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The GH-Method

A Comparison Study of Two Effective Glucose Equations Combined with Average Glucose and Average Glucose Fluctuations with Different Split Ratios Using Time Domain and Frequency Domain Analyses for 3+ Years of Data Based on GH-Method: Math-Physical Medicine (No. 459)

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Abstract

The author utilized a flash glucose monitoring (FGM) technique with a 14-day system of continuous glucose monitoring (CGM) sensor device and a customized Bluetooth signal transferring device to collect glucose data (sensor glucose) from 5/5/2018 to 5/31/2021. As a result, over the 1,218 days with 96 glucose data per day, a total of 116,928 glucose data was recorded and stored on a US-based cloud server for data analysis and medical research work. Along with the hardware devices, he developed a customized software with artificial intelligence capability to conduct his desired data analysis and medical research work on the iPhone and PC. This investigation contains two parts. The first part is the study of his average glucose (eAG) which includes 4 segments: fasting plasma glucose (FPG), postprandial plasma glucose (PPG), between meals glucose, and pre-bed glucose. The second part consists of his average glucose fluctuations (GF) every 4 hours each day. GF is defined as the maximum glucose value (peak) minus the minimum glucose value (nadir) in a day which describes the degree of glucose fluctuation that is oscillation or vibration. He applied a time domain (TD) analysis to obtain the magnitude (the Y-amplitude of TD space) of the average amplitudes of glucose itself and glucose fluctuation. He then applied the Fast Fourier Transform (FFT) technique to conduct his frequency domain (FD) analysis to obtain the estimated relative energy associated with his daily glucose and daily GF (the Y-amplitude of FD space). In his previous research papers, he has proven that the Y-axis magnitude (Y-amplitude) of FD is directly proportional to the relative energy level associated with glucose amplitude value in TD that is the glucose magnitude or Y-amplitude of TD. In this way, he can quickly estimate the relative energy levels associated with different glucose levels in order to understand the varying degree of organ impact due to these relative energies. The relative energies are generated by the glucose wave itself and its wave fluctuation amplitude are carried by red blood cells (RBC) circulating in the blood vessels throughout the body. In summary, human organs and glucose have their biochemical reasonings and needed operations, but they also present certain biophysical phenomena following the physics theories and principles which can be interpreted or solved using various mathematical equations or statistical tools. The following paragraphs describe his two equations along with his major findings from this study: Effective glucose equation no. 1 = (0.29*eAG + 0.71*GF), Effective glucose equation no. 2 = (0.5*eAG + 0.5*GF). In TD analysis, the ratio of eAG (124) over GF (96) is 129%. However, in FD analysis, the ratio of GF energy (863) over eAG energy (339) is 255%. This means that the energy associated with the difference between wave extremities (GF) is much higher than the energy associated with mean value of wave (eAG). In TD analysis, using two different combinations of eAG split and GF split, the model of (0.29*eAG + 0.71*GF) has a lower effective glucose value (104) than the effective glucose value (110) of the model of (0.5*eAG + 0.5*GF) with a small difference of 5%. However, in FD analysis, the model of (0.29*eAG + 0.71*GF) has a moderately higher associated energy (658) than the associated energy (522) of the model of (0.5*eAG + 0.5*GF) with a moderate difference of 26%. This means that the energy associated with the model of (0.29*eAG + 0.71*GF) is 26% higher than the energy associated with the model of (0.5*eAG + 0.5*GF). This higher energy difference is a result from the model of (0.29*eAG + 0.71*GF) which contains a higher component contribution (971% > 50%) from GF than the model of (0.5*eAG + 0.5*GF). Again, the relative energies associated with GF values are 1.55x (or 155%) higher than the relative energies associated with eAG. Although the Y-amplitude of a FD space is directly proportional to the relative energy level of the glucose in the TD space, this finding reveals the significance of GF in diabetes control. In other words, the commonly adopted concept of using average glucose values, such as the popular biomarker of HbA1C, is still useful in diabetes practice. However, the mean value itself alone is not a sufficient diabetes control biomarker. The importance of glucose fluctuation between its peak and nadir should not be ignored or overlooked in overall diabetes control, particularly for situations of complex diabetic complications, including macro-vascular diseases, such as stroke, cardiovascular disease, and micro-vascular diseases, such as peripheral neuropathy, retinopathy, nephropathy, and even cognitional disorders.

