

Conducting Polymer Wires for Intravascular Neural Recording

by

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B.S. Mechanical Engineering
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ABSTRACT

Brain-machine interfaces are a technology with the potential to fundamentally change the way people interact with their environment, but their adoption has been hampered by the invasiveness of conventional implanted cortical microelectrode arrays. Llinás et al. have proposed a novel design for intravascular nanowire electrode arrays, which promise to be less invasive than current technology. Early work utilizing platinum nanowires showed that metal wires are too stiff for this application. Conducting polymer nanowires could be used in place of metal to build electrodes with far lower stiffness and high conductivity. This thesis describes several all-polymer electrode architectures and the fabrication techniques used to build them. Polypyrrole microwire electrodes were first built in order to demonstrate the feasibility of an all-polymer neural recording electrode, and were shown to give high-fidelity intravascular recordings. Polyaniline nanowires were then fabricated by coaxial electrospinning, which was shown to be a viable technique for the manufacture of such wires. These wires will be integrated to form complete nanowire electrodes and tested in animals before moving towards human applications.

Thesis Supervisor: Ian W. Hunter
Title: Professor of Mechanical Engineering

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TABLE OF CONTENTS

List of Figures.....	8
1—Introduction.....	9
2—Intravascular Neural Recording.....	10
2.1 System Architecture.....	10
2.2 Limitations of Current Approach.....	12
3—Conducting Polymers.....	13
3.1 History and General Properties.....	13
3.2 Polymers of Note.....	13
3.2.1 Polypyrrole.....	14
3.2.2 Polyaniline.....	14
3.2.3 Others.....	15
4—Sliced Polypyrrole Electrodes.....	16
4.1 Electrode Design.....	16
4.2 Electrode Fabrication.....	16
4.2.1 Polymer Fabrication.....	16
4.2.2 Slicing Procedure.....	17
4.2.3 Electrode Assembly.....	17
4.3 Results.....	18
4.3.1 Wire Morphology.....	18
4.3.2 Neural Recording.....	19
4.4 Discussion.....	21
5—Electrospun Polyaniline Nanowires.....	22
5.1 Motivation.....	22
5.2 Electrode Design.....	23
5.3 Apparatus Design.....	24
5.4 Wire Fabrication.....	25
5.4.1 Solution Preparation.....	26
5.4.2 Electrospinning Procedure.....	26
5.5 Results.....	27
5.6 Discussion.....	28
6—Future Work.....	29
6.1 Improved Electrospinning Apparatus Design.....	29
6.2 Nanowire Electrode Fabrication.....	29
6.2.1 Electrode Tip Adornment.....	30
6.2.2 Electrode Base Attachment.....	30
7—Conclusions.....	31
References.....	32
Appendix—Electrospinning Apparatus Block Diagram.....	35

LIST OF FIGURES

1	Neuron Schematic.....	10
2	Intravascular Electrode Specifications.....	11
3	Conducting Polymer Structures.....	14
4	Polypyrrole Microwire Electrode.....	16
5	Microwire Slicing Jig.....	17
6	Polypyrrole Microwire, Low Magnification.....	18
7	Polypyrrole Microwire, High Magnification.....	19
8	Polypyrrole Microwire, Insulated.....	20
9	Intravascular Neural Electrode Recording Experiment.....	20
10	Neural Signals Detected by Polypyrrole Microwire Electrode.....	21
11	Whipping Instability in Electrospinning.....	23
12	Electrospinner Schematic.....	25
13	Electrospinner Photograph.....	26
14	Polyaniline Nanowire Light Micrograph.....	27
15	Polyaniline Nanowire Electron Micrograph.....	27

1: INTRODUCTION

Since the dawn of computing, technologists have dreamed about the possibility of using brain-machine interfaces. By communicating directly with the human brain, computers could become an extension of the mind, seamlessly allowing communication, enhancing memory, and performing computations. Furthermore, the machine connected to a brain-machine interface could include sensors and mechanical devices as well as computational hardware, providing extensions to the body as well as the mind[21].

Today, we are on the cusp of achieving this brain-machine interface revolution. Cochlear implants have restored some hearing to thousands of deaf patients[21]. Microelectrode implants have allowed monkeys to control robot arms as if they were their own[5]. Each new experiment improves our understanding of the mechanisms behind neural control and sensory input. Moreover, a perfect understanding of these mechanisms is not required, as the natural plasticity of the brain allows it to reprogram itself to accommodate new brain-machine interfaces[5].

At present, brain-machine interface applications are limited to animal experiments and to restoration of lost bodily functions in humans. The most powerful brain-machine interfaces currently consist of microelectrode arrays, which are directly implanted in nervous tissue. This implantation is a major surgical procedure that requires opening of the skull, and may damage brain tissue around the implantation site. Furthermore, over time brain tissue reacts to the presence of microelectrodes by forming scar tissue, which increases the electrical impedance between neurons and the electrodes[17]. These problems limit the application of brain-machine interfaces to people suffering from sufficiently serious medical conditions to warrant brain surgery, such as paralysis, and to devices interacting with peripheral nerves, such as cochlear implants.

In order to expand the range of situations in which brain-machine interfaces can be used, a less invasive technique for recording the activity of small neuron populations must be developed. Recently, Prof. Rodolfo Llinás of the NYU School of Medicine has proposed a brain-machine interface using electrodes placed within cranial blood vessels rather than electrodes implanted directly into neural tissue[16,17]. This technique, which I will refer to as intravascular neural recording throughout this thesis, promises to provide the same wealth of information available from implanted microelectrode arrays without requiring brain surgery or forming neural scar tissue.

2: Intravascular Neural Recording

Intravascular neural recording is a technique developed by our collaborator, Prof. Rodolfo Llinás, that promises to provide high-fidelity neural recordings with a less invasive implantation technique than current technology. In this section I will explain how Prof. Llinás's technique is different.

2.1: System Architecture

Intravascular neural recording requires a very different kind of electrode system from conventional microelectrode techniques. In a conventional system, sharp microelectrodes are arranged in a closely spaced grid, and attached to a rigid or semi-rigid backplane[8]. Amplifier electronics are frequently placed directly on this backplane. Amplified and/or processed neural signals exit the skull either via a penetrating wire or via wireless communication. The microelectrode array is implanted by simply pushing the array into the relevant part of the brain; the sharp electrode tips and small electrode size minimize tissue damage.

In intravascular neural recording, electrodes are placed individually in the vasculature, preferably in capillaries. As shown in Figure 1, the capillary bed is in intimate contact with all parts of the neuron. Experiments have demonstrated that the electrical impedance of the blood-brain barrier is minimal, allowing the electric potential of the neuron near a capillary to be sensed by an electrode within the capillary[17]. The ability of a microelectrode array to sample

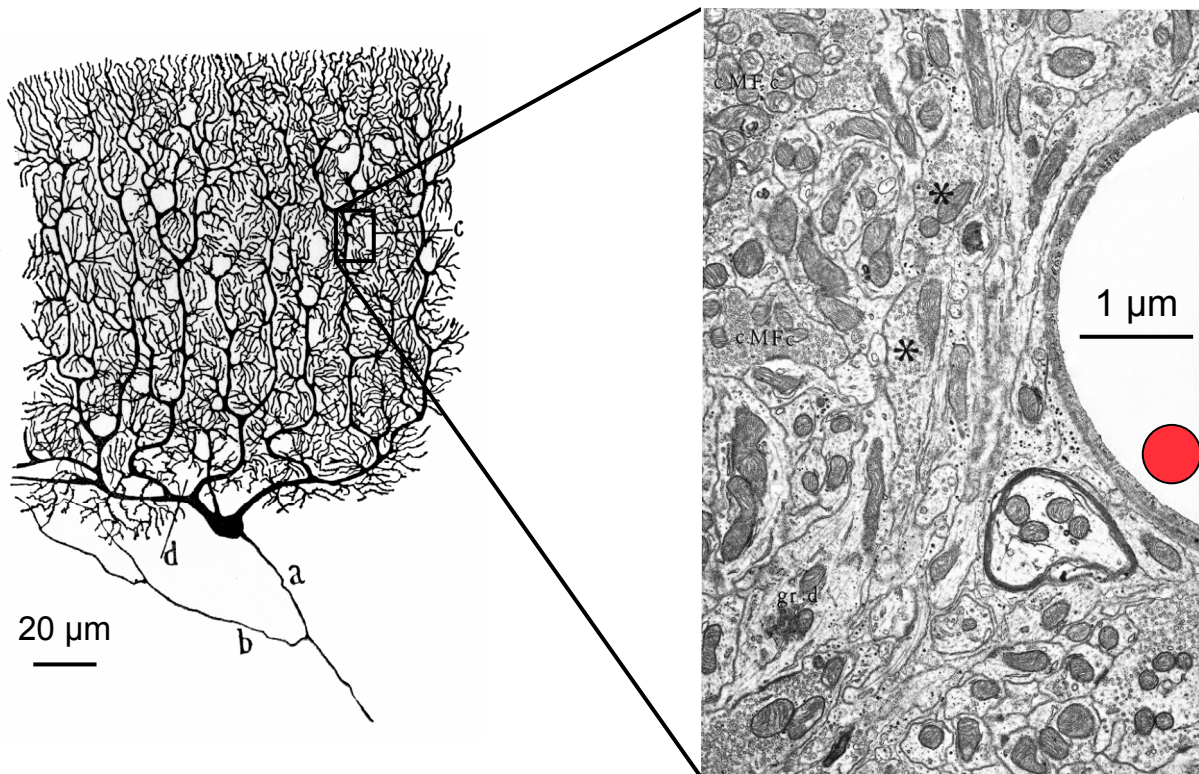


Figure 1: (Left) A schematic view of a typical neuron, illustrating the locations of capillaries (empty circular areas) relative to the dendrites. (Right) A transmission electron microscope (TEM) image showing a capillary in neural tissue. The structures outside the capillary wall are parts of neurons; the red dot is 500 nm in diameter, for scale. Image courtesy of Rodolfo Llinas.

numerous neurons within a small brain region may be duplicated by placing multiple intravascular electrodes in nearby portions of the vasculature.

