Special Issue 5
2022

https://www.theghmethod.com

The GH-Method

Viscoelastic Medicine Theory (VMT #406): Relationships Between Three Glucose Biomarkers, TIR, TBR, TAR, and Six Diseases, T2D, CVD, CKD, Alzheimer's, Parkinson's, Cancers, Using Viscoplastic Energy Model of GH-Method: Math-Physical Medicine (No. 1008)

Gerald C. Hsu*

eclaireMD Foundation, USA

Abstract

According to ADA's 2019 report, for adults with diabetes, over 70% TIR is deemed good control, with TBR ideally under 4% and TAR under 25%. Therefore, the author selected his normalization factors of 71 for TIR, 4 for TBR, and 25 for TAR.

He tracked his daily HbA1C using four daily finger-prick tests and a continuous glucose monitoring (CGM) device every 15 minutes since May 1, 2018. He also gathered his quarterly lab HbA1C test results. He then used these three annual average HbA1C values from 2018 to 2023 to conduct his viscoplastic energy analyses of six mortality diseases resulting from his TIR, TBR, and TAR.

In summary, the ranking of three averaged input values are: TIR% = 90.5%; TBR% = 1.4%; TAR% = 2.1%. The ranking of six averaged strain (i.e., disease risk) values are T2D (114); CKD (68); CVD (54); AD (45); PD (40); and Cancers (39). The ranking of six strain change rates over the years are T2D (-2.7); AD (-0.7); PD (-0.7); CKD (-0.5); CVD (-0.3); and Cancers (0.2). Therefore, the ranking of total energy values (the area underneath the stress-strain curve) from SD-VMT analysis are T2D (107) > CKD (15) > AD (14); CVD (12) > PD (9) > Cancers (2).

Explanation: The author has had Type 2 Diabetes (T2D) since 1995. Although it is well-managed, it remains uncured. The higher T2D energy is resulted from using 5.7% to normalize his Lab A1C values. From 1994 to 2005, he experienced five cardiovascular incidents, influenced by both diabetes (eAG at 280 mg/dL, A1C at 11%, triglyceride at 1160) and high business stress. Between 2006 and 2012, he also faced kidney issues with a high ACR of 150. However, thus far, he has not exhibited signs of dementia or cancer.

His six SD-VMT stress-strain energy curves displayed unique curvatures and shapes. Yet, the averaged SD-VMT energy ratios from three metrics - TIR, TBR, and TAR - were similar. These energy sources reflect the varying extents of organ damage he sustained from six mortality diseases: TIR energy = 82%; TBR energy = 16%; TAR energy = 2%.

Key message:
This report presents the author's current health status. His diabetes is under control, as indicated by TIR, TBR, and TAR metrics. His previous issues with cardiovascular disease (CVD) and chronic kidney disease (CKD) appear to be receding, though the near experience with kidney issues is still more significant than heart issues. Despite controlled diabetes, there remains a concern about hypoglycemia's role as an influencer in cognitive and memory impairments, such as Alzheimer's. The risk of developing Parkinson's disease, associated with movement, seems less likely compared to Alzheimer's. Fortunately, the risk of cancer, his greatest concern, remains the lowest among the six major diseases discussed. This report also highlights the effectiveness of using the viscoplastic energy method in his biomedical research.

Keywords: Viscoelastic; Viscoplastic; Diabetes; Glucose; Biomarkers; Insulin; Hyperglycemia

Abbreviations: CGM: continuous glucose monitoring; T2D: type 2 diabetes; PPG: postprandial plasma glucose; FPG: fasting plasma glucose; SD: space-domain; VMT: viscoelastic medicine theory; FFT: Fast Fourier Transform; MI: Metabolism Index; TIR: Time in Range; TBR: Time Below Range; TAR: Time Above Range

Available online: 30 March 2024

*Corresponding author: Gerald C. Hsu, eclaireMD Foundation, USA

1. INTRODUCTION

According to ADA's 2019 report, for adults with diabetes, over 70% TIR is deemed good control, with TBR ideally under 4% and TAR under 25%. Therefore, the author selected his normalization factors of 71 for TIR, 4 for TBR, 25 for TAR.

