Surface Characterization of Modified Neural Implants

by

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“Nobody can go back and start a new beginning, but anyone can start today and make a new ending.”

Maria Robinson
Neural implants represent a new hope for the rising number of patients with neurodegenerative diseases. These electrode-neuronal tissue interfaces are capable of recovering sensory and functional losses by stimulation of neuronal cells or monitoring the CNS by the recording of nerve signals. However, the implantation of devices in the CNS still remains one of the biggest challenges of neurosciences, due to the immune reactions that follow their insertion into the human body. Glial scar formation causes the implant’s encapsulation, increasing the distance between the electrode and neurons, which will induce the decrease of the signal-to-noise ratio. This violent response, also results in both electrode and neuronal tissue deterioration.

The main objective of the present work was the development of coatings intended to improve silicon-based neural implants biocompatibility. The proposed materials were silicon dioxide, as insulator, silver and copper as antibacterial agents, and gold which will permit the implant’s identification in imaging exams, and will induce silver/copper’s oxidation, which only are effective in their oxidized form. Therefore, the work was based in the surface characterization of modified Si with thin films of SiO$_2$, Au, Ag and Cu, as well as with thin films of three different systems: SiO$_2$/Au, SiO$_2$/Ag e SiO$_2$/Cu, varying the percentage of the metallic element. Chemical composition, wettability and morphology/topography were the surface properties analyzed. From the monolithic thin films, only copper’s has not shown a biocompatible behavior, presenting hydrophobic characteristics and poor adhesion to the silicon wafer. From the SiO$_2$/metallic element systems, it was verified that the metallic element deposition induced a general increase in contact angles, but also a general improvement in the thin film’s topography. Silver’s release in in vitro tests, which has been concluded to be related to its film’s initial at.%, was achieved specially for the 24.3% Ag, with an increase of the average roughness. The only film that induced the release of copper ions was 10.5% Cu. However, this thin film presented inadequate surface wettability properties for the application in study. Future work should include a new characterization of SiO$_2$ doped with both Ag and Au, where the systems with the best characteristics should be submitted to in vitro cell tests.
Resumo
Faculdade de Ciências e Tecnologia da Universidade de Coimbra
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Os implantes neuronais representam uma nova esperança para o número em crescente de pessoas que sofrem de doenças neurodegenerativas. Estas interfaces eléctrodo-tecido nervoso são capazes de restituir perdas sensoriais e funcionais pela estimulação de células nervosas, ou de monitorar o SNC, pelo registo de impulsos nervosos. Contudo, a implantação de dispositivos no SNC é, ainda, um dos maiores desafios das neurociências, devido às reacções imunitárias que advêm da sua inserção no corpo humano. A formação de tecido cicatricial das células da glia provoca o encapsulamento do implante, levando ao afastamento do eléctrodo aos neurónios, induzindo a diminuição da razão sinal-ruído. Esta resposta violenta resulta ainda numa deterioração do implante e do tecido nervoso.

O presente trabalho teve como objectivo o desenvolvimento de revestimentos de modo a optimizar a biocompatibilidade de implantes neuronais de silício. Os materiais propostos para o efeito são dióxido de silício como isolante, prata e cobre como agentes antibacterianos, e ouro que permitirá a identificação do implante em exames imagiológicos e induzirá a oxidação da prata e do cobre, que apenas serão eficazes na sua forma oxidada. Assim, procedeu-se à caracterização de superfícies de Si modificadas com filmes finos de SiO$_2$, Au, Ag e Cu, bem como com três sistemas diferentes: SiO$_2$/Au, SiO$_2$/Ag e SiO$_2$/Cu, com percentagens variáveis do elemento metálico. As propriedades de superfície analisadas foram composição química, molhabilidade e morfologia/topografia. Dos filmes monolíticos, apenas o de cobre demonstrou não ter um comportamento biocompatível, com características hidrofóbicas e fraca adesão à superfície de silício. Dos sistemas SiO$_2$/elemento metálico, verificou-se que a deposição do elemento induziu um aumento geral do ângulo de contacto, mas uma melhoria geral da topografia dos filmes finos. A libertação da prata em testes in vitro, que se concluiu estar relacionada com a sua %at. inicial, foi conseguida com um consequente aumento da rugosidade média, para o filme de 24,3% Ag. O único filme que induziu libertação de íões de cobre foi o de 10,5% Cu, no entanto este filme possuía molhabilidade de superfície menos adequada à aplicação em estudo. Propõe-se, como trabalho futuro, uma nova caracterização de filmes finos de SiO$_2$ dopados com Ag e Au em simultâneo, onde os sistemas com melhor características seriam submetidos a testes in vitro com cultura de células.
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<tr>
<td>AFM</td>
<td>Atomic Force Microscopy</td>
</tr>
<tr>
<td>CNS</td>
<td>Central Nervous System</td>
</tr>
<tr>
<td>CVD</td>
<td>Chemical Vapor Deposition</td>
</tr>
<tr>
<td>DC</td>
<td>Direct Current</td>
</tr>
<tr>
<td>EDS</td>
<td>Energy Dispersive Spectrometer</td>
</tr>
<tr>
<td>EPMA</td>
<td>Electron Probe MicroAnalyzer</td>
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<tr>
<td>Form.</td>
<td>Formamide</td>
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<tr>
<td>Glyc.</td>
<td>Glycerol</td>
</tr>
<tr>
<td>MEMS</td>
<td>Micro Electro Mechanical Systems</td>
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<tr>
<td>PVD</td>
<td>Physical Vapor Deposition</td>
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<tr>
<td>RF</td>
<td>Radio Frequency</td>
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<tr>
<td>SBF</td>
<td>Simulated Body Fluid</td>
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<tr>
<td>SEM</td>
<td>Scanning Electron Microscopy</td>
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<tr>
<td>SFE</td>
<td>Surface Free Energy</td>
</tr>
<tr>
<td>% at.</td>
<td>atomic percentage</td>
</tr>
<tr>
<td>Ag</td>
<td>Silver</td>
</tr>
<tr>
<td>Au</td>
<td>Gold</td>
</tr>
<tr>
<td>Cu</td>
<td>Copper</td>
</tr>
<tr>
<td>H$_2$O</td>
<td>Water</td>
</tr>
<tr>
<td>Si</td>
<td>Silicon</td>
</tr>
<tr>
<td>SiO$_2$</td>
<td>Silicon dioxide</td>
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## Symbols

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<th>Symbol</th>
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<tr>
<td>$R_a$</td>
<td>Roughness average</td>
<td>nm</td>
</tr>
<tr>
<td>$R_t$</td>
<td>Maximum height of the profile</td>
<td>nm</td>
</tr>
<tr>
<td>$R_{tm}$</td>
<td>Average maximum height of the profile</td>
<td>nm</td>
</tr>
<tr>
<td>$S$</td>
<td>Sputter Yield</td>
<td>atoms/ion</td>
</tr>
<tr>
<td>$\gamma_c$</td>
<td>Critical surface tension</td>
<td>mJ.m$^{-2}$</td>
</tr>
<tr>
<td>$\gamma_{LV} \ or \ \gamma_L$</td>
<td>Surface tension of the liquid</td>
<td>mJ.m$^{-2}$</td>
</tr>
<tr>
<td>$\gamma_{SL}$</td>
<td>Interfacial free energy between the liquid and the solid</td>
<td>mJ.m$^{-2}$</td>
</tr>
<tr>
<td>$\gamma_{SV} \ or \ \gamma_S$</td>
<td>Surface free energy of the solid (SFE)</td>
<td>mJ.m$^{-2}$</td>
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<tr>
<td>$\theta$</td>
<td>Contact angle</td>
<td>$^\circ$</td>
</tr>
<tr>
<td>$\theta_a$</td>
<td>Advancing contact angle</td>
<td>$^\circ$</td>
</tr>
<tr>
<td>$\theta_r$</td>
<td>Receding contact angle</td>
<td>$^\circ$</td>
</tr>
<tr>
<td>$\Delta \theta$</td>
<td>Hysteresis of the contact angle</td>
<td>$^\circ$</td>
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Introduction

Neurological disorders are one of the most challenging medical problems faced by science today. Nowadays, diseases from the nervous system affect around 50 million people in the European Union and have significant impact not only on patients lives, but also on their families and society as a whole. According to the European Brain Council, there will be an increase of 20% in these diseases in the next years, which is a serious economical concern since they are currently costing nearly 400 billion euros annually to the health care systems. [3] [4]

In the last decade, biomaterials have been widely used, not only in the treatment of neurological disorders, but also to improve functional recovery in the central nervous system. Neural implants are systems that connect electrode probes to the neuronal tissue and that are capable of stimulate neuronal cells or recording neuronal stimulus. These neural interfaces are currently implanted in more than 237 000 patients around the world. [5]

One successful example of neural implants are deep brain stimulators, which have been implanted in patients for pain management and control of motor disorders of many neurological disorders, such as epilepsy, Parkinson’s and Alzheimer’s disease. Nerve excitability results in the release of neurotransmitters capable of relieving the symptoms of such diseases, improving the quality of life of the patients. Recording interfaces, on the other hand, allow the understanding of physiological processes in neurosciences and help restoring functions in the nervous system. [6]

The major problem related to neural implants is their long-term viability and stability, since it is important that these probes remain entirely functional for a long period of time within the organism. Otherwise, patients would frequently be submitted to invasive surgeries to exchange the implant which, adjacently, suggests an economic impact.
However, although over the years biocompatibility has been significantly improved, long-term implanted biomaterials still lead to unwanted tissue reactions. These reactions, in the particular case of central nervous system’s applications, result in the proliferation of a glial scar around the implant, deteriorating not only the surrounding neural elements, but also the electrodes. [7] [8]

Several studies have proved that although mechanical and bulk properties are important for the performance of the implant, the key for biocompatibility is at the material’s surface. Acceptance of the biomaterial might be predicted at tissue-material interfaces by surface characteristics, like surface morphology and topography, surface chemistry and surface wettability. The problem comes when the materials that have the favorable bulk properties for any biomedical application, have the inadequate surface biological properties. [9]

Some approaches have been made in order to achieve the best neural probes structure. Nowadays, neural implants are made of silicon, the main component of most semiconductor devices. However, after some time and due to adverse reaction of biological tissue, the impedance around the electrode increases, leading to the loss of the signal and to the failure of neurostimulation and recording.

Consequently, in order to improve tissue reaction and to optimize signal reception, the material surface may be modified without affecting the desirable implant bulk attributes. In fact, the deposition of thin films from and over materials that already were established as biocompatible, will increase their performance. Varying the deposition parameters, the surface modification process may induce changes in structural and chemical composition of the surface.

The aim of this project is to perform the surface characterization of modified silicon-based electrodes, with silicon dioxide (SiO₂) thin film coatings, doped with silver, gold and cooper, separately. The characterization of the films will be performed, before and after its immersion in simulated biological fluid. The exhaustive characterization of the modified materials is the only way to properly relate the properties of its surface with their desired biological functions. After that, reproducibility can be ensured, leading to the industrialization of the device under this study. The general proceedings of the present work are chronologically represented in the timetable from Figure 1.
In the first chapter of this dissertation, it will be made a brief review about the state of art of the neural implants, and also how the interaction between the electrode and the neural tissue is done. Furthermore, it will be discussed some biocompatibility aspects, as well as be explained the brain immune response to these neural implants.

After that, it will be highlighted the importance of implant-neural tissue interface to the performance of the neural probe and to the tissue’s immune response. Moreover, it will be explained how to improve surface’s biocompatibility in order to decrease, for example, electrode’s impedance. Also, the technique used to modify the surface of the materials used in the present investigation will be clarified.

In the second chapter, some of the surface properties that most influence biocompatibility will be presented. The methodologies used in order to characterize such properties, and how to evaluate the implant’s performance towards the physiological environment, will be described.

In the third and last chapter, the experimental surface characterization results will be compared and discussed.

To sum up, this dissertation will end with the conclusions of the present work, namely whether the results obtained were as expected and if they do answer the main goals of the project, and how. Finally, some guidelines for future work in this field will be suggested.
Chapter 1

Fundamentals of Neural Implants

Neural interfaces connect electronic circuitry and neurobiological substrate to provide exchange of information with the nervous system. This exchange can occur either by electrical stimulation, for the rehabilitation of sensory and motor functions in patients with neurological disorders or by electrical recording, which gives detailed access to neural signals and can be used to determine the internal state of an organ or organism.

In this chapter some aspects about the nervous system and its connection to the neural electrodes will be reviewed. Furthermore, several types of neural probes will be presented, and also explained the organism response to their implantation. Moreover, it will be clarified the importance of surface modification modification of the material as a solution in the optimization of implant’s biocompatibility. As the samples used in this work were obtained by a specific modification technique, such technique will be briefly presented.

1.1 Communication with the Nervous System

Communication and information processing within the nervous system are based in action potentials: electrical signals produced by excitable cells. These cells, known as neurons, are the basic components of the nervous, glandular and muscular tissue. The cell is electrically polarized if there is an electrical potential difference between its internal and external environment, which is maintained by transmembrane proteins or ion channels. When this difference is properly stimulated and the potential inside the
cell increases beyond some threshold, the excitable cell will create an action flow of charged ions across the permeable cell membrane with the ions passing through the ion channels (Figure 1.1). Axons and dendrites, the branched filaments extending from the neuron body, are then responsible to transfer these action potentials to adjacent cells, generating an electric field that propagates through the biological tissue. [10]

![Figure 1.1: Propagation of the Action Potential on a neuron. The current flow spreads farther along the axon.](image)

By connecting a neural implant to nervous tissue, action potentials may be artificially generated through electrical stimulation or even transduced in an external electric signal, that is then further amplified and recorded without tissue and electrodes damage.

