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Understanding and Predicting Postprandial Plasma Glucose (PPG) to Control Type 2 Diabetes (Math-Physical Medicine)

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1. Introduction

The author has type 2 diabetes (T2D) for 25 years. For the past 8 years, he collected approximately 1.5 million data of his lifestyle details and medical conditions. His approach is a "math-physical medicine" based on mathematics, physics, optical and electronics physics, engineering modeling, signal processing, computer science, big data analytics, statistics, machine learning, and artificial intelligence. His main focus is on preventive medicine using prediction tools. He believes that the better the prediction, the more control of your chronic diseases you have [1-4].

2. Method

The author's research approach is based on his solid inter-disciplinary academic background and successful industrial experiences. His 17-years of college education and 36-years of working experience have prepared him to take on these 20,000 hours for the past 8 years of diabetes research. He has conducted his diabetes research by taking the following thorough process and carefully chosen steps:

A. Observing phenomena, identifying basic characters of a system, and then collecting relevant data carefully as a true physicist.
B. Developing related but rigorous mathematical equations and studying statistical variances of data as a true mathematician.
C. Applying suitable engineering models and conducting related numerical analyses to address the real-world challenges, as a professional engineer.
D. Using modern computer science tools and sophisticated artificial intelligence techniques to aid in problem solving via big data analytics.

The step-by-step research method in chronological order on this specific subject is described as follows:

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1. During 2010-2011, he studied six chronic diseases: obesity, diabetes, hypertension, hyperlipidemia, heart attack, and stroke. Concurrently, he developed a customized software to collect related data of both lifestyle management details and medical conditions. Thus far, using this computer program, he has collected 8,878 glucose data: 7,206 postprandial plasma glucose (PPG) and 1,672 fasting plasma glucose (FPG) for the past 4.7 years from 1/1/2014 to 8/25/2018. After learning the important role that food plays in chronic diseases, he delved further into food nutritional science from 2012 to 2013. During this time, he collected and organized six million food material data from the U.S. Department of Agriculture (USDA) and hundreds of thousands of menu items from more than 500 international franchise restaurants. Later, he added more than 4,000 photos with the detailed information from his own meals to build a large database of food and meals.

2. After studying these six medical conditions and how they result from metabolic disorders, he spent the year 2014 living in a desert city and developed a mathematical governing equation of the human body's metabolism. He used 10 categories and then added in "time" as the 11th category to get the "dynamic" effect of each variable's behavior over time. Within the medical output categories, there are four medical conditions: weight, glucose, blood pressure, and lipid. Within lifestyle input categories, there are six lifestyle management details: food, exercise, water, sleep, stress, and life pattern regularity. He further identified a total of about 500 elements within these ten categories to define and describe his desired metabolic model. This work ended with a 14-page long equation of the human metabolic model. At last, he created two new terms which use simple numbers or percentages to effectively describe his overall metabolism and health status at any time. These two new terms are Metabolism index (MI) and General health status unit (GHSU).

   The metabolism curve is similar to the ocean waves by going up and down with various waveforms. Their building components and control methods are very different and complicated. You cannot analyze your metabolism based on your medical conditions alone since it only provides a partial picture. You must include detailed lifestyle data in order to get a total picture about your health. At present, the healthcare community generally focuses on disease status and treatment methods, but paying less attention on the causes and prevention. Furthermore, the inter-relationship between disease and lifestyle is not only nonlinear (i.e. it is complicated), but also dynamic (i.e. it varies with time constantly) which makes it an impossible task for most healthcare professionals who do not have sufficient mathematical training to understand this problem quantitatively.

   During the author's research process; he has utilized advanced mathematics, statistics, and physics, structural engineering modeling, certain powerful techniques from optical physics and electronic wave theory, and modern computer science algorithms and calculation tools. Mathematics includes partial differential equation, nonlinear algebra, topology concept, complex variables, and statistics. Structural engineering modeling includes finite element method to convert the human body's "continuum" or "analog" system into a "digital" system in order to take advantage of modern computing power to handle its associated big data. In his opinion, at present, the general practice of the medical community is heavily relying on "hardware" power (such as EKG and CT machines that is comparable to bones and muscles) and not enough on "software" power (such as sophisticated software programs that is comparable to nerves and brain). Software is much more flexible and powerful than hardware. Furthermore,

the author applied what he learned from his engineering thesis work at MIT; the concept of "plastic" state of a material similar to a "non-reversible" diabetes condition of a chronic disease patient vs. "elastic" state of a material similar to a "reversible" common illness of a healthy person. In addition, he also utilized optical physics and signal processing in developing his PPG prediction model.

