5 msec and their third area at the anterior end of the lateral

sulcus also as 8.5 msec. However, in the diagrams published by Marshall et al. (1941) and Darian-Smith et al. (1966) the latent period is similar for the three regions described; in the diagrams of Marshall et al. the latent period in response to a stimulus applied to the forepaw is approximately 14 msec.

The latent period of the responses evoked in the association areas is longer than in SI and SII according to Thompson et al. (1963). In their diagrams, these responses have a latent period of approximately 30 msec.

Using cats under barbiturate anaesthesia, Oscarsson & Rosén (1963) studied the afferent pathways concerned in the transmission of information from the contralateral forepaw to the cerebral cortex via the thalamus and the part of the cortex to which the different pathways projected. They found that stimulation of Group I muscle afferents in the contralateral fore-limb evoked responses in the post-cruciate cortex in the rostral region of SI. By placing lesions in different parts of the afferent projections, they found the pathway responsible was the dorsal funiculus-medial lemniscus system. Stimulation of

cutaneous afferents, however, such as those of the superficial radial nerve, evoked potentials with maximum amplitude in both somatic areas I and II, as well as in a region which corresponds with the classical motor region; this is rostral to SI. The latent period was the same for the three areas. There were two spinal pathways for the cutaneous afferents, the first being the dorsal funiculus route which activated most effectively the caudal region of SI and the second was the spino-cervical tract activating the motor area rostral to SI (Oscarsson & Rosén, 1966). From a study of the effects of electrolytic lesions of the thalamus, it was observed that the nucleus responsible for relaying forelimb afferent impulses to SI was the ventralis posterolateralis nucleus of the ventro-basal complex (Hand & Morrison, 1970).

Landgren, Silfvenius & Wolsk (1967) have reported electrophysiological evidence that muscle afferents project to the anterior end of the suprasylvian gyrus (SII), with group I afferents projecting to the upper limb and groups II and III to the lower limb of the suprasylvian sulcus. Using degeneration studies, DeVito (1967) also showed an

anatomical pathway from the posterior nuclear group of the thalamus to SII.

There is less evidence concerning the projection pathways to the association areas. Albe-Fessard & Rougeul (1958) have produced evidence to suggest that there is a pathway to these areas which passes through the medium centranum of the thalamus.

Unitary responses to stimulation of the contralateral forepaw or forepaw nerve have been observed in SI (Amassian & Thomas, 1952; Perl & Whitlock, 1955; Mountcastle, Davies & Berman, 1957). Mountcastle (1957) observed that stimulation of a small area of the contralateral forepaw evoked discharges in a small vertical column of cells within the cortex of SI. Likewise Hubel & Wiesel (1962) have observed that the visual cortex of cats was divisible into discrete columns, all the cells in one column responding to similarly orientated bars of light.

Unitary discharges, evoked by contralateral forepaw stimulation, have been observed at a depth of 1.0-1.5 mm in the cortex of SII (Amassian & Thomas, 1952). Some columnar organisation of evoked units in SII has been

noticed (Carreras & Andersson, 1963). The majority of units were modality and place specific but some were non-specific, responding to stimulation of many parts of the body.

Units, evoked by stimulation of the skin and exposed nerves of the contralateral forepaw, have also been recorded in the somatic association areas, (Amassian, 1954). The latent period of these units was long and variable (28-100 msec); these units often responded to stimulation of all four limbs.

Thus there is general agreement about the form of responses evoked, in both the primary somatic sensory areas and association areas, by contralateral forepaw stimulation and also about the afferent pathways to these areas. The early mass potential, elicited by contralateral forepaw stimulation from the surface of the cat cortex, consists of a positive-negative deflexion in SI, a pure positive deflexion in SII and an initially negative wave seen in the region medial to SI (the post-cruciate gyrus). Evoked unitary activity has been observed in SI (Mountcastle, 1957) and in SII (Carreras & Andersson, 1963). In

the present work, an attempt has been made, by means of micro-electrode penetrations into the cortex of SI and its surrounding regions, to elucidate the origin of the various waves and, in particular, the negativity recorded from the surface of the cat cerebral cortex in response to contralateral forepaw stimulation.

Potential evoked from cortex by peripheral stimulation:
rat, rabbit and coypu

In a rat anaesthetised with urethane, the cerebral response to contralateral forepaw stimulation is variable and depends upon the state of spontaneous activity of the cortex at the instant of arrival of the afferent volley (Bindman, Lippold & Redfearn, 1964). In the small region where the latent period of onset is a minimum (the forepaw primary receiving area of Dawson & Holmes 1966) the response is usually a small positive wave, followed by a larger positive or negative wave (Ennever, 1969; Holmes & Short, 1969a). The initial positive wave is seen only in the primary receiving area (Holmes & Short 1970). The second larger, positive wave, with a peak about 11 msec

after the stimulus, can also be recorded over an extensive area of the cortical surface (Carter et al. 1969a); this wave is only seen if the cortex is quiet when the afferent volley arrives. The later negative component of the response of initially active cortex is confined to the primary receiving area (Carter et al. 1969a).

Each component of the waveform so far described is coincident with negativity in regions of the subjacent cortex (Carter et al. 1969a). The initial positivity is associated with a region of negative potential at depths between 0.6 and 1.4 mm. Underlying the whole of the large area of cortex which shows the surface positivity of the response in quiescent cortex, there is an intense negativity which can be recorded at a depth of about 1.2 mm. The late negative wave seen at the surface in active cortex is associated with a region of intense negativity in more superficial layers of the cortex (0.5 mm) and can only be recorded in the primary receiving area. According to Carter et al. (1969a), these observations are compatible with the following hypothesis. In active cortex, the forepaw response is confined to a small

cylinder of nerve elements responsible for the initial positive wave, together with a superficially situated disk of elements responsible for the negative wave. In quiescent cortex, these same elements respond to stimulation in a similar way, but in addition, more deeply situated elements over a wider area of cortex are involved to give the widespread late surface positive wave.

In support of this hypothesis the temporal and spatial distribution of evoked extracellular unitary discharges are highly correlated with the occurrence of regions of mass negativity. For example, a group of cells with a latent period of about 11 msec and at a depth of around 1.2 mm, responded only if contralateral forepaw stimuli were given when the cortex was quiet (Carter et al. 1969a).

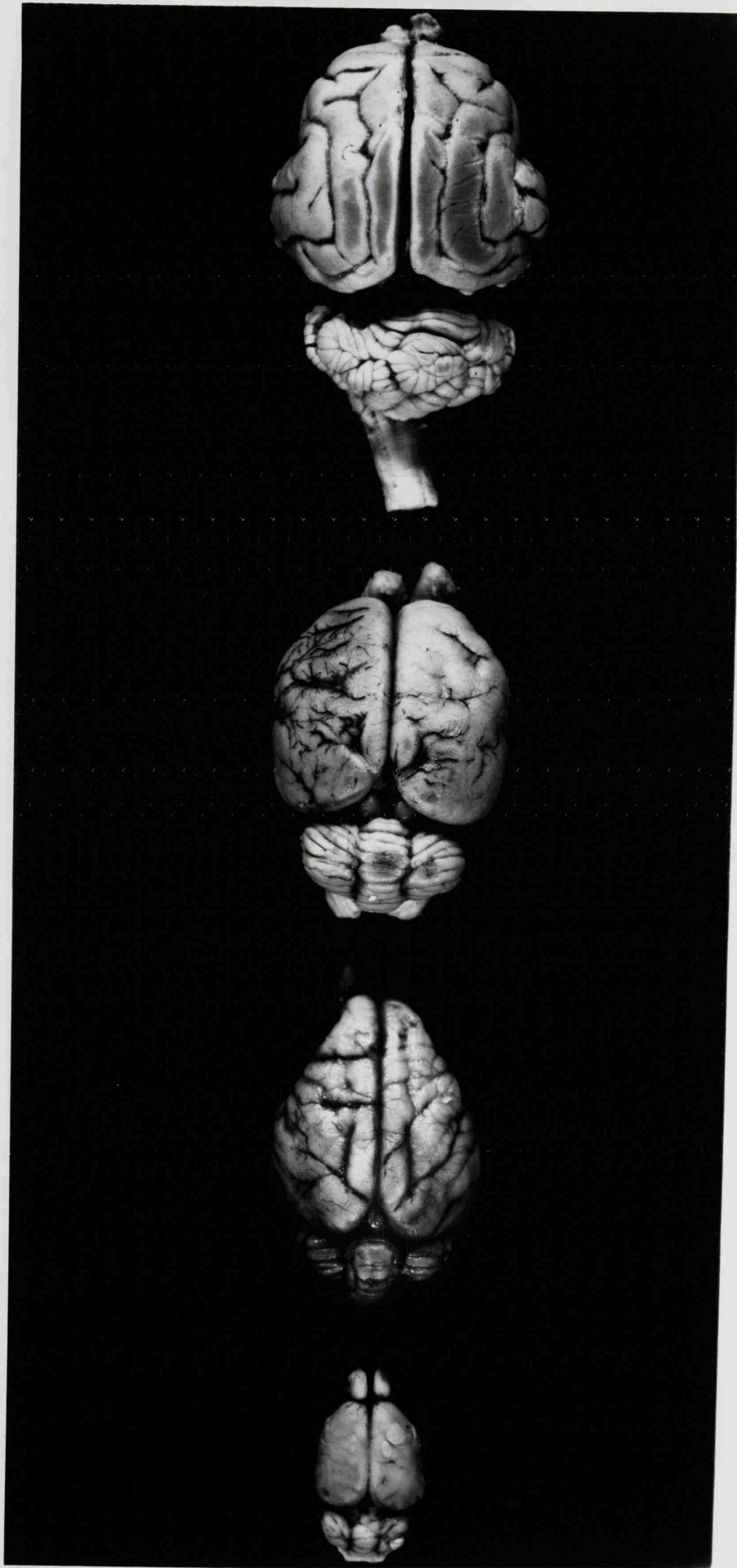
In the rabbit anaesthetised with barbiturate, Woolsey & Wang (1945) found two discrete areas responding to forepaw stimulation, which they named somatic areas I and II. Chang (1955) and Angel (1967) both described the response at the surface as a large positive wave followed by a negative deflexion. Angel (1967) pointed out that the negative deflexion was larger when the animal was

lightly anaesthetised by comparison with the response under deep anaesthesia. In the former condition the cortex was more spontaneously active than in deep anaesthesia and these observations were therefore similar to those on the responses recorded from the rat.

Both the rat and rabbit have flat cortical surfaces (termed Lissencephalic by Ariëns Kappers, Huber & Crosby, 1963). The cat, however, has a convoluted cortex (Gyr-encephalic). One difference between the responses evoked by contralateral forepaw stimulation in the cat and the lissencephalic species is the initially negative surface response which can be recorded in the cat. This difference may be due to one or more of many factors e.g. the difference in number or type of sensory projections to the cortex, or to the difference in architecture or size of the cortices.

The effect of brain size on the form of response evoked by stimulation of the contralateral forepaw is investigated by a comparative study of the rat, rabbit and cat with the coypu. This last mentioned animal is a large rodent, with a brain similar in size to that of the cat, but with a flat cortex like the rat (see Fig. 4).

Fig. 4. Dorsal view of the brain surfaces of the various species studied in this work. Only the cat (top brain) has a deeply convoluted cortex. Next to the cat brain is the coypu, followed by rabbit and rat. Calibration mark - 1 cm.



I

Fig. 4

Useful information about the origin of cerebral evoked potentials has been gained by the study of the responses recorded at depths in the cortex of the rat. (Calvet, Calvet & Scherrer, 1964; Holmes & Houchin, 1967). This method has been applied, in the present work, to elucidating the origin of these mass potentials in rabbits and coypu.

Potential evoked from cortex by stimulation of the contralateral cortex

The cerebral hemispheres are connected by commissures, the largest of which in the species considered is the corpus callosum. Most authors agree from histological evidence that pyramidal cells located in layers 5 and 6 of the cerebral cortex are the origin of callosal fibres (Curtis, 1940b, and Chang, 1953a in the cat; Pines & Maiman, 1939 in dogs and humans). The site of termination of callosal fibres, however, in the opposite hemisphere is still in doubt. Chang (1953a) and Curtis (1940b) suggested that they ended in superficial layers of the cortex, whilst Nauta (1954) considered that they ended

in the deeper layers and Jacobson (1965) found callosal endings in all but the most superficial layers in the rat cortex. Nauta (1954) noted that callosal fibres ended mainly on axons or dendrites and very rarely on the soma. This observation was confirmed by Globus & Schiebel (1966 & 1967) using a technique to measure the loss of dendritic spines after sectioning the corpus callosum; they found that the fibres ended on the oblique branches of the pyramidal cell dendrites.

In the monkey, Jones & Powell (1969) found no histological evidence of callosal connections of regions of cortex representing the distal parts of the limbs. They also found that, in monkeys, callosal fibres from somatic area I entered the contralateral cortex vertically. This finding suggests a precise organisation of these fibres with respect to the topographic and functional properties of individual cell columns. Fibres from somatic area II, however, entered the cortex obliquely, which suggests a less discrete organisation. These anatomical observations, together with electrophysiological observations of the receptive fields to peripheral stimulation (Woolsey, 1947),

reflect the discrete topography of SI and the more diffuse nature of SII.

In the rat, Jacobson (1965) has produced anatomical evidence of callosal fibres connecting somatosensory areas. Evidence for the callosal connection of distal regions of the limbs has been furnished by electrophysiological observations. Thus in rats (Holmes & Short, 1970) and cats (Perl & Whitlock, 1955), electrical potentials could be evoked in the cerebral cortex, by stimulation of that area of the opposite hemisphere responding to forepaw stimulation; the recording site was homotopic to the site of stimulation. Direct electrical stimulation of a point on the cerebral cortex evoked a positive - negative wave, which was largest in that region of contralateral cortex homotopic to the point of stimulation (Carter, et al. 1969b in rats; Curtis, 1940a and Chang, 1953a, in cats). The latent period of onset of the response was 3.5-5 msec in rats anaesthetised with urethane (Carter et al. 1969b) and about 4 msec in cats anaesthetised with barbiturate (Chang, 1953a).

The latent period of contralateral stimulation is

long enough for the volley to travel by a route other than the corpus callosum, e.g. via the thalamus to the contralateral cortex. Such routes exist, as was shown by Girardo & Purpura (1958), who stimulated the corpus callosum and recorded discharges, at a latent period of 2.5 msec, at the mid olivary level. However the response to contralateral cortical stimulation was abolished if the corpus callosum was sectioned in a line directly between the stimulating and recording electrodes; lesions placed either side of this line had no effect on the response (Curtis, 1940a in cats; Holmes & Short, 1970 in rats). This evidence indicates that the response is mediated via the corpus callosum.

Direct electrical stimulation of the corpus callosum, in rats anaesthetised with urethane, evoked potentials similar in form to those evoked by contralateral cortical stimulation, but with a shorter latent period of 2 msec. (Carter et al. 1969b). Similar observations were noted by Chang (1953a) in cats anaesthetised with pentobarbitone sodium. The difference in latent period between the responses to contra-cortical and callosal stimulation

was thought to be due to the time taken for the initiation of action potentials in the stimulated cortex (Holmes & Short, 1970).

In his analysis of the potential evoked by contralateral cortical stimulation in cats under barbiturate anaesthesia, Curtis (1940b) applied drugs locally to the recording site. With nembutal the amplitude of the early positive wave increased and the later negative wave decreased in amplitude; strychnine however, potentiated the later negative wave. The two waves were thus distinct. Curtis (1940b) observed that certain narcotics reduced the amplitude of the negative wave. Chang (1953a) found that surface application of novocaine was effective immediately and deduced that the elements responsible for the negative wave were situated in the superficial layers of the cortex.

The delivery of two closely timed stimuli to different parts of the body, has been used by several authors to demonstrate the presence or absence of elements which are influenced by both stimuli (Chang, 1953b; Perl & Whitlock, 1955; Holmes & Short, 1970). Thus Chang (1953b)

found that the surface positive wave evoked by auditory stimulation was severely inhibited by a preceding callosal volley and concluded that common elements were involved. Chang (1950; 1953b) found that callosal afferents terminated in the superficial layers and thalamic afferents arrived at the fourth layer of the cortex; he concluded that the common elements must be predominantly those pyramidal cells which have apical dendrites in the first layer and cell bodies at deeper levels in the cortex (Chang, 1953b) and it is here that the inhibitory influences occur. Perl & Whitlock (1955), however, considered that both callosal and thalamo-cortical fibres terminated in deeper layers of the cortex. This would also provide an anatomical explanation for the observed ability of callosal volleys to drive cortical neurons also activated by thalamic projections (Perl & Whitlock, 1955; Holmes & Short, 1969a).

Simultaneous stimulation of contralateral forepaw and cortex evoked a positive wave at the surface and a negative wave at a depth of 1-1.4 mm (Holmes & Short 1969b). However, the response to simultaneous stimulation

of the two sites was smaller than the sum of the responses to the stimuli given separately and the deficit was confined to the second positive wave of the forepaw response. The occlusion evident in the mass response is paralleled by an occlusion at the cellular level (Holmes & Short, 1969a). Units were found, also at a depth of 1-1.4 mm, which showed a single spike in response to either contralateral cortical or contralateral forepaw stimuli with a latent period of 3-9 and 10-13 msec respectively. These units also showed single spike responses to stimuli applied simultaneously to the two sites. Unitary discharges responding to contralateral cortical stimulation have also been observed by Perl & Whitlock (1955) at a depth around 1.2 mm in the cat cortex; more superficial units were also found, but they were not stable enough to allow investigation.

As already mentioned, in rats anaesthetised with urethane, certain components of the cortical response to a forepaw stimulus are affected by the presence of spontaneous cortical activity (Holmes & Short, 1969a). Evidence has also been put forward correlating certain

components of the forepaw response with regions of negativity and the discharge of unitary potentials in the subjacent cortex (Carter et al. 1969a). In the present work, an investigation has been made of the relationship between the mass and unitary responses to stimulation of the contralateral cortex and the spontaneous cortical activity.

CHAPTER II

MATERIALS AND METHODS

Anaesthetics

Anaesthesia was induced in rats and coypu with ethyl-chloride vapour. This was followed by an intraperitoneal injection of urethane. In the rabbit, urethane solution was injected, over a period of ten minutes, into the marginal ear vein. Intraperitoneal injection of urethane was used in cats. In all species the initial dosage was 2 g.urethane/kg body weight; it was administered at a concentration of 25% in 0.9% saline. Three experiments were performed on cats anaesthetised with sodium pentobarbitone injected into the saphenous vein after ether induction; the dosage was 50 mg/kg body weight.

In all animals supplementary doses of anaesthetic were given, sufficient to abolish the withdrawal reflex produced by a hard pinch applied to the hind paw.

Surgery

A tracheal cannula was inserted and mucus secretions sucked out periodically. The rectal temperature was monitored and kept as close to 38°C as possible by means

of a water heated pad placed under the animal.

Since electrophysiological recordings required a stable brain, the head was immobilized. In the case of the rat, the head was clamped at three points; (i) by two conical bars, one inserted into each external auditory meatus and (ii) by a nose clamp (Dawson & Holmes 1966).

A similar head holder was used for the other species.

Two bars, both grooved at one end, fitted over the zygomatic arches and a third bar supported the lower jaw. The nose clamp was similar to that used for the rat.

The scalp was incised in the midline from the level of the eyes and back to the posterior margin of the skull. Some of the temporal muscle was removed and the periosteum scraped away. When a large craniotomy was needed a rectangular piece of bone, varying in size with the animal concerned, was drilled out with a flat fissure dental drill. When only a small craniotomy was needed, (e.g. in experiments involving stimulating or micro-electrode penetrations of the cortex) a small (2 mm) trephine drill was used. In all animals the craniotomy was made in the region of the forepaw receiving area of

the cortex. In the rat, the bony landmarks of the skull (Fig. 5) bore a fairly constant relationship to the area of cerebral cortex where the electrical response to contralateral forepaw stimulation had a minimum latent period (Dawson & Holmes, 1966). It was found, in the present work, that bony landmarks also bore a fairly constant relationship to the forepaw receiving area in the other species.

After removal of the bone, the dura mater was incised with a needle and reflected with fine forceps. The incised skin was sewn to a ring and paraffin, equilibrated with physiological saline at 37°C, was poured on the cortex.

Electrical stimulation

Except where otherwise stated, the stimulus consisted of a rectangular voltage pulse applied to the skin of the second and fourth digits, by means of curved needles inserted subcutaneously. The stimulus, varying between 30-80 V, with a duration of 0.5 msec, was delivered by a Devices isolated stimulator. The stimulus was usually

Fig. 5. Dorsal view of rat skull. Position of the craniotomy, used in the present experiments, is marked by the dashed line. F.- fronto-parietal suture.

42.

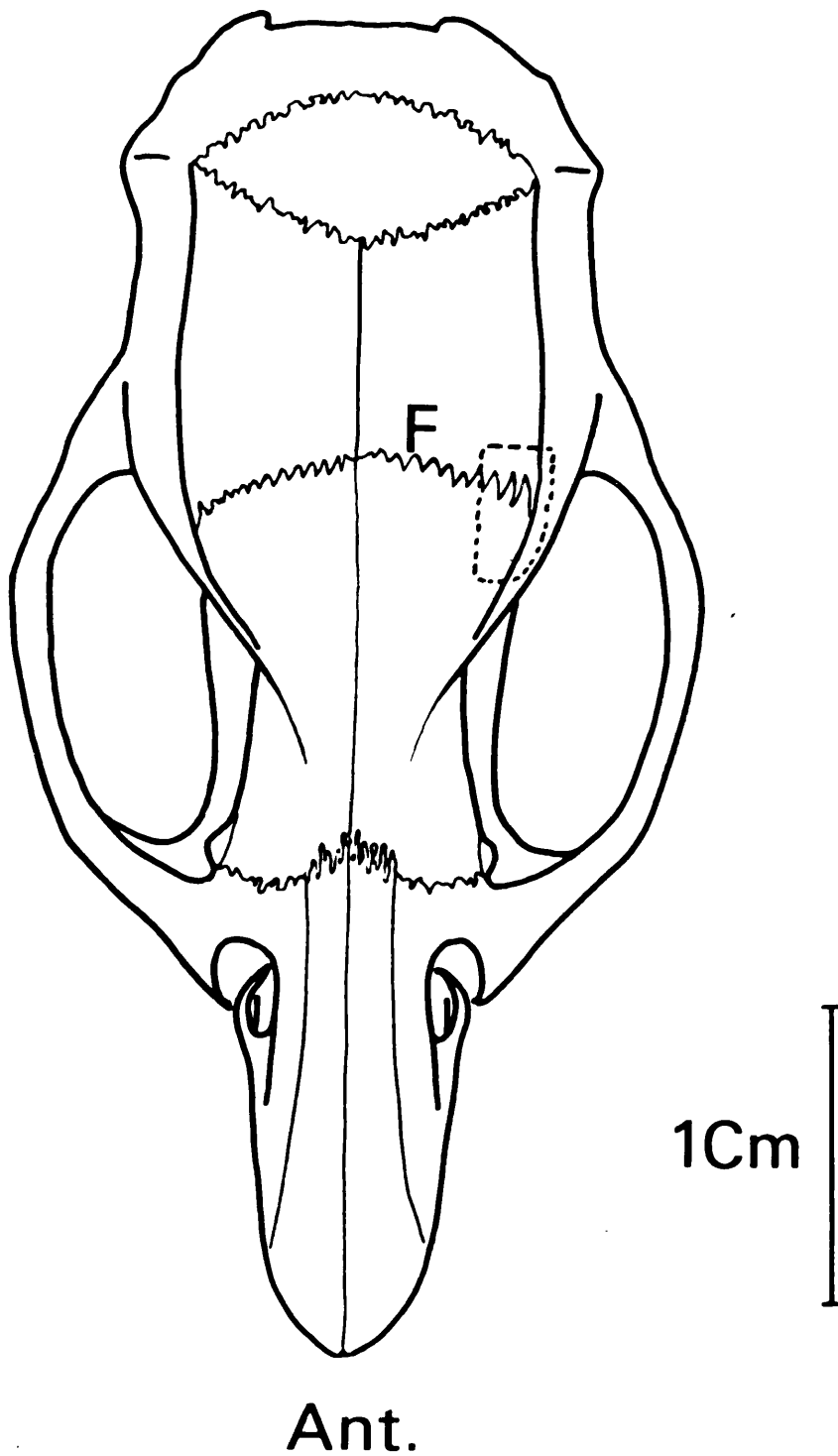


Fig. 5

just sub-liminal for the production of a flexion of the digits. The contralateral cortex was stimulated via a concentric stimulating electrode lying on the surface; this electrode consisted of a steel cylinder of 1.25 mm external diameter, insulated by portex tubing from a central stainless steel core of 0.4 mm diameter. The stimulus duration was 0.1 msec and the voltage used was from 10-20 V. The inner pole was negative with respect to the outer. Intra-cortical stimulation was achieved via a 3 M-NaCl filled micro-electrode, similar to those used for recording. Neither of these types of direct cortical stimulation produced any observable muscular contraction in the animal.