The passage of current through the extracellular electrodes, positioned near neurons, results in the depolarization of the cells membrane and in the generation of an action potential. More specifically, a stimulation pulse is applied at tissue-electrode interface and numerous electrochemical mechanisms will contribute to the transduction of the electronic pulse into ionic current in the tissue. Neural interfaces may also modulate or even block ongoing neuronal firing by controlling the magnitude, polarity and distribution of the potentials. [12] [13] The currents required to excite single cells are in the
range of picoamperes. However, to stimulate neurons in the treatment of Parkinson’s disease for example, hundreds of microamperes need to be applied. [14]

Furthermore, by delivering high frequency electrical stimulation to target regions of the brain, deep brain stimulation not only aims to treat Parkinson’s disease, but also epilepsy, depression and obsessive-compulsive disorders. [6] Another example of implantable neural interfaces, commercially available, and that have been successfully applied are cochlear implants. These implants can restore the sense of sound for many varieties of hearing loss, by stimulation of auditory nerve. [15]

As it was already mentioned, the flow of ionic current gives rise to potentials within the tissue. These potentials are usefully converted into electronic current, and recorded in order to extract information from the nervous system. It is possible to record, at specific regions of the brain, the activity from single neurons or the activity of large populations of neurons. [12] Besides monitoring the activity of the nervous system, another very interesting application of recording electrodes is the extraction of information about intentional brain processes, and then translating these signals into algorithms that are able to control artificial limbs. This approach, which is still in research, would be hopefully useful for amputees and paralyzed patients. [16]

1.2 Neural Implants: State of Art

It was back in the year of 1757 the first documented usage of electrical current to attempt the treatment of a neural disease. In the year of 1939, Hodgkin and Huxley demonstrated, for the first time, recordings of action potentials directly from nerve tissue. After that, in 1952, they found out how to analytically describe nerve stimulation and the subsequent generation of action potentials. [17]

Since then, neural electrodes became subject of huge interest for research and development, and a key tool to, on the one hand, stimulate specific brain regions and, on the other hand, to record the action potentials from neurons. In the fifties, single wire metal microelectrodes have been commonly used to record extracellular activity and, later in the seventies, Wise and Angell reported the first silicon-based microprobes to interface neural tissue. Thereafter, silicon has been abundantly used in the field of neural interfaces, leading to the development of miniaturized neural probes and probe arrays, and
to the establishment of Neural MEMS (Micro-Electro-Mechanical Systems) field. Surface and bulk micromachining techniques have brought an improvement in production of neural microinterfaces, with very well defined shanks and precise placement of recording sites at very low cost. Consequently, higher accuracy and repeatability of the probes were achieved. [12] [17]

1.2.1 Types of Neural Probes

Metal microelectrodes are fine wires typically made of tungsten, platinum, stainless steel or gold and have no more than 100 µm in diameter. These electrodes are completely insulated except for a small exposed area at the tip, the stimulation and recording site. These neural probes are still successfully employed for long-lasting single neurons recordings, and also in deep brain stimulation, thanks to their unique shape which allows them to access specific regions that are located deep into brain. [12] Unfortunately, these type of neural interfaces can only record at their exposed tip. This would require the increase of the number of recording sites and thus an increase on overall probe, leading to neural tissue damage. [17] [18]

In contrast to what happens with microelectrodes, silicon based implants can carry many recording sites without affecting the overall size of the probe, which make them a much more attractive option when compared to the metal ones. Thanks to photolithography (a microfabrication process widely employed to create desired patterns onto a material), and due to its mechanical advantages, the recording site size, texture, shape and spacing may be perfectly controlled enabling multiple recording. Several silicon-based microelectrode arrays have been studied. The most outstanding were Michigan and Utah electrodes.

The Michigan probes, developed in the Michigan University, have numerous advantages over microelectrodres, such as, higher reproducibility of geometrical and electrical characteristics, higher density recording sites while reducing the displaced tissue and the ability to integrate circuits directly on the probe. There were developed several layouts for Michigan electrodes, including single-shaft, multi-shaft (Figure 1.2 (c)) and 3-D arrays (Figure 1.2 (d)). These probes, in spite of being successful in several neuroscience applications, have some disadvantages related to thickness and durability. As Michigans
shanks are only 15 $\mu$m thick, they are fragile, being difficult to handle and leading to the probes to crack.

The Utah Electrode Array, developed in the Utah University, does not have thickness problems. Utah shanks diameter ranges from 100 $\mu$m at the base, to less than 1 $\mu$m at the tip. However, Utah has the particularity of having its arrays vertically oriented, as opposed to the others silicon-based, which are horizontal oriented. The problem is that, due to this fact, the probe length is limited by the silicone wafer thickness, which 1.5 mm is the longest reported length. Another disadvantage stands on the fact that as arrays are glued to the skull and as each probe shaft has just one recording site, the depth of the electrode site related to the skull is fixed. If, after surgery, cortical surfaces move, the electrodes may also move, leading to the failure of the recording. This situation also happens with microelectrodes, so it was accepted that Michigan probes offer better access to neurons. [17] [18]

In the recent times, polymeric probes have received great attention due to their flexibility, biocompatibility and simple fabrication process. Different polymeric materials such as
Polyimide (Figure 1.3) and Parylene-C, have been used to cover the metal and silicon region of the probes in order to improve interface’s biocompatibility.

Although this new technology is an advantage because improves the malleability match between a rigid electrode and a soft tissue, it is also a disadvantage, since electrodes are not stiff enough to pierce brain tissue on their own, resulting in tissue damage if the electrode moves relative to the brain. Furthermore, this type of probes have the tendency to failure since the polymer may absorb possible moisture from the surroundings. Given this, neural implants based of silicon continue to be the more successful option, taking into account silicon mechanical properties and patterning flexibility brought by microfabrication techniques. [17]

![Flexible Polymeric Neural Probes](image)

**Figure 1.3:** Flexible Polymeric Neural Probes: electrode arrays in two (above) and three dimensions (below). The cable is made of Polyimide and is $10 \ \mu\text{m}$ thick. [23]

### 1.3 Biocompatibility

The greatest setback in the usage of neural implants is the inevitable tissue response. As a normal physiological response, any surgical intervention is accompanied by an inflammatory response. When an implant enters the body, that response tends to be increased: the organism recognizes it as a foreign body and rapidly activates its defenses against it. The type of the encapsulation tissue and the cellular participants in immune reaction, depend on the site of implantation and the nature of tissue that hosts the implants. Sometimes, this encapsulation might be useful regarding to implant’s spatial fixation. However, since one is dealing with implants that record neural signals and stimulate neural cells, this encapsulation leads to a decrease of recording’s signal-to-noise ratio and an increase of current threshold for neuron stimulation. [12] [8]
A good performance, with an appropriate host response, towards a specific application, means the material is biocompatible (Williams, 1987). With regard to neural implants, it is expected they do not harm their host response in any way, being as inert as possible, performing their intended function within the organism without suffering of any allergic, carcinogenic, irritating or toxic action. Neural electrodes must be optimized to have, for long-term, stable impedance, no corrosion and no degradation or delamination of the insulation layers. The maintenance of the implant’s viability, for long periods of time, at the desired site, would also avoid frequent painful invasive surgeries to its exchange. [6] [24] [8]

Although the key for implant’s acceptability by the organism is at its surface, one should refer that physical properties such as size, shape and stiffness are also important parameters related to the success of the implantation. The electrodes must have a similar size to neurons, and be positioned deep within the nervous system in order to optimize the neuronal recording and stimulation, since electrode efficacy decreases rapidly with distance. [7] [4]

1.3.1 Immune Brain Response

Although in short-term (acute) applications the performance of microelectrodes arrays is acceptable, chronic performance remains inconsistent and unstable. In order to optimize the implantable electrodes, and to minimize the undesirable immune response of the Central Nervous System (CNS), it is important to understand the physiological mechanisms involved. [15]

As already stated, neural networks are responsible for the control of body functions and information processing. Still, neurons constitute only 25% of the cells in the brain, with glial and vascular-related tissue consisting the remaining tissue. Glial cells are divided in oligodendrocytes, which are the CNS myelin forming cells, and astrocytes and microglia which are the main effectors of the brain’s response to injury. [16] In opposition to what happens in the Peripheral Nervous System, where injured axons can regrow through a Schwann cell scaffold, it is believed this cells manufacture products that may be inhibitory to axon regeneration and replacement. [12]
The implantation of any object into the brain starts with the damage of the cortical tissue, and results in a gradual scar formation. During the moment of insertion, multiple structures are damaged, including neurons that are ripped or sliced, and blood vessels and nerves that are disrupted. [15] [25] This is where the Acute Response begins, an early reactive response, which rounds from one to three weeks, and it is characterized by the activation of microglia and its migration to the site of injury (Figure 1.4 - A). The number of reactive astrocytes and microglia increases around the insertion site, so that this area may extend up to a few hundred microns. The influence of the acute’s response in the following events is still unclear, but it is believed that this response is proportional to the cross section of the implant. [6] [15] [16]

The other component of the neural tissue response to implant is Chronic Response, a prolonged reactive response characterized by the encapsulation of the implanted electrode (Figure 1.4 - B), where the main component of this encapsulation is astrocytes. Astrocytes normally perform vital functions in the CNS, such as releasing neurotransmitters and forming the blood-brain barrier, but when reactivated they secrete proteoglycans and form a barrier around the implant. Astrocytes sheath grows in size for several weeks, becoming thinner and denser and eventually stabilizing after six to eight weeks. [25]

As it can be seen in Figure 1.5, by week four a great concentration of astrocytes stands near the implant, up to 500 µm around the insertion site. By week six, the glial scar is already completed, with the formation of a more dense sheath around the implanted probe. This effect varies with the biocompatibility of the materials used in the implant manufacturing and the properties of the coating. [15] [16] In addition to the glial scar,
it is observed that the number of neurons close to the probe decreased, suggesting neurons death or migration. This local neurodegeneration may lead to, on the one hand, the increase of electrode impedance, and on the other hand, a possible worsening of neurodegenerative disease. [25]

Definitively, there is an obvious need to improve the characteristics of neural implants to avoid such a violent response from the brain tissue. The strategy used for this purpose, in this project, will be discussed below.

1.4 Surface Modification

The undesirable inflammatory response of the CNS is unforgiving. Glial scar density increases with time, the electrodes become isolated from neurons and, as brain experiences micro-motion in response to those physiological processes, there is also motion of the electrodes, resulting in the damage of neural tissue. [17] A biocompatible neural implant must have better specific cell interactions and low protein adsorption. It should also promote tissue integration, in order to minimize encapsulation and long-term performance of the neural probe. [15]

Several approaches around the optimization of neural implant’s biocompatibility have been devised. Such strategies include the optimization of the probe design or the improvement of the neuron-implant interface. Conversely, many studies proved that the size of the implant might at first minimize acute response, but long-term response turns
out to be similar regardless to the implants design. While appropriate mechanical properties and functionality of the device are primarily derived from the bulk of the material in use, physiological responses to materials are affected by their surface properties. Such properties will determine the performance of cell adhesion to the implant. [10] The problem is, sometimes, one has the desirable bulk properties for a given application, but not the compatible interface.

Some of the approaches for interface’s improvement that are currently in research include enhancing electrode surface by the application of more biocompatible materials and coatings; these electrode coatings might have antibacterial agents incorporated or microfluidic channels that deliver drugs into the insertion site. Some investigations used as drugs proteins that encourage neural growth, like Dexamethasone and Cyclosporine A. However, it is complicated to incorporate these channels without increasing the size of the electrode tip. Other studies include the creation of nano scale surface features by etching the electrodes surface to increase neuronal cell adhesion, or application of conductive polymers to silicon-based probes to decrease site impedance. Many of these methods are promising, but none have emerged as a definitive solution to the problem of reactive tissue response. [17] [27] [28] [29]

In this project, the strategy adopted in order to reduce immune response was electrode surface modification with more biocompatible materials, from which desirable surface properties would be achieved, without affecting the bulk properties of the material. [15]

Within the various existing techniques for surface modification, the one explored in this project was Radio Frequency Magnetron Sputtering, a type of Physical Vapor Deposition, where it was obtained silicon dioxide thin film coatings doped with silver, gold and copper, separately.

As the scope of this work does not focus in surface modification per se, the samples to be characterized in this thesis have been previously modified. However, it is considered important to understand the influence of the modification technique in use on the surface properties of the final samples. Throughout the next sections it will be explained how does work such deposition technique, its advantages and disadvantages and also discussed the purpose of the materials used during this investigation.
1.4.1 Deposited Materials

As mentioned before, the approaches in the improvement of tissue-implant interfaces include electrode surface modification, which is the one adopted in this work. In Section 1.2.1 it was referred that silicon-based neural probes were the more promising among the other materials-based electrodes. However, they are still facing biocompatibility problems that jeopardize their long-term viability.

In order to maintain their internal functionality and mechanical properties, what it is proposed in this thesis is the coating of silicon electrodes with thin films of silicon dioxide (also known as silica, SiO$_2$) doped with silver (Ag), copper (Cu) and gold (Au) [scheme in Figure 1.6]. Silicon dioxide, a ceramic and bio-active material with mechanical stability, biocompatibility and inertness, would serve as the electrical insulator; and Silver and Copper, in their oxidized form, would act as antibacterial agents. Gold, besides inducing silver and copper oxidation, would allow the detection of the implant at imaging examinations. The utilization of both copper and silver materials comes from the fact that copper has higher reducing power than silver, allowing an easier oxidization of the copper and maybe a more quicker antibacterial action. Currently, silicon dioxide films have been widely used in microelectronics and MEMS as structural and sacrificial layers. [30]

![Design of the surface modification of the electrode with the coating made of the proposed materials: SiO$_2$, Au, Ag/Cu.](image)

**Figure 1.6:** Design of the surface modification of the electrode with the coating made of the proposed materials: SiO$_2$, Au, Ag/Cu.

- Antibacterial activity

Silver is a metal known for its broad-spectrum antimicrobial activity against bacteria, fungi and certain viruses. The growing interest in materials containing silver is due
to the fact that, besides being long-lasting biocidal materials with high temperature stability and low volatility, there is a large increase in the number of antibiotic-resistant bacterial strains.