The author named his approach as "math-physical medicine" where medicine is the subject and math-physical is adjective. In other words, his intention is to research on medicine problems but utilizes mathematics, physics, and engineering as tools of research. The author has a master's degree in the field of biomechanics. In his opinion, many schools offering "bio-engineering or medical engineering" curriculums with their emphasis on demonstrating engineering's beauty and power (engineering or mechanics are subjects here) using medicine as an application domain, instead of really solving medical problems (medicine is an adjective here).

3. For the period of 2015-2017, the author focused on developing five prediction tools - Weight, FPG, PPG, Adjusted Glucose, and Estimated Hemoglobin A1C (A1C). In traditional western medicine, most of the emphasis is placed on treatment of existing medical conditions instead of prediction and prevention. From an engineering standpoint, having prediction tools and developing early warning capabilities are extremely important to prevent negative outcomes. Similarly, by nature, these medical prediction tools would be very useful in preventive medicine as well. The better you can predict glucose behavior, the better chance you can reduce their damage on your internal organs; therefore, eliminating frustration, pain, expense, and risk down the road that are often associated with treatment of complications. This is especially true for chronic diseases since most of them are non-curable (i.e. non-reversible) in the foreseeable future; and therefore, the best and only hope of a patient relies on controlling these diseases and reduce risks from complications.

During the course of his investigation of risk probability of having a heart attack or stroke resulting from chronic diseases, the author realized and verified that diabetes (high glucose) is the fundamental "trouble maker" which combined with the extra damages caused by hyperlipidemia (high cholesterol) and hypertension (high blood pressure) to cause blood flow blockage and blood vessel rupture. In 2010 when he started his own research work, he made a promise to himself that he would spend the rest of his natural life to find all of the causes and consequences of his diabetes complications. Now, not only has he saved his own life, he is also convinced that his research work on diabetes is both important and necessary for other patients.

2.1 Weight

Weight control is critical for all chronic diseases and as everyone knows weight management is a difficult task for most people. The author took 3-years to bring his BMI down from 32.5 (220 lbs. or 100 kg) to 24.5 (167 lbs. or 76 kg) and 5-years to reduce his waistline from 46 inches (112 cm) to 32 inches (81 cm). He has monitored and analyzed his weight situation since 2012. One thing he has analyzed is the causes and rough percentages of weight loss at night due to: quantitatively measurable factors, such as urination and bowl movements, unable to be measured factors, such as vaporization and internal organ operations, as well as some special factors, such as sudden stress, sleep disturbance, and illness. For the past 3-years, both of his average weight gain during daytime and weight loss at night are ~2.8 lbs. (1.3 kg) per day. That is why he is able

to maintain his body weight around 170 lbs. (77 kg) and BMI at 25. Based on all of these, his weight computing model can predict his next morning's weight and it has reached to 99.9% of linear accuracy.

2.2 FPG

Conceptually, it is beneficial to discuss FPG a little bit before we dive into the details of PPG. In the early morning of March 17, 2016, he discovered the hidden high correlation coefficient of 86% between his weight and his FPG values based on data available at that time. Using his 1,672 days data of FPG and Weight, his calculation also revealed a 94% of FPG data variance coverage from a +/- 20% "skewed band". Because of this, his weight prediction serves a direct and most important role on his FPG prediction. In summary, Weight contributes about 80% to 85% influence on long-term FPG formation and the other four factors only contribute about 15% to 25%.

During sleep, our body does not have many observable activities related to energy infusion and diffusion. The combined weight loss at sleep from vaporization and urination and internal organ operations (energy diffusion), and weight gain at daytime from eating (energy infusion) minus exercising and internal organ operation (energy diffusion) determine our weight fluctuations. Weight is a mere physical representation of our body's internal energy exchange. Thus, this weight changes lead directly into the wave fluctuations of both FPG and PPG. In a short sentence, FPG changes are the results of our body energy change at nighttime with weight functioning as the physical representation of this internal energy exchange. I have analyzed this problem using my mechanical engineer's training on "energy".

