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Development of an Inflammatory Joint Fluid Corrosion Assessment Method for Metallic Biomaterials

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Abstract

There is currently no systematic way to analyze the corrosion response of orthopedic alloys in contact with human joint fluid. The goal of this project was to design and test a small device that can successfully run electrochemical tests on retrieved inflamed joint fluids. Methods of fluid testing analysis were also explored. The a small electrochemical cell was created using polypropylene for the body and an electrode cartridge that could be disposed of after each test. In total the device could hold 4 mL of liquid. Testes were preformed using titanium, stainless steel, and CoCrMo alloys as the working electrodes and were tested in solutions of PBS and AMEM (10% fetal bovine serum) and additions of 0.1 mM of $FeCl_3$ and H_2O_2 (5, 10, 25 mM) to simulate the inflamed joint fluid created by the oxidative burst reaction.

Three electrochemical tests were run to evaluate the cell and included open circuit potential, impedance, and anodic polarization. The results of these tests indicated that the device can be used to analyze the corrosion response of metallic alloys in joint fluid, and that the additions of $FeCl_3$ and H_2O_2 increased potential of these alloys to corrode.

Executive Summary

This project explores the hypothesis that an electrochemical relationship exists between inflamed synovial joint fluid and the level of inflammatory cell induced (ICI) corrosion acting on a metallic implant. A recent study reported on direct ICI corrosion of the surfaces of CoCrMo implants that had been retrieved and studied for failure analysis, and provided new evidence of this corrosion through microscopic observation. ICI corrosion is caused by cellular reaction mechanisms that produce reactive oxygen species that can significantly alter the implant surface topography. This type of corrosion can be recognized by the characteristics of its morphology and resembles biological patterns that have been derived from cellular reactions and remnants. The corrosion behaviors of these surfaces depend heavily on the material interactions with its environment, including interactions with the synovial joint fluid, and its constituents.

The major goals of this project were to design, build and evaluate an electrochemical cell to assess the joint fluid inflammatory state. A prototype was modeled with respect to considerations for sterility, volumetric capacity, and ease of use. The final chosen design consisted of a three-part system that included a disposable cartridge that contained electrodes, a polypropylene tube that could be autoclaved, and a cap that could be pierced by a needle. After completion of the final design, the cell was evaluated for electrochemical behavior using a potentiostat - an instrument that controls the voltage between electrodes to make electrical measurements.

The cell contained three electrodes: working, counter, and reference. The working electrode provides the surface for which the electrochemical reaction takes place and for corrosion experiments, this is the material that represents the corroding metal structure. Stainless steel, titanium, and cobalt-chromium were chosen for working electrodes due to the popularity of

these metals for orthopedic implants. A reference electrode is used to provide a comparison for the potential measurement of the working electrode. In the absence of current, the reference electrode has a known, constant electrochemical potential. The material used in the set up was Ag/AgCl. The counter electrode completes the circuit in the cell by providing an exit for the current flow in the solution from the working electrode and a thin rod of graphite carbon was used for this purpose. The electrodes were made small and thin so that the device was able to hold small amounts of fluid (~4 mL). This is because it is unknown how much fluid can be extracted from a joint and is dependent on the patient.

A protocol was developed for the testing of the device and was followed through the project. Each cell was run through three electrochemical tests (open circuit potential, impedance, and anodic polarization) and repeated using different solutions. To test the cell for simple functionality and durability, .01 M of phosphate buffered saline (PBS) was used, which has similar osmotic and ion concentrations as the fluids in the human body. Next, a solution of PBS with hydrogen peroxide and iron (iii) chloride was used to mimic the reactive, or inflamed, environment inside the joint, and these additives more closely resemble ions conducive to a Fenton-like reaction, which is thought to play a major role in the cell attack on the implant. Three molarity of the hydrogen peroxide were used in PBS to compare the effects of an increasing concentration of hydrogen peroxide on the electrochemical environment. Lastly, AMEM (a type of cell culture medium) with 10% fetal bovine serum (FBS) with the same concentrations of hydrogen peroxide and iron additions was used to further simulate the conditions in the body, and this solution would best represent the chemistry and reactivity of true inflamed joint fluid.

Three electrochemical tests were used to evaluate the cell. An open circuit potential (OCP) test shows the voltage of the working electrode relative to the reference electrode. Corrosion reactions on the surface of the working electrode cause the open circuit potential, or corrosion potential. It should be noted that this potential cannot be measured directly, and therefore must be compared to that of a known system, which is why a reference electrode is used. The second test that was run was impedance, which measures the resistance of the working electrode in the set up of the cell. The information provided by this test can also be used to determine the surface area of the electrode, which has a significant impact on current flow and the comparability of the data sets gathered form each test. The last test run on the cell was anodic polarization. This type of test scans the voltage in the positive direction in small increments where the working electrode acts as an anode and corrodes or forms an oxide.

Upon completion of the project, this device could be used as a diagnostic tool for inflammatory-corrosion index in humans and perform short-term human retrieved inflammatory cell interactions with medical alloys to assess the severity of corrosion. This means that extensive revision surgery could be avoided because the conditions inside the joint would be able to be monitored and analyzed quickly with mild invasion to the patient and knowing the corrosion state of the implant will help surgeons take the most appropriate course of action for treatment of a patient.

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INTRODUCTION

Much of the research in the Gilbert Laboratory is related to the retrieval and failure analysis of metallic hip implants. The major types of metallic alloys used for these implants include both cobalt-chromium-molybdenum (CoCrMo) and titanium (Ti). Although considered highly biocompatible, these materials do have the potential to corrode inside the body, which can lead to implant failure and eventually removal from the body [1].

For years it was thought that wear caused corrosion, and corrosion caused release of small particle debris and ions into the surrounding fluids and/or tissues. This corrosion process has been thought to consist of mechanically assisted crevice corrosion, or tribocorrosion [1-4], which is a process that combines a cyclic motion between two contacting surfaces in the presence of a fluid [5]. Pitting is another corrosion process that results from the lowering of the pH of the environment surrounding the implant [1]. As the surfaces degrade over time, particles are released which then trigger an immune/inflammatory response from the local tissues [6,7].