The antibacterial properties of silver, which have been known for centuries, are nowadays used in the treatment of burned areas, for water treatment and to prevent bacterial colonization in medical devices and in textile fabrics. [31]

The antibacterial activity of silver is mainly due to its chemical nature. Electron donor groups containing nitrogen, oxygen and sulfur, that are present in proteins, enzymes and cell-membranes, are capable of attracting silver cations, Ag\(^+\) (see Figure 1.7). As a heavy metal, silver is known to react readily with compounds that contain sulfur. This binding results in conformational change and disruption of the function of bacterial cell membranes and crucial metabolic proteins and enzymes, leading to cell death. It was demonstrated that this antibacterial properties are effective against a broad spectrum of pathogens, and generally accepted that Ag\(^+\) antibacterial properties are such that bacteria will not develop resistance. [32] [33]

![Figure 1.7: Oxidized silver, Ag\(^+\), interacting with enzymes and other proteins in bacterial membrane, causing cellular distortion and loss of viability. In this figure, it might be also seen that Ag\(^+\) may inhibit bacterial replication, by binding bacterial DNA and RNA. [34]](image)

Researchers deposited several silver films by different deposition processes, and after immersing them in simulated physiological fluid, only the Physical Vapor Deposition (PVD) originated films showed silver oxides that exhibited inhibition of bacterial growth. Ag\(_2\)O would dissolve from silver material, resulting in the formation of silver ions that became antimicrobially active. [31] [35] Sometimes, silver coatings fail to demonstrate decreased bacterial adhesion. The reason for this to happen is that the antibacterial
properties of silver have been attributed to its oxidized form and silver coatings do not actively release silver ions. This form of silver does not need to be present at the surface coated with metallic silver.

Antibacterial performance enhancement is currently associated with an increased $\text{Ag}^+$ concentration. However, the usage of silver in medical implants must be taken with caution, because it has been shown that toxicity is often related to high levels of silver cations. [31] In order to increase the levels of $\text{Ag}^+$ delivered from metallic silver surface coatings, Dowling et al. decided to incorporate platinum into the coatings. Platinum is more cathodic than silver in the galvanic series, so when the two metals are electrically coupled, silver oxidation is enhanced through galvanic action. Platinum doped silver coatings resulted in $\text{Ag}^+$ increase and in enhanced antibacterial efficacy, without altering the coatings toxicity. [36] It was demonstrated by Saravanapavan et al. that the minimum bactericidal concentration of silver was 0.1 ppm and that the cytotoxic concentration was 1.6 ppm for human cells. Nevertheless, it is still unclear whether these levels were total values or rates in days, hours, etc. [31]

Copper is now also recognized as one of the best antibacterial agents. Besides the fact living organisms require copper, at low concentrations, as cofactors for metalloproteins and enzymes, it has been proved that $\text{Cu}^{2+}$ induces an inhibition growth in bacteria. It is then speculated that this effect might involve substitution of essential ions and the blocking of functional groups of proteins and inactivation of enzymes, which lead to alterations of membrane integrity, in a similar mechanism of action as the one for silver. [37] [38]

### 1.4.2 Depositing Techniques

A wide range of processes are used to deposit metal, ceramic and organic coatings or combinations of these materials (composite coatings). Each has their own distinct processing parameters, such as pressure, time, temperature, its own advantages and limitations.

Among the numerous depositing techniques, Chemical Vapor Deposition (CVD) and Physical Vapor Deposition (PVD) are those that have suffered a major technological and scientific development. The PVD technique is based on formatting vapor of the
material to be deposited as a thin film. The material in solid forms is either heated until evaporation (Thermal Evaporation) or sputtered by ions (Sputtering). The CVD technique is a deposition process where chemical precursors are transported in the vapor phase to decompose on a heated substrate to form a film. The high deposition temperatures for many CVD processes (often exceeding 600 °C), the toxicity or the expensive cost of some precursors utilized to reduce such temperatures, make PVD more attractive for some applications. There are still a large number of parameters that must be optimized to produce good films through CVD processes. [39] [40]

One significant advantage of Sputtering is that it gives a better composition control for multi-component thin films, where the deposited films have the same composition as the source material. As the sputter efficiency depends on the atomic weight of the atoms in the target, this may sound surprising. It might be expected that one component of an alloy or mixture would sputter faster than other components, resulting in an enrichment of that component in the deposit. Since only surface atoms can be sputtered, the faster ejection of one element will leave the surface enriched with the others, which will counteract the difference in sputter rates. This is an advantage over Thermal Evaporation, where deposited films have different composition from the source, because one of the component’s source may have higher vapor pressure. Additionally, in Sputtering technique the lateral thickness uniformity is better, due to the superposition of multiple point sources. [41]

1.4.3 Sputtering Technique

Sputter deposition is a method for depositing thin films, having as benefits the deposition of alloys and insulators as composite materials. Over high electric field and low pressure, material is ejected from a target and deposited on a substrate.

In spite of existing various sputtering techniques, like DC (Direct Current) sputtering, RF (Radio Frequency) and pulse magnetron sputtering, reactive sputtering, etc., the fundamentals of each process are the same.

Sputtering process takes place in a vacuum chamber, where the substrate and the target, serving as electrodes, face each other. Substrates are pumped into the chamber, maintained under high vacuum. An inert gas, which is typically argon, is placed in the
chamber at very low pressure. Sputtering starts when an electric field of several keV is applied between cathode and anode (target and substrate) causing a plasma to be maintained between the electrodes. Plasma region induces the accelerating of free electrons and the creation of positive charged gas ions that are attracted to the negatively biased target plate at a very high speed. This collision creates a momentum transfer and ejects atomic size particles from the target which are then deposited into the substrate’s surface. [42] [43]

Researches demonstrated that biomaterials surface modification, induced by sputtering, may promote desirable reactions and prevent undesirable effects. Such modification may result in a better attachment of the surrounding tissue to the biomaterial surface, changes in healing process and minimized foreign body response. [44]

a) Physics of Sputtering

The only way the target atoms get sputtered is if there is enough energy transferred in order to overcome the forces binding them. The threshold energy $E_{th}$, i.e., the minimum energy needed to unbind them, depends on the nature of the incident ion and on the atomic and mass number of the target atoms. The typical value of this energy is between 5 eV and 40 eV. Not less important is the energy that binds the atoms, $U_s$, and that should be taken into account. This energy is typically assumed to be the heat of sublimation, ranging from 2 eV and 5 eV. Sputtering is usually characterized by the sputter yield $S$ (sputtering efficiency), defined as the number of atoms removed from the surface of a solid per incident ion and is given by

$$S = \frac{\text{Number of Sputtered Atoms}}{\text{Incident Particles}}. \quad (1.1)$$

The sputter yield is influenced by several factors, such as RF power, gas pressure, target material and target structure and topography. [43] [45]

Observing Figure 1.8 one may rapidly conclude the dependence of the target material on the sputtering yield. As different materials have different binding, the greater the binding energy of a target’s material, the lower will be its sputtering rate and yield. Thus, in order to efficiently detach atoms from the target, more energetic ions are needed. That
is why sputtering yield is shown to increase with ionizing energy. As it was mentioned before, with incident ions that have smaller energy than the binding energy of the target material, atoms are not removed. [45]

In RF Sputtering it is used a RF power supply at high frequency (commonly 13.56 MHz) and a matching network. Increasing the RF power, there is also an increase of the ion bombardment energy and of the discharge current, resulting in an increased sputter rate. [45]
b) Magnetron

In conventional diode sputtering, some of the electrons created escape the effective ionized plasma area near the target. The wasted electrons fly around the chamber, creating undesirable side effects, such as radiation and subsequent heating the tooling.

Magnetron sputtering is an enhanced sputter method where a magnetron source addresses the electron problem by placing the magnets behind, and sometimes, at the sides of the target. These magnets capture the escaping electrons and confine them to the immediate vicinity of the target. This is achieved by applying a magnetic field perpendicular to the electric field of the target electrons. The crossed fields force the electrons to follow a closed drift path, as if they were trapped in a channel. The magnet behind the target increases the ionization efficiency significantly (a factor of ten over conventional diode systems) and effectively directs the sputtered atoms towards the substrate. Thus, faster deposition rates at lower pressures are achieved, which helps to produce cleaner films. Also, as the target temperature is lower with magnetron sputtering, the films are deposited with higher quality. [42] [48]

1.4.4 Film morphology controlled by Sputtering parameters

The tendency the cells have to adhere or not to the implant’s surface is crucial to its performance. As one will see in the next chapter, cellular response depends, among other surface characteristics, on the surface morphology and topography.

It has been proved that film morphology may be controlled by depositing parameters. Figure 1.10 shows the influence of the depositing pressure and the substrate temperature in the final film’s morphology. With low temperature and low ion energy (low RF power) or higher pressures, there will be less acceleration between collisions which will result in a poor surface mobility, leading to a porous and/amorphous surface (Zone 1).

On the other hand, higher surface mobility is achieved with higher temperature or ion energy, and then the surface will be smooth, small grain polycrystalline, dense, compact and with high reflectance (Zone T). Further increases in surface mobility will result in columnar grains with rough surfaces, leading to poor coverage in later steps (Zone 2). Continuing to further increase the surface mobility, will lead to large, non-columnar grains (Zone 3). As there are fewer grains in this state, and thus less grain
boundary diffusion, these grains can be useful for diffusion barriers. However, due to light scatter off of large grains there may exist problems for some applications, for example lithography. Furthermore, as these thin films tend to be more rigid, it can result in failures and cracking. Film thickness is also easily controlled by fixing the operating parameters and adjusting deposition time.

Concluding, parameters may be adapted in order to fulfill the surface characteristics of the material’s final application. [39] [50]

The innovation of this project stands in the possible combination of silver/copper with gold deposited on silicon dioxide coatings. It would be expected gold, like platinum does, to induce silver/copper’s oxidation and consecutively the release of $\text{Ag}^+ / \text{Cu}^{2+}$. As one knows, when any material is a candidate for implant application, material’s biocompatibility is of major importance. The material should be explored and studied without any coatings, in order to evaluate its biocompatibility and long-term functionality in the human organism. Also, the coating and the base material should be connected with a stable bond. Consequently, there will be several thin films to be analyzed. First of all, each of the four materials ($\text{SiO}_2$, Au, Ag and Cu) will constitute one thin film, so that the material may be characterized alone. After that, there will be three different systems composed by silicon dioxide and the respective metallic element: $\text{SiO}_2$/Au,
SiO$_2$/Ag and SiO$_2$/Cu. In each system there will be several samples, each one with different concentrations of the metallic element.

Each of the modified thin film will be characterized before and after being immersed in simulated biological fluid. The surface properties to be characterized are those that most directly influence the biocompatibility of neural implants.

In Chapter 2, it will be discussed the surface properties on which depends biocompatibility, and also explained the surface characterization techniques developed in the current work.
Chapter 2

Experimental Characterization Techniques

The concept of biocompatibility is not limited to bulk characteristics of the material in use. It is already understood that nervous tissue response to the implantation of a neural probe, as well as for all the implantable biomaterials, is closely connected to its surface properties. The only way to predict this response is to properly characterize them. The major material variables that might influence on the host response, and that were explored in the current work, are surface wettability, surface morphology/topography and surface chemistry. [10]

By understanding the surface characteristics given by each property and combining all of them, it will be possible to predict the improvement biocompatibility and the long-term performance of the implant, resulting in the success of the device and its industrial acceptability. In order to study such surface properties the several techniques presented in the Table 2.1 were used.

<table>
<thead>
<tr>
<th>Surface Property</th>
<th>Surface Characterization Technique</th>
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</thead>
<tbody>
<tr>
<td>Chemical Composition</td>
<td>Electron Probe Microanalysis (EPMA)</td>
</tr>
<tr>
<td>Wettability</td>
<td>Contact Angle</td>
</tr>
<tr>
<td>Morphology</td>
<td>Scanning Electron Microscopy (SEM)</td>
</tr>
<tr>
<td>Topography</td>
<td>Atomic Force Microscopy (AFM)</td>
</tr>
</tbody>
</table>

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During this chapter, it will be discussed the techniques of surface characterization presented in Table 2.1. These techniques were used for the characterization of the thin films produced by the sputtering technique, explained in the previous chapter. The same characterization was performed before and after the immersion of the films in simulated biological fluid.

2.1 Chemical Composition

The surfaces of the samples used in the present study were chemically modified via sputtering, by the deposition of materials that are expected to improve implant’s biocompatibility.

With regard to neural implants, in order to achieve long term stability and to minimize electrode impedance, it would be important to chemically resist to protein adsorption and also to enhance cortical neuronal attachment and differentiation. Besides, no corrosion is allowed, thus insulating materials must be stable and maintain their insulating properties, without degradation and the release of products that may be harmful to the host organism. [6] [51] In order to evaluate the chemical composition of the deposited films, they were submitted to the Electron Probe Microanalysis (EPMA).

2.1.1 Electron Probe Microanalysis

The electron probe microanalyzer is capable of yield both qualitative identification and quantitative compositional information from very small areas, with just some micrometers in diameter.

In this method, a beam of accelerated electrons is focused on the surface in analysis using a series of electromagnetic lenses. These electron-sample interactions induce the emission of characteristic X-rays of the several material compounds. Then, detectors receive the characteristic X-rays at their particular wavelengths, and the respective intensities are converted into concentrations. As any chemical element emits a specific set of X-rays (except H, He, and Li), they all can be detected. The structure of the EPMA system is represented in Figure 2.1, where it may be seen the electron beam producer and the X-rays detector.
This analytical method requires short time to be performed, and has high spatial resolution and sensitivity. EPMA analysis is also considered to be "non-destructive", where the X-rays created do not lead to volume loss of the sample. Thus, the same sample may be re-analyzed more than one time. A data acquisition and processing system is coupled to the electron beam producer and to the X-ray detector system. [53] [54]

In this study, a Cameca/Camebax SX50 with two wavelength dispersive spectrometers and six different crystals was used. The calibration and analysis of all elements was performed using a tension of 10 keV and a current of 40 mA.

2.2 Wettability

Surface wetting properties have a great effect on numerous physiological events at subcellular and cellular level, including protein adsorption, cell attachment and spreading.
The assessment of wettability properties was made with contact angle measurements through the sessile drop technique, with a Krüss GmbH G-23 goniometer. In this experiment, a droplet of a liquid is placed on the solid surface. The angle between the drop (liquid-vapor interface) and the substrate (solid) is determined. [9] [10]

![Picture of sessile drop technique](image1)

![Diagram of contact angle and wettability](image2)

**Figure 2.2:** a) A drop on a glass surface from the sessile drop technique [55], b) Relationship between the contact angle and wettability. [56]

Depending on the contact angle, one can determine the wetting character of a surface. Therefore, as it can be seen in Figure 2.2 (b), if the used liquid is water, high contact angle values do imply a less wettable surface, which can be considered as a hydrophobic surface. On the contrary, low contact angle values, refer to hydrophilic surfaces, which present a more wettable surface. Researchers have demonstrated that proteins tend to be adsorbed in hydrophobic surfaces when compared to hydrophilic surfaces. [57]

### 2.2.1 Surface Free Energy

Solid’s wettability is mainly influenced by the Surface Free Energy, and if this concept is quantitatively known, the wetting behavior of the surface can be predicted.