2.3 PPG

PPG is quite a different concept from FPG. The author spent 2-years studying food nutrition, 1-year collecting related food data, and then 3-years researching the effects of various foods on his PPG situation from a math-physical point of view. At the end, he has identified about 19 influential factors related to PPG changes. Among those, two are the major influential factors. Food (carbs & sugar intake) has a 38% contribution rate with +57% positive-correlations to PPG. Exercise (post-meal walking) has a 41% contribution rate with -80% negative-correlations to PPG. Using a mathematical algorithm to calculate the influence of contributing factors on PPG is one thing; however, building an accurate and effective PPG prediction model is a different and difficult task. He graphed his medical conditions and lifestyle details, including weight, blood pressure, glucose, food intake, exercise, etc. and saw that those curves fluctuate like waves. Therefore, the author decided to apply wave theory from classical physics to conduct his research work on understanding PPG phenomena. Over the summer months of 2015, by accident, he observed the color change of oranges in his backyard. He suddenly visualized a continuous picture of a hidden relationship diagram, including color of fruit or food material at different stage, wavelength difference associated with each color, changes of food molecular structure, changes of food nutrition ingredients, nutrition amount to glucose, glucose to A1C, and A1C to diabetes condition. This realization led him into the specific investigation of PPG by applying his domain of knowledge in optical physics and signal processing. The signal processing technique has been frequently and heavily utilized by geophysicists and communication electronics engineers. The author worked in the semiconductor industry for 14 years and is familiar with the signal processing techniques. He first decomposed his PPG wave into 19 "linear" (i.e. having simpler and linear mathematical relationship) component waves. He then re-integrated those 19 "linear" component waves back into one combined "nonlinear" wave (more random shape and complex pattern) which is the

predicted PPG wave. Actually, this decomposition and reintegration process is very similar to the concept of finite element structural engineering modeling which he already used to develop his metabolism index model in 2014.

In the early stages of using his PPG prediction model, there was a bigger gap that existed between the actual measured PPG curve and predicted PPG curve, i.e. a lower linear accuracy (<90%). He then applied many practical engineering methodologies, such as trial-and-error and curve-fitting (from his aerospace and defense industrial experience), safety margin (from his nuclear power industrial experience), numerical simulation (from his computer-aided-design system experience), AI (from his semiconductor chip design automation experience), etc. to continuously improve its linear accuracy until it reached 99.9% by the end of 2017.

During this research period, he also identified some seemingly-trivial factors which actually have quite a significant impact on the creation of both FPG and PPG. For example, after 6-months of research in 2017, he identified that other than weight (80%-85%), weather related ambient temperature contributes approximately 10% to both FPG and PPG creation models. This is an example of maintaining harmony or achieving balance between the human body and environmental conditions. By now, the author realized that each human body has an existing biorhythm which is the natural outcome from million years of evolutionary improvement and continuous adaption of human body with environment. Actually, selecting right food to eat and exercising are also acts matching with our body's natural bio-rhythm. We should respect this biomedical rhythm and environmental harmony and try our best not to interrupt, intrude, or destroy it. In his opinion, chronic diseases are resulted from these "imbalance of our bio-rhythm".

2.4 Adjusted glucose & hemoglobin A1C

The author created a new term of "adjusted glucose" with different weighting factors for contributions from FPG and PPG, respectively. In order to combine FPG and PPG into one unified daily glucose number and then to determine the predicted A1C level (i.e. mathematical A1C, not lab-tested A1C), the author examined many stages of glucose formation and variations. In order to get an accurate, effective, and practical predicted A1C values, this task cannot be done via a simple conversion factor as indicated in some published medical documents.

As we know, even a lab-tested A1C result can be influenced by many factors, such as chemical, environmental, operational, etc. which may contribute to a margin of 15% to 30% build-in error. However, A1C value has been adopted by the medical community as the yardstick of diabetes diagnoses. Therefore, the author adopts the same standard to make sure that his predicted A1C result is as close as possible to the lab-tested A1C results.

He further borrowed one idea from his previous industrial experience in nuclear power plant design and earthquake engineering, the idea of "safety margin". Since the intention of this algorithm is to provide an "early-warning" capability to diabetes patients, he designed his final A1C prediction tool to contain only 95% linear accuracy which is about 5% higher than lab-tested A1C results. He did this intentionally to add-in a minimum safety margin of 5%. In another word, his safety margin increases his predicted A1C value by at least 5% higher than lab-tested A1C value in order to "scare" the diabetes patient's a bit and allow them to modify their lifestyle behavior before the actual lab-testing is conducted, without losing its desired accuracy.

3. Results

The author spent three years (2015-2017) to develop five prediction models to achieve approximately 95% (for A1C) to 99% for both FPG and PPG of linear accuracy with high correlations (pattern similarity) between two biomedical signal waves, predicted and measured glucose.

