

Investigation of GH Modulus on the Linear Elastic Glucose Behavior Based On Three Diabetes Patients' Data using the GH-Method: Math-Physical Medicine, Part 3 (No. 350)

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Abstract

This article is Part 3 of the linear elastic glucose research work. It is also the continuation of the simple linear equation for the predicted postprandial plasma glucose (PPG) in References 2, 3, and 4.

Here is the formula

Predicted PPG = $(FPG * 0.97) + (\text{carbs/sugar grams} * M2) - (\text{post-meal waking K-steps} * 5)$

The author connected his biomedical equation with a basic concept of linear elasticity which includes stress and strain, along with the Young's modulus of strength of materials in structural & mechanical engineering. By using the collected data of glucose, food, and exercise from three different type 2 diabetes (T2D) patients, he demonstrated once again that a "pseudo-linear" relationship existed in all three clinical cases, between the carbs/sugar intake amount and incremental PPG amount, with a newly defined coefficient of "GH modulus" (same as the M2 multiplier) cited in References 7 and 8. The linear elastic glucose behavior is similar to the Young's modulus (E) linking stress and strain of engineering strength of materials.

He selected three T2D patients with different levels of severity. For data consistency purposes, he has chosen data from 7-monthly sub-periods of equal length from 3/18/2020 - 10/18/2020. The main objective of this study is to prove that GH-modulus (M2) indeed vary with the severity of diabetes for these three clinical cases.

The 7-month average value of each monthly M2 variables (i.e., GH-modulus) are 3.7, 2.6, and 1.0, and with an average measured PPG values at 122 mg/dL, 114 mg/dL, and 109 mg/dL, for Case A, Case B, and Case C, respectively, which are ranked according to the severity of their diabetes conditions.

In summary, the higher the M2, the higher values of both x (carbs/sugar intake amount) and y (incremental PPG amount) become, and the higher predicted and measured PPG values are. The key conclusion from these three clinical observations is that the M2 values are varying based on patients' body conditions (liver and pancreas), especially their diabetes severity. This is similar to the different inorganic materials having the different Young's modulus values, such as nylon ~3 versus steel ~200.

The article represents the author's special interest in using math-physical and engineering modeling methodologies to investigate various biomedical problems. The methodology and approach are a result of his specific academic background and various professional experiences prior to the start of his medical research work in 2010. Therefore, he has been trying to link his newly acquired biomedical knowledge over the past decade with his previously acquired mathematics, physics, computer science, and engineering knowledge over 40 years.

The human body is the most complex system he has dealt with, which includes aerospace, navy defense, nuclear power, computers, and semiconductors. By applying his previous acquired knowledge to his newly found interest of medicine, he can discover many hidden facts or truths inside the biomedical systems. Many basic concepts, theoretical frame of thoughts, and practical modeling techniques from his fundamental disciplines in the past can be applied

to his medical research endeavor. After all, science is based on theory via creation and proof via evidence, and as long as we can discover hidden truths, it does not matter which method we use and which option we take. This is the foundation of the GH-Method: math-physics medicine.

The author has spent four decades as a practical engineer and understands the importance of basic concepts, sophisticated theories, and practical equations which serve as the necessary background of all kinds of applications. Therefore, he spent his time and energy to investigate glucose related subjects using variety of methods he studied in the past, including this particular interesting stress-strain approach. On the other hand, he also realizes the importance and urgency on helping diabetes patients to control their glucoses. That is why, over the past few years, he has continuously simplified his findings about diabetes and derive more useful formulas or practical tools for meeting the general public's interest on controlling chronic diseases and their complications to reduce their pain and death threat probability.

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He selected three T2D patients with different levels of severity. For data consistency purposes, he has chosen data from 7-monthly sub-periods of equal length from 3/18/2020 - 10/18/2020. The main objective of this study is to prove that GH-modulus (M2) indeed vary with the severity of diabetes for these three clinical cases.

Methods

Background

To learn more about the author's GH-Method: math-physical medicine (MPM) methodology, readers can refer to his article to understand his developed MPM analysis method in Reference 1.

Highlights of his Previous Research

In 2015, the author decomposed the PPG waveforms (data curves) into 19 influential components and identified carbs/sugar intake amount and post-meal walking exercise contributing to approximately 40% of PPG formation, respectively. Therefore, he could safely discount the importance of the remaining ~20% contribution by the 16 other influential components.

