The GH-Method

# Viscoelastic or Viscoplastic Glucose Theory (VGT #126): Estimation of Self-Repair Rate on the Damaged Pancreatic Beta Cell's Insulin Resistance Situation Using HbA1C Level, Triglyceride and Glucose Index Biomarker (TyG), Along with Fasting Plasma Glucose Level in the Early Morning as Three Inputs and Applying Three Different Medical Research Tools of Time Domain, Space Domain Energy, Frequency Domain Energy from a Type 2 Diabetes Patient's 13-Year Record from Y2010 to Y2022 Based on GH-Method: Math-Physical Medicine (No. 717)

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**Keywords:** Viscoelastic; Viscoplastic; Insulin; Triglyceride; Cardiovascular disease; Postprandial plasma glucose; Fasting plasma glucose; Type 2 diabetes; Fast Fourier transform

**Abbreviations:** IR: insulin resistance; TG: triglycerides; CVD: cardiovascular disease; FFT: fast Fourier transform; T2D: type 2 diabetes; PPG: postprandial plasma glucose; FPG: fasting plasma glucose; FD: frequency domain; SD: space domain; TD: time domain; MPM: math-physical medicine

## 1. INTRODUCTION

The primary purpose of this study is to estimate the self-repair rate of insulin resistance (IR) of pancreatic beta cells over a long period of 13 years from 1/1/2010 to 8/8/2022.

Doctors often order the fasting plasma glucose (FPG) test or HbA1C test from a medical laboratory to diagnose prediabetes or diabetes. Less often, they use the oral glucose tolerance test (OGTT). The HbA1C test reflects your average blood glucose over the past 3 to 4 months, actually ~115 days. Insulin testing may be ordered with glucose test and C-peptide test. Insulin levels are also sometimes used in conjunction with the glucose tolerance test (GTT). In this situation, both glucose and insulin levels are measured at pre-established time intervals to evaluate insulin resistance. However, these tests are more expensive and not as easy to obtain needed information.

The laboratory tests would most likely include blood lipids. Diabetes conditions contend with both the production and storage of glucose in the liver and insulin secretion (quantity) or insulin resistance (quality) from the pancreatic beta cells. The triglycerides (TG) biomarker of blood lipids is also utilized in evaluating the situation of insulin resistance through a defined biomarker of triglyceride and glucose index (TyG). This description demonstrates the connectivity of diabetes with glucose and lipids in blood vessels and their relationships with the liver and pancreas' health conditions.

The author has had 40+ blood draws at medical laboratories or hospitals for the past 13 years. Approximately 90% of them were performed at the same location; therefore, the consistency and reliability of the test results are not a concern.

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A more detailed description of TyG can be found in the Method section but 2 slightly different TyG equations are listed below:

TyG = ln [Fasting triglyceride (mg/dl) * Fasting glucose (mg/dl)] / 2

or,

TyG = ( ln[Fasting triglyceride (mg/dl)] + ln[Fasting glucose (mg/dl)] ) / 2

This article's data are based on his finger-pierced glucose which is measured 4 times a day, once in the early morning for FPG and three times for postprandial plasma glucose (PPG) at 2 hours after the first bite of his meals. On 5/8/2018, he applied a continuous glucose monitoring (CGM) sensor device on his upper arm and then collected 288 times of glucose data each day. Since this article is covering a longer period of 13 years from Y2010 to Y2022, the finger-pierced glucose data are only used in the analysis.

The author has self-studied and researched diabetes and its related complications during the past 13 years and published 700+ medical papers. Among them, almost 50% are related to diabetes. Therefore, he understands the linkage of glucose biophysical characteristics and their mathematical interpretations along with the actual progression of his diabetic complications. For example, he has written around 10 papers regarding the self-repair rate of his pancreatic beta cells using various math-physical medicine tools.

