GluMo: A Noninvasive Blood Glucose Monitor

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***Abstract*—Diabetics are used to pricking their fingertips in order to check their glucose level. In an effort to sunset that practice, Santa Clara University's Ethical, Pragmatic, and Intelligent Computing (EPIC) Laboratory has envisioned, designed, and prototyped a portable noninvasive glucose monitoring medical instrument which we have dubbed GluMo. In place of a drop of blood GluMo uses Infrared (IR) light emitters and receivers as part of a small form factor Internet of Things (IoT) medical instrument which calculates the amount of the IR wave's interaction with glucose molecules within the blood stream. The information is then transmitted to a database for tracking, history building, and data visualization for the patient (and potentially the patient's doctor if authorized). Since current single droplet blood glucose meters are attainable as cheap as 10 USD, in order to keep GluMo's cost under 100 USD without diminishing the accuracy of the reading outside of an acceptable bounds, Near Infrared (NIR/IR-A DIN) emitters at the 1300 nanometer (nm) wavelength and corresponding receivers were chosen for the prototype. The choice of 1300nm NIR/IR-A comes from the fact that 60% of human blood is water (H_2O) and 1300nm NIR/IR-A has the largest positive difference between its absorbance in glucose and its absorbance in water among the other wavelengths of IR in the NIR/IR-A range.**

Keywords–Blood Glucose Monitor; Infrared (IR); Internet of Things (IoT); Medical Instrumentation; Non-invasive.

I. INTRODUCTION

Diabetes is a chronic disease caused by an inherited and/or acquired deficiency in the production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. Such a deficiency results in increased concentrations of glucose in the blood, which in turn damage many of the body's systems such as the vision and digestive systems, as well as organs such as the heart, blood vessels, nerves, kidneys, and even skin [1]. Diabetes is thus the seventh leading cause of death in the United States as it is a factor in causing serious health complications including heart disease, blindness, kidney failure, and lower-extremity amputations [2]. According to the International Diabetes Federation, in 2017, over 425 million adults suffered from diabetes. This number is estimated to increase to over 629 million within a generation (2045) [3].

With regular glucose monitoring, patients can maintain normal glucose levels and thus can prevent or delay the aforementioned diabetes-related complications. The current method for monitoring blood glucose levels requires a drop of blood to be obtained by pricking a finger tip with a retractable needle. However, this method is invasive, painful, and sometimes messy for the users. It can also cause infections over time with regular use [4] due to the usage of un-sterilized needles, repeated usage of needles which were designed for single usage, or the sharing of needles/prickers between patients.

The replacement of this painful, messy, and unsafe method of blood glucose monitoring is thus under much research and development as is explored in the Related Work Section below. Sections II and III will cover the consumer needs and existing efforts respectively. Section IV will delineate GluMo's design and implementation and Section V will report on GluMo's preliminary results. Finally, Section VI previews the many redesigns, improvements, and additions currently under research and development at Santa Clara University's Ethical, Pragmatic, and Intelligent Computing (EPIC) research lab which aims to create GluMo's Minimal Viable Product (MVP).

II. CONSUMER NEEDS

With a significant and rapid increase in the prevalence of type II diabetes in the world's population, the ability to continuously detect the amount of glucose in the blood is particularly relevant. Diabetics must be able to quickly and accurately test their blood glucose level in order to appropriately regulate their blood sugar level in response. Current single drop blood glucose meters allow the patient to self-monitor their blood glucose levels regularly throughout the day in an accurate way. However, because they must directly analyze blood to determine its concentration of glucose, patients are forced to prick their fingers for each reading, making monitoring blood sugar an inherently noncontinuous, invasive, painful, and potentially unhygienic process. In addition, the single-use test-strips required by these meters represent an ongoing expense for the patients, which is especially costly for those requiring multiple tests throughout the day. The quality of the test-strips does also effect the accuracy of the blood glucose level readings especially if damaged or expired.

Therefore, although currently available meters allow patients to accurately meter their blood glucose concentration, they do not make the experience pleasant nor completely safe. Pricking the skin for the extraction of blood does pose a potential health hazard. The finger pricker's needle may accumulate microbes and/or viruses and thus inject the patient with them inadvertently. Also, patients report that to save money they often reuse their prickers' needles even up to several days or a week. The pricking needle is also not considered safe for children and can be very harmful if used improperly. The needle, just for instance, is capable of damaging the eye if accidentally or maliciously used in that area.

Therefore, what diabetic patients need, is a continuous, painless, hygienic, and safe alternative which also does not incur an indefinite cost of test-strips and needles.