Keywords: Average glucose; Time domain; Frequency domain; Continuous glucose monitoring; Fasting plasma glucose; Postprandial plasma glucose

Abbreviations: CGM: continuous glucose monitoring; FPG: fasting plasma glucose; PPG: postprandial plasma glucose; GF: glucose fluctuation; TD: time domain; FFT: Fast Fourier Transform; FD: frequency domain; HbA1C: glycated hemoglobin; MPM: math-physical medicine

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1. INTRODUCTION

The author utilized a flash glucose monitoring (FGM) technique with a 14-day system of continuous monitoring glucose (CGM) sensor device and a customized Bluetooth signal transferring device to collect glucose data (sensor glucose) from 5/5/2018 to 5/31/2021. As a result, over the 1,218 days with 96 glucose data per day, a total of 116,928 glucose data were recorded and stored on a US-based cloud server for data analysis and medical research work[1,2].

Along with the hardware devices, he developed a customized software with artificial intelligence capability to conduct his desired data analysis and medical research work on the iPhone and PC.

This investigation contains two parts. The first part is the study of his average glucose (eAG) which includes 4 segments: fasting plasma glucose (FPG), postprandial plasma glucose (PPG), between meals glucose, and pre-bed glucose. The second part consists of his average glucose fluctuations (GF) every 4 hours each day. GF is defined as the maximum glucose value (peak) minus the minimum glucose value (nadir) in a day which describes the degree of glucose fluctuation that is oscillation or vibration[3,4].

He applied a time domain (TD) analysis to obtain the magnitude (the Y-amplitude of TD space) of the average amplitudes of glucose itself and glucose fluctuation. He then applied the Fast Fourier transform (FFT) technique to conduct his frequency domain (FD) analysis to obtain the estimated relative energy associated with his daily glucose and daily GF (the Y-amplitude of FD space). In his previous research papers, he has proven that the Y-axis magnitude (Y-amplitude) of FD is directly proportional to the relative energy level associated with glucose amplitude value in TD that is the glucose magnitude or Y-amplitude of TD. In this way, he can quickly estimate the relative energy levels associated with different glucose levels in order to understand the varying degree of organ impact due to these relative energies. The relative energies are generated by the glucose wave itself and its wave fluctuation amplitude are carried by red blood cells (RBC) circulating in the blood vessels throughout the body[5,6].

2. METHODS

2.1 MPM background

To learn more about his developed GH-method: math-physical medicine (MPM) methodology, readers can read the following three papers selected from the published 400+ medical papers.

The first paper, No. 386, describes his MPM methodology in a general conceptual format[1]. The second paper, No. 387, outlines the history of his personalized diabetes research, various application tools, and the differences between the biochemical medicine (BCM) approach vs. the MPM approach[2]. The third paper, No. 397 depicts a general flow diagram containing ~10 key MPM research methods and different tools[3].

2.2 The author's case of diabetes

The author was a severe type 2 diabetes patient since 1996. He weighed 220 lb. (100 kg) at that time. By 2010, he still weighed 198 lb. with an average daily glucose of 250 mg/dL (HbA1C of 10%). During that year, his triglycerides reached 1161 and the albumin-creatinine ratio (ACR) at 116. He also suffered from five cardiac episodes within a decade. In 2010, three independent physicians warned him regarding his need for kidney dialysis treatment and his future high risk of dying from his severe diabetic complications[7].