He tracked his daily HbA1C using four daily finger-prick tests and a continuous glucose monitoring (CGM) device every 15 minutes since May 1, 2018. He also gathered his quarterly lab HbA1C test results. He then used these three annual average HbA1C values from 2018 to 2023 to conduct his viscoplastic energy analyses of six mortality diseases resulting from his TIR, TBR, and TAR.

1.1 Biomedical information:

The following sections contain excerpts and concise information drawn from multiple medical articles, which have been meticulously reviewed by the author of this paper. The author has adopted this approach as an alternative to including a conventional reference list at the end of this document, with the intention of optimizing his valuable research time. It is essential to clarify that these sections do not constitute part of the author's original contribution but have been included to aid the author in his future reviews and offer valuable insights to other readers with an interest in these subjects.

Physiological explanations regarding relationships between HbA1C and TIR, TBR, TAR:

HbA1c (haemoglobin A1c) and the metrics TIR (Time in Range), TBR (Time Below Range), and TAR (Time Above Range) are all measures related to blood glucose control in diabetes. Each metric provides a different perspective on long-term and short-term glucose management, and understanding their pathophysiological implications is important in diabetes care.

HbA1c reflects average blood glucose levels over a period of approximately 2-3 months by measuring the percentage of haemoglobin that is glycated. It provides an indication of overall long-term glucose control and risk for diabetes-related complications. A higher HbA1c level indicates higher average blood glucose levels over the prior months, which is associated with an increased risk of diabetic complications such as retinopathy, neuropathy, and cardiovascular diseases.

In contrast, TIR, TBR, and TAR assessed through continuous glucose monitoring (CGM) offer a more comprehensive view of short-term glucose control. TIR reflects the percentage of time spent within a target glucose range, providing insights into how well blood glucose levels are managed throughout the day. TBR and TAR further provide information about the frequency and duration of hypoglycemic (low) and hyperglycemic (high) episodes, respectively. However, if a longer period of data regarding TIR, TBR, and TAR are available, they can also provide useful information on the patient's glucose co-trim in addition to HbA1C values.

From a pathophysiological standpoint, TIR, TBR, and TAR metrics help to assess how well glucose levels are managed in real time, revealing fluctuations, trends, and patterns in blood glucose control. This information is valuable in understanding the impact of diet, physical activity, insulin or medication dosing, stress, and other factors on day-to-day glucose variability. It allows for the identification of specific areas for improvement and targeted interventions to optimize glycemic control and reduce the risk of acute and chronic complications.

In summary, while HbA1c provides a retrospective average of blood glucose control over an extended period, TIR, TBR, and TAR offer real-time data to evaluate short-term fluctuations and patterns in glucose control, which is essential in developing personalized diabetes management strategies to optimize overall health outcomes.

Pathophysiological explanations of relationships between TIR, TBR, TAR and CVD, CKD, Alzheimer's, Parkinson's, and cancers:

The relationships between Time in Range (TIR), Time Below Range (TBR), Time Above Range (TAR), and various diseases such as Cardiovascular Disease (CVD), Chronic Kidney Disease (CKD), Alzheimer's diseases, Parkinson's diseases, and various cancers involve complex pathophysiological mechanisms.

TIR, TBR, TAR, and Cardiovascular Disease (CVD):

TIR: Maintaining glucose levels within a target range reduces the risk of atherosclerosis and hypertension, common in CVD.

TBR: Frequent hypoglycemia (low sugar levels) can increase the risk of arrhythmias and ischemic events.

TAR: Persistent hyperglycemia (high sugar levels) contributes to endothelial dysfunction, oxidative stress, and inflammation, exacerbating atherosclerosis.