As can be seen in the right half of Figure 1, an intravascular electrode must be very small in order to avoid obstructing blood flow through a capillary. To be specific, such an electrode must be under one micrometer in diameter, considerably smaller than a standard microelectrode[8]. To bring the measured electrical signal to the outside world, the electrode must be connected to a larger wire, which can either exit the body via a catheter for short-term implantation or be connected to an implanted signal processing device for long-term implantation. As the larger wire must terminate in a relatively large blood vessel to avoid flow obstruction, the electrode must be long enough to exit the capillary bed, a distance of 20 to 30 millimeters[16].

The first electrode system utilized by Prof. Llinás and his research group is shown in Figure 2. The electrode consisted of an insulated platinum nanowire, 600 nanometers in diameter. The tip was adorned with a deposit of platinum black, which served the dual purposes of reducing the impedance of the electrode and serving as a “sail” to guide the electrode in the bloodstream. This wire was connected to a larger silver wire by co-fabrication; i.e. the platinum wire was drawn as the core of the silver wire, and the nanowire portion was formed by etching the silver away.

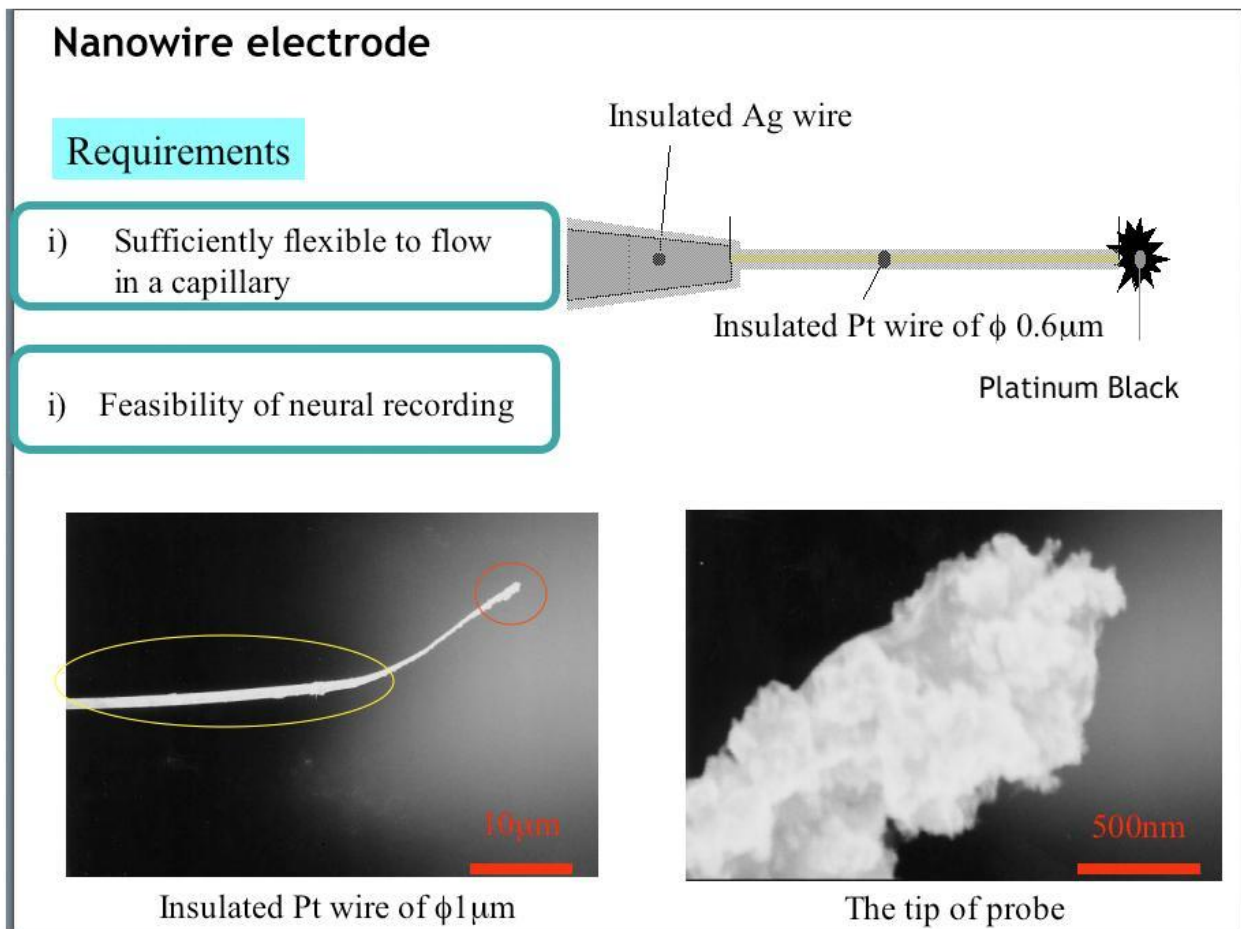


Figure 2: The first electrode system used by the Llinas group to demonstrate intravascular neural recording. Figure courtesy of Rodolfo Llinas.

2.2: Limitations of Current Approach

While the Llinás group was able to use the platinum electrode system to obtain proof-of-concept intravascular neural recordings, it displayed critical flaws that needed to be addressed in future systems. Most prominently, the platinum nanowire was too stiff to easily negotiate the tortuous paths of the capillary bed. Individual vessels and vessel branch points frequently have radii of curvature under 30 micrometers[17]; rather than bend so sharply, the platinum wires would instead puncture the vessel wall. Such an event is clinically unacceptable, so the bending stiffness of the electrode must be reduced. We proposed to achieve this stiffness reduction by replacing the metallic conductor in the wire with a conducting polymer.

3: Conducting Polymers

Conducting polymers are an unusual class of materials that combine the mechanical properties of engineering plastics, the electrical properties of metals, and chemical properties unlike those of any other class of materials. In this section, I will describe the class of conducting polymer materials, then talk in greater depth about the properties of the conducting polymers polypyrrole and polyaniline.

3.1: History and General Properties

In general, conducting polymers are polymers whose backbone structure contains alternating single and double bonds capable of forming a delocalized electron cloud. While some conducting polymers may have been accidentally produced as early as the 19th Century, none were prepared in sufficient purity for characterization until the 1970s[9,13]. After the first well-characterized conducting polymer, polyacetylene, was shown to be electrically conductive in 1977 (work recognized with a Nobel Prize in 2000), numerous other conducting polymers were prepared and described[7].

When pure, most conducting polymers are semiconductors. In an infinitely long chain of alternating single and double bonds, it has been shown that the chain is not fully conjugated, like a benzene molecule, but rather has an electronic structure characterized by a band gap, like silicon. With the addition of dopants by oxidation or reduction, conducting polymers can be made to be highly conductive, displaying metallic conductivity under certain conditions[30]. Conducting polymers are generally highly active in oxidation and reduction (redox) reactions involving both electrochemical processes and chemical reagents. This chemical sensitivity, combined with the associated doping effect, allows many conducting polymers to serve as chemical sensors. With careful control of the polymer purity, some conducting polymers can be used, like silicon, to make transistors[22]. Others can be used to make high-efficiency light sources[4].

The molecular electronic structure of conducting polymers also has important implications for their processing. The partially-conjugated polymer backbone is very stiff, as any bending of the chain tends to reduce the degree of conjugation. Thus, many conducting polymers do not melt or dissolve in solvents, making them difficult to process.

3.2: Polymers of Note

Conducting polymers are a very broad class of materials. The number of possible variants is nearly infinite, and new conducting polymer syntheses are frequently reported in the literature. Certain polymers stand out as being stable, highly conducting, and well characterized, however, and the Hunter group has focused its efforts on a small number of these materials. Of particular relevance are the conducting polymers polypyrrole and polyaniline; polypyrrole attracts notice due to its stability and very high conductivity, while polyaniline is of note due to the wide range of techniques by which it may be processed. Representative structures for these polymers are shown in Figure 3.

