ECEN 403
Electrical Design Laboratory I
GlycoTrem: Benchmarking Assignment

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"An Aggie does not lie, cheat or steal or tolerate those who do."

Abstract

Diabetic patients struggle with regulating their blood sugar levels, as well as they suffer from low blood sugar level unawareness. Many tools are offered that aim to make blood sugar level measurement easier; however, these tools have proved to be expensive and invasive in nature. GlycoTrem is a proposed product that hopes to facilitate the process of detecting low blood sugar levels. This paper will touch upon GlycoTrem's design, along with the existing solutions' modes of action and comparing them to GlycoTrem's.

Contents

List of Acronyms and Abbreviations

Near Field Communication: NFC

Continuous Glucose Monitor: CGM

Bluetooth Low Energy: BLE

Application: App

1 Introduction & Overview

1.1 Problem Statement

Diabetic patients suffer from poor blood sugar regulation. Also called glycemia, these blood sugar levels may increase and cause hyperglycemia, or decrease and cause hypoglycemia. Hyperglycemia most commonly occurs when a person consumes food, meaning that a patient would know when to expect a hyperglycemic event. Hypoglycemia, on the other hand, may occur at any given time and, according to current research, many patients suffer from hypoglycemia unawareness [1].

Many products do exist in the market; however, patients often report that they're invasive and too expensive. Low blood sugar in the body leads to the release of hormones that attempt to regulate blood sugar levels, and a common side effect of these hormones is tremors (a feeling of shakiness)[2]. Therefore, the proposed solution GlycoTrem exploits these tremors using wearables such as smartwatches. The following sections will discuss the existing solutions and comparing them to GlycoTrem, along with their standards, as well as their constraints.

1.2 GlycoTrem's Design

GlycoTrem aims to detect hypoglycemic events through physiological tremors using wearables. This would be achieved through a multi layered system.

The first layer is the smartwatch application, which is responsible for collecting accelerometer data and continuously sending it to the smartphone application, the second layer of the system. The users would mainly interact with the smartphone application, which allows them to view their data and manage their user profiles. All data received from the smartwatch would then be sent from the smartphone application to the database and the data analysis servers, which form the third and fourth layers respectively. The database is responsible for storing all of the data and relaying it to any layer that requires it. Finally, The data analysis server oversees the computationally heavy aspects of the process that cannot be performed by other layers.

For the smartwatch application to be able to collect the data and then transfer it, the smartwatch itself must be equipped with a triple axis accelerometer and Bluetooth low energy support. Most smartwatches in the market already possess these two features, as well as the applications would be designed for most platforms, GlycoTrem to be available to most vendors. Therefore, users' smartphone/smartwatch preferences would not form an issue to GlycoTrem's accessibility.

1.2.1 Standards

Multiple standards exist that govern the secure handling of healthcare data. In addition, there are technical standards for some technologies used by GlycoTrem such as Bluetooth.

HIPAA and HITECH standards regulate the transmission, handling, and storage of patient healthcare data. Stringent safety precautions are to be set in place to protect the anonymity and confidentiality of this sensitive information in the dedicated server. In addition, the IEEE P1752 Standard for Mobile Health Data is applicable due to the handling

of the data through a smartwatch and smartphone application. As the smartwatch and smartphone both make use of Bluetooth Low Energy, the Bluetooth standard[3] also applies - and GlycoTrem's design ought to be compliant.

The app-to-server communication should be encrypted using a TLS socket, GlycoTrem's design aims to make use of the latest TLS 1.3 standard for optimal security and safety while maintaining good latency through TLS 0-RTT. Should a Web API be developed for integration with third-party tools, it would comply with the JSON:API specification (v1.0)[4].

1.2.2 Constraints

Many factors come into play that may hinder achieving GlycoTrem's goals. From filtering unwanted "noisy" data, to protecting the privacy of the users, as well as matching their preferences, all form constraints on the product's design.

Physiological tremors may be due to several factors other than hypoglycemia, such as fatigue, consuming too many caffeinated beverages, certain medications, or due to Parkinson's disease. Singling out the tremors that result solely from hypoglycemic events remain as an active constraint to the project's design. This constraint therefore leads to the following one: accelerometer quality. Hypoglycemic tremors range from 10 to 14 Hz [5]. Since the sampling rate must be at least twice the maximum frequency, any smartwatch that samples at a frequency starting from 30 Hz should be sufficient.

