Engineering Principles and Medical Discoveries

Edward H Mathews [a] and Leon Liebenberg [b]

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Engineering researchers often tackle problems slightly differently from medical researchers. Engineers usually try to model a phenomenon and then test its validity. Medical researchers on the other hand usually do large empirical studies and derive models from the statistical analyses. In this paper we show the value of the engineering approach as applied to the problem of carbohydrate (CHO) metabolism into blood glucose in the body. We show that the engineering approach leads to a more acceptable description than the one currently used for food labelling. It is also more practical than other detailed attempts to solve the historical problem. The CHO metabolism model is used to simulate the full blood glucose cycle, using engineering equivalents. Correct modelling of this cycle is valuable as blood glucose inter alia influences cancer, cardiovascular disease, diabetes, and the performance of sportspeople. Clinical verification of the model showed that it was within 1 mmol/L from more than 600 measurements for 80 % of the time. It can be deduced that the engineering approach and experience in engineering systems were vital in making these discoveries and developing the models in an important field of medicine.

Additional keywords: Energy modelling

1. Introduction

Engineers know that the energy converted from matter can be different for different conversion processes. For example, the energy released from combusting a given amount of matter is much smaller than the energy which can be released by a nuclear conversion process and it also differs from the amount released by a chemical conversion process, etc..

Let us see what the current medical thinking and also the current practice are regarding the energy conversion of carbohydrates (CHO) by a living creature. Atwater and Bryant[1, 2] described a method in 1900 to find metabolized CHO energy through bomb calorimeter measurements and the 'difference' method. With a few modifications, these measurements known as metabolizable energy (ME) have been the currency of food energy ever since[3,4]. These measurements are also reported on nutrition labels as per the United States of America Food and Drug Administration (FDA) requirement as the total carbohydrate count[5] .

In 1970, Southgate and Durnin[6] added a factor for available carbohydrate expressed as monosaccharide (16 kJ/g [3.75 kcal/g]). This change recognized the fact that different weights for available carbohydrate are obtained depending on whether the carbohydrate is measured by difference or directly.

In recent years, an energy factor for dietary fibre of 8.0 kJ/g (2.0 kcal/g) has been recommended, but has not yet been implemented[3,5]. In arriving at this factor, fibre is assumed to be 70 % fermentable[3,5].

Metabolized CHO has an approximate energy content of 4 kcal/g of CHO when calculated with the Atwater *general* factor system[1,3]. However, energy conversion factors calculated with the Atwater *specific* factor system range from 2.4 kcal/g for certain types of fruit, to 4.12 kcal/g for wheat[3,7]. Both the *general* and *specific* food energy factors are under strain; the *specific* factor system because of its complexity (with different factors being used for different foods), and the *general* factor system because of inaccuracies relative to the specific factors[3,7].

The above values derived from bomb calorimeter measurements are of course only *approximate*, as our bodies do not incinerate food, they digest it. And digestion takes a different amount of energy for different foods, quantified by the ME values. These can be modified further to account for energy that is lost as heat from different substrates via heat of fermentation and obligatory thermogenesis, i.e. energy that would not be available for the production of the energy storage and transfer molecule adenosine triphosphate (ATP) to fuel metabolism.

This procedure results in the so-called net metabolizable energy (NME) factors[8, 9]. The NME system retains a general factor approach, i.e. a single factor each for protein, fat, available carbohydrate, dietary fiber, alcohol, etc. that can be applied to all foods. Despite the NME system's improved accuracy, it has been rejected worldwide due to its complexity [1, 3, 7, 10-12].

In practice, over the past 100 years, the Atwater *general* factor system has been used on nutrition labels (as required by the FDA). This system assumes that similar amounts of energy is made available by the body's blood glucose (BG) energy conversion process (metabolism) as that made available by the conversion process in a bomb calorimeter (complete combustion), i.e. 4 kcal/g of metabolised carbohydrate [3,7,10-12] .

However, as engineers we know that the two conversion processes (i.e. full combustion and human metabolism) are very different. Therefore, contrary to popular practice, we suspect that different amounts of energy will be released by the two processes (less by metabolism than by full combustion).