The following sections cover point by point the information in TABLE 1: Summarized Characteristics of PPG.

TABLE 1. **Summarized Characteristics of PPG.**

Comparison between FPG and PPG:	**PPG**
Measurements per day	3
Measurement timing	two hours after first-bite of meal
Total identified number of influential factors	19
Primary influential factors & Contribution %	Carbs/sugar intake for 38%; Exercise for 41%
Primary factors conversion to Glucose value	carbs/sugar (gram) and Walking (steps) to PPG (mg/dL)
Secondary influential factors & Contribution %	Weather temperature for 10%
Secondary factors conversion to Glucose value	Each degree increase (above 77F) to PPG (mg/dL)
All other remaining factors & Contribution %	Total 16 remaining factors for 11%
Glucose contribution % on A1C formation	~75%-85%
Period of Waveform	Shorter
Frequency of Waveform	Higher
Vibration Amplitude of Waveform	Higher
Intensity and Energy Associated with Waveform	Bigger
Range of Value Variance	Wide
Correlation between FPG and PPG	PPG has no correlation with FPG (or Weight)
Correlation with Blood Pressure	Significant (if patient has hypertension)
Relationship with Food	Food quality (carbs & sugar) influence PPG, Not food quantity
Key Techniques to build Glucose Prediction Model	Signal Processing to decompose and re-integrate a wave
Accuracy of predicted vs. measured glucose	99.9%
Correlation between predicted & measured glucose	84.4%

3.1 Glucose measurement frequency and timing

Most Type 2 Diabetes (T2D) patients dislike finger-piercing measurements due to its associated inconvenience, pain, cost, and psychological reactions. In order to conduct his research, the author diligently measured his blood sugar four times a day during the past 6.5 years (more than 2,000 days), once in early morning for FPG and 2 hours after each meal (3 times a day) for PPG. He collected data since 1/1/2012 and recorded all of his measured data and associated lifestyle details into his customized software on his iPhone. It should be noted that if a patient encountering a limitation on measurement frequency, he or she should at least measure once a day by recording his/her measured PPG data at two hours after first bite of meal which has the heaviest contents of carbs/sugar and largest food portion.

3.2 Total identified influential factors and their contributions on PPG

There are 19 factors for PPG formation identified and used in his research. Quality of Food and Meal (i.e. carbs and sugar intake) contributes about 38% (averaged amount of <15 gram per meal) with +57% correlation coefficient (it is a positive relationship, the more you eat, the higher your PPG). Exercise (walking within 2 hours after eating, an average of 4,200 steps after each meal, 2.8 km, 1.8 mile) contributes 41% with -80% correlation coefficient (it is a negative relationship, the more you walk, the lower your PPG). Weather temperature contributes about 10% and all of the other 16 factors contribute approximately 11% of PPG.

3.3 PPG impact by primary influential factors

Using machine learning technique and AI algorithm, his customized software can automatically calculate the following conversion factors. It should be pointed out that these results are subjected to patient's age, diabetes history, and disease severity.

PPG fluctuation amount in mg/dL by each gram of carbs/sugar intake.

PPG reduction amount in mg/dL by each 1,000 steps of post-meal walking within 2 hours after first bite of meal.

3.4 PPG Impact by weather temperature

For FPG, when weather is below 67 degrees Fahrenheit (19.4 degrees Celsius), FPG drops in certain amount of mg/dL by each degree of Fahrenheit decrease, and when weather is above 77 degrees Fahrenheit (25 degrees Celsius), PPG rises in certain amount of mg/dL by each degree of Fahrenheit increase. His customized AI software can automatically calculate all of these quantities.

3.5 Contribution of FPG and PPG on adjusted glucose (as well as on estimated A1C)

FPG: approximately 15% to 25%

PPG: approximately 75% to 85%

This ratio is constantly being self-learned and self-adjusted when a new lab-tested A1C value is entered into the system. This is an example of "machine learning" application.

3.6 PPG data and waveform

Generally speaking, in comparison with PPG waves, FPG waves have longer period, lower frequency, and lower amplitude. Therefore, FPG wave has lower peak and shallower valley, i.e. the "vibration amplitude" is smaller. This is due to the fact that energy diffusion at night is less intensive in comparison with PPG at daytime, and also due to weight does not fluctuate much from day to day. On the other hand, PPG waves have much higher peak and deeper valley, i.e. the vibration amplitude is higher, with shorter period, and higher frequency.

