Novel Electrodes for Deep Brain Implantation

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1 Abstract

As more applications emerge for brain-machine interfaces and neuroscience research, there arises a need for an electrode that better matches the mechanical properties of the brain. Such an electrode would allow for longer-duration electrode implantation as well as a greater variety of circumstances in which electrodes could be used. This paper aims to demonstrate that an electrode made of strands of carbon fiber fabric is sufficiently conductive to function as an electrode, besides having a density and stiffness much closer to that of the brain than typical metal electrodes. Difficulties in constructing a flexible electrode include insertion methods, insulation materials, and methods of connecting the electrode to the rest of a sensory circuit. Temporary reinforcement of the electrode was done using a gelatin coating that allowed the carbon fiber strands to penetrate a gelatin approximation to brain tissue. Metal clips were used to attach to the electrodes for measurements of resistivity and for viewing of waveforms successfully acquired through the gel. Recommendations are made for insulative materials and for the future testing of these electrodes in vivo.

2 Introduction

If reverse-engineering the brain is one of the fourteen grand challenges of the 21st century, as the National Academy of Engineering has said [12], then building a better electrode is fundamental to solving that challenge. Electrodes are the connection between nerves and computers, the critical link in a brain-machine interface (BMI) that allows scientists to gather EEG data on the one hand and directly stimulate targeted points of the central nervous system on the other. Gleaning electrical signals from the brain allows scientists to gain information on where and how various mental processes occur in the brain, which is useful for research (for example, the work done by the Nicolelis lab to discern the signals that correspond to monkey limb movement [1]), diagnosis (e.g. implantable electrode arrays used to identify the source of seizure activity in epileptic patients [2]), and potentially prostheses. Active stimulation of the brain can be used for sensory prosthesis, as in cochlear implants [4], or even for therapeutic deep-brain stimulation for Parkinson's or severe depression [11]. The applications of BMIs are enormous, but depend strongly on the reliability and biocompatibility of the electrodes used, especially in the long term.

Electrode design is overconstrained by the many requirements that biocompatibility imposes [5]. For an electrode to perform its function, it must be highly conductive. This conductivity can allow corrosive chemical reactions to occur at the electrode's surface, depending on the relative stability of the oxidized metal, the pH and temperature of the environment, and the specific chemicals and mechanical stressors that the electrode is exposed to. The typical human body temperature is 37° C (98.6° F), but can range between 36° and 40° C. Typical human pH is slightly alkaline at 7.4, but can also vary because of infection or hematomas to be as low as 4 or as high as 9 [5]. Body fluids that the electrode is exposed to generally contain both organic compounds and salts, which allow electrical current to flow that can create an electrochemical reaction with the metal surface of the electrode. And mechanical stressors can break the electrode or rub away at its insulative, non-reactive surface and provide additional surface area for corrosion to occur.

Another issue with biocompatibility is the damage caused by insertion and subsequent mechanical abrasion. The electrode requires rigidity to pierce the surface of the dura and for its position to be controlled as it is placed, but this same inflexibility provides a source of mechanical incompatibility that can cause friction between the electrode and the tissue over time. This increases the damage to local neurons and can cause microglia to accumulate around the stab wound, followed by astrocytes and eventually scar tissue [8]. Not only are the neurons local to the electrode damaged, but the scar tissue can form an insulative barrier around the electrode. Both of these can impede the electrode's continued function.

Further issues particular to the Injury Biomechanics Lab in which I work is the density mismatch between the metal electrode and brain tissue. Although potentially negligible in normal daily activity, when subjected to sudden force, the difference in local mass can cause the electrode and local tissue to accelerate at different rates and collide with one another. In our lab, the response of a brain to a shock wave or blast is of great interest, but data can only be gathered before and after a blast. Supplementing this with EEG data taken during the blast would be helpful in increasing our knowledge of blast-induced brain damage.

The goal of this project was to identify a material that more closely matches the mechanical properties of the brain, while still maintaining necessary conductivity and biocompatibility requirements. Better mechanical compatibility will allow for less invasive electrodes with better chronic stability, with applications in research and prosthetics.