We investigate the blood glucose response in rats to ingested CHOs. We attempt to obtain a better insight of metabolized BG energy from CHO using engineering principles, i.e. by deriving the CHO metabolic energy equations from first principles. We hope to arrive at an easy-to-use practical solution.

a, b Centre for Research and Continued Engineering Development, North-West University, (Pretoria Campus), Suite no. 93, Private Bag X30, Lynnwood Ridge, 0040, South Africa.
Contract Professors and consultants to TEMM International (Pty) Ltd. and MCI (Pty) Ltd.
a Director
E-mail: ehmathews@researchtoolbox.com
b E-mail: LLiebenberg@researchtoolbox.com

2. Experiment and Discussion

Nine groups, each consisting of eight healthy Sprague Dawley rats, were clinically investigated. All rats were of the same age and received the same kilocalories per body mass. The food energy (kcal) values were determined by the following energy equation[13] for recommended daily allowance (RDA) for rats:

$$RDA[\text{kcal}] = 0.45 \times body\ mass^{0.75} \quad (1)$$

Each of the groups received different foods containing a high percentage of CHO with low fructose count, namely: barley (1), Provita (2), Strawberry Pops (3), chickpeas (4), toasted muesli (5), Pronutro flakes (6), Special K (7), All Bran Flakes (8) and Nutrific (9), refer to figure 1. The energy content of the foods was measured with a bomb calorimeter. The mass loss/gain for each group was measured weekly for three weeks.

As the energy supplied to the rats (calculated in the "conventional" way or "Atwater *general* system") is their RDA, we would expect that the mass of the rats should not change. However, if there is a small mass loss/gain due to an error in equation 1, this loss/gain should be the same for each group as they all received the same amount of kcal per body mass.

Our experimental results in figure 1, however, show that all the groups actually lost mass. (We had to stop the experiment after three weeks as the ethical allowable loss limit of 15 % was exceeded very quickly.) The results also show that these losses were not the same for the different groups consuming different types of "isocaloric" food.

Our suspicion was confirmed: the full four kilocalories per gram of CHO were not converted into blood glucose energy which the body could use. Furthermore, the metabolic efficiencies of different CHOs also differ.

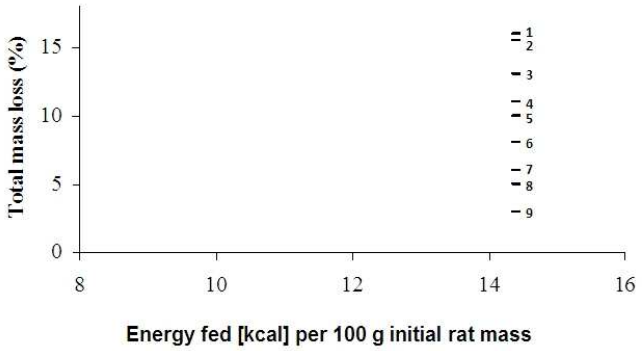

Figure 1: Relationship between mass loss and "isocaloric" kcal ingested for 9 different foods (kcal calculated in the "conventional" way)

3. Derivation of Equations: Metabolic Efficiency of Carbohydrates

In the previous section we have shown that our 100 year's understanding of energy from carbohydrates (CHO) may be wrong. We must try to find a better way to estimate the blood glucose energy metabolized from CHO. However, to accomplish this we first have to find the true metabolic efficiency of any CHO. We use the engineer's tool of mathematics to accomplish this.

Only CHO in a meal is directly metabolized into blood glucose during digestion. The metabolic conversion efficiency (η_{CHO}) of CHO estimates the amount of energy which is converted into blood glucose by a typical person. All losses, including energy needed for digestion, incomplete digestion, gas and heat production, etc., are accounted for in η_{CHO}. This value can be measured (as discussed later) and is a property of the meal. It depends on many factors including the content of dietary fibre, fat and protein in the meal.

Energy from CHO which can be metabolized by a person (E_{CHO} [kcal]) in the form of blood glucose is then a function of the mass of CHO (including fibre) in the meal (m_{CHO} [g]), the full energy content per mass of the CHO (k_{CHO} [kcal/g]) measured outside the body by means of a bomb calorimeter and the metabolic efficiency (η_{CHO}) of the meal which accounts for how efficiently the energy can be extracted inside the body as blood glucose.