A Devices Digitimer was used to trigger the stimulators and oscilloscope time base and also to provide a time calibration. The stimuli were applied at 4 sec intervals unless otherwise stated.

Mechanical stimulation

This was achieved by means of a piezo-electric crystal. 1 msec pulses were applied to the crystal and

the voltage was such that a displacement of 2 mm occurred. A fine glass insulating rod with a beaded end, coupled the crystal to the animal's skin. The stimulus could just be discerned when applied to the finger of the experimenter.

Stimulus control

In rats under urethane anaesthesia, the corticogram shows bursts of spontaneous activity separated by periods of cortical quiescence (Bindman et al. 1964). In some experiments it was necessary to deliver stimuli only when the cortex was quiescent. For this purpose a system of electronics was made which triggered a stimulus only when the corticogram was quiet. When it was necessary to deliver stimuli during periods of cortical activity, the stimuli were triggered by hand. Another method of recording the responses to stimuli delivered during cortical activity was to precede the test stimulus by a conditioning stimulus applied to the contralateral forepaw (Houchin, 1969b). The test stimulus was delivered at least 100 msec afterwards. The oscilloscope was

triggered to display the response to the latter stimulus. A comparison of the response to contralateral cortical stimulation during hand selected and evoked activity is shown in Fig. 6. It can be seen that the two are similar.

Recording

A chlorided silver ball electrode, 0.5 mm in diameter, was used to record the slow mass potential waves at the surface of the cerebral cortex. Narishige or Baltimore stereotaxic manipulators clamped to the recording table were used to hold and position the electrodes.

Two types of micro-electrode were used to record both fast extracellular action potentials and slow mass activity at depth. The first type was made from Jencons glass (1.5 mm external and 0.75 mm internal diameter) drawn to a fine taper on a vertical Narishige electrode puller. The electrodes were then filled with 3 M sodium chloride solution by boiling under reduced pressure. The resistance of these electrodes was between 2-10 M Ω and their frequency response flat from D.C. to 10 KHz. A chlorided silver wire connected the saline of the

Fig. 6. Comparison of the response evoked at the cerebral cortex by contralateral cortical stimulation during evoked activity (upper trace) and spontaneous activity (lower trace) as described in the text. Both records show five superimposed transients. In this and subsequent figures, an upward deflexion indicates that the recording electrode has become positive with respect to a reference electrode lying on the skull.

46.

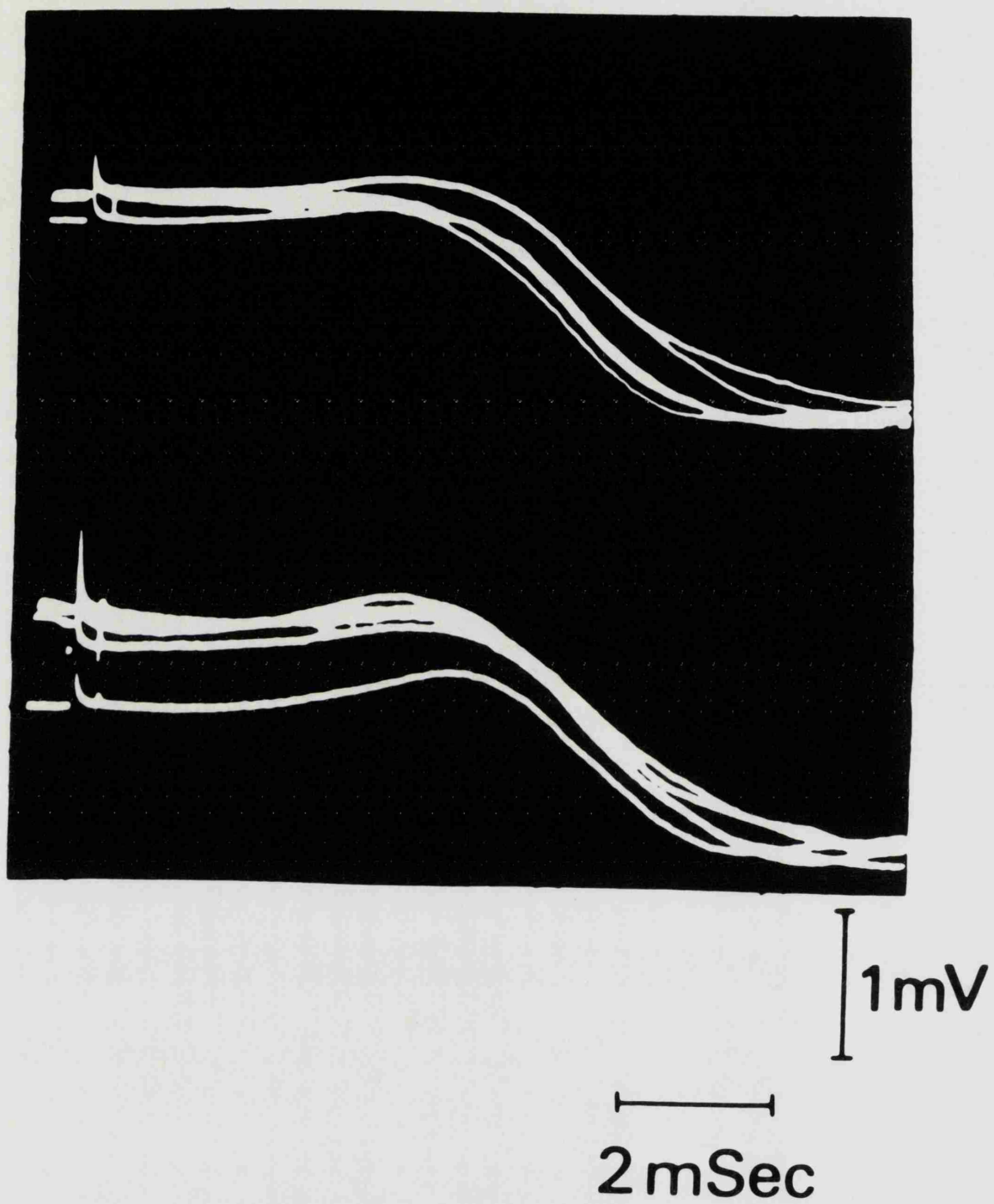


Fig. 6

electrode to a source follower, whose input resistance was 50 M Ω .

The second type of micro-electrode was a tungsten wire etched electrolytically in saturated potassium nitrate to a fine point (Hubel, 1957). All but a small area around the tip was then covered with an insulating varnish (Insl.-X). The electrodes were tested for resistance and insulation by Hubel's method (Hubel, 1957) and had a resistance of 0.2-1 M Ω at 1KHz. The noise level was consequently low, making them suitable for recording small extracellular discharges such as those seen at superficial depths in the cortex (Holmes & Houchin, 1966⁷; Block, 1968).

Amplification, processing and display

Conventional amplifying techniques were used. The characteristics of the recording apparatus are illustrated in Fig. 7. This shows the distortion introduced by the whole of the recording system when a rectangular voltage pulse of 1 mV amplitude and 10 msec duration was applied to the input of the source follower via a 1 M Ω resistance and displayed on the oscilloscope. The time constant of

Fig. 7. Characteristics of the recording apparatus.

A pulse of 1 mV was applied to the input of the source follower via a series resistance of 1 M Ω . The time scale is in msec.

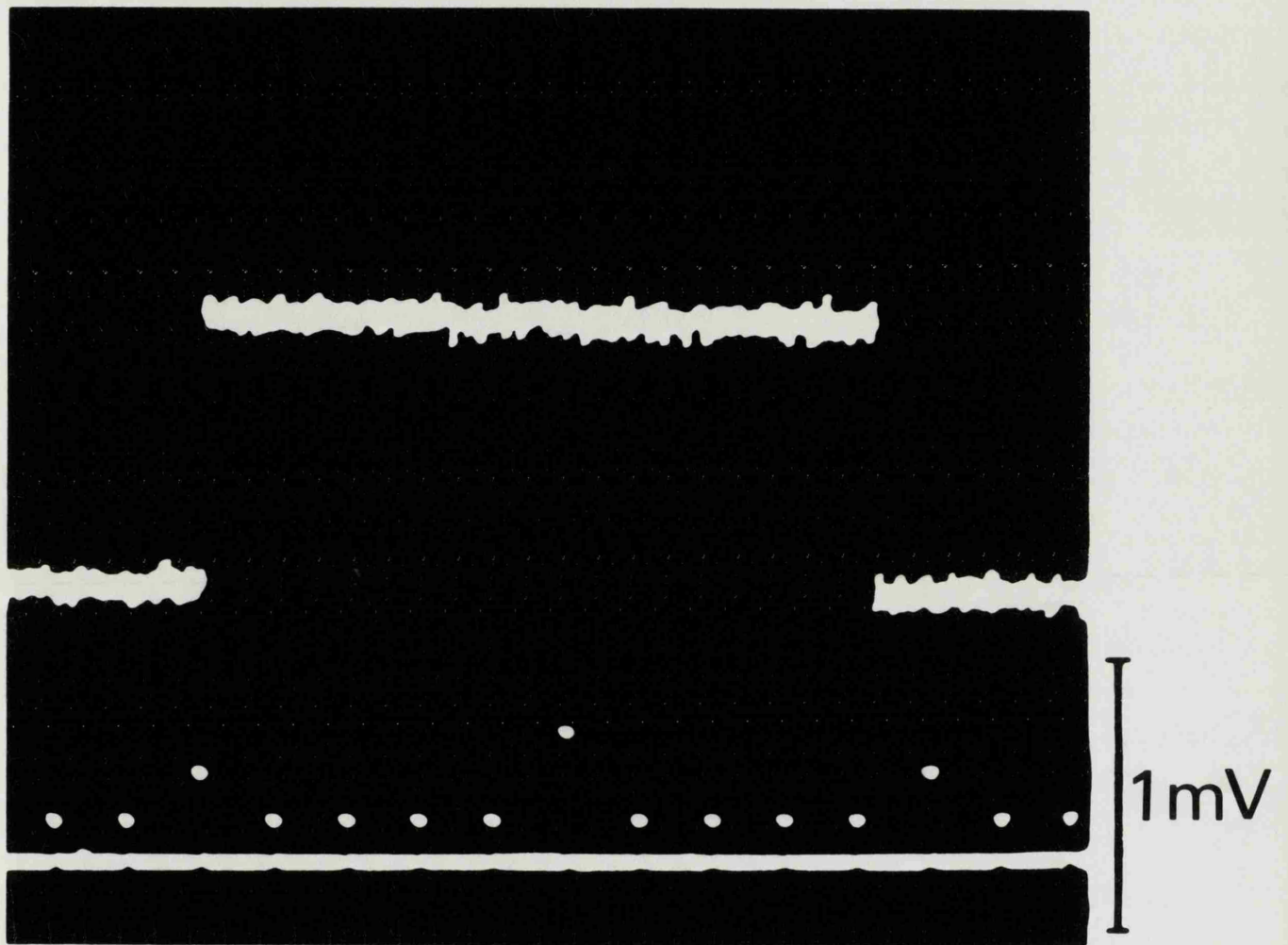


Fig. 7

decay was 200 msec. Records were photographed with an oscilloscope camera.

To keep the stimulus artefact within acceptable limits, all recordings were made differentially with reference to a second silver ball electrode placed on the skull. In the case of the rat the first 20 msec and in the other animals the first 40 msec only of the evoked response was usually observed. In all records, an upward deflexion indicates that the active electrode has become positive with respect to the indifferent electrode.

Some of the records are of individual responses. Others are sets of transients superimposed on film or drawn out on paper with the aid of an enlarger. Many of the records, however, are the digital average of a number of transients, usually 16, computed by a Data Laboratories Biomac 1000 computer. These averages were stored on paper tape and plotted out after the experiment on a Bryans X-Y plotter.

Electrode placement

Micro-electrode tracks were located histologically in the cortex by the method of Houchin (1969a). Formalin

fixation was carried out with the electrode in situ for about 12 hours. A block of tissue with four faces parallel to the electrode track was cut out with a needle inserted in the electrode holder. 20μ sections were cut on a Leitz freezing microtome, stained with Ehrlich's acid haematoxylin and eosin and mounted. In such sections, electrode tracks could be easily identified.

Shrinkage of the tissue during this treatment was kept to a minimum by using freezing microtomy and aqueous staining. The amount of shrinkage was tested by drawing around the enlarged images of the same section before and after staining; it was 5% or less.

The largest error in recording the depth was in the occasional dimpling of the cortex before the electrode penetrated it. On withdrawal of the electrode, the exact position at which contact with the cortex was lost was determined by the sudden increase in interference. The discrepancy in depth between the original zero on the manipulator and the zero on withdrawal was between 0 and 0.2 mm in the rat and between 0 and 0.4 mm in the larger animals. With electrodes left in the brain for fixing

purposes it was difficult to judge accurately the amount of dimpling and therefore to know the exact depth. However an experiment was undertaken illustrated in Fig. 8, to find out how much of an electrode track was identifiable. A glass micro-electrode was plunged vertically 5 mm into a cat brain. In the same coronal place a thicker stainless steel electrode was moved 5 mm lateral to the first and advanced into the brain at an angle of 45° . The second electrode was then pointing to the tip of the glass electrode. On fixing and sectioning it was clear that the glass electrode could be traced to within 0.2 mm of its tip. For the physiological experiments this error was ignored and the depth recorded by the manipulator was used. This amount of error was accepted by Perl & Whitlock (1954).

Experimental Stock

Males and females of all four species were used. The rats were an albino C.F.E. strain weighing 150-250 g. White rabbits varying from 2-4 kg and cats from 2-5 kg were used. Coypu were also used, ranging from 1.5-5 kg.

Fig. 8. Outline of a coronal section through part of the left cerebral hemisphere of a cat, showing the visible part of the electrode tip (T). The oblique, dashed line points to the calculated depth of 5 mm. (see text).

50.

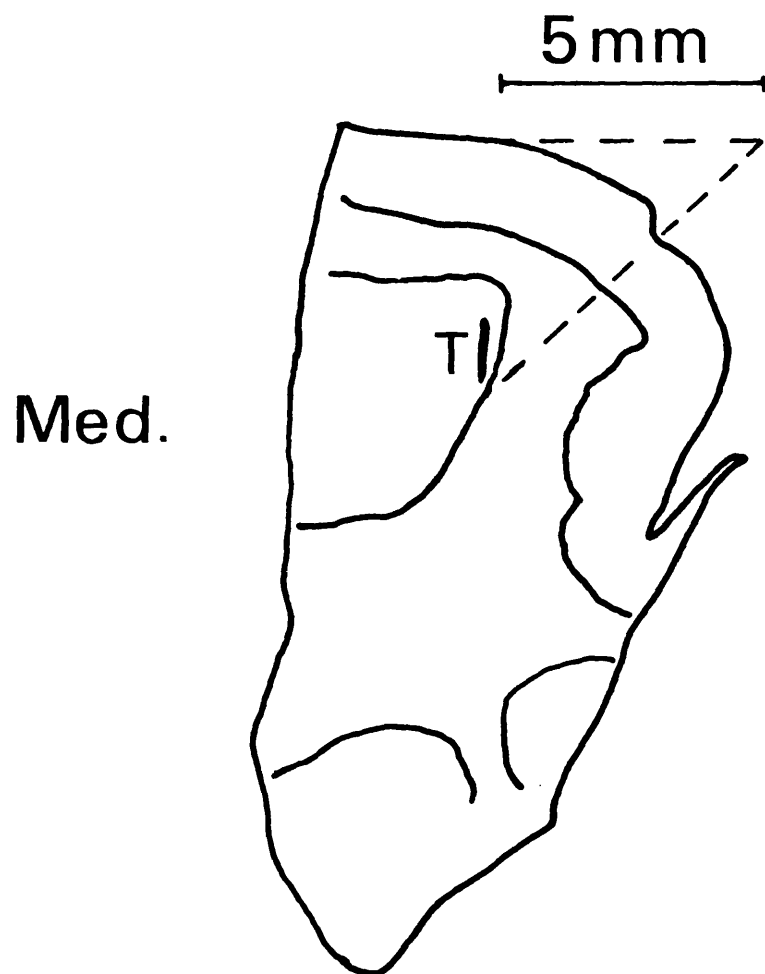


Fig. 8

53.

For the work involving stimulation of the contralateral cortex, thirty rats were used. For the rest of the present work, results were obtained from sixteen cats, seven rats, sixteen rabbits and ten coypu.

CHAPTER III

RESULTS

The potential evoked by forepaw stimulation in the cat

Surface response Fig. 9 shows the area of cortex studied and the surface electrical potentials evoked by stimulation of the contralateral forepaw in a cat anaesthetised with urethane. An electrical stimulus was applied between the second and fourth digits of the right forepaw. The region from which a response could be recorded covers both the classical somatic sensory areas, SI around the coronal sulcus and SII in the anterior ectosylvian gyrus (Woolsey, 1947), the area anterior to the cruciate sulcus and also some of the somatic association areas in the posterior regions of the exposure (Thompson et al. 1963).

The form of the response is different at different sites; posteriorly there is a region showing a pure positive response, medially a region showing an initially negative response and contiguous with these areas the response is positive followed by a negative wave. The latent period of the response is constant, within experimental error, over the whole of the region from

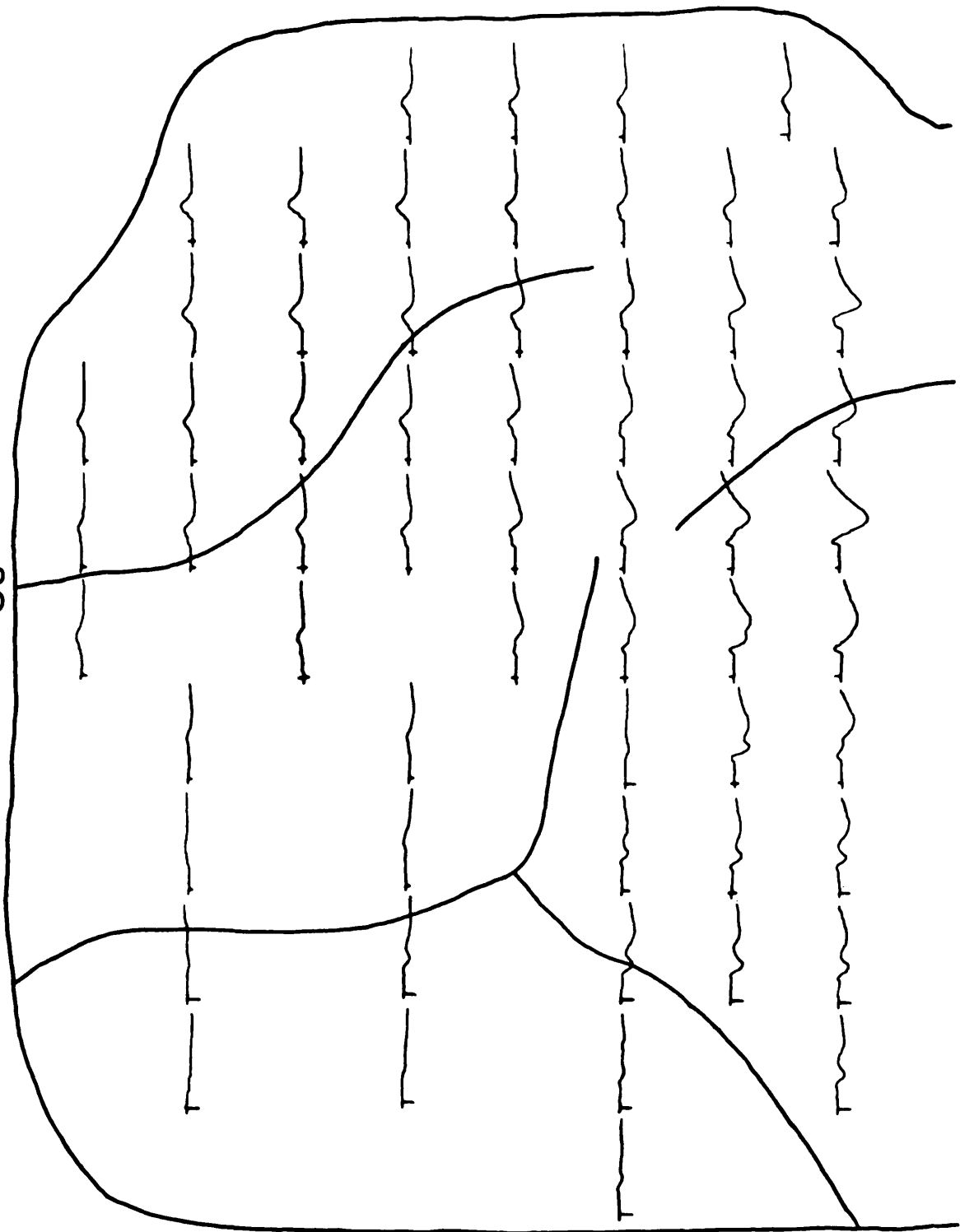
Fig. 9. Responses evoked at the surface of the cat left cerebral cortex by electrical stimulation applied between the second and fourth digits of the contralateral forepaw. L.- lateral; A.- ansate; Cr.- cruciate; Co.- coronal and Ss.- suprasylvian sulci respectively. Records taken over a 1 mm grid. Each record is the Biomac average of 16 transients.

Post.

L

Ss

A



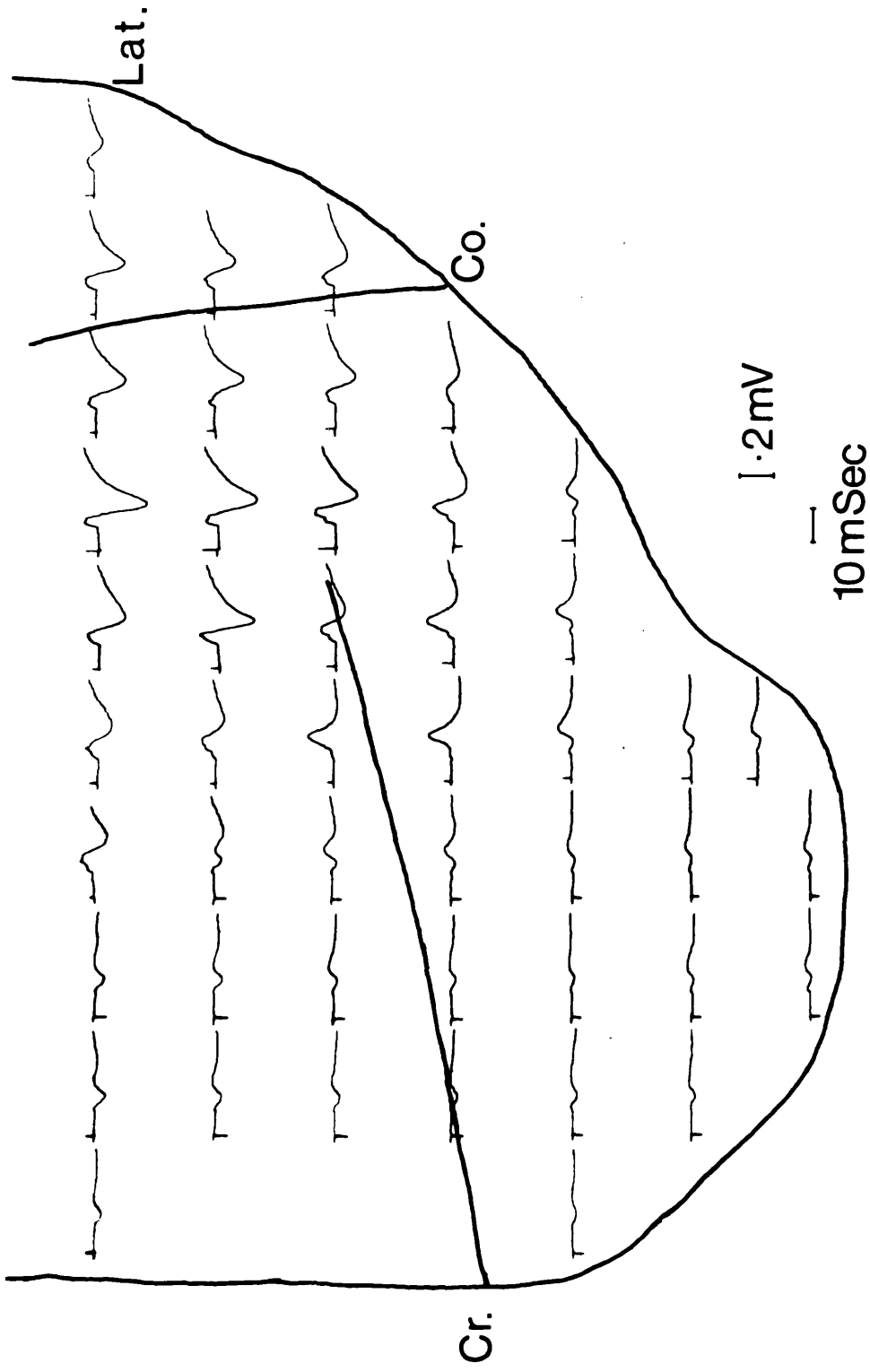


FIG. 9

which a response is elicited (see Figs. 9 and 10). Other experiments have given results which differ from fig. 9 only in detail.

