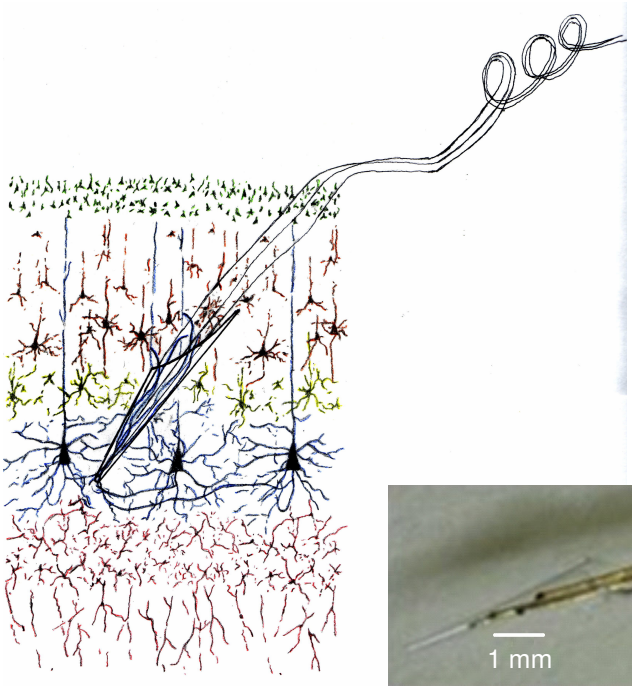
### 2.1 Diagram of electrode in cortical layers




The basic format of the electrode lying within cortical tissue is shown in fig. 1. The six layers of cortex are diagrammed with the electrode tip in position near layer five that contains corticospinal tract cells. Neurites are shown growing into the tip, through the cone, and out the top end so as to hold the glass cone tip in position. The tip is introduced at an angle of 45 degrees from the surface of the cortex, and inserted for a distance of 5 to 6 mms until the part of the wire on the surface of the cortex limits its insertion depth. The wire is brought along the surface and then rises above it with continuous coiling until it reaches its connector on the skull. The coiling provides strain relief in the X,Y and Z dimensions, operating like a 'slinky' child's toy that can move side to side in any direction as well as in and out. The inset shows an actual four wire glass cone tip. The scale bar is 1.0 mm.

### 2.2 Histology

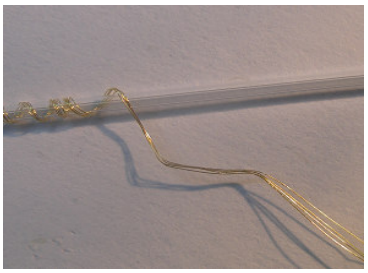
Histological preparation and analysis has been described previously (1,2). We have employed light and EM microscopy in rats and monkeys. No human histology is available for logistical and technical reasons. The histology is discussed below in section 3.2.

### 2.3 Electrode assembly

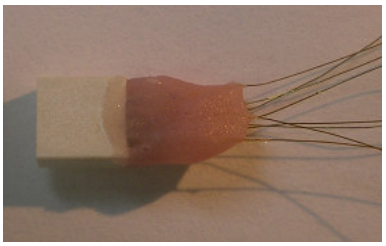
The electrode consists of coiled gold wires with a glass cone tip on one end and a connector on the other. Initial attempts at assembly produced only one wire inside the cone, then two, now we have three wires in an implanted subject, and have produced four wire versions of the electrode as shown in the inset of fig. 2.3.1. Other recent improvements include smaller connectors, specifically those from Omnetics Inc.'s Nanoconnectors series. We describe here the complete method updated from our original description (1).

Assembly of the four-wire version is usually begun by taking a long length of 2 mil

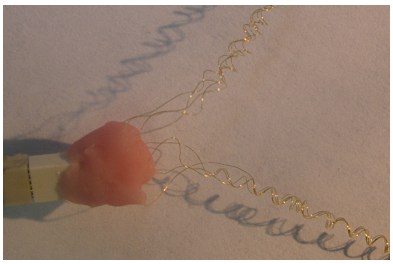
Teflon coated gold wire (California Fine Wire Inc). The length is estimated by multiplying the final length by four or five. Therefore if a one-inch electrode is required, 16 inches of wire are used, 4 inches by 4 wires. This is first coiled on a hand wound mandrill as shown in fig. 2.3.2a. Next, the lower (cone) end is bent at 45 degrees and then a second bend is added at 45 degrees in the opposite direction as shown. These bends limit the possible implantation depth as shown in fig.2.3. 2b. The final bend at 45 degrees directs the wire into the cortex at the correct 45 degrees angle.