This is due to both carbs/sugar intake (energy infusion) and exercise (energy diffusion) being stronger influential factors (meaning stronger impact) with higher speed of change (meaning rapid changes). The characteristics mentioned above can be easily analyzed, interpreted, and understood via wave theory and signal processing techniques.

3.7 Correlation between PPG and weight

Investigating Weight and Glucose reveal that FPG is highly related to Weight, which is further related to food portion (total food "quantity"). On the other hand, PPG is highly related to carbs/sugar intake amount (nutrition contents or food "quality"), not related to Weight directly. Based on the author's experience, by simply reducing his weight while he was obese (BMI>30), his overall diabetes conditions improved rapidly and significantly. However, while in "overweight" stage (BMI between 25 and 30), it was more difficult for the author to lose weight and the task becomes harder in terms of obtaining rapid and clear effectiveness of diabetes control.

During this stage, the above-mentioned knowledge of FPG and PPG helped him to effectively control his T2D conditions. In conclusion, the more you know about the differences between fasting and postprandial glucoses, the easier and more effective job you will do in terms of diabetes control via this "divide and conquer" approach to face these two glucose challenges.

3.8 Correlation between FPG and PPG

The correlation coefficient between FPG and PPG is below 20% which means there are no direct links between these two glucose values.

3.9 Relationship between PPG and Blood Pressure (BP)

There is a significant correlation between PPG and BP. However, it should be noted that the above conclusion only applies to cases of patients having both diabetes and hypertension conditions. If a T2D patient who does not have hypertension, you will not observe any correlation between elevated glucose and "normal" BP.

3.10 Techniques used to build PPG prediction models

The PPG prediction model utilized mathematics and the three statistical methods: time-series, spatial analysis, and frequency domain analysis, but is further enhanced by using optical physics, wave theory from physics, and signal processing from electronic engineering. The two glucose prediction models have utilized heavy mathematics and modern computational tools, such as database, parallel processing, big data analytics, machine learning, and artificial intelligence.

3.11 Linear accuracy and correlation coefficients between predicted and measured PPG

By mid-2018, predicted PPG values have achieved 99.9% of linear accuracy in comparison with measured values using the finger-piercing method. PPG has 84.4% correlation between predicted and measured values with "phase shift" phenomenon due to its data complexity and interference among multiple influential factors. It should be noted that, from a purely statistical point of view, any two sets of data with more than 60% of correlation coefficient are considered "highly correlated" already.

Finally, FIG. 1 through FIG. 6 further illustrates the contents described in this article and TABLE 1.

FIG. 1 depicts accuracy and correlation (R) of FPG, PPG, and A1C between predicted and measured values. FPG has 99.9% of accuracy and 97% of R, PPG has 99.9% of accuracy and 84% of R with some phase shift situations, A1C has ~95% accuracy due to build-in 5% safety margin during the period of 6/1/2015-8/29/2018.

