SAND2015-9741R

# Handheld Microneedle-Based Electrolyte Sensing Platform

## FINAL REPORT

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**Period of Performance: June 11, 2015 to October 15, 2015**

**SNL Project 27202**
**New Mexico Small Business Assistance (NMSBA) Program**

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# Handheld Microneedle-Based Electrolyte Sensing Platform

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**Statement of Work:** Sandia National Laboratories will provide technical assistance, within time and budget, to Requester on testing and analyzing a microneedle-based electrolyte sensing platform. Hollow microneedles will be fabricated at Sandia and integrated with a fluidic chip using plastic laminate prototyping technology available at Sandia. In connection with commercial ion selective electrodes the sensing platform will be tested for detection of electrolytes (sodium and/or potassium) within physiological relevant concentration ranges.

**Results:**

A combination potassium ion selective electrode was purchased from Cole Parmer and tested for efficacy to detect potassium in synthetic interstitial fluid in a large volume beaker as presented in Figure 1. The formulation of the synthetic interstitial fluid composition consisted of 2mM $CaCl_2$, 5.5mM glucose, 10mM Hepes buffer, 0.7mM $MgSO_4$, 123mM NaCl, 1.5mM $NaH_2PO_4$, 9.5mM Na-gluconate and 7.4mM sacharose (Methods section of thesis from University of Berlin: http://www.diss.fuberlin.de/diss/servlets/MCRFileNodeServlet/FUDISS_derivate_000000003040/4_04MaterialandMethods.pdf).

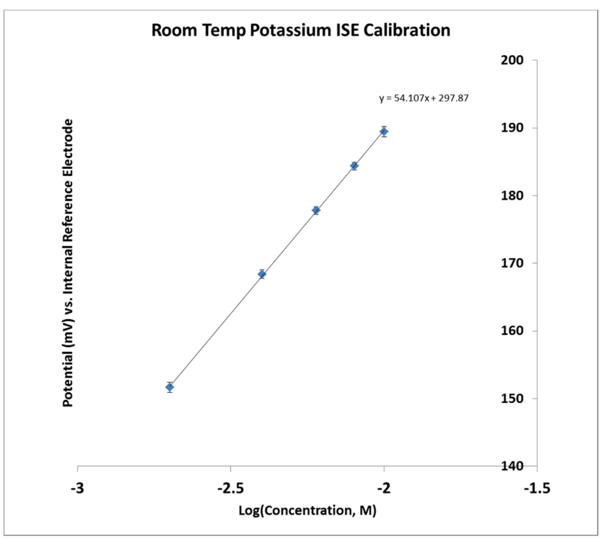


**Figure 1.** Analytical results from testing of commercial ion selective electrode in synthetic interstitial fluid.

A commercial pH probe station interface was used to take measuremetns at an open circuit potential every minute for 10 minutes over 0-10 mM potassium spikes at room temperature. Three tests were performed over a three day period with great consistency demonstrated and the representative results shown in Figure 1. A near immediate sensor response time was observed for each potassium spike. A linear response was observed over the concentration ranges measured with a ~54mV/decade response indicating typical Nernstian behavior and proving that the commercial electrode can accurately detect potassium over physiologically relevant concentration ranges which is typically 3.5 – 5.2 mM potassium.

The sensor was then tested in a small volume (10 µl) that is anticipated to reflect the amount of interstitial fluid that is able to be extracted in a human subject, presented in Figure 2. Comparable results were seen over the same potassium range as the large volume beaker experiment indicating that the surface area of the working part of the electrode is suitable for detecting the volume of fluid expected from real samples. While it is unknown exactly the volume of interstitial fluid that can be extracted using microneedles the 10 µl range was used as an approximation based on preliminary experiments done in pig skin using single microneedles. The true volume able to be extracted is the subject of ongoing research using human subjects in collaboration with the Department of Emergency Medicine at the University of New Mexico.