Liquid molecules are connected to each other by cohesive forces. Since molecules at the surface do not have other like molecules on all of their sides, they cohere more strongly to those directly associated with them, exhibiting stronger attractive forces on the surface. This phenomenon, named as Surface Tension, $\gamma_L$, is the reason for being more difficult to move an object through the liquid surface, than to move it when it is completely submerged. In solids, this analogous quantity is called Surface Free Energy (SFE), defined as the work required to increase the area of a substance by 1 cm$^2$. The higher the surface free energy per unit area, the greater the possibility of reactions between the
material’s surface the host tissue. If a liquid has a surface tension smaller than the SFE of a solid, then the liquid-solid interface will increase in order to minimize energy. High SFE values correspond to hydrophilic surfaces and, on the contrary, low SFE values correspond to hydrophobic surfaces. It should be clear that the SFE of a solid is not a measure of its reaction with any one liquid, but it is a solid-defined parameter, measured through its interactions with multiple liquids. [58]

Since SFE cannot be directly measured, its estimation was made through contact angle measurements. At the three-phase equilibrium (Figure 2.3), the interfacial tensions of the solid-vapor, liquid-vapor and solid-liquid interface, and the contact angle are related through Young’s Equation,

\[ \gamma_{LV} \cos \theta = \gamma_{SV} - \gamma_{SL}. \]  

![Figure 2.3: Representation of the surface free energies between the three phases in contact. Where \( \theta \) is the contact angle, \( \gamma_{LV} \) (or \( \gamma_L \)) is the liquid surface tension, \( \gamma_{SL} \) is the solid/liquid interfacial free energy and \( \gamma_{SV} \) (or \( \gamma_S \)) is the solid surface free energy. [59]]

However, while the quantities \( \gamma_{LV} \) and \( \theta \) can be easily measured, the quantity \( \gamma_{SL} \) remains unknown. Therefore, in order to determine the required \( \gamma_{SV} \) (SFE), a further relationship is necessary and many different approaches have been proposed. [9] [60]

Owens and Wendt’s model assume that dispersive and polar intermolecular forces operate across the interface and, therefore, the value of the total surface tension is the sum of two components,

\[ \gamma = \gamma^d + \gamma^p, \]  

being \( \gamma^d \) and \( \gamma^p \) the dispersive and polar components respectively. The solid interfacial tension can be given as

\[ \gamma_{SL} = \gamma_{SV} + \gamma_{LV} - 2\sqrt{\gamma_{SV} \gamma_{LV} \gamma^d} - 2\sqrt{\gamma_{SV} \gamma_{LV} \gamma^p}. \]
Combining the Equations 2.1 and 2.3 it is obtained

\[ \gamma_{LV}(\cos \theta + 1) = 2\sqrt{\gamma_{SV}^d\gamma_{LV}^d} + 2\sqrt{\gamma_{SV}^p\gamma_{LV}^p}. \] (2.4)

Finally, \( \gamma_{SV} \) and \( \gamma_{SL} \) can be determined from the equations above and from the values of static contact angles measured with testing liquids whose surface tension components are already known. The liquids used in the current study were water, glycerin and formamide, all belonging to the same homologous series by having non-null values for every surface tension components. The choice of liquids from the same series is important for a good contact angle comparison, where the difference between them is due to surface characteristics and not due to chemical interactions created from some difference between the liquids. The surface tension values of the liquids used in the experiment are exposed in Table 2.2. [9] [61]

<table>
<thead>
<tr>
<th>Liquid</th>
<th>( \gamma_{LV} ) (mJ.m(^{-2}))</th>
<th>( \gamma_{LV}^d ) (mJ.m(^{-2}))</th>
<th>( \gamma_{LV}^p ) (mJ.m(^{-2}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>72.8</td>
<td>29.1</td>
<td>43.7</td>
</tr>
<tr>
<td>Glycerin</td>
<td>63.4</td>
<td>37.4</td>
<td>26.0</td>
</tr>
<tr>
<td>Formamide</td>
<td>58.2</td>
<td>35.1</td>
<td>23.1</td>
</tr>
</tbody>
</table>

As the contact angle can vary with the volume of the deposited drop, measurements were made with drops with the same volume (10 \( \mu \)L), controlled by a micrometer screw, which is attached to the syringe plunger. [62] The reading of the values of the contact angle was made at least eight times for each sample/liquid system. The mean value was considered as the value of the contact angle for the respective testing liquid and the surface in study. The same proceeding was made for each liquid, in three different spots of the sample.

Due to studies related to the influence of surface free energy on bioadhesion, it is general accepted nowadays that cells spreading on implant’s surfaces is related to its polar and dispersion components. Additionally, it has been proved that when the value of the polar component if higher, there is also higher cell spreading around the surface. [63]
a) Critical Wetting Tension: Zisman Plot

The Zisman method is used to determine the critical wetting tension of a solid, $\gamma_c$. This tension differs from the quantity $\gamma_{SV}$ that appears in Equation 2.1. According to Zisman, the value of $\gamma_c$ of a solid equals the $\gamma_{LV}$ of a liquid when the contact angle between both is zero. This method is executed by the sessile drop technique, where the contact angle determinations are performed with at least three pure compounds on the surface and the cosines of the contact angles are plotted versus the superficial tensions. The extrapolation of the mathematical fitting of the experimental values to the point of $\cos \theta = 1$ yields the estimation of the critical wetting tension $\gamma_c$, equal to $\gamma_{LV}$ at this point. [60] [64]

![Figure 2.4: Determining the critical surface tension according to Zisman. [65]](image)

The value of $\gamma_c$ indicates that only the liquids with $\gamma_{LV} \leq \gamma_c$ are able to completely wet the surface, while liquids with $\gamma_{LV} > \gamma_c$ will partially wet the surface.

In the case of neural implants, it is desired that the material placed in the body integrates with the surrounding tissue with successful attachment of neural cells to the material. Thus, it is necessary a material with a high surface tension, on which the cells readily spread and wet, so that they can create an intimate intermolecular contact with the surface, leading to strong adhesion. [66]

b) Hysteresis

Surface free energy is also related to contact angle hysteresis. Hysteresis is defined as the difference between the advancing and receding contact angles (Figure 2.5). Although Young’s Law (Equation 2.1) gives one value of the contact angle, the one that is associated with a drop minimizing the total interfacial energy, hysteresis proves that there
exists a whole range of stable contact angles. Actually, since there are free energy barriers, it is impossible to find an equilibrium contact angle. Therefore, what is observable is that advancing and receding contact angle are rarely the same and this difference is induced by some heterogeneities at materials surface. Is then important to explore the contact angle hysteresis in order to fully characterize any surface. [67] In this work, the hysteresis of the contact angles was determined using water as the liquid.

![Advancing and receding contact angles](Picture from ramé-hart instrument co.)

It has been demonstrated that SFE may be a more important surface property than surface roughness for cellular adhesion strength and proliferation. Wettable characteristics of a surface may be modified by changing surface roughness or chemistry, by for example sputtering techniques. [10]

### 2.3 Surface Morphology/Topography

The topography and the roughness of a surface are important factors in determining the response of cells to an implanted material. As it was mentioned before, one can control surface morphology by varying deposition parameters.

Surface’s topography is related to wettability and interfacial energy. It has been proved that surface roughness can affect cell’s adhesion due to increased or decreased contact area, which is proportionate to interfacial adhesive force. Therefore, the contact area of the cell membrane with the implant’s surface may be influenced by roughness parameters. If it is intended a minimal cell adhesion, thus surfaces should be done as smooth as possible. However, if cell adhesion is favorable to the implantation, rough surfaces are the most advantageous. A surface with grooves might induce "contact guidance", affecting the cell movement direction. Besides, the numerous nanoscale features found
in the neural tissue, represented by the extracellular microtubules and proteins, are also implying that neurons are accustomed to interact with nanoscale featured surfaces. However, the electrodes used nowadays for chronic applications have been smooth at the nanoscale. [51] [68] [69] The morphology and topography characterization of the surfaces in study was made by Scanning Electron Microscopy and Atomic Force Microscopy, to be described below.

2.3.1 Scanning Electron Microscopy

Scanning Electron Microscopy (SEM) is a very powerful instrument that permits the observation and characterization of the materials surface. The basis of SEM is very similar to EPMA’s; a beam of electrons is focused on a small region of the sample, where energy is transferred, causing the deceleration of the incident electrons. These bombarding electrons, also known as primary electrons, interact with the sample by scattering and absorption within the specimen. The energy exchange between the electron beam and the sample results in ions’ displacement from the specimen itself. This electrons, referred as secondary electrons, are collected by specialized detectors, and finally translated into a signal. The SEM image is performed by the amplification of the signals produced when the electron beam sweeps across the sample’s region, i.e. amplification of the beam current absorbed by the specimen. The signals, after their amplification, are analyzed and translated into images. [70] [71] In this study, the coatings morphology were obtained by the use of a Philips XL30 SEM equipment, with accelerating voltage of 10 keV and magnifications of 5000 or 10000 times. The equipment does also possess an Energy Dispersive Spectrometer (EDS) detector, which allows a rapid and qualitative composition of a specific spot or area of the sample.

2.3.2 Atomic Force Microscopy

Surface’s topography was analyzed by Atomic Force Microscopy (AFM) in tapping mode. The surface study through this technique is made at the microscope level, allowing a very high accurate three-dimensional characterization resolution, ranging from 100 µm to less than 1 µm. [72] The microscope used was the Veeco di-Inova System (Figure 2.6), which is equipped with a large area scanner capable of 90×90 µm² coverage and sample size up to 45 mm in diameter. [73] All images were obtained at room temperature, from
coatings deposited on Si wafers. For each sample three scans were made corresponding to areas of $5.0 \times 5.0 \, \mu m^2$, $1.0 \times 1.0 \, \mu m^2$ and $0.3 \times 0.3 \, \mu m^2$.

The basis operation of AFM is illustrated in Figure 2.7. A sharp tip, usually some microns long and with less than 100 Å in diameter, is either in contact or in very close proximity to the surface sample to be imaged. In the present case this contact will be intermittent (tapping mode), inducing less surface damage of the samples. This tip is at the end of a cantilever, usually with a length of 100 $\mu m$ to 200 $\mu m$. During the scanning, different forces acting on the cantilever will be directly related to the displacements (deflections) of the cantilever. These deflections are measured by focusing a laser on the tip of the cantilever and calculating the changes in the reflected beam as the cantilever changes its position during the scan. These detections are recorded and processed using imaging software. [74] [72]

It is possible to collect amplitude, topography and phase images while working in tapping mode. Given in volts, the amplitude image is the raw data collected by the photodiode. This image leads to the creation of the topography image, which is the distance the tip traveled to return the amplitude to the set point. The topographic image may be two dimensional or in three-dimensions. On the other hand, phase images come from a secondary signal, in this case from the phase lag of the cantilever relative to the drive signal. This phase change in the oscillation may be related to energy dissipation. [75] It is complicated to understand the physical meaning of this signal. However, in addition to topographic information, relative softness/hardness of the sample may affect the phase. Other application for phase imaging is the detection of distribution of

Figure 2.6: On the left the Veeco di-Innova AFM System and on the right the imaging process NanoScope Analysis Software.
composition variation on the surface, even when topography does not change. Generally, in heterogeneous samples, it is easy to get a contrast in the phase, but interpreting such signal is more complicated. In this work, AFM image analysis was made by using the free data analysis software WSxM 4.0 Beta 4.1.

Compared with SEM, AFM provides a greater topographic contrast and resolution. However, both are complementary techniques that give a more complete representation of a surface when used together than if each were the only technique available.

a) Roughness Parameters

Roughness is a topographic concept often used in surface’s characterization. WSxM Software provides many roughness amplitude parameters, and those adopted in this work will be described in Table 2.3.
Table 2.3: Roughness amplitude parameters. [1]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roughness average, $R_a$</td>
<td>Average deviation of all points in the roughness profile from a line over the evaluation length.</td>
</tr>
<tr>
<td>Maximum height of the profile, $R_t$</td>
<td>Maximum peak-to-peak-valley height, i.e the absolute value between the highest and lowest peaks.</td>
</tr>
<tr>
<td>Average maximum height of the profile, $R_{tm}$</td>
<td>Difference between the highest peak and the lowest valley within multiple samples in the evaluation length.</td>
</tr>
</tbody>
</table>

2.4 In vitro tests

To predict the success of the inclusion of a new material in the organism, it is important to simulate the process of interaction between the physiological environment and the implant itself. As stated before, surface characteristics are the key to the acceptability of the material, however these characteristic might change as the material spend some time implanted in the organism, compromising its functionality.

In order to verify the behavior of the thin films in physiological environment, the samples were immersed in Simulated Body Fluid (SBF), a solution that, according to Kokubo et al. [2], simulates the human plasma inorganic form. This immersion will also allow the analysis of the release of $\text{Ag}^+/\text{Cu}^{2+}$, which will then act as antibacterial agents. The Table 2.4 contains the ion concentrations and the pH of both SBF and human blood plasma. In Table 2.5 are presented the regents used in the preparation of the SBF of the present work.

