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Using Transmission Properties to Determine Blood Glucose Levels

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***Abstract*— A non-intrusive technique based on modeling the body as a transmission channel was tested in vitro and was shown to perform equally with a commercial OTS glucose meter on saline-glucose solutions of concentrations of glucose from 30 to 300 mg/dL. The technique uses an initial frequency sweep to locate a frequency where a resonant response occurs. At that position the phase is changing rapidly and can therefore be used more easily to measure a phase difference. This sweet spot can be natural or assisted. Present efforts are toward a system which uses a feedback amplifier with a low phase margin in order to easily find the the region of rapid phase change. Initial tests measuring known glucose concentrations with an OTS glucose meter and then using the proposed technique were shown to correlate with the actual concentrations with an $R^2 = 0.9879$ and $R^2 = 0.9952$ respectively (with one outlier data point removed). Further tests are being conducted in vitro on whether other interfering agents may disrupt results. The ultimate goal of the development of this technique is to fabricate a device that is worn externally on the upper arm and does not require blood for testing. A device is being built and is scheduled for human subject testing in Summer 2013. Some results of human testing may be available at the EMBC conference. Human testing will involve measurements done with our device against an OTS glucose meter and results compared. The future goal is to refine the device so that it can be worn 24 hours a day and will automatically test the wearer at a user specified interval such as 10 or 20 minutes by transmitting a low power signal for a few microseconds. Power levels are still being determined but, in simulation, nano-watts was sufficient for the distance needed to travel which is orders of magnitude less than present day cell phones. To evaluate safety of the system, 3D electromagnetic simulations are being carried out with the device positioned strapped to the upper arm. Simulations show transmission along the targeted paths which suggests that affective glucose sensing is possible with this device.**

I. INTRODUCTION

A common technique to test blood for glucose levels requires a blood sample that is put through an analysis device. This method has many drawbacks: The fact that blood has to be drawn may make the test uncomfortable to do in front of other people. This and the fact that pricking ones fingers is not a pleasant activity contributes to people not always testing themselves as often as they should. Additionally, the high-cost of test strips may also be a deterrent to regular glucose level testing. Regular glucose testing is the key to keeping glucose levels in a healthy range and preventing serious health issues. In an effort to remove barriers to regular testing, the development of a device based on a new non-intrusive technique to monitor blood glucose has been designed. The system evaluates glucose levels by watching the behavior of a signal that has been transmitted through the human body.

The technique introduced in this paper is non-invasive and has shown high accuracy in in vitro testing. The team developing a system using this technology is continuing lab experiments to gather further details of the biological, chemical and electrical mechanisms that are responsible for the success of this technique. In parallel they are building a device that will be used in human testing in May of 2013. Results of the testing should be available for the 2013 EMBC conference. The technique requires the transmission of a MHz frequency signal through the upper arm for an interval of micro-seconds and then observing the received signal. Power levels for the transmitted signal will be orders of μ Watts which is magnitudes lower than that of a cell phone and, in the final device, will only be transmitted at a selected intervals by the user such as 5, 10 or 30 minutes.

Other related research in this area includes [2] where a frequency sweep was done and the dielectric constant change was observed. Change in the dielectric constant changes the speed that a signal travels through a medium and therefore the time of arrival and magnitude of phase difference between transmitted and received signals. This is related to the behavior that we observed in 2010 that inspired this approach but the work reported in this paper includes a simple mechanism to more easily observe the exact glucose levels plus the mechanism used here is not simply a result of the change in the dielectric constant. It is thought that bioimpedance is also a contributor. [3] finds the relative dielectric constant for sugar-water solutions at a range of frequencies but extremely high sugar concentration were used and the frequencies examined were in the 1 to 5 GHZ range. Low GHz range devices may have interference from mobile devices using 3G and 4G technologies and other common devices such as microwave ovens (2.45GHz). Technology has advanced enough that GHz transmitters are relatively easy to build so the creation of a device to run at these frequencies is not as problematic as it may have been at one time but research on safety of devices has suggested that devices that are to be worn for an extended period of time should pay attention to power levels and frequency usage [4]. Though [4] is generally aimed at cellphone frequency ranges, the fact that information about the dangers of extended exposure to electromagnetic transmissions at cell phone frequencies should inspire us to find lower power, shorter duration and safer frequencies to use in sensor devices.