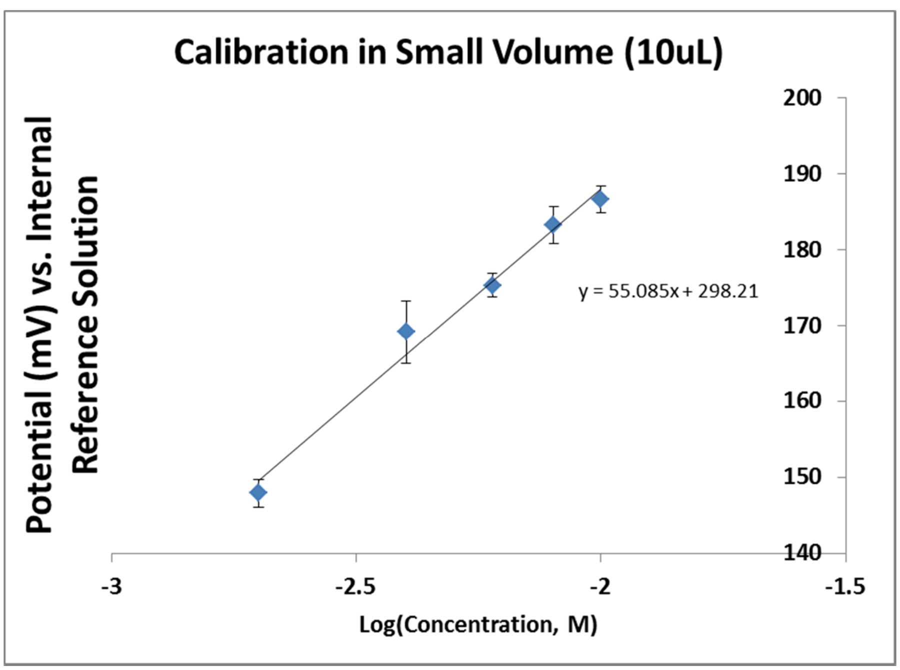


**Figure 2.** Calibration of the commercial ion selective electrode in small volume experiment

Similar experiments were performed over the same concentration ranges of potassium with a Fluke multimeter and compared to the pH probe station interface at a physiological temperature of 37 C presented in Figure 3. The commercial pH probe station is bulky and therefore incompatible with real world measurements, which is why the small and portable Fluke mulitmeter was tested as it is more suitable for integration with the hand held device. A caveat exists however in the fact that the commercial pH probe station has existing calibration software built in where the Fluke mulitmeter requires in-house software to be written to perform the same tasks. As can be seen, both meters had linear responses over the range of potassium measured. However, a significant shift in open circuit potential is also observed. This is due to the standard calibration software in the commercial pH meter over temperature differences as measured between an internal thermocouple. This is significant as there is expected to be a likely temperature shift that occurs when measuring in live subjects as interstitial fluid is extracted out of the body. Therefore when the miniature multimeter is eventually incorporated into the final device a special calibration software will have to be written (combined with an internal thermocouple) to account for temperature variations. This is however outside the scope of the current NMSBA.

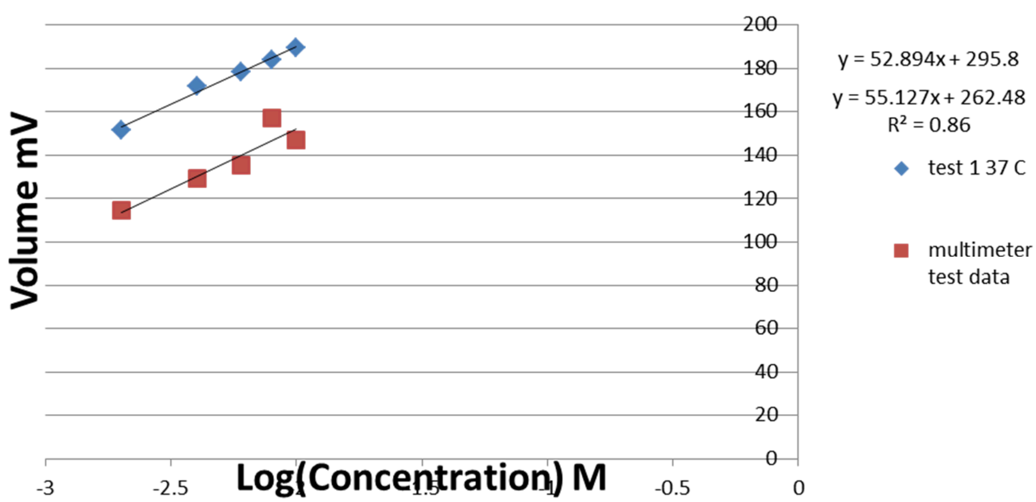


**Figure 3.** Comparison of Fluke multimeter to pH probe station response at 37 C over 0-10 mM potassium in synthetic interstitial fluid.

Computer renderings of the handheld portion of the device are presented in Figure 4. Salient features include 1: plastic casing, 2: miniature multimeter and 3: commercial potassium ion selective electrode (A). The device fabricated at Aquila and was designed as ergonomically accessible when held, even if the user is wearing a cumbersome glove as is the case with healthcare workers in many infectious disease scenarios. The multimeter snaps into place and fits into an open window fabricated in the front to have access to read the multimeter screen and also be able to be operated through a simple push button. The ion selective electrode fits into a port in the bottom that has four protruding posts designed to mate with the disposable microneedle cartridge. The fully assembled rendering is shown in Figure 4B.