In the present work it has not been possible to separate, by criteria such as latent period or peak to peak voltages, discrete areas of the cortex responding to contralateral forepaw stimulation. Fig. 10 shows the responses obtained, simultaneously, from four sites on the cortex, including SI, SII and the region between them (the anterior suprasylvian gyrus). A large pure positive wave is seen at SII and a large positive-negative wave at SI. In between SI and SII, the response is intermediate.

The stimulation used was just sufficient to cause a small contraction of the digits. Decreasing the stimulus strength so that no contraction was seen made little difference either to the form of response or to the area from which it could be recorded. Fig. 11 shows two sets of records from the same points across a coronal line through somatic sensory area I. Responses evoked with stimulation subliminal for a twitch are shown on

Fig. 10. Surfaces responses, evoked by electrical stimulation of the contralateral forepaw, at SI, SII and two points from the cortex between them. Records taken simultaneously. (Biomac averages).

57.

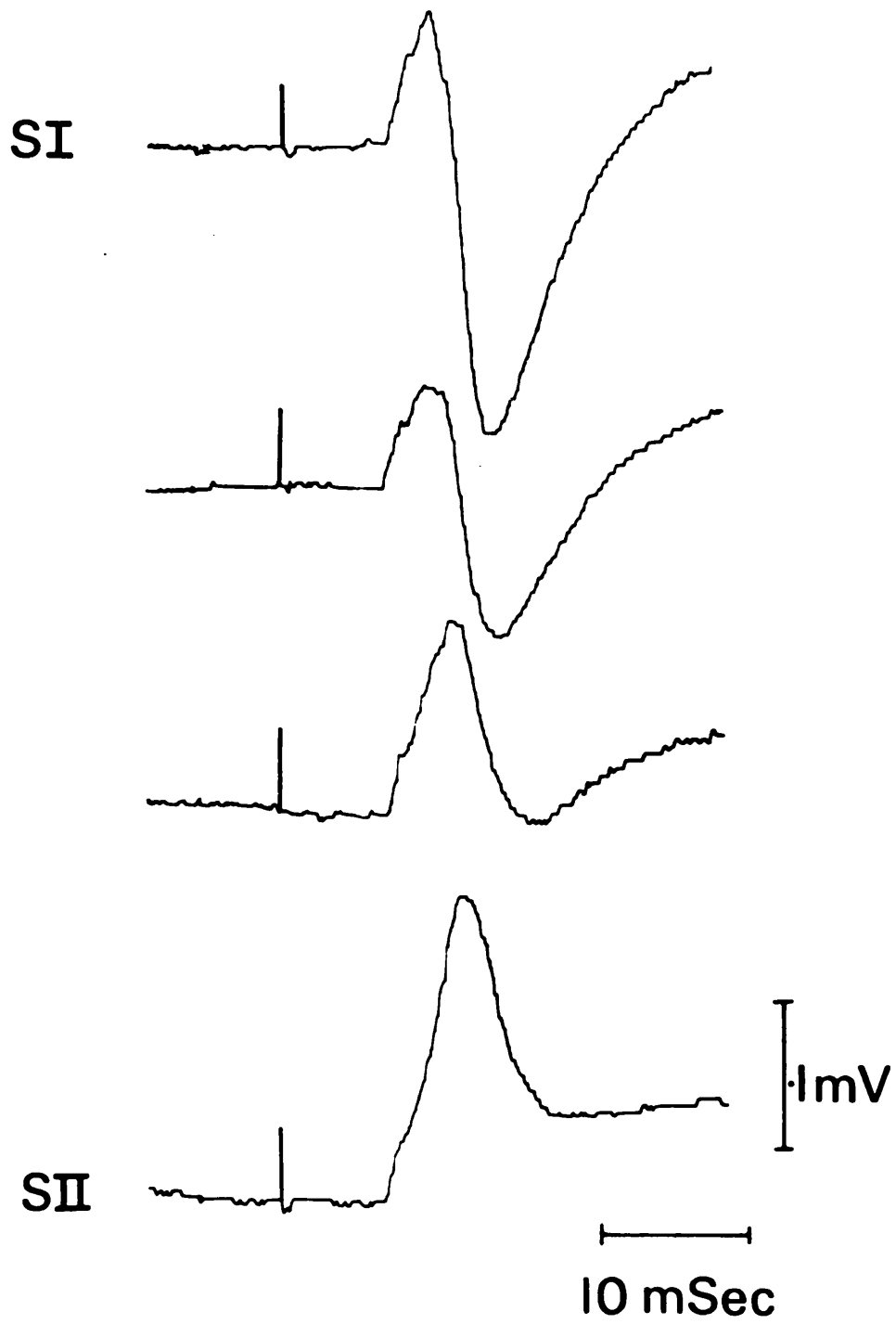
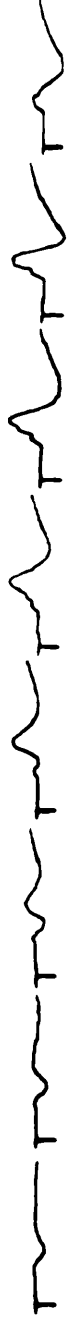


Fig. 11. Two sets of records obtained at 1 mm intervals from the same coronal line through SI in the cat. Stimulus subliminal for a twitch (upper trace); supra-liminal for a twitch (lower trace). The stimulus strengths were 27 V and 63 V respectively; in both cases the stimulus duration was 0.1 msec. (Biomac averages).



Med.



Ant.

the upper set and supraliminal for a twitch on the lower set.

The responses shown in figs. 9, 10 & 11 were all obtained with electrical stimulation. With mechanical stimulation of the contralateral forepaw the picture is little changed (see Fig. 12), except that the amplitude is less; there is a region of initial negativity still apparent in the cruciate region, positive - negative response are recorded around the coronal sulcus (SI) and pure positive responses more laterally in SII (Fig. 12). Mechanical stimulation was used in three cats. Likewise the surface responses are little altered by the use of an alternative anaesthetic, sodium pentobarbitone.

Depth response With the aim of determining the origin of both the surface negative and surface positive waves, a series of micro-electrode penetrations was made into the cerebral cortex of cats. In all cases saline-filled glass micro-electrodes were used, since these micro-electrodes do not distort mass potentials.

The first penetration was made vertically into the

Fig. 12. Cat. Surface cortical responses to mechanical stimulation of the fourth digit of the contralateral forepaw. Records taken over a 1 mm grid. Notation as in fig. 9, but gain different. (All records are Biomac averages).

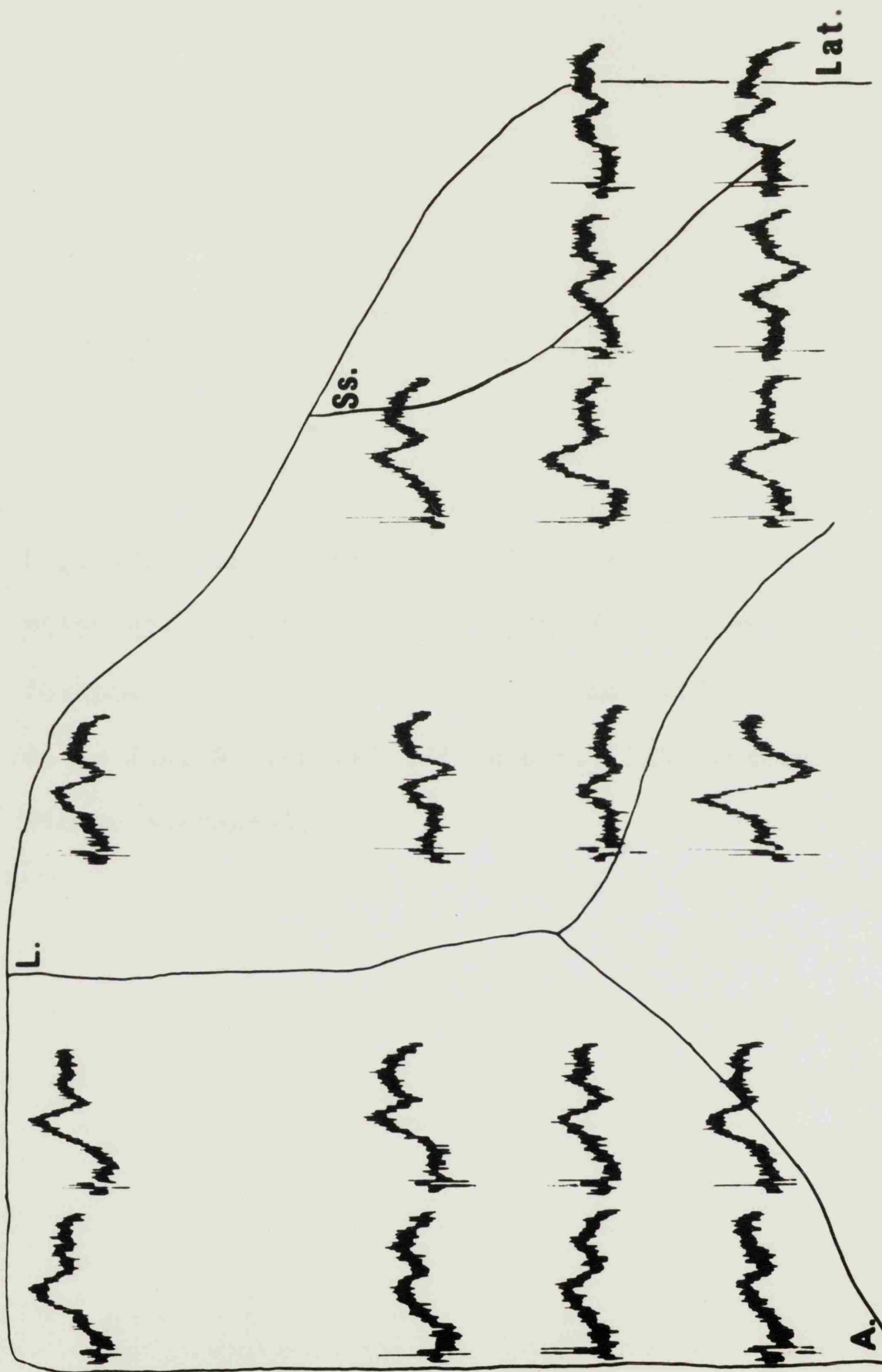
Post.

L.

Ss.

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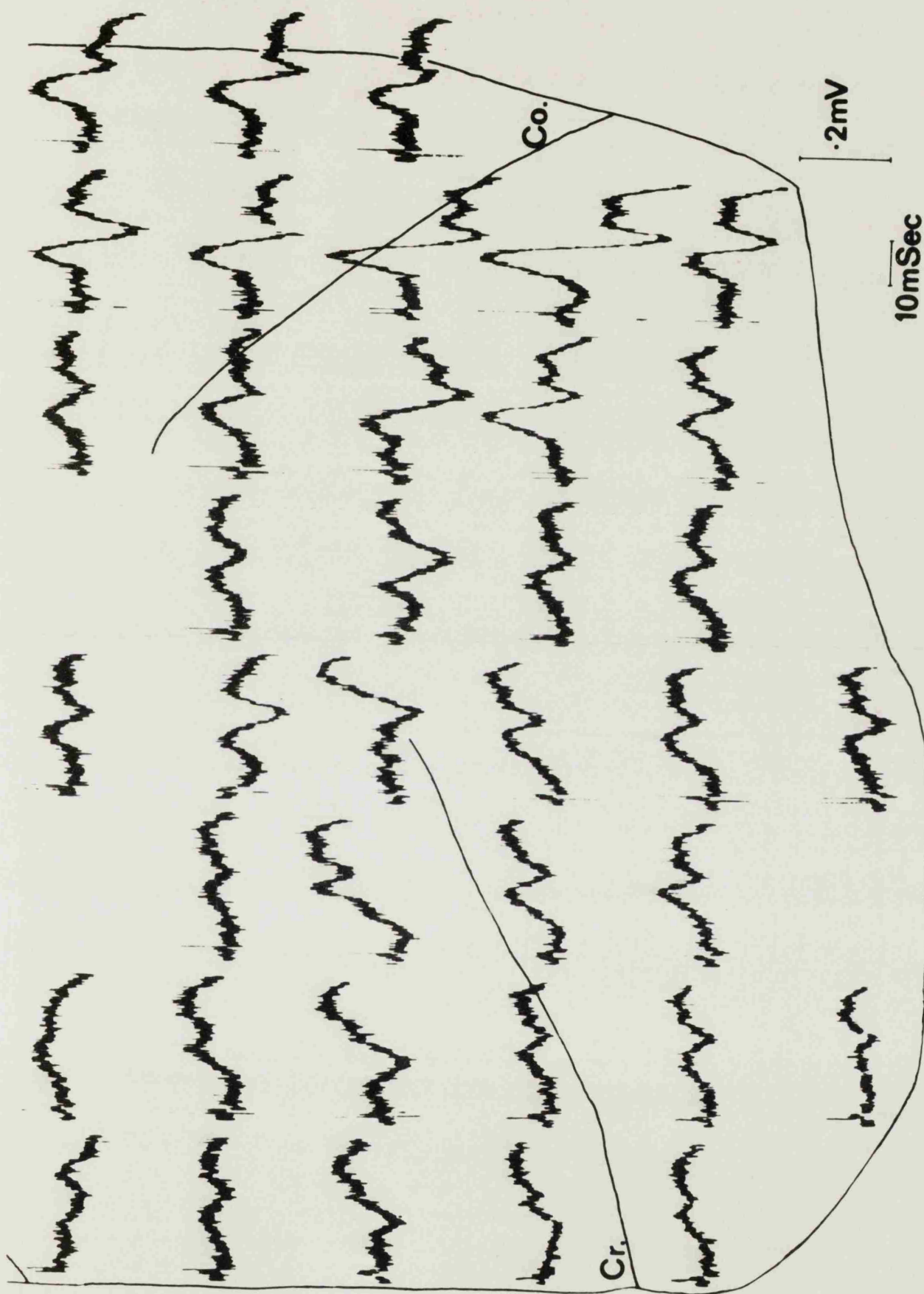


Fig. 12

region which showed an initial negativity at the surface. Fig. 13 shows the mass responses obtained; these remained negative throughout the course of the penetration. In this particular experiment the histology (Fig. 14) shows that the electrode passed through a small arm of white matter at a depth of 2 mm, before returning to the cortex of the cruciate sulcus and finally reaching a depth of 5 mm. At 1 mm depth the negativity was three times the amplitude on the surface and it remained at this level throughout the penetration. In this and all subsequent depth plots the latent period was the same at all depths. Fig. 14 is a photograph of a coronal section in which the electrode track is seen.

The records obtained from a penetration, perpendicular to the surface of the initially positive region, are shown in fig. 15. The surface positive wave (0.05 mV) increases in peak amplitude to over 0.1 mV at 1.75 mm depth. The response becomes progressively more negative from 2 mm, down to 5 mm where it is a maximum of 0.6 mV. The gain of the recording amplifier was reduced by half at depths between 3.0 and 6.0 mm. At 6 mm depth the

Fig. 13. Cat. Depth responses obtained from a vertical micro-electrode penetration into the region of initial negativity. Depth indicated on the left. Control surface records on the right. Unless otherwise stated, in this and subsequent depth plots, the stimulus is an electrical pulse applied between the second and fourth digits of the contralateral forepaw. Likewise all depth records are the Biomac average of 16 transients.

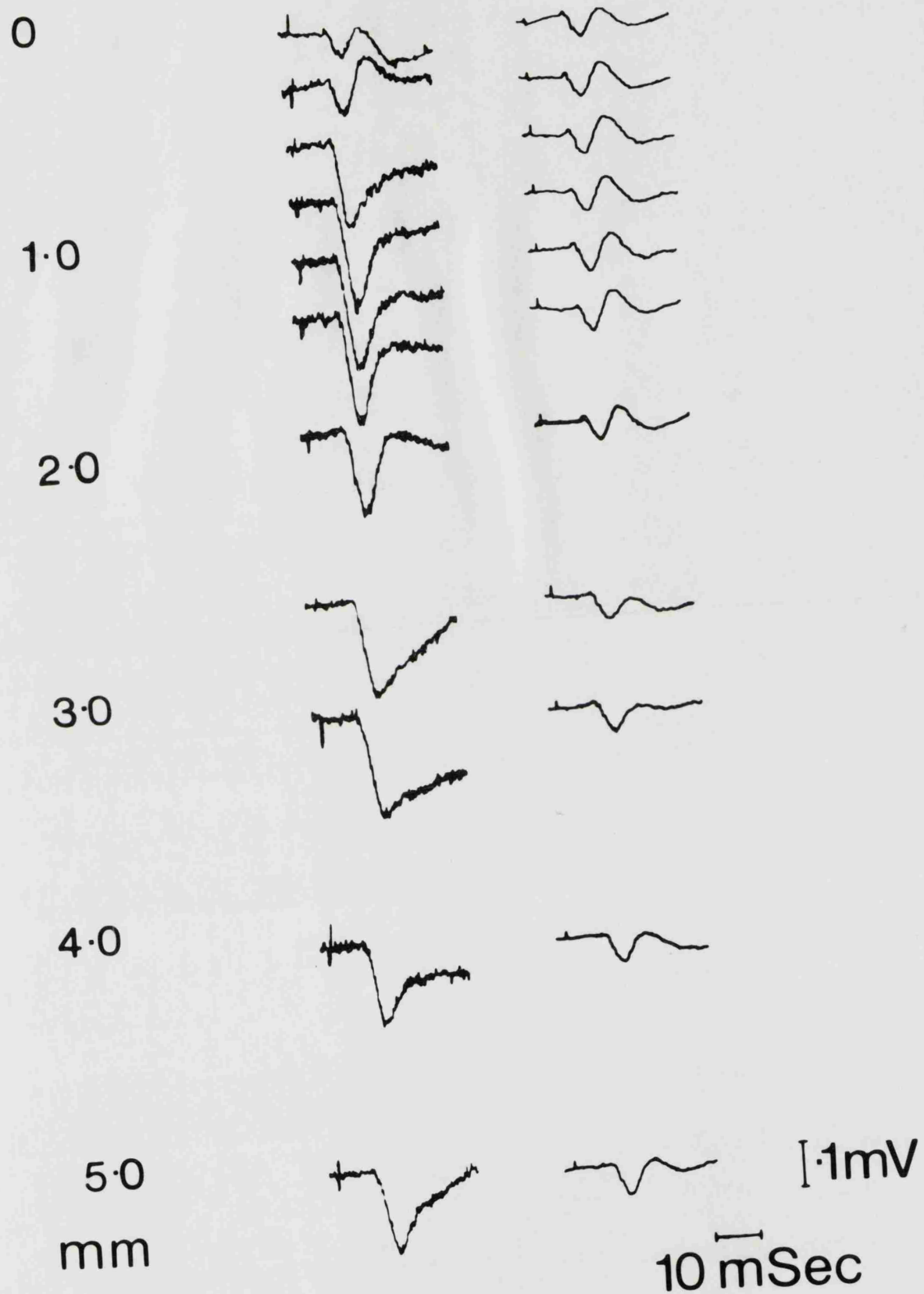


Fig. 13

Fig. 14. Coronal section through part of left cerebral hemisphere of cat, showing the histology of the penetration of fig. 13. Arrow indicates position of electrode track as deep as could be seen in this section. Calibration mark 5 mm.

63.



Fig. 14

Fig. 15. Depth responses obtained from a micro-electrode penetration, perpendicular to the surface of the region of initial positivity, just medial to the coronal sulcus in the cat. Depth indicated on the left. Control surface records on the right. Between 3.0 mm (indicated by the bar) and 6.0 mm the gain was reduced by half.

64.

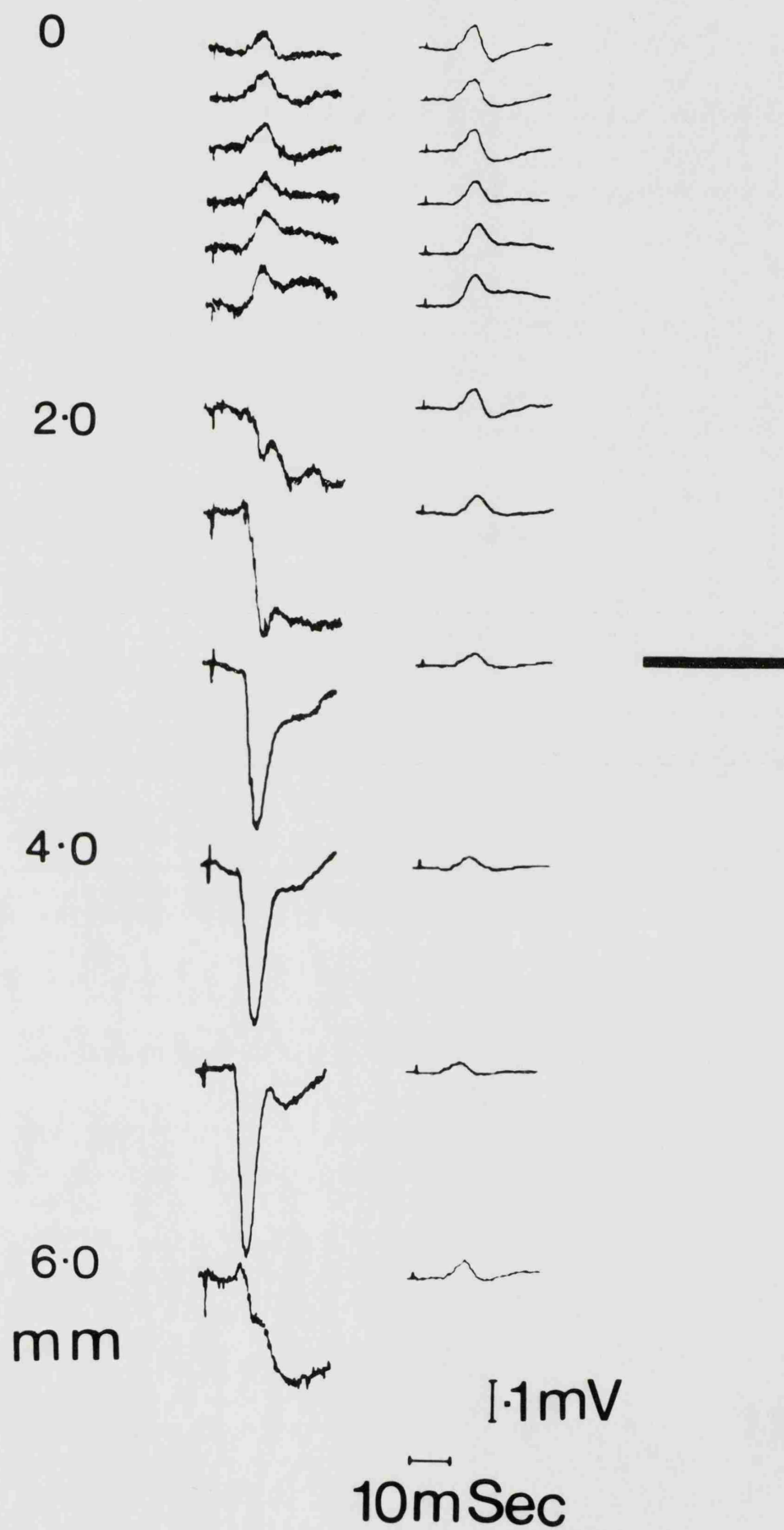


Fig. 15

amplitude of the negative response decreases. This penetration into the region of initial surface positivity was made 2 mm lateral to the penetration into the region of initial negativity in the same cat. This lateral track could not be identified histologically.