Next the connector is soldered onto the wire ends. A small load of solder is applied to the pin connectors. The wires are bared for 1 – 2 mm by scraping away the Teflon coating. The bare end is placed against the pin loaded with solder and heated until the solder is seen to begin to melt. The heating iron must be rapidly removed to avoid melting back the gold wire. The solder will be seen to envelop the gold wire end.



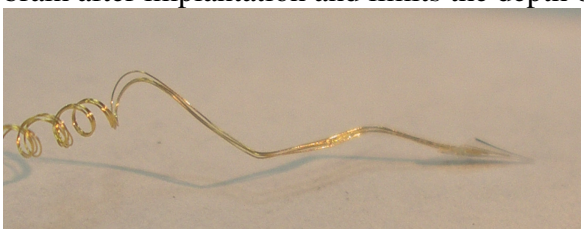
Finally, a coating of dental acrylic is applied to the connections to protect them from trauma. In the latest version of the electrode we are using Nanoconnectors from Omnetics Connector Corporation (7260 Commerce Circle East, Minneapolis MN - 55432). An example of these tiny connectors with acrylic covering the wire origins is shown here in fig. 2.3.2c. A further example is shown below with two coiled wires.



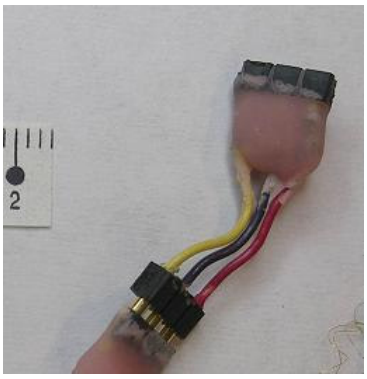
The next step is to manufacture and attach the cone. The glass cone is shaped by heating and pulling a thin walled borosilicate microfilament glass rod of wall thickness 0.125mm and diamter 1 mm (AM Systems Inc). The electrode puller (Kopf model 720) has settings of 12.5 for the heater and 1.0 for the solenoid that applies the pull. The lower

end is shaped by breaking the tip with forceps until the tip diameter is 50 to 100 microns. The upper end is shaped by using a diamond knife to cut the glass. Prior to cutting, a piece of fine wire (one strand of a stainless steel wire) or fine hair is inserted into the lower end so that when it is cut off and moves away, it can be easily retrieved and held with fine forceps. The upper end is broken back with forceps until it measures about 300 -

400 microns in diameter, and has a shelf extension. The covered area of the electrode should be about 1 to 1.5 mm. The final result is shown in fig.2.3.2d with the hair inside. Scale is in mms. The figure below (2.3.2e) shows another view of the final curvature of the wires. Note that the section parallel to the table surface lies along the surface of the brain after implantation and limits the depth of the tip.



To attach the cone to the four gold wires, the cone is manipulated by holding the hair and approximated to the four wires until they are all inside. To hold the wires together, a dab of glue is placed along their lengths near the turns. The wires are trimmed with a new blade by cutting across their ends at an angle before the glue is used to keep them together. The exposed surface is over 50 microns in diameter and produces an impedance of 500 to 1000 kohms when measured with a 1 kHz AC current. This impedance drops over the initial weeks of implantation as discussed below. The final step is to fix the wires inside the cone. Fixation is achieved by applying the cyanoacrylate gel glue to the wires and cone. The shelf is very useful in this regard because it allows a large surface for fixation. This minimizes the possibility of glue covering the tips of the wires. The glue is applied in stages with each stage drying overnight until the gold wires and shelf are completely covered with glue. This is shown in fig. 2.3.2e.




Finally, a removable handle is made by soldering larger diameter wires to a plug that inserts into the electrode connector. This allows for easy handling of the delicate electrode. The handle, shown here in fig.2.3.2f as three colored wires plugged into the electrode's connector, is itself connected to plugs in a sealed container box. The container allows safe storage and transport prior to implantation. Scale to the left of figure is in mms.

**3.1 Diagram of electrode in cortical layers**

This design has withstood the test of time. First used in 1984, it has been implanted in over 40 rats, seven implantations in five monkey cortices, and now five humans. Placement in or near the corticospinal tract neurons assures that motor activity will be recorded. Such placement was studied using tract tracing in rats as described in the next section. However, there can be no guarantee that other neurons and interneurons don't send processes into the cone. They probably do. It is worth noting also that no

neurons reside within the cone itself but they send processes into it, which become myelinated and thus essentially axons. Thus, the recordings consist of action potentials or compound action potentials as described in sections 2.8 and 3.8. The tissue is encouraged to grow into the cone tip using trophic factors contained within small segments of sciatic nerve placed within the cone just before implantation or by using growth factors such as Nerve Growth Factor (NGF). Trophic factors encourage tissue growth into the cone tip.

