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Case Study

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Methodology of Math-Physical Medicine (GH-Method)

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Introduction

This paper discusses the "math-physical medicine (MPM)" approach of a non-traditional methodology in medical research. The author uses his own type 2 diabetes (T2D) metabolic conditions control as a case study for some detailed illustration and explanation of this methodology.

Math-physical medicine starts with the observation of the human body's physical phenomena (not biological or chemical characteristics), collecting elements of the disease related data (preferring big data), utilizing applicable engineering modeling techniques, developing appropriate mathematical equations (not just statistical analysis), and finally predicting the direction of the development and control mechanism of the disease.

Diabetes example

Diabetes is a multi-system disease, affecting the endocrine system, cardiovascular system, metabolism, and even psychological well-being of patients. Regulation of glucose is the cornerstone of all diabetes control. Newer medications focus on glycemic control in T2D, but do not address the origin of diabetes, which is the progressive loss of ß-cell function [1].

Liu from University of Virginia School of Medicine, and Yang from the Center for Drug Evaluation and Research, Food and Drug Administration, advance the notion that one of the most important factors in developing Type II diabetes (T2D) is "positive energy balance," e.g. surplus energy intake (over-eating) over expenditure (exercise), which is at the core for developing metabolic syndrome and T2D [1].

Other factors complicating management of T2D are the discrepancies between A1C and self-monitoring of blood glucose data, which led Hirsch et al to advocate the value of using patients' own glucose data to consolidate therapeutic, educational, and behavior-change objectives [2].

This paper presents a system to more accurate prediction of glucose if possible, and measure of A1C glycohemoglobin, to achieve better control of the disease processes of T2D, and to predict untoward cardiovascular events.

The author describes his math-physical medicine approach (MPM) to reach more accurate glucose predictions and A1C readings, utilizing mathematics, physics, engineering modeling, and computer science tools, instead of the current biochemical medicine approach (BCM) that mainly utilizes biology and chemistry. The attached Table 1 illustrates some fundamental differences between the traditional bio-chemical medicine (BCM) methodology and the non-traditional math-physical medicine (MPM) methodology.

Comparison of Methodology	*Bio-Chemical Medicine (BCM)*	*Math-Physical Medicine (MPM)*
Academic Foundation	Based on both Biology and Chemistry, which are both based on Physics and Math	Based on Engineering and Physics, which are both based on Mathematics
Precision and Accuracy of Results	It appears that most likely the results are less precise and less accurate than MPM	Most likely more precise and accurate than BCM due to mathematics and physics
Data Size	It seems that most of the data size is smaller (hundreds to thousands)	Most of the data size are larger (thousands to millions)
Application of Mathematics	It appears that mostly utilizing statistics (an extension of mathematics)	Mostly utilizing mathematical equations, including many branches of mathematics
Distinguish by Importance Level (Weighting Factors)	It appears that mostly no weighting factors are considered before analysis	Figuring out various weighting factors and then assigned to key influential factors (Engineering Concept for approximation)
Data Collection and Cleaning	It seems that most of work spends 50% to 80% on data collection, cleaning, and organization	Spend only 10% to 30% on data collection, cleaning, and organization by utilizing computer technology, including AI

Table 1: Comparison of BCM versus MPM

Methodology of Math-Physical Medicine (MPM)

One of the most valuable tools for physicians is a method which allows them to give advice to a patient, to improve treatment outcome. This requires a predictive analytic method, which can only be derived from a retrospective analysis of multiple data points, looking for a pattern common to a certain outcome. Once a retrospective analysis of pattern recognition has been conducted, then a prospective testing, to see the accuracy of the predictive model needs to be done. This process is complicated by the multi-factorial origins of a medical event. As an example, "metabolism" should be considered as a nonlinear, dynamic, and organic mathematical system having at least 10 categories with ~500 elements as defined by the author. This multi-factorial origin of "metabolism" equation can be better derived with the use of topology concept with partial differential equation and nonlinear algebra to construct a "metabolism equation." (*Topology* studies properties of spaces that are invariant under any continuous deformation. Similarly, human body's metabolic properties remain unchanged despite of the variance and deformation of human body's physical shapes). The formula for the "metabolism equation" can be calculated and clearly expressed using two new variables defined by the author: a) metabolism index - MI, and b) general health status unit - GHSU. If and when both MI and GHSU are below 73.5%, then the patient is in a "healthy" condition, and when above 73.5%, the patient is "unhealthy".