A recent study reported on evidence of direct inflammatory cell-induced (ICI) corrosion of CoCrMo implant surfaces and demonstrated that cells that are part of the mononuclear phagocytic cell line have the ability to cause corrosion to the surfaces of CoCrMo devices [8]. The corrosion patterns on the surfaces of retrieved hip and knee implants were analyzed and documented using both optical and scanning electron microscopy (SEM), and the corrosion morphology and cellular remnants indicated an attack from inflammatory cells that were

migrating or had been adhered to the surface (Figure 1). This type of corrosion was found first on the CoCrMo heads and liners near the tapers, but later it was found on all of the components, suggesting that these inflammatory cells attack both CoCrMo and Ti alloys [9]. This type of corrosion was found on metal-on-metal (MoM) and metal-on-polymer (MoP) components.

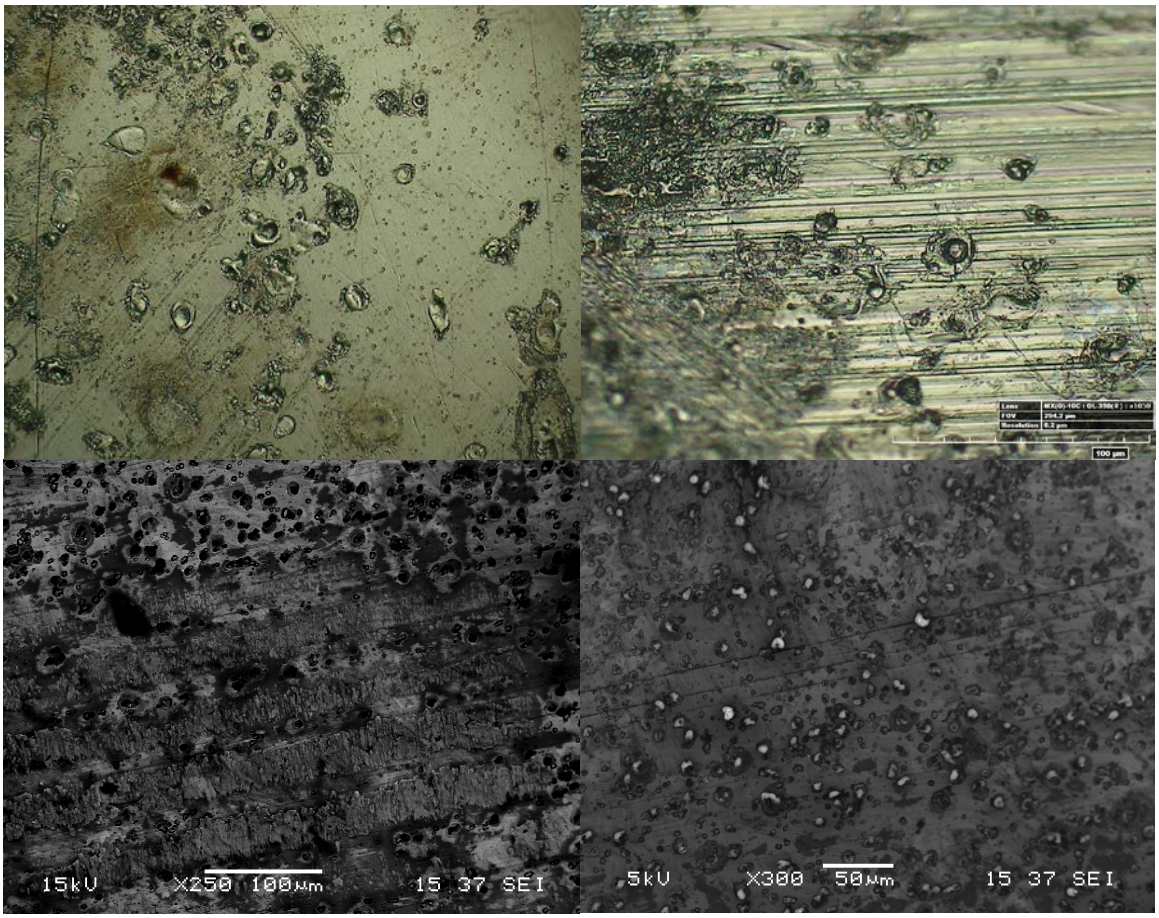


Figure 1: Optical microscope image of ICI corrosion surface of CoCrMo liner (A, B). SEM image of ICI corrosion at 15kV(C) and 5kV(D). Note the cell remnants present under 5kV observation (bright regions in D).

The mechanism by which ICI corrosion happens on these metal alloy surfaces by the oxidative burst reactions (Figure 2) [9], which is the quick release of reactive oxygen species (including hydrogen peroxide) from the cell. When exposed to iron (Fe^{2+}/Fe^{3+}) the hydrogen peroxide forms hydroxyl radicals, which are extremely reactive [8,9]. When exposed to the implant surface, H_2O_2 can increase the oxidizing power of the environment, and it can also

damage the oxide film that forms on the metal surface of implants making it less resistant to corrosion[1,10]. In other words, an increase in H_2O_2 delivered by inflammatory cells, will increase the corrosion rate of the implant [1]. Corrosion releases small particles and ions into the joint cavity and will aggravate the surrounding tissues which may lead to tissue reactions and eventually to implant removal [9].