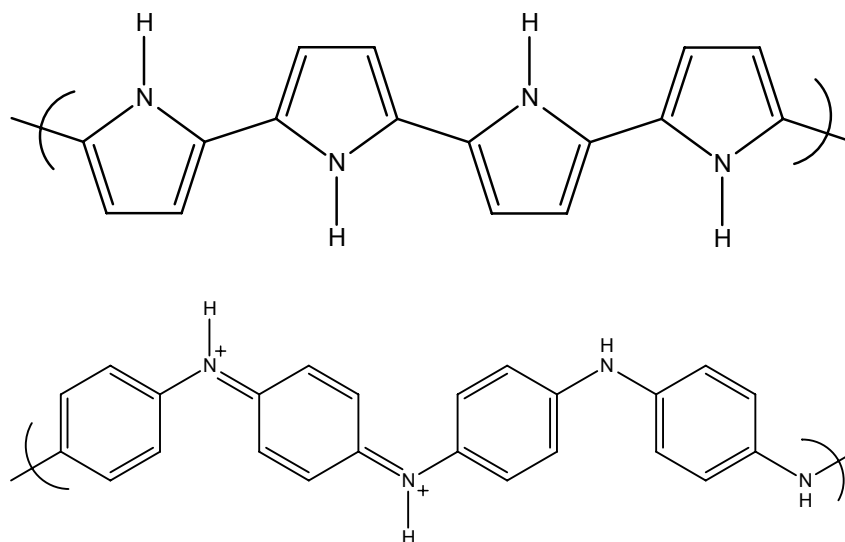


Figure 3: (Top) Chain repeat unit of undoped polypyrrole. (Bottom) Chain repeat unit of the emeraldine salt form of polyaniline.

3.2.1: Polypyrrole

Polypyrrole is a conducting polymer frequently used as an “artificial muscle,” and also noted for its relative environmental stability and high conductivity[20]. Typically, polypyrrole is prepared in the Hunter group by electrodeposition with a tetraethylammonium hexafluorophosphate dopant; the synthesis method will be described in more detail in section 4.2.1. Electrodeposition produces a strong, coherent black film 10 to 50 micrometers thick, with typical conductivities ranging from 10^4 to 10^5 S/m. No additional doping or other processing is required to achieve these conductivities, which remain stable for years in dry films. Additional physical properties of polypyrrole can be found in Table 1.

Unfortunately, polypyrrole is not amenable to melt or solution processing. The films decompose on heating above approximately 200 °C, and do not dissolve in any solvent. Polypyrrole can be prepared in a water-soluble form through the use of macromolecular dopants; however, the resulting material has a very low conductivity. Thus, polypyrrole films can only be processed by cutting, which we can do with a blade, using a carbon dioxide laser, or by electrical discharge machining.

3.2.2: Polyaniline

Polyaniline is currently the most widely used conducting polymer in industry, primarily as an additive in anti-static plastics. It is most frequently prepared as a powder by oxidative polymerization; depending on the polymerization conditions, the powder can be composed of nanofibers, globules, or mixtures thereof[12]. Polyaniline can also be purchased from chemical supply houses in a variety of molecular weights and oxidation states.

Polyaniline has a somewhat unusual chemistry among conducting polymers, as it participates in acid-base reactions as well as redox reactions, and exists in three oxidation states. The form most often available commercially is known as the emeraldine base; this form is very intensely blue in color, and is highly soluble in N-methyl pyrrolidone. Treatment with strong

acid converts the blue emeraldine base to the green emeraldine salt form, which is the only conductive form of polyaniline. The acid serves as a dopant in the polymer, giving it conductivity as high as 10^4 S/m. Depending on the dopant acid, emeraldine salt may be insoluble in all solvents or it may be soluble in numerous organic solvents. Both emeraldine forms of polyaniline can undergo redox reactions, being reduced to leucoemeraldine (clear) or oxidized to pernigraniline base (violet) or salt (blue).

Through the use of suitable dopant acids, particularly organic acids such as camphorsulfonic acid, the emeraldine salt can be rendered soluble in a number of solvents, including formic acid, dimethyl sulfoxide, and *m*-cresol[23]. The resulting solutions can be drop cast or spin coated to yield thin polyaniline films. Adding another wrinkle to polyaniline chemistry, when camphorsulfonic acid-doped polyaniline is processed with *m*-cresol, it achieves the highest conductivities observed in polyaniline, about 10^4 S/m[23]. Polyaniline can also be melt processed to a limited extent; blends of polyaniline with engineering thermoplastics retain their conductivity through the injection molding process. Additional properties of polyaniline can be found in Table 1.

3.2.3: Others

While polypyrrole and polyaniline are among the most common conducting polymers, and were the focus of the studies presented in this thesis, certain other conducting polymers bear mention. Polyacetylene was the first conducting polymer to be studied, and is also the simplest. As such, it has been very well characterized in the ~30 years since the discovery of its conductivity. It also has the best material properties of any conducting polymer: it is as conductive as copper, as soft as rubber, and yet as strong as mild steel[6,18,30]. Unfortunately, it is highly unstable in air, and degrades in a matter of hours.

Polythiophene and its derivatives form another major class of conducting polymers, primarily with applications in organic electronics. Alkyl derivatives of polythiophene are high-mobility semiconductors, and can be processed in nonpolar solutions. Ether derivatives have low bandgaps and are extremely stable, making them useful as transparent electrical conductors.

Table 1: Comparative material properties of several conducting polymers. Polypyrrole properties were taken from measurements made in the Hunter lab[1]. Polyaniline[11,23,27] and polyacetylene[6,18,30] properties were taken from the literature. Platinum properties were taken from an online database¹.

	Platinum	Polypyrrole	Polyaniline	Polyacetylene
Conductivity	10^7 S/m	10^5 S/m	10^4 S/m	10^7 S/m
Elastic Modulus	171 GPa	0.8 GPa	2.3 GPa	0.2 GPa
Tensile Strength	200 MPa	40 MPa	60 MPa	150 MPa

¹ MatWeb, <http://www.matweb.com/>

4: Sliced Polypyrrole Electrodes

As a preliminary step towards the development of proper conducting polymer intravascular neural recording electrodes, we first developed polymer electrodes at larger size scales. These electrodes, while too large to be placed in the capillary bed, were nonetheless sufficient to demonstrate the viability of using a conducting polymer wire to detect neural signals. Here I will discuss the design and fabrication of oversize polypyrrole electrodes, including the polypyrrole synthesis technique, the wire production process, and the assembly of complete wires. I will then show micrographs of the polypyrrole wires, as well as neural recordings obtained by Hirobumi Wantanabe in Prof. Rodolfo Llinás's group at NYU using polypyrrole microwire electrodes.

4.1: Electrode Design

The goal of our preliminary work on conducting polymer intravascular neural recording electrodes was simply to demonstrate the feasibility of such recording. The electrodes produced in this work were to be used to measure signals on the sciatic nerves of dead frogs from within their sciatic arteries. Therefore, they did not need to be compatible with blood, nor did they need to be less than one micrometer in diameter so as to fit into capillaries. Furthermore, it was desired to produce these electrodes as quickly as possible.

In light of these relaxed constraints and the tight schedule, the electrodes were made using materials and equipment already present in the BioInstrumentation Lab. A square cross-section polypyrrole wire approximately 20 micrometers across would form the core of the electrode, and be fabricated from the same films as are commonly used for actuator development. The wire would be attached to a larger carrier wire by means of electrically conductive epoxy, and the system would be insulated by a solvent-applied coating after assembly. A photograph of an assembled electrode is shown in Figure 4; no tip adornment is required for an electrode this large.

4.2: Electrode Fabrication

Electrode fabrication using this design is a three-step process: first, a polymer film must be synthesized, then it must be sliced into square wires, and finally the wires must be assembled with other components and insulated.

4.2.1: Polymer Fabrication

Polypyrrole films were prepared by low-temperature, non-aqueous electro-polymerization. A propylene carbonate

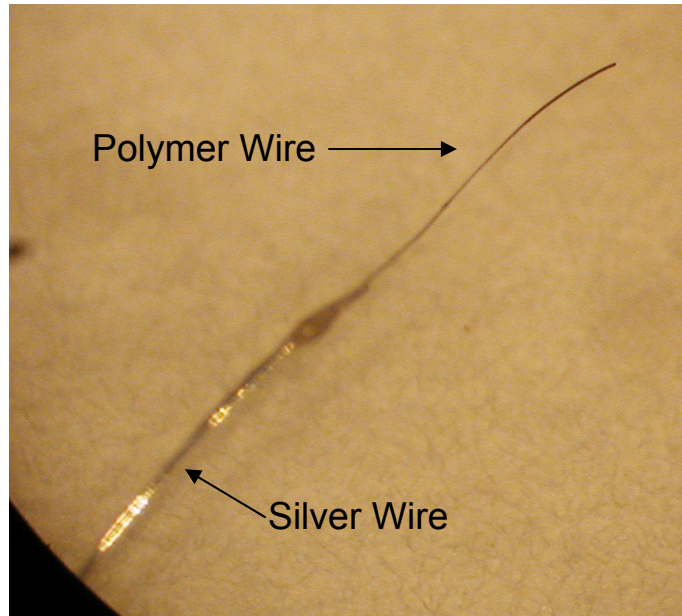


Figure 4: A completed polypyrrole microwire electrode. The polymer wire is attached to the silver wire with silver-bearing epoxy, and the assembly is insulated with poly(ethylene oxide). Image courtesy of Rodolfo Llinas.