In 2010, he decided to self-study endocrinology, diabetes and food nutrition. During 2015 and 2016, he developed four prediction models related to diabetes conditions i.e., weight, PPG, FPG, and HbA1C (A1C). As a result, from using his developed mathematical metabolism index (MI) model and those four prediction tools, by end of 2016, his weight was reduced from 220 lbs. (100 kg) to 176 lbs. (89 kg), waistline from 44 inches (112 cm) to 33 inches (84 cm), averaged finger glucose from 250 mg/dL to 120 mg/dL, and HbA1C from 10% to ~6.5%. One of his major accomplishments is that he no longer takes any diabetes medication since 12/8/2015[8,9].

In 2017, he had achieved excellent results on all fronts, especially glucose control. However, during the pre-COVID period of 2018 and 2019, he traveled to approximately 50+ international cities to attend 65+ medical conferences and made ~120 oral presentations. This hectic schedule inflicted damage to his diabetes control, through dining out frequently, post-meal exercise disruption, jet lag, and overall metabolism impact due to his irregular life patterns through a busy travel schedule; therefore, his glucose control was affected during this two-year period[10].

By 2020, his weight was further reduced to 165 lbs. (BMI 24.4) and his HbA1C was at 6.2% without any medication intervention or insulin injection. Actually, during 2020 with the special COVID-19 quarantined lifestyle, not only has he published approximately 400 medical papers in journals, but he has also achieved his best health conditions for the past 26 years. These good results are due to his non-traveling, low-stress, and regular daily life routines. Of course, his strong knowledge of chronic diseases, practical lifestyle management experiences, and his developed various high-tech tools contribute to his excellent health status since 1/19/2020.

On 5/5/2018, he applied a CGM sensor device on his upper arm and checks his glucose measurements every 15 minutes for a total of ~96 times each day. He has maintained the same measurement pattern to the present day.

Therefore, during the past 11 years, he could study and analyze his collected ~2 million data regarding his health status, medical conditions, and lifestyle details. He applies his knowledge, models, and tools from mathematics, physics, engineering, and computer science to conduct his medical research work. His medical research work is based on the aim of achieving high precision with quantitative proof in his medical findings[11].

2.3 Glucose and HbA1C

Using signal processing techniques, the author identified approximately 20 influential factors of physical behaviors for glucose. From these 20 factors, he further outlined the following six most prominent conclusions for his glucose and HbA1C values:

(1) The CGM sensor based A1C variances have the following contributions: 29% from FPG, 38% from PPG, and 33% from between meals and pre-bedtime periods. Therefore, all three segments contributed to HbA1C value almost equally.

(2) FPG variance due to weight change with ~77% contribution.

(3) Colder weather impact on FPG with a decrease of each Fahrenheit degree caused 0.3 mg/dL decrease of FPG.

(4) PPG variance due to carbs/sugar intake with ~39% weighted contribution on PPG.

(5) PPG variance due to post-meal walking with ~41% weighted contribution on PPG.

(6) Warm weather impact on PPG with an increase of each Fahrenheit degree caused 0.9 mg/dL increase of PPG.

It is common knowledge that HbA1C is closely connected to the average glucose for the past 90 days. Actually, the average human RBC, after differentiating from erythroblasts in the bone marrow, are released into the blood and survive in circulation for approximately 115 days. Although the author has adopted the 120-day model in his previous sensor HbA1C studies, he uses the 90-day model in this particular study. It should also be pointed out that he utilized the CGM collected sensor glucose and calculated HbA1C to compare against his collected nine lab-tested HbA1C data, while the lab A1C data actually contained a large margin of error due to various reasons[12-15].

2.4 GF and diabetic complications

The following are excerpts taken from two references[16,17]:

"From reference 16: Diabetes mellitus is a world-wide health issue with potential for significant negative health outcomes, including microvascular and macrovascular complications. The relationship of hemoglobin HbA1c and other glycosylation end products (AGEs) to these complications, particularly microvascular disease, is well understood. More recent evidence suggests

that glycemic variability may be associated with diabetes macrovascular complications. As HbA1c is better representative of average glucose levels and does not account as well for glycemic variability, hence new methods to assess and treat this variability is needed to reduce incidence of complications.