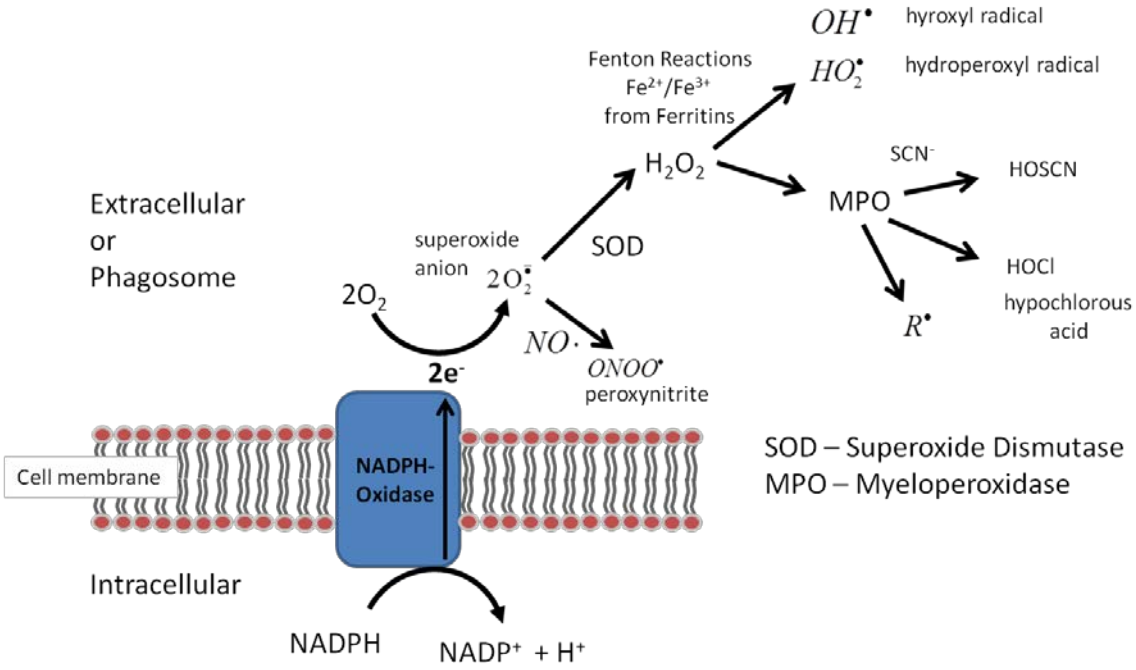


Figure 2. Schematic of the oxidative burst reaction. Note, cells make super oxide anions that react into other species (H_2O_2, HClO, etc.), which are reactive with CoCrMo alloy surfaces [9].

To date, there have been no systematic analyses of the corrosion response of orthopedic alloys in contact with human joint fluids. In addition, variations in corrosion response with variations in joint fluid inflammatory state is unknown. Knowledge of the corrosion response of orthopedic alloys in human joint fluids would provide significant insight into the range of possible corrosion processes that are affected by the inflammatory state of the patient.

The goal of this project is to design and evaluate an electrochemical cell to assess the joint fluid inflammatory state and to evaluate methods of analysis that can provide direct

measurement of inflammatory state of the fluid. This device will then be used as a diagnostic tool for an inflammatory corrosion index in humans, and will give insight to inflammatory cell interactions with medical alloys. This particular portion of the project aims to design and build a working prototype for a small electrochemical cell and evaluate it for its electrochemical behavior using different solutions including phosphate buffered saline (PBS), PBS with $FeCl_3$ and H_2O_2 additions, and cell culture media and fetal bovine serum (FBS) with the same additions [7,10]. These solutions may simulate the environment of the interior of an inflamed synovial joint. After completion of the cell and its preliminary evaluation, it would be ready for tests using retrieved human joint fluids, and could then be used for a systematic, quantitative measurement of an inflammatory index.

MATERIALS AND METHODS

Device design

Several specifications for the design of the cell were taken into consideration. The device needed to be kept sterile or be able to be sterilized. Because it is unknown how much fluid can be extracted from each joint, the device needed to hold small quantities of liquid and still be able to function with only 5 – 10 mL of fluid [10]. Finally, the cell needed to use three electrodes and be able to connect to a potentiostat for electrochemical testing. The cell consisted of three parts including a cap, cell body, and electrode cartridge. (Figure 3)

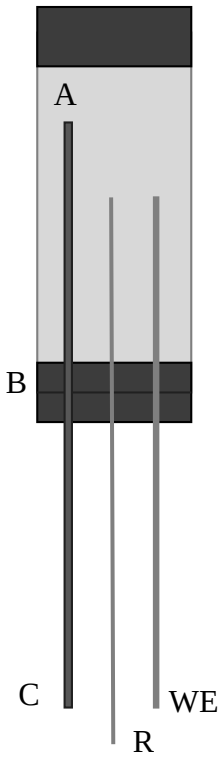


Figure 3: Components of electrochemical cell. (A) cap and cell body made of polypropylene test tube, (B) Electrode cartridge containing the working (WE), reference (R) and counter (C) electrodes.

Cell Body

A custom three-electrode cell with a volume capacity of 4 mL was designed for the testing of small liquid quantities. A 12 mL *Simport* polypropylene test tube was cut in half to use for the walls of the cell. The bottom half was discarded, leaving the top portion with the original "cap friendly" end. A hole to allow gas exchange in the chamber was pierced through the side of the tube approximately 4 mm from the cut edge using an 18-gauge needle. The tube was then wiped down with 70 percent ethanol.

Electrodes

Working electrodes were made out of stainless steel or Titanium wire. Wire lengths of 6 cm were cut and rolled straight. The wire was then polished through several grits to 600 grit with emery paper and rinsed with deionized water and wiped down with 70 percent ethanol [11]. The

reference electrode was prepared using 8 cm of Ag wire. Wire was held over a Bunsen burner to remove oxides and contamination and then wiped with ethanol to sterilize and clean the surface. It was then placed in bleach for 15 minutes to allow AgCl to build up on the surface. A Steadtler carbon 9 mm rod was used for the counter electrode, and the surface was sterilized with ethanol.

Cartridge

The disposable cartridge was made using a *Simport* Pierce-It cap. The cap was wiped down with 70% ethanol and the indentation on the top was filled with 100 percent silicone gel and set aside to cure for 24 hours. The tube facing side of the cap was then also filled with silicon gel and set aside for 24 hours. The electrodes were fed through the cap from top to bottom using an 18-gauge needle for the working and counter electrodes, and a 21-gauge for the reference. The stainless steel and titanium electrodes had 0.49 and 0.56 cm^2 of exposure in the cell and silicone gel was used to seal around each one after placement.

Assembly

The cartridge was fit into the top of the tube and pressed into place. Another *Simport* cap was sterilized with ethanol and fit into the cut side of the tube to close the cell. The potentiostat was connected to the electrode portions that were left exposed out of the cartridge. (Figure 4)

Figure 4: Assembled cell with hole near top for gas exchange.