3 Related Research

3.1 Electrical Properties of Commonly-Used Electrodes

Both external cup or plate electrodes and implanted, needle-like electrodes are generally metallic. Typical electrical characteristics of metal electrodes were obtained from Tallgren et al. (2004) [13], *The Handbook of Materials for Medical Devices* (2003) [5], and *Modern Techniques in Neuroscience Research* [18], and include impedances, noise, some mechanical properties, and signal stability over time. Impedance information is most important for cup electrodes, which become more effective when impedances are matched between electrode, gel, and skin. For subdural electrodes, the most common types of metal used are the precious metals (gold, platinum, iridium, rhodium, and palladium) due to their nonreactivity. Additional preferred metals (especially for applications that require resistance to stress) include tungsten, 315L stainless steel, tantalum, titanium, and cobalt allows Eligoy and MP35N.

Metal electrodes require insulation in order to retain a specific area of conduction on their tips. Insulation can be provided by glass, lacquer, epoxy, parylene-C. Teflon, or other smooth and non-reactive materials [18].

For the purposes of comparison, a 30 μ m diameter tungsten wire was obtained from Dr. Dzirasa's Neurobiology laboratory. A tungsten electrode is stiff and able to hold a very narrow tip that can be inserted into a single neuron. The density of tungsten is 19.25 g/cm³, with a Young's modulus of 411 GPa and a resistivity of 50 n Ω ·m [17].

3.2 Alternative Materials

The creation of more flexible electrodes has been attempted by several labs, including MIT's Mechanical Engineering Department [14], the Neuronano Research Center at Lund University, Sweden [8], the Fraunhofer-Institute for Biomedical Engineering [16], and the Department of Polymer Science and Engineering at Sungkyunkwan University, Republic of Korea [7]. A list of the conductive polymers used by these labs is shown in Table 1.

Polymer	Fabrication	Features
Polyacetylene [14]	· unspecified	conductivity: 10 ⁷ S/m, elastic mod-
		ulus: 0.2 GPa, tensile strength: 150
		MPa, degrades quickly
Polyaniline [14]	· nanowires are electro-	conductivity: 10 ⁴ S/m, elastic mod-
	spun via a specially de-	ulus: 2.3 GPa, tensile strength: 60
	signed apparatus	MPa; easily processed
Polyimide [16]	· used as a flexible back-	tensile strength: 0.34 GPa, elonga-
	bone for metallic conduc-	tion: 25%, Young's modulus: 8.375
	tors: layers of polyimide	GPa, density: 1.07 g/cm ³ , resistiv-
	are spun and cured, alter-	ity: >10 ¹⁶ Ω ·cm
	nating with metal sputter	
	deposition	
Poly(methyl methacry-	\cdot dispersed in solution,	10^{-2} S/cm, brittleness of carbon
late) with carbon nan-	film deposition, sliced into	overcome by polymer surroundings
otubes [7]	strips	while conductivity and biocompati-
		bility are presumably preserved
Polypyrrole [14]	\cdot electropolymerized from	conductivity: 1.2×10^5 S/m, elastic
	solution to create a thin	modulus: 0.8 GPa, tensile strength:
	film, cut with a knife,	40 MPa; stable
	laser, or machining tool	

Table 1: Flexible Polymers Used for Electrode Fabrication

3.3 Insulators

These polymers have to be insulated by a material that is also flexible. Some insulators mentioned included poly(ethylene oxide) [14], cathodic electrophoretic paint [19], and polyvinylphenol [20]—and in the case of the polyimide, the polymer itself was the insulator. The poly(ethylene oxide) insulation was incorporated into the polyaniline electrode during fabrication using a modification to the electrospinning apparatus. The electrospinner works by jetting a conductive polymer in solution through a low-flow nozzle in the presence of an electric field, which causes the jet to stretch out as it falls. This allows the solvent to evaporate so that the end result is a thin polymer strand. By modifying the nozzle of the electrospinner so be coaxial, a poly(ethylene oxide) solution could be ejected around the fluid stream of the polyaniline, drying on its surface and insulating it. This method had the added benefit of providing stabilization for the polyaniline solution as it was ejected, since the poly(ethylene oxide) solution has a higher viscosity.