In 2016, he utilized optical physics, big data analytics, and arti-

cial intelligence (AI) techniques to develop a computer software to predict PPG based on the patient's food pictures or meal photos. This sophisticated AI approach and iPhone APP software product have reached to a 98.8% prediction accuracy based on ~6,000 meal photos.

In 2017, he also detected that body weight contributes to over 85% to fasting plasma glucose (FPG) formation. Furthermore, in 2019, he identified that FPG could serve as a good indicator of the pancreatic beta cells' health status; therefore, he can apply the FPG value (more precisely, 97% of FPG value) to serve as the baseline PPG value to calculate the PPG incremental amount in order to obtain the predicted PPG.

In 2018, based on his collected ~2,500 meals and associated sensor PPG waveforms, he further applied the perturbation theory from quantum mechanics, using the first bite of his meal as the initial condition to extend and build an entire PPG waveform covering a period of 180 minutes, with a 95% of PPG prediction accuracy.

In 2019, all of his developed PPG prediction mathematical models achieved high percentages of prediction accuracy, but he also realized that his prediction models are too difficult for use by the general public. The above-mentioned sophisticated methods would be difficult for healthcare professionals and diabetes patients to understand, let alone use them in their daily life for diabetes control. Therefore, he supplemented his complex models with a simple linear equation of predicted PPG (see References 2, 3, and 4).

Here is his simple linear formula:

$$\text{Predicted PPG} = \text{FPG} * M1 + (\text{carbs-sugar} * M2) - (\text{post-meal walking k-steps} * M3)$$

Where M1, M2, M3 are 3 multipliers.

After lengthy research, trial and error, and data tuning, he finally identified the best multipliers for FPG and exercise as 0.97 for M1 and 5.0 for M3. In comparison with PPG, the FPG is a more stabilized biomarker since it is directly related to body weight. We know that weight reduction is a hard task. However, weight is a calmer and more stabilizing biomarker in comparison to glucose which fluctuates from minute to minute. The influence of exercise (specifically, post-meal walking steps) on PPG (41% contribution

and >80% negative correlation with PPG) is almost equal to the influence from the carbs/sugar intake amount on PPG (39% contribution and >80% positive correlation with PPG). In terms of intensity and duration, exercise is a simple and straightforward subject to study. Especially, normal-speed walking is a safe and effective form of exercise for the large portion of diabetes patients, the senior people.

The parameters, FPG and walking, have a lower chance of variation for the author. However, for some diabetes patients, he recommends them to keep the multiplier M3 as a variable if their exercise patterns are different and changing.

The relationship between food nutrition and glucose is a complex and difficult subject to fully understand and effectively manage due to many types of food and their associated carbs/sugar contents. For example, in the author's developed food material and nutrition database, it contains over six million data. As a result, the author decided to implement two multipliers, M1 for FPG and M3 for exercise, as the two "constants" and keep M2 as the only "variable" in his PPG prediction equation and the linear elastic glucose research in this article.

The more simplified linear equation for predicted PPG is listed below:

$$\text{Predicted PPG} = (0.97 * \text{FPG}) + (\text{Carbs \& sugar} * M2) - (\text{post-meal walking } k\text{-steps} * 5)$$

Where he created three new terms:

Term 1
GH modulus = M2

Term 2
The incremental PPG amount
= Predicted PPG - PPG baseline
(I.e., 0.97 * FPG) + exercise effect
(i.e., walking k-steps * 5)

Term 3
GH modulus
= (Incremental PPG) / (Carbs & sugar)

Stress, Strain, & Young's Modulus

Prior to his medical research work, he was an engineer in the various fields of structural engineering (aerospace, naval defense, and earthquake engineering), mechanical engineering (nuclear power plant equipments, and computer-aided-design), and electronics engineering (computers, semiconductors, and software robot).

The following excerpts comes from internet public domain, including Google and Wikipedia:

Strain - ϵ

Strain is the "deformation of a solid due to stress" - change in dimension divided by the original value of the dimension - and can be expressed as
 $\epsilon = dL / L$

where

ϵ = strain (m/m, in/in)

dL = elongation or compression (offset) of object (m, in)

L = length of object (m, in)

Stress - σ

Stress is force per unit area and can be expressed as

$$\sigma = F / A$$

where

σ = stress (N/m², lb/in², psi)

F = applied force (N, lb)

A = stress area of object (m², in²)

Stress includes tensile stress, compressible stress, shearing stress, etc.