Electrochemical testing

To assess the cell and its ability to measure changes in corrosion performance of alloys in different solutions, simulated inflammatory solutions were synthesized and used to corrode CoCr, Ti, and stainless steel alloys. Systematic changes in response to different solutions were measured for each alloy. Solutions with increasing complexity from phosphate buffered saline (PBS) to cell culture medium with proteins and the addition of reactive oxygen species were assessed [7]. (Figure 5)

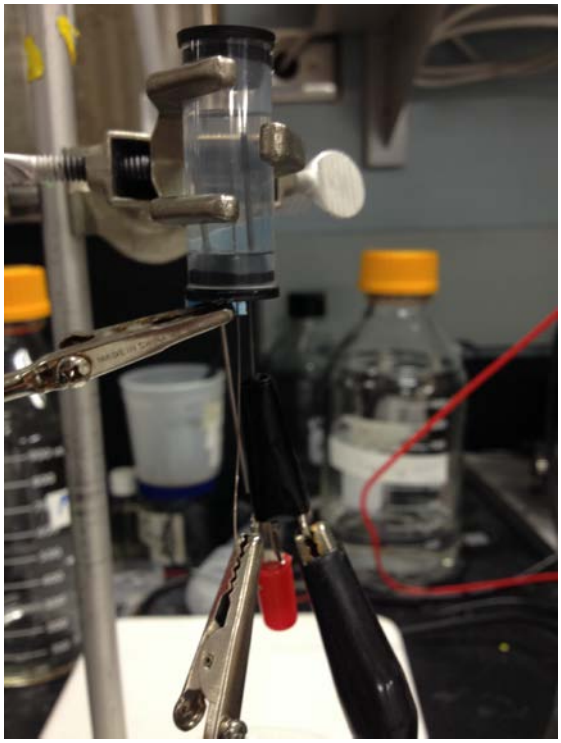


Figure 5: Test setup of functional cell holding PBS solution.

A potentiostat (Solartron 1380) was used to run electrochemical tests and software (Corrware, Corrview) was used to configure controls and collect data from each test. The test methods used included Open Circuit Potential (OCP) and polarization testing. Phosphate buffered saline (PBS) was used as the initial electrolyte solution to determine the functionality of the cell set up and to show any leaks or flaws in the system. PBS with additions of $FeCl_3$ (0.1 mM) and H_2O_2 (10 mM) was then used for each type of test. This solution more closely represents the corrosion conditions inside the synovial joint.

Solutions and alloys to test

Three metal alloys were chosen for the working electrodes and included titanium, cobalt chromium and stainless steel. The stainless steel surface area was measured to be 0.49 cm^2 and the titanium was 0.56 cm^2. Because the metals were in wire form, the surface area was calculated using the cylindrical surface area equation:

$$SA = 2\pi rh + \pi r^2$$

Where r is the radius and h is the length of the wire. The area of the circle is only counted once because there is no bottom of the wire, only sides and a top. The surface area of the CoCrMo electrodes was calculated using the surface area equation:

$$A = 2(wl + hl) + hw$$

Where l, w, and h are length, width, and height, respectively. Just like in the cylinder equation, the bottom of the electrode is not counted.

Along with PBS the series of tests was also run using culture media with Fetal Bovine Serum (FBS, 10%) and $FeCl_3$ (0.1 mM) and H_2O_2 (5 mM, 10 mM, 25 mM) additions to further simulate the conditions inside the inflamed joint[7,10]. The $FeCl_3$ was added into the base solution, and the H_2O_2 was added after five minutes of sitting at OCP. This solution adds proteins and other components to the cell that could potentially hinder or change the functionality of the cell or show different results. Each solution combination was tested three times with the different alloys and an average was taken and graphed for each.

OCP

The OCP of both the stainless steel and Titanium electrodes was monitored for thirty minutes in 4 mL of each type of solution. In the tests that involved H_2O_2, the addition was added after ten minutes to show the sharp voltage increase as a result of the presence of H_2O_2 in the environment.

Impedance

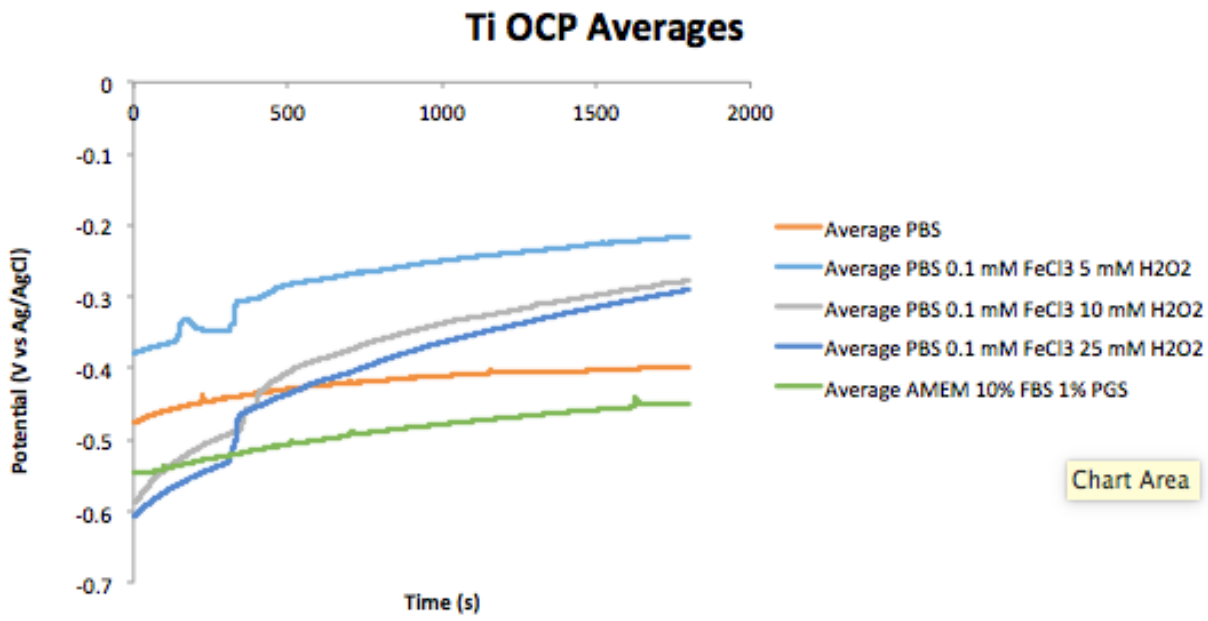
A test was run for impedance to determine the exact surface area of the working electrode [12]. A program was set up with Zplot (Scribner Associates, North Carolina USA) and run through Corrware with reference to OCP.