The polypyrrole electrodes were also insulated with poly(ethylene oxide), which was applied in concentrated solution form directly on their surfaces. The electrophoretic paint was applied in several layers to electrodes using electrodeposition, with excess paint washed away each time using distilled water before the layer was heat-cured. An alternative method of applying insulation to an electrode involves spraying a solution uniformly using a modified ink-jet printer or a spray gun [20]. In the paper just cited, the insulative polymers used were polyarylate and polyvinylphenol. However, these were used as a substrate and spun film coating, respectively. Given an insulative polymer in solution, however, the sprayprinting technique should be viable for uniformly coating an electrode as desired, with viscosity compensated for by changing the pressure of the gas used to aerosolize the solution.

3.4 Mechanical Properties of the Brain

The primary criteria of the new electrode design was to select a conductive and biocompatible material with a density and stiffness that could match the brain's. Identifying specific parameters for "typical" brain tissue is difficult, as brain tissue is not homogeneous [6], is poorly studied, and tissue properties are likely to be different in vivo and ex vivo. Furthermore, biological tissue is not purely elastic and can exhibit increasing deformation over time under the same force conditions. However, it is reasonable to assume a brain density slightly above that of water (0.993 g/cm³ \approx 1 g/cm³ at 37° C), given that gray matter has an average density of 33 Hounsfield units [3], which is slightly more dense than blood and less dense than muscle (which has a density of 1.0597 g/cm³ [15]). Given that biocompatibility requirements already overconstrain the design of an electrode and that metals tend to have a density that is around twenty times greater than the density of water (19.25 g/cm³ for tungsten, 21.45 g/cm³ for platinum), decreasing the density by an order of magnitude without perfectly matching brain density will be sufficient to dramatically improve the mechanical matching between electrode and brain tissue.

Data on brain stiffness was even more elusive than data on density. To match brain stiffness requirements, a tray of ballistic gelatin was mixed to be used as a model.

4 Materials Selection

To expand beyond the conductive polymers that were identified during the background research stage of this project, I decided to focus on the potential of flexible carbon fiber electrodes. Carbon composites tend to be conductive as well as highly biocompatible, and by using a composite material, one can avoid the typical brittleness of pure-carbon materials such as graphene or pure carbon nanotubes.

An added benefit of carbon fiber is that it is relatively cheap and easy to acquire. 5 g of polypyrrole from Sigma-Aldrich costs \$107 and arrives in sulfonic acid solution that needs to be chemically processed (as alluded to in Table 1) before it can be cut, using lasers or blades, into needle-like wires. The carbon fiber fabric I chose was HexTow fabric from Hexcel, obtained from leftover scraps donated to the Duke University Motorsports group. The fabric is woven carbon fiber and epoxy, with the mechanical data provided in datasheets online [9] and relevant values reproduced in Table 2.

Because the carbon fiber was donated five years ago, the Motorsports club could not tell me the specific fabric type. I gathered the above values from the AS4 carbon fiber datasheet [10], which appeared to be the closest match. However, density values were all very similar (the average is 1.80 g/cm^3 , with $\pm 0.02 \text{ g/cm}^3$ variation among fabric types), and fiber moduli and strengths varied from each other by less than 5%. The properties in the table above refer to the properties

Density	1.79 g/cm^3
Tensile Modulus	141 GPa
Tensile Strength	2,205 MPa
Filament Diameter	7.1 microns
Carbon Content	94.0%
Resistivity	$1.7 \times 10^{-3} \Omega \cdot cm$

Table 2: HexTow Carbon Fiber (AS4) Properties

of individual fibers; 3000 fibers are wound together in a tow for use in weaving the carbon fiber fabric.

4.1 Insertion Methods

Lowering the stiffness of an electrode can pose problems for insertion. Given that a certain degree of rigidity may be necessary to penetrate the brain surface and to allow precision and control in placement, research was done to find options for a temporary sheath. Materials considered are summarized in Table 3.