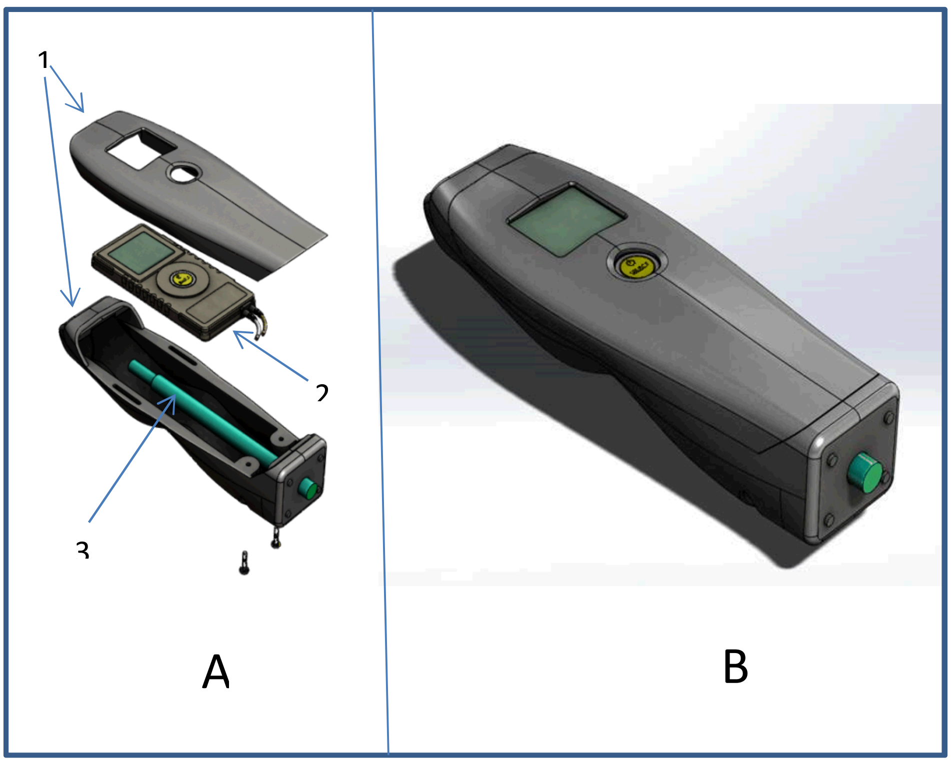


**Figure 4:** A) Blown up rendering containing 1- bottom and top casing of handheld portion, 2- multimeter and 3- internal potaasium ion selective electrode. B) Rendering of completely assembled handheld portion.

The disposable microneedle cartridge was fabricated in a multilayer 3-channel microfluidic fixture via $CO_2$ laser machining of plastic polymethylmethacrylate and polyethyleneterapthalate laminates by ablation. Acrylic adhesive coatings on the plastic sheets provided a route to multilayer structures via simple hydraulic pressing at room temperature presented as renderings in Figure 5 and fully fabricated in Figure 6. The design is engineered to snap into the bottom portion of the handheld analyzer and contains a vacuum port as well as a centered opening for placement of microneedles. It was also designed to interface with the extruded portion of the potassium sensor such that a minimal volume of fluid (down to low µl levels) would be necessary to cover the working portion of the electrode. The fully fabricated handheld microneedle-based electrolyte sensing platform containing internal potassium ion selective electrode, multimeter, and fitted with disposable microneedle cartridge are shown in Figures 7.