For the past nine years, the author has spent ~23,000 hours to self-study and research six chronic diseases and food nutrition science. Furthermore, he has collected and processed more than 1.5 million data points of his body and health conditions. From these data, he developed predictive models, i.e. equations (not just relying on statistics like BCM approach), for weight, glucoses, and hemoglobin A1C. Glucoses include both postprandial plasma glucose (PPG) and fasting plasma glucose (FPG). Nineteen influential factors were identified for PPG formation and five factors for FPG formation. Primary influential factors according to their respective contribution margin are summarized as follows:

PPG Influential factors and their relative contribution margin:
- Post-meal exercise (41%)
- Carbs & sugar intake amount (38%)
- Ambient temperature (weather 10%)
- All other 16 secondary factors, such as stress, sleep, diseases, water, food quantity, and more (combined 11%)

FPG Influential factors and their relative contribution margin:
- Body weight in the morning (80% to 85%)
- Ambient temperature (weather 10%)
- All other three secondary factors, i.e. stress, sleep, and disease (5% to 10%)

Each factor has a different contribution weight or significance impact to the formation of glucose. The initial weighting factors assigned to influential factors for the calculation of predictive values are further modified or enhanced via mathematical and computer science tools, such as big data analytics and artificial intelligence (AI).

It should be noted that the author was a trained mathematician and computer scientist who focuses on precision but also an engineer and industrialist who focuses on solving practical problems with the best approximated answers which combines cost, effectiveness, and accuracy. A professional engineer or practical industrialist would not waste lots of time and energy to continue on investigating some minor influence factors once they have achieved accurate-enough answer of their problem. This is the reason the author applied many engineering modeling techniques in his MPM research work.

The PPG model was developed using optical physics at the front-end and signal processing at the back-end. These various physics theories and geophysics and electronics engineering tools help the author understand and calculated the relationship between diet and glucose as well as the detailed characteristics of PPG variances. During the process of data collection and processing, many different waveforms are generated to represent characteristics of different diseases, including diabetes. In fact, any fluctuation of physical representation (either causes or symptoms of a disease) is a "wave" which can not only revels the specific disease symptoms but also possess certain specific characteristics, such as wavelength, period, frequency, amplitude, etc. From these numerical characteristics and using energy theory from both mechanical engineering and structural engineering, an associated differential "energy" level generated by this specific wave can also be calculated or estimated. This excessive "leftover" energy circulates inside human body which can cause damages on our internal organs. In summary, by combining both wave theory and energy theory, a mathematical model was able to derive for assessment of the risk probability of cardiovascular disease (CVD) or stroke due to chronic diseases. In his detailed calculation of this risk assessment, he must also establish a proper model of human blood vessels. He then applied structural mechanics concepts, such as elasticity, dynamic plastic behavior & fracture mechanics, to simulate artery rupture (about 20% to 30% of CVD/Stroke occurrence rate). He also applied fluid dynamics concepts to simulate artery blockage (about 70% to 80% of CVD/Stroke occurrence rate).

In order to link psychological behavior and physiological characteristics together to understand certain specific disease deeper, the author decomposed ~1,200 glucose waveforms with ~21,000 data points, and then re-integrated them into 3 distinctive PPG waveform types which revealed different personality traits and psychological behaviors associated with T2D patients. After identifying these three distinctive PPG waveforms and their associated contribution percentages, the author then created a "progressive behavior modification" model to gradually guide these patients to modify their behaviors in order to change or improve their lifestyle progressively.

For single time-stamped variable, he used traditional time-series analysis, similar to EKG cardiology chart with time as its X- or horizontal axis. For interactions between two variables, he used spatial analysis to identify some hidden characteristics or relationships among two different sets of variables (e.g. metabolic symptom). This spatial analysis using two different variables as two axes has not been widely utilized in medical research arena in the past. Actually, one of its early applications was done by Dr. John Snow of London, UK showing clusters of cholera cases in the 1854 Broad Street cholera outbreak. This was one of the first uses of map-based spatial analysis in medicine. The author found this tool is quite powerful for data analysis, especially to identify the close relationship between multiple variables, such as weight and FPG, diet/exercise and PPG, blood pressure and glucose, etc. Furthermore, he also applied Fourier Transform to conduct frequency domain analyses to discover some hidden characteristics of glucose waves. Using frequency domain analysis, he was able to identify some interesting hidden evidences, for example, the impact of trauma, diseases, and medications on FPG. But a deeper study, investigation, and results interpretation regarding frequency-oriented data are still needed by the author in order to maximize his knowledge and experience of using frequency as an effective tool to study human biomedical signals.

The author also developed an AI Glucometer software, which required entering the following data into this iPhone and web-based APP:

1. Entering food intake quantity and bowel movement quantity to get predicted body weight.
2. From body weight in the morning to get predicted FPG value.
3. Take a meal picture and entering into APP, and also enter post-meal walking time (between 0 and 40 minutes). These two inputs will provide predicted PPG value. If the predicted PPG is too high, patient can either reduce his carbs/sugar intake or increase his post-meal walking exercise time.
4. Based on predicted values of FPG and three PPG, an estimated "dynamic" A1C value will be shown.