Material	Proposed application method	Expected function	
sucrose Electrode dipped in solution and		Hard surface. Dissolves in vivo.	
solution allowed to evaporate.		Well-tolerated compound.	
Layers added as necessary.			
hollow needle to	Electrode size predetermined	Similar or greater brain injury	
guide insertion	and uniform to fit inside needle.	upon insertion as compared to	
		traditional metal electrodes.	
gelatin	Electrode coated with liquid	Flexible exterior is still rigid	
	gelatin and allowed to dry.	enough to permit penetration [8]	

Table 3: Possible Sheath Materials Considered for Aiding Insertion

According to Gustav Lind et al. [8], a gelatin coating provides sufficient stability to allow electrode penetration, and is even rigid enough to penetrate the dura by itself. Gelatin also dissolves within minutes without any apparent adverse effects, and a smooth, thick coating is associated with lower levels of reactive microglia and astrocytes in the weeks immediately following implantation. A thick gelatin coating leads to smaller areas of scar tissue 12 weeks after implantation even when the core electrodes have the same diameter and the extra gelatin smooths the insertion at the cost of a larger initial diameter. Given these reported advantages, I chose to use gelatin for the electrode sheath.

5 Manufacture of Electrodes

5.1 Electrode Creation

Fibers were separated from each other and twisted into strands of different thicknesses, with lengths close to 60 mm long. Ballistic gelatin was prepared using approximately 10 g gelatin powder and 150 g hot water, and strands were dipped into the solution while it was still liquid. The gelatin was allowed to cool and solidify overnight, while the strands were placed on a sheet of paper and allowed to dry. The liquid gelatin tended to form balls on the strands and did not form an even coat (see Figure 1). To see if this would affect the insertion, extra strands were created and coated with Elmer's glue, which did form an even coat.



Figure 1: Uneven gelatin coagulation

An additional problem that arose was that not all fibers extended throughout the entire length of the electrode, and thicker/smoother coatings were necessary to prevent stray fibers from poking out.

Tips were cut off using scissors after the coating had dried. This was to ensure an even, perpendicular tip for better penetration. This would also be necessary to expose the uninsulated carbon fiber core of the electrode, given that future electrodes will have an insulative layer underneath the gelatin coating.

5.2 Tungsten Electrode for Comparison

The 30 μ m tungsten electrode taken from Dr. Dzirasa's lab was used as a basis for comparison. The tungsten wire is coated with a thin layer of insulation and is attached via surface-mount soldering to a printed circuit board, from which wires can carry the electrode's signal to a 2× low-noise amplifier.

5.3 Insulation and Attachment

No insulation was chosen for the initial tests, which were primarily to ensure that the electrode could penetrate the gelatin. Leaving off insulation also allowed the conductivity of the electrodes to be tested without requiring special attachments to be made to the ends. However, as a finished electrode would require some sort of connection to allow it to link with a sensing/amplification

circuit, an attempt was made to connect one of the carbon fiber electrodes to a wire using solder, as with the tungsten electrode. A multi-stranded wire was stripped and the ends were twisted with an uninsulated carbon fiber strand. Solder was applied to the joint. Conductivity was tested along the length of the electrode and then from across both the electrode and the wire.

6 Testing of Electrode Performance

6.1 Conductivity Testing

The conductivity of the gelatin-coated and glue-coated carbon fiber electrodes were tested from end to end, from the end to the middle, and from one end to a quarter of the way down the length of the electrode to determine the electrodes' resistance and its dependence on length. Three additional, uncoated strands were created, of larger width, to determine the effect of diameter on resistivity. The tip of the tungsten electrode was too small to contact with a multimeter, and also difficult to connect to a larger wire via solder. The resistance of the tungsten electrode was obtained by gently scraping the side of the wire in several places to remove the insulation and then measuring the resistance from those points.

6.2 Insertion of Electrodes into Gelatin

Four electrodes were manually inserted into the ballistic gelatin: one glue-coated electrode, two gelatin-coated electrodes (one of thicker diameter than the other), and the tungsten electrode. Attempts were made to insert the electrodes in as perpendicularly as possible, with fingers holding the electrode at a point very close to the surface of the gelatin to reduce buckling. Electrodes were pushed in until buckling prevented any further penetration. The distance to the end of the strand below the meniscus was then measured.