(HPLC grade, Aldrich²) solution containing 0.05 M tetraethylammonium hexafluorophosphate (99%, Aldrich) and 0.05 M pyrrole (Aldrich, purified by vacuum distillation), along with 1% (V/V) distilled water, was prepared with vigorous stirring. Nitrogen gas was bubbled through the solution to eliminate as much oxygen as possible. The solution was then chilled to -40 °C in an environmental chamber (Cincinnati Sub-Zero³).

Electropolymerization was carried out in a two-electrode cell under galvanostatic conditions. The cell possesses a glassy carbon anode and a copper foil cathode; polypyrrole is produced on the glassy carbon electrode. The current was chosen to deliver 0.5 A/m² of anode area, resulting in a deposition rate of 2-3 micrometers per hour (2×10^9 C/m³). The resulting film was opaque black; the film used to slice wires had a conductivity of 1.2×10^4 S/m and a thickness of 17 micrometers.

4.2.2: Slicing Procedure

Polypyrrole microwires were prepared by slicing a film mounted perpendicular to the stage of a cryo-microtome. To prepare the film for slicing, it was first cut into approximately a 10×20 millimeter rectangle. A small plastic box (50×50×20 millimeters) was then filled halfway with distilled water, and the film was floated on the water surface. The box was then placed in a freezer at -20 °C until the water was completely frozen. Additional distilled water was then added to fill the box, taking care not to dislodge the film from the ice surface, and the box was returned to the freezer. The resulting ice block was removed from the box and trimmed until approximately 5 millimeters of ice remained around all of the edges of the embedded polypyrrole film.



Figure 5: Mounted ice block with embedded polypyrrole film.

The ice block was then attached to a microtome sample holder using standard embedding compound (Tissue-Tek O.C.T.⁴) such that the short edge of the rectangular film was perpendicular to the sample holder, as shown in Figure 5. The holder was mounted in a cryo-microtome (Vibratome UltraPro 5000⁵) with its stage maintained at -25 °C and its blade maintained at -20 °C such that the long axis of the film was parallel to the direction of blade travel. The microtome was set to cut sections equal in thickness to the measured film thickness, so as to give square cross-section wires. Wires were produced by repeatedly cutting sections and collecting them on glass slides; each section resulted in the production of a single wire with a cross section of approximately 17×17 micrometers and a length of 20 millimeters (an aspect ratio of 1000:1).

4.2.3: Electrode Assembly

Electrodes were assembled from sliced polypyrrole wires by Prof. Llinás's group at NYU. The polypyrrole microwires were attached to larger silver wires, as shown in Figure 4,

² <http://www.sigmaaldrich.com/>

³ <http://www.eszinc.com/>

⁴ Electron Microscopy Sciences: <http://www.emsdiasum.com/>

⁵ <http://www.vibratome.com/>

using silver-bearing epoxy (Transene Nanopoxy 60). The assembly was then insulated by application of a saturated solution of poly(ethylene oxide) (Aldrich, MW = 2×10^6) in dichloromethane; the tip was left exposed to ensure a low-impedance electrical interface.

4.3: Results

The sliced polypyrrole microwires were able to become successful intravascular neural recording electrodes, collecting clean signals from the frog sciatic nerve. This process was likely assisted by the smooth surface morphology of the wires and by the high conductivity of the film from which they were made.

4.3.1: Wire Morphology

Representative scanning electron micrographs of a polypyrrole microwire are shown in Figures 6 and 7. Figure 6 shows the large-scale morphology of the fiber; there are very few defects in the 2 millimeter section shown, and the defects present are smaller in size than the wire diameter. Figure 7 shows a closer view of the same wire. The side of the wire cut by the microtome can be identified by the wavy striations; these striations are very small in comparison to the size of the wire. The side of the film exposed to the solution is visible on the bottom of the wire. The extremely smooth solution-side surface is characteristic of high-conductivity films produced in the BioInstrumentation Lab[1]. The small, rounded defects on the surface (one of which was sliced by the microtome) typically appear opposite small holes on the electrode-side surface; these features appear to be related to flaws on the surface of the glassy carbon electrode.

Figure 8 shows a different polypyrrole microwire that was coated in poly(ethylene oxide). This wire was made from a slightly lower-quality film, and thus has a higher concentration of bubble-shaped defects. The edges of the defects have been noticeably rounded over by the adherent layer of poly(ethylene oxide), which appears to be 1 to 2 micrometers thick. The bright bands at the edges of the wire also indicate the presence of a continuous layer of insulating material surrounding a conductive core.

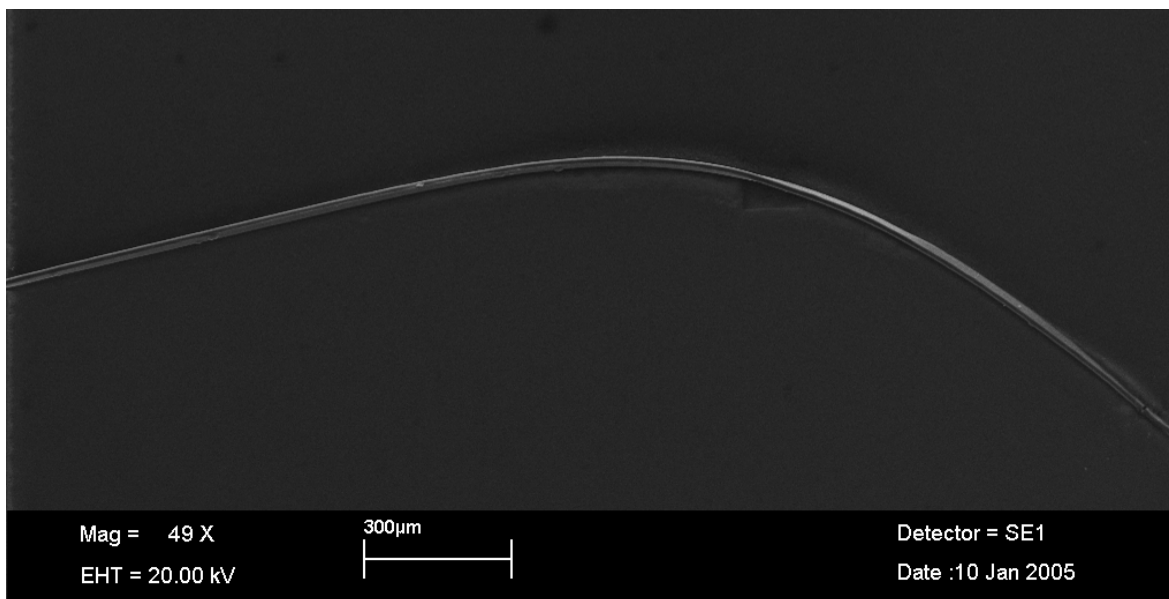


Figure 6: Low-magnification view of a sliced polypyrrole microwire.

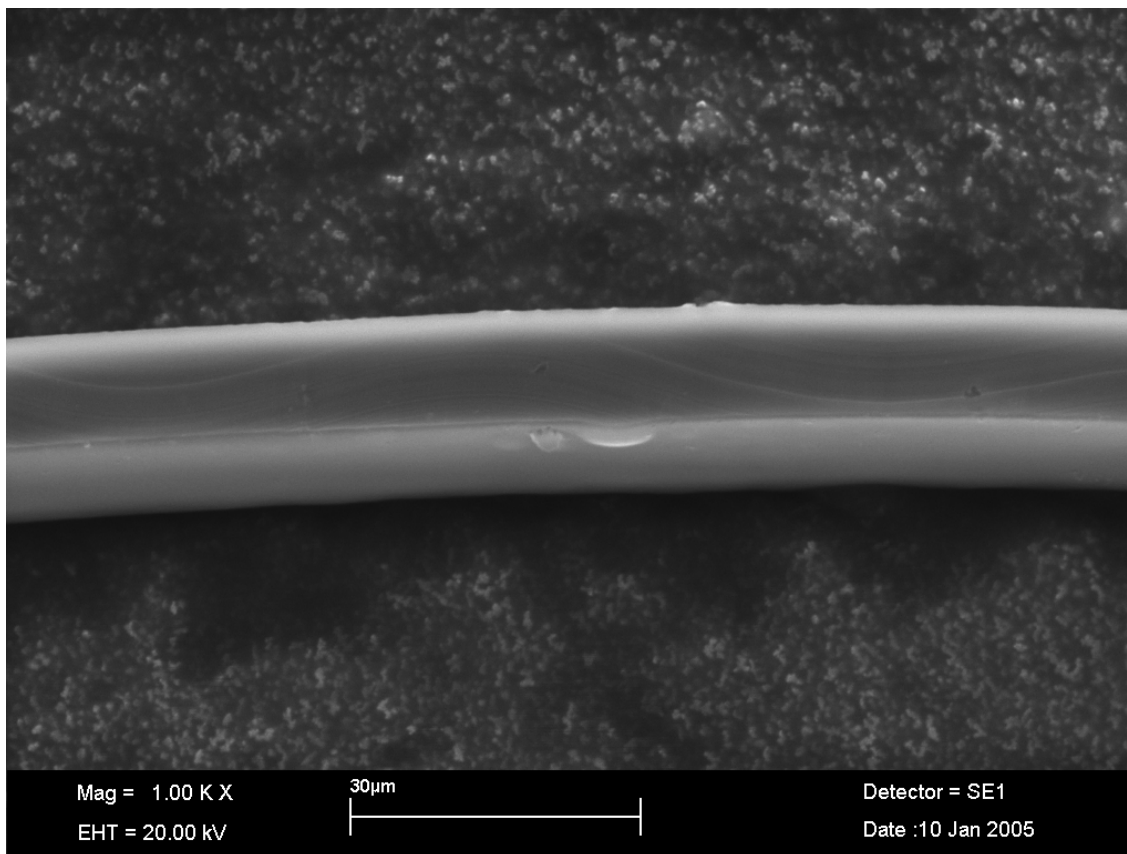


Figure 7: High magnification view of the same polypyrrole microwire as shown in Figure 6. The portion of the wire bearing wavy striations was cut by the microtome, while the smooth wire surface visible in the lower portion of the image was on the solution side of the film during electrodeposition.