Fig. 16 shows the records obtained from an oblique penetration into the lips of the coronal sulcus, with the electrode almost horizontal. The surface response is a typical positive-negative wave (0.2 mV); the peak to peak voltage increases in amplitude down to 2.5 mm. A negative wave is seen at 3.5 mm and maximum negativity is at 4.0 mm. This maximum negativity is found, from the histology, to be in the upper limb of the cortex at the base of the coronal sulcus. Further records deeper than 4.0 mm show a decrease in negativity down to a final depth of 6.45 mm, where the electrode was in the white matter. Here the response is a small negative wave. A photograph of the track is shown in Fig. 17. The electrode is only seen from 3.5 mm depth onward, where disruption of the tissue of the pit of the coronal sulcus is seen.

Fig. 16. Responses obtained from a micro-electrode penetration into the coronal sulcus of a cat. An intense negativity is noted at 4.0 mm depth (the base of the coronal sulcus). Depth indicated on left.

66.

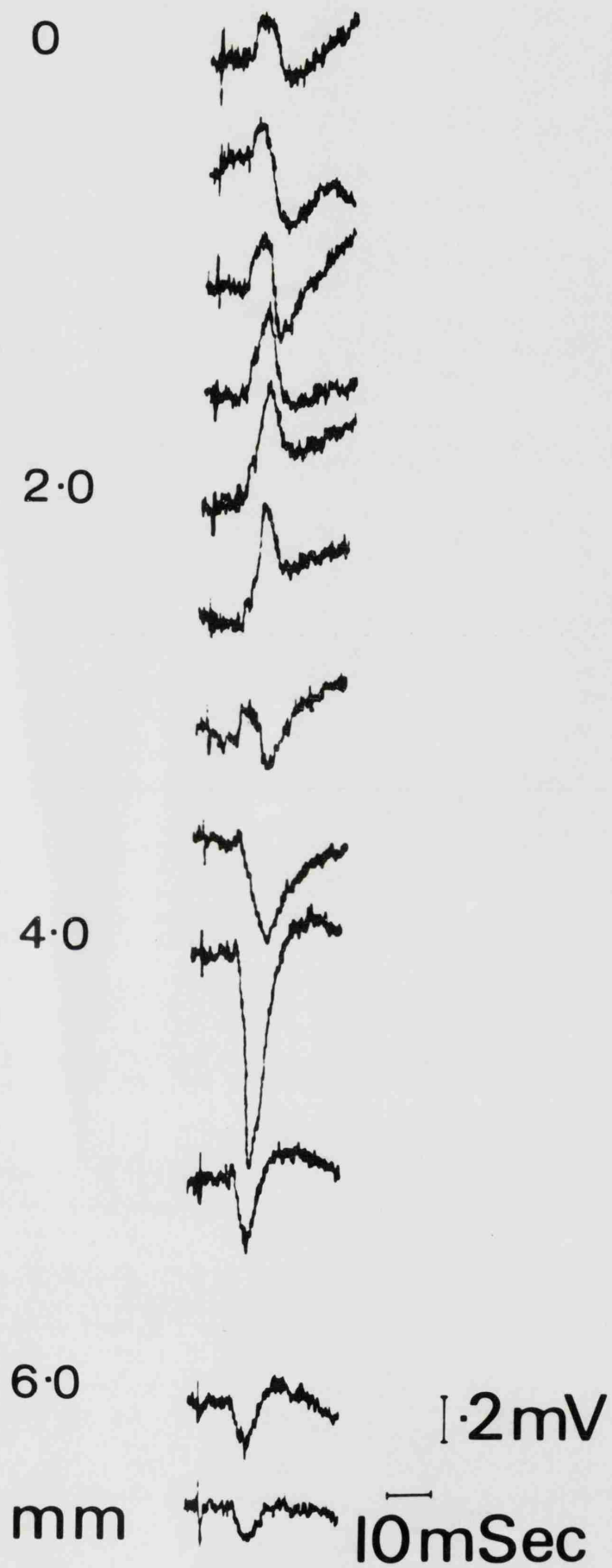


Fig. 16

Fig. 17. Photograph of a coronal section of cat left cerebral hemisphere showing the histology of the penetration of fig. 16. Calibration 5 mm. Electrode track marked by dashed line. End of track in this section marked by an arrow.

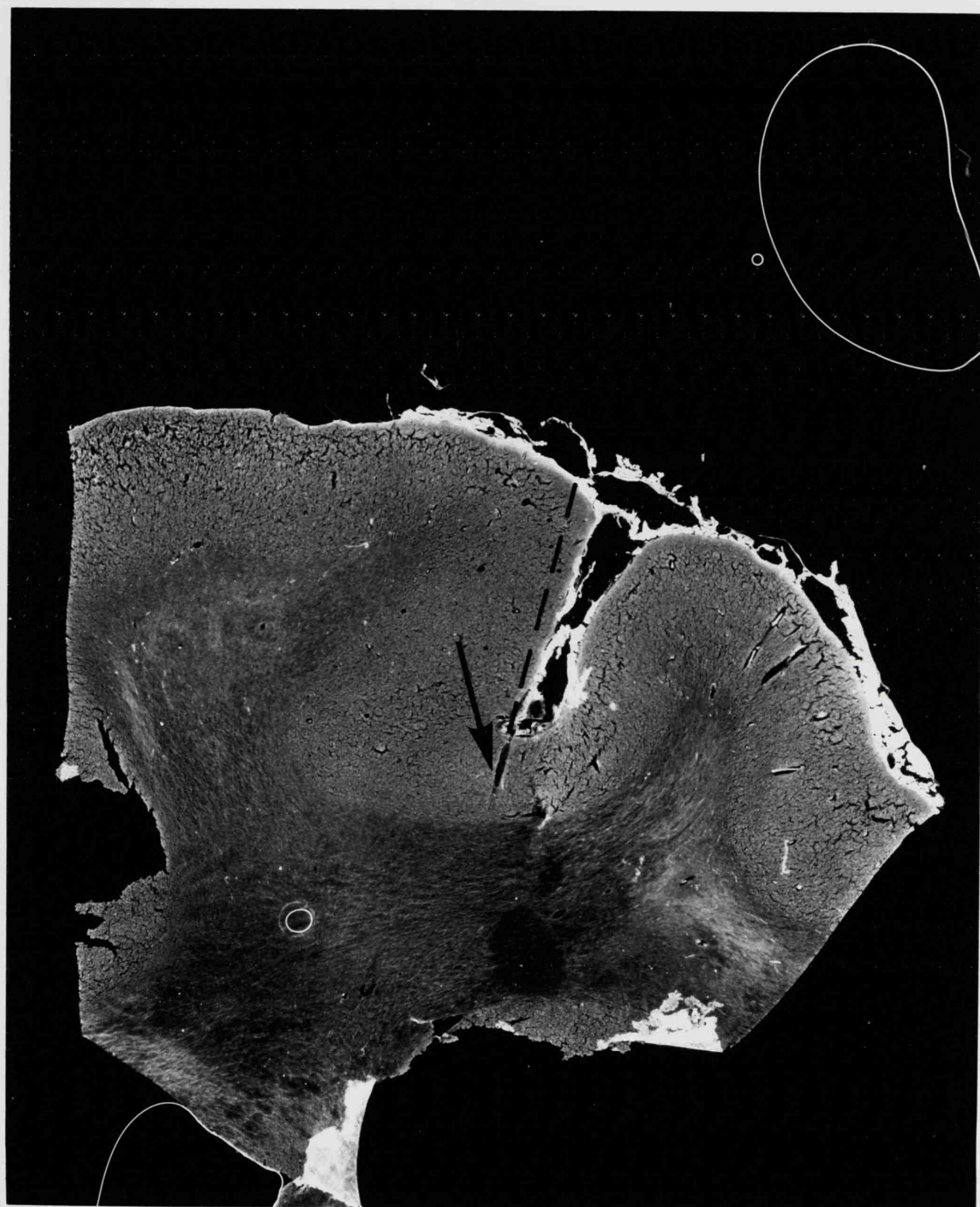


Fig. 17

An electrode penetration was made obliquely, starting in the region showing a surface negative response and ending in the base of the coronal sulcus. The records are shown in Fig. 18. Evoked responses were observed, without interruption, from the surface to the bottom of the sulcus and the latent period of onset remained constant throughout the depth plot. At the surface the negative wave was small; it continuously increased in amplitude with depth until 6.25 mm was reached. At this depth the electrode track was lying in the grey matter of the coronal sulcus (Fig. 19). Deep to 7 mm the response was a small positive deflexion. A drawing of the track is shown in Fig. 19. The sections were oblique to the track and two sections, one showing the electrode at the surface and the second showing it at the base of the coronal sulcus have been enlarged and superimposed. The latter section was as far as the track could be followed; by direct measurement this was 6.5 mm. The maximum recorded depth during the experiment was 8 mm, so presumably the electrode penetrated the opposite limb of the coronal sulcus, but could not be identified histologically.

Fig. 18. Cat. Responses obtained from a micro-electrode penetration starting at the surface of the initially negative region and going obliquely down to the pit of the coronal sulcus. An intense negativity is seen at about 6.0 mm (in the cortex of the pit of the coronal sulcus). Control surface records on right.

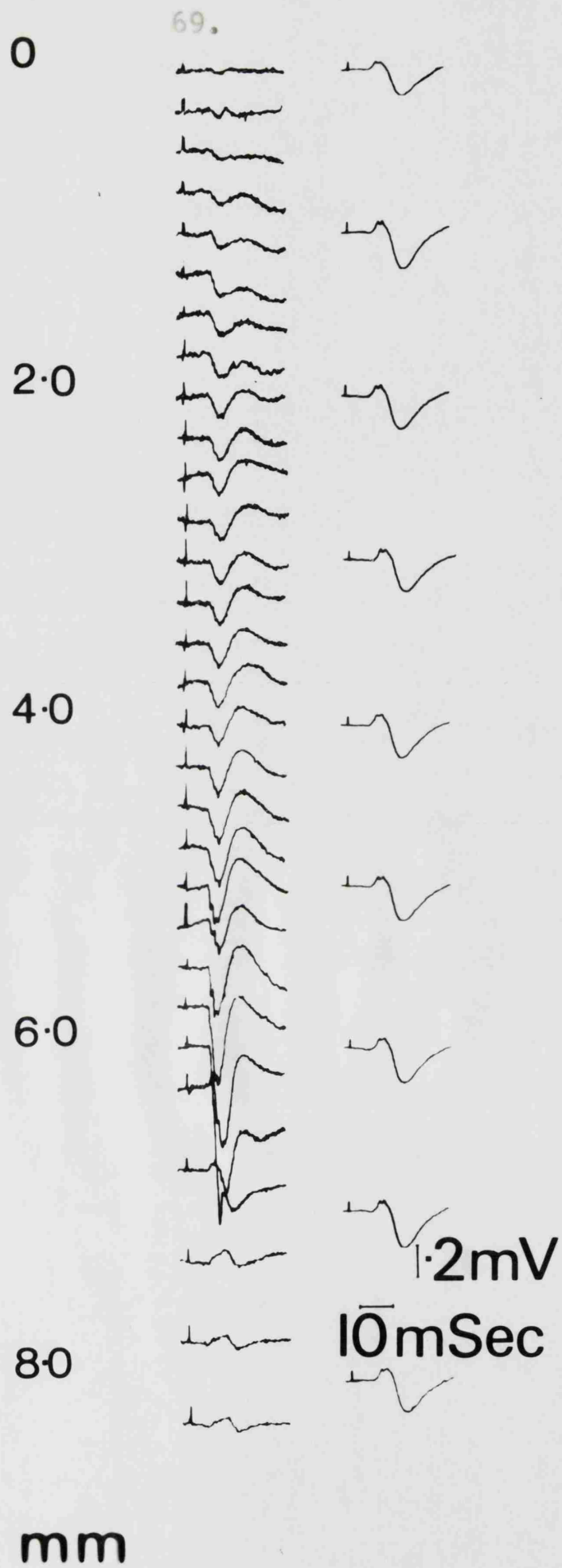


Fig. 18

Fig. 19. A reconstruction of the electrode track of fig. 18. The sections were oblique to the track. The thick outline is the most anterior section showing the electrode's point of entry. The thin line is the most posterior section in which the track is still visible. Co.-coronal; Cr.- cruciate and PreS.- presylvian sulci respectively. T.- electrode track.

Dorsal

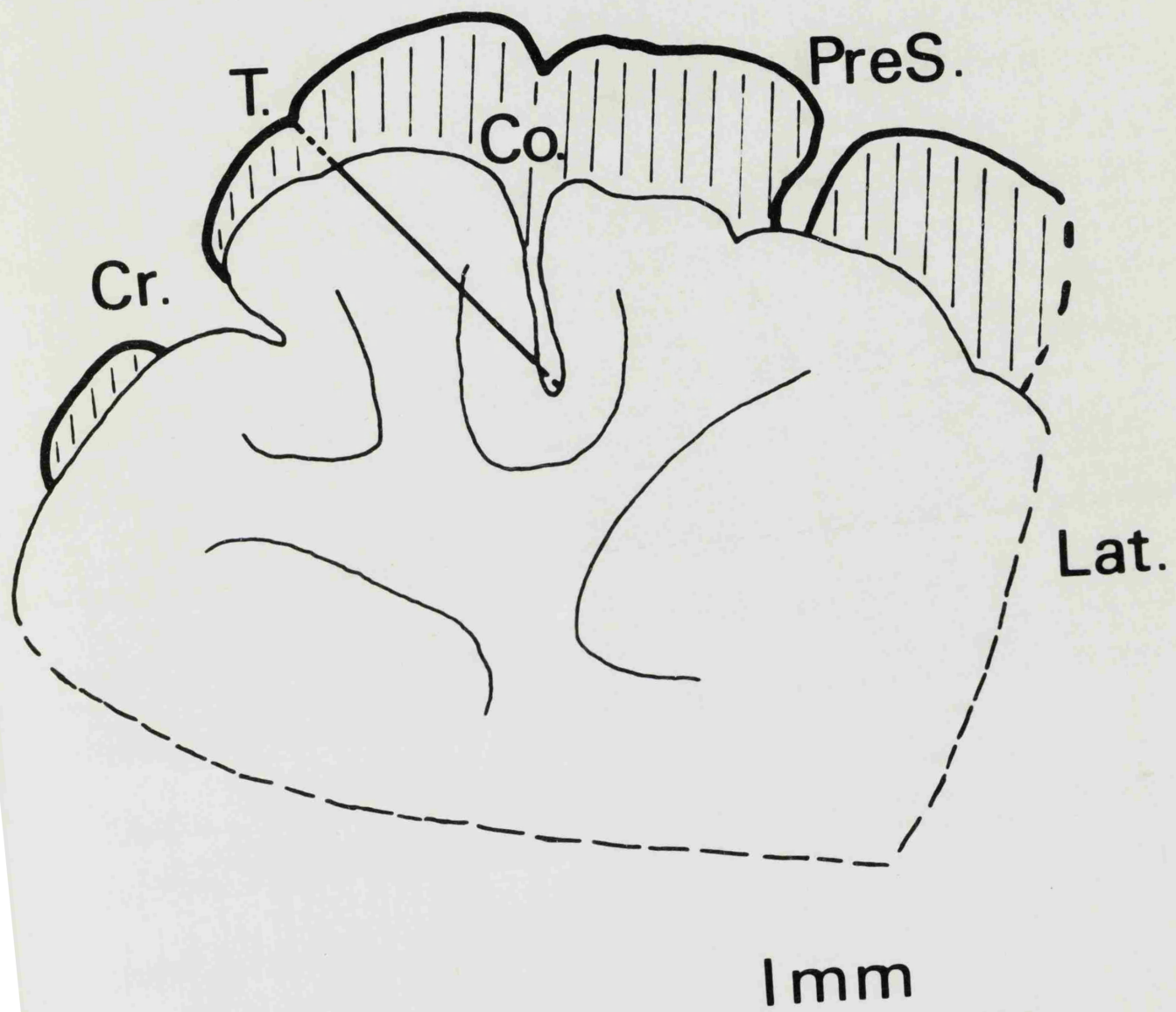


Fig. 19

Depth responses to mechanical stimulation are similar to those evoked by electrical stimulation, indicating that similar elements in the cortex are being activated by the incoming afferent volley. Fig. 20 shows responses on the surface and at depth to mechanical stimulation during a micro-electrode penetration perpendicular to the surface of the region of initial positivity, close to the coronal sulcus. These records are similar to those obtained with electrical stimulation (see Fig. 16).

Further micro-electrode penetrations were made, from various sites and at different angles, into and around the coronal sulcus. These records substantiated the observation that an intense negativity was present in the upper limb of the cortex at the base of the coronal sulcus. A less intense negativity was observed in the structures subjacent to the region of surface initial negativity. A micro-electrode penetration, perpendicular to the region of positivity on the surface of SII, was also made. This showed rapid voltage changes to occur within the thickness of the cortex (2.0-2.5 mm). A negativity was observed at 0.5 mm depth and an intense negativity

Fig. 20. Responses, from the surface and at depth, evoked by mechanical stimulation of the fourth digit of the contralateral forepaw of the cat. The penetration was perpendicular to the surface of the region of initial positivity (just medial to the coronal sulcus).

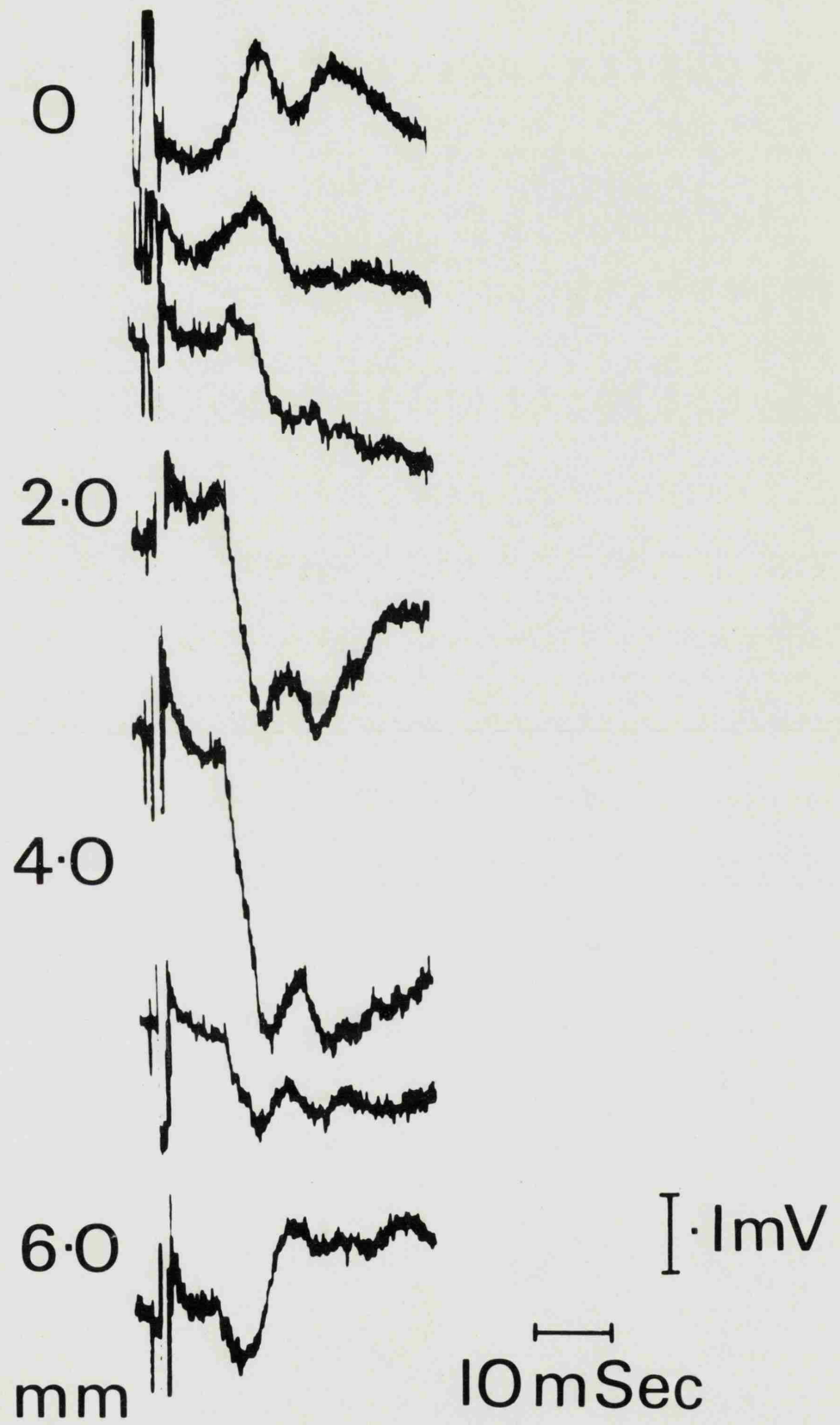


Fig. 20

at 1.5 mm. At 2.5-3.0 mm the response was small and the electrode was in the white matter. It would thus appear that the forepaw receiving area of SII is situated in the exposed cortex of the anterior ectosylvian gyrus.

In summary, the response at the surface of the cerebral cortex of the cat, to contralateral forepaw stimulation, was a positive-negative wave in SI, an initially negative wave in the post cruciate gyrus and a pure positive wave in SII. As the response was observed only for 40 msec after the stimulus, association responses (Amassian, 1954) have been excluded in the present work. A micro-electrode penetration into the centre of SI shows rapid changes in voltage with depth and an intense negativity in that region of cortex lying at the base of the coronal sulcus. A penetration into the negative region shows low voltage gradients and if the penetration is from the surface negative region to the base of the cortex underlying SI, the gradients get larger as the base of the coronal sulcus is reached. Depth records taken from a penetration into SII showed an intense negativity at 1.5 mm depth, subjacent to the surface

positivity; the negativity decreased with further depth penetration.

From theoretical considerations (Holmes & Houchin, 1967), the initially positive wave seen at SI can be explained by the depolarisation, deep in the cortex, of a localised group of pyramidal cells. This is supported by the observation of localised intense negativity at the base of the coronal sulcus. Although SII has not been studied in such detail as SI, a separate region of negativity has been observed, at a depth of 1.5 mm; this underlies the pure positive wave observed on the surface of SII.

There are several explanations which may be put forward to account for the appearance of a surface negative wave in the post-cruciate cortex. The first is that an afferent volley hyperpolarises the somata of a localised group of pyramidal cells in the cortex subjacent to this region (Fig. 21). In this case a positivity would be expected at depth, within the cortex subjacent to the surface negativity; since no such positivity is observed (Fig. 13), this explanation seems unlikely.

Fig. 21. Extracellular current and voltage fields generated by the hyperpolarisation of a pyramidal cell body and its basal dendrites in layer 4 of the cortex. Arrows indicate the flow of positive current (solid lines) and dashed lines represent points of equal voltage numbered on an arbitrary scale. Surface - cortical surface.