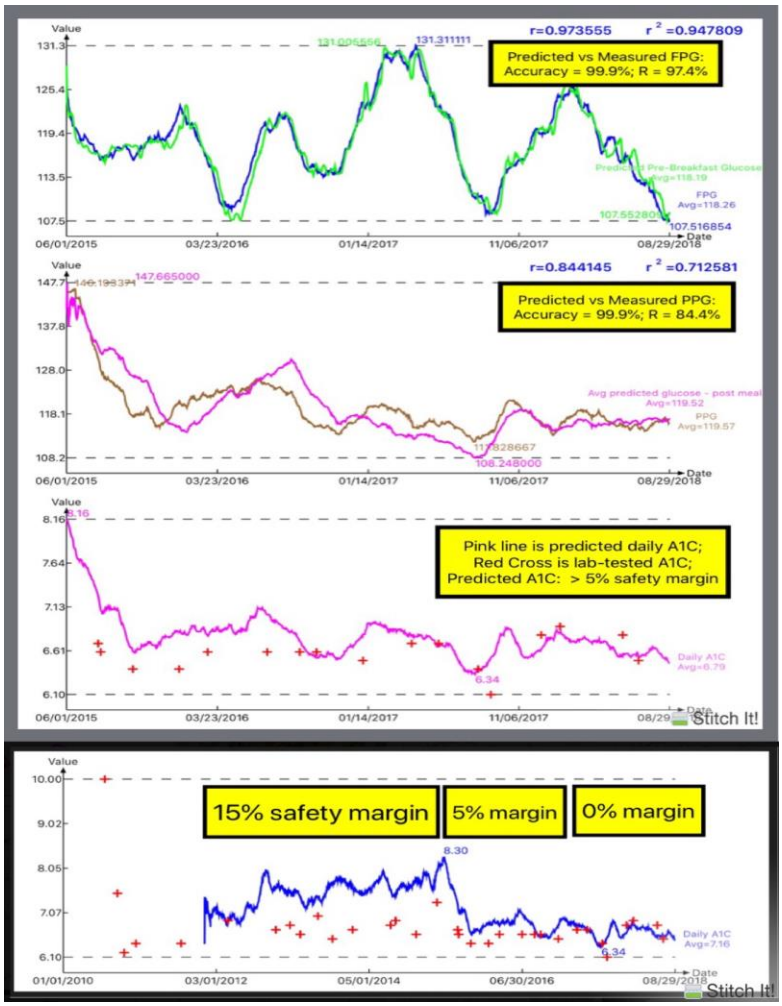

FIG 1. **Results of Prediction Models for FPG, PPG, and A1C.**

FIG. 2 shows pie charts of element contribution percentages of Weight, FPG, PPG, and A1C.

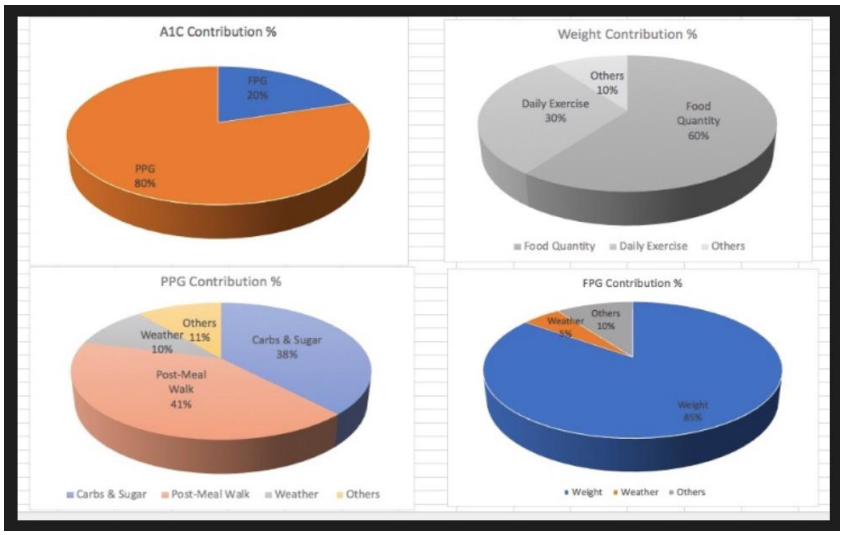

FIG 2. **Contribution % of Weight, FPG, PPG, and A1C.**

FIG. 3 shows decomposition of PPG Signal wave into four Major Sub-Waveforms. From this diagram, you can see the contribution margin and glucose value created by each component (sub-wave) of PPG. The PPG value used here is the average PPG at 119mg/dL during the period of 6/1/2015 to 8/25/2018.

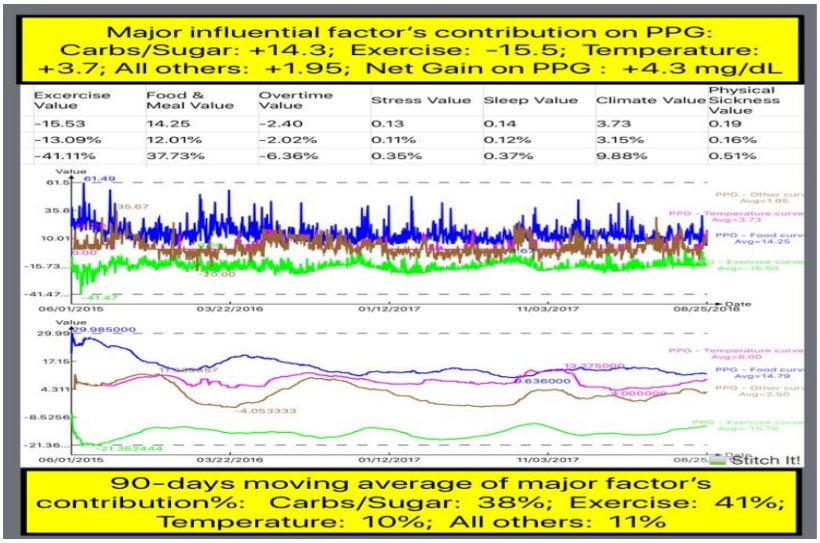

FIG 3. **Decomposition of PPG into four Major Sub-Waveforms.**

FIG. 4 shows an extremely low correlation (7%) existing between FPG and PPG, as well as a low correlation (19%) existing between PPG and weight.