III. RELATED WORK

As reported by researchers McNicoles and Coté [5] back in the year 2000 ”over 100 small companies and universities were working to develop noninvasive or minimally invasive glucose sensing technologies". Yet, a 2019 search of online retailers such as Amazon, Ebay, and Alibaba results in a scant number of extremely expensive devices such as the Glucose Wizard [6] at a price tag of nearly 1150 USD or OMELON B-2 [7] at a price tag of nearly 400 USD and an overarching number of reviews which report the device's inaccuracy in measuring blood sugar levels yet doing well as a blood pressure meter.

Glucose detection using IR spectroscopy is not a new discovery [8]. In fact, among the aforementioned 100 ventures of the two past decades, McNicoles and Coté [5] report that the optical methods for measuring glucose levels had the biggest share. More specifically, they indicate that the NIR/IR-A DIN (DIN standing for the Deutsches Institut für Normung or the German Institute for Standardization) region of the infrared optical spectrum has been the primary region of focus in academia and industry as it has the least IR radiation absorbance in water in comparison to the other IR spectrum regions such as the short-wavelength IR (SWIR/IR-B DIN) and mid-wavelength IR (MWIR/IR-C DIN) regions. However, much of the early work in the NIR/IR-A have been of purely proof-of-concept nature and thus have used large and relatively expensive bench-top machines [9] such as the Fourier Transform Infrared (FTIR) [10] instruments and grating spectrometer [11] instruments.

Many researchers have also suggested that the thickness of the human skin can cause the scattering of the IR signal. For instance in 1982, researchers suggested measuring the glucose level of the aqueous humor of the eye as a measure of the blood glucose concentration in the blood [12]. They indicated that this would lead to the development of noninvasive blood glucose meters for public usage but as of 2019 no such publicly available devices have been found in the market by the authors.

In a different approach, GlucoTrack is a noninvasive non-IR solution through combining ultrasonic, electromagnetic, and thermal technologies for the measurement of glucose in the blood through the ear lobe [13]. However, because the device is so close to the patient's ear, and the fact that numerous studies such as [14], [15], and [16] exist which link ultrasonics to human ear damage and thus hearing degradation, the device has the potential of damaging the eardrum due to its continued bombardment with ultrasonic waves. More time and usage data are necessary to ascertain the true health effects of the device on longtime users.

IV. Design and Implementation

GluMo is a multi-phased research project. Phase 1, which will be expand on in this section, was the proof of concept and prototyping phase. Phase 2 is the MVP phase in which the size of the instrument is reduced to pocket-sized and potential IR frequency changes outside of NIR/IR-A are explored for further increasing accuracy. Much work on this phase has also been completed or is near completion. However, a thorough cost-benefit analysis will contrast the accuracy gain of the system against the higher cost of the non-NIR/IR-A LEDs which will need to be used instead. And phase 3 consists of a robust human subject field testing of GluMo beyond the laboratory setting which included carefully crafted test tubes containing precise glucose solutions. The inherent uncertainty and messyness of the real world will thus help fine-tune GluMo's design in preparation for the next phase. Lastly, phase 4 is the further reduction of the size to a system on a chip for the incorporation of the bio-medical instrument within common wearables such as smart watches.

A. Electronics

The electronics of GluMo consists of 2 closed circuits. One for an IR emitter at the 1300nm wavelength, and another for an IR receiver - a photodiode designed to be able to detect IR signals around 1300nm. The choice of 1300nm NIR/IR-A is due to two separate requirements of the system: low cost, and accuracy. Since current single droplet blood glucose monitors are purchasable from online retailers as cheap as 10 USD, in order to satisfy the market imposed requirement of keeping GluMo's prototype's cost under 100 USD, the emitter chosen for the prototype needed to be a Near Infrared (NIR/IR-A DIN) LED as LEDs in this range are attainable off the shelf at under 20 USD.

However, another requirement for the GluMo prototype is to maintain a glucose measurement accuracy within an acceptable bounds. Due to the fact that 60% of human blood is water (H_2O) and that among the other wavelengths of IR in the NIR/IR-A range the 1300nm NIR/IR-A has the largest positive difference between its absorbance in glucose and in water [17], the 1300nm NIR/IR-A satisfies the requirement for maintaining a glucose measurement accuracy within the acceptable bounds.