This AI-based Glucometer was developed utilizing various computer science IT tools, including big data analytics, machine learning (self-learning, self-correction, and self-simplification), and artificial intelligence based on ~8 million food nutrition data, including author's own history of 4,600 meal photos.

T2D case study results

In 2010, the author had an averaged glucose of 280 mg/dL and A1C was above 10%. His weight was 210 lbs. (95 kg), BMI was 32, waistline was 44 inches (112 cm). During the period of 1994 through 2006, he suffered 5 cardiac episodes. Now, in 2019, after using these five prediction models and the AI Glucometer developed by himself, his average glucose is 116 mg/dL and A1C is 6.5%. His weight is 170 lbs. (77 kg), BMI is 24.7, waistline is 32 inches (82 cm). Since his health condition is stable, he no longer suffers from repetitive cardiovascular episodes, as he had in the past. (See Table 2: Comparison of health conditions)

Health Examination Record	2010	2017	
A1C (<6.4%)	10	6.1	
90-days Average Glucose (<120 mg/dL)	279	113	
ACR (<30)	116.4	12.3	
Triglyceride (<150)	1161	67	
HDL (>40)	24	48	
LDL (<130)	174	74	
Total Cholesterol (<200)	253	118	
Blood Pressuire Index M3 (<1.0)	1.2	0.7	
BMI (<25.0)	31.0	24.7	
Weight (lbs)	210	167	
Waistline (inch)	44	32	
Matabolism Index (MI / GHSU: <73.5%)	140% / 103%	49% / 55%	
Heart episodes(1994 - 2006)			5 times
Kidney			Yes
Blader			Yes
Foot Ulcer			Yes

Discussion

Physicians are always looking for ways to encourage people to adopt a healthier lifestyle by exercising more and/or decreasing caloric intake [1]. However, they are compromised by the accuracy of testing methods. Patients with diabetes rely on blood glucose (BG) monitoring devices to manage their condition. As some self-monitoring devices are becoming more and more accurate, it becomes critical to understand the relationship between system accuracy and clinical outcomes, and the potential benefits of analytical accuracy. In one study of simulated meter models derived from the published characteristics of 43 commercial meters researcher isolated the differences in clinical performance that are directly associated with the meter characteristics [3]. The researchers reported that a meter's systematic bias has a significant and inverse effect on HbA1c ($P < .01$), while also affecting the number of severe hypoglycemia events. On the other hand, error, defined as the fraction of measurements beyond 5% of the true value, is a predictor of severe hypoglycemia events ($P < .01$). Both bias and error have significant effects on total daily insulin (TDI) and the number of necessary glucose measurements per day ($P < .01$). Furthermore, these relationships can be accurately modeled using linear regression on meter bias and error [3]. Two components of meter accuracy, bias and error clearly affect clinical outcomes. While error has little effect on HbA1c, it tends to increase episodes of severe hypoglycemia. Meter bias has significant effects on all considered metrics: a positive systemic bias will reduce HbA1c, but increase the number of severe hypoglycemia attacks, TDI use, and number of finger-sticks per day [3].

The author has written quite a few papers on comparison of glucose measurement results between finger-piercing and a particular brand of continuous monitoring sensor. The sensor measurement results in comparison with finger-piercing measurements have the following: average PPG is +17% higher and peak PPG is +38% higher. The most shocking finding is PPG peaks happen around 45 minutes to 75 minutes (around 60 minutes) after the first bite of meal, not the conventional knowledge of two hours after the first bite.

The use of the AI Glucometer testing affords physicians a mechanism to assist their patients to gain better control over the A1C glycohemoglobin, and lessen the cardiovascular risk associated with diabetes, while motivating them to engage in a healthier lifestyle. This is done without the need for finger-sticks, which most patients find objectionable [4].

The MPM methodology used in the author's research is compared and contrasted to current mechanisms in common use today (BCM), as shown in Table 1 below, and achieved to an accuracy level of 99%. Clearly, a non-invasive technique using AI Glucometer which has a high degree of accuracy is preferable to current BCM method.

Conclusion

More importantly, in the author's opinion, his non-traditional research methodology of MPM can provide a quantitative proof with very high accuracy on other disease research work as well. After all, medicine is based on biology and chemistry while biology, chemistry, and engineering are based on physics. Mathematics is the mother of all sciences; even physics is based on mathematics. When we dig into our application problems down to their foundation level, we are bound to be able to find out more facts and truth. This is what "math-physical medicine" is about.

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