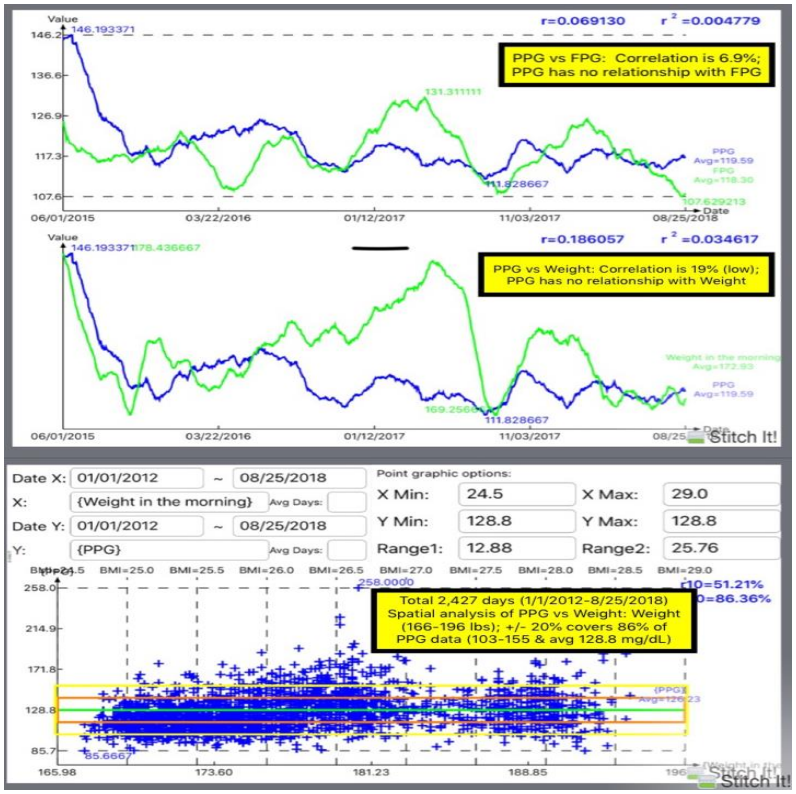

FIG 4. **Low Correlation Existed Between PPG vs. FPG and PPG vs. Weight.**

FIG. 5 depicts a formation of annually accumulated "cluster data clouds" for both FPG and PPG. PPG has a constant value regardless of weight changes; however, FPG has a linear relationship with a skewed angle with weight changes. This means that FPG expands its value when weight increases.

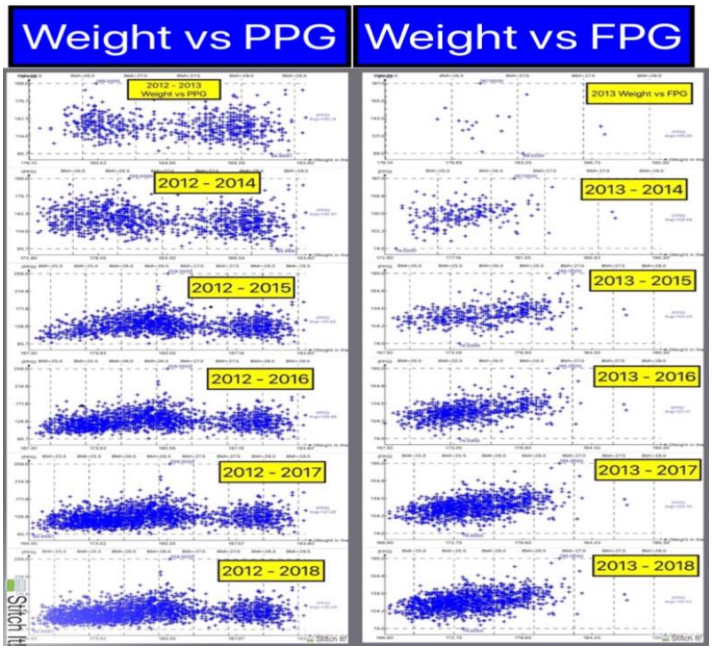

FIG. 5. **Constant PPG values, regardless of Weight changes, whereas FPG has a linear relationship with Weight (2012 - 2018).**

FIG. 6 shows the screen of an AI Glucometer which is a medical product that brings theoretical research results for practical disease control. Diabetes patients do not have to suffer from daily finger-piercing or laboratory blood-drawing test. This AI tool can help T2D patients to predict their glucose values and therefore to control their T2D conditions using math-physical medicine research results.