4.3.2: Neural Recording

The physiological layout of the neural recording experiment performed by the Llinás group is shown in Figure 9. The stimulating electrode near the top of the image is used to apply an electrical pulse to the sciatic nerve, so as to induce an action potential. The external electrode mounted directly on the nerve below the stimulating electrode measures the propagating action potential, as does the polymer electrode located within the sciatic artery. The experiment was performed on a dead and partially dissected frog, so there were no spontaneous neural signals.

The action potentials recorded by the two electrodes are shown in Figure 10. The intravascular polymer electrode observed a higher amplitude signal than the standard surface electrode. The surface electrode also appears to observe the action potential through a low-pass filter compared to the polymer electrode, smearing out details of the waveform.

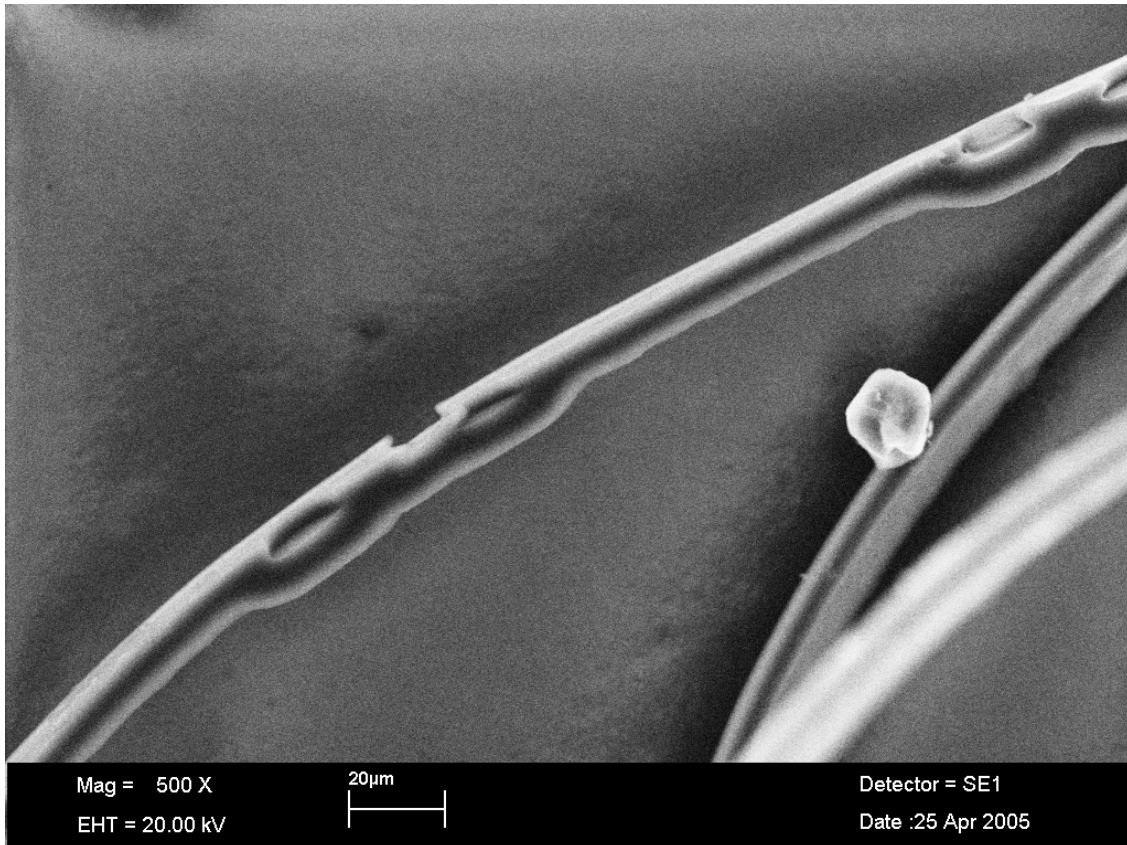


Figure 8: High-magnification view of poly(ethylene oxide) coated polypyrrole microwires. The coating has rounded the edges of the bubble-shaped defects, and allowed charging from the electron beam to occur at the edges of the wires.

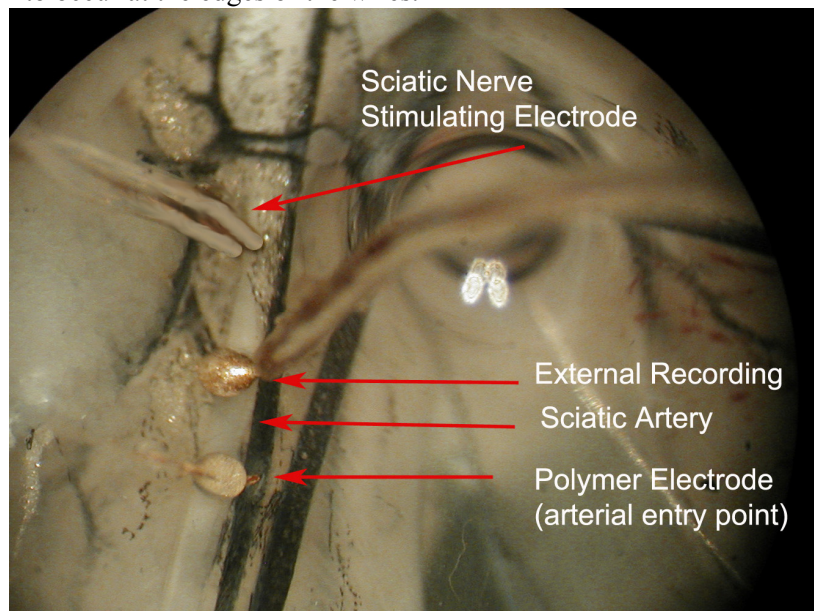


Figure 9: Experimental setup for intravascular recording of sciatic nerve signals in a frog. The stimulating electrode produces an action potential on the sciatic nerve, which is recorded by the external recording electrode placed on the surface of the nerve and by the intravascular polymer electrode. Image courtesy of Rodolfo Llinas.

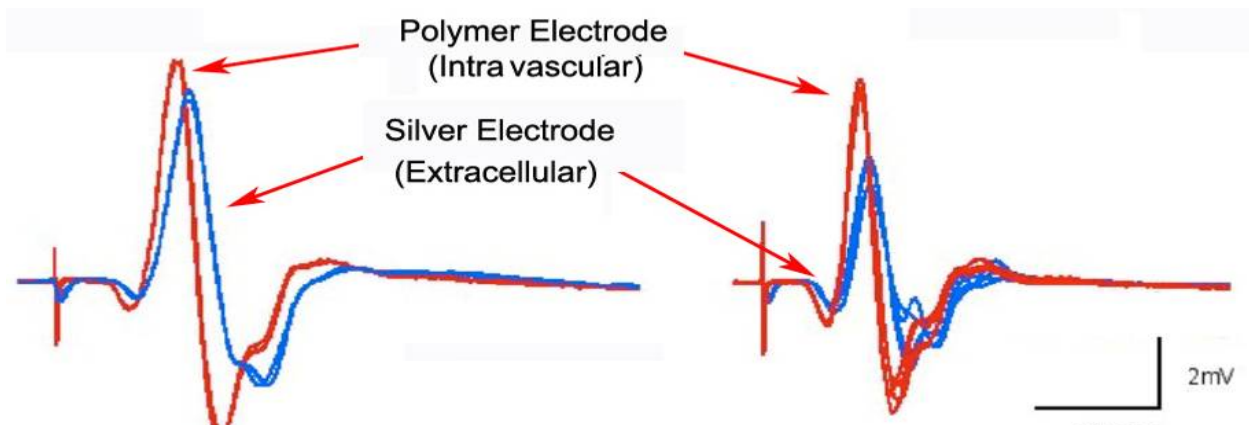


Figure 10: Electrode signals recorded from the frog sciatic nerve after stimulation. The polymer electrode displays faster response time and higher signal amplitude than the silver electrode mounted directly on the nerve. Figure courtesy of Rodolfo Llinas.