B. Software

Arduino C code is used to control the instrument, to analyze the data from the IR receiver, and to transmit the results to a computer for analysis. Using built-in Arduino functions, 1000 voltage-readings from the photodiode are averaged and after observing 10 of these values, the most frequently occurring value is recorded. Furthermore, a delay of 1 second between readings is established and the voltage values from the IR receiver are converted to percentage of transmittance and then inverted into absorbance. These absorbance values are then converted to blood glucose values given an experimentally derived equation for a standard curve of glucose concentration vs. absorbance as follows:

$$Glucose = \frac{Absorbance - 0.2671}{0.4665} \quad (1)$$

However, due to the indeterminate nature of reality, the aforementioned 1 second spaced readings are not constant and fluctuate slightly around the actual value. This can be remedied by increasing the number of readings to 10,000 values instead of 1000 and averaging the results. It therefore follows that obtaining even more readings and averaging their value should result in a more accurate value. However, the patience of a user must be here considered. How long would a diabetic patient be willing to wait with his or her finger inside of the instrument in order to get an accurate reading? Therefore, a band-pass software filter was created to exclude outlying values in order to increase the accuracy of the average value even on fewer reading samples. The final decision on the number of readings necessary as well as the exact values to set the band-pass filter to, are yet to be determined as further human subject testing is necessary to fine tune these values. Though we do foresee this fine-tuning to be also individual based and perhaps even part of an automated initial calibration step when a patient utilizes the device for the first time.

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C. 3D printed Casing

The circuitry was placed in a 3D-Printed box, made from PLA, designed to minimize interference from outside light in order to focus the infrared light through the patient's finger's tissue and onto the photo-diode receiver. The box consists of a lid and a main body, as seen in Figure 1, with two openings: one for a USB cable that powers the system and transmits the results to a connected computer, and another for the patient's finger. The main body and the top have screw holes at each corner so that the box can be sealed securely from any interfering light.

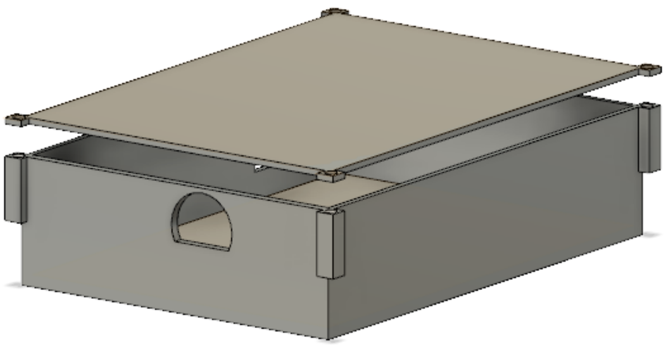

Figure 1. 3D-Printed GluMo Housing

V. RESULTS

To calibrate, test, and validate GluMo a series of test tubes with varying levels of glucose concentration were built and utilized repeatedly to test accuracy in face of both variance and strain of continued usage. In order to best resemble the human skin, the test tubes were built from powder-less and lubricant-free condoms. The error in measurements were under 10% With a high average level of accuracy at 99.2%. However, since this will be a medical device which millions will rely upon for regulating their blood glucose levels, we are aiming for 100% accuracy.

Human subject testing was also conducted on team members and verified against traditional single blood droplet glucose meters with the same levels of error and accuracy when multiple results are averaged. As an example, the table in Figure 2 shows 5 consecutive measurements for a single subject. The average blood glucose concentration measurement taken by the noninvasive meter was 113.65mg/dL. This value represents a 0.6% error compared to the value given by the commercial meter, suggesting that the meter is highly accurate. However, as the calculated p-values comparing each measurement to this average value indicate, the precision of each individual measurements was not as ideal. The p-values indicate the certainty with which each measurement can be assumed to be equal to the average value, with a maximum value of one. There is 90% confidence in the measurement for each of the five trials, with two trials indicating that their respective values are definitively different from the average measurement with p-values of almost zero.

The high accuracy of the average glucose measurement despite this lack of precision was caused by a fairly even distribution of individual measurements above and below the average value. Many more human subject test are necessary

	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5
[Blood glucose], (mg/dL)	113.42	107.92	115.31	119.10	112.48
p-value[1]	0.902	0.002	0.362	0.003	0.523

[1] p-values calculated using two-tailed z test comparing each blood glucose concentration measurement to the average measurement of 113.65mg/dL

Figure 2. Blood glucose concentration measurements and p-values from glucose meter testing.

in order to validate the accuracy levels. However, due to the COVID19 Pandemic at the time of this writing the human subject testing was very limited and insufficient to validate that the high level of accuracy will be maintained across a wide verity of patient skin types. A more extensive human subject testing will be conducted once the second phase prototype is completed as delineated further below.

VI. WORK IN PROGRESS

The first prototype of GluMo has been produced as a proof of concept. The second pocket-sized GluMo prototype is under development as an MVP for a marketable alternative to today's blood droplet glucose meters.