E, Young's Modulus

It can be expressed as:

$$E = \text{stress} / \text{strain}$$

$$= \sigma / \epsilon$$

$$= (F / A) / (dL / L)$$

where

E = Young's Modulus of Elasticity (Pa, N/m², lb/in², psi) was named after the 18th-century English physicist Thomas Young.

Elasticity

Elasticity is a property of an object or material indicating how it will restore it to its original shape after distortion. A spring is an example of an elastic object - when stretched, it exerts a restoring force which tends to bring it back to its original length (Figure 1).

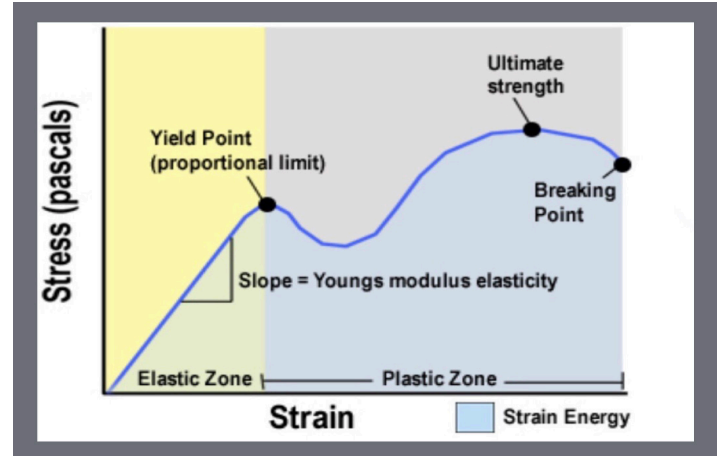


Figure 1: Stress-Strain-Young's modulus, Elastic Zone vs. Plastic Zone

Plasticity

When the force is going beyond the elastic limit of material, it is into a "plastic" zone which means even when force is removed, the material will not return back to its original state (Figure 1).

Based on various experimental results, the following table lists some Young's modulus associated with different materials:

Nylon: 2.7 GPa

Concrete: 17-30 GPa

Glass fibers: 72 GPa
Copper: 117 GPa
Steel: 190-215 GPa
Diamond: 1220 GPa

Young's modules in the above table are ranked from soft material (low E) to stiff material (higher E)."

Professor James Andrews taught the author linear elasticity at the University of Iowa and Professor Norman Jones taught him non-linear plasticity at Massachusetts Institute of Technology. These two great academic mentors provided him the foundation knowledge to understand these two important subjects in engineering.

Linear Elastic Glucose Research

In this particular study, he uses the analogy of relationship among stress, strain, and Young's modulus to illustrate a similar relationship among carbs/sugar intake amount, incremental predicted PPG, and GH modulus (i.e., M2). They are listed below for a closer comparison.

GH modulus (M2) = (Incremental PPG)/(Carbs&sugar)

Young's modulus E = stress / strain = σ / ϵ

Where Incremental PPG is the incremental amount of predicted PPG (note: the predicted PPG is also replaced by the measured PPG in order to conduct a sensitivity study of glucose behaviors.).

The author visualizes the carbs/sugar intake amount as the stress (the force or stimulator) on his liver and the incremental PPG amount as the strain (the response or stimulation) from the liver. The GH modulus (i.e., M2) is similar to the Young's modulus (i.e., E) which describes the "pseudo-linear" relationship existing between the carbs/sugar intake amount (stress) and the incremental predicted PPG (strain).

In Part 1 of the linear elastic glucose study (Reference 7), he proved the existence of the linear relationship between carbs/sugar intake amount and incremental PPG amount. In Part 2, two T2D patients within the same 9-month period (Reference 8), he proved that the more severe a T2D patient is, then the higher GH-modulus. In Part 3, he uses three clinical cases within the same 7-month period to prove again that the orders of magnitude in the GH-modules are following the severities of diabetes conditions in the patients.

Data Collection

Case A (the author) is a 73-year-old male with a 25-year history of T2D. He began collecting his carbs/sugar intake amount and post-meal walking steps on 7/1/2015. From 7/15/2015 to 10/18/2020 (1,935 days), he has collected 6 data per day, 1 FPG, 3 PPG, carb/sugar, and post-meal walking steps. He utilized these 11,610 data of 1,935 days to conduct his prior research work on the subject of linear elastic glucose study (Reference 7). In addition, on 5/5/2018,

he started to use a continuous glucose monitoring (CGM) sensor device to collect 96 glucose data each day.