During sleep hours in the night, diabetes patients would not be eating or exercising. Therefore, the FPG level in the early morning serves as a good indicator of pancreatic beta cells' health condition i.e. insulin resistance. Based on the research results in his case, he has identified that the FPG level was at 74% of his PPG level in Y2010, and at 94% of his PPG level during the long period of 13 years from Y2010 to Y2022. That is why he considers his FPG level as the baseline component of the PPG formation. In addition, the daily estimated average glucose (eAG) is defined as: "eAG = 0.25*FPG + 0.75*PPG". As a result, FPG contributes around 95% of eAG which is the outcome from 0.25+0.75*0.94 = 0.95. Finally, his estimated HbA1C values have a high prediction accuracy of >99% from the lab-tested HbA1C results.

Based on the description in the above paragraph, he has decided to choose A1C, TyG, and FPG as the three input variables for the output variable of beta cells insulin resistance (IR).

## 2. METHODS

### 2.1 TyG index

The "triglyceride and glucose index" is a screening method for insulin resistance, which is simple to use, and only requires two laboratory determinations: serum triglycerides and serum glucose. According to a study by Salazar et al., the insulin resistance cut-off is placed at the TyG index value of 4.49, with a sensitivity of 82.6% and specificity of 82.1% (AUC=0.889, 95% CI: 0.854-0.924). Subjects with an index of 4.49 or greater are likely to suffer from insulin resistance (References 1, 2, 3, 4, and 5).

The TyG equation is:

TyG = ln [Fasting triglyceride (mg / dl) * Fasting glucose (mg / dl)] / 2

or,

TyG = ( ln[Fasting triglyceride (mg / dl)] + ln[Fasting glucose (mg / dl)] ) / 2

Furthermore, let us re-express it with an abbreviated format as follows:

TyG = (ln(TG) + ln(FPG)) / 2

The TyG is considered a screening tool for large-scale medical studies. Its accuracy and simplicity can be calculated with data obtained from medical records.

According to Fedchuk et al., the TyG values above 8.38 indicates a positive predictive value (PPV) of 99% in predicting steatosis equal to or greater than 5%. A recent cross-sectional study by Zhang et al. aimed to determine whether TyG has any predictive value for non-alcoholic fatty liver disease (NAFLD) by comparing the predictive value of TyG with the determinations of ALT (alanine aminotransferase) in a cohort of 10,761 patients.

The association between a screening method using triglycerides and glucose should not come as a surprise as NAFLD is considered the liver manifestation of metabolic syndrome, while triglycerides and serum glucose are key components of this process.

The following table summarizes the two cut-off points identified for insulin resistance and NAFLD positive diagnosis likelihood:

| Condition | Cut-off value | Values below cut-off | Values above cut-off |
|---|---|---|---|
| Insulin resistance | 4.49 | Insulin resistance unlikely | Suggestive of insulin resistance |
| Nonalcoholic fatty liver disease | 8.5 | NAFLD diagnosis is unlikely | High likelihood of NAFLD |

### 2.2 New TyG index (TyG-B)

In order to develop any mathematical equation for describing an observed biophysical phenomenon, scientists should not only demand high accuracy of biophysical description via mathematical equation in reflecting the background physical concept or mathematical theory, but the equation must also be practical for real-life applications. The author is an engineer with a mathematics background and a long-term severe type 2 diabetes (T2D) patient. To date, he has collected and processed 3+ million data on his overall health conditions and lifestyle details and he understands his data very well. He wants to develop an easier way to interpret his complex pancreatic beta cells status in regard to insulin resistance and to find a quicker path to achieving the goal of his diabetes control. Therefore, he made some simple modifications of the above defined TyG equation and developed an alternative New TyG or TyG-B equation as follows:

$$\text{TyG-B} = \ln(\text{TG}+\text{FPG}) - \ln(2)$$

Or

$$\text{TyG-B} = \ln((\text{TG}+\text{FPG}) / 2)$$

### 2.3 Sensitivity analysis

The most common blood test used to check triglyceride levels is called a lipid panel. A standard lipid panel will test for the following:

- Total cholesterol
- LDL (bad) cholesterol
- HDL (good) cholesterol
- Triglycerides
- Cholesterol/HDL ratio
- Non-HDL cholesterol

Normal triglyceride levels are < 150 mg/dL. Triglyceride levels between 150 and 199 mg/dL are borderline high. High triglyceride levels occur at 200–499 mg/dL. Anything over 500 mg/dL is considered extremely high. (Note: The author had a triglyceride value of 1,161 mg/ dL and an FPG value of 280 mg/dL in 2010 with a TyG level of 6.58).