The correct equation for CHO energy in a meal which can be metabolized inside the body (E_{CHO}) is then given by:

$$E_{CHO} = \eta_{CHO} m_{CHO} k_{CHO}. \quad (2)$$

Efficiency towards metabolizing the CHO from a meal (equation 2) into blood glucose varies among people. We represent this personalised CHO efficiency by the term f_{CHO}. (Remember that f_{CHO} is a function of a specific person while η_{CHO} is a function of a meal.) The total energy metabolized as blood glucose for a specific person is then given by

$$E_{Metab} = f_{CHO} E_{CHO} = f_{CHO} \eta_{CHO} m_{CHO} k_{CHO} \quad (3)$$

As E_{Metab} [kcal] is the CHO energy metabolized into blood glucose for a specific person, E_{Metab} can also be found by means of blood glucose measurements for that specific person. First we have to integrate the response curve for blood glucose concentration ($\int BG(t)dt$) over a period in which the blood glucose rises above basal level. This period is usually in the order of 120 minutes and is the period used in glycaemic index (*GI*) methodology[14]. The resulting integral value is called area under the curve (*AUC*).

AUC now gives us the time integrated concentration of blood glucose in [mmol.min/L]. We then need to multiply the concentration by the total volume of blood of the person (Vol) [L] to find the total amount of extra glucose in the blood due to the meal. Finally, E_{Metab} [kcal] is then found by multiplying with e [kJ/mmol], the energy value of glucose and dividing by the integration period of 120 minutes and equation the result to equation 3.

$$E_{Metab} = \frac{Vol.e}{120} \int_{t_0 = start\ of\ meal}^{t = t_0 + 120\ \text{min}} BG(t)dt = \frac{Vol.e}{120} AUC = f_{CHO} \eta_{CHO} m_{CHO} k_{CHO} \quad (4)$$

The energy absorption for any CHO relative to that of glucose is then given by the following equation:

$$\frac{E_{Metab|CHO}}{E_{Metab|Glucose}} = \frac{120.Vol.e.AUC|_{CHO}}{120.Vol.e.AUC|_{Glucose}} = \frac{f_{CHO}\eta_{CHO}m_{CHO}k_{CHO}}{f_{Glucose}\eta_{Glucose}m_{Glucose}k_{Glucose}} \quad (5)$$

Accounting for the facts that for the same person, $f_{CHO} = f_{Glucose}$ and $k_{CHO} = k_{Glucose}$ as measured in a bomb calorimeter as well as $m_{CHO} = m_{Glucose}$ (eating the same amounts of CHO and glucose namely 50 g) and assuming $\eta_{Glucose} = 1$ (assuming 100 % metabolic efficiency for ingested glucose to blood glucose although we know it will be slightly less) the following equation results:

$$\eta_{CHO} = \frac{AUC|_{CHO}}{AUC|_{Glucose}} \quad (6)$$

But according to the definition of *GI* [14,15]

$$GI_{CHO} = 100 \times \frac{AUC|_{CHO}}{AUC|_{Glucose}} \quad (7)$$

By comparing equations 6 and 7 we have proven that the metabolic efficiency (η_{CHO}) of a CHO (times 100) is its *GI* value! The metabolic efficiencies of many CHOs are therefore available through their *GI* values. This unexpected finding also leads us to conclude that current thinking on *GI* may be wrong. This will be explained in a later paper.

4. Derivation of Equations: Estimating Energy Metabolized from Carbohydrates

In section 2 we have shown that a better method than the one used during the past century is needed to calculate the carbohydrate energy metabolized by a living creature. It was also shown there that, contrary to popular belief, the metabolized energy from different CHOs can differ vastly.

Based on these findings we suspect that we have to account for the metabolic conversion efficiencies (η) for each different CHO as derived in section 3. Here we again use the engineer's tool of mathematics to derive the necessary final energy equations and we then verify them.

The energy E_{CHO} [kcal] converted into blood glucose from a CHO with a metabolic conversion efficiency of η_{CHO} and a mass of m_{CHO} [g] (including fibre), can be given by equation 8. All losses, including energy needed for digestion, as well as incomplete digestion, gas and heat production, etc., are accounted for in η_{CHO}.

$$E_{CHO}[kcal] = \eta_{CHO}\, m_{CHO}[g]\, 4[kcal/g] \quad (8)$$

We want to express the energy content in any CHO with a unit which is easy to understand and visualise for the layperson, say a teaspoon of sugar. There are many other advantages for choosing this unit which will be described in more detail in future papers.