Table 2.4: Comparison of pH and ion concentration between SBF and human blood plasma. [2]

<table>
<thead>
<tr>
<th>Ion</th>
<th>Na$^+$</th>
<th>K$^+$</th>
<th>Mg$^{2+}$</th>
<th>Ca$^{2+}$</th>
<th>Cl$^-$</th>
<th>HCO$_3^-$</th>
<th>HPO$_4^{2-}$</th>
<th>SO$_4^{2-}$</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBF [mM]</td>
<td>142.0</td>
<td>5.0</td>
<td>1.5</td>
<td>2.5</td>
<td>147.8</td>
<td>4.2</td>
<td>1.0</td>
<td>0.5</td>
<td>7.25</td>
</tr>
<tr>
<td>Human Plasma [mM]</td>
<td>142.0</td>
<td>5.0</td>
<td>1.5</td>
<td>2.5</td>
<td>103.0</td>
<td>27.0</td>
<td>1.0</td>
<td>0.5</td>
<td>7.20-7.40</td>
</tr>
</tbody>
</table>

As the interest in the immersed samples was not based on studying the metallic elements release kinetics, the study was conducted in static conditions [see Figure 2.8]. The aim of the experiment was to understand what type of changes occurred on the surface of
Table 2.5: Simulated Body Fluid detailed composition. The salts were dissolved in Milli-Q water. [2]

<table>
<thead>
<tr>
<th>Compound</th>
<th>Concentration (mol/dm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl</td>
<td>1.5</td>
</tr>
<tr>
<td>NaHCO$_2$</td>
<td>1.8</td>
</tr>
<tr>
<td>KCl</td>
<td>2.0</td>
</tr>
<tr>
<td>CaCl$_2$·2H$_2$O</td>
<td>2.0</td>
</tr>
<tr>
<td>MgCl$_2$·6H$_2$O</td>
<td>1.3</td>
</tr>
<tr>
<td>Na$_2$SO$_4$</td>
<td>1.4</td>
</tr>
<tr>
<td>K$_2$HPO$_4$·3H$_2$O</td>
<td>1.5</td>
</tr>
</tbody>
</table>

each thin film after fixed time intervals, and realize the release of the elements by their static deposition and fixation on the surface.

The Si wafers in which the films were deposited, were submersed into the SBF over a maximum of fourteen days at room temperature. After day one, two, four, seven and fourteen each sample was removed from the fluid and carefully washed with Milli-Q water, in order to avoid the formation of any precipitate or salts derived from fluid. The samples were then observed by SEM and AFM. Also, qualitative chemical composition of some interesting features of the surfaces was achieved by EDS.

Figure 2.8: Some of the samples immersed in approximately 10 mL of SBF. In the picture one can also see that one of the samples was already collected, washed and stored after day 1.
Chapter 3

Analysis and Discussion of Results

This chapter presents the analysis and discussion of results from the experimental surface characterization techniques mentioned in Chapter 2. This includes not only the elementary characterization of the coatings, but also the study of their behavior towards an environment similar to the organism. Hopefully, the analysis may determine the selection of the thin films that have the best performance and, maybe, the most biocompatible properties, meeting then the objective that motivated this work.

The monolithic thin films (SiO$_2$, Au, Cu and Ag) were deposited by sputtering from pure targets. The systems SiO$_2$/Au and SiO$_2$/Cu, were sputtered with two targets, varying the metallic target deposition powder, in order to achieve different contents of the metallic element in each thin film. Finally, in the sputtering deposition of the system SiO$_2$/Ag, the SiO$_2$ target was doped with Ag foils (10×10 mm$^2$), varying the number of metallic foils.

The first characterization, immediately after sputtering deposition, was made by EPMA in order to access the elemental composition. Afterward, wettability tests were performed by contact angle measurements through the sessile drop technique, and the hysteresis of the contact angle determined by the dynamic method. The topographic characteristics of the thin film’s surface were evaluated by AFM. The samples were, then, immersed in SBF over a period of two weeks. After those fourteen days, the samples were characterized again by AFM. SEM images from days 1, 2, 4, 7 and 14 were also
obtained in order to study the morphologic evolution of the surfaces. Therefore, it was possible to verify the influence of the biological environment at the implant’s surface and also to evaluate the release of silver and copper ions.

### 3.1 Surface Chemical Composition

The elemental composition of thin films was determined, as already mentioned, by EPMA. The designation and composition of the films is shown in Table 3.1.

<table>
<thead>
<tr>
<th>System</th>
<th>Film Designation</th>
<th>at. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monolithic Films</td>
<td>SiO₂</td>
<td>100% SiO₂</td>
</tr>
<tr>
<td></td>
<td>Au</td>
<td>100% Au</td>
</tr>
<tr>
<td></td>
<td>Cu</td>
<td>100% Cu</td>
</tr>
<tr>
<td></td>
<td>Ag</td>
<td>100% Ag</td>
</tr>
<tr>
<td>SiO₂/Ag</td>
<td>Si₆Ag₀.₃</td>
<td>0.3% Ag</td>
</tr>
<tr>
<td></td>
<td>Si₆Ag₂</td>
<td>2.7% Ag</td>
</tr>
<tr>
<td></td>
<td>Si₆Ag₂₄</td>
<td>24.3% Ag</td>
</tr>
<tr>
<td></td>
<td>Si₆Ag₃₁</td>
<td>30.9% Ag</td>
</tr>
<tr>
<td>SiO₂/Au</td>
<td>Si₉Au₁</td>
<td>0.9% Au</td>
</tr>
<tr>
<td></td>
<td>Si₆Au₆</td>
<td>5.9% Au</td>
</tr>
<tr>
<td></td>
<td>Si₆Au₁₁</td>
<td>10.8% Au</td>
</tr>
<tr>
<td>SiO₂/Cu</td>
<td>Si₅Cu₅</td>
<td>5.5% Cu</td>
</tr>
<tr>
<td></td>
<td>Si₆Cu₆</td>
<td>6.0% Cu</td>
</tr>
<tr>
<td></td>
<td>Si₆Cu₁₁</td>
<td>10.5% Cu</td>
</tr>
</tbody>
</table>

The concentrations of the doping elements were controlled by the variation of sputtering’s powder deposition. In the specific case of silver, the number of metal foils was varied. As expected, for the SiO₂/Au and SiO₂/Cu systems the metallic element content increased with the increase of the deposition powder. For the SiO₂/Ag system, the increase in the number of foils corresponded to an increase in silver’s concentration, although no linear relation was observed.
3.2 Surface Wettability

The term "wettability" refers to how a fluid interacts with a solid surface, analyzing how easily it spreads on the surface. This characteristic is often determined by measuring the contact angle of the material. Therefore, the mean values of the contact angles measured on the thin film’s surfaces in study are found in Table 3.2.

<table>
<thead>
<tr>
<th>Table 3.2: Mean Values of the Contact Angles.</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIQUID</td>
</tr>
<tr>
<td>Water</td>
</tr>
<tr>
<td>Glyc.</td>
</tr>
<tr>
<td>Form.</td>
</tr>
</tbody>
</table>

In order to compare the wetting character of the surfaces in study, the mean values of the water contact angles obtained for each sample were plotted on the histogram in Figure 3.1.

For the monolithic thin films, it is shown in Figure 3.1 that Ag and SiO$_2$ films are those with the lowest contact angle mean values, which indicate that those are also the most

![Figure 3.1: Histogram showing the variation of the water contact angles for each surface. In each system, the thin films are in ascendent order of at % of the metallic element.](image-url)
hydrophilic monolithic surfaces. Regarding the Au coating, with higher mean value of contact angle than the other two films, can be considered as slightly hydrophilic, having $\theta = 73.7^\circ$. The thin film of Cu, on the contrary had $\theta = 92.9^\circ$, being a hydrophobic surface.

Considering the three ceramic/metallic systems, it may be observed that the deposition of the metallic element has induced a global increase in the contact angles values when compared to SiO$_2$ film alone. However, there does not seem to exist any relationship between the increase of the atomic percentage of the metallic element and the value of the contact angle. This can be due to the fact that the contact angle measurements are restricted to the 10-20 nm of the surface, while the chemical composition incorporates the information of almost all the thickness of the thin films. As a consequence, the distribution of the metallic element on the surface of the thin film can differ from its content, determined by EPMA. Between the three systems, Ag/SiO$_2$ is the one showing the greatest wetting properties, having the highest hydrophilic character, followed by Cu/SiO$_2$ and Au/SiO$_2$, which presents hydrophobic character.

The variability of the static contact angle values is mainly related to specific kinds of atoms and surface terminations present at the liquid-solid-vapor interfaces.

The atomic structure inside silicon dioxide is considered to be a network of SiO$_4$ tetrahedra linked together. However, at the surface, this network abruptly ends, and, due to oxygen deficits, Si pendant bonds are left at the surface. Additionally, there are also some superficial tetrahedral units, that present high energy Si-O-Si bonds, thus making them unstable. This results in an increased tendency to chemically adsorb water molecules, leading to the formation of silanol groups (Si-OH) at the surface. The presence of hydrophilic silanol groups at the surface will provide silicon dioxide good wetting properties, as it was verified in the histogram in Figure 3.1. [78] [79]

As the metallic element is sputtered into the SiO$_2$ surface, the number of pendant bonds will be decreased. With the decrease of Si pendant bonds at the surface, the probability of the formation of the silanol groups becomes reduced, which results in the prevalence of hydrophobic siloxane groups (Si-O-Si) at the surface. [80] [81] This is why in each system it is noticed an increase in the value of the contact angle for the thin films with initial levels of the metallic element (SiAg$_{0.3}$ for silver, SiAu$_1$ for gold and SiCu$_5$ for copper) when compared with SiO$_2$ alone.
There is, however, one exception for the 2.7% Ag thin film (SiAg$_3$) which shows a decrease in the contact angle when compared to the thin film of SiO$_2$ alone. This fact was probably due to an increased number of pendant bonds at the silicon dioxide’s surface which would react with the H$_2$O molecules present at humidity, leading to the formation of the silanol and other functional groups. [82]

As for the differences in the wetting character between the three different systems, those may be related to the bond nature between the oxygens in the SiO$_2$ structure and the atoms of the doping elements. Among the three systems, Ag/SiO$_2$ demonstrated the lowest contact angle values. Therefore, between the doping elements, Ag atoms seemed to have the weakest bonds with oxygen atoms. [82] [83] Data in [84] shows bond strengths between Ag-O lower than Cu-O and Au-O, which would support these results.

The surfaces with higher levels of the metallic element, those are also the thin films submitted to the highest pressures during the sputtering process, caused by the increase of chemical particles in the plasma as a consequence of the increased deposition powder. Different chemical species from the plasma might have induced the contamination of the surface with the deposition of different hydrophobic functional groups, such as hydrocarbons (-C$_m$H$_{2m+1}$). [85]

Surface roughness also plays an important role in the wettability of a surface. In fact, according to Wenzel’s Law, roughness on a surface will decrease the contact angle for a droplet on a hydrophilic surface, and increase the contact angle on a hydrophobic surface. [86] The influence of this factor will be considered later.

### 3.2.1 Surface Free Energy (SFE)

When two condensed phases are in contact, interactions based on chemical and physical forces immediately occur between them. When these phases are, respectively, the surface of a solid and a liquid, the interactions can be described in terms of surface free energy. As already mentioned, one method to calculate the polar and dispersive components of such energy is by measuring the contact angles between the solid and liquids of well-known characteristics. Young’s Equation can be used to calculate this quantity (Equation 2.1). The equation describes the thermodynamic balance of surface
free energies that exist within the boundary of a drop of liquid on a solid surface. However, as it consists of variables that are not experimentally accessible, it was derived in Chapter 3 an equation (Equation 2.4) for the specific case of a drop of liquid on a solid surface, referring to the measured values of the contact angles, as well as to the values of surface tensions of the liquids used during the activity.

The SFE values of the thin films, as well as their polar and dispersive components, are presented in Table 3.4 and also as an histogram in Figure 3.2.

Table 3.3: Surface free energy values for the thin film coatings, and their respective polar and dispersive components.

<table>
<thead>
<tr>
<th>Thin film</th>
<th>$\gamma_S^d$ (mJ.m$^{-2}$)</th>
<th>$\gamma_S^p$ (mJ.m$^{-2}$)</th>
<th>$\gamma_S$ (mJ.m$^{-2}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SiO$_2$</td>
<td>23.9</td>
<td>81.4</td>
<td>105.3</td>
</tr>
<tr>
<td>Ag</td>
<td>16.8</td>
<td>95.6</td>
<td>112.4</td>
</tr>
<tr>
<td>Au</td>
<td>8.0</td>
<td>101.4</td>
<td>109.4</td>
</tr>
<tr>
<td>Cu</td>
<td>33.6</td>
<td>9.9</td>
<td>43.5</td>
</tr>
<tr>
<td>SiAg$_{0.3}$</td>
<td>18.5</td>
<td>38.6</td>
<td>57.1</td>
</tr>
<tr>
<td>SiAg$_3$</td>
<td>30.3</td>
<td>86.6</td>
<td>116.9</td>
</tr>
<tr>
<td>SiAg$_{24}$</td>
<td>34.7</td>
<td>58.3</td>
<td>93.0</td>
</tr>
<tr>
<td>SiAg$_{31}$</td>
<td>23.5</td>
<td>44.6</td>
<td>68.1</td>
</tr>
<tr>
<td>SiAu$_1$</td>
<td>26.3</td>
<td>10.1</td>
<td>36.4</td>
</tr>
<tr>
<td>SiAu$_6$</td>
<td>21.5</td>
<td>20.3</td>
<td>41.8</td>
</tr>
<tr>
<td>SiAu$_{11}$</td>
<td>30.4</td>
<td>11.4</td>
<td>41.8</td>
</tr>
<tr>
<td>SiCu$_5$</td>
<td>46.9</td>
<td>10.8</td>
<td>57.6</td>
</tr>
<tr>
<td>SiCu$_6$</td>
<td>29.7</td>
<td>13.6</td>
<td>43.3</td>
</tr>
<tr>
<td>SiCu$_{11}$</td>
<td>38.5</td>
<td>22.8</td>
<td>61.3</td>
</tr>
</tbody>
</table>

From the observation of the histogram in Figure 3.2 is clear that the surfaces previously mentioned as the most hydrophilic ones, are now those with the highest values of surface free energy, $\gamma_S$. One of the reasons for this to happen is that, as such surfaces have higher $\gamma_S$ than water’s $\gamma_L$ (72.8 mJ.m$^{-2}$), water has to spread around the surface to minimize energy, resulting in low contact angle values.

The monolithic thin films of SiO$_2$, Au and Ag presented very high values for surface free energy, with the three having $\gamma_S > 100$ mJ.m$^{-2}$. On the opposite, 100% Cu film showed the lowest value of surface free energy among the four pure thin films, with a $\gamma_S$ of 43.6 mJ.m$^{-2}$.
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Figure 3.2: Histogram representing the SFE and respective dispersive and polar components of all the surfaces. In each system, the thin films are in ascendent order of atm % of the metallic element.