The author's TG record during the past 13 years (2010-2022) shows a data range of coverage from the lowest at 39 to the highest at 1,161, with an average value of 166 mg/dL. His 90-day moving average data of FPG during the same time period reflects a data range from the lowest 89 mg/dL to the highest 220 mg/dL with an average value of 120 mg/dL. However, the extremely high TG or FPG occurred only in Y2010.

### 2.4 The author's case of diabetes

The author has been a severe T2D patient since 1996. He weighed 220 lb. (100 kg, BMI 32.5) at that time. By 2010, he still weighed 198 lb. (BMI 29.2) with average daily glucose of 250 mg/dL (HbA1C of 10%). During that year, his triglycerides reached 1161 and albumin-creatinine ratio (ACR) at 116. He also suffered from five cardiac episodes within a decade. In 2010, three independent physicians warned him about his need for kidney dialysis treatment and his future risk of dying from his severe diabetic complications. Other than the cerebrovascular disease (stroke), he has suffered most of the known diabetic complications, including both macro-vascular & micro-vascular complications as well as nerve damage.

In 2010, he decided to launch his self-study on endocrinology, diabetes, and food nutrition to save his own life. During 2015 and 2016, he developed four prediction models related to diabetes conditions: weight, PPG, fasting plasma glucose (FPG), and A1C. As a result, from using his developed mathematical metabolism index (MI) model in 2014 and the four prediction tools, by end of 2016, his weight was reduced from 220 lbs. (100 kg, BMI 32.5) to 176 lbs. (89 kg, BMI 26.0), waistline from 44 inches (112 cm) to 33 inches (84 cm), average finger glucose reading from 250 mg/dL to 120 mg/dL, and lab-tested A1C from 10% to ~6.5%. One of his major accomplishments is that he no longer takes any diabetes medications as of 12/8/2015.

In 2017, he has 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 along with the overall metabolic impact due to his irregular life patterns through a busy travel schedule; therefore, his glucose control and overall metabolism state were somewhat affected during this two-year heavy traveling period.

Since early 2020, living in a COVID-19 quarantined lifestyle, not only has he written snd published ~500 medical papers in 100+ journals, but he has also reached his best health conditions in the past 26 years. By the beginning of 2022, his weight was further reduced to 168 lbs. (BMI 24.8) along with a 5.8% A1C value (beginning level of pre-diabetes), without having any medication interventions or insulin injections. These good results are due to his non-traveling, low-stress, and regular daily life routines. Of course, his knowledge of chronic diseases, practical lifestyle management experiences, and development of various high-tech tools contribute to his excellent health status since 1/19/2020, the beginning date of his self-quarantined life.

On 5/5/2018, he applied a continuous glucose monitoring (CGM) sensor device on his upper arm and checks his glucose measurements every 5 minutes for a total of ~288 times each day. He has maintained the same measurement pattern to the present day. In his research work, he uses his CGM sensor glucose at a time interval of 15 minutes (96 data per day). Incidentally, the average sensor glucoses between 5-minute intervals and 15-minute intervals has only a 0.6% difference (average glucose of 111.86 mg/dL for 5 minutes and average glucose of 111.18 mg/dL for 15 minutes with a correlation of 94% between these two sensor glucose curves) during the period from 2/19/20 to 7/22/22.

Therefore, over the past 13 years, he could study and analyze his collected 3+ 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 research work has a goal of achieving both “high precision” and “quantitative proof” in the medical findings for the ultimate objectives of “preventive medicine”.