Other non-obtrusive techniques are being investigated but are not as directly related to this work. These include electromagnetic coupling-based sensors [5], work which

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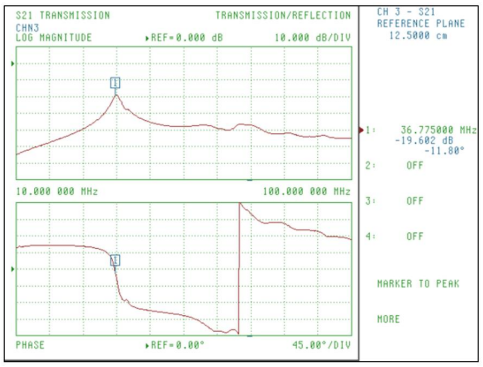

Fig. 1. Example of data capture for use in determining blood glucose.

use permitivity changes [6], Raman spectroscopy [7], and bioimpedance [8].

Hereafter, the technique described in this paper will be called BBGSS (bioelectromegnetic blood glucose sensing system).

II. Behavior of interest and testing

The behavior that provides the glucose information is the phase value of S21. S21 is the scattering parameter (S-parameter) associated with a ratio of the signal out over the signal in in systems where traveling waves are scattered or reflected by the component under investigation. To gather data, the frequency was swept and phase data was taken. Most of the sweep range gave little to no information on the glucose level so selecting the point at which to sample phase information is crucial. The sweet spot found is where a *resonant* frequency of a sample is found. An example reading is shown in Fig. 1 and shows a resonant frequency of 36.775MHz. To detremine glucose levels, the resonant frequency is found for a user when they are in the center of their normal range and, when their glucose level changes, the phase at that frequency changes as a directly correlating value to the glucose level. Plotting the phase values against concentrations provides a repeatable, accurate and wide range correlation in vitro as shown in Fig. 5 [1]. Tests will also be done to verify if the effects of skin can be identified and then removed by receiving a transmission through a path with less opportunity to travel through blood and body fluid.

The sweet spot can be *assisted* - a field of research that is being pursued by our group. *Assisting* the sweet spot consists of putting the arm in the feedback loop for an amplifier with a small phase margin. The spike in amplitude caused by the small phase margin makes identification of the sweet spot easier and can further be improved by placing both the dominant and secondary poles near each other.

III. Lab Testing

In lab testing, four types of solutions were used. Distilled water, saline solutions of various concentrations, glucose solutions of various concentrations and glucose/saline mixtures of various concentrations. Distilled water and saline solution did not display the behavior shown for the glucose mixture. Additionally, the technique used here showed not to be affected by saline levels in the glucose mixtures. Results for in vitro testing agreed for the pure glucose solution and for the glucose saline solution.

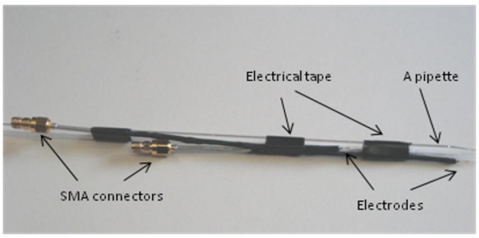

Fig. 2. Electrodes used in graphed data.