Upon surveying a sample of 184 people [6], out of which around 100 were diagnosed with diabetes [7], it was evident that not all patients experience tremors; in fact, it was mostly the younger population that confirmed experiencing tremors often, and this frequency decreased as the age range increased. A possible hypothesis is that the more the patients are subjected to tremors, the less they notice them over time due to being desensitized. Further testing is necessary in order to reach a concrete conclusion.

1.3 Competitor Product Selection

There exist a wide selection of products for diabetic patients to choose from that help manage their blood sugar levels. There's a different feature set for each tool depending on the manufacturer. The choice of products was based on the mode of action of the tool, along with its popularity among patients according to the aforementioned survey [6].

Different types for blood sugar regulation exist. The first at-home blood glucose measurement tool was the blood glucose meter (glucometer) using electrochemical test strips: with a small device, the patients would have to prick their finger with a needle and take a swab of blood using the strips. Those were then inserted back into the device which would calculate the current blood sugar level. The chosen product for the glucometer is the **Bayer Contour NEXT**.

Later on, the Continuous Glucose Monitoring (CGM) tool was released, which eliminated the need to prick a finger in order to measure glycemia levels. These coin sized sensors would be inserted into the skin (on the upper arm) are to be left there for approximately 14 days, at which point it must be replaced with a new one. The sensors are equipped with Near-field Communication (NFC) chips that can be scanned with the companion device

(the reader) in order to retrieve current glycemia levels. The chosen product for the CGM is **Freestyle Libre**.

1.3.1 Standards

The Near-field Communication (NFC)[8] standard is used by the chosen CGM device (Freestyle Libre). In addition, the Freestyle Libre reader device makes use of Bluetooth for syncing data to a third-party device. The Bayer Contour NEXT does not use any communication protocol aside from optional USB support (USB standard v2.0)[9].

1.3.2 Constraints

All alternative solutions to GlycoTrem are inherently invasive as they rely on blood samples. Glucose levels needs to be measured constantly in order to be able to detect highly fluctuation blood sugar levels, over time, this invasive procedure takes its toll.
Furthermore, the high cost of consumables with these competitor solutions forms a significant economic barrier. This raises a few ethical and economic concerns that should be taken into account when comparing these products to GlycoTrem. Indirectly, these products also have environmental issues that will need to be studied due to the bio-hazardous waste and plastics that are generated from needles and other consumables. On the plus side, all three products have a positive impact on public health to varying degrees.

1.4 Methodology

The products will be compared using the specifications outlined in their respective datasheets and support materials. Due to the early stages of development of GlycoTrem, some assumptions will be made regarding some features of the product.
To maintain objectivity and reduce any subjective cherry-picking, the results of the customer survey will be used to highlight the features that users care about the most and to define their weighting in terms of importance.

1.5 Limitations

Due to the early stage of development of GlycoTrem, a direct comparison to third-party solutions is not feasible. In addition, because these are medical products, testing on humans is not a trivial task. As a result, the products will be compared using the specifications and provided data from the manufacturer rather than field studies or real-life comparisons. This method of product evaluation does not highlight the faults and defects of products that are encountered over a long time of use - it rather compares the ideal use-case of each product which may not be entirely accurate.

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2 Benchmarking

The following primary performance metrics were chosen for the comparison using the results of the customer survey and the ethnographic study video[10]: sampling rate, invasiveness, ease of use, price, and accuracy.
The comparison will also include the differences in modes of action of the three devices along with their “pros” and “cons”.

2.1 Comparison Results

	GlycoTrem	**Bayer Contour NEXT**	**Freestyle Libre**
			
Mode of Operation	Smartwatch and Smartphone Application Accelerometer Based No Needle	Device, Needle, and Test Strip Setup.	Sensor, Applicator, and Reader Needle in Applicator, 14-day Application.
Sampling Rate	100 accelerometer samples per second.	1 sample on demand.	1 sample every 15 to 30 minutes.
Accuracy	Medium to Low.	High.	High.
Invasiveness	Non-Invasive.	Very Invasive.	Somewhat Invasive.
Ease of Use	No User Interaction.	Moderately Easy to Use.	Complicated Applicator Procedure.
Cost Breakdown	Cost of Smartwatch ($100-$300) + 5$/month.	$8.25 Reader + $21 Test Strips (14 days) + $10 Needles (28 days).	$280 Reader + $115 Sensor & Applicator Combo (14 days).
Cost per Month	$105 First Month + $5 Monthly Afterwards.	$60.25 First Month + $52 Monthly Afterwards.	$510 First Month + $230 Monthly Afterwards.
Cost per Year	$160	$632.25	$3040
% Cost	100% (baseline).	395.15% (∼x4 times).	1900% (x19 times).