The following timetable provides a rough sketch of the emphasis in his medical research during each stage:

2000-2013: Self-study diabetes and food nutrition, developing a data collection and analysis software.

2014: Develop a mathematical model of metabolism, using engineering modeling and advanced mathematics.

2015: Weight & FPG prediction models, using neuroscience.

2016: PPG & HbA1C prediction models, using optical physics, artificial intelligence (AI), and neuroscience.

2017: Complications due to macro-vascular research, such as Cardiovascular disease (CVD), coronary heart diseases (CHD), and stroke, using pattern analysis and segmentation analysis.

2018: Complications due to micro-vascular research such as kidney (CKD), bladder, foot, and eye issues (DR).

2019: CGM big data analysis, using wave theory, energy theory, frequency domain analysis, quantum mechanics, and AI.

2020: Cancer, dementia, longevity, geriatrics, DR, hypothyroidism, diabetic foot, diabetic fungal infection, and linkage between metabolism and immunity, learning about certain infectious diseases, such as COVID-19.

2021: Applications of linear elastic glucose theory (LEGT) and perturbation theory from quantum mechanics on medical research subjects, such as chronic diseases and their complications, cancer, and dementia.

2022: Applications of viscoelastic/viscoplastic glucose theory (LEGT) on 121 biomedical research cases and 5 economics research cases.

Again, to date, he has spent ~40,000 hours self-studying and researching medicine and he has read ~3,000 published medical papers online. He has collected and calculated more than three million pieces of data regarding his own medical conditions and lifestyle details. In addition, he has written and published 700+ medical research papers in 100+ various medicine, physics, mathematics, and engineering journals. Moreover, he has also given ~120 presentations at ~65 international medical conferences. He has continuously dedicated his time (11-12 hours per day and work each day of a year, without rest) and efforts to his medical research work and shared his findings and learnings with other patients worldwide. In addition, he has also spent the past 10+ years developing and maintaining a medical and health software APP on the iPhone which functions as his private numerical laboratory to process various experimental datasets of his medical conditions and lifestyle details.

## 2.5 TD, SD, and FD analysis tools

This section has brief descriptions of time-domain (TD) correlation analysis with other observational results, space-domain (SD) VGT analysis with hysteresis loop area's energy results, and frequency-domain (FD) analysis with frequency curve area's energy results.

First of all, using a TD analysis tool, we can examine the curves' moving trend and pattern visually, and also the curves' correlation numerically. We can also study those extremely high or low data values in the dataset. The visual observation or calculation-derived interpretations are a part of statistical analysis results which can indeed provide some useful hints or even derive some accurate conclusions. However, we must be aware of the limitations of the data we select and be cautious of the appropriate statistics tool we choose.

The author would like to describe the essence of his developed "hybrid model" that combines both space-domain (SD) viscoelastic/plastic VGT analysis method and frequency-domain (FD) fast Fourier transform (FFT) analysis method together with a comparison against the traditional time-domain statistical correlation analysis.

It is described in 10 steps in the English language instead of using mathematical equations to explain it. In this article, he has applied the SD-VGT operations (steps 1-7) and the FD-FFT operations (steps 8-10). As a result, it is aimed at readers who do not have an extensive background in those academic subjects of engineering, physics & mathematics.

The first step is to collect the output data or symptom (strain or ε) on a time scale. The second step is to calculate the output change rate with time (dε/dt), i.e. the change rate of strain or symptom over each period. The third step is to gather the input data or cause (viscosity or η) on a time scale. The fourth step is to calculate the time-dependent input or cause (time-dependent stress or σ) by multiplying dε/dt and η together. The "time-dependent input or cause equation" of "stress σ = strain change rate of dε/dt * viscosity η" is the essential part of "time-dependency". The fifth step is to plot the input-output (i.e. stress-strain or cause-symptom) curve in a 2-dimensional space domain or SD (x-axis versus y-axis) with strain (output or symptom) on the x-axis and stresses (time-dependent inputs, causes, or stresses) on the y-axis. The sixth step is to calculate the total enclosed area within these stress-strain curves or input-output curves (i.e. the hysteresis loops), which is also an indicator of associated energies (either created energy or dissipated energy) of this input and output dataset. These energy values can also be considered as the degrees of influence on output by inputs. The seventh step is assembling the area values of selected periods to compare the "progression and contribution of condition" over certain time periods.