Initial testing was done in an electronics lab where tests were carried out on distilled water, various concentrations of saline solutions, various concentrations of glucose solutions and various concentrations of saline and glucose combined solutions. Care was taken to measure exact amounts of D-glucose (dextrose) and non-iodized salt that were dissolved in distilled water to create the test *"blood"* that had concentration in line with actual values that might be seen in a human [10]. Tests on pure distilled water showed no response to the technique. Tests behaved independently of saline concentration and saline was determined to have no affect on the results. Glucose concentrations used were: 30 mg/dL, 40 mg/dL, 50 mg/dL, 60 mg/dL, 70 mg/dL, 90 mg/dL, 110 mg/dL, 130 mg/dL, 180 mg/dL, 200 mg/dL, 220 mg/dL, 250 mg/dL and 300 mg/dL. 8.41 grams of Mortons table salt (without iodide) was mixed with 100ml of distilled water to prepare a concentrated saline solution. Distilled water was added to it to prepare 8.12mg/ml saline solution which is the normal saline level in blood [10]. After testing the pure glucose samples, 5 drops of 8.12mg/ml saline solution were added to each sample.

Electrodes were fabricated such that cables were shielded and the distance between the electrodes were fixed as shown in Fig. 2. Tests were carried out on the VNA (vector network analyzer) on each sample as shown in Fig. 3. Tests were first done using an OTS hand held glucose sensor (Kroger blood glucose monitoring system) against the various concentrations of solutions. Results are shown in Fig. 4. Correlation between the concentration of the solutions and the readings off the glucose meter were recorded and an R^2 was found of 0.9879.

Next the same solutions were tested using BBGSS. The results are shown in Fig. 5 and though there was only one outlier, in this particular case, two points were removed resulting in an R^2 of 0.9952.

IV. Simulation Testing

In order to better understand the mechanism that allowed this accurate sensing ability, 3D electromagnetic FDTD (Finite-difference time-domain) simulations were done on a virtual beaker of blood and on a 3D model of an arm. In

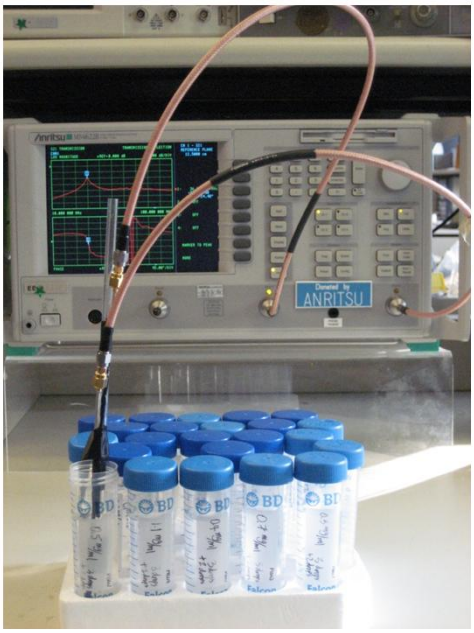

Fig. 3. Testing setup and spectrum analyzer.

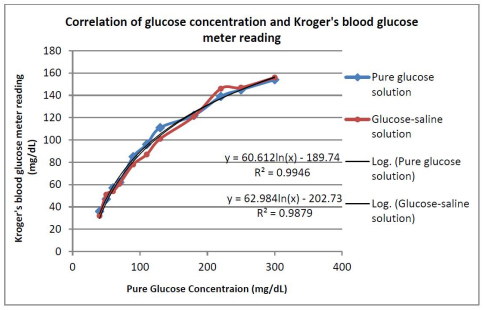

Fig. 4. Two logarithmic trend lines were added to best-fit the data. Krogers blood glucose monitoring system outputs LO for 30mg/dL pure and glucose-saline solution, so 30mg/dL is not included in the graph.

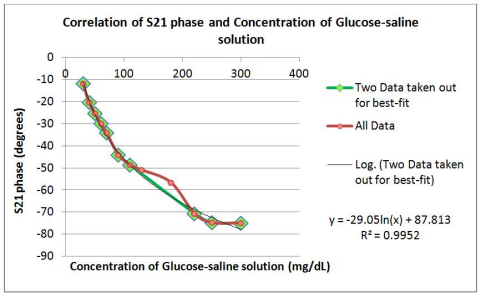

Fig. 5. Two logarithmic trend lines were added to best-fit the data. BBGSS vs solution glucose concentrations.