4.4: Discussion

The successful production of sliced polypyrrole microwire electrodes and their use for high-fidelity neural recording through a blood vessel wall were crucial milestones for the project as a whole. We demonstrated that conducting polymers can be used to replace metals for neural recording without any inherent loss of performance. Microtome slicing, a technique that was born out of a need for haste and allowed wires to be produced and delivered to the Llinás group within a week of the collaboration's start, proved to be a high-quality manufacturing techniques for wires greater than about 10 micrometers in minimum cross-sectional dimension. Unfortunately, polypyrrole films thinner than 10 micrometers are generally fragile and porous, and are not suitable for slicing. Thus, slicing is not a manufacturing technique capable of meeting the ultimate production goal of submicron wires.

It is interesting to compare the theoretical performance of this electrode to that of the platinum nanowire electrode used in the Llinás group's early work. Using the material properties in Table 1, the platinum nanowire has a resistive impedance of 370 k Ω /m. Using the measured polypyrrole conductivity, the microwire has a resistive impedance of only 280 k Ω /m. Both resistances are small compared to the typical interface impedance at the end of an electrode in a biological system[8]. The polymer wire has a flexural rigidity 5000 times greater than that of the platinum wire (5×10^{-12} N \cdot m² versus 1×10^{-15} N \cdot m²), but is 200 times stronger in tension (10 mN versus 50 μ N). The high stiffness and strength of the polypyrrole microwires arises from their large size. In order to match the flexural rigidity of the platinum wire, the polymer wire would have to shrink to a 3 micrometer thickness, at which point the polymer wire would still be 6 times stronger in tension than the platinum wire (360 μ N), but have 25 times more resistance, at 9.1 M Ω /m. Even still, the resistive impedance of a microwire electrode on the order of a centimeter long would be substantially lower than the interface impedance.

5: Electrospun Polyaniline Nanowires

Electrospinning was selected as the fabrication method of choice for conducting polymer electrodes capable of intravascular neural recording from within the capillary bed. Coaxial electrospinning, a technique developed in 2003, allows simultaneous fabrication of a sub-micrometer wire and an insulating coating[26]. As these wires are very difficult to manipulate, special attention must be paid to the design of the overall electrode design so as to minimize the amount of mechanical manipulation of nanowires required. Coaxial electrospinning is a new technique for the BioInstrumentation Lab, so an appropriate apparatus had to be designed and constructed. To date, complete nanowire electrodes have not been assembled, so the only well-developed experimental protocols relate to the production of the wires themselves. These wires have been characterized by light microscopy and transmission electron microscopy, and shown to be continuous and conductive over lengths of 10 millimeters or more.

5.1: Motivation

The slicing technique described in the previous chapter, despite its ease of use and development, proved inadequate for the production of sub-micrometer wires. Thus, a broad set of possible fabrication techniques for sub-micrometer wires were investigated. These techniques divide themselves into three main categories: templated deposition, template-free techniques, and post-fabrication size reduction.

In a templated deposition technique, a pre-existing, non-conducting-polymer structure is prepared and used to control the morphology of nascent conducting polymer nanowires. There are several ways in which this can be done: for example, conducting polymer can be polymerized directly onto a lithographically patterned electrode; it can be polymerized onto a carbon nanotube or other nanofiber[19,31]; or it can be polymerized into a nano-scale mold, such as a polycarbonate track-etched membrane[14]. While these techniques can provide tight control over the wire size and shape, they have several drawbacks. Coherent, free-standing submicron films are extremely difficult to make on electrodes, both because they are difficult to remove and because typical film morphologies are not smooth. Nanofiber templates limit the conducting polymer content of the finished wire, and tend to produce wires with very rough surface morphologies. Mold templates are very difficult to prepare with the extreme (>10,000:1) aspect ratios sought for the final nanowires. All of these techniques require independent application of an insulator coating to the conducting polymer nanowire.

Some techniques can produce conducting polymer nanowires without any explicit template. During chemical oxidative polymerizations, nanowires can be produced by self-assembled surfactant micelle templates[32] or inherently by the polymerization process itself[12]. Electrospinning employs electric fields to stretch a jet of polymer dissolved in solvent into a nanofiber, and can be applied to conducting polymers under certain conditions[19,26]. These techniques provide less control than templated techniques, but do not require the preparation and maintenance of sub-micrometer templates. The nanowire-producing chemical polymerizations do not produce long enough nanowires for the neural electrode application; however, electrospinning can produce single fibers meters in length. The coaxial electrospinning technique[26] can also fabricate the insulator coating simultaneously with the nanowire, eliminating a potentially difficult electrode fabrication step.

Nanowires could also potentially be produced by a fiber drawing technique, similar to that pioneered by Yoel Fink's research group[3]. A preform of melt-processable conducting polymer, insulation, and easily removed filler could be prepared, and thermally drawn for a size reduction of two to three orders of magnitude. Multiple stages of preform preparation and fiber drawing may be required to produce the desired nanowires. This technique could produce single fibers many meters in length with near-perfect control of fiber morphology. However, it would require considerable physical plant investment, and there are very few readily melt-processed conducting polymers, such as poly(alkylthiophene).

After considering these options, I selected coaxial electrospinning as the fabrication technique of choice. Its ability to directly produce long, insulated nanowires using relatively simple equipment and from a variety of materials outweighs the relative lack of control of fiber morphology.

5.2: Electrode Design

In broad terms, the design of the electrospun nanowire electrode is very similar to that of the platinum electrode previously used by the Llinás group. As shown in Figure 2, the main body of the electrode consists of an insulated wire under a micrometer in diameter, with a length of up to 20 millimeters. The tip is adorned with a high-surface-area deposit to reduce electrical impedance and guide the electrode in the vasculature, and the base is fastened to a larger carrier wire. The nanowire and tip deposit are now simply made from conducting polymer rather than platinum. The detailed design of the tip deposit and the base attachment will be discussed in the next chapter.

The choice of coaxial electrospinning guides the choice of specific materials for the conducting polymer nanowire and its insulation. Electrospinning processes, in general, only work with certain polymer solutions due to the process physics. Traditional electrospinning operates by pumping a polymer solution out of a nozzle at a low flow rate and with a large electrical potential relative to a grounded collector plate placed some distance away from the nozzle. The electric field causes the polymer solution to form a Taylor cone and jet[28,29], which is then stretched and accelerated by the electric field. When the jet reaches a critical diameter, it undergoes an electrohydrodynamic instability and begins to whip violently[15]. A photo of this whipping instability observed with my apparatus is



Figure 11: A view of the whipping instability when electrospinning poly(ethylene oxide). The electrospinning conditions included a 10 kV nozzle voltage, 170 mm electrode separation, 2% (w/w) polymer solution in distilled water, 2×10^6 molecular weight, and 0.5 mL/hr flow.

shown in Figure 11. This whipping process stretches the jet even further, resulting in a final jet diameter as low as 10 nanometers. As this very fine jet travels towards the collector plate, the solvent evaporates, leaving behind a solid polymer fiber. A good recent review of electrospinning can be found in[15]. The electrospinning process is not yet well understood, and there is some debate in the literature as to the influences of various parameters, such as electric field, nozzle-plate separation, solution concentration, and polymer molecular weight, on the final fiber diameter. It is clear, however, that the polymer solution to be spun must have pronounced viscoelastic properties, which are related to the flexibility, molecular weight, and concentration of polymer chains[24].

Conducting polymers typically possess very rigid chains, so they do not form viscoelastic solutions and are therefore difficult to electrospin. The coaxial electrospinning technique developed by Sun et al. gets around this problem by using a compound, core-shell jet emitted from a coaxial nozzle[26]. The shell layer contains a highly viscoelastic solution that could easily be spun by itself, while the core of the jet can contain nearly any fluid. The viscoelasticity of the shell stabilizes the core through the electrospinning process, forming a coaxial polymer nanofiber. As the core and shell solutions are in intimate contact, they cannot react with each other to form precipitates or decompose. Furthermore, the core of the jet will be more stable if it contains a similar solvent to the shell, so as to minimize the interfacial surface tension.

The physics of electrospinning, then, dictate that the conducting polymer electrode must be a highly conductive, soluble polymer, while the insulating layer (which serves as the shell layer in the coaxial electrospinning process) must be a high molecular weight, flexible polymer soluble in a solvent similar to that of the conducting polymer. Very few conducting polymers remain soluble in their conductive forms—of those, most are not very conductive. The soluble polymer with the highest conductivity is polyaniline doped with organic acid[23]. In particular, polyaniline doped with 10-camphorsulfonic acid (PAni-CSA) has the highest conductivity yet measured in a polyaniline, and is readily soluble in formic acid, dimethyl sulfoxide, and *m*-cresol. Of these solvents, only formic acid readily evaporates at room temperature. This choice then limits the available insulation materials to polymers that dissolve in formic acid; fortunately, poly(ethylene oxide) (PEO) does so and is also very easily electrospun.

5.3: Apparatus Design

The key functional requirements for a coaxial electrospinning system are twofold: it must produce a coaxial fluid jet with no leakage between the core and shell fluids, and it must sustain a sufficient electric field for electrospinning (~ 100 kV/m) over a gap of several hundred millimeters. In the process of achieving those requirements, it must also protect the operator from dangerous voltages and withstand the powerful, corrosive solvents used in the polymer solutions. We also wished to have as adaptable and expandable a design as possible, to accommodate future electrospinning research.