Polarization testing

After running OCP for thirty minutes with each solution type, the cell was held at -1 V for ten seconds to prevent any spikes in current from interfering with the polarization results. The cell was the scanned from -1 V to +1 V in increments of 5 mV/s.

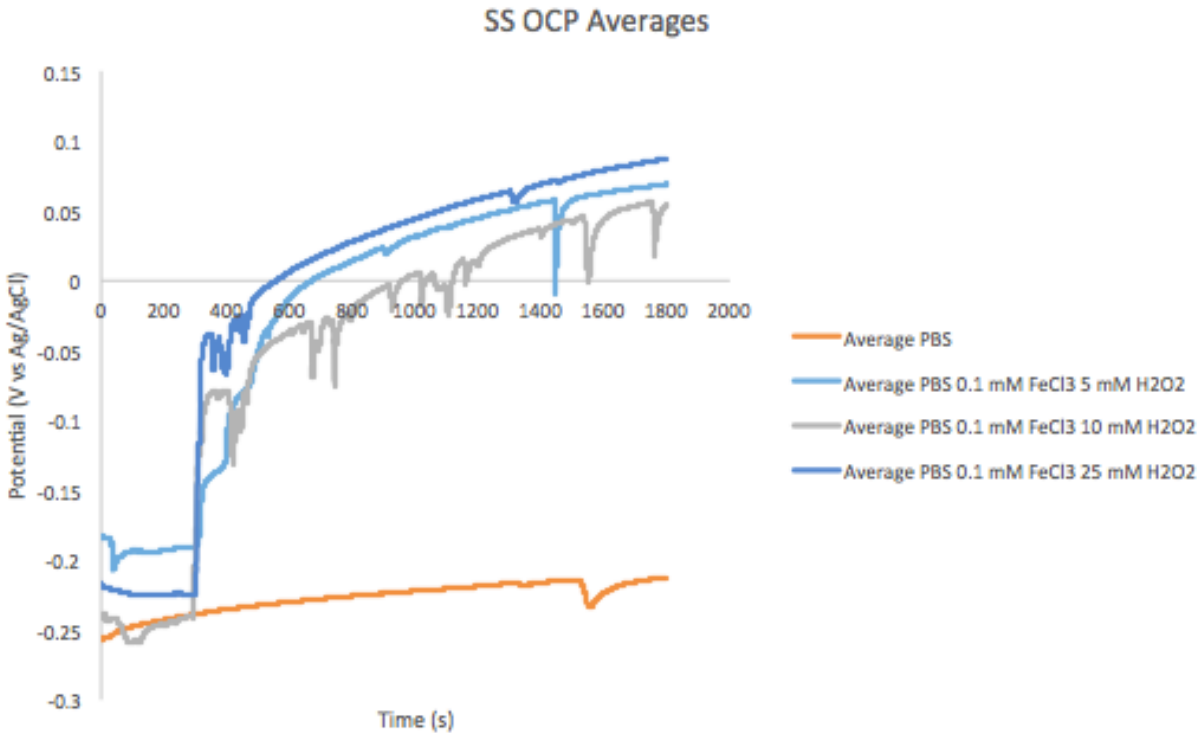
To reuse the cell for testing purposes, the electrode cartridge was detached from the cell body, rinsed with deionized water and wiped dry. The reference electrode was then dipped in bleach for 10 minutes and the working electrode was freshly polished. The cell body and cap were rinsed in deionized water and wiped with 70 percent ethanol.