From reference 17: Few physicians recognized that only 6.6% of the variation in risk of retinopathy for the entire study cohort was explained by the difference in the treatment groups, although it was widely appreciated that nearly all of this treatment group effect was explained by differences in the mean level of HbA1C over time. The trial results also considered the instantaneous risk of retinopathy (i.e., whether a patient would develop retinopathy at a particular point in time during the study) rather than eventual risk of retinopathy (whether a patient would develop retinopathy over his or her entire life). However, this latter outcome is not feasible to study because it would require lifetime follow-up of patients.

Similarly, HbA1C and duration of diabetes (glycemic exposure) explained only about 11% of the variation in retinopathy risk for the entire study population, suggesting that the remaining 89% of the variation in risk is presumably explained by other factors independent of HbA1C. Given the magnitude of the effect of unmeasured elements in the Diabetes Control and Complications Trial, identification of these elements is critically important for designing more effective therapy for type 1 diabetes.

What factors not captured by HbA1C measurements might explain the remaining 89% of microvascular complications risk? Possible factors unrelated to blood glucose levels include genetics, environmental toxins, and metabolic consequences of abnormal insulinization such as increased free fatty acid levels. Possible factors related to blood glucose levels most likely reflect the fact that since HbA1c represents the time-averaged mean level of glycemia, it provides no information about how closely the fluctuations of blood glucose levels around that mean mimic the normal narrow range of blood glucose excursion. In addition, patients with identical HbA1C values differ significantly in amplitude and duration of glycemic spikes."

2.5 Glucose fluctuation (GF)

Another excerpt regarding glucose and glucose fluctuation is listed below[18]:

"A variety of stimulations and mechanisms tightly regulates blood sugar levels. This is important for metabolic homeostasis. Levels may fluctuate after fasting for long periods of time or an hour or two after food consumption. Despite this, the fluctuations are minor. Normal human blood glucose levels remain within a remarkably narrow range.

Blood sugar fluctuations:
In most humans, this varies from about 82 mg/dl to 110 mg/dl (4.4 to 6.1 mmol/l) and the author takes the averaged glucose fluctuation from the mid-point value of 96 mg/dL. The blood sugar levels rise to nearly 140 mg/dl (7.8 mmol/l) or a bit more in normal humans after a full meal. In humans, normal blood glucose levels are around 90 mg/dl, equivalent to 5mM (mmol/l). Since the molecular weight of glucose, C6H12O6, is about 180 g/mol, when calculated, the total amount of glucose normally in circulating human blood is around 3.3 to 7g (assuming an ordinary adult blood volume of 5 liters)."

2.6 GF-influenced eAG equations

In this study, he has defined the following two effective glucose equations which combine eAG and GF with two different weighting splits between eAG and GF:

Effective glucose equation no. 1 = (0.29*eAG + 0.71*GF)

Effective glucose equation no. 2 = (0.5*eAG + 0.5*GF)

3. RESULTS

Figure 1 shows the daily data and curves of both eAG and GF with FD curves of eAG and GF.