For the frequency domain, the eighth step is to define a "hybrid input variable" by using "strain*stress" which yields another accurate estimation of energy ratio similar to the SD-VGT energy ratio associated with the hysteresis loop. The ninth step is to present these hybrid models' results of (strain*stress) in a time domain and then perform the fast Fourier transformation (FFT) operation to convert them into a frequency domain. The enclosed area of the frequency curve (where the x-axis is the frequency and the y-axis is the amplitude of energy) can be used to estimate the total FD-FFT energy. The tenth step is to compare these FD energy results against the SD-VGT energy results, or even TD energy results.

After providing the above 10-step description, the author would still like to use the following set of VGT stress-strain mathematical equations in a two-dimensional SD to address the unique "time-dependency characteristics" of selected medical variables:

Strain
= $\varepsilon$
= individual strain value at the present time duration

Stress
= $\sigma$ (based on the change rate of strain multiplying with a chosen viscosity factor $\eta$)
= $\eta$ * ($d\varepsilon/dt$)
= $\eta$ * (d-strain/d-time)
= (viscosity factor $\eta$ using individual viscosity factor at present time duration) * (strain at present quarter - strain at previous time duration)

Some of these inputs (causes or viscosity factors) are further normalized by dividing them or being divided by a normalization factor using certain established health standards or medical pieces of knowledge. Some examples of normalization factors are 6.0 for HbA1C, 120 mg/dL for glucose, 25 for body mass index (BMI), 4,000 steps after each meal, 10,000 or 12,000 steps for daily walking exercise depending on time-period selection, 15 or 20 grams of carbs/sugar intake amount per meal depends on time-period selection. If using the originally collected data, i.e. the non-normalized data would distort the numerical comparison of the hysteresis loop areas. Using this "normalization process", we can remove the dependency of the individual unit or certain unique characteristics associated with each viscosity factor. This process allows us to convert the originally collected variables into a set of "dimensionless variables" for easier numerical comparison and result interpretation.

In this particular study, he uses the following 3 "normalization factors" of 100 mg/dL for FPG, 4.49 for TyG, and 5.6% for HbA1C.

**2.6 Time-frequency analysis**

In signal processing, the time-frequency analysis comprises those techniques that study a signal in both the time domain and frequency domain simultaneously, using various time-frequency representations. Rather than viewing a 1-dimensional signal (a function, real or complex-valued, whose domain is the real line) and some transform (another function whose domain is the real line, obtained from the original via some transform, such as fast Fourier transform), time-frequency analysis studies a two-dimensional signal – a function whose domain is the two-dimensional real plane, obtained from the signal via a time-frequency transform.

The mathematical motivation for this study is that functions and their transform representation are tightly connected, and they can be understood better by studying them jointly, as a two-dimensional object, rather than separately.

The practical motivation for time-frequency analysis is that classical Fourier analysis assumes that signals are infinite in time or periodic, while many signals in practice are of short duration, and change substantially over their duration."

**Note:** For a more detailed description, please refer to the "consolidated method" section which is given at the beginning of the special issue.

## 3. RESULTS

Figure 1 shows the background information charts, background data table and his processed data table.

Figure 2 shows his time-domain, space-domain, and frequency-domain energy analysis results.