RESULTS

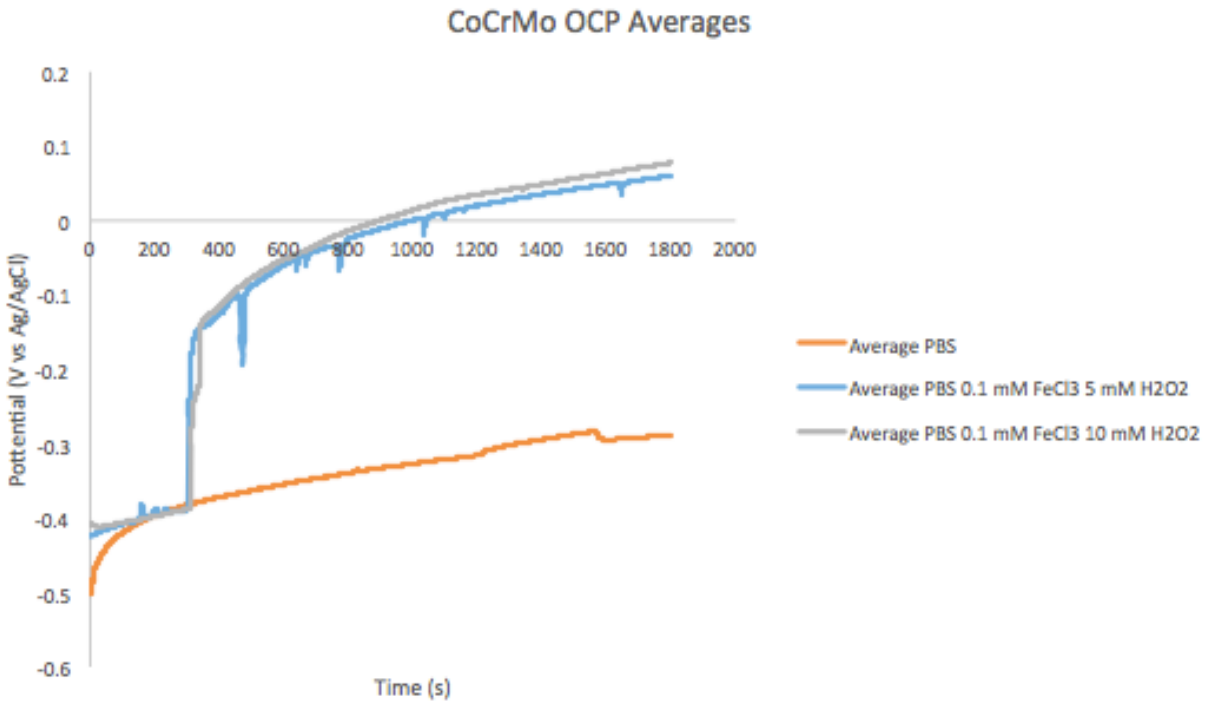


The results of Titanium averages for OCP show an increase in potential when $FeCl_3$ and H_2O_2 are added to the solution. The concentrations of H2O2 appear to play less of a role on OCP , as there is no correlation with concentration and the resulting potential increase. The PBS

(Orange) shows a base line value for OCP under ‘normal’ or “not inflamed’ conditions, as does the AMEM with no additions (Green)

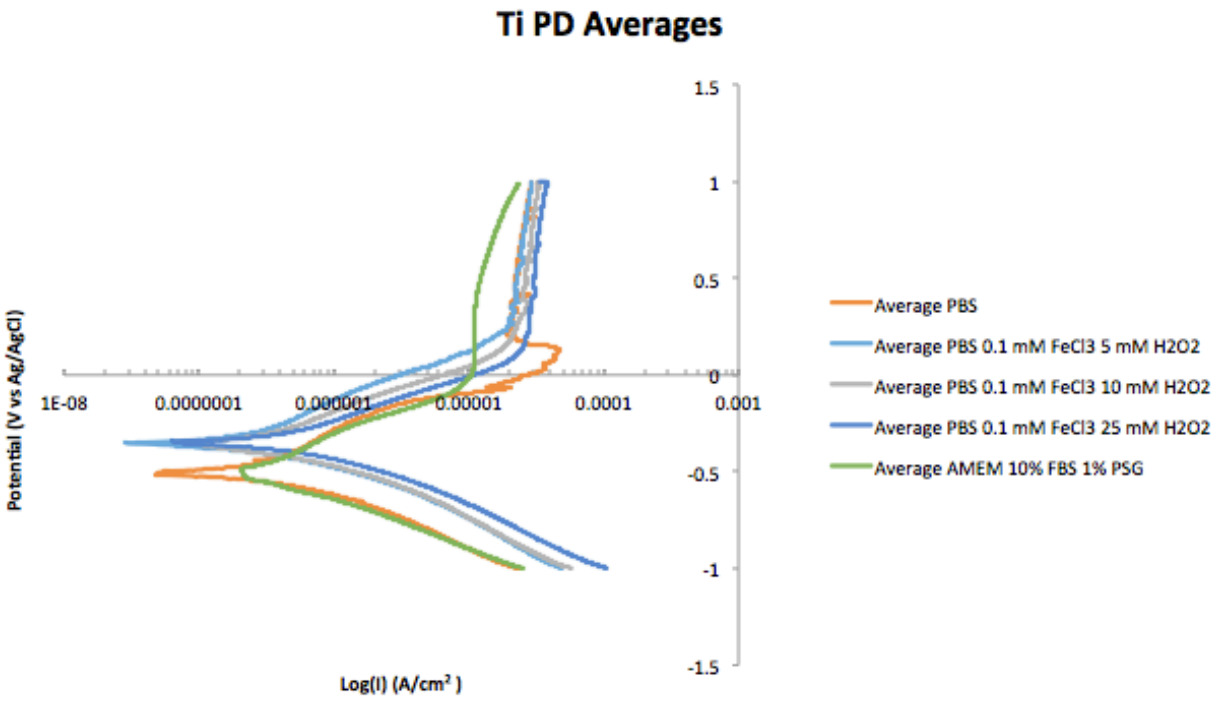


The OCP of the stainless steel after averaging the results of the different concentrations shows a similar pattern to that of titanium, where the addition of Fe and H_2O_2 has an increasing effect on the OCP compared to the baseline condition (orange). Again, there does not appear to be a strong correlation between concentration of H_2O_2 and the voltage value.