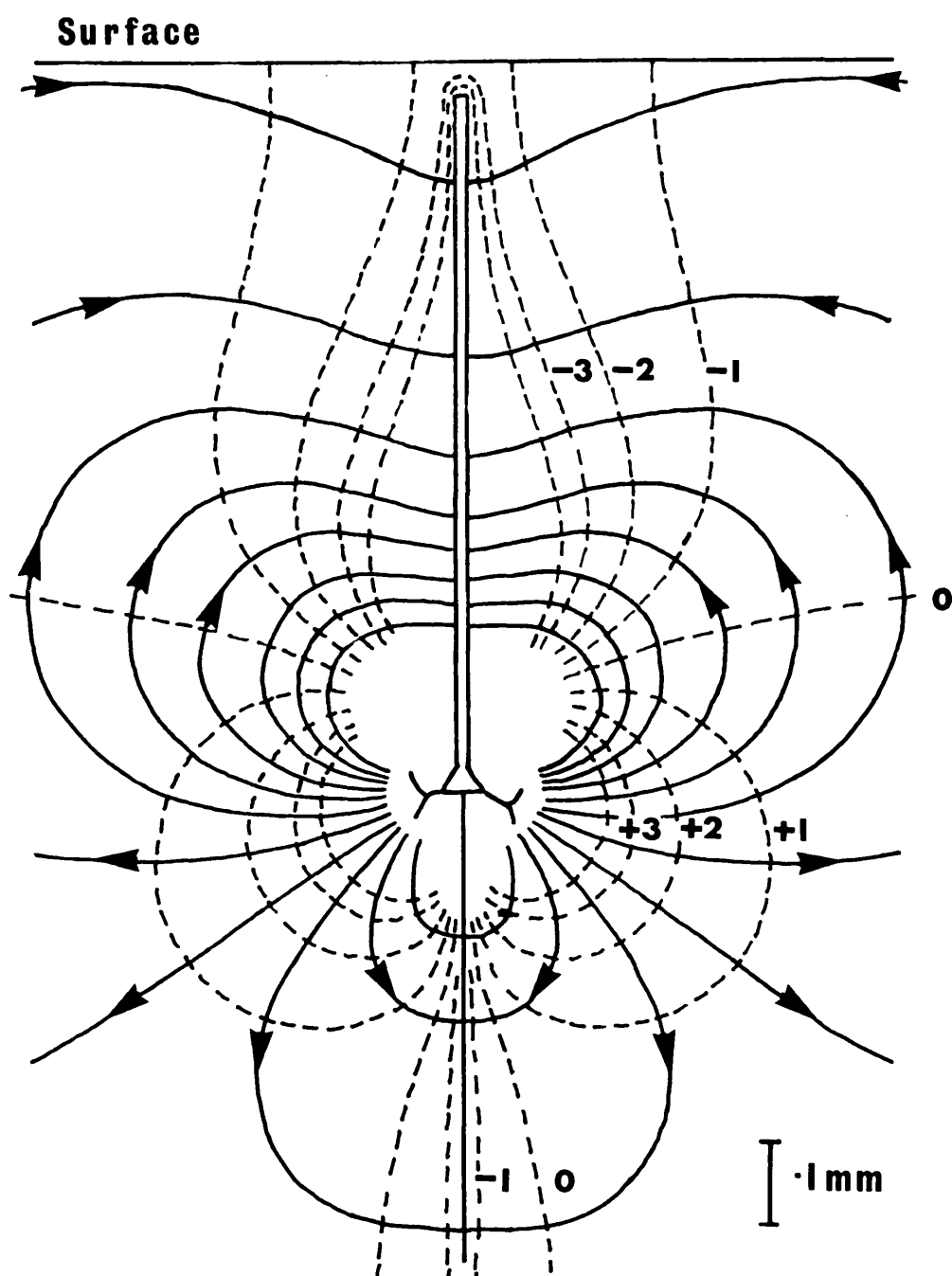


Fig. 21

The second explanation is that the afferent volley depolarises a more superficial region, such as the apical dendrites of a group of pyramidal cells (Fig. 22). In this circumstance it would be expected that, as the recording electrode penetrated the cortex, the potential would become more negative and then reverse to give a positive deflexion. Experimentally no superficial negativity nor depth positivity were observed. Hence this explanation also seems unlikely.

A third hypothesis is that the surface negativity is a reflection of the intense depolarisation recorded in the cortex, at the base of the coronal sulcus. Fig. 23 is a reconstruction of the voltage and current fields produced by the depolarisation of a localised group of pyramidal cells lying in the upper limb at the base of the coronal sulcus. This depolarisation produces a negative field which extends to the cortical surface. All the observations, made on the surface and at depth, concur with the field illustrated in Fig. 23. These results suggest that the whole field is generated by the depolarisation of a localised group of cells in the upper limb

Fig. 22. Extracellular current and voltage fields generated by depolarisation of a superficial region of an apical dendrite. Notation as in fig. 21.

77.

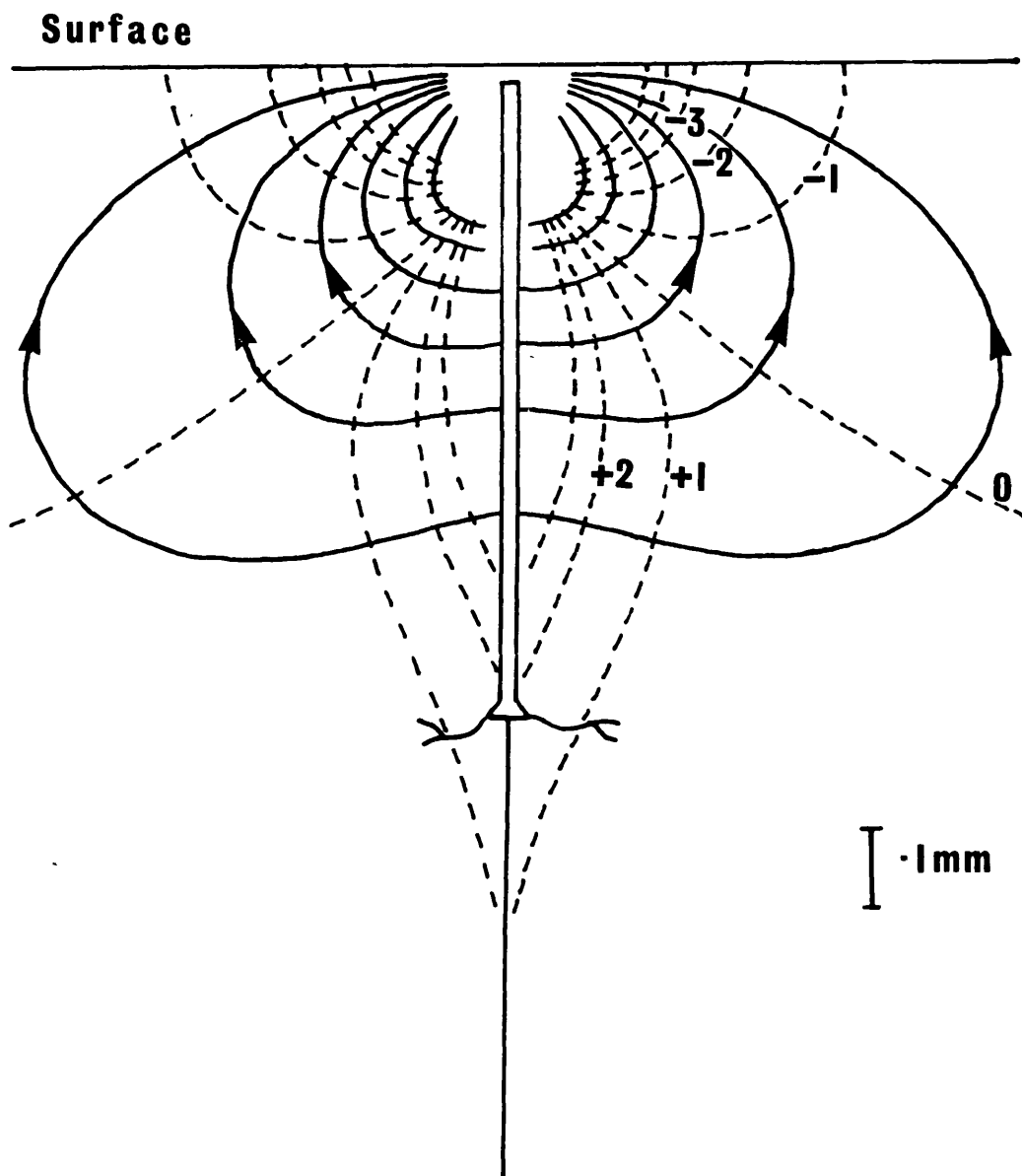


Fig. 22

Fig. 23. Extracellular current and voltage fields generated by the depolarisation of a pyramidal cell body and its basal dendrites, situated in the upper limb of the cortex at the base of the coronal sulcus. Notation as in fig. 21. The field has been constructed on the assumption that the whole system (cortex and coronal sulcus) is homogeneously conducting.

78.

Surface

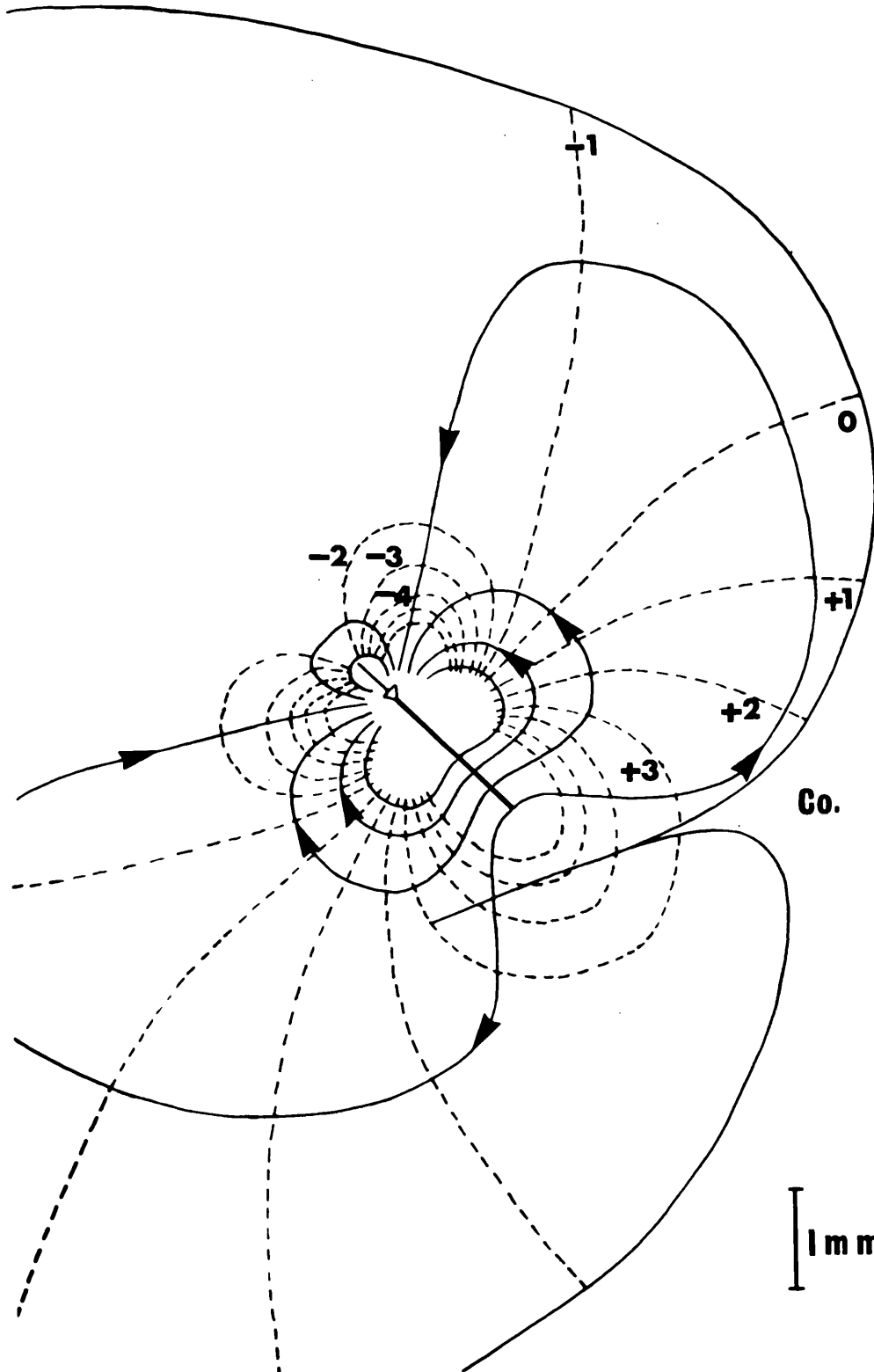


Fig. 23

of the cortex at the base of the coronal sulcus.

Records have also been made of extracellular unitary discharges, in the cerebral cortex, evoked by stimulation of the contralateral forepaw. Only the cortex in and around SI was searched systematically; no thorough search for such units was made in the region of SII. Such units have only been found in the cortex lying at the base of the coronal sulcus. Fig. 24 shows three consecutive responses recorded simultaneously from a surface electrode and from a micro-electrode whose tip was lying in the upper limb of the grey matter at the base of the coronal sulcus. The latent period of the unitary discharge coincided with the peak of the surface positivity. Most of the units encountered gave a single discharge to the contralateral forepaw stimulus. The site and latent period of these units is thus consistent with the hypothesis (illustrated in Fig. 23) based on mass responses.

A further confirmatory experiment was performed in which, when SI unitary responses described above had been recorded, a stimulus was applied to the micro-electrode.

Fig. 24. Unitary discharges from the same cell in response to contralateral forepaw stimulation. Depth of cell was 5.54 mm into the upper limb of the cortex of the coronal sulcus. Interval between successive stimuli was 4 msec. Upper trace of each pair is the micro-electrode recording. Lower trace is the surface record. The unitary discharge co-incides with the peak of the surface positivity. (Individual responses).

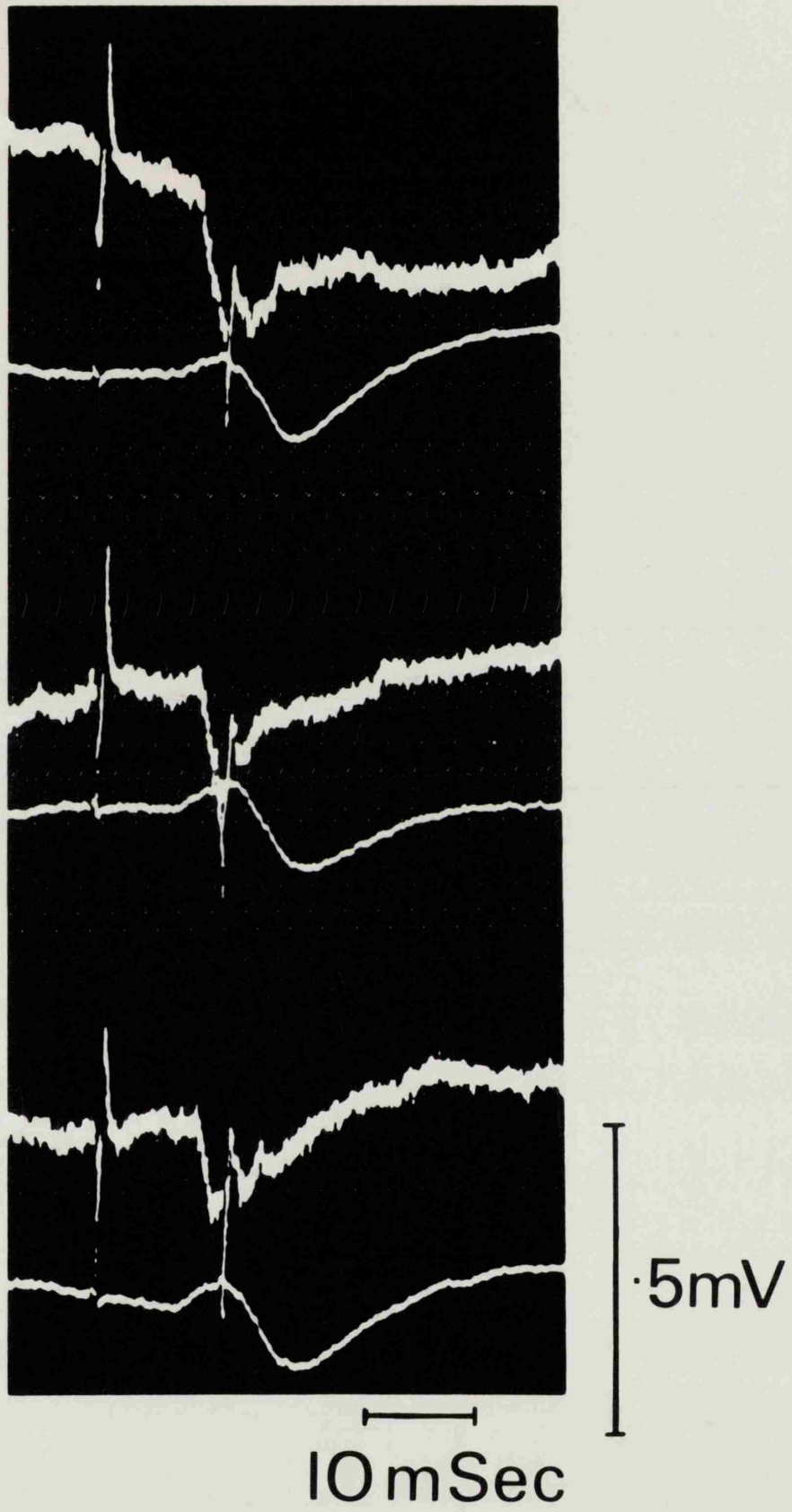


Fig. 24

The stimulus was a negative rectangular wave of 81 V lasting 0.1 msec. Fig. 25 shows that the resultant surface potential was a large positivity directly over the stimulating site and a negative wave medial to this. The depth of the micro-electrode was 3.6 mm into the upper limb of the coronal sulcus. These responses are thus of similar polarity but more rapid time course than those obtained by stimulation of the contralateral forepaw. Stimulation through the micro-electrode, with a pulse of reverse polarity produced no surface response.

The potential evoked by forepaw stimulation in the rat, rabbit and coypu

Of the four species studied, rat, rabbit, coypu and cat, only the cat has a deeply convoluted cerebral cortex. Fig. 4 shows a dorsal view of the cortical surface of the four species. Blood vessels can be seen ramifying over the cortical surface in the rabbit and coypu. The potentials evoked at the cortex in rat, rabbit and coypu exhibit certain common features and so these species will be considered together. All three species exhibit an initially

Fig. 25. Right.- Mass responses, from the surface of the cat cerebral cortex, evoked by antidromic stimulation at a depth of 3.6 mm into the cortex of the upper limb of the coronal sulcus. (see text). Upper trace:- positive-negative wave directly over the stimulating electrode. Lower trace:- initially negative wave recorded medial to the stimulating electrode.

Left.- Control records, taken from the same surface positions, but evoked by electrical stimulation of the contralateral forepaw.

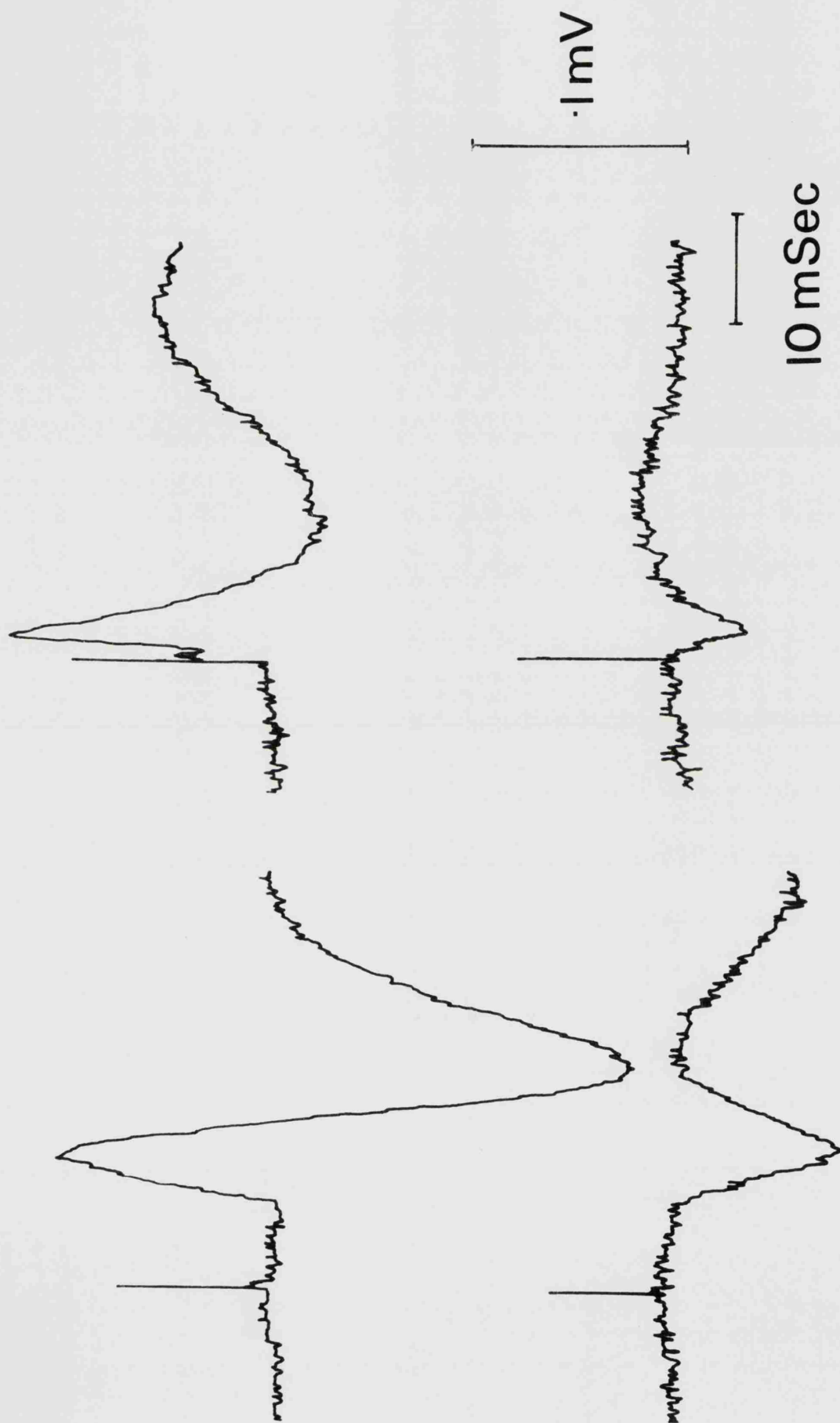


Fig. 25

positive and often pure positive wave at the cortical surface, in response to contralateral forepaw stimulation. Another common feature is that two latent periods can be distinguished; an area where the responses have a short latent period is observed in the centre of the forepaw receiving area and around this is another area where responses of longer latent period can be recorded.

Surface response The form of the potential, evoked at the cortical surface by contralateral forepaw stimulation, in the rat anaesthetised with urethane has been described by Bindman et al. 1964; Dawson & Holmes, 1966; Holmes & Short, 1970. The present work has repeated and confirmed these previous observations.

In the rabbit, the response evoked at the cortical surface is a large positive wave, about 1 mV in amplitude in the region of greatest voltage (the forepaw primary receiving area). The latent period in this region is 9 msec, with a peak positivity occurring at 16-17 msec (Fig. 26). The response rapidly decreases in amplitude, with distance from this region. It can be seen from

Fig. 26. The potential evoked at the surface of the rabbit cerebral cortex by electrical stimulation of the contralateral forepaw. Records taken over a 1 mm grid. C.- coronal suture, equivalent to the fronto-parietal suture of the rat. All records in this section are the Biomac average of 16 transients. An electrical stimulus, applied between the second and fourth digits of the contralateral forepaw was always used in this section.

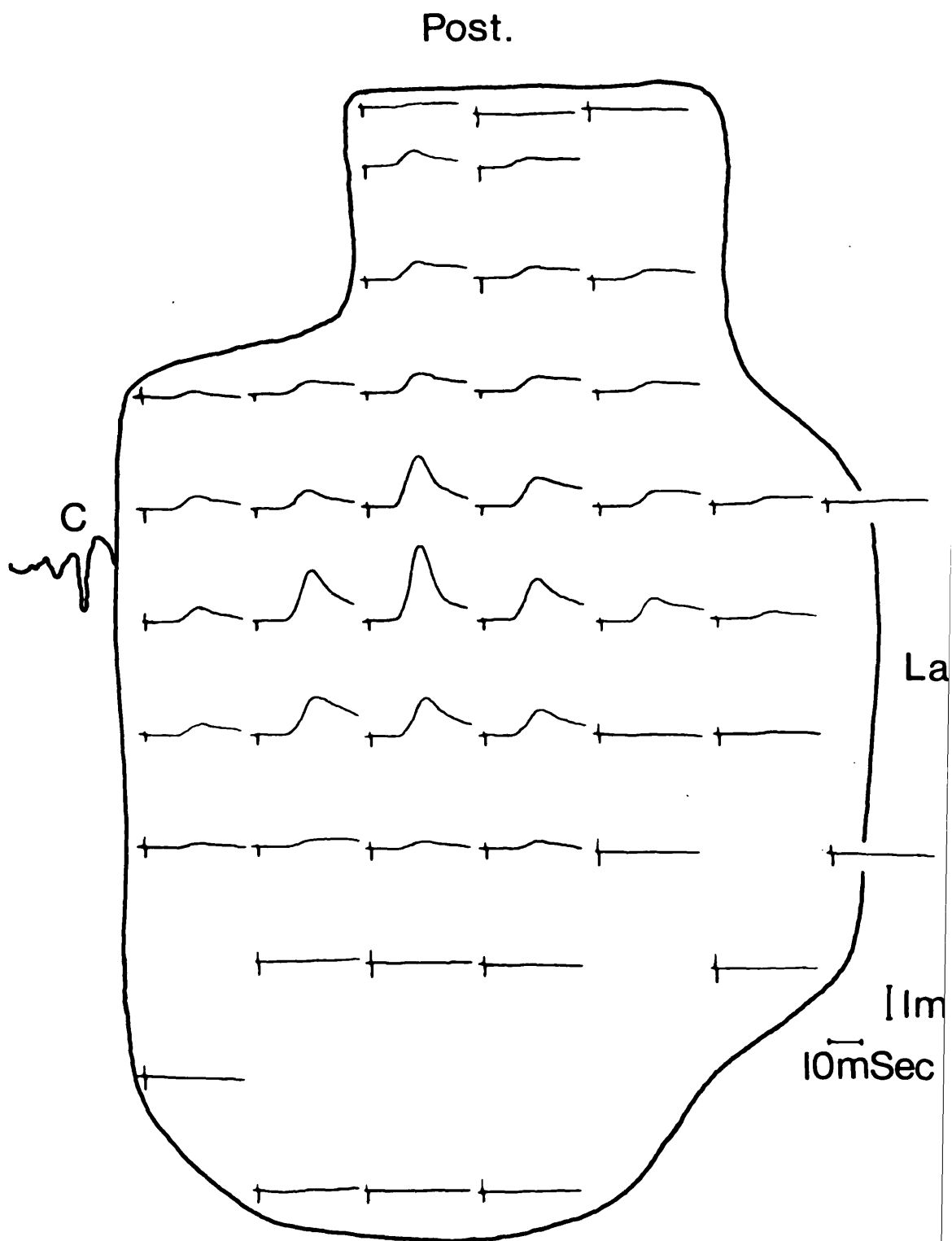


Fig. 26

fig. 26 that, as in the rat, the latent period is longer at points outside the forepaw primary receiving area. This point is emphasised by reference to Fig. 27, which is an enlargement of one anterior-posterior line of responses from the surface of the rabbit cortex.