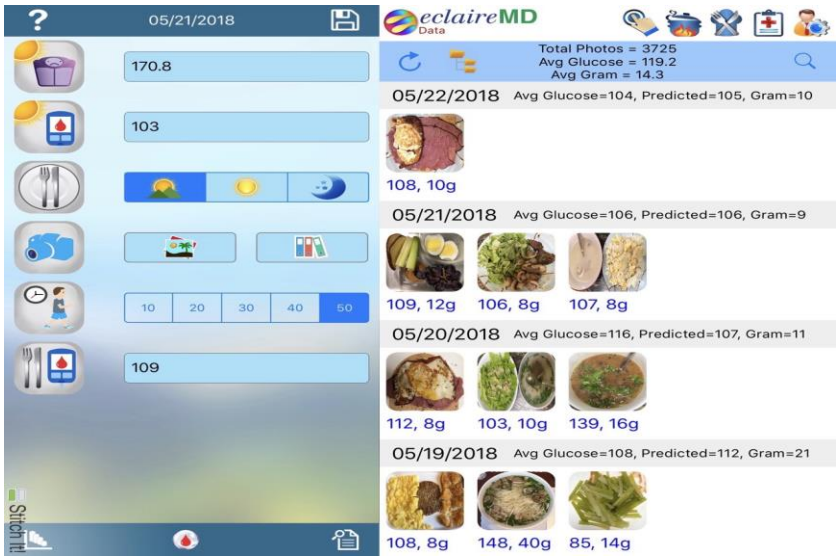

FIG 6. **AI Glucometer Screen Design to Predict Glucose Value via Meal Photos.**

4. Conclusion

After 2015, the author's severe T2D condition is completely under control using his developed "math-physical medicine" approach, including metabolism model (MI and GHSU), and five glucose prediction tools. The author has acquired extensive knowledge and useful experience from his own 8-years and 20,000 hours of self-study and research. He also wants to share his knowledge and experience with other T2D patients through medical professionals. He firmly believes that a deeper understanding, quantitative knowledge, and precise pictures of both FPG and PPG will also benefit worldwide healthcare professionals with their tasks of effectively controlling diabetes.

5. Biography

The author received an honorary PhD in mathematics and majored in engineering at MIT. He attended different universities over 17 years and studied seven academic disciplines. He has spent 20,000 hours in T2D research, initially studying six metabolic diseases and food nutrition during 2010-2013, then conducting his own diabetes research during 2014-2018. His approach is a "quantitative medicine" based on mathematics, physics, optical and electronics physics, engineering modelling, signal processing, computer science, big data analytics, statistics, machine learning, and artificial intelligence. He named it math-physical medicine (MPM). His main focus is on preventive medicine using prediction tools. He believes that the better the prediction, the more control you have.

The author created this "math-physical medicine" approach by himself in order to save his own life. Although he has read many medical books, journals, articles, and papers, he did not specifically utilize any data or methodology from other medical work. All of his research is his original work based on data he collected from his body and using his own computer software developed during the past 8-years. Therefore, no major problems were associated with data interference or data contamination since he has been dealing with a homogenous genetic condition and lifestyle environment. He could dig into one single variable very deeply to extract valuable information. In addition, his knowledge, information, technique, and methodology of mathematics, physics, engineering, and computer science came from his lifelong learning from schools and industries and should not be listed as medical references. This is the reason his references only contain his own published papers.

6. Limitation of Research

This article is based on data of metabolic conditions and lifestyle details collected from one T2D patient (himself). It does not cover genetic conditions and lifestyle details of other diabetes patients. Therefore, his conclusions and findings should be re-verified and used with caution when being applied to other patients who are under different metabolic conditions or lifestyles.

7. Other Declarations

For the past 8-years of self-study and research, the author has never hired any research assistant or medical research associate to help with his work. He applied his own invention of a "Software Robot" created during 2001-2009, his AI knowledge, and his previous programming experience (close to 1 million lines) to produce the system architecture, design structure, and some special code of this customized computer software. He used this software to collect and analyze his big data, conduct his medical research, and to control his diabetes disease.

This project was 100% self-funded by using his own money that was earned from a successful high-tech venture in Silicon Valley. He did not receive any financial assistance or grants from any public, private institution or organization. Therefore, there are no concerns regarding any conflict of interest.

8. Acknowledgement

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