6.3 Performance in Gelatin

A function generator was set to provide a 70 mVpp, 1 kHz sine wave (70 mV is the cell potential of a neuron, and a 1 kHz signal is two orders of magnitude greater than typical repeated neuron depolarization). It leads were clipped to either end of a gelatin-coated electrode. An oscilloscope was used to measure the voltage across the electrode to ensure predictable function generator output.

The positive lead from the function generator was then inserted into the gelatin while the negative lead was attached to the electrode. The electrode was inserted into the gelatin to complete the current path through the gelatin. The oscilloscope was used to measure the voltage between the electrode and ground (probe 1), and the output of the function generator (probe 2). The function generator lead was removed from the gelatin and reinserted and graphs were taken of the change in waveform to verify operation was as predicted.

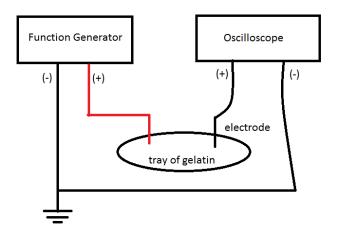


Figure 2: Electrode-testing circuit configuration

7 Experimental Results

7.1 Conductivity

The carbon fiber fabric had a fairly constant resistance of around 20-30 Ω when measured with a multimeter, regardless of distance between probes. However, initial measurements of resistance across the smaller gelatin-coated electrode were surprisingly high. More methodical measurements were taken along the lengths of all the electrodes, and the measured resistances are listed in Table 4. Electrode lengths were between 62 and 66 mm, and because there tended to be a lot of variability even in repeated measurements, the effect of the difference in length on the precision of the measurements was considered negligible. The general trends are more important than the specific numbers.

Electrode	1/4 way resistance	1/2 way resistance	tip to tip resistance
Thick strand (gelatin)	118 Ω	330Ω	448 Ω
Thin strand (gelatin)	115 Ω	$277 \ \Omega$	628 Ω
Glue-coated strand	2663 Ω		2671 Ω
Tungsten		1.7 Ω	

Table 4: Electrode resistances

The glue-coated electrode had higher resistance because the probes were not in direct contact with the carbon fibers. The resistance of the tungsten electrode is very low, so that changes in resistance are indiscernible throughout its length. There seems to be a general trend of increasing resistance with length, in a more or less linear fashion. To determine whether or not resistance was also affected by width, thicker strands were measured as shown in Figure 3. Again, the gen-

eral trends are more important than the specific numbers, as the probe orientation changed the measured values greatly (though I tried to be consistent). It appears that a larger diameter means more interconnected paths for electrons to travel down, which effectively puts all the resistance of individual strands in parallel, significantly decreasing the resistance.

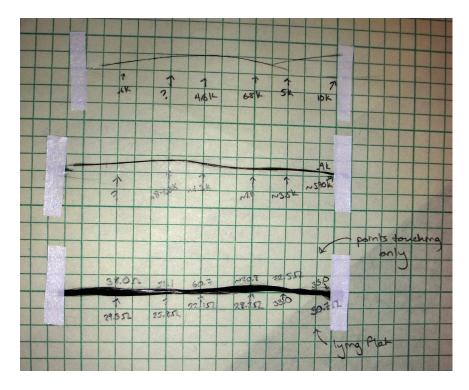


Figure 3: Measuring resistances of carbon fiber strands of different widths

The end result is that conductivity is high enough for carbon fiber to be used as an electrode, but if impedance matching becomes important, variation of resistance with respect to length and width could be an issue that needs to be taken into account.

The carbon fiber electrode is difficult to connect to via typical circuit methods such as soldering. However, using a metal clip to attach to an uninsulated part of a carbon fiber strand seemed to work. Releasing the electrode had to be done gently to prevent tearing it.

7.2 Gelatin Penetration

The distances that each electrode was able to penetrate are shown in Table 5.