Considering the three silicon dioxide systems, Ag/SiO$_2$ was the system with the highest values of surface free energy, followed by Cu/SiO$_2$ and finally Au/SiO$_2$ system. From the histogram it is observed that these last two systems were also composed by the surfaces with highest dispersive component, when compared to the polar component. Therefore, while hydrophobic surfaces had as highest values their surface tension dispersive component, hydrophilic surfaces had their surface tension polar component with the largest values, as expected.

The deposition of the metallic elements into the SiO$_2$ thin film led to the general decrease of the surface free energy value. These results have confirmed both the decrease of silicon and oxygen pendant bonds and the no formation hydrophilic silanol groups at the film’s surface, which would had increased SFE. Once again, with the exception for SiAg$_3$ (2.7% Ag), which is the thin film with the highest SFE value (109.4 mJ.m$^{-2}$).

Surface free energy of implant’s surface has a great influence on their acceptability in the human body. Hydrophobic surfaces and thus with low SFE values promote the ability of proteins to attach the implant. Protein adsorption to the implant’s surface will induce the activation of glial cells, leading to the formation of scar tissue around the implant’s site. These reactions will decrease the long-term functionality of the neural implant.
Furthermore, the lower the polar component of the surfaces, the less tendency neurons have to adhere and spread around those surfaces. Copper’s thin films, having such lower values of surface free energy and of its polar component, might bring some concerns about its biocompatibility.

### 3.2.2 Critical Wetting Tension

An approach to determine the critical wetting tension of a solid is based on Zisman Plot, which, as explained in Section 2.2.1 a), measures the variation of the contact angle as a function of the surface tension of a well-known series of liquids. The tension value for which \( \cos(\theta) = 1 \) is the critical wetting tension, \( \gamma_c \). This value is conceptually related to the specific SFE of the material, being thus a measure of the surface’s wettability. Therefore, if a liquid has a surface tension equal to or less than the critical surface tension of a material, such liquid will be capable of completely wet and spread on that surface. [87] In Figure 3.3 are represented the Zisman plots for the several surfaces in study.

The first plot (Fig. 3.3 (a)) was made in order to compare the critical surface energy of the four monolithic thin films. Sorting in ascending order, the results were:

\[
\gamma_c(\text{SiO}_2) < \gamma_c(\text{Cu}) < \gamma_c(\text{Ag}) < \gamma_c(\text{Au}).
\]

Therefore, these results indicate that 100% Au is the thin film with the better surface wetting, since it was the surface that had the closest \( \gamma_c \) to the \( \gamma_L \) of the water (72.8 mJ.m\(^{-2}\)). In fact, this affinity with water is not surprising. From the histogram in Figure 3.2 it is possible to observe that Au is the surface with the largest value of polar component.

The remaining plots represent the Zisman plots of the three systems SiO\(_2\)/Ag (Fig. 3.3 (b)), SiO\(_2\)/Cu (Fig. 3.3 (c)), SiO\(_2\)/Au (Fig. 3.3 (d)). The results indicate that in neither of the systems seems to be a dependence between the increase of the critical wetting tension and the atomic percentage of the metallic elements. This might be, once more, related to the fact that the chemical composition found by EPMA was referent to all the thickness of the thin films, while the contact angle measurements are restricted to the surface of the films, which results in a different distribution of the metallic elements in both cases. The ascending sequences of the \( \gamma_c \) values are:
Figure 3.3: Representation of the Zisman plots of all the surfaces and determination of the respective $\gamma_c$. (a) Monolithic thin films, (b) Ag/SiO$_2$ system, (c) Cu/SiO$_2$ system and (d) Au/SiO$_2$ system.

**Ag:** $\gamma_c$(SiAg$_{31}$) < $\gamma_c$(SiAg$_{03}$) < $\gamma_c$(SiAg$_{24}$) < $\gamma_c$(SiAg$_3$)

**Cu:** $\gamma_c$(SiCu$_{66}$) < $\gamma_c$(SiCu$_{55}$) < $\gamma_c$(SiCu$_{11}$)

**Au:** $\gamma_c$(SiAu$_{11}$) < $\gamma_c$(SiAu$_1$) < $\gamma_c$(SiCu$_6$)

In the plots SiO$_2$, SiAu$_6$, Au, Cu and Ag, $\cos(\theta)$ and $\gamma_L$ did not seem to exhibit a linear relationship, but rather demonstrated a curve tendency, so they have had an exponential fit. The argument to support the linear method is only valid for apolar and low energy surfaces. This is not the case of those samples, which have, not only high surface tension value, but also low surface free energy dispersive component value. [88]

The critical wetting tension values of the surfaces given by the Zisman method are represented in Table 3.4.

As already mentioned, in biomedical electrode applications, the material implanted in the body should integrate with the surrounding tissue and successfully promote the
attachment of neural cells to his surface. For that purpose, only a high surface energy surface can induce the cells to create intermolecular contact with the surface. Thus, a material with low surface energy would not be expected to elicit great adhesion of neural tissue to the surface. R. E. Baier stated a relationship between critical surface tension and bioadhesion, where surfaces with measured $\gamma_c$ values between 20 and 30 mJ.m$^{-2}$ have minimum adhesion, being least retentive. Therefore, materials for neural implants, which require strong adhesion, should avoid this range. [89]

In the histogram represented in Figure 3.4 are the values of surface free energy measured through the Zisman method and also a beige region that includes the range stated by R. E. Baier as the values that promote minimum bioadhesion, that are not in the interest of this work’s application.

The surfaces included in the beige region are SiAg$^{0.3}$ and SiAu$^{11}$, leading to, at first sight, their exclusion of the hypothetic possibility of being good surfaces for the present application. Moreover, both surfaces SiAg$^{31}$ and SiCu$^{6}$ show to have low $\gamma_c$ values, leading to the speculation that these, too, are not suitable for a maximum spread and attachment of nervous tissue to the implant’s surface. However, when considering that these surfaces are intended to modify the surface of neural implants additional factors

---

### Table 3.4: Surface tension values of the thin films.

<table>
<thead>
<tr>
<th>Film</th>
<th>$\gamma_c$ (mJ.m$^{-2}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SiO$_2$</td>
<td>44.7</td>
</tr>
<tr>
<td>Au</td>
<td>53.4</td>
</tr>
<tr>
<td>Cu</td>
<td>45.9</td>
</tr>
<tr>
<td>Ag</td>
<td>49.1</td>
</tr>
<tr>
<td>SiAg$^{0.3}$</td>
<td>27.7</td>
</tr>
<tr>
<td>SiAg$^{3}$</td>
<td>48.6</td>
</tr>
<tr>
<td>SiAg$^{24}$</td>
<td>41.7</td>
</tr>
<tr>
<td>SiAg$^{31}$</td>
<td>17.9</td>
</tr>
<tr>
<td>SiAu$^{1}$</td>
<td>36.1</td>
</tr>
<tr>
<td>SiAu$^{6}$</td>
<td>52.7</td>
</tr>
<tr>
<td>SiAu$^{11}$</td>
<td>21.7</td>
</tr>
<tr>
<td>SiCu$^{6}$</td>
<td>16.8</td>
</tr>
<tr>
<td>SiCu$^{5}$</td>
<td>34.0</td>
</tr>
<tr>
<td>SiCu$^{11}$</td>
<td>34.6</td>
</tr>
</tbody>
</table>
must be considered. In fact, although the attachment and spread of neurons is welcome, the same is not applied for other cells of the CNS such as astrocytes and glial cells. Therefore, cell adhesion must be selective in order to avoid the formation of glial scar, which leads to the encapsulation and isolation of the implant.

### 3.2.3 Hysteresis

Contact angle hysteresis, $\Delta \theta$, was measured by the major difference between advancing and receding contact angles. The advancing angle, $\theta_a$, is measured when the solid/liquid contact area increases, while the receding angle, $\theta_r$, is measured when the contact area shrinks. The existence of hysteresis implies the existence of hydrophilic domains and functional groups at the surface of the thin films.

In Table 3.5 are the dynamic contact angle values, as well as the respective hysteresis of the surfaces in study. The variation of the drop volume was plotted against the advancing and receding contact angles of each thin film in Figures 3.5, 3.6, 3.7 and 3.8.

In Figure 3.5 is the hysteresis of the surfaces composed by the materials alone: $\text{SiO}_2$ (a), Au (b), Cu (c) and Ag (d).
Table 3.5: Dynamic Contact Angles and Hysteresis of the thin films, with $\theta_a$ being the advancing and $\theta_r$ the receding contact angles.

<table>
<thead>
<tr>
<th>Film</th>
<th>$\theta_a$ ($^\circ$)</th>
<th>$\theta_r$ ($^\circ$)</th>
<th>$\Delta \theta$ ($^\circ$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SiO$_2$</td>
<td>49.4</td>
<td>12.2</td>
<td>37.2</td>
</tr>
<tr>
<td>Au</td>
<td>33.9</td>
<td>14.3</td>
<td>19.7</td>
</tr>
<tr>
<td>Ag</td>
<td>70.3</td>
<td>18.1</td>
<td>52.2</td>
</tr>
<tr>
<td>Cu</td>
<td>96.3</td>
<td>25.1</td>
<td>71.2</td>
</tr>
<tr>
<td>SiAg$_{0.3}$</td>
<td>86.1</td>
<td>30.4</td>
<td>55.7</td>
</tr>
<tr>
<td>SiAg$_3$</td>
<td>33.4</td>
<td>5.2</td>
<td>28.3</td>
</tr>
<tr>
<td>SiAg$_{24}$</td>
<td>59.6</td>
<td>6.2</td>
<td>53.4</td>
</tr>
<tr>
<td>SiAg$_{31}$</td>
<td>59.3</td>
<td>14.6</td>
<td>44.7</td>
</tr>
<tr>
<td>SiAu$_{1}$</td>
<td>96.5</td>
<td>28.2</td>
<td>68.3</td>
</tr>
<tr>
<td>SiAu$_{6}$</td>
<td>103.3</td>
<td>29.6</td>
<td>73.7</td>
</tr>
<tr>
<td>SiAu$_{11}$</td>
<td>99.8</td>
<td>19.5</td>
<td>80.3</td>
</tr>
<tr>
<td>SiCu$_5$</td>
<td>90.2</td>
<td>27.7</td>
<td>62.5</td>
</tr>
<tr>
<td>SiCu$_6$</td>
<td>100.7</td>
<td>28.1</td>
<td>72.6</td>
</tr>
<tr>
<td>SiCu$_{11}$</td>
<td>93.1</td>
<td>24.1</td>
<td>69.0</td>
</tr>
</tbody>
</table>

From the results, it is seen that while SiO$_2$ and Au thin films have the lowest values of hysteresis, having respectively $37.2^\circ$ and $19.7^\circ$, Cu and Ag surfaces show higher difference between the advancing and receding angles, with $71.3^\circ$ and $55.7^\circ$ of hysteresis. This difference might be related to the value of the SFE polar component of each surface. In fact, observing Table 3.4 it appears that between the four monolithic thin films, Au has the highest value of $\gamma_{sp}$, while, on the other hand, Cu presents the lowest one.

Generally from the plots, it is evident the non-linearity of the advancing angles of SiO$_2$ in Figure 3.5 (a) and Au in Figure 3.5 (b), in opposition to what happens with Cu in Figure 3.5 (c), for example. This probably happened because, as it may be seen in the histogram from Figure 3.2, SiO$_2$ and Au dispersive SFE is quite low when compared to dispersive SFE of the Cu thin film (c). Dispersive forces, mainly due to Van der Waals forces, are responsible for the advancing angles, so that high SFE dispersive component will lead to relatively contact advancing contact angles. On the other hand, polar forces are responsible for the receding angles. Copper is also presenting the highest value of advancing angle from the monolithic films, which might be related to the fact that it is the monolithic thin film with the lowest value of surface free energy. Advancing angles are expected to be lower in surfaces with high $\gamma_{sp}$. 
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(a)

(b)

(c)

(d)

Figure 3.5: Dynamic contact angles of the monolithic thin films surfaces (a) SiO$_2$, (b) Au, (c) Cu and (d) Ag.

In Figure 3.6 are the plots representing the dynamic angles of the surfaces belonging to the Ag/SiO$_2$ system.

The observation of the results demonstrated that, with the exception of SiAg$_3$ (Fig. 3.6 (b)), the deposition of silver into the SiO$_2$ surface induced the general increase of the hysteresis value, as well as it had increased the contact angle values and the hydrophobic character. SiAg$_3$ has showed a hysteresis value of 28.3$^\circ$, being the film with the most outlier value when compared with the rest of the films of the system, whose behavior seemed similar to Ag surface’s behavior (Fig. 3.5 (d)). As seen in the histogram from Figure 3.2, SiAg$_3$ is, between the four surfaces of the system, the surface with the highest value of polar SFE, which is probably the reason for having the lowest advancing angles. The plot highlights the non-linearity in both advancing and receding angles, which might be due to, not only the low values of dispersive SFE, but also to the chemical heterogeneity of the surface. This chemical heterogeneity probably related to the fact of SiAg$_3$ being the only thin film of SiO$_2$ doped with silver (or a metallic element) that has seen its contact angle values decrease and its surface free
Figure 3.6: Dynamic contact angles of silver system surfaces (a) SiAg$_{0.3}$, (b) SiAg$_3$, (c) SiAg$_{24}$ and (d) SiAg$_{31}$.

energy values increase, when compared to the thin film of SiO$_2$ alone. These results lead to the conclusion of the possible presence of hydrophilic functional groups at SiAg$_3$ surface, which is in agreement with the observations in the wetting character analysis. As expected, SiAg$_{0.3}$ thin film was the surface with the highest advancing angle value, since it was also the thin film with the lowest $\gamma_S$ and respective $\gamma_p^S$.