### 3.2 Histology

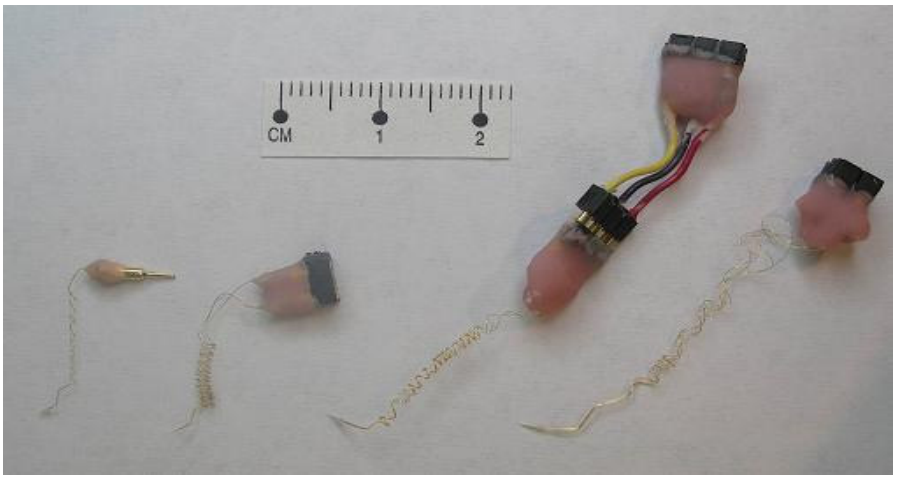
As previously reported (1,2) and summarized here, the content of the electrode's glass tip consists of myelinated axons. Axo-dendritic synapses are present but not neurons. There are no microglial cells or other evidence of gliosis. Oligodendroglial cells are seen indicating that myelination occurs within the cone. Blood vessels and supporting stroma are seen. In essence, the cone tip contains normal neuropil except that neurons are absent. There is no evidence of any remnants of the sciatic nerve that had been placed inside the tip in many rats and some monkeys. Other trophic agents such as Nerve Growth Factor, used in some rats and monkeys, are not in evidence.

Tracing techniques have demonstrated that the myelinated processes arise from corticospinal tract neurons (1). Fluorogold dye was placed within the corticospinal tract in the posterior column of the rat and was then found to be present in many of the myelinated axons of the neuropil extracted from the cone tips. Thus in fig. 1 the neurites are shown to arise from the corticospinal tract neurons. This does not imply that they cannot arise from others cells such as interneurons. However, it does allay the concern that all the neurites grow into the cone from superficial layers above the wide top end. A bridge of tissue grows through the cone and anchors the cone within the brain. The single units appeared at the lower end first as shown in fig. 3 (1). This is the basis for the stability of recordings. As will be described below, the recording is obtained by placing one or more wires along the inside of the cone tip.

### 3.3 Electrode assembly

The various types of electrodes are shown in fig. 3.3.1. On the left is an original single wire electrode that is still intact 20 years after manufacture. The glass tip was stressed by pushing on it with a forceps and did not detach from the wire. The next electrode was manufactured in 1990 and was a double wire electrode. Its tip is still intact. The 2000 electrode is a longer, three-wire electrode and is for use in human cortex. The three-colored wire extension is a temporary 'handle' for ease of handling especially at surgery (as shown in the Methods section). The final electrode is a four-wire version for human implantation. Note also the longer length of the final wires carrying the glass cone tip.

1986 1990 2000 2006

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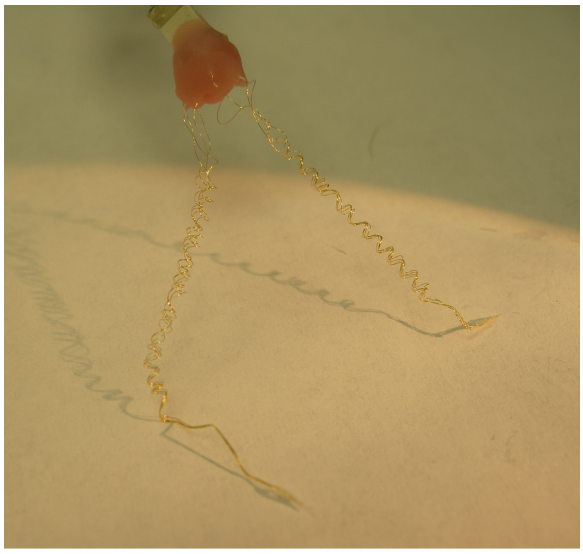

Summary: We have described in some detail how to build the Neurotrophic Electrode. We have discussed the histological results. We will soon discuss other features of these techniques in future uploads. References are listed in the reference section of this web site.