Table 1: Product Comparison Table.

* Calculations assume that measurements are taken at least 3 times a day.

2.2 Analysis & Discussion

As shown from the table above, GlycoTrem provides a supplementary solution that reduces the need for frequent invasive measurements of blood sugar levels. GlycoTrem does not aim to replace existing solutions, it aims to complement them.

It is apparent that GlycoTrem excels in being non-invasive, extremely easy to use, and requiring no user interaction while logging continuously. While our proposed solution does not measure actual blood sugar levels, the ability to alert for hypoglycemic events and to log with high resolution the dips in blood sugar level over extended periods of time will surely prove useful to end users. Furthermore, GlycoTrem's design does not use consumable expensive components, which makes the product cost-effective and competitive with the other solutions.

The two competing products are able to provide accurate numerical values of blood sugar levels. However, they require expensive dispensable sensors, needles, and glucose test strips that pose ethical, economical, and environmental challenges.

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3 Conclusion

GlycoTrem is capable of providing a complementary solution that reduces the reliance on current blood sugar measurement devices. This would reduce the environmental and economical burden these devices typically inflict on diabetic patients. While all three devices have a place in the market, GlycoTrem can fill the non-invasive and user-friendly continuous logging niche.

REFERENCES — NEXT PAGE

4 References

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5 APPENDIX A

Technical Information

Accuracy

The CONTOUR®NEXT blood glucose monitoring system was tested using 100 capillary blood samples and three lots of CONTOUR®NEXT test strips. The results were compared to the YSI® Glucose Analyzer laboratory reference method, traceable to the CDC hexokinase method. The tables below show how well the two methods compared.

Table 1 - System accuracy results for glucose concentration < 75 mg/dL

Difference range in values between YSI laboratory reference method and CONTOUR NEXT meter	Within ± 5 mg/dL	Within ± 10 mg/dL	Within ± 15 mg/dL
Number (and percent) of samples within specified range	74 of 78 (94.9%)	77 of 78 (98.7%)	78 of 78 (100%)

Table 2 - System accuracy results for glucose concentration ≥ 75 mg/dL

Difference range in values between YSI laboratory reference method and CONTOUR NEXT meter	Within ± 5%	Within ± 10%	Within ± 15%	Within ± 20%
Number (and percent) of samples within specified range	390 of 522 (74.7%)	513 of 522 (98.3%)	521 of 522 (99.8%)	522 of 522 (100%)

Acceptance criteria in ISO 15197: 2003 are that 95% of all differences in glucose values (i.e., between reference method and meter) should be within 15 mg/dL for glucose values less than 75 mg/dL, and within 20% for glucose values greater than or equal to 75 mg/dL.

Technical Information

Precision

To assess precision under repeatability conditions, venous human blood samples were pooled and adjusted to a hematocrit of 42%. Blood was collected in tubes using sodium heparin as the anticoagulant. The glucose levels of the test solutions were prepared either by allowing samples to age to a final concentration or by using the aqueous 20% glucose solution to adjust the final test concentration. Five glucose levels were evaluated.

For each of 3 lots of sensors, ten CONTOUR®NEXT instruments were tested with ten replicates. In total three hundred replicates were used for each blood glucose level. The mean blood glucose levels, pooled standard deviations and %CVs were calculated and are presented here.

Repeatability

Glucose Level (mg/dL)	40	87	122	206	327
Pooled SD	0.8	1.2	1.6	2.7	4.6
%CV	2.1	1.4	1.3	1.3	1.4

To assess intermediate measurement precision, the performance of ten CONTOUR®NEXT meters was evaluated with three lots of sensors. The evaluation was performed by three operators who utilized three liquid control glucose levels under normal conditions of use over the course of 10 days. In total, three hundred sensors were used for each glucose level. The Grand Mean, pooled standard deviation and pooled %CV for each glucose level were calculated and are presented here.

Intermediate Precision

Glucose Level (mg/dL)	Glucose Level (mg/dL)	Pooled SD	Pooled CV (%)
Low (30 - 50)	43.4	0.7	1.6
Normal (96 - 144)	129.0	1.8	1.4
High (280 - 420)	383.8	6.3	1.6

Symptoms of High or Low Blood Glucose

You can better understand your test results by being aware of the symptoms of high or low blood glucose. According to the American Diabetes Association, some of the most common symptoms are:

Low blood glucose (Hypoglycemia):

- shakiness
- sweating
- fast heartbeat
- blurred vision
- confusion
- passing out
- seizure
- irritability
- extreme hunger
- dizziness

High blood glucose (Hyperglycemia):

- frequent urination
- excessive thirst
- blurred vision
- increased fatigue
- hunger

Ketones (Ketoacidosis):

- shortness of breath
- nausea or vomiting
- very dry mouth

WARNING

If you are experiencing any of these symptoms, test your blood glucose. If your test result is under 50 mg/dL or above 250 mg/dL, contact your health care professional immediately.