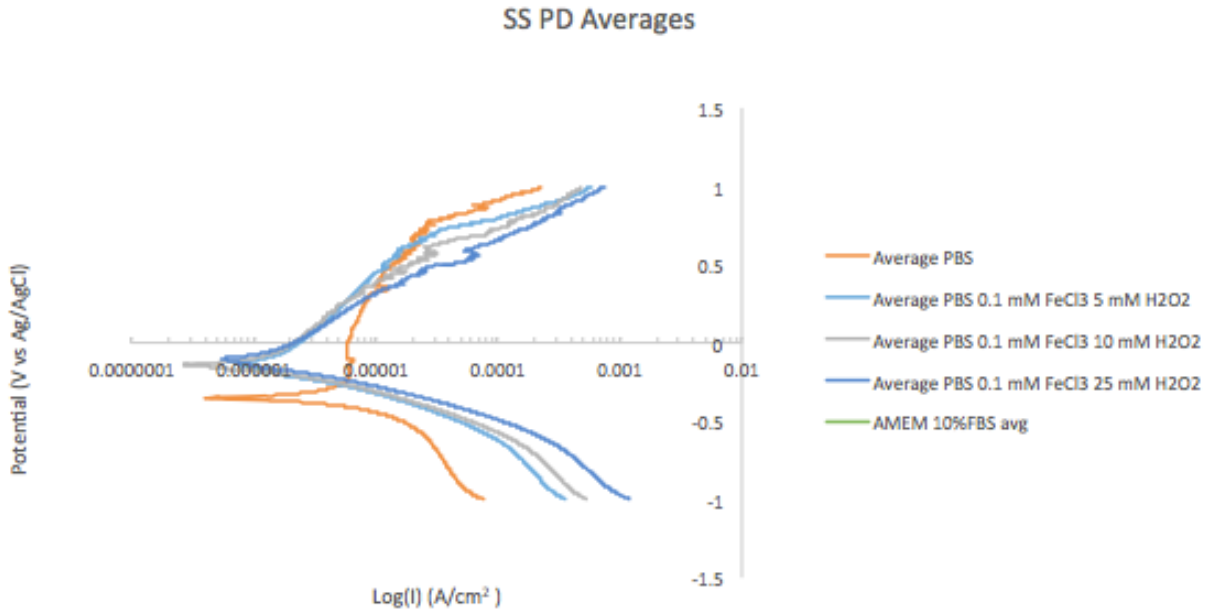


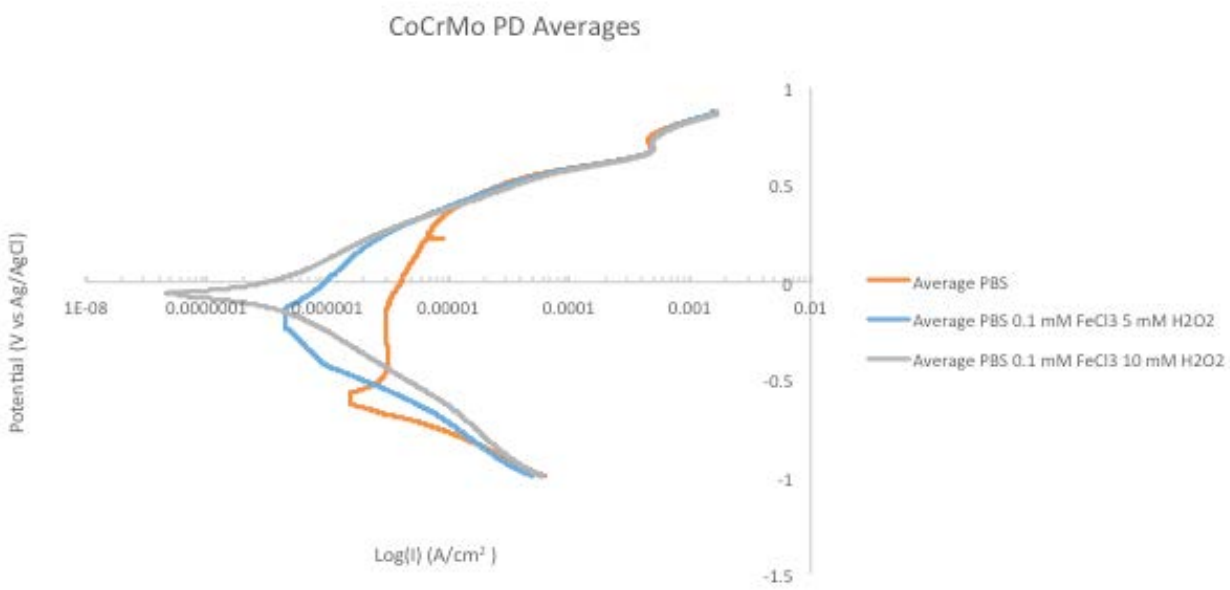
CoCrMo behaves in a similar way to both titanium and stainless steel. The resulting graph of the data reveals that the OCP is also effected by the addition of H_2O_2. Because of time constraints, all testing solutions could not be performed for this material.

In all three of the graphs of OCP there is a spike in voltage upon the addition of H_2O_2. After some time the potential began to level out as it did in the baseline solutions.



Anodic polarization testing revealed that titanium is affected by the addition of Fe and H_2O_2. It can be seen that the current has increased compared to the baseline solution (orange).





Due to time constraints, not all testing was concluded for CoCrMo and stainless steel, however both seem to increase with the addition of H_2O_2, much like that of titanium.

DISCUSSION

Design

A standard design process was followed to complete the electrochemical cell. One of the priorities of the design was to make it sterile. This meant that it either needed to be disposable or able to be sterilized. Electrode reactivity becomes compromised after running a polarization test, and would need to be re-polished before using again. This is a time consuming process, so instead, the electrode cartridge was designed to be disposed after one use, while the body of the cell could be sterilized. A polypropylene test tube was used for the walls because it can be sterilized by ethyl alcohol or an autoclave – which uses steam heat and pressure.

A sealable cap that can be pierced by a needle was used for both the cartridge and the top. Because joint fluid is a biohazard, this will allow fluid to be taken from the patient in a syringe and then directly added to the cell. The use of a syringe will also limit the exposure of the fluid

to the atmosphere. There is a small hole in the top of the polypropylene tube to allow gas exchange in order to prevent pressure build up in the cell, but it was placed very close to the cap and protected by silicone to prevent liquid from getting out.

The electrodes were pushed through the cartridge using a needle and then sealed in place with aquarium glue. Aquarium glue is made out of silicone and is waterproof, inert and bio-safe. This means that it will not interfere with the biology or and electrochemical testing done with the device.

Three electrodes were used in this design : a working, reference, and counter. The working electrode represents the surface (in this case, the implant) that is being evaluated [13]. A reference is used because the electrochemical values cannot be directly measured, they can only be observed with respect to another material. Ag/AgCl was chosen because it has a known electrical potential and can be made to fit into small applications. All of the results of the tests are then scaled to this value. The counter electrode is used to complete the circuit and supplies electrons to the cell [13]. This design used a carbon rod, however, because it is so brittle, a platinum wire may have been a more suitable choice to make the cartridge less fragile.

The cartridge was designed to be at the bottom of the device because the test results depend on surface area of the working electrode. Since the amount of fluid that can be extracted from the joint can vary – this design will allow the electrode to always be completely covered, and therefore the surface area is always the same, no matter how much fluid is present.

How it works

When a metallic implant is placed into the body, it is essentially placing a metal in a salt solution. When this is done, the atoms on the metal surface become oxidized and escape into the solution and the surface is left with electrons [1]. This is called oxidation. (Figures 6 and 7). The

water and oxygen present in the surrounding solution cause a reduction reaction, and the transference of electrons creates a closed electrical circuit that can be measured. Simply put, if the electrical data of the system is known, the chemical conditions of the environment are known, and therefore the state of the corrosion and the oxide on the metal surface are also known.