TIR, TBR, TAR, and Chronic Kidney Disease (CKD):

TIR: Good glycemic control slows the progression of kidney damage.

TBR: Severe hypoglycemia may worsen renal ischemia.

TAR: Chronic hyperglycemia leads to glomerular hyperfiltration and kidney damage.

TIR, TBR, TAR, and Alzheimer's:

TIR: Stable glucose levels may reduce the risk of dementia by preventing microvascular and macrovascular complications in the brain.

TBR: Hypoglycemia can cause cognitive impairment and may accelerate neurodegeneration.

TAR: Hyperglycemia is linked to increased amyloid-beta accumulation, a hallmark of Alzheimer's.

TIR, TBR, TAR, and Parkinson's:

TIR: Adequate glycemic control might protect against neurodegeneration.

TBR: Repeated hypoglycemia may contribute to neuronal loss in brain areas affected by Parkinson's.

TAR: Chronic high glucose levels may exacerbate oxidative stress and mitochondrial dysfunction in Parkinson's.

TIR, TBR, TAR, and Cancers:

TIR: Balanced glucose levels may reduce the risk of some cancers, as many cancer cells preferentially use glucose for growth.

TBR: There's less direct evidence linking hypoglycemia to cancer progression.

TAR: Sustained high glucose levels can create a favourable environment for cancer cell growth and proliferation.

Overall, maintaining glucose levels within a target range (TIR) is beneficial for preventing or slowing the progression of these diseases, while deviations (TBR and TAR) can exacerbate their progression through various mechanisms.

1.2 MPM Background:

To learn more about his developed GH-Method: math-physical medicine (MPM) methodology, readers can read the following three papers selected from his published 760+ papers.

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

The author's diabetes history:

The author was a severe T2D patient since 1995. 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 at 10%). During that year, his triglycerides reached 1161 (high risk for CVD and stroke) and his albumin-creatinine ratio (ACR) at 116 (high risk for chronic kidney disease). He also suffered from five cardiac episodes within a decade. In 2010, three independent physicians warned him regarding the need for kidney dialysis treatment and the future high risk of dying from his severe diabetic complications.

In 2010, he decided to self-study endocrinology with an emphasis on diabetes and food nutrition. He spent the entire year of 2014 to develop a metabolism index (MI) mathematical model. During 2015 and 2016, he developed four mathematical prediction models related to diabetes conditions: weight, PPG, fasting plasma glucose (FPG), and HbA1C (A1C). Through using his developed mathematical metabolism index (MI) model and the other four glucose prediction tools, by the 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), average finger-piercing glucose from 250 mg/dL to 120 mg/dL, and A1C from 10% to ~6.5%. One of his major accomplishments is that he no longer takes any diabetes-related medications since 12/8/2015.

In 2017, he achieved excellent results on all fronts, especially his glucose control. However, during the pre-COVID period, including both 2018 and 2019, he travelled to ~50 international cities to attend 65+ medical conferences and made ~120 oral presentations. This hectic schedule inflicted damage to his diabetes control caused by stress, dining out frequently, post-meal exercise disruption, and jet lag, along with the overall negative metabolic impact from the irregular life patterns; therefore, his glucose control was somewhat affected during the two-year travelling period of 2018-2019.

He started his COVID-19 self-quarantined life on 1/19/2020. By 10/16/2022, his weight was further reduced to ~164 lbs. (BMI 24.22) and his A1C was at 6.0% without any medication intervention or insulin injection. In fact, with the special COVID-19 quarantine lifestyle since early 2020, not only has he written and published ~500 new research articles in various medical and engineering journals, but he has also achieved his best health conditions for the past 27 years. These achievements have resulted from his non-travelling, low-stress, and regular daily life routines. Of course, his in-depth knowledge of chronic diseases, sufficient practical lifestyle management experiences, and his own developed high-tech tools have also contributed to his excellent health improvements.