The period of 7/1/2015 to 10/18/2020 is his "best-controlled" diabetes period, where his average daily glucoses is maintained at 116 mg/dL (<120 mg/dL). He named this as his "linear elastic zone" of diabetes health. It should also be noted that in 2010, his average glucose was 280 mg/dL and HbA1C was 10%, while taking three diabetes medications. Please note that the strong chemical interventions from various diabetes medications would seriously alter glucose physical behaviors. He called the period prior to 2015 as his "nonlinear plastic zone" of diabetes health.

The second set of data comes from his wife (Case B) with a 22-year history of T2D. She began to collect her glucose data via finger-piercing method (finger glucose) since 1/1/2014. However, she does not keep a detailed record of her diet and exercise. Both patients eat almost the same meals prepared by the author, except that she consumes more meat which partially affects her hyperlipidemia and hypertension conditions. From the diabetes research viewpoint, he decided to use 80% of the Case A's carbs/sugar amount for her and use 50% of the Case A's post-meal walking steps for her. On 1/1/2020, she began using the same brand of CGM device to collect her sensor glucose data at the same rate of 96 data per day since 1/1/2020.

Case C is 47-year-old male with a 4-year history of T2D. He started to collect his glucose data using the same model of CGM sensor on 3/18/2020. Through a telephone interview, the author discovered that over the past 7-month period, his average carbs/sugar intake amount is about the same amount as Case A, and his average post-meal walking steps is at ~25% level compared to Case A.

It should be mentioned here, other than the male case who has collected a complete dataset of diet and exercise, both female and young cases are using the best guess-estimated percentages of male case amount of diet and exercise. Therefore, these data differences would definitely create some degree of result deviation.

In order to maintain data consistency for a fair and accurate comparison, the author took the CGM sensor glucose data from Cases A, B, and C from 3/18/2020 through 10/18/2020 and subdivided them into 7-monthly sub-periods of equal length to study their glucose fluctuation patterns and data. The reason for using sensor glucose data over finger glucose is because they are 13% to 18% higher. Therefore, the sensor data would be more conservative in terms of diabetes severity. Finally, the author calculated the three GH-modulus values via the approach of matching the predicted PPG values with the yardstick of measured PPG values.

Results

Figure 2 shows the raw data collected from the three cases and their respective predicted PPG values of each sub-period.

Male Sensor	3/18-4/18	4/18-5/18	5/18-6/18	6/18-7/18	7/18-8/18	8/18-9/18	9/18-10/18	Average
PPG (peak)	141	133	128	134	120	125	119	129
Male Measured PPG	136	125	117	128	115	119	112	122
FPG (Average)	114	105	96	101	100	99	91	101
Carbs/Sugar (grams)	12.73	16.18	12.55	9.79	10.67	12.93	11.81	12.38
Walking (K-steps)	4.528	4.268	3.895	4.039	4.009	4.148	4.252	4.163
Male predicted PPG	133	139	119	113	116	122	110	122
Female Sensor	3/18-4/18	4/18-5/18	5/18-6/18	6/18-7/18	7/18-8/18	8/18-9/18	9/18-10/18	Average
PPG (peak)	120	118	116	128	118	119	113	119
Female Measured PPG	115	114	113	118	112	113	110	114
FPG (Average)	98	103	107	103	97	101	106	102
Carbs/Sugar (grams)	10.18	12.94	10.04	7.83	8.54	10.34	9.45	9.90
Walking (K-steps)	2.264	2.134	1.948	2.020	2.005	2.074	2.126	2.08
Female predicted PPG	110	122	120	110	106	114	116	114
Young Sensor	3/18-4/18	4/18-5/18	5/18-6/18	6/18-7/18	7/18-8/18	8/18-9/18	9/18-10/18	Average
PPG (peak)	132	102	108	105	123	106	107	112
Young Measured PPG	125	101	108	105	121	102	104	109
FPG (Average)	117	100	107	106	115	94	95	105
Carbs/Sugar (grams)	12.73	16.18	12.55	9.79	10.67	12.93	11.81	12.38
Walking (K-steps)	1.132	1.067	0.974	1.010	1.002	1.037	1.063	1.041
Young Predicted PPG with Fixed M2 of 1.0323	121	108	112	108	118	100	99	109
Young Predicted PPG with variable M2	125	101	108	105	121	102	104	109

Figure 2: Raw data and predicted PPG for the 7-month period of three patients

Figure 3 lists a data table of calculated x- and y- components, where

x is $(carbs \& sugar * M2)$

and

y is $(measured\ PPG - (FPG * 0.97) + (walking\ k-steps * 5))$.