The response obtained from the surface of the cerebral cortex of a coypu (Fig. 28) is very similar to that of a rat. There is a central region where the response is largest (0.8 mV) and has the shortest latent period (9 msec). Here the response consists of two or more positive waves; at surrounding points it is a single positive deflexion with a latent period of 11 msec. Fig. 29 emphasises the difference in latent period at the primary forepaw receiving area and at surrounding regions.

Responses at depth The results described so far in this section have been of potentials recorded at the cortical surface. At depth, Holmes & Short (1970) recorded, in rats, a large negativity at 1.0-1.4 mm in the cortex beneath the forepaw primary receiving area. This negativity was co-incident, in time, with the later surface positive wave.

Fig. 27. Line of surface responses taken and enlarged from fig. 26. In the region of large positivity the latent period is 9 msec. On either side of this region the latent period increases to 10 msec. Responses recorded at 1 mm intervals. (Biomac averages).

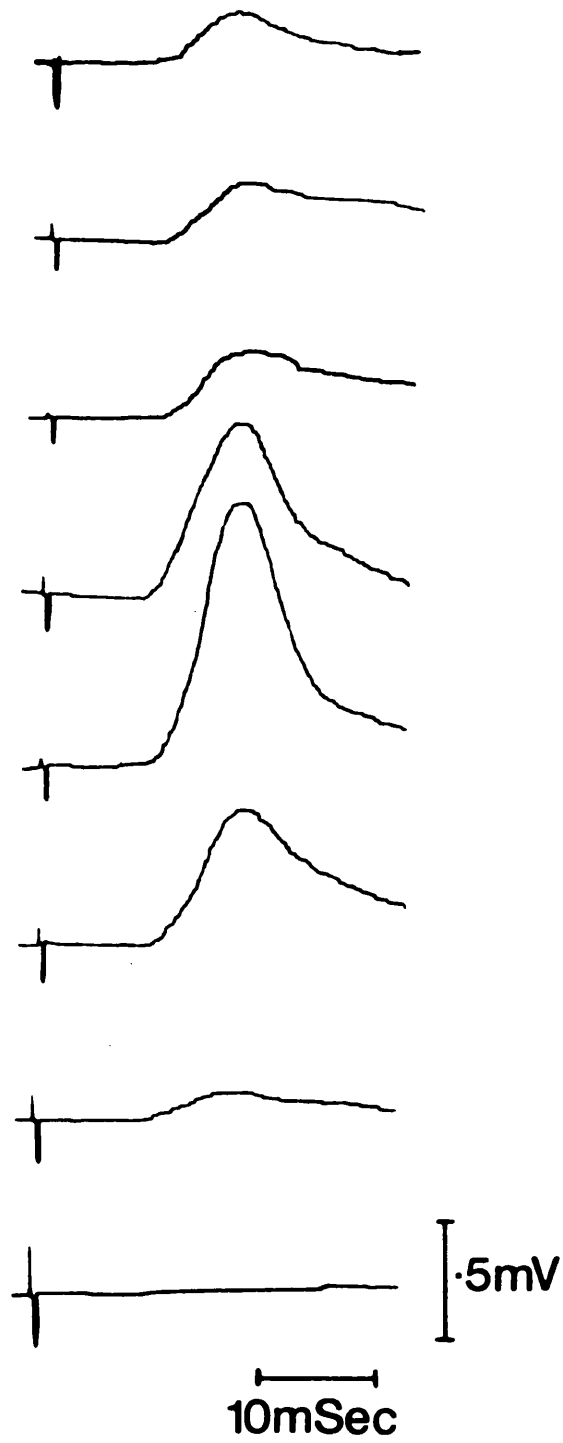
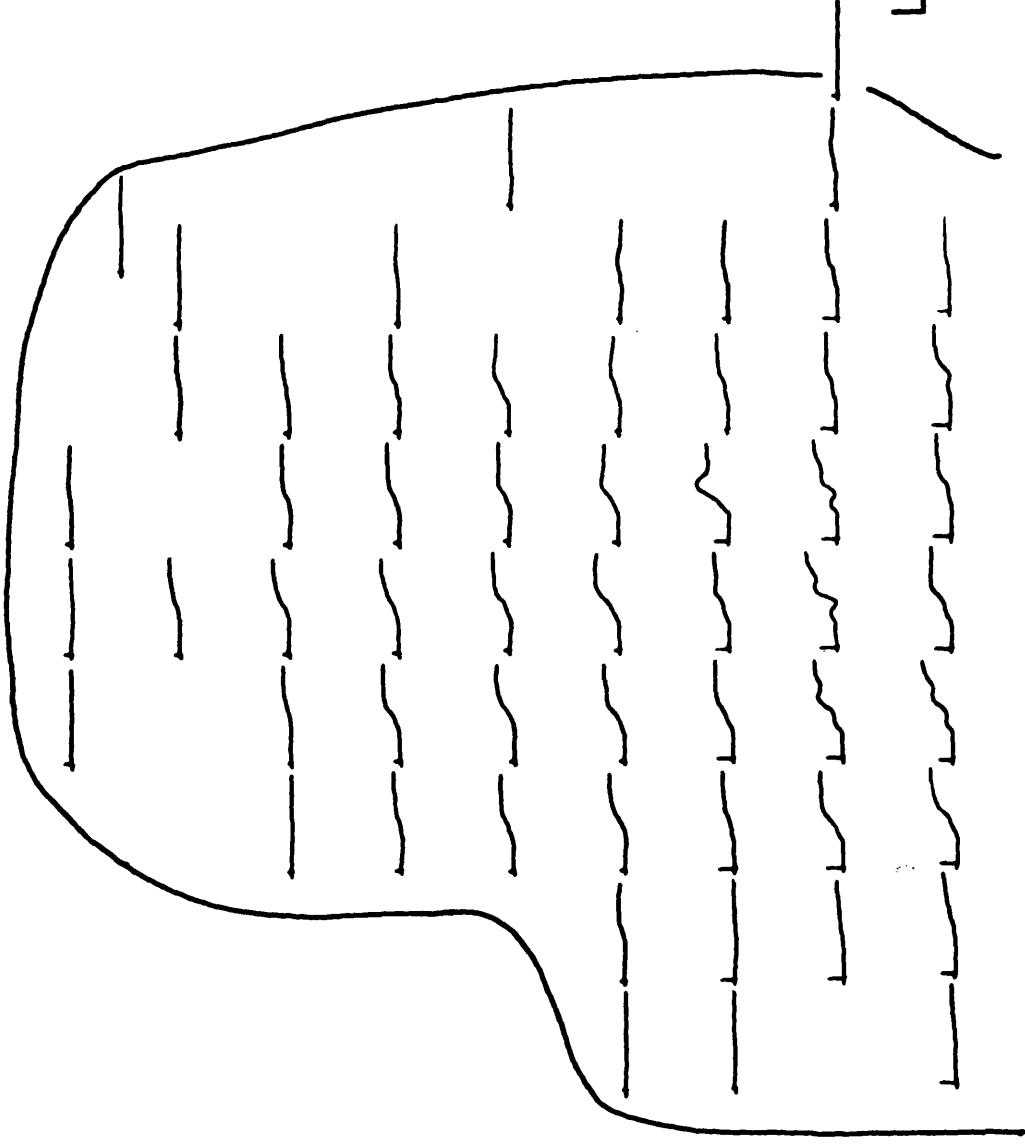


Fig. 27

Fig. 28. Records obtained from the surface of the left cerebral hemisphere of a coypu, in response to electrical stimulation of the contralateral forepaw.

Records taken over a 1 mm grid. F.- fronto-parietal suture.

Post.



Lat.

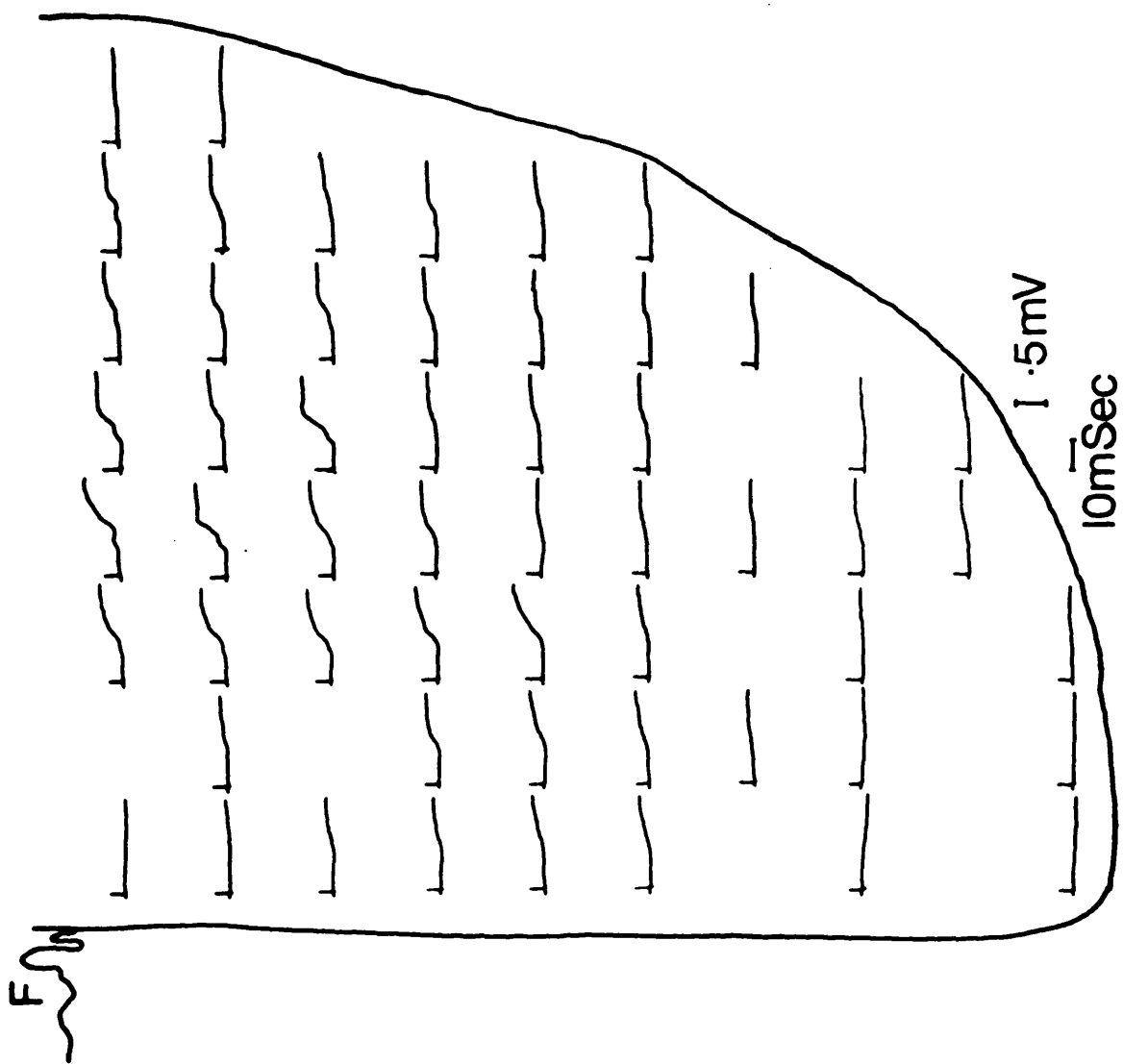
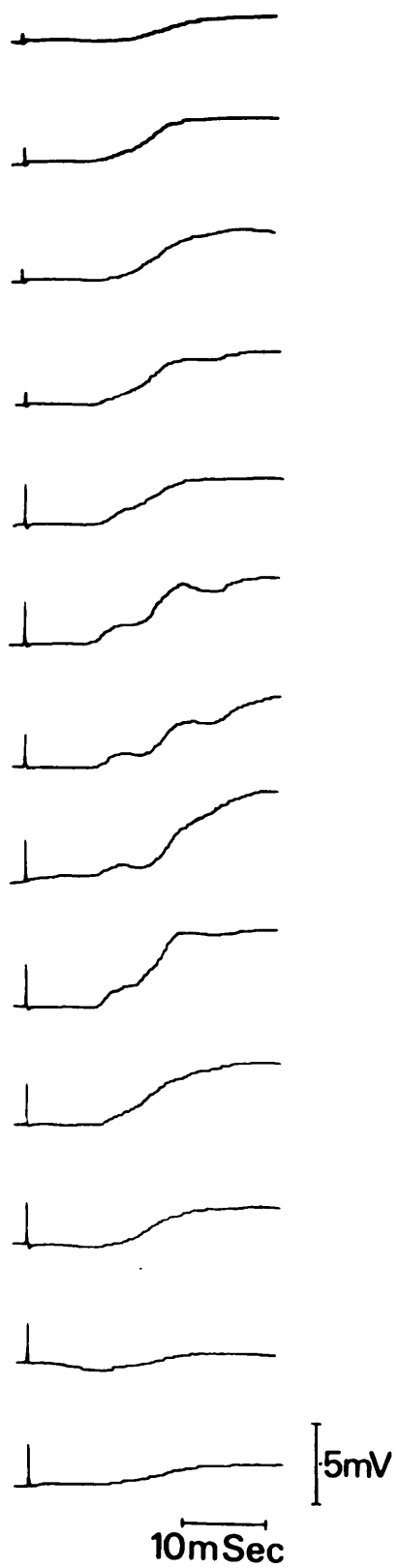


Fig. 23

Fig. 29. Line of surface responses taken and enlarged from fig. 28. The responses are taken from an anterior-posterior line through the forepaw receiving area of the coypu at 1 mm intervals.

37.



A similar picture is seen in the rabbit when a micro-electrode penetrates the cortex at a point where the response is largest (Fig. 30). At a depth of 0.4 mm the initial positive wave seen on the surface gives way to a positive-negative wave. At depths in excess of 0.6 mm the response is a pure negative wave with a maximum negativity at 0.9 mm. The time to peak negativity at 0.9 mm coincides with the time to the peak of the surface positive wave. At 2 mm depth the cortex ends and the response is a small negative wave. Surface records taken simultaneously with the depth records are seen on the right of Fig. 30; these show no significant change during the course of the penetration so that the comparison of depth responses is valid.

A micro-electrode penetration into the forepaw primary receiving area of the coypu is shown on the left in Fig. 31. The response is a pure negative wave at depths in excess of 0.8 mm and is intensely negative between 1.0 and 1.4 mm. With further increase in depth the response decreases in size. At this depth the micro-electrode is in white matter. No depth responses are observed at a

Fig. 30. Depth responses to contralateral forepaw stimulation in the rabbit. Depth indicated on left. Surface control records on right.

10.

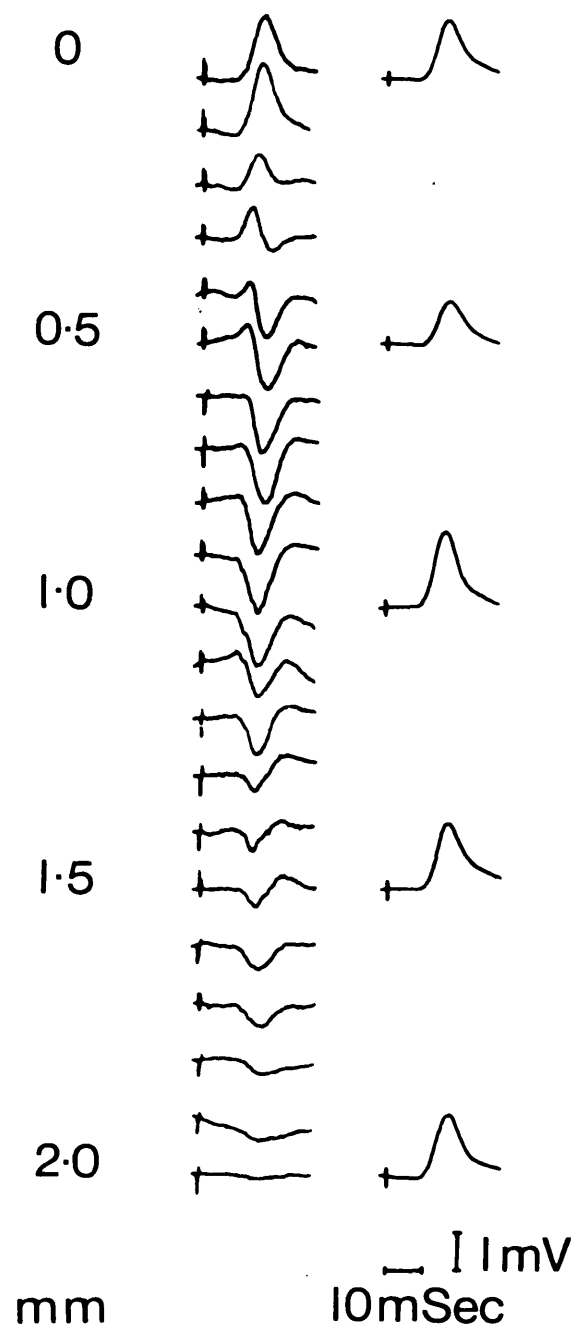


Fig. 30

Fig. 31. Depth responses to contralateral forepaw stimulation in the coypu. Depth indicated on the left. Control surface records on right.

90.

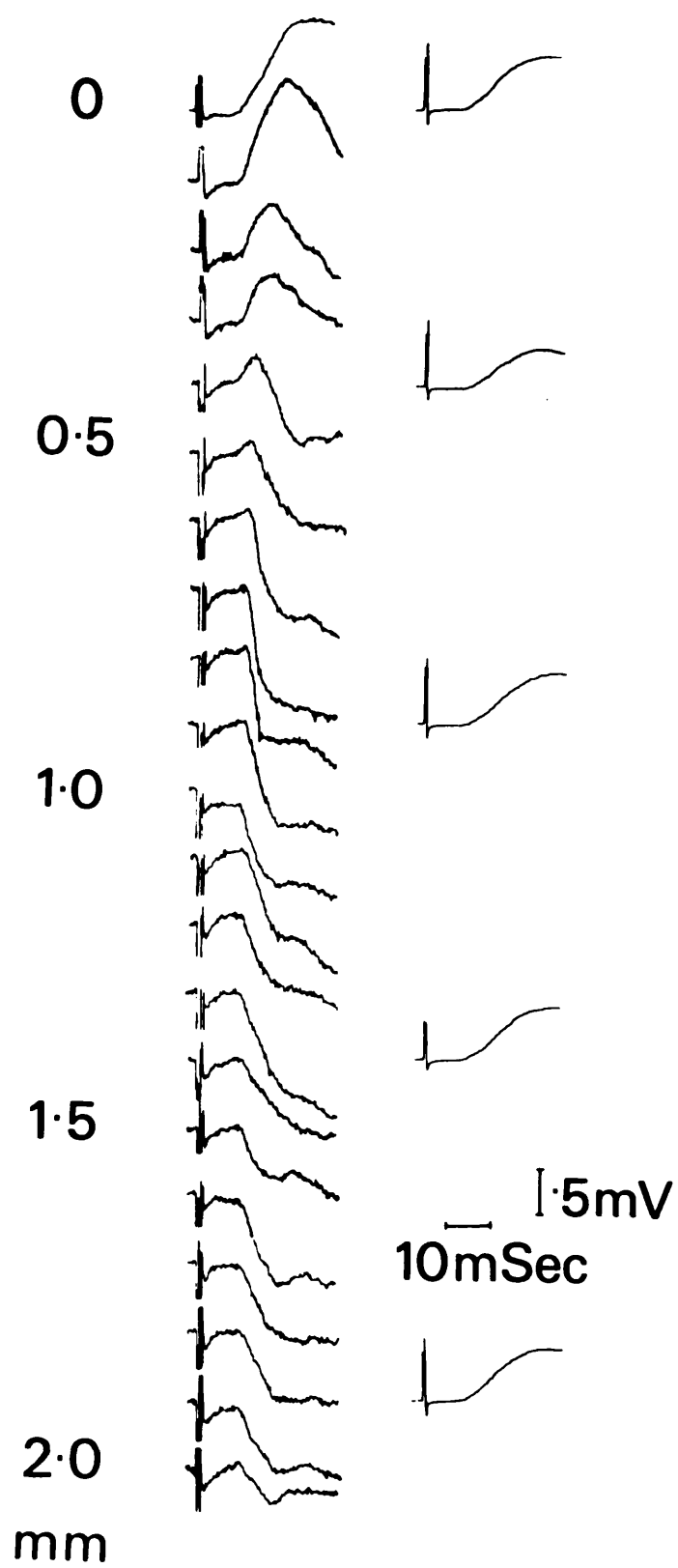


Fig. 31

distance from the primary receiving area, where there is no surface response to contralateral forepaw stimulation, in this or any of the species studied in this work.

The conclusion to be drawn from this section is that the responses evoked on the surface of the cortex and at depth, by stimulation of the contralateral forepaw, are similar in the rat, rabbit and coypu. Anatomically these three species are similar, in that they all have flat brains, but differ in size. The cat is gyrencephalic and has a brain about the same size as that of the coypu. The evoked potentials in the cat are different from those in lissencephalic species (vide supra). It seems that size is less important than cortical architecture in its effect on evoked responses.

The potential evoked by contralateral cortical stimulation in the rat

Surface response Some components of both mass and unitary potentials evoked by a peripheral stimulus depend upon the absence of spontaneous cortical activity at the instant of arrival of the afferent volley (Bindman et al., 1964; Carter et al., 1969b). Fig. 32 illustrates the

Fig. 32. Response evoked at the surface of the rat cerebral cortex by electrical stimulation of the contralateral forepaw during the absence (Q) and presence (A) of spontaneous cortical activity. Both records are the Biomac average of 16 transients. Records taken from the forepaw primary receiving area.

91.