On 5/5/2018, he applied a continuous glucose monitoring (CGM) sensor device on his upper arm and checked his glucose measurements every 5 minutes for a total of 288 times each day. Furthermore, he extracted the 5-minute intervals from every 15-minute interval for a total of 96 glucose data each day stored in his computer software.

Through the author's medical research work of over 40,000 hours and reading over 4,000 published medical papers online in the past 13 years, he discovered and became convinced that good life habits of not smoking, moderate or no alcohol intake, avoiding illicit drugs; along with eating the right food with well-balanced nutrition, persistent exercise, having a sufficient and good quality of sleep, reducing all kinds of unnecessary stress, maintaining a regular daily life routine contribute to the risk reduction of having many diseases, including CVD, stroke, kidney problems, micro blood vessels issues, peripheral nervous system problems, and even cancers and dementia. In addition, a long-term healthy lifestyle can even "repair" some damaged internal organs, with different required time lengths depending on the particular organ's cell lifespan. For example, he has "self-repaired" about 35% of his damaged pancreatic beta cells during the past 10 years.

Energy theory:

The human body and organs have around 37 trillion live cells which are composed of different organic cells that require energy infusion from glucose carried by red blood cells, and energy consumption from labor-work or exercise. When the residual energy (resulting from the plastic glucose scenario) is stored inside our bodies, it will cause different degrees of damage or influence to many of our internal organs.

According to physics, energies associated with the glucose waves are proportional to the square of the glucose amplitude. The residual energies from elevated glucose are circulating inside the body via blood vessels which then impact all of the internal organs to cause different degrees of damage or influence, e.g., diabetic complications. Elevated glucose (hyperglycemia) causes damage to the structural integrity of blood vessels. When it combines with both hypertension (rupture of arteries) and hyperlipidemia (blockage of arteries), CVD or Stroke happens. Similarly, many other deadly diseases could result from these excessive energies which would finally shorten our lifespan. For example, the combination of hyperglycemia and hypertension would cause micro-blood vessel leakage in kidney systems which is one of the major causes of CKD.

The author then applied Fast Fourier Transform (FFT) operations to convert the input wave from a time domain into a frequency domain. The y-axis amplitude values in the frequency domain indicate the proportional energy levels associated with each different frequency component of input occurrence. Both output symptom value (i.e., strain amplitude in the time domain) and output symptom fluctuation rate (i.e., the strain rate and strain frequency) influence the energy level (i.e., the Y-amplitude in the frequency domain).

Currently, many people live a sedentary lifestyle and lack sufficient exercise to burn off the energy influx which causes them to become overweight or obese. Being overweight and having obesity leads to a variety of chronic diseases, particularly diabetes. In addition, many types of processed food add unnecessary ingredients and harmful chemicals that are toxic to the bodies, which lead to the development of many other deadly diseases, such as cancers. For example, ~85% of worldwide diabetes patients are overweight, and ~75% of patients with cardiac illnesses or surgeries have diabetes conditions.

In engineering analysis, when the load is applied to the structure, it bends or twists, i.e., deforms; however, when the load is removed, it will either be restored to its original shape (i.e., elastic case) or remain in a deformed shape (i.e., plastic case). In a biomedical system, the glucose level will increase after eating carbohydrates or sugar from food; therefore, carbohydrates and sugar function as the energy supply. After having labour work or exercise, the glucose level will decrease. As a result, the exercise burns off the energy, similar to load removal in the engineering case. In the biomedical case, both processes of energy influx and energy dissipation take some time which is not as simple and quick as the structural load removal in the engineering case. Therefore, the age difference and 3 input behaviours are "dynamic" in nature, i.e., time-dependent. This time-dependent nature leads to a "viscoelastic or viscoplastic" situation. For the author's case, it is "viscoplastic" since most of his biomarkers have continuously improved during the past 13-year time window.