When we now use equation 8 for one teaspoon of sugar containing 5 g of CHO, it results in the following:

$$E_{TeaspoonSugar}[kcal] = \eta_{Sugar}\, 5[g] \times 4[kcal/g] \quad (9)$$

Let us now relate the metabolized blood glucose energy from each different CHO (E_{CHO}) to equivalent teaspoons sugar (—ets). We can achieve this by dividing equation 8 with equation 9 for sugar to find the amount of —ets in any CHO, namely —ets$_{CHO}$:

$$\text{—ets}_{CHO} = \frac{E_{CHO}}{E_{Teaspoon\ Sugar}} = \frac{\eta_{CHO}\, m_{CHO} \times 4[kcal/g]}{\eta_{Sugar}\ m_{Teaspoon} \times 4[kcal/g]} = \frac{\eta_{CHO}}{\eta_{Sugar}}\ \frac{m_{CHO}}{5} \quad (10)$$

In the previous section we proved that $\eta_{CHO} \approx GI/100$, where *GI* is a well known entity [15]. We therefore have measured values for η_{CHO} for most of the important CHOs. (It must be remembered that η_{CHO} will become even smaller than these measured values in a meal high in fat and/or protein.)

Using equation 9 and keeping in mind that $GI_{sugar} = 65$, thus having a metabolic conversion efficiency (η) of 0.65, the equivalent energy in one teaspoon sugar (—ets) is 13 kcal as calculated using equation 9).

$$E_{Teaspoon\ Sugar}[kcal] = one\ \text{—ets}\ [\text{kcal}] = 0.65 \times 5 \times 4 = 13\ \text{kcal.} \quad (11)$$

The new energy value for a meal consisting of CHO, fat and protein is then given by equation 12. The energy unit for this new equation is called —ets *cal*, to avoid confusion with standard kcal.

$$\text{—ets}\ cal = 13[\text{kcal/—ets}] \times \text{—ets}_{CHO} + 9[\text{kcal/g}] \times mass_{Fat}[\text{g}] + 4[\text{kcal/g}] \times mass_{Protein}[\text{g}] \quad (12)$$

The important difference between equation 12 and the conventional equation is that the energy value per gram of carbohydrates is no longer a constant value of 4 kcal/g. It now depends upon the metabolic efficiency of the specific type of carbohydrate.

By utilising experimental data from section 2, and calculating the energy with the new equation 12, figure 2 was constructed. A linear relationship is found between the —ets cal values of a food containing primarily CHO's and the percentage mass loss. A Pearson's R^2 value of 0.68 results.

It is again important to note that the rats received isocaloric diets according to the popular historical way of calculating the energy. This means that each rat received the "same calories" per body mass daily. This is shown in figure 1 where all data points are located on a single line (the historically calculated energy intake is approximately 14.5 kcal/[100 g initial rat mass] for the different feeds).

In figure 2 the same mass loss data were used but the energy was now calculated in *ets* cal (not kcal) by using the new equation 12. Because the metabolic efficiencies of each type of feed are different and now taken into account, the energy measured in the new unit *(ets cal)*, for the different feeds, was not equal as was the case when using the historical 4 kcal/g of CHO measured in kcal.

Therefore the data in figure 2 are spread over the *ets* cal energy range unlike the data in figure 1. Obviously this makes more sense than figure 1 as we would expect the mass loss to be a function of the true metabolized energy values, exactly as figure 2 indicates.

This shows that the *ets* cal equation is more representative of the metabolized glucose energy of CHO in a body than the constant 4 kcal/g historically used, shown in figure 1. However, note that the full effect of fructose energy intake is not accounted for in equation 12. A separate term should in future be added to account for it.

By utilising experimental data from section 2, figure 2 was constructed. A linear relationship is found between the *ets* cal values of a food containing CHO and the % mass loss with a resulting Pearson's R^2 correlation value of 0.68. This shows that the *ets cal* equation is more representative of the metabolized energy of CHO in a body than the constant 4 kcal/g historically used, shown in figure 1. The *ets* concept is not only easy to visualise and to use, but also practical to establish as the *GI* values of CHOs are already available.