For additional information and a complete list of symptoms, contact your health care professional.

Specifications

Test Sample: Capillary whole blood

Test Result: Glucose measurements are reported as plasma equivalents.

Sample Volume: 0.6 µL

Measuring Range: 20 - 600 mg/dL

Countdown Time: 5 seconds

Memory: Stores most recent 800 test results

Battery Type: Two 3-volt lithium batteries (DL2032 or CR2032)

Battery Life: Approximately 1000 tests (1 yr. average use)

Control Solution Operating Temperature Range: 59°F–95°F

Meter Operating Temperature Range: 41°F-113°F

Humidity: 10 - 93% RH

Dimensions: 3.15" (H) x 2.09" (W) x 0.50" (T)

Weight: 1.6 oz. (45 grams)

Meter Life: 5 years

Sound Output: 55 to 80 dBA at a distance of 10 cm

Electromagnetic Compatibility (EMC): The CONTOUR®NEXT meter complies with the electromagnetic requirement specified in ISO 15197:2013. Electromagnetic emissions are low and unlikely to interfere with other nearby electronic equipment, nor are emissions from nearby electronic equipment likely to interfere with the CONTOUR NEXT meter. The CONTOUR NEXT meter meets the requirements of IEC 61000-4-2 for immunity to electrostatic discharge. Avoid use of electronic devices in very dry environments, especially if synthetic materials are present. The CONTOUR NEXT meter meets the requirements of IEC 61326-1 for radio frequency interference. To avoid radio frequency interference, do not use the CONTOUR NEXT meter near electrical or electronic equipment that are sources of electromagnetic radiation, as these may interfere with the proper operation of the meter.

6 APPENDIX B

System Specifications

Sensor Specifications

Sensor glucose assay method	Amperometric electrochemical sensor
Sensor glucose reading range	40 to 500 mg/dL
Sensor size	5 mm height and 35 mm diameter
Sensor weight	5 grams
Sensor power source	One silver oxide battery
Sensor wear period	Up to 14 days

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Sensor memory	Up to 14 days (glucose readings stored every 15 minutes)
Operating temperature	50 °F to 113 °F
Sensor Applicator and Sensor Pack storage temperature	39 °F to 77 °F
Operating and storage relative humidity	10-90%, non-condensing
Sensor water resistance	IP27: Can withstand immersion into 3 ft (one meter) of water for up to 30 minutes
Operating and storage altitude	-1,250 ft (-381 meters) to 10,000 ft (3,048 meters)

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Reader Specifications

Reader size	95 mm x 60 mm x 16 mm
Reader weight	65 grams
Reader power source	One lithium-ion rechargeable battery
Reader battery life	2 weeks of typical use
Reader Sensor memory	1 Sensor
Reader operating temperature	50 °F to 113 °F
Reader storage temperature	-4 °F to 140 °F
Operating and storage relative humidity	10-90%, non-condensing
Reader moisture protection	Keep dry

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Operating and storage altitude	-1,250 ft (-381 meters) to 10,000 ft (3,048 meters)
Reader display timeout	60 seconds
Radio Frequency	Near Field Communication* (13.56 MHz RFID); ASK Modulation; 124 dBuV/m; 1.5 inch communication range
Data port	Micro USB
Minimum Computer Requirements	System must only be used with EN60950-1 rated computers
Mean service life	3 years of typical use
Power Adapter	Abbott Diabetes Care PRT25611 Operating temperature: 50 °F to 104 °F
USB Cable	Abbott Diabetes Care PRT21373 Length: 37 inches (94 cm)

* Security measures: The communication between Reader and Sensor is a short range near field communication method making it difficult to interfere with or intercept data that is being transferred. The Sensor and Reader are protected by proprietary data format, memory mapping, and cyclic redundancy check (CRC) generation and verification of data.
Quality of Service (QoS): QoS for the FreeStyle Libre Pro Reader and Sensor wireless communications using the near field communications is assured within the effective range of 4 cm between the Sensor and Reader that is specified to occur within 15 seconds.

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