Male X: (Carbs*M2)	48	45	44	51	38	44	45	45
Male Y: (Meas PPG)-(0.97FPG)+(Steps*5)	48	45	44	51	38	44	45	45
Female X: (Carbs*M2)	32	25	19	29	27	26	18	25
Female Y: (Meas. PPG)-(0.97FPG)+(Steps*5)	32	25	19	29	27	26	18	25
Young X: (Carbs*M2)	13	17	13	10	11	13	12	13
Young Y: (Meas. PPG)-(0.97FPG)+(Steps*5)	13	17	13	10	11	13	12	13
Male M2 (Variable)	3.8	2.8	3.5	5.2	3.6	3.4	3.8	3.7
Female M2 (Variable)	3.1	1.9	1.9	3.6	3.2	2.5	1.9	2.6
Young M2 (Variable)	1.3	0.6	0.7	0.7	1.4	1.2	1.4	1.0

Figure 3: Calculated x and y components using variable M2 values for the 7-month period of three patients

This table provides the most suitable GH-modulus (i.e., M2) values for each month which allows the predicted PPG to match the measured PPG via trial-and-error.

The 7-month average value of each monthly M2 variables (i.e., GH-modulus) are 3.7, 2.6, and 1.0, and with an average measured PPG values at 122 mg/dL, 114 md/dL, and 109 mg/dL, for Case A, Case B, and Case C, respectively, which are ranked according to the severity of their diabetes conditions.

Listed below are the values of the individual M2 multiplier (i.e., GH-modulus) for each of the 7 months in 2020 which are listed in the order of (Case A, Case B, Case C):

3/18 - 4/18: (3.8, 3.1, 1.3)

4/18 - 5/18: (2.8, 1.9, 0.6)

5/18 - 6/18: (3.5, 1.9, 0.7)

6/18 - 7/18: (5.2, 3.6, 0.7)

7/18 - 8/18: (3.6, 3.2, 1.4)

8/18 - 9/18: (3.4, 2.5, 1.2)

9/18 - 10/18: (3.8, 1.9, 1.4)

Variable M2: (3.7, 2.6, 1.0)

Fixed M2: (3.6, 2.6, 1.0)

Case A with the fixed M2 as 3.6, both x and y are within the range of 38 to 48 with an average value of 45 are observed in Figure 4. Case B with the fixed M2 as 2.6, both x and y are within the range of 18 to 32 with an average value of 25 are observed in Figure 5. Case C with the fixed M2 as 1.0, both x and y are within the range of 11 to 17 with an average value of 13 are observed in Figure 6.

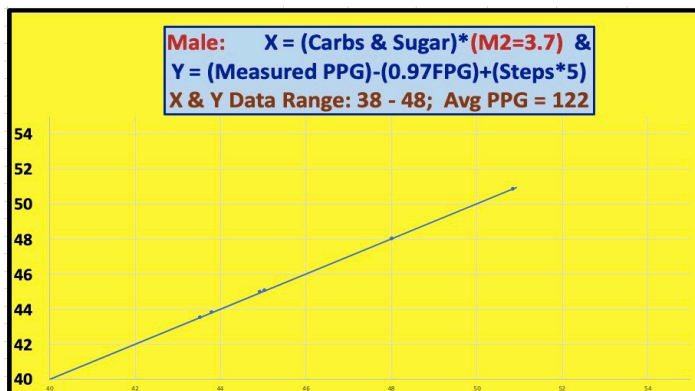


Figure 4: Linear elastic glucose behavior between cars/sugar input and incremental PPG output for male case A during the 7-month period

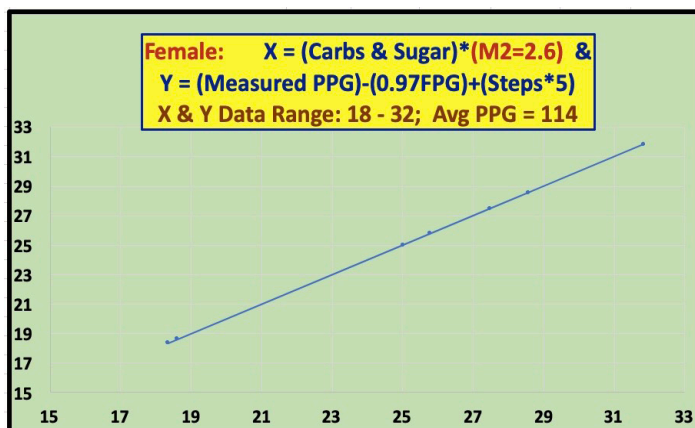


Figure 5: Linear elastic glucose behavior between cars/sugar input and incremental PPG output for female case B during the 7-month period