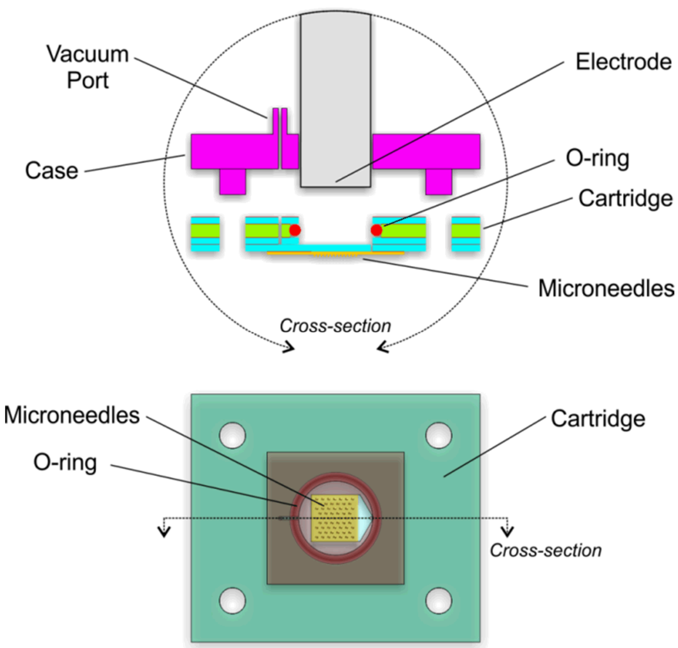


**Figure 5:** Rendering of disposable microneedle cartridge

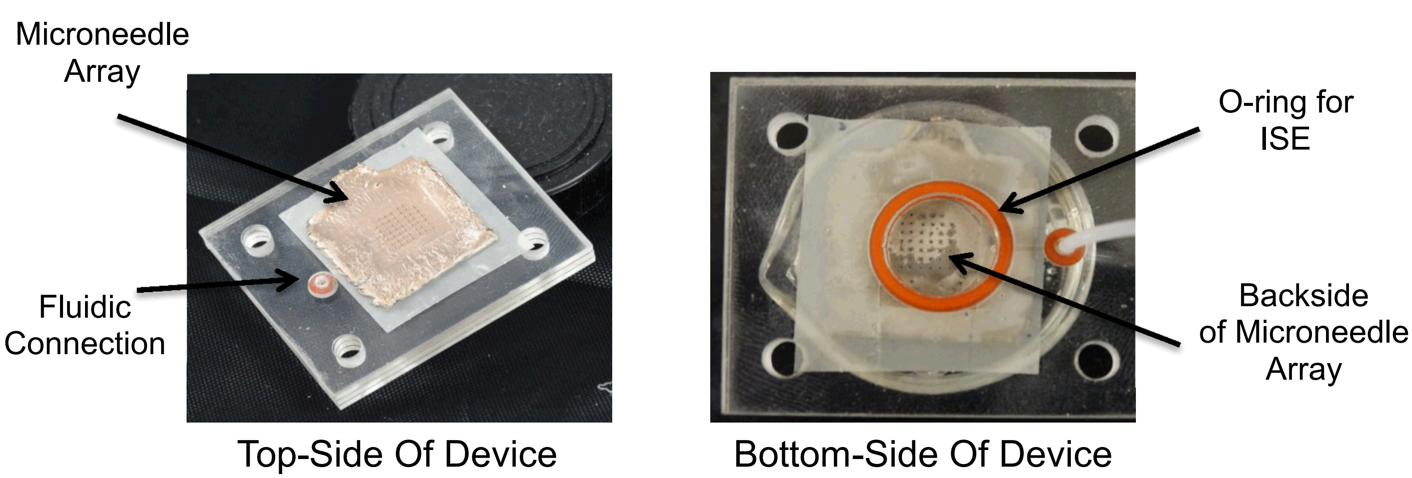

**Figure 6:** Fully fabricated disposable microneedle cartridge

**Figure 7:** Fully fabricated handheld microneedle-based electrolyte sensing platform fitted with disposable microneedle cartridge.

**Conclusions and Future Perspective:**

Significant progress was made towards the construction of a handheld microneedle-based electrolyte sensing platform in accordance with the statement of work put forth in the original proposal under the scope and budget of the project. Firstly, a commercial potassium ion selective electrode was tested for efficacy towards detecting physiologically relevant concentrations of potassium in synthetic interstitial fluid and tested for suitability to analyze the small volumes of interstitial fluid that are expected to be extracted in live subjects. A small multimeter was also tested in connection to the ion selective electrode to take measurements. A plastic laminate cartridge was then fabricated that contained a microneedle array that could interface with a handheld device. Finally, a 3D printed handheld casing was fabricated at Aquila that contained the ion selective electrode and multimeter that was designed to be ergonomically handled by a user.

The actual testing of the device in live subjects and the complete integration of all components was beyond the scope of this project. Rather, the proof of concept of the design was demonstrated. The ultimate goal of realizing the autonomous integrated sensor will require further advancements including, but not limited to, internal electronic connections of electrode and multimeter, the design of software for temperature and calibration control, a pumping mechanism to control interstitial fluid extraction and Bluetooth capabilities to electronically transmit data. These key aspects will be pursued for future directions and will be dependent on evolving results from current projects as well as funding resources.