A. Spectroscopy

In order to find the optimal IR wavelength to absorb glucose in water, the full range of IR is being explored. As seen in Figure 3, at around 1650nm, the absorbance of IR in water is zero [18]. Hence, this region provides a unique opportunity for testing the accuracy of measuring glucose in blood. Thus, the entire absorbance recorded by the system should only be the absorbance of IR in glucose without needing to subtract the absorbance of water. However, this will cause the instrument to be more expensive than 100 initially until economies of scale lower the product's cost of production.

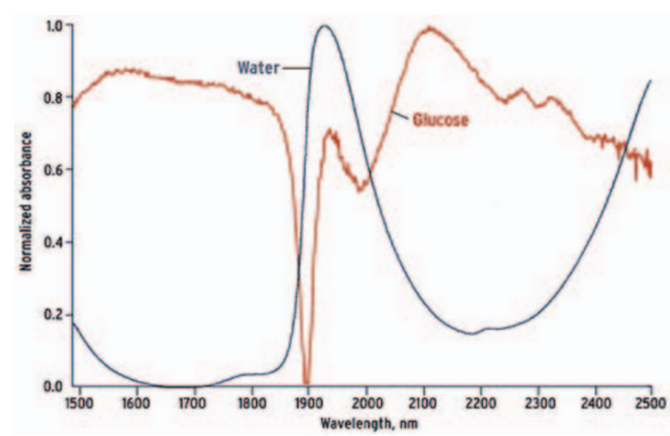

Figure 3. Water and Glucose Solution Absorbance spectra 1500nm – 2500nm. [18]

However, a complete IR spectroscopy of glucose vs water will be conducted in order verify this finding or to better select the IR range which will have the highest absorbance in glucose, yet lowest absorbance in water.

B. Pocket sized MVP with 3D-Printed casing

The current GluMo prototype, even though light weight and robust, is still too big for every day usage. Granted that competitor devices such as the Glucose Wizard or OMLEN B-2 are still bigger than GluMo in size, GluMo's circuitry can still me shrunken down substantially with low cost off-the-shelf available components alone. The packaging of the MVP in a custom 3D-Printed casing also allows for a lot of flexibility in the design of both the internal and overall looks and feel of the instrument. The intricate design details of the Pocket sized GluMo MVP and its results, will be the subject of the authors' next paper; but it is noteworthy that the completion of the MVP enables consumer testing of the instrument.

C. Rechargeable Battery and apparatus for USB charging

The GluMo MVP will be a portable pocket-sized device. Hence, it will need to operate even when not plugged in to a power source. Therefore, the MVP will include a small, internal, and rechargeable battery and a charging board. The USB port which serves as a data port in the Phase 1 prototype will then be re-purposed for charging the battery. There will also be a small OLED to display the battery status and the current blood glucose level.

D. Wireless communication

The GluMo prototype in phase 1 is designed to utilize serial communication using a USB cable. However, a point to point communication system consisting of nrf24 transceivers was tested as a proof of concept. GluMo's pocket-size MVP in phase 2 will have WiFi capabilities in order to allow the instrument's direct connection to the home or facility WiFi router for its independent access to an online database. This will allow the centralization of the patient's glucose reading history for easier access by the patient as well as the patient's care taker and/or doctor.

E. Web application

Our current prototype's data visualization is merely numeric based, with minimal explanatory details, and geared towards researchers and experts in the domain. In order to enable the mass usage of the instrument by users, a web based Graphical User Interface (GUI) is being developed. The interface will include numeric results of the readings as well as interactive graphs to help patients, their care takers, and physicians to better track their glucose levels across time periods. Furthermore, user's will be able to view their glucose readings over a specified period of time, such as the past day, week, or month. The application will also feature an alert capability which can automatically send messages to the patient's authorized care taker(s) or health provider(s) in case of a sustained abnormal glucose reading level, provided such alerts are set up.

VII. CONCLUSION AND FUTURE STEPS

An alternative to the classical single droplet blood glucose monitors which are prevalent today is a painless, hygienic, noninvasive glucose monitoring system utilizing infrared light waves; and it does not have to cost 1150 USD. There is at least 3 decades worth of evidence that researchers in companies and universities have been working on noninvasive blood glucose meters with most of them utilizing optics of some sort. The physics and chemistry of the absorbance of IR in glucose is thus not a new discovery, yet no reliable, portable, low cost, noninvasive blood glucose meter has made its way to the market. GluMo is an attempt at that and as the preliminary prototype results indicate it is a promising attempt. Once GluMo's pocket-sized MVP is completed and the limitations imposed by the COVID-19 pandemic are alleviated, a period of rigorous human subject field testing will finally present GluMo as the light at the end of the more than 3 decade long effort to enhance the lives of those struggling with diabetes by lessening their pain by a few needle pricks a day.

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