The electrospinner design chosen uses as many off-the-shelf parts as possible. The core and shell polymer solutions are delivered to the nozzle assembly by a dual-channel syringe pump (Harvard Apparatus model 33⁶). The nozzle assembly, shown in a cutaway view in Figure 12, uses standard hypodermic tubing held by standard compression fittings. The large blocks serve to channel the fluid flow into the hypodermic tubing and hold the compression fittings in the correct coaxial alignment. The nozzle assembly is made entirely from 316 stainless steel, to

⁶ <http://www.harvardapparatus.com/>

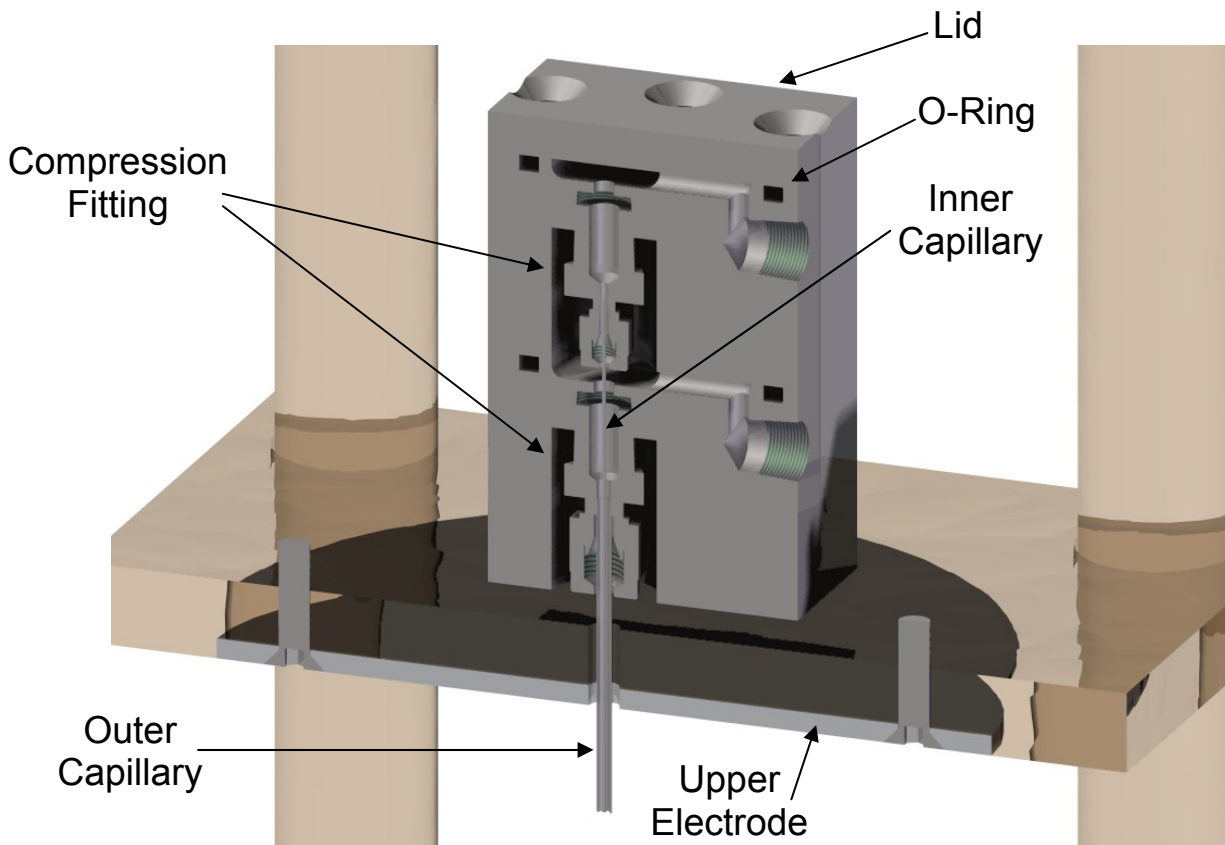


Figure 12: Cutaway schematic view of the electrospinner nozzle assembly. Polymer solutions enter the nozzle assembly from the two ports on the right.

prevent corrosion and resulting contamination of the polymer solutions. Voltage is applied to the nozzle assembly using a high voltage power supply with a 30 kV capacity (Spellman CZE1000R⁷). An upper electrode is used in addition to just the nozzle so as to obtain a more uniform and controllable electric field in the electrospinner. The protrusion of the nozzle beyond the plate is adjustable over a 20 millimeter range; further adjustment can be made by using longer or shorter lengths of hypodermic tubing.

The nozzle assembly is held in position by a poly(methyl methacrylate) structure, seen in Figure 13. This structure encloses the nozzle assembly and all high voltage connections, and partially guards the upper electrode. The nozzle assembly is supported on four rods, allowing the gap to be adjusted to a maximum size of 300 millimeters. A block diagram of the electrospinner can be found in the appendix.

5.4: Wire Fabrication

In order to produce electrospun conducting polymer nanowires, polymer solutions must be prepared and run through the electrospinning device. The polymer solutions do not have a long shelf life, so they must be prepared within a few days of running an electrospinning experiment.

⁷ <http://www.spellmanhv.com/>

5.4.1: Solution Preparation

To prepare PAni-CSA, 0.962 g of polyaniline emeraldine base (Aldrich, $M_w = 3 \times 10^5$) and 1.283 g (5.5 mmol) (\pm)-10-camphorsulfonic acid (Aldrich, 98%) were dissolved in 500 mL of chloroform (EM Science, 99.8%) and stirred for 24 hours. The chloroform was then evaporated at room temperature to give PAni-CSA (100% yield). A 10% (w/w) solution of PAni-CSA in formic acid (Fluka, 98%) was prepared by mixing on an orbital shaker for 72 hours. The solution was then filtered with a 1 micrometer glass fiber filter (Gelman Glass Acrodisc⁸), giving an opaque green solution measured to contain 9% (w/w) PAni-CSA.

A 2% (w/w) solution of PEO (Aldrich, $M_w = 2 \times 10^6$) in formic acid was prepared by mixing on an orbital shaker for 72 hours, yielding a slightly cloudy, strongly viscoelastic solution. The viscoelasticity was observed to degrade after several weeks of storage, most likely due to acid-catalyzed ether bond breakage in the PEO chains.

5.4.2: Electrospinning Procedure

For all experiments, the electrospinner was configured with a 23 gauge inner nozzle (635 μm OD, 508 μm ID), a 13 gauge outer nozzle (2413 μm OD, 1956 μm ID), and 260 mm of electrode separation. All experiments were performed with a core:shell flow rate ratio of 1:3, theoretically yielding fibers composed of 60% PAni-CSA and 40% PEO by mass. Fibers were successfully produced with total flow rates from 4 mL/hr to 20 mL/hr, and electrode potentials from 16 kV (62 kV/m) to 30 kV (120 kV/m). As the flow rate was increased, the voltage required for steady electrospinning also increased.

Fibers collected as green mats on and around the ground electrode. As spinning progressed, new fibers were deposited preferentially on existing fibers and the support rods, causing cobweb-like deposits to grow upwards towards the nozzle. If the fibers reached the positive electrode, a short circuit condition developed and stopped further electrospinning. Nanowire samples were collected on glass slides and stainless steel foils by placing the slide or foil directly below the nozzle and just above the ground electrode for a few seconds. The



Figure 13: Photograph of completed electrospinner. The clear plastic parts are all made from poly(methyl methacrylate), and the nozzle assembly from Figure 12 is visible in the center of the photo.

⁸ <http://www.pall.com>

operator's arm served to ground the collection devices, and had to be connected directly to the power supply ground to minimize electrical shocks.

5.5: Results

Electrospun nanowire samples were examined by light microscopy and transmission electron microscopy. A light micrograph of nanowires produced at a total flow rate of 4 mL/hr and an electric field of 120 kV/m is shown in Figure 14. The brightly colored polyaniline cores are continuous over tens of millimeters on the slide. The fiber diameter appears to be approximately 3 micrometers, with a 1 micrometer core; however these features are close in size to the spatial resolution of the microscope, and so their measured sizes may not be reliable.

A transmission electron micrograph of an electrospun nanowire is shown in Figure 15. The PEO shell has been removed by the electron beam in the center of the image, exposing a resistant core of PAni-CSA. The core is 650 nanometers in diameter, and the wire outside diameter is 1950 nanometers. The PEO shell is very sensitive to beam damage; the slight blurring at the ends of the exposed region is due to the continued ablation of PEO as the image was taken.

In order to estimate the fiber conductivity, a PAni-CSA film was drop cast at 100° C from the same 9% solution as was used for electrospinning. The conductivity of the resulting film was 3 S/m. Treating the film with a drop of *m*-cresol and allowing it to evaporate at 100 °C raised the conductivity to 1360 S/m.

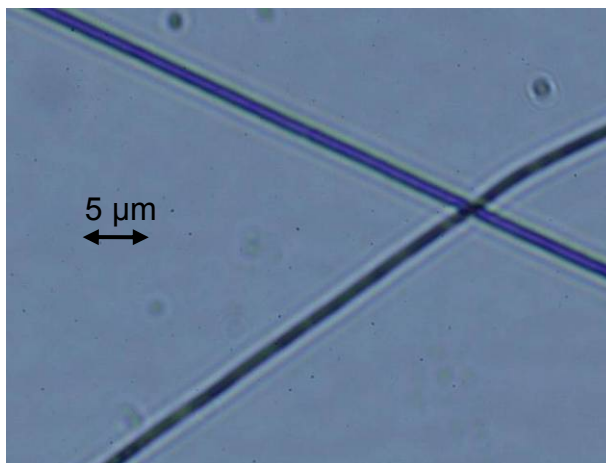


Figure 14: Light microscope image of two electrospun nanowires produced at a total flow rate of 4 mL/hr and an electric field of 120 kV/m.