eAG / GF = 1.29
GF energy / eAG energy = 2.55
R of 90-days eAG & GF = 64%

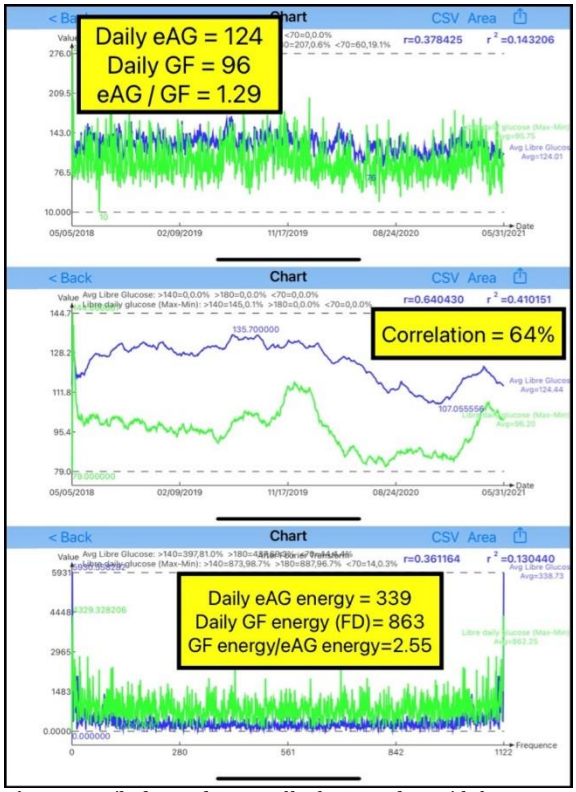


Figure 1: Daily data and curves of both eAG and GF with frequency domain curves of eAG and GF.

Figure 2 reflects the average eAG of 124 mg/dL and average GF of 96 mg/dL in TD with a 29% difference on glucose level in mg/dL.

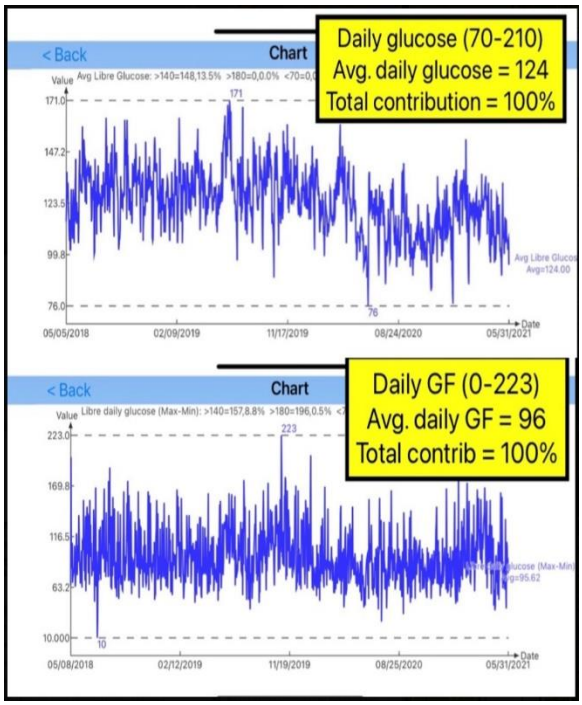
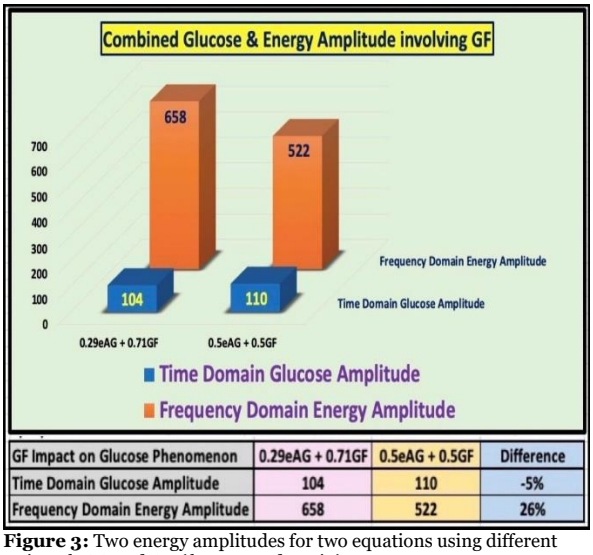


Figure 2: Averaged eAG is 124 mg/dL and averaged GF is 96mg/dL (time domain).

Figure 3 depicts 2 energy amplitudes for 2 equations using different ratios of eAG and GF in FD.



GF Impact on Glucose Phenomenon	0.29eAG + 0.71GF	0.5eAG + 0.5GF	Difference
Time Domain Glucose Amplitude	104	110	-5%
Frequency Domain Energy Amplitude	658	522	26%

Figure 3: Two energy amplitudes for two equations using different ratios of eAG and GF (frequency domain).