Time-dependent output strain and stress of (viscous input*output rate):

Hooke's law of linear elasticity is expressed as:

Strain (ε: epsilon) = Stress (σ: sigma) / Young's modulus (E)

For biomedical glucose application, his developed linear elastic glucose theory (LEGT) is expressed as:

PPG (strain) = carbs/sugar (stress) * GH.p-Modulus (a positive number) + post-meal walking k-steps * GH.w-Modulus (a negative number)

where GH.p-Modulus is the reciprocal of Young's modulus E.

However, in viscoelasticity or viscoplasticity theory, the stress is expressed as:

Stress = viscosity factor (η: eta) * strain rate (dε/dt)

where strain is expressed as Greek epsilon or ε.

In this article, in order to construct an "ellipse-like" diagram in a stress-strain space domain (e.g., "hysteresis loop") covering both the positive side and negative side of space, he has modified the definition of strain as follows:

Strain = (body weight at a certain specific time instant)

He also calculates his strain rate using the following formula:

Strain rate = (body weight at next time instant) - (body weight at present time instant)

The risk probability % of developing into CVD, CKD, and Cancer is calculated based on his developed metabolism index model (MI) in 2014. His MI value is calculated using inputs of 4 chronic conditions, i.e., weight, glucose, blood pressure, and lipids; and 6 lifestyle details, i.e. diet, drinking water, exercise, sleep, stress, and daily routines. These 10 metabolism categories further contain ~500 elements with millions of input data collected and processed since 2010. For individual deadly disease risk probability %, his mathematical model contains certain specific weighting factors for simulating certain risk percentages associated with different deadly diseases, such as metabolic disorder-induced CVD, stroke, kidney failure, cancers, dementia; artery damage in heart and brain, micro-vessel damage in kidney, and immunity-related infectious diseases, such as COVID death.

Some of explored deadly diseases and longevity characteristics using the viscoplastic medicine theory (VMT) include stress relaxation, creep, hysteresis loop, and material stiffness, damping effect based on time-dependent stress and strain which are different from his previous research findings using linear elastic glucose theory (LEGT) and nonlinear plastic glucose theory (NPGT).

2. RESULTS

Figure 1 shows data tables. Figure 2 shows the inputs and SD-VMT energy output diagram.

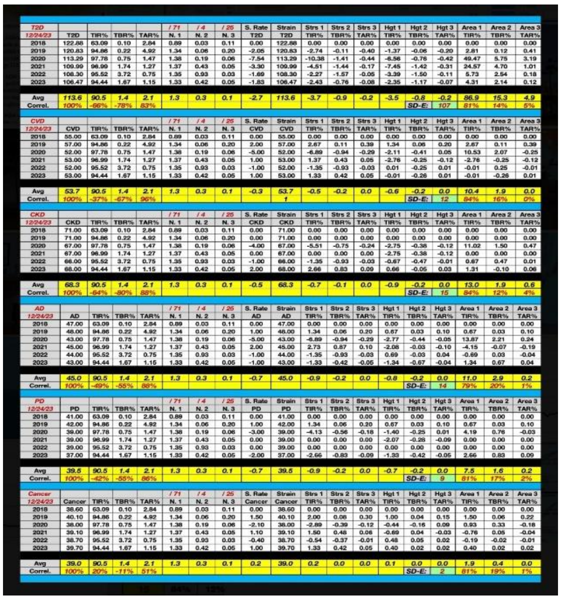


Figure 1. Data table, inputs, and SD-VMT energy output diagram.