Oxidation

$$m \rightarrow m^{+} + e^{-}$$

in solution — on metal

$$m + H_2O \rightarrow mO + 2H^{+} + 2e^{-}$$

passive oxide film

Reduction

$$\tfrac{1}{2} O_2 + H_2O + 2e^{-} \rightarrow 2OH^{-}$$

Figure 6. Chemical equation for the oxidation and reduction reactions showing the formation of the oxide.

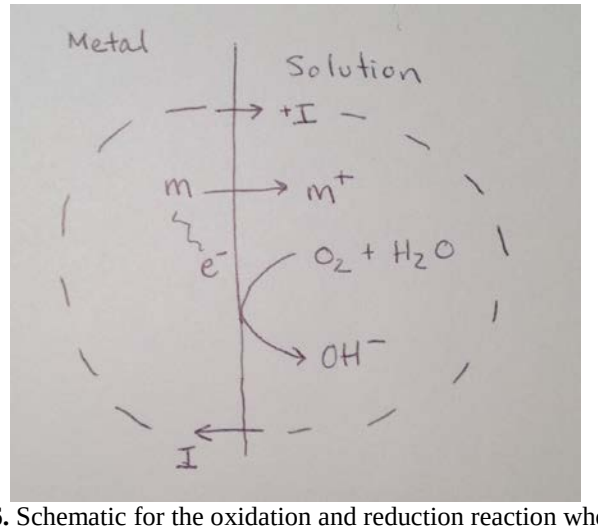


Figure 6. Schematic for the oxidation and reduction reaction where m is a metal atom and m+ is the ion.

In a polarization test, a current is generated as the voltage of the metal is increased. (Figure 8). The voltage versus log of current density is graphed and changes in the oxide can be seen by this graph [5]. The addition of H_2O_2 to this system affects the oxide behavior of the oxide and will shift the graph.

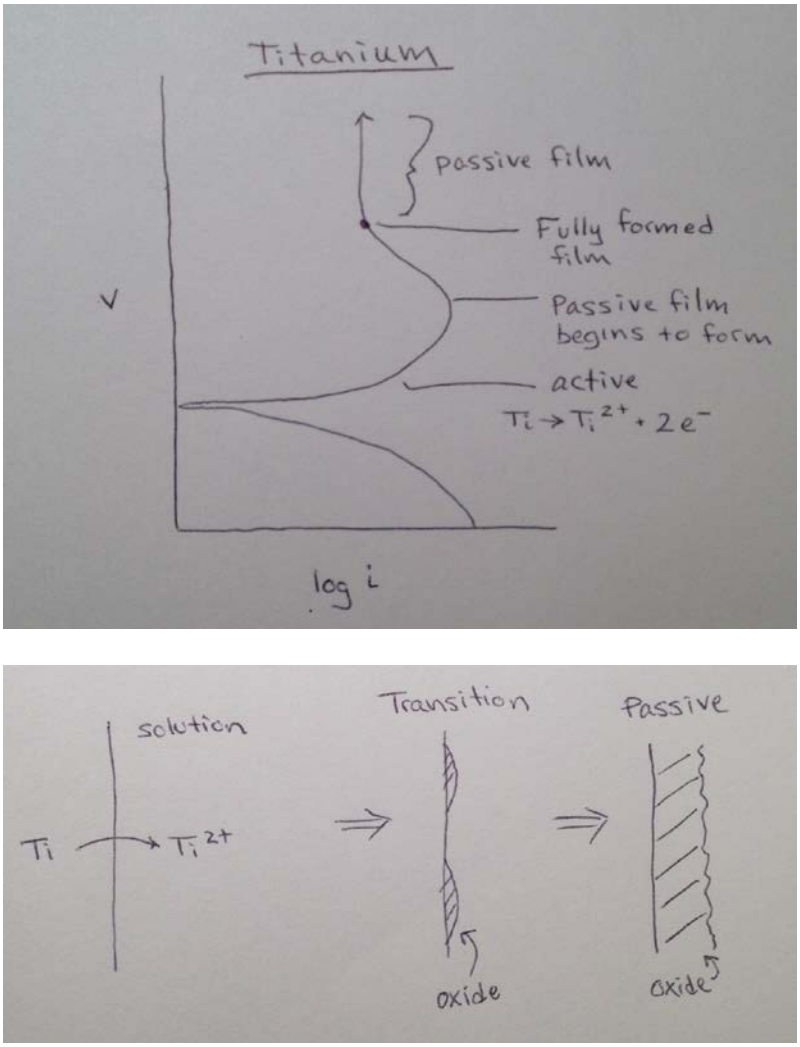


Figure 8. Anodic polarization graph of titanium. As voltage increases the oxide layer on the surface of the metal begins to form.

Test results

OCP values show the metal – solution system when it is at equilibrium. Values that appear higher than OCP indicate an accelerated oxidation reaction, while values lower represent an accelerated reduction reaction. Because the Fe and H_2O_2 additions increased the value of the OCP this means that the implant in this inflammatory environment in the body experiences more rigorous oxidation reactions and this increases its potential to corrode [7].

Anodic polarization curves show the behavior of the formation of the oxide layer on the metal [5,14]. The changes in the graph with the additions indicate that the H_2O_2 is affecting the oxide. Because the oxide protects the metal surface from the surrounding environment, the exposure of the surface of the metal to the solution will allow for corrosion.

CONCLUSION

A device was successfully created to run electrochemical tests of small amounts of fluid. It was created to be sterile upon use and to also keep a sterile boundary between the joint fluid and the outside environment. The design also allowed for easy joint fluid addition and connection to a potentiostat for evaluation.

The results of the electrochemical testing indicates that the presence of inflammatory solutions have the ability to affect the corrosion potential of the implant through the oxidative burst reaction.

Future work on this project will include finishing the testing with stainless steel and CoCrMo in the remaining solutions. The results can be used to create a diagnostic tool for an

inflammatory corrosion index in humans, and eventually the corrosion level of the implant can be assessed based on the inflammatory state of the joint fluid, rather than surgery.

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