The important limitation of this study is that only blood glucose (and not fructose) metabolized from CHO is addressed. Although the current work is relevant to our investigation into blood glucose simulation, etc. (which only depends upon blood glucose), equation 12 will not be correct for weight loss calculations where the CHOs may contain large amounts of fructose. A separate term for fructose energy should in future be added to account for that.

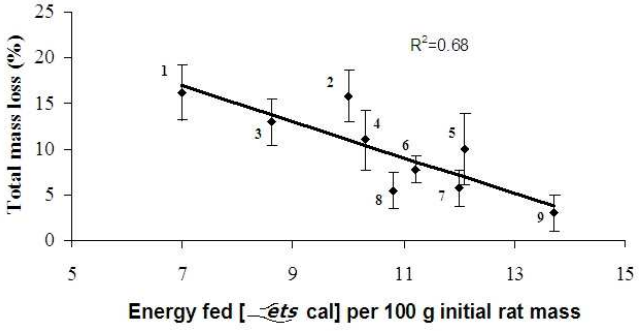

Figure 2: Relationship between mass loss and *ets* cal

It is apparent that engineering principles can add value across the discipline barrier to medical research. In the process an improved and easy-to-use equation for energy metabolized from carbohydrates was developed. This information is crucial to predicting correct blood glucose levels which impacts on cancer, heart disease and diabetes. We next show how engineering principles guided us to develop a new blood glucose simulator.

5. Simulating Blood Glucose Control

Engineers want to understand a phenomenon and build models to simulate it rather than gaining understanding through empirical methods as is preferred in the medical field. We have shown how engineering principles can be used to model the true metabolized energy from carbohydrates.

With this new insight we can proceed to model the full blood glucose cycle using engineering equivalents. Correct modelling of this cycle is valuable as blood glucose *inter alia* influences cancer, cardiovascular disease, diabetes, the performance of sports people and maybe even Alzheimer's disease.

Let us first investigate blood glucose and cancer. Cancer is a condition where normal cells become malignant, requiring large amounts of energy to sustain their uncontrolled growth rate. Cancer cells usually prefer glucose as an energy source, as opposed to fatty and amino acids [16-18]. This effect is *inter alia* used in positron emission tomography (PET) scans to track tumours[19]. The link between cancer and blood glucose must be investigated and should profit from a correct blood glucose simulation. With this insight a better lifestyle for the lowering of cancer risk could result. A correct simulation model for blood glucose control could thus be of value.

Blood glucose also influences coronary heart disease (CHD). CHD is the product of a pathogenic process associated with the development of arteriosclerotic plaque in the arteries [20,21]. High blood viscosity creates stress areas in the arteries which are prone to arteriosclerotic lesion formation[22]. There is a significant correlation between blood glucose levels and blood viscosity [23].

High levels of low density lipoproteien (LDL, or 'bad' cholesterol) and low levels of high density lipoprotein (HDL, or 'good' cholesterol) also affect the relative risk of coronary heart disease [24]. High blood glucose levels reduce HDL cholesterol levels and enhance the synthesis of very low density lipoprotein (VLDL) [25].

A high insulin level has also been shown to be a risk factor for CHD [26, 27]. Insulin levels are increased with blood glucose increase. Furthermore, high blood glucose increases the potential for inflammation which was also shown to increases the risk for CHD [28]. It is unclear which of the above mentioned is the major CHD risk factor. However, what we know is that high blood glucose levels adversely influences all of them.

Let us now investigate blood glucose and endurance sport. Hypoglycaemia ("hypo") describes a state of low blood glucose[29]. Since the brain's primary fuel is blood glucose[30] it becomes "confused" when in a hypoglycaemic state. This can happen to an athlete during endurance events where the liver is depleted of its blood glucose stores (glycogen)[31]. It can also occur when under high stress situations such as during the writing of a long examination paper.

It should be clear from the above that understanding of the blood glucose cycle is important and warrants a more detailed investigation. Let us now discuss our philosophy of using our engineering experience to develop a blood glucose simulation model. The detailed derivation of equations for the full model will be discussed in later papers.

6. Blood Glucose Simulation

6.1 How did we as engineers approach the problem?

We first ensured that we understood engineering systems which are analogous or "equivalent" to human systems. These engineering systems were easier to manipulate, measure and therefore to understand. We also had more experience and background in these.

We mostly used inexpensive postgraduate engineers who first helped us to understand the engineering equivalent systems. After understanding these we could look for the similarities in the human system. It was easier, as the human system was not as well understood or mathematically described as the engineering systems.