**Figure 1:** Background information chart, background data table, and processed data table.

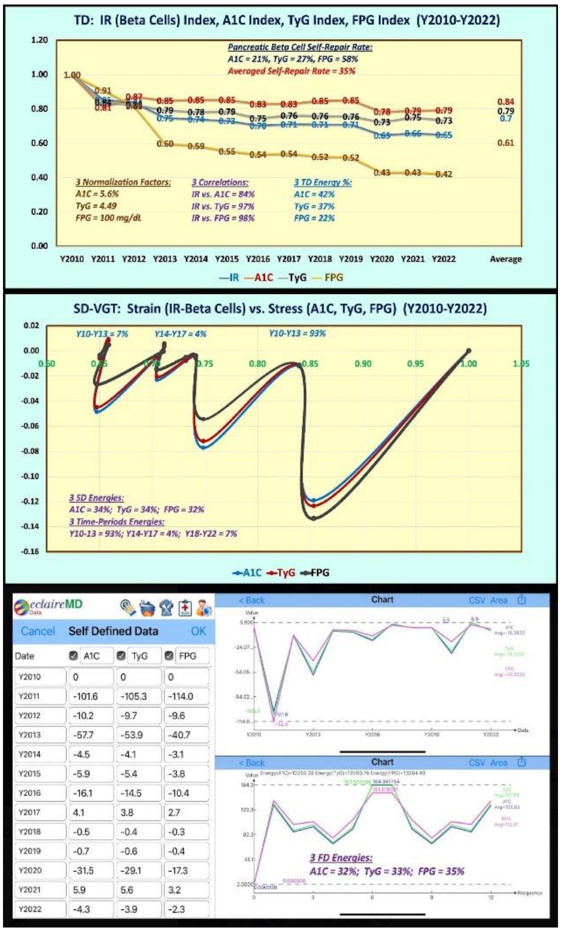

**Figure 2:** Time-domain, space-domain, and frequency-domain energy analysis results.

# 4. CONCLUSION

In summary, he has 3 key observations described as follows:

(1) From the TD analysis, the most important finding is his overall pancreatic beta cells' IR self-repair amount: A1C = 21%, TyG = 27%, FPG = 58%, the overall average rate = 35%. There are two less important TD information from this analysis: (a) correlations between IR and 3 inputs: A1C = 84%, TyG = 97%, FPG = 98%. (b) TD energy via squared amplitude associated with 3 inputs are: A1C = 42%, TyG = 37%, FPG = 22%. This energy distribution pattern is somewhat different from both SD and FD energy distribution patterns.

(2) From the SD-VGT energy analysis, the three hysteresis loop areas, i.e. SD energies are: A1C = 34%, TyG = 34%, FPG = 32%. This means that the 3 inputs contribute an almost equal amount of influences, i.e. energies, on IR. Furthermore, the 3 time-period energies are: Y10-Y13 = 93%, Y14-Y17 = 4%, Y18-Y22 = 7%. This means that the earlier 4-years contribute the most energy to IR formation due to his high glucoses (FPG and A1c) and high TyG (FPG with TG) within this timeframe of Y10-Y13.

(3) From the FD-FFT energy analysis, the three frequency curve areas, i.e. FD energies are: A1C = 32%, TyG = 33%, FPG = 35%. This FD energy distribution pattern is almost identical to the SD energy pattern, but both SD and FD energy patterns are quite different from the TD-squared amplitude energy pattern.

Finding from this article using 3 different research methods has yielded a 35% self-repair rate of insulin function and capability of damaged pancreatic beta cells over the past 13 years. From his previous various studies, he has already identified the self-repair rates of his damaged pancreatic beta cells are within 28% to 33% for 7 to 10 years. These findings are pretty much consistent with each other.

The author has tried to search for information regarding the lifespan of pancreatic beta cells but could not find any concrete answer except its lifespan is very long, unlike the 3-4 months for red blood cells and ~1 year for liver cells. If based on the conclusion of this article and applying a linearly stretched model, the author guesses that the lifespan of pancreatic beta cells is around 30 to 40 years, which is a long time. No wonder diabetic conditions can be controlled but are difficult to cure.

## 5. REFERENCES

For editing purposes, the majority of the references in this paper, which are self-references, have been removed for 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.