The plots representing the dynamic angles of the surfaces from the Cu/SiO$_2$ system are in Figure 3.7. The three Cu/SiO$_2$ surfaces seem to be pretty similar to each other regarding to their hysteresis, having values of approximately 72.6° (SiCu$_6$, 3.7 (b)), 62.5° (SiCu$_5$, 3.7 (a)) and 69.0° (SiCu$_{11}$, 3.7 (c)). The high values of both hysteresis and advancing angles might be confirmed by the histogram in Figure 3.2 where it is possible to note the relative poor SFE polar component belonging to those surfaces. Furthermore, specially in SiCu$_6$ and SiCu$_5$ thin films, also the abundant dispersive SFE is visible in the plots, by the general stability of the advancing contact angles. SiCu$_{11}$ is showing the least regular advancing angles probably since is the one that presented the lowest dispersive/polar rate, between the three films. Comparing the system with
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Figure 3.7: Dynamic contact angles of copper system surfaces (a) SiCu$_5$, (b) SiCu$_6$ and (c) SiCu$_{11}$.

the SiO$_2$ thin film, hysteresis has had an increase induced by the deposition of metallic copper in the ceramic surface.

Finally, in Figure 3.8 are represented the dynamic contact angles of gold’s system surfaces. The three SiO$_2$/Au surfaces appear to be quite similar between each other and present a contact angle hysteresis very different from the Au surface, having higher hysteresis values. In fact, in their SFE values this difference is evident too, since Au is the sample with the highest polar SFE, in opposition to SiAu$_1$ (a), SiAu$_6$ (b) and SiAu$_{11}$ (c) which happen to be the surfaces with the lowest ones. Each of the three have also more dispersive than polar component, which might have resulted in the constant advancing contact angles that may be visible in the plots. Inclusively, since they also have the highest advancing angles, these surfaces were originally the most hydrophobic. Comparing the system to the thin film of 100% SiO$_2$, once again is visible that the presence of gold has turned the surface more hydrophobic, since the hysteresis values of the Au/SiO$_2$ are larger than hysteresis from SiO$_2$. 
Hysteresis values are also influenced by rearrangements of the solid surface when in contact with a liquid and by surface roughness. Smooth surfaces with chemical homogeneity will measure a contact angle hysteresis close to zero. On the contrary, increased roughness or more chemical heterogeneity will increase contact angle hysteresis. Surfaces topography will be analyzed in the following sections.

3.3 Surface Morphology/Topography

Although the results of the wettability of the surfaces provide some information concerning to their potential biocompatibility, topographic and morphological characterization of the same surfaces is also important to predict the behavior of such materials in biological environment. It is well known that the surface microstructure of biomaterials plays a fundamental role in the behavior of the attached cells. Researchers have reported that porous silicon promoted a better neuron’s spreading than bulk silicon. Furthermore, it...
has been stated that nanometer-scale columnar structures in Si might improve astrocytes adhesion. [90]

In order to analyze the topographic features of the surfaces, the samples were characterized by AFM, before and after their immersion in the SBF, being taken in addition to 2-D and 3-D topographic images and phase images, the roughness parameters from each scan. SEM images were also obtained after the immersion, with the complement of EDS information where it was possible to achieve elemental composition of some spots of interest.

- Monolithic Coatings

The coatings of the monolithic materials will be compared, since, as already mentioned, materials by them selves must meet compatibility requirements in order to be considered to be included in any implant.

Observing the SiO$_2$ surface three-dimensional topographic images in Figure 3.9 (A), there are some differences to point on the surface before and after SBF immersion. On day zero, the thin film presented a wavy surface, with some irregularities. After fourteen days of being immersed into the SBF, the film was more uniform, with a granulated surface and, although did not present peak-to-peak values as large as the surface before the immersion, showed a topography less smoother and less softer. The immersion resulted in the decrease of the roughness parameters, where the average roughness, $R_a$, has changed from 7.9 nm to 2.7 nm. SEM images from day 4, in Figure 3.10 (A) have demonstrated little irregularities, however EDS information has proved that these were only small NaCl deposits from the liquid (Figure 3.9). As neural implants are supposed to be coated mainly by SiO$_2$, it is important the maintenance of the properties of this material.

In (B) from Figure 3.9 is represented Au thin film. Before the immersion into SBF, the thin film presented a very granular surface, with protruding and large-sized grains ($\simeq 0.13 \mu m$). After the fourteen days, the grains became from circular to a more elongated and smaller structure ($\simeq 0.07 \mu m$). Furthermore, due to the immersion, roughness parameters have modified. Average roughness, $R_a$, increased from 6.6 nm to 7.6 nm, and the maximum peak-to-peak-valley height, $R_t$, from 56.5 nm to 119.4 nm. Observing SEM images from Figure 3.10 (B), it is noticed from day 2 until the end of the period
vertical/horizontal irregularities, which might be the cause for the roughness differences. There are also some tiny and white spots, which might be related to the heterogeneity observed in AFM phase image. The spots probably are, once more, just salts left from the fluid.

The thin films of Cu have suffered a great both texture and chemical modification during the time of immersion, where by days 7 and 14 the surfaces were completely damaged. So, in SEM images from those days (Figure 3.10 (C)) one is just in the presence of the Si wafer, on where the coating was sputtered. As the copper thin film has detached and released into the SBF during the days, it were also obtained AFM images of the surface from first day (Figure 3.9 (C), middle).

Observing three-dimensional topographic images, one notices that, after one day of being immersed into the SBF, Cu thin film has changed from a lamellar to a granular surface. Roughness parameters increased, where the average roughness, $R_a$, before the immersion was 2.6 nm, and after was 11.5 nm. Despite these changes, looking at SEM images in Figure 3.10 (C) it is observable that only by day 2 surface demonstrated any significant change in its morphology, with some deposits on it.

The thin film’s surface from day 4 was submitted to EDS and, as one can see in SEM Figure 3.10 (C), at the fourth day there seems to be the release of copper oxide which has accumulated at the film’s surface. After that, in day 7 and 14, the oxide detached from the film dissolving in the fluid, resulting in the damage of the coating.

The thin film of 100% Ag, represented in Figure 3.14 did show significant topography changes, where the average roughness, $R_a$, decreased from 3.2 nm to 1.6 nm. While the sample before immersion into the SBF had a rough layer exhibiting a pitted structure, after the fourteen days of immersion the surface was more smoother, although having some irregularities on the surface higher height. These are easily identified in phase image, implying a possible heterogeneity of the surface after the time of immersion, which might be due to the deposition of salts from the fluid. In fact, observing the SEM images from Figure 3.12, one can notice what looks like crystals deposits, probably of NaCl. Silver oxide, did not seem to release from the film as copper oxide did in Cu. This fact is not surprising since as it was mention before, copper has a more greater ability to oxidize than silver.
The histogram in Figure 3.13 compares the roughness average before and after the immersion of the four monolithic thin films. The immersion of the thin films into the SFB induced some changes, more noticeable to some surfaces than to others, in the topography. While SiO$_2$ and Ag have seen their $R_a$ decrease after the immersion, Au thin film surface became less smoother, resulting in a slightly increase of the $R_a$. Meanwhile, Cu could not resist until the end of the period with the total release of copper coating from the silicon wafer, which lead to a significant increase in the $R_a$. The detachment of Cu coating means that probably copper does not show adequate adhesion to Si surface, not being appropriate to the application of the present work.
Figure 3.9: AFM topographic images (1.0×1.0 μm²): (A) SiO₂, before (above) and after (below) 14 days of immersion in SBF. (A.1) EDS from day 4 of immersion of SiO₂. (B) Au before (above) and after (below) immersion. (C) Cu, before (above), at day 1 (middle) and after (below) immersion. (C.1) EDS from day 4 of Cu’s immersion.
Figure 3.10: SEM images of the monolithic thin films: (A) SiO$_2$, (B) Au and (C) Cu. Days 1, 2, 4, 7 and 14 of the immersion in SBF.
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**Figure 3.11:** AFM topographic 2-D and 3-D and phase images (1.0×1.0 µm$^2$): Monolithic Ag, before (above) and after (below) 14 days of immersion in SBF.

**Figure 3.12:** SEM images from the monolithic Ag thin film. Days 1, 2, 4, 7 and 14 of the immersion in SBF.
Figure 3.13: Variation of the $R_a$ values of the monolithic thin films, before and after the immersion in SBF. (Values taken from 1.0×1.0 $\mu$m$^2$ scan.)

- **Ag/SiO$_2$ System**

Silicon dioxide films doped with silver will be now analyzed. In Figure 3.14 (A) are contained the AFM results of surface SiAg$_{0.3}$, the thin film with the lowest levels of silver. Although the average roughness, $R_a$, had not seen its value increase significantly, the three-dimensional topographic image from day 0 seems less harsh than the one from the fourteenth day. Images from the day 14 reveal a smaller surface grain size with columnar morphology. Looking at SEM images (Figure 3.15 (above)), it is possible to see, from the second day, the deposition of small residues at the surface. As seen in Figure 3.16 the chemical characterization by EDS of such deposits indicated that these were just crystals derived from the SBF, composed by NaCl. Silver’s release was not achieved during the immersion period, which indicates that probably the levels of sputtered silver should be increased or perhaps the time of immersion. The first solution should be the most appropriate, since the inflammatory response to the implant initiates in the first few seconds after the material’s insertion. Therefore, the earlier the release of silver ions, the faster starts its antibacterial action preventing acute response.

Figure 3.14 (B) represents AFM images of thin film SiAg$_3$. The three-dimensional topographic image did not show significative changes of roughness parameters with the immersion of the film into SBF, although the day 14 surface seemed to exhibit a more granular and less smoother surface. Average roughness, $R_a$, decreased from 7.0 nm to 6.7 nm and the average maximum height of the profile, $R_{tm}$, increased from 37.8
nm to 49.8 nm. The evolution of the SiAg$_3$ thin film’s surface during the immersion period is presented in SEM images of Figure 3.15 (B). Looking at the micrographs, it is possible to easily identify small deposits on the surfaces, particularly since day 4. After submitting the regions of the deposits to EDS, it was possible to conclude that those deposits were referent to oxides, chlorides and carbonates of silver that have accumulated on the surface (Figure 3.16 (B)). However, observing the micrographs from seventh and fourteenth day, the percentage of elements accumulated on the surface did not seem to increase with time, being, since approximately day 4, the same amount of deposits at the film’s surface.

Considering SiAg$_{24}$, its 3-D topographic images in Figure 3.14 (C) reveal very significant differences induced by the immersion of the samples into the SBF. Before the immersion, the layer exhibited a slightly rough and granular surface, while after being immersed it became softer but irregular and with a large groove at the center of the surface sample. These changes resulted in an enormous difference between the before and after roughness parameters, where the average roughness, $R_a$, increased from 9.8 nm to 90.4 nm. There was an increase in the other roughness parameters, particularly in the maximum peak-to-peak-valley height, $R_t$, which increased from 110 nm to 773 nm. Figure 3.15 (C) shows the evolution of the thin film SiAg$_{24}$ surface during the immersion period. The morphological changes began to appear from the very first day, with small deposits at the surface, which significantly increased in size by the second day. From the fourth day until the end of the immersion period, the amount of deposits seems to remain constant. The chemical characterization of three different regions from day 4 surface, performed by EDS, is presented in Figure 3.16 (C). While in the first two graphics is represented the elemental composition of two regions with high amounts of accumulated deposits on the surface (C.I and C.II), the third and last chart is pointing to an area where, apparently, there were no accumulations (C.III). The graphics show that those deposits were mainly composed by silver oxides and chlorides, and on the other hand, the spots with no accumulations appeared to have the film’s initial elemental composition: silver and silicone dioxide. Once again, the immersion of the film in simulated biological fluid resulted in the release of silver ions, indispensable for the antibacterial activity desired for neural interfaces applications. Comparing with SiAg$_3$, the amount of deposits on SiAg$_{24}$ thin film’s surface is much larger, which might confirm that probably the release of silver is related to the initial percentage of metallic silver of the coatings.
For the SiAg$_{31}$ thin film, are presented in Figure 3.17 two 3-D topographic images with different magnifications. The differences in the surface induced by the immersion into SBF are clear in the 5.0$\times$5.0 $\mu$m$^2$ images. While before immersion, the surface presented a very rough and lamellar structure, after the fourteen days the coating exhibited a smoother surface, with some sharp irregularities. Considering now 1.0$\times$1.0 $\mu$m$^2$ 3-D image, one may see that the surface has also became more granular. This changes resulted in the general decrease of the roughness parameters, where $R_a$ decreased from 26.8 nm to 9.1 nm.

The morphological evolution of SiAg$_{31}$ surfaces is presented in Figure 3.18 (A), and is possible to observe that since day 2 and day 4 small deposits start to accumulate in the film’s surface. However, it is by day 7 that the major difference is noticed and the sample is filled with structures deposited on its surface. In order to conclude about the elemental composition of such deposits, EDS was performed (see Figure 3.18 (B)). The results demonstrated that, while in day 4 the deposits were mainly composed by silicon, with small amounts of silver and fluid salts, by day 7 the quantity of AgCl has drastically increased leading to the conclusion that silver has effectively oxidized after, at least, seven days of immersion and has accumulated on the thin film’s surface, fulfilling the objective of the work.

As it can be seen in the histogram from Figure 3.19, for the thin films with the highest levels of silver, the deposition of this element into SiO$_2$ surface has increased the average roughness of the thin films. SiAg$_{0,3}$ and SiAg$_3$ have average roughness value before immersion lower than the 100% SiO$_2$ thin film. The fact that silver may induce an increase in the roughness parameters of SiO$_2$ surface is a very good principle, meaning that silver improves topography of silicon dioxide, since roughness is fundamental for neuron spreading. After the immersion of the ceramic/silver films into the SBF, only the thin films with the highest levels of the metallic element, SiAg$_{24}$ and SiAg$_{31}$, noticed a significative change in the roughness parameters. However, although both thin films met the objective of the silver’s ions release, only SiAg$_{24}$ has seen its $R_a$ increase which might indicate that this might be the surface with the most appropriate morphological/topographic properties for the applications of this project. SiAg$_{0,3}$ and SiAg$_3$ demonstrated to have a poor release of silver’s ions and low roughness parameters.
Figure 3.14: SiO$_2$/Ag system AFM images (1.0×1.0 µm$^2$): (A) SiAg$_{0.3}$, (B) SiAg$_3$ and (C) SiAg$_{24}$, before (above) and after (below) 14 days of immersion into SBF.
Figure 3.15: SEM images: (A) SiAg$_{0.3}$, (B) SiAg$_3$ and (C) SiAg$_{24}$. Days 1, 2, 4, 7 and 14 of the immersion in SBF.
Figure 3.16: EDS: Chemical characterization after SBF of (A) SiAg$_{0.3}$, day 4; (B) SiAg$_3$, day 4; (C.I) and (C.II) SiAg$_{24}$, day 4 at two different spots with deposits; and (C.III) SiAg$_{24}$, day 4 at spot with no deposits.
Figure 3.17: AFM images 2-D and 3-D, 1.0×1.0 μm², and 3-D, 5.0×5.0 μm²: SiAg₃₁, before (above) and after (below) 14 days of immersion in SBF.