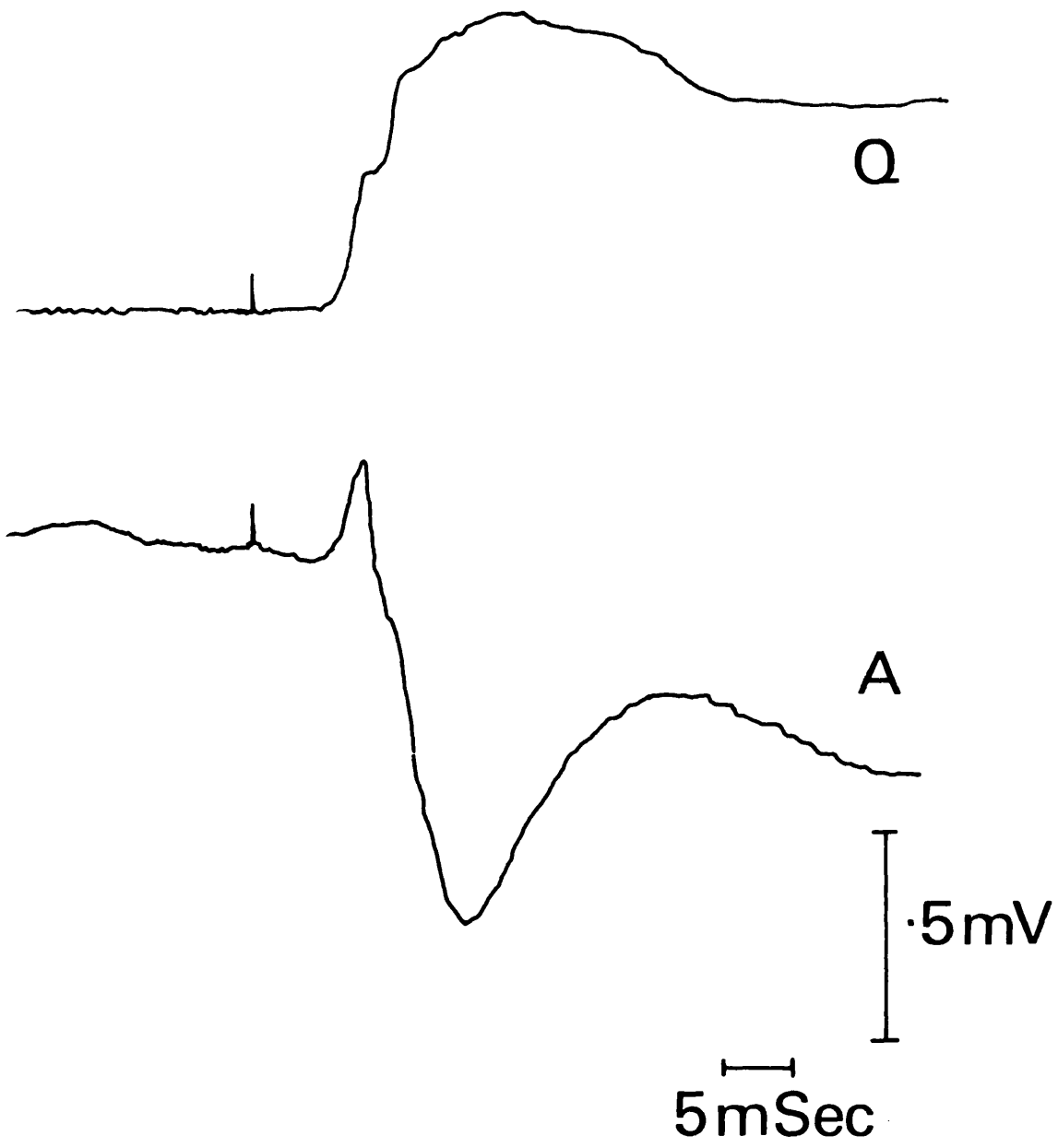


Fig. 32

effect of spontaneous cortical activity on the response; in the absence of spontaneous cortical activity (Q), stimulation of the contralateral forepaw evoked an initial positive wave followed by a larger, long lasting positivity (the Pq wave of Carter et al., 1969a). When the stimulus was delivered during spontaneous cortical activity (A), a large negativity followed the initial positive wave.

To investigate whether potentials evoked by electrical stimulation of the contralateral cortex in the rat behaved similarly, a point on the forepaw receiving area of the contralateral cortex was stimulated. The response to this type of stimulus could be recorded over a large continuous area of the cortex, but points at which the response showed the shortest latent period and least variation were found to be homotopic to the point of stimulation. This confirms the results of Curtis (1940a) and Chang (1953a) in cats. Fig. 33 shows the point of stimulation on the right cortex and the point of largest response, homotopic to it, on the left cortex.

The form of the surface mass response was affected,

Fig. 33. Photograph of rat brain exposed for recording the response evoked by stimulation of the surface of the contralateral cortex. The point (■) gave the largest response, with the shortest latent period, to an electrical stimulus applied at point (●). B.-bregma.

94.

Post.

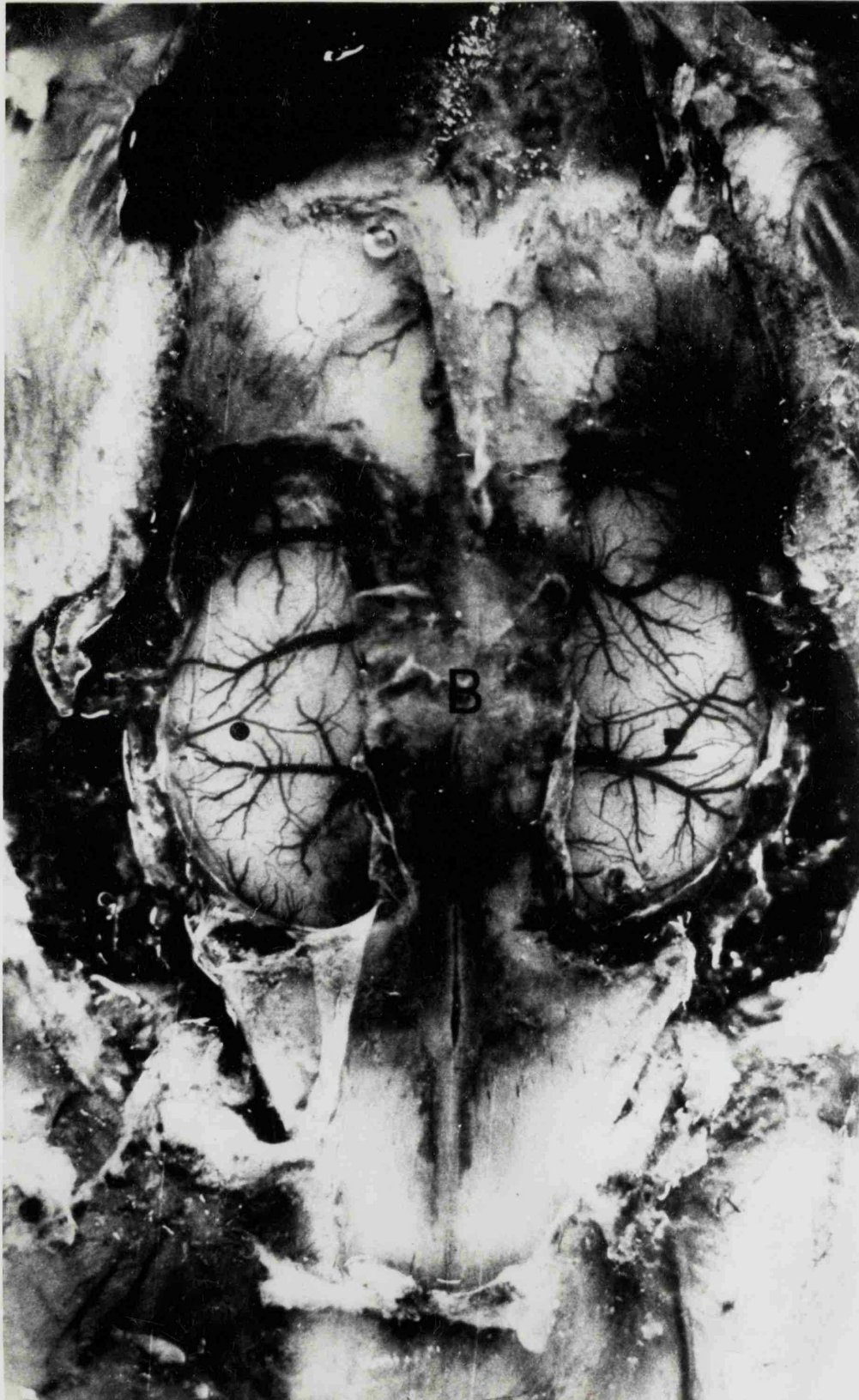


Fig. 33

as in the forepaw evoked response, by the spontaneous activity of the cortex. If a stimulus was given when the cortex was quiet, the response was a positive deflexion, with a latent period of 3 msec and a peak positivity of approximately 1 mV after 15 msec (Fig. 34Q). If a stimulus was given when the cortex was spontaneously active, the response showed a small initial positivity, with a latent period also of 3 msec, followed by a large negative wave with a peak after 15 msec (Fig. 34A). However the area of cortex over which the response could be recorded was the same in both cases.

Responses at depth A glass micro-electrode was advanced into the region of largest surface response and depth records were taken at regular intervals. Responses to contra-cortical stimuli delivered during cortical quiescence were taken for Fig. 35 and during spontaneous cortical activity for Fig. 36. The responses were plotted in contour form as described by Holmes and Short (1970). This involved plotting points of equal potential with depth in the cortex, against the time after the stimulus.

Fig. 34. Responses evoked at surface of the rat cerebral cortex, by electrical stimulation of the contralateral cortex during the absence (Q) and presence (A) of spontaneous cortical activity. Stimulating and recording positions as in fig. 33. Both records are the Biomac averages of 16 transients.

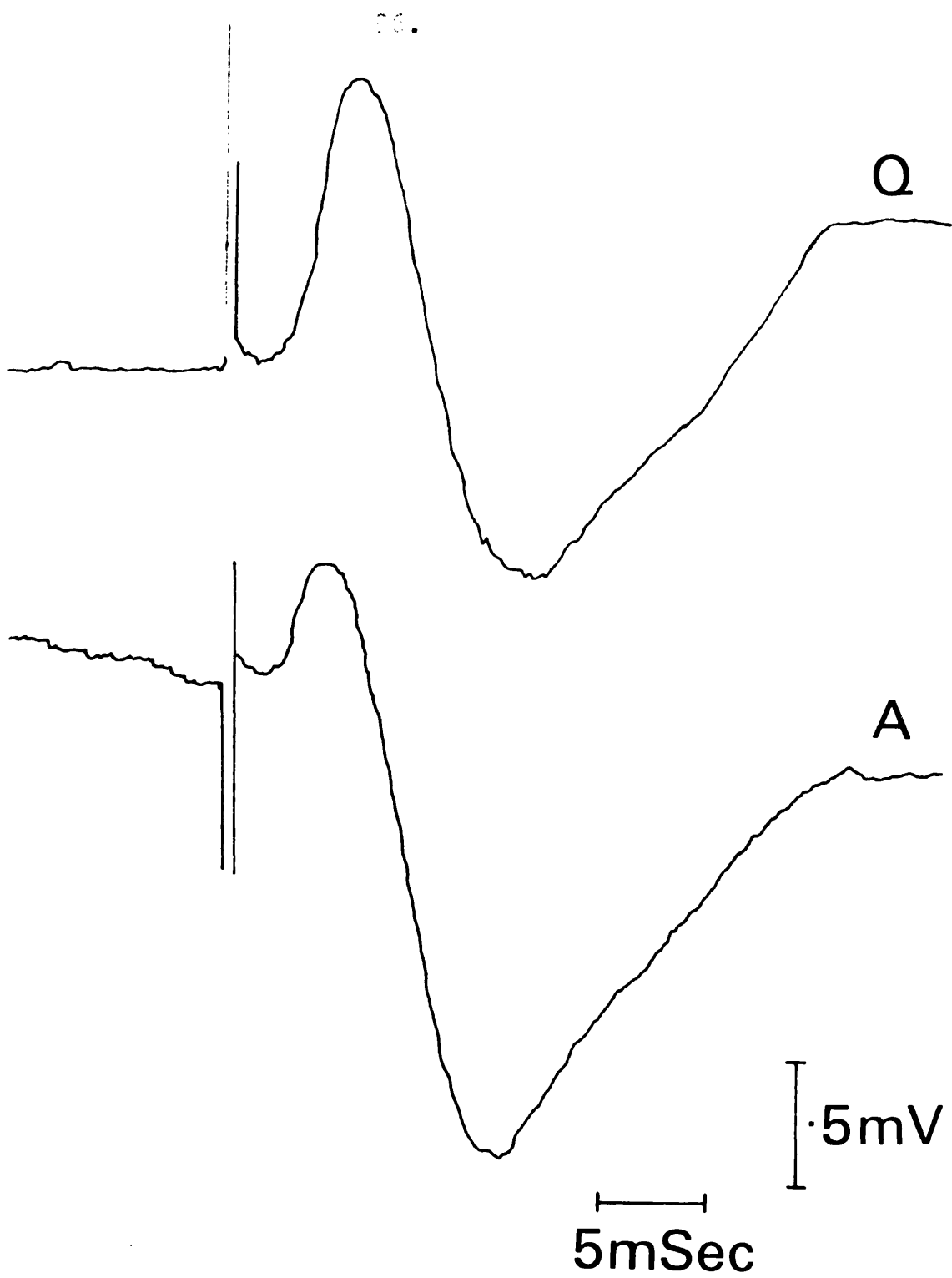


Fig. 24

Fig. 35. Potentials evoked at depths within the cortex, by stimulation of the contralateral cortex during cortical quiescence. The potential, plotted as a function of depth and time after the stimulus, is represented by contour lines and shading (squares.- positive, vertical lines.- negative). The closer the squares or vertical lines, the greater the potential, positive or negative. In both figs. 35 and 36 records were taken at 0.05 mm intervals down to 0.5 mm depth. Deep to this records were only taken at 0.1 mm intervals. (see text for explanation).

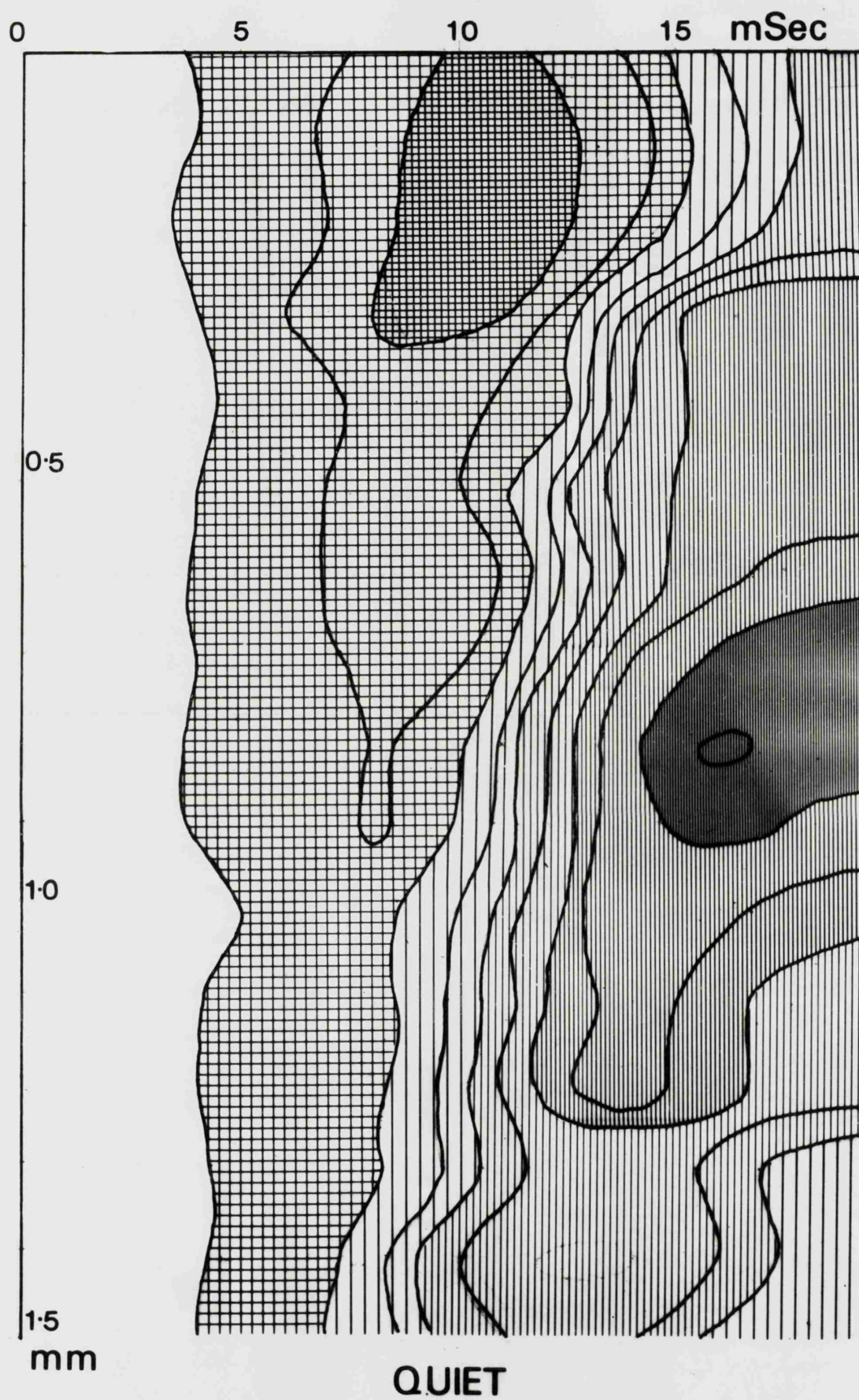


Fig. 35

Fig. 36. Same as fig. 35, but all records taken during periods of spontaneous cortical activity.

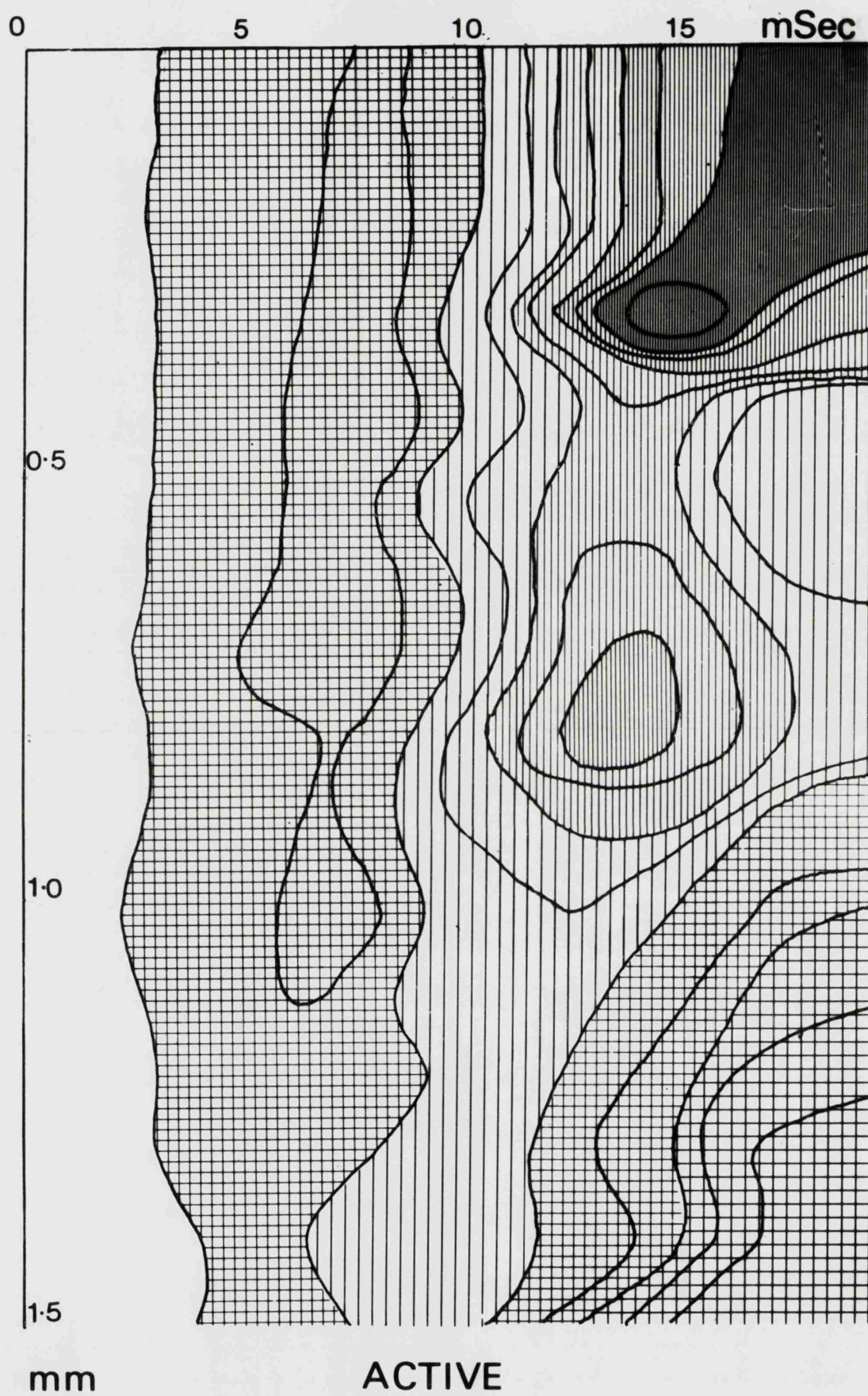


Fig. 36

Each individual response was drawn out in the form of a depth plot, as previously described (c.f. Fig. 27 - depth responses in the rabbit). Arbitrary units of potential were selected and the time after the stimulus that each unit occurred was plotted. This was done for each depth response; lines of equal potential were then joined in order to produce a contour plot. Positive potential is represented by squares and negativity by vertical lines; the closer the squares or lines, the greater the potential. In this way peaks of potential are displayed with respect to depth and time. Both plots are from records taken during a single penetration.

Fig. 35 is a contour plot of the depth responses evoked during cortical quiescence. A small peak positivity is seen superficially, with a latent period of about 10 msec. A larger depth negativity (at 0.8 mm) occurs at a latent period of about 17 msec. The contour plot of responses evoked during cortical activity is shown in Fig. 36. Two peak negativities are seen, one superficially with a latent period of about 15 msec and another at depth (0.8 mm) with a latent period of 14 msec.

There was some variation from one experiment to the next but in all experiments the difference in response in the two circumstances was seen at points down to 0.6 mm depth.

Of the nine contour plots drawn, seven had regions of peak negativity in the superficial layers of the cortex, only in the response to stimuli given in active periods. All except one had a peak negativity deep in the cortex in both quiet and active periods. The consistent difference between the response in the two states is the large superficial negativity, maximum at approximately 0.3 mm, recorded only when the cortex was active. Although there are differences in the peak negativity of the quiet and active response, recorded at a depth of 0.8 mm, examination of records from all the experiments reveals that differences at depths greater than 0.6 mm are inconsistent.

At a depth of 1.0-1.5 mm a positivity is seen in the active response. By referring to Fig. 22 it can be seen that this is the extracellular potential distribution to be expected from the depolarisation of a superficial region of the cortex, by an afferent volley. A description of unitary potentials follows, which supports the

hypothesis that superficially situated cell bodies are depolarised by an afferent volley, more frequently during spontaneous cortical activity.

To make sure that changes in the responsiveness of the cortex did not occur, the surface response was monitored continually throughout these experiments. As a further control, in two experiments simultaneous records were taken on the surface and at 0.5, 1.0 and 1.5 mm depth, in both active and quiet cortex (Fig. 37). The records taken during these experiments showed the same features as records taken consecutively at different depths. This suggests that no appreciable alteration of the response occurred during consecutive recordings.

The cortex in the forepaw primary receiving area was explored for extracellular unitary responses to contralateral cortical stimulation. Observations were confined to units firing with a latent period of less than 15 msec. Such unitary potentials were found at depths ranging from 0.2-1.5 mm in 21 experiments (Fig. 38). The majority of units fired with a single discharge, but occasionally two or even three discharges were observed.

Fig. 37. Responses recorded on the surface and at depths in the cortex, to contralateral cortical stimulation delivered during cortical quiescence (Q) and activity (A). Depth indicated on the left. The four responses were recorded simultaneously first during cortical quiescence and secondly, during cortical activity. Each record is the Biomac average of 16 transients. The responses are similar to those taken during the course of a penetration lasting 1 hr.