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# Viscoelastic and Viscoplastic Glucose Theory Application in Medicine

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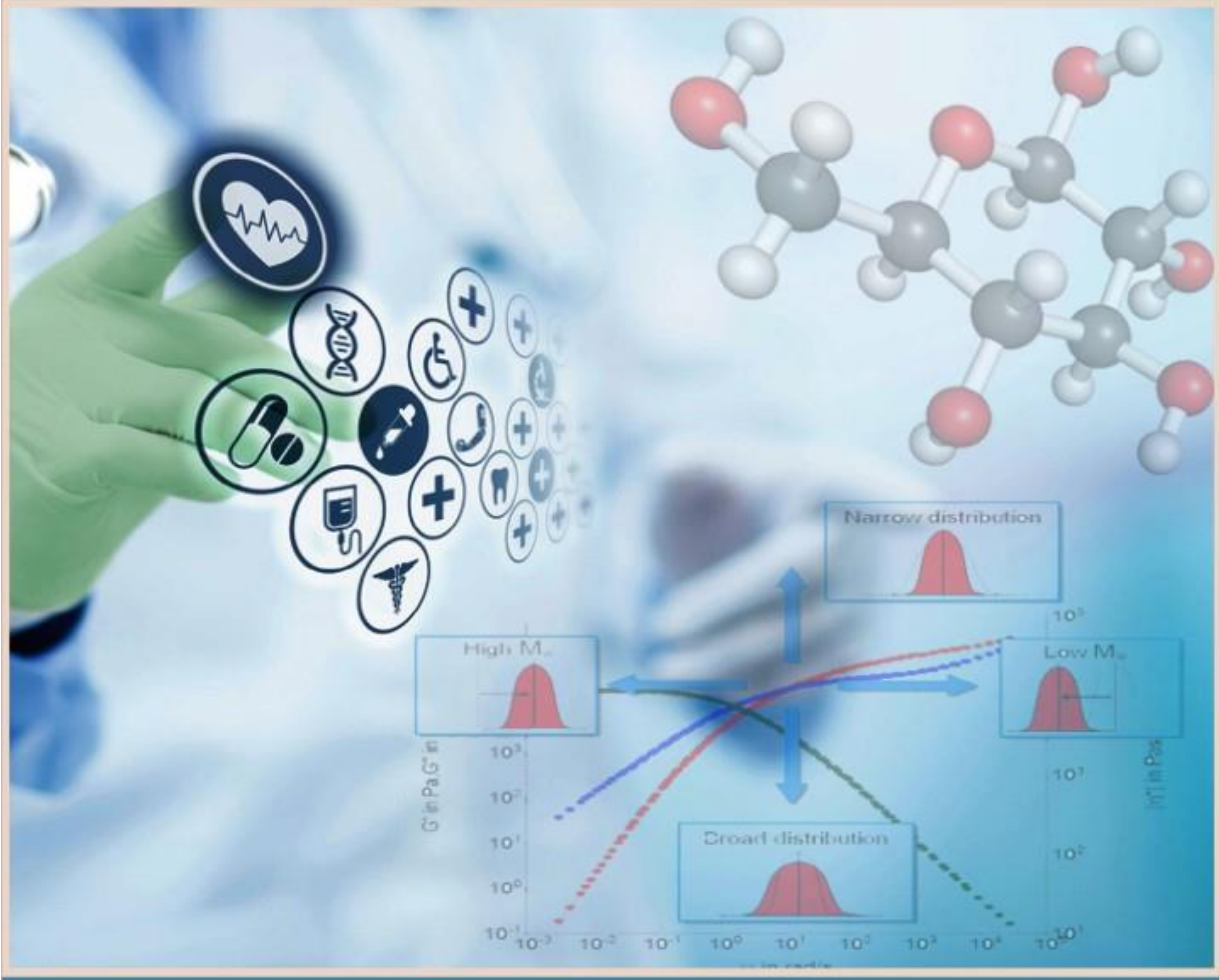


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