Figure 3.18: SEM images: SiAg₃₁. Days 1, 2, 4, 7 and 14 of the immersion in SBF. EDS of days 4 and 7.
Figure 3.19: Variation of the $R_a$ values with the levels of metallic silver, before and after the immersion in SBF. (Values taken from 1.0×1.0 $\mu$m$^2$ scan.)

- **Au/SiO$_2$ System**

In Figure 3.20 (A) are the AFM images of SiAg$_1$ thin film, with 3-D topographic images having two different magnifications. Comparing the three-dimensional topographic images of 5.0×5.0 $\mu$m$^2$, one notices that the surface corresponding to day 0 appeared to be rougher than the one corresponding to day 14, which in spite of having some spark irregularities, exhibits a more regular and flatter surface. Also, looking at the 1.0×1.0 $\mu$m$^2$ 2-D and 3-D images, while before immersion, the surface showed more grouped and stacked grains with higher height values, after the fourteen days the surface exhibited a more columnar structure. Average roughness, $R_a$, decreased from 15.6 nm to 7.7 nm and the average maximum height of the profile, $R_{tm}$, decreased from 66.3 nm to 32.8 nm.

The SEM figures from the immersion period in the SBF are represented in Figure 3.21 (A). It is possible to observe, in each day’s picture, the formation of residues on the thin films surface. These residues, specially in day 2, appear to simply be deposits of salt crystals from the fluid, which accumulated in result of a poor sample’s washing. The deposits on day 4 did not seem to be just crystals, so in order to evaluate their chemical composition, EDS was performed (Figure 3.22 (A)). The results showed that the deposits were mainly formed by Si, O and by a very few percentage of Au.
In (B) from Figure 3.20 are presented the AFM images from surface of the SiAu\textsubscript{6} thin film. Looking at the 3-D topographic images, it is seem that SiAu\textsubscript{6} surface before the period of immersion in the SBF had a wavy and compact structure, which has became columnar sharpened after the fourteen days period. Roughness parameters had a slightly decrease, where $R_a$ changed from 8.5 nm to 5.3 nm. The images presented in Figure 3.21 (B), obtained by SEM, are showing the evolution of the surface during the fourteen days. Since the first day, there are little residues on the surface, which tend to increase at the second day. With the EDS was achieved the elemental composition of such spots. The results tell that the deposits were mainly constituted by Si, O and Au (Figure 3.22 (B)).

In Figure 3.20 (C) are presented the images of SiAu\textsubscript{11} surface, after and before the immersion in SBF, obtained by AFM technique. Both surfaces presented great topographic differences, and roughness parameters from the two different magnifications showed different conclusions. Considering the 3-D images, while in day 0 the surface showed a rough texture with elongated and diagonally oriented grains, the 3-D images from the fourteenth day showed a more smoother surface, with compact grains. However, considering $5.0 \times 5.0 \mu\text{m}^2$, roughness parameters increased with the immersion into the SBF. On the other hand, regarding $1.0 \times 1.0 \mu\text{m}^2$, roughness parameters decreased after the immersion. SEM images (Figure 3.21 (C)) revealed the appearance of small deposits since the first day. Submitting the day 4 surface to EDS (Figure 3.22 (C)), it was discovered that such deposits corresponded to Si but, specially, to Au and O. These results mean that gold oxidized under the SBF and accumulated at the film’s surface. The release of gold ions might be related to the levels of gold by which the thin film was initially composed, since this surface was the one with the highest levels of this metal. The deposition of oxidized gold at the surface might be the cause for the large increase of the roughness parameters in magnification $5.0 \times 5.0 \mu\text{m}^2$, since there can be seen large and high amounts on the 3-D image.

The histogram in Figure 3.23 shows the variation of average roughness with the levels of Au, before and after the 14 days of immersion in the SBF. The surface that has not seen its values change significantly was surface SiAu\textsubscript{6}. Its texture became from wavy to sharpened, which may bring some advantages to neuron adhesion. However, this thin film is the one that presents the lower values of roughness parameters. On the other hand, SiAu\textsubscript{11} is the film from the SiO\textsubscript{2} system with the higher roughness parameters.
This film had also showed the oxidation of gold during the immersion, which might lead to the conclusion that, when together, gold may be effective in silver’s oxidation, instead of oxidize itself.
Figure 3.20: AFM images (Topographic 2-D and 3-D 1.0×1.0 µm² and 3-D 5.0×5.0 µm²): (A) SiAu₁, before (above) and after (below) 14 days of immersion in SBF. (B) SiAu₆, before (above) and after (below) immersion in SBF. (C) SiAu₁₁, before (above) and after (below) immersion in SBF.
Figure 3.21: SEM images: (A) SiAu$_1$, (B) SiAu$_6$ and (C) SiAu$_{11}$. Days 1, 2, 4, 7 and 14 of the immersion in SBF.
Figure 3.22: EDS: Chemical characterization after SBF of (A) SiAu1, day 4; (B) SiAu6, day 4; (C) SiAu11, day 4.

Figure 3.23: Variation of the $R_a$ values with the levels of gold, before and after the immersion in SBF. (Values taken from 1.0×1.0 µm² magnification.)
Cu/SiO$_2$ System

The topographic images of SiCu$_5$ thin film are represented in Figure 3.24 (A). Comparing both three-dimensional topographic images, it may be seen the decrease of smoothness after the period of immersion in the SBF. In fact, the average roughness value, $R_a$, increased from 5.5 nm to 11.5 nm, and the average maximum height of the profile, $R_{tm}$ increased from 17.2 nm to 64.5 nm. Observing Figure 3.25 (A), it is possible to notice the appearance of some deposits, which EDS from the fourth day proved them to be just NaCl crystals from the fluid (Figure 3.26 (A)).

In Figure 3.24 (B) are represented the AFM images from SiCu$_6$ surface. The values of the roughness parameters suffered from a general slightly decrease, where the average roughness, $R_a$, decreased from 5.5 nm to 4.7 nm after the immersion period. Although both before and after surface showed to be granular, at the end of day 14, the thin film seemed to have larger grains and a more wavy texture. From the SEM micrographs in Figure 3.25 (B), it is possible to see that, probably, such texture was given by the deposits that were found at the surface from day 4. Figure 3.26 (B) represents the chemical composition of the deposit found on day 4 surface. The graphic reveals that it was composed, in addition to copper oxides and silicone, by salts and elements from the fluid, such as Cl, Ca, Mg, C and S.

Considering now SiCu$_{11}$ thin film, observing the topographic pictures from Figure 3.24 (C) it is possible to conclude that the immersion of this sample during fourteen days in SBF did induce the decrease of the roughness parameters. While before the immersion the surface seemed more granular and with a deep groove, after the immersion the surface exhibited a more pitted and lamellar structure. The surface from day 0, although seems smoother, presents a larger average heigh value. In SEM micrographs from Figure 3.25 (C) it is possible to notice the formation of some deposits over the period of immersion. Those deposits, as one sees in EDS information in Figure 3.26 (C), were proven to be copper oxides and also silicon.

In Figure 3.27 it is possible to see the variation of $R_a$ values before and after the fourteen days of immersion in the SBF, and the levels of copper in the thin film. Observing the histogram it is noticed, as it has happened with silver and gold, the deposition of copper in the SiO$_2$ only induced an increase in the roughness average for the thin film with higher level of the metallic element. Thin film SiCu$_6$ is the one showing the biggest
maintenance of the average roughness, $R_a$, values. Considering the other two surfaces belonging to SiO$_2$/Cu system, while SiCu$_5$ thin film had an increase in the roughness average after the immersion, SiCu$_{11}$ had a significative decrease. Despite this decrease, SiCu$_{11}$ was the only thin film surface that proved to induce the release of copper oxides during the immersion.
Figure 3.24: AFM topographic 2-D and 3-D, 1.0×1.0 μm², and 3-D 5.0×5.0 μm² images: (A) SiCu₅, before (above) and after (below) 14 days of immersion in SBF. (B) SiCu₆, before (above) and after (below) immersion in SBF. (C) SiCu₁₁, before (above) and after (below) immersion in SBF.
Figure 3.25: SEM images: (A) SiCu₅, (B) SiCu₆ and (C) SiCu₁₁. Days 1, 2, 4, 7 and 14 of the immersion in SBF.
Chapter 3. Analysis and Discussion of Results

Figure 3.26: EDS: Chemical characterization after SBF of (A) SiCu₅, day 4; (B) SiCu₆, day 4; (C) SiCu₁₁, day 4.

Figure 3.27: Variation of the $R_a$ values with the levels of copper, before and after the immersion in SBF.
Conclusions

In this study, it was proposed the development of coatings that are intended to improve the biocompatibility and long-term functionality of silicon-based neural implants. Therefore, the work was based on the characterization of the modified silicon, in order to be able to predict their behavior when inserted into the human body.

The materials assessed for the optimization of the implant’s performance were silicon dioxide as insulator and encapsulator material, silver and copper as antibacterial agents, and gold which induces silver and copper’s oxidation, and leads to the implant’s identification in imaging examinations.

The main conclusions of the developed work can be summarized as follows:

**Monolithic thin films:**

- SiO$_2$, Ag and Au thin film surfaces presented good wetting, hydrophilic character and high values of surface free energy and critical surface tension. Important factors for neuron spreading and to avoid protein adsorption.

- Cu, although had high critical surface tension, presented poor wetting and hydrophobic character, with high values of surface free energy dispersive component.

- SiO$_2$ $R_a$ decreased with the immersion of the thin film into SBF. However, SEM images from the period of immersion revealed no significative alteration of the morphology of the surface. SiO$_2$ did not release from the sample, showing a good adhesion to the Si wafer, which means SiO$_2$ will serve as a good insulator/base material for the implant.

- Au $R_a$ increased after being submitted into SBF, which although it might modify its hydrophilic character, it also might be good to neuronal adhesion.
Conclusions

- During the 14 days of immersion in the SBF, 100% Cu thin film completely detached from the Si substrate.

- 100% Ag $R_a$ values were low, did not significantly change after the 14 days of immersion.

Therefore, SiO$_2$, Ag and Au thin films seem to have biocompatibility characteristics and it is expected that they will not intensify or anticipate the inflammatory response from the CNS. Cu thin film bring some concerns about its acceptability in the human body. From there results, Ag is a better antibacterial agent than Cu for neural interfaces applications.

Ceramic/Metallic Systems:

- SiO$_2$ hydrophilic character and surface free energy decreases with the deposition of metallic elements.

- The increase in the contact angle in the systems is not proportional to the increase of the content of the deposited metallic element.

- There does not seem to exist any direct relation between the increase in roughness parameters with the deposition of the metallic element. However, it seemed that for the highest levels, the average roughness was higher too.

The overall properties/characteristics of the SiO$_2$/Ag and SiO$_2$/Cu thin films are synthesized in the tables, from which can be concluded that the more advantageous thin films are SiAg$_{24}$ from the ceramic/silver system and SiCu$_{11}$, from the ceramic/silver system. Between both, SiO$_2$ doped with Ag would be preferential to the present application.

<table>
<thead>
<tr>
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<td>+</td>
<td>+</td>
</tr>
<tr>
<td>$\gamma_c$</td>
<td>(Baier)</td>
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<td>+</td>
</tr>
<tr>
<td>$\Delta\theta$</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
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<td>–</td>
<td>–</td>
<td>+</td>
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<tr>
<td>Ag$^+$</td>
<td>–</td>
<td>–</td>
<td>+</td>
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<table>
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<td>–</td>
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<tr>
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<td>+</td>
<td>(&lt;Baier)</td>
</tr>
<tr>
<td>$\Delta\theta$</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>$R_a$</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cu$^{2+}$</td>
<td>–</td>
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</tr>
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</table>
Conclusions

- Gold deposition into SiO$_2$ induced a general increase in the contact angle values, and a decrease in surface free energy. However, while one of the thin films (10.9%) was between Baier’s range, other one was well above the limit (5.9%). This one is also the one with the higher polar component. However, presented the lowest roughness parameters values from the three thin films, a possible addition of silver into the coating might compensate this low, and increase roughness average.

Although monolithic SiO$_2$ roughness parameters have not been high, it was visible an increase in the roughness parameters with the 24.3% Ag thin film. The same has happened with the deposition of gold for some of the percentages. These results lead to the conclusion that a SiO$_2$ coating doped with both Ag and Au will have an even higher average roughness, promoting neuron adhesion.

Future work can include the deposition and, again, a thoroughly characterization of SiO$_2$ thin films doped with both silver and gold. New experimental surface characterization techniques may be added to the study of the surfaces, such as surface charge characterization. It has been demonstrated that, in many cases, the mechanism of protein adsorption is mainly due to electrostatic interaction. The electrostatic interaction of the nanoparticles may be controlled by the variation of their surface charges, which can be determined by the Zeta Potential of these particles. [91] The systems with the best set of properties/characteristics should be afterward submitted to in vitro cell tests, to conclude about the capacity of neuronal cells to adhere to the new coatings. After that, it will be possible to find a balance that minimizes adverse response and enhances the implant’s performance. In longer term, the new coatings would be able to induce adhesion, activation or repulsion of specific cell types of the CNS that are in contact with the modified surface, promoting a maximum incorporation into the tissue and avoiding both the violent responses of the immune system and the damage of the electrodes.

I sincerely hope the developments in the field of neural implants to continue the good way and that they bring hope to such a great number of patients suffering from neurodegenerative diseases and functional or sensory loss. I am sure they will.
Bibliography


[40] Andrew R. Barron. Chemical vapor deposition. This module was developed as part of the Rice University course CHEM-496: Chemistry of Electronic Materials. This module was prepared with the assistance of Scott Stokes, July 2009.


[48] Muhammad Maqbool. *Target temperature is lower with magnetron sputtering enhancing the deposition of high quality films*. PhD thesis, Department of Physics and Astronomy (College of Arts and Sciences), Ohio, August 2005.