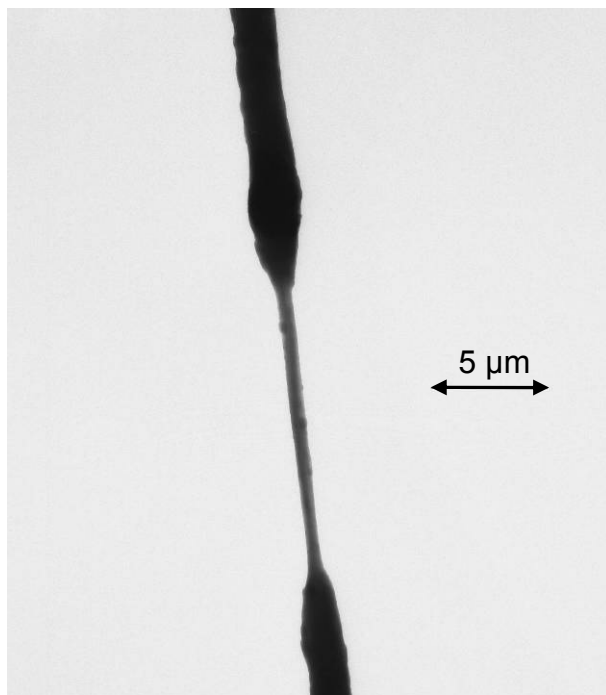


Figure 15: Transmission electron micrograph of an electrospun nanowire produced at a total flow rate of 4 mL/hr and an electric field of 120 kV/m. The electron beam has ablated the PEO coating in the center of the image, exposing the PAni-CSA core. Image courtesy of Rachel Pytel.

5.6: Discussion

No previous author has published the production of electrospun fibers from PANi-CSA, or any other form of polyaniline doped with organic acid. The only previous electrospinning involved polymer blends[10] or inorganically doped polyaniline[19]. While the current conductivity of the fibers is poor, the results of *m*-cresol treatment show that considerably higher conductivities should be available given changes in the solvent system. These fibers are slightly larger than was specified, but there is no reason to believe that additional adjustment of spinning parameters will not shrink the nanowires to the nanoscale.

The relative proportions of the fibers are somewhat unexpected. Theoretically, the fibers should be 60% PANi-CSA and 40% PEO by mass; assuming that PANi-CSA is 50% denser than PEO[25], a 650 nanometer core should correspond to a 920 nanometer fiber outside diameter. The observed structure is instead consistent with a mass composition of just 16% PANi-CSA and 84% PEO. The gross excess of PEO is most likely caused by some sort of dripping behavior; there must be other portions of the wire with very thin insulation. If this is the case, it will have to be remedied in order to produce high-quality nanowires.

6: Future Work

Our efforts to produce a conducting polymer-based intravascular neural recording system have only just begun to bear fruit. In this chapter I will discuss some of the next steps that need to be taken towards achieving a fully functional electrode system. In particular, I will discuss the design of an improved electrospinning apparatus that will be able to produce nanowires of higher conductivity and with a broader range of insulations. I will also discuss some ideas about the procedures that might be used to assemble a complete nanowire electrode system.

6.1: Improved Electrospinning Apparatus Design

The current electrospinning system, as described in the previous chapter, is missing a key capability for the production of highly conductive nanowires. PANi-CSA only possesses a high conductivity when it is treated with *m*-cresol, or cast from *m*-cresol solution. Furthermore, PEO dissolves rapidly in water and blood when used as a coating on such a small wire, rendering it unsuitable; polyurethane is frequently used as a blood-contacting polymer, and it dissolves readily in *m*-cresol. However, *m*-cresol has a very high boiling point, (203 °C) and a correspondingly low vapor pressure at room temperature. It is therefore unable to evaporate from a jet electrospun at room temperature before it reaches the ground electrode, leading to the deposition of a puddle in place of a mat of nanowires. In order to use *m*-cresol as an electrospinning solvent, then, the temperature at which the electrospinning takes place must be raised to approximately 100 °C.

Electrospinning at high temperature requires an apparatus that operates in an isolated atmosphere, and that is composed entirely of materials suitable for use at such temperatures. To ensure that high-temperature electrospinning works the same way as room temperature electrospinning, the polymer solutions must exit the nozzle at the correct temperature, and the air and radiative heat transfer environment surrounding the polymer jet must also be at the correct temperature.

Changing the materials from which the electrospinner is made, building an environmental isolation chamber around it, and controlling the air temperature within the chamber are relatively simple tasks. Controlling the temperature of the polymer solutions, however, is made a bit more complex by the fact that the solutions are at an electrical potential of up to 30 kV relative to ground. The nozzle assembly, which is essentially a large stainless steel block, has a very slow thermal time constant. It will thus not be sufficient to simply heat the polymer solutions at the pump, or to rely on the hot air in the chamber to heat the nozzle assembly—the block will need to be directly heated to provide reasonable control bandwidth. In order to heat the assembly, I will need to construct an isolated power supply to run a temperature sensor and a resistive heater, as such supplies are not readily commercially available. I will construct a motor-generator set with a ceramic shaft for use as a high-isolation-voltage power supply.

6.2: Nanowire Electrode Fabrication

A simple insulated conducting polymer nanowire is not sufficient for neural recording. It must be attached to the outside world in some manner, and it must communicate with the neural environment with as low an electrical impedance as possible. These tasks are made more challenging by the incredibly small size of the nanowire—it cannot be manipulated by hand.

Fortunately, there are techniques available for both the growth of electrode tip adornments and for attaching nanowires to larger wires that do not require direct manipulation of the nanowire.

6.2.1: Electrode Tip Adornment

Just as the platinum nanowire electrode could have a high-surface-area platinum tip electroplated onto it, a conducting polymer nanowire electrode can have a high-surface-area conducting polymer tip electrodeposited onto it. Ideally, such an electrodeposition would be non-contact, as it is rather difficult to locally remove the insulation on a nanowire in order to make external electrical contact. Fortunately, for high-aspect-ratio structures like nanowires, a technique called bipolar electrochemistry allows electrochemical reactions to take place in the presence of just a static electric field[2].

Bipolar electrochemistry exploits the fact that the surface of a good conductor is an equipotential surface. If a long, narrow conductor lies parallel to an electric field, it will be at the average of the potential along its length. At one end, the potential on the conductor is higher than the surrounding free-space potential; at the other end, the potential is lower. These underpotentials and overpotentials can be sufficient to drive electrochemical reactions; all that is required is that the conductivity of the conductor be much greater than the conductivity of its environment. On metallic conductors, the typical reactions are electroplating on the end with an underpotential and dissolution on the end with an overpotential, resulting in a simple net migration of metal.

Conducting polymers undergo very different electrochemical reactions than metals, allowing for richer behavior. If a monomer, such as pyrrole, is present in the environment, electropolymerization will take place at the end of the a conducting polymer structure bearing an overpotential, but the end of the structure with an underpotential will simply be reversibly reduced to a non-conductive state. In a DC electric field and a pyrrole-bearing electrolyte solution, a conducting polymer nanowire would grow a polypyrrole tip on one end, without needing to make any actual electrical contact to the nanowire and without disrupting the insulation on the wire.

6.2.2: Electrode Base Attachment

A conducting polymer nanowire can also be attached to a larger wire by bipolar electrochemistry. If a metal wire is used as the negative electrode in a cell containing pyrrole, a metal salt, and a single nanowire, with a flat plate serving as the positive electrode, the nanowire will attach itself to the metal wire. The nonuniform potential gradient near the metal wire will attract the nanowire; meanwhile, a polypyrrole deposit will grow on the end of the nanowire closest to the negative electrode, and a metal deposit will grow on the metal wire. When the nanowire makes contact with the negative electrode, metal will be deposited to reinforce the joint between metal wire and nanowire, as well as on the nanowire tip. After the assembly is removed and the wire junction is insulated, the metal on the tip of the nanowire can be removed by oxidation, leaving an all-polymer nanowire electrode attached to a larger metal wire.

7: Conclusions

Substantial progress has been made in the collaboration between the BioInstrumentation Lab and Prof. Llinás's group towards the production of all-polymer intravascular neural recording electrodes. Such electrodes promise to substantially reduce the risks involved with the use of high-information-content brain-machine interfaces, enabling their wider use. We have produced an all-polymer demonstration microelectrode, and shown that it can make high-fidelity neural recordings. We have also produced the first electrospun fibers of organically-doped polyaniline, and taken steps towards improving them to meet required specifications for small size and high conductivity. Within a few short years, we expect to be able to produce electrode systems small enough to fit into capillaries and conductive enough to record nerve impulses, and in the process bring nanotechnology into the world of macroscale applications.

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Appendix: Electrospinning Apparatus Block Diagram