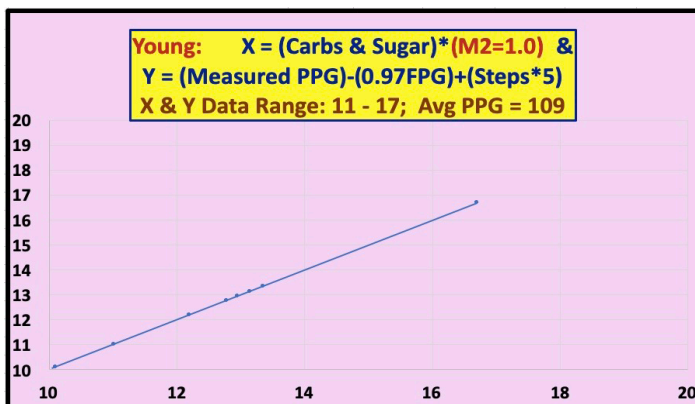


Figure 6: Linear elastic glucose behavior between cars/sugar input and incremental PPG output for young case C during the 7-month period

7-month period.

In summary, the higher the M2, the higher values of both x (carbs/sugar intake amount) and y (incremental PPG amount) become, and the higher predicted and measured PPG values are. The key conclusion from these three clinical observations is that the M2 values are varying based on patients' body conditions (blood, liver, pancreas), especially their diabetes severity. This is similar to the different inorganic materials having the different Young's modulus values, such as nylon ~3 versus steel ~200.

Discussion

The raw data table in Figure 2 and the calculation of x, y, variable M2 in Figure 3, along with the three graphs in Figures 4, 5 and 6, the author utilized variable M2 values for each month in order to make the calculated x-component values to match with the calculated y-components values during each monthly sub-period; therefore, to “force” the predicted PPG value to match with the measured PPG value in each month. As a result, a linear or “pseudo-linear” relationship between x-component and y-component could be created and observed.

This forced “pseudo-linear” relationship makes sense in the biomedical field since red blood cells and liver cells are organic materials which are different from those inorganic materials in the engineering systems, such as rubber or steel. The human organ cells are not only organic but also have different lifespans, where they can mutate, change, repair, or die. For example, the lifespan of the red blood cells is 115 to 120 days, the lifespan of liver cells is 300 to 500 days, and the lifespan of pancreatic beta cells is unknown with a slightly adaptive change. As indicated in his previous research, the pancreatic beta cells' self-repair process is extremely slow, taking approximately 2.7% per year for the author. Not all of the body cells die at the same moment. At any given instance, an organ would have different combination of new cells, sick cells, dying cells, and mutated cells that can mix together. It is an overly complex and extraordinary situation; therefore, the author has chosen variable M2 values for different months in order to achieve his prediction accuracies for all sub-periods. This would be a reasonable approach for this particular biomedical research. These data have demonstrated that the variable M2 values of different months resulted from the T2D conditions varying month to month for each patient, precisely the combined situation of liver, blood, and pancreas. This means that glucose is a very “dynamic” function instead of being a “static” function. The above discussions are the major differences between the linear elasticity *organic* glucoses and the traditional linear elasticity of strength of *inorganic* engineering materials.

Conclusions

The article represents the author's special interest in using math-physical and engineering modeling methodologies to investigate various biomedical problems. The methodology and approach are a result of his specific academic background and various professional experiences prior to the start of his medical research work in 2010. Therefore, he has been trying to link his newly acquired biomedical knowledge over the past decade with

his previously acquired mathematics, physics, computer science, and engineering knowledge for over 40 years.

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Acknowledgement

Foremost, I would like to express my deep appreciation to my former professors: professor James Andrews at the University of Iowa, who helped develop my foundation in basic engineering and computer science, and professor Norman Jones at the Massachusetts Institute of Technology, who taught me how to solve tough scientific problem through the right attitude and methodology.

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