Many young people find it difficult to multi-task. Our young engineers were therefore not informed that they had to produce bioengineering results. They were also too inexperienced and often not creative enough to make the engineering to medicine link.

The project coordinator and sometimes the project engineer used the young engineers' findings on the engineering systems to investigate the similarities and differences between these systems and the human energy system. Although this approach is unconventional, we will show that it was successful.

6.2 Common units

In the engineering field we could only start to successfully model complex systems consisting of interplay between chemical, mechanical, electrical, and other elements after we could describe their respective energy effects in a common unit. The unit that was developed is called the Joule. We now have the same problem for our blood glucose simulation as the engineers of old had before the Joule was developed. Let us explain.

It is known that various factors influence blood glucose, namely food intake, dietary fibre intake in addition to a meal, exercise, and stress. However, they are all measured in different units, e.g., for food intake we use grams of carbohydrates and the glycaemic index; for fibre we use grams; for exercise it is kcal expended, and stress is usually reported as low, medium, high, etc..

Before we investigate the impact of these factors on blood glucose, we must develop a common unit to describe the blood glucose effect of all these factors as the engineers did more than a century and a half ago with the Joule.

We decided to use the equivalent teaspoons sugar *ets* concept (equations 10 and 11) as our common unit. Various advantages of using this unit will be described in another paper. As non-technical people must also use this unit, one of the main advantages is that it is easy to visualize and therefore to understand, even for children.

The relevant impacts in *ets* have been quantified and are given elsewhere [32, 33]. The most important impact of food ingestion was described in section 4 of this paper.

6.3 First engineering equivalent: Building HVAC (Heating, Ventilation and Air-Conditioning) systems

The first simplified blood glucose simulation[34] was developed based on knowledge from an engineering simulation of building thermal analyses [35, 36]. Our logic was that there are various "similarities" between the two problems. For example in both simulations, results must fall within certain boundaries and have certain controls. For buildings the inside dry bulb temperature must typically be between 20 °C and 24 °C while the human metabolism is typically set for blood glucose control between 4 mmol/L and 8 mmol/L.

Furthermore, when the temperature or blood glucose goes over the maximum limit, respectively air-conditioning will engage while in the human case insulin will be secreted by the pancreas. This will reduce the building's indoor temperature and for the human, the blood glucose value.

If the temperature in the building goes below a certain temperature, the heaters will come on to rectify the problem. In the human the counter regulation (i.e. the liver) will engage to prevent the blood glucose from going too low. If the blood glucose value drops too low the person can become comatose or even die.

6.4 Second engineering equivalent: Pumping systems

If we look at the full network for a typical large-scale engineering pumping system (see figure 3) and compare it to the metabolic system (see figure 4), one can see that there are similarities. The same integration network analyses as well as characterisation methods for elements in the system can be used. For this reason a lot of effort was spent to understand the engineering pumping systems [37 - 44] then to investigate their "similarities" with human systems.

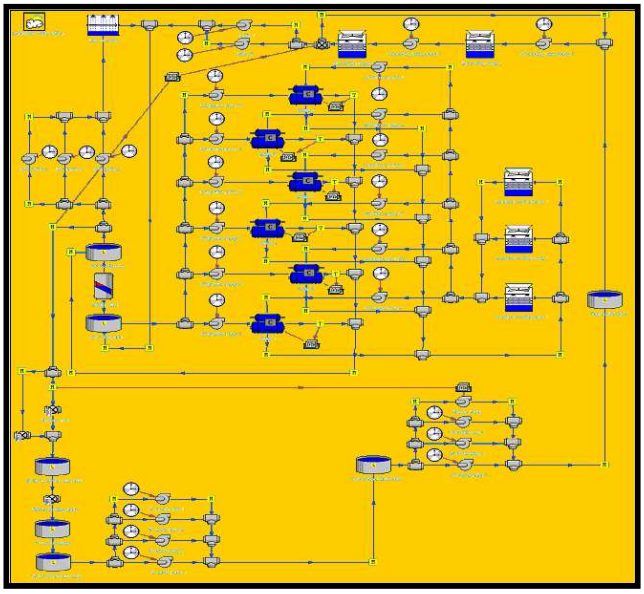

Figure 3: Engineering pumping system