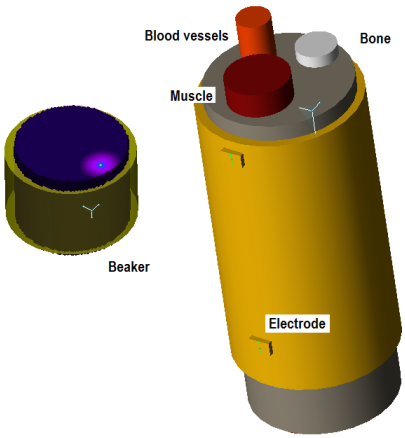

Fig. 6. Simplified models used in investigation of device.

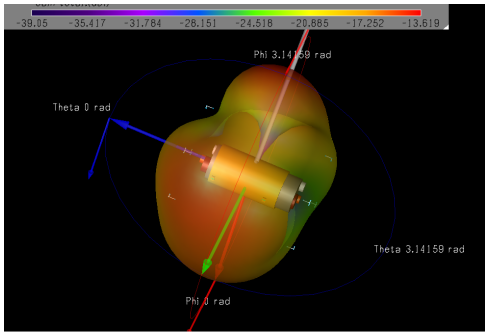

Fig. 7. Radiation pattern from device run at 15mW.

simulation, for the distance that the signal would need to travel, power in the microwatts was sufficient. This is a level of power orders of magnitude smaller than cell phones. This level is also small enough such that it shouldn't interfere with medical equipment. Tests have not been done to evaluate the sensitivity of the device to environmental noise. Examples of models for use for investigating transmission through the arm and for better understanding the behavior observed in the lab (in vitro beaker testing) can be seen in Fig. 6. Simulations are ongoing but preliminary results suggest that signal paths are successfully following paths that would be affected by a change in glucose levels such as blood and muscle.

Safety is a concern for a device that is worn for long periods of time and with recent research into cell phone dangers [12] radiation must also be well investigated. The 3D simulator, with sources at 15mW, produced the radiation pattern shown in Fig. 7. RF dangers have been attributable to frequent changes in RF signals rather than steady contnuous signals which this device would use, but the radiation from the device must not be ignored. The electrodes can be seen on the front of the model. What this result means is yet to be evaluated but standards [11] have been set and are available to analyze the dangers that such a field may produce.

V. Sensor Device

A mock up of the device is shown in Fig. 8.

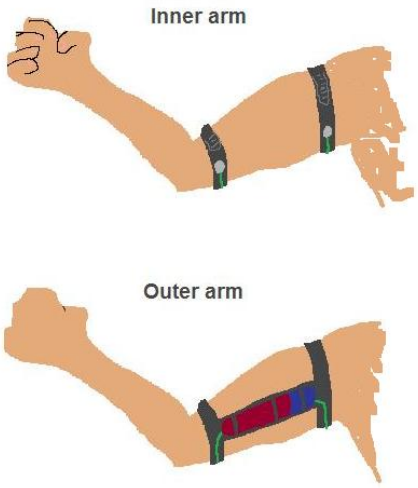

Fig. 8. Mock up of glucose sensor.

Timers will be set to only turn on the device for less than 10 milliseconds at an interval that can be set by the user and actual transmissions will be a few microseconds or less. A user may set the device to test, for example, every 10 or 30 minutes as well as having a manual button so the user can test if needed at times off the schedule. The short amount of time that the device will run will guarantee long battery life.

VI. Human Subject Testing

Human subject testing will be carried out upon completion of the device. Some results may be available at the 2013 EMBS conference in Osaka, Japan.

VII. Conclusions

A promising method for an unobtrusive measurement of blood glucose has been proposed and verified in vitro to agree with an OTS commercial glucose tester with an an $R^2 = 0.9952$ and $R^2 = 0.9879$ respectively when compared to the actual glucose concentrations.

VIII. Future Topics

Research is continuing in our group into assisting response, comfort and in electrode research to make the glucose testing device 24/day wearable.

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