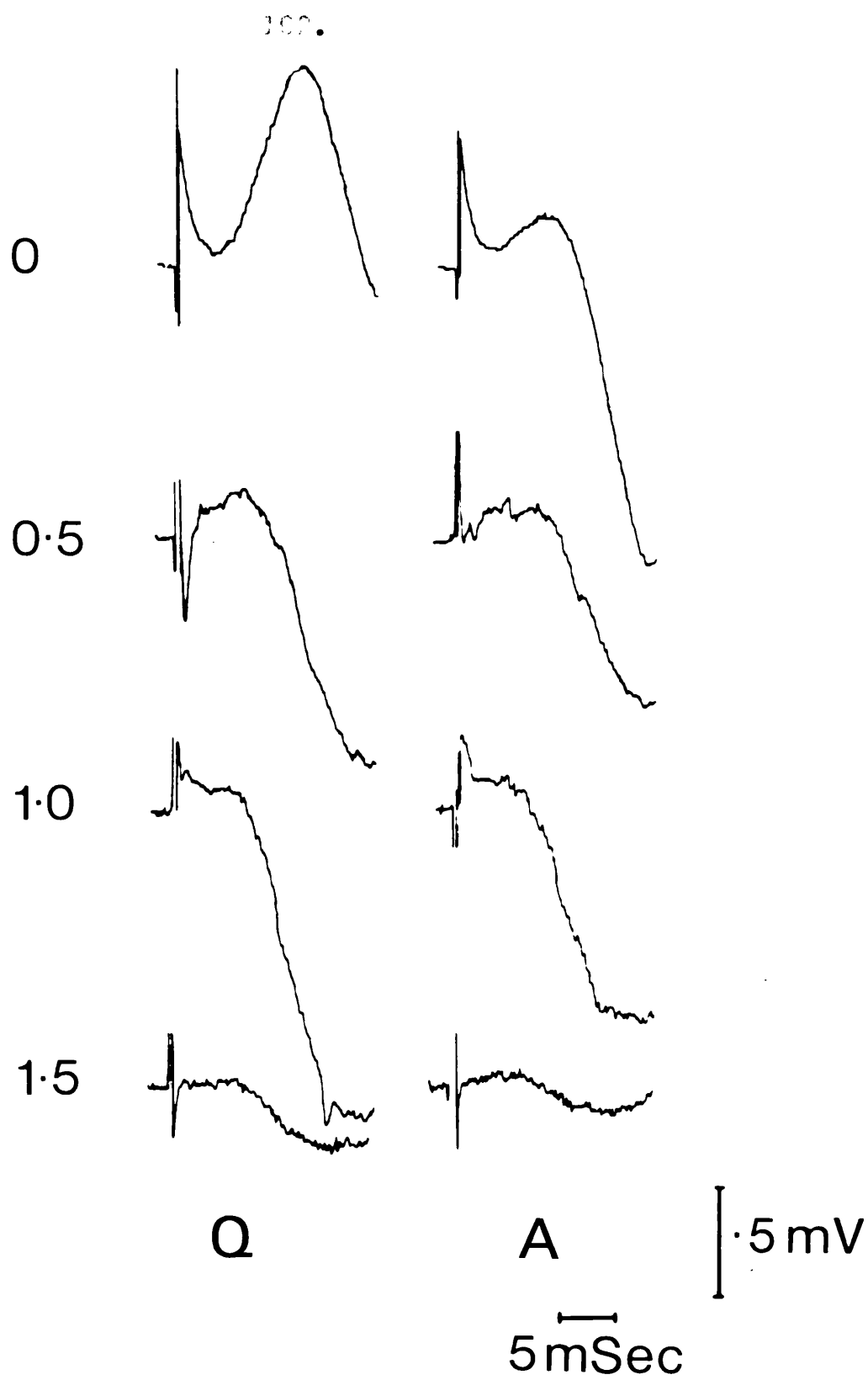


Fig. 38. Summary of units evoked by contralateral cortical stimulation in 21 experiments. Responses are plotted as a function of depth within the cortex and time after the stimulus. Each symbol represents one unitary discharge. ● - units responding in both active and quiet cortex. □ - units responding more frequently in active cortex.

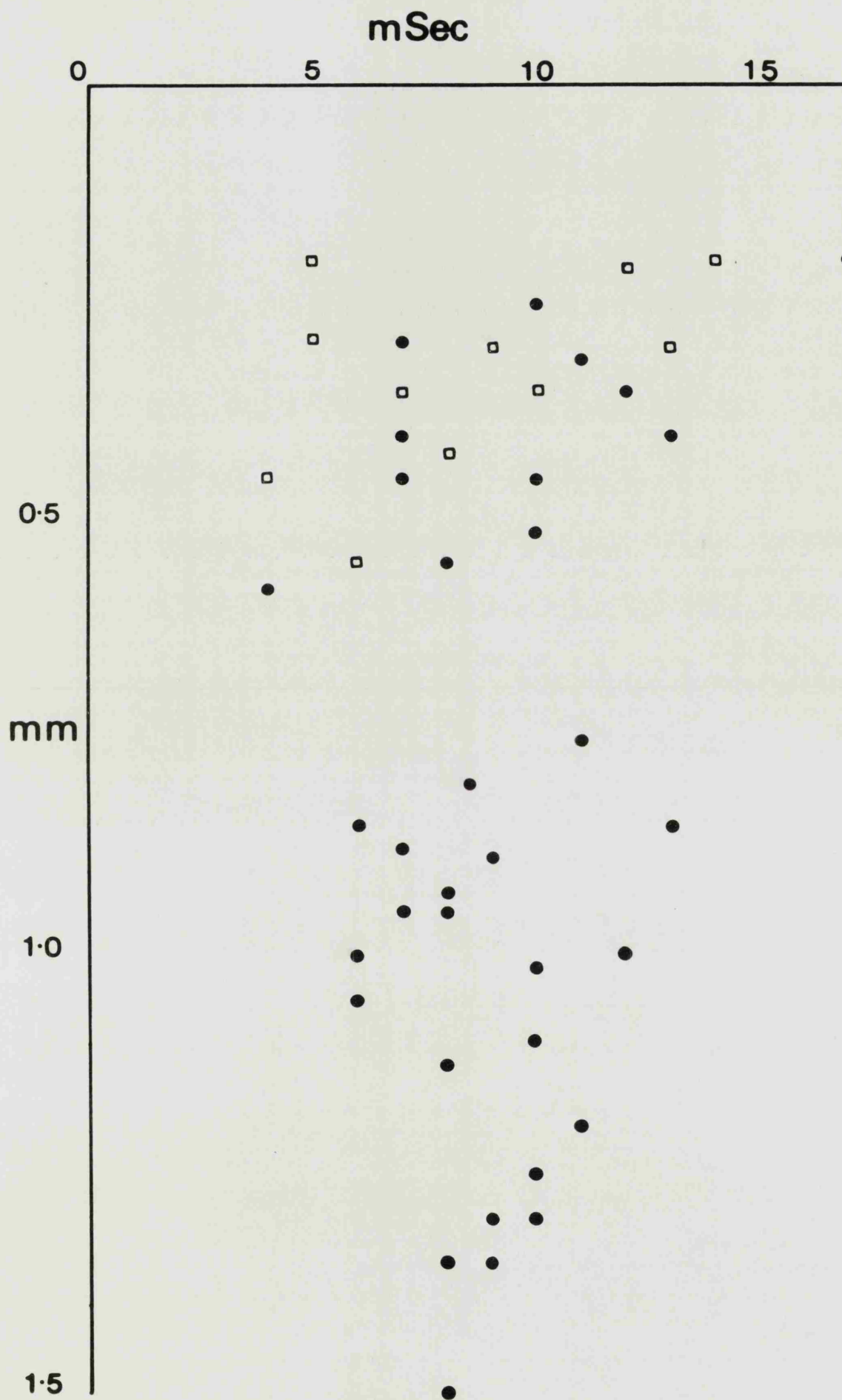
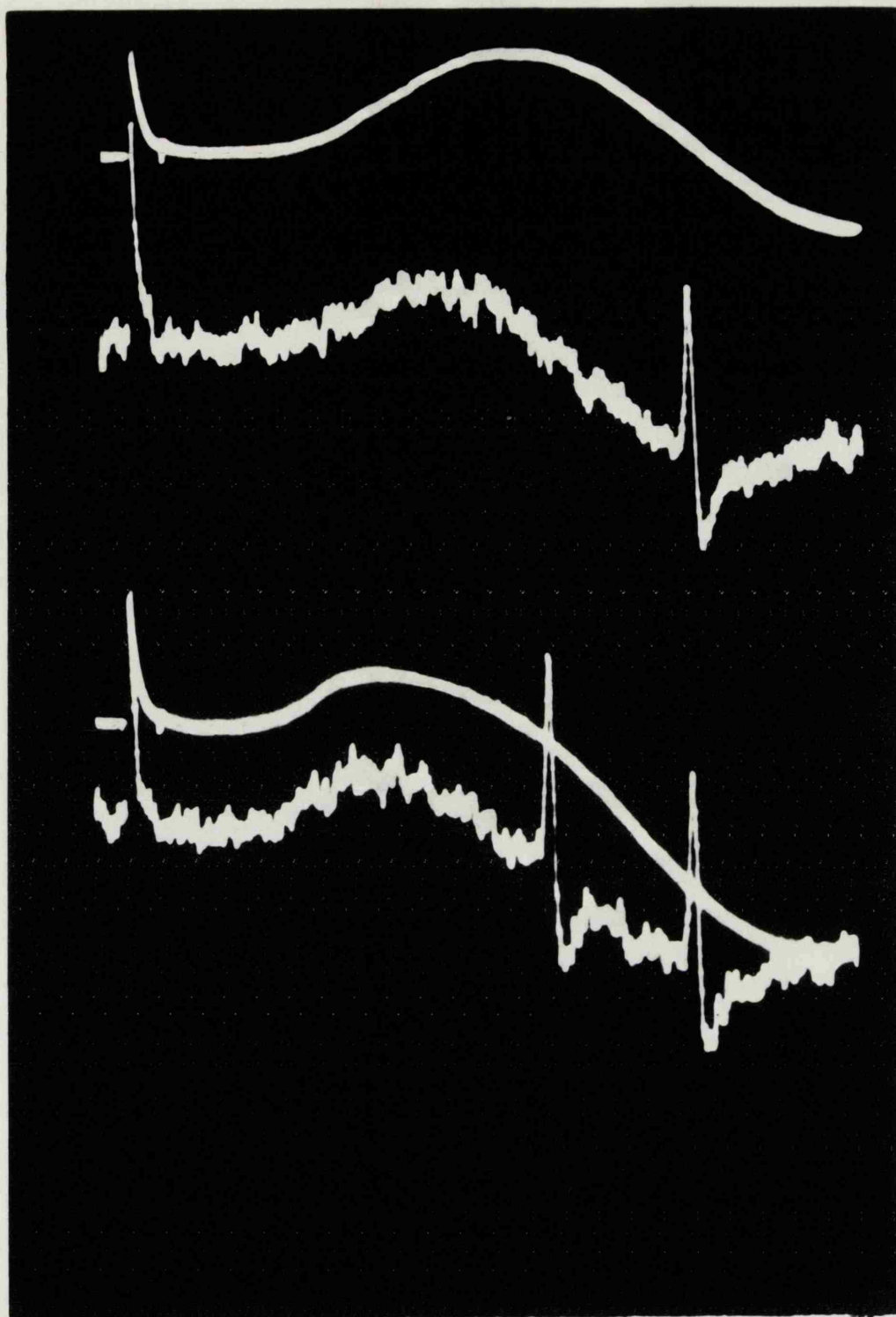


Fig. 38

All evoked units below a depth of 0.7 mm responded to stimulation, irrespective of the presence or absence of spontaneous cortical activity. Of the more superficial units, 11 out of the 23 studied showed different characteristics in active and quiet periods. The response of these units correlated closely with the form of the simultaneously recorded surface mass response. When the surface response showed the large positive deflexion, typical of the quiet state, superficial units fired only once. However, if the surface response had a large, later negativity, the unit fired more than once in 50% of the trials (Fig. 39). When a unit fired more than once, the latent period of one of the unitary potentials coincided with the latent period of the unitary response in the quiet state (Fig. 39).

In some experiments the contralateral forepaw was stimulated to discover whether this form of stimulation would influence the behaviour of units evoked by contralateral cortical stimulation. Only three units responded to contralateral forepaw stimulation as well as to contralateral cortical stimulation. On one occasion a unit was inhibited

Fig. 39. Mass and unitary responses to contralateral cortical stimulation delivered during periods of cortical quiescence (upper pair) and activity (lower pair). The upper trace of each pair is the surface mass response and the lower trace the mass and unitary response at a depth of 0.35 mm within the cortex.



5mSec

5mSec

1mV

Fig. 39

by simultaneous stimulation of the contralateral forepaw; it did not respond to forepaw stimulation alone.

In general, the extracellular action potentials found in superficial layers of the cortex are of lower voltage than those found in deeper layers. This corresponds with the observation that larger pyramidal cells are found in the deeper layers of the cortex, such as layer 4, than in more superficial layers (Scholl, 1956).

The evidence taken from depth penetrations and unitary activity suggests that the positive wave, evoked by contralateral-cortical stimulation during the absence of cortical activity, is the product of the depolarisation of a localised group of cells at a depth of about 0.8 mm in the cortex. Although these cells have not been identified histologically, previous evidence from forepaw stimulation (Holmes & Short, 1970) points to the fact that they are pyramidal cells. The negative wave, evoked by contralateral cortical stimulation during spontaneous cortical activity, is associated with the depolarisation of a superficially situated (0.3 mm) group of cells. This hypothesis is further substantiated by the evidence

from extracellular unitary discharges within the cortex.

Thus a higher frequency of discharge, in response to contralateral cortical stimulation, has been observed in superficial cells during spontaneous cortical activity.

CHAPTER IV

DISCUSSION

The waves evoked in the cerebral cortex, by peripheral stimulation, in the rat, rabbit, coypu and cat

From the results of previous authors (Angel & Holmes, 1967; Carter et al. 1969a) it is known that, in the cortex of a rat, a peripheral stimulus elicits a mass response consisting of a surface positive wave and a more intense depth negativity. This is the field which would be anticipated from the depolarisation of the somata and basal dendrites of a group of pyramidal cells (see Fig. 1). Unitary discharges occur in the same regions and with the same latent period as the intense depth negativity of the mass response (Carter et al. 1969a). Hence predictions from volume conductor theory have been substantiated by experimental observation in this species.

In the present work, observations of a similar nature have been made on two other lissencephalic species, the rabbit and coypu. As in the rat, responses with two discrete latent periods are evoked at the cortical surface of both species. An initial positivity, at the centre of the receiving area, is observed in the coypu; this is presumably analagous with the P_1 wave observed in the

rat (Carter et al. 1969a) and is responsible for the short latent period in this region. No wave analagous to the P_1 wave is seen in the rabbit, although a short latent period is evident in the centre of the receiving area. This short latent period is presumably due, however, to a small initially positive wave which, in the centre of the receiving area, merges with the late positivity and is not seen as a discrete wave.

Micro-electrode penetrations into the centre of the forepaw receiving area in rabbit and coypu show similar features to a penetration into the analagous region of the rat cortex. The surface positive wave is paralleled by a negativity at depth in all three species.

In the cat, by contrast to the lessencephalic species, the surface response shows a diversity of form dependant upon the site of the recording electrode. Adrian (1941) reported that, in anaesthetised cats, two discrete areas of the cortex responded to contralateral forepaw stimulation; these areas were found around the coronal sulcus and in the anterior ectosylvian gyrus. Woolsey (1947) named these areas somatic areas I and II respectively

(SI and SII). The response in these areas was usually a positive wave, sometimes followed by a negativity. Initially negative waves have been recorded, however, in the region medial to the coronal sulcus. (Malcolm & Darian-Smith, 1958; Whitehorn et al. 1969). In addition to these areas, association responses, more variable in nature and of longer latent period than those described above, to contralateral forepaw stimulation have been recorded over a wide area of the cortex (Thompson et al. 1963).

In the present work, the region around the coronal sulcus (SI) and medial to it has been studied in detail. Only that part of the response within 40 msec after the stimulus was recorded and this excludes any observations on association responses. As described by previous authors, the evoked potential consisted of a pure positive wave at SII, a positive-negative wave at SI and an initially negative wave medial to SI in the post-cruciate cortex. However in the present work, the discrete nature of SI and SII was not clear. Even with a small electrical or mechanical stimulus applied to the contralateral fore-

paw the regions between SI and SII yielded evoked potentials; these were intermediate in form between the responses characteristic of SI and SII. It would appear that the stimuli used were sufficient to activate a number of receptors sending afferent volleys to both SI and SII.

Micro-electrode penetrations of the cat's cortex have been made in order to discover the sites of the sources and sinks of current provoked by stimulation of the contralateral forepaw. The distribution of potential in spatial and temporal dimensions has been measured. It was found that the voltage was most negative in a region of grey matter in the upper limb of the cortex at the base of the coronal sulcus. Voltage gradients were steepest in the immediately surrounding regions. At the surface of the coronal sulcus (SI), the initial deflexion was positive; medially the surface response was initially negative. The mass potentials which have been described at these various sites occurred at about 10 msec delay after the stimulus. Taken together, these results indicate an intense sink situated in the region of grey

matter in the upper limb at the base of the coronal sulcus, with a source in the overlying cortex. From the theoretical considerations of Holmes & Houchin (1967) such a mass potential may be attributed to depolarisation in the cell bodies of a localised group of pyramidal cells. A semi-quantitative plot has been made of the electrical field to be anticipated from the depolarisation of a cell body of a pyramidal cell lying in the region of the observed intense negativity (Fig. 23).

When an afferent volley of nerve impulses arrives at the cortex, the volley would be expected to initiate post-synaptic potentials, both excitatory and inhibitory and also unitary discharges in cortical cells. These physiological responses generate the extracellular current which is responsible for extracellularly recorded potentials. With methods as coarse as those used in this work, subtle patterning in time and space of those various electrophysiological effects would be missed. Indeed, the only effect of an afferent volley, recorded by the technique used in the present work, is post-synaptic activation in or near the somata of a group of

pyramidal cells confined to a small region of cortex.

Extracellular unitary discharges have been recorded in response to contralateral forepaw stimulation. In the region of grey matter showing the intense negative deflexion in the mass response, many evoked units were recorded. The latent period of these evoked units was about the same as the peak negativity of the evoked mass potential recorded at depth. In the regions immediately surrounding SI and medial to it, evoked unitary responses have not been observed. No study has been made of units in SII. However, previous authors have observed evoked units in SII at a depth of 1.0-1.5 mm (Amassian & Thomas, 1952; Carreras & Anderson, 1963).

Stimulation, through a micro-electrode which had previously recorded unitary activity in SI, elicited a surface mass response consisting of a large positive wave immediately over the stimulating electrode and a smaller negative wave medial to this. This is the same distribution of voltage as the response to forepaw stimulation (Fig. 25). This provides confirmatory evidence that the forepaw response reflects the discharge of a localised

group of pyramidal cells.

Although the response at different points on the surface of the cat cortex can be attributed to a number of different electrical models, from depth plot and volume conductor considerations the number of these possibilities may be reduced. Thus the hypothesis that the variety of surface responses around SI and medial to it is due to separate groups of elements within the cortex would require a model with two sinks and sources. A separate sink and source is not observed in the cortex subjacent to the surface negative wave. The simplest model to account for the observed mass and unitary potentials is a single sink, situated in the grey matter of the upper limb at the base of the coronal sulcus, and a more diffuse source in the overlying cortex. Due to the geometry of the cat cortex, the coronal sulcus provides an appropriate orientation of pyramidal cells which, when depolarised, produce an overlying positivity and a negativity on the surface at a distance (Fig. 23). The geometry of the cortex and the corresponding orientation of pyramidal cells also provides the simplest explanation

for the differences observed between the surface mass responses of the lissencephalic species and the cat.

The waves evoked in the cerebral cortex of the rat, by contralateral cortical stimulation

The response evoked at the surface of the cerebral cortex of a rat by stimulation of a homotopic point on the contralateral cortex is a positive wave followed, sometimes, by a negative wave (Curtis, 1940a; Chang, 1953a; Carter et al. 1969b). The observations made in the second part of this work support this finding as long as the stimulus is delivered only during periods of cortical quiescence. During periods of spontaneous cortical activity, however, the response is a small positive wave followed by a larger negativity. In these respects the surface response to contra-cortical stimulation behaves in a similar manner to the response evoked by contralateral forepaw stimulation (Ennever, 1969; Carter et al. 1969b). Thus in both cases the later, negative component is more noticeable when the stimulus is delivered during spontaneous cortical activity. Carter et al. (1969b) have provided a hypothesis to explain

the different forms of response evoked by contralateral forepaw stimulation during the presence and absence of spontaneous cortical activity. They suggest that different parts of the waveform are associated with the activity of different cylinders of elements in the subjacent cortex. Thus in active cortex, the forepaw response is confined to a small cylinder of elements responsible for the early positive wave or series of waves together with a superficially situated disk of elements responsible for the later negative wave. In quiet cortex the same elements respond in a similar way but, in addition, deeply situated elements over a wider area of cortex are responsible for the late widespread positivity, typical of the forepaw response in quiescent cortex. In support of this hypothesis Carter et al. (1969b) found unitary discharges, evoked by contralateral forepaw stimulation, at a depth of around 1.2 mm, only in quiescent cortex. No superficial unitary discharges, correlating with the superficial disk of negativity, were observed.

Micro-electrode penetrations into the cortex have

shown that there are two pockets of negativity found in the mass response to contra-cortical stimulation. A deep pocket, maximal at about 0.8 mm, is present irrespective of the presence or absence of spontaneous cortical activity. A more superficial pocket, maximal at about 0.3 mm depth, is only seen when the stimulus is delivered during spontaneous cortical activity.

Unitary discharges have been found, in response to contra-cortical stimulation, at the same depth as units responding to contralateral forepaw stimulation (Holmes & Short 1970). In this work units responding to the stimulation during the presence and absence of cortical activity have been observed throughout the depth of the cortex (0.2-1.5 mm). However, units which respond more frequently during spontaneous activity have been found at superficial levels in the cortex (0.2-0.6 mm). This additional unitary evidence further substantiates the observations of Carter et al. (1969a) that a separate, superficial group of elements is responsible for the appearance of a large negative wave in active cortex.

From the previous discussion on the nature of the

response evoked by contralateral forepaw stimulation, it can be seen that the depolarisation of a local group of pyramidal cells at depth would be reflected as a surface positivity. The surface positive response to contracortical stimulation delivered during the absence of spontaneous cortical activity in the rat may be explained in a similar manner. In fact, intense negativity and extracellular unitary discharges are seen at depth in both active and quiet cortex. The early, small positive wave of active cortex may also be explained by this deep depolarisation. It is probable that the later, large negativity seen in the active cortex is the product of the superficial depolarisation seen only during spontaneous cortical activity (see Fig. 36) and that the surface positive wave is diminished by this superficial depolarisation. Additional evidence for this hypothesis is furnished by the observation that the surface application of narcotics rapidly diminishes the amplitude of the later negative wave indicating that the elements responsible for this wave are situated superficially in the cortex (Chang, 1953b).

The effect of delivering stimuli to both the contralateral cortex and forepaw of the rat, either simultaneously or at close intervals, has been studied by Holmes & Short (1970). They found that the second positive wave of the forepaw response and the response to contralateral cortical stimulation interacted. These authors concluded that the interaction involved common cortical elements. They also found that the simultaneous stimulation of the contralateral cortex sometimes inhibited the firing of a forepaw unit. In the present study, unitary discharges to contralateral-cortical stimulation have been recorded superficially (0.2-0.6 mm) and at depth (0.7-1.5 mm) within the cortex. Of the 45 units recorded, only 3 responded to both forepaw and contra-cortical stimulation. On only one occasion was a unit inhibited by simultaneous stimulation of the contralateral forepaw; this unit was observed at a depth of 1.2 mm. These observations on unitary discharges conform with the observations of Holmes & Short (1970).

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APPENDIX

It is important to note that the latent period of onset of the surface response to contralateral forepaw stimulation in the cat is the same over the whole of the cortex from which a response is recorded. The fact that it is constant within the limits of experimental error ($8\frac{1}{2} \pm \frac{1}{2}$ msec) supports the hypothesis that both the initially negative wave, recorded in the cruciate region, and the initially positive wave, recorded over the coronal sulcus can be ascribed to active depolarisation of only one region of the cortex. This is further supported by the observation that unitary discharges, recorded at the base of the coronal sulcus, which coincide with the peak of the surface positivity also coincide with the peak of the surface negative wave.

Interpretation of the depth records obtained in fig. 16 is made difficult by the fact that the electrode track, illustrated in the following diagram (fig. 17) appears to penetrate the cortex very close to the coronal sulcus. Records obtained from such an electrode penetration should yield only pure positive responses,

according to the hypothesis illustrated in fig. 23.

The fact that negative responses were recorded in the lower part of the track indicates that the track is not the one shown in fig. 17. It is considered probable that the electrode was parallel to the track shown, but situated about 1 mm medial (to the left) of it.

Further experiments which could be performed to substantiate this hypothesis will be briefly mentioned. First, a local anaesthetic agent could be applied to the medial limb of the infolded grey matter of the coronal sulcus. If the hypothesis is correct, any effect which this agent has on the waves recorded in the cortex above the coronal sulcus should also be evident in the negative waves elicited in the region of the cruciate sulcus. Secondly, it is known that a preceding contra-cortical volley reduces the amplitude of the surface positive wave evoked by contralateral forepaw stimulation (Perl & Whitlock, 1955). This interaction occurs in the cortex (Chang 1953b). Any reduction in size of the positive wave should be accompanied by a reduction in size of the negative wave.

ERRATA

Pg. 16. The calibration should read 1 cm.

Pg. 19. Marshall et al. (1941) should read Malcolm & Darian-Smith (1958).

Pg. 60. The calibration should read $\cdot 05$ mV.

Pg. 78. The extracellular current and voltage fields in diagram 23 are taken from the work of Holmes & Houchin (1967).

Pg. 95. Line 2. If a stimulus was given when the cortex was quiet, the response was a positive-negative deflexion, with a latent period of 3 msec and a peak positivity of approximately 1 mV after 5 msec (Fig. 34Q).