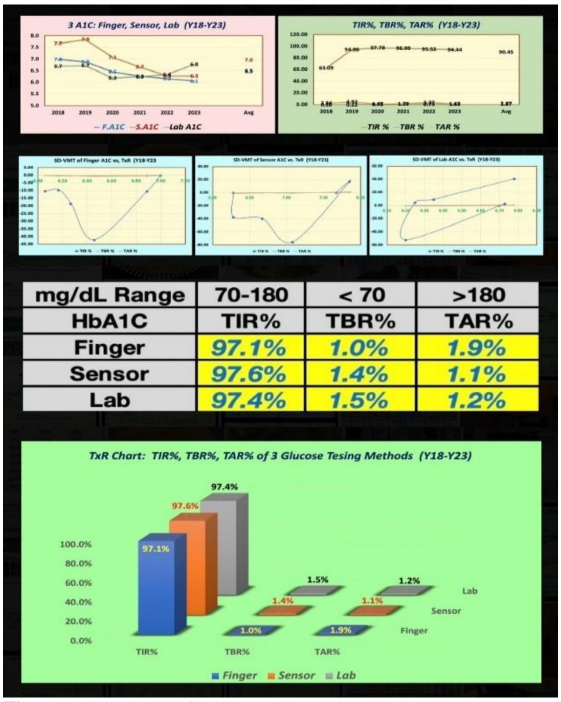


Figure 2: Inputs and SD-VMT energy output diagram.

3. CONCLUSION

In summary, the ranking of three averaged input values is:

- TIR% = 90.5%; TBR% = 1.4%; TAR% = 2.1%.

The ranking of six averaged strain (i.e., disease risk) values are:

- T2D (114); CKD (68); CVD (54); AD (45); PD (40); Cancers (39)

The ranking of six strain change rates over the years are:

- T2D (-2.7); AD (-0.7); PD (-0.7); CKD (-0.5); CVD (-0.3); Cancers (0.2)

Therefore, the ranking of total energy values (area underneath the stress-strain curve) from SD-VMT analysis are:

- T2D (107) > CKD (15) > AD (14); CVD (12) > PD (9) > Cancers (2)

Explanation: The author has had Type 2 Diabetes (T2D) since 1995. Although it is well-managed, it remains uncured. The higher T2D energy is resulted from using 5.7% to normalize his Lab A1C values. From 1994 to 2005, he experienced five cardiovascular incidents, influenced by both diabetes (eAG at 280 mg/dL, A1C at 11%, triglyceride at 1160) and high business stress. Between 2006 and 2012, he also faced kidney issues with a high ACR of 150. However, thus far, he has not exhibited signs of dementia or cancer.

His six SD-VMT stress-strain energy curves displayed unique curvatures and shapes. Yet, the averaged SD-VMT energy ratios from three metrics - TIR, TBR, and TAR - were similar. These energy sources reflect the varying extents of organ damage he sustained from six mortality diseases:

- **TIR energy = 82%**
- **TBR energy = 16%**
- **TAR energy = 2%.**

Key message:

This report presents the author's current health status. His diabetes is under control, as indicated by TIR, TBR, and TAR metrics. His previous issues with cardiovascular disease (CVD) and chronic kidney disease (CKD) appear to be receding, though the near experience with kidney issues is still more significant than heart issues. Despite controlled diabetes, there remains a concern about hypoglycemia's role as an influencer in cognitive and memory impairments, such as Alzheimer's. The risk of developing Parkinson's disease, associated with movement, seems less likely compared to Alzheimer's. Fortunately, the risk of cancer, his greatest concern, remains the lowest among the six major diseases discussed. This report also highlights the effectiveness of using the viscoplastic energy method in his biomedical research.

4. REFERENCES

For editing purposes, the majority of the references in this paper, which are self-references, have been removed from this article. Only references from other authors' published sources remain. The bibliography of the author's original self-references can be viewed at www.eclairemd.com.

Readers may use this article as long as the work is properly cited, their use is educational and not for profit, and the author's original work is not altered.