Glue-coated electrode	14 mm
Gelatin-coated electrode (thick)	12 mm
Gelatin-coated electrode (thin)	3.5 mm
Tungsten electrode	25 mm

 Table 5: Gelatin Penetration Depth

The tungsten electrode was by far the easiest to insert because of both its smoothness and rigidity, although even it began to curve slightly at the 25 mm mark. If the gelatin had been deeper, however, it could have been pushed in farther. The gelatin coating was sufficiently hard to allow the two gelatin-coated electrodes to be inserted, even with the unevenness of the coating, although buckling precluded further insertion much more quickly with the thinner electrode than the thicker one. The glue-coated electrode started to curve immediately the first time I attempted to insert it into the gelatin; I withdrew it and began again but some of the dried coating had already begun to dissolve. This left the tips of the fibers bare and able to splay, preventing reinsertion on the same side. Turning the electrode around and inserting the other end first worked well and penetrated more deeply than all other tested electrodes except for the tungsten wire. I attempted to insert one uncoated electrode, to see if reinforcement by the gelatin was indeed necessary. The fibers easily separated from each other, splaying and buckling at the surface of the gelatin rather than penetrating. Images of the electrodes inserted into the gelatin are found in the Appendix (Figures 5, 6, and 7).

7.3 Performance in Gelatin

When connected as shown in Figure 2, the oscilloscope measured both the voltage at the electrode (probe 1, top waveform) and the output voltage of the function generator (probe 1, bottom waveform) as can be seen in Figure 4.

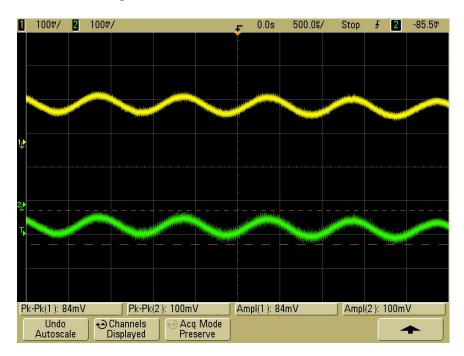


Figure 4: Voltage obtained by carbon-fiber electrode

The resistance of the gelatin was measured to be around 200 k Ω from one side of the dish to the other, but took a long time to stabilize and may be as imprecise as the resistance measurements of the carbon fiber strands in Figure 3. The output waveform of the function generator and the

voltage of the electrode match each other very well, and the difference in measured amplitudes (commonly, between 0 and 20 mV) appears to be largely due to noise fluctuations throwing off the oscilloscope's determination of the maximum and minimum voltages.

Waveforms taken when either the electrode or function generator were disconnected from the gelatin show a flat line waveform for probe 1, as expected.

8 Conclusion

An electrode made of strands of carbon fiber twisted together appears to be sufficiently conductive to function as an electrode when tested in a gelatin environment. It is discernibly more flexible and has a density approximately an order of magnitude lower than a traditional metal electrode. Literature suggests that in vivo, the carbon-fiber electrode would be chemically innocuous and that a thick gelatin sheath would allow for clean insertion with minimal local tissue trauma. An appropriate insulation material has yet to be chosen for this particular electrode, and would be important to keeping carbon fibers contained smoothly within the electrode's body to prevent mechanical degradation that could cause irritation of tissue. The insulation will also serve to ensure that signals are only acquired from the target neuron(s) at the electrode's tip. Both epoxy and poly(ethylene oxide) have been mentioned as possible solutions, although testing (in gelatin and in vivo) would be necessary to determine biocompatibility and continued electrode functionality.

Future improvements could be made by mechanizing the process of twisting carbon fiber strands together. This would allow for more precisely known dimensions of the electrodes as well as uniformity in their production. A more uniform gelatin sheath could be applied using an ink-jet printer or spray gun, and if the coating were made sufficiently thick, the gelatin would dissolve slowly enough to allow removal and reinsertion in the case of improper initial placement.

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A Additional Figures



Figure 5: Gelatin-coated electrodes



Figure 6: Glue-coated electrode



Figure 7: Tungsten electrode