The model of (0.29*eAG + 0.71*GF) has a lower effective glucose value (104) than the effective glucose value (110) of the model of (0.5*eAG + 0.5*GF) with a small difference of 5%. However, in the FD analysis, the model of (0.29*eAG + 0.71*GF) has a moderately higher associated energy (658) than the associated energy (522) of the model of (0.5*eAG + 0.5*GF) with a moderate difference of 26%.

In Figure 4, the conclusive diagram illustrates the comparison results from two different equations of the combined eAG and GF in both TD and FD.

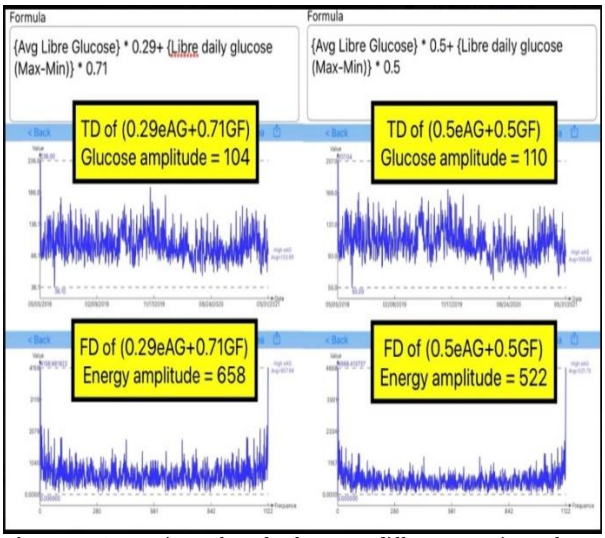


Figure 4: Comparison of results from two different equations of combining eAG and GF (both TD and FD).

4. CONCLUSION

In summary, human organs and glucose have their biochemical reasonings and needed operations, but they also present certain biophysical phenomena following the physics theories and principles which can be interpreted or solved using various mathematical equations or statistical tools[19,20].

The following paragraphs describe his two equations along with his major findings from this study:

Effective glucose equation no. 1 = (0.29*eAG + 0.71*GF)

Effective glucose equation no. 2 = (0.5*eAG + 0.5*GF)

In TD analysis, the ratio of eAG (124) over GF (96) is 129%. However, in FD analysis, the ratio of GF energy (863) over eAG energy (339) is 255%. This means that the energy associated with the difference between wave extremities (GF) is much higher than the energy associated with mean value of wave (eAG)[21,22].

In TD analysis, using two different combinations of eAG split and GF split, the model of (0.29*eAG + 0.71*GF) has a lower effective glucose value (104) than the effective glucose value (110) of the model of (0.5*eAG + 0.5*GF) with a small difference of 5%. However, in FD analysis, the model of (0.29*eAG + 0.71*GF) has a moderately higher associated energy (658) than the associated energy (522) of the model of (0.5*eAG + 0.5*GF) with a moderate difference of 26%. This means that the energy associated with the model of (0.29*eAG + 0.71*GF) is 26% higher than the energy associated with the model of (0.5*eAG + 0.5*GF). This higher energy difference is a result from the model of (0.29*eAG + 0.71*GF) which contains a higher component contribution (971% > 50%) from GF than the model of (0.5*eAG + 0.5*GF)[23-25].

Again, the relative energies associated with GF values are 1.55x (or 155%) higher than the relative energies associated with eAG. Although the Y-amplitude of a FD space is directly proportional to the relative energy level of the glucose in the TD space, this finding reveals the significance of GF in diabetes control. In other words, the commonly adopted concept of using average glucose values, such as the popular biomarker of HbA1C, is still useful in diabetes practice[26-30]. However, the mean value itself alone is not a sufficient diabetes control biomarker. The importance of glucose fluctuation between its peak and nadir should not be ignored or overlooked in overall diabetes control, particularly for situations of complex diabetic complications, including macro-vascular diseases, such as stroke, cardiovascular disease, and micro-vascular diseases, such as peripheral neuropathy, retinopathy, nephropathy, and even cognitional disorders[31-36].

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