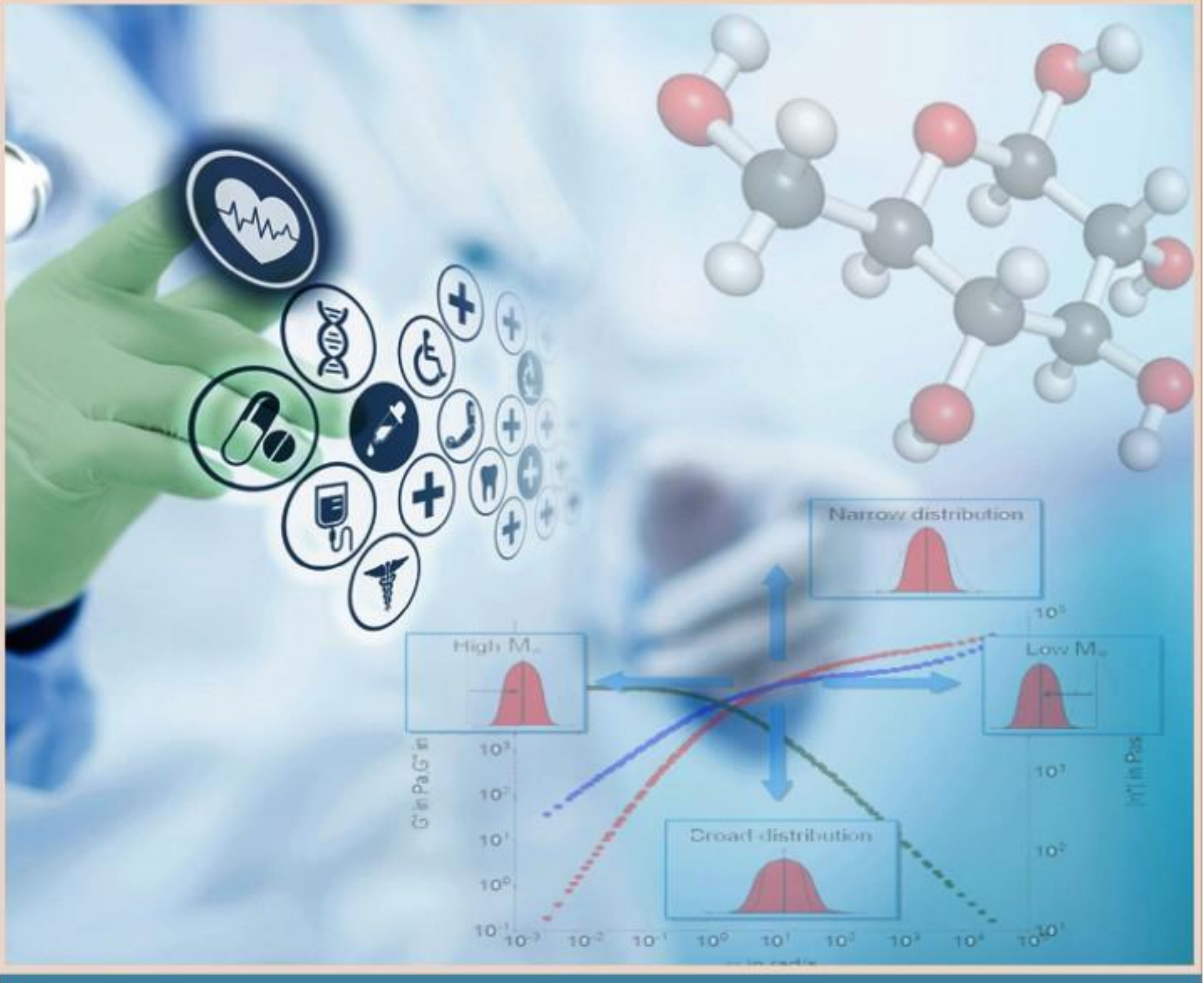
For reading more of the author's published VGT or FD analysis results on medical applications, please locate them through platforms for scientific research publications, such as ResearchGate, Google Scholar, etc.

Special Issue | Issue No. 5

The GH-Method

Viscoelastic and Viscoplastic Glucose Theory Application in Medicine

Gerald C. Hsu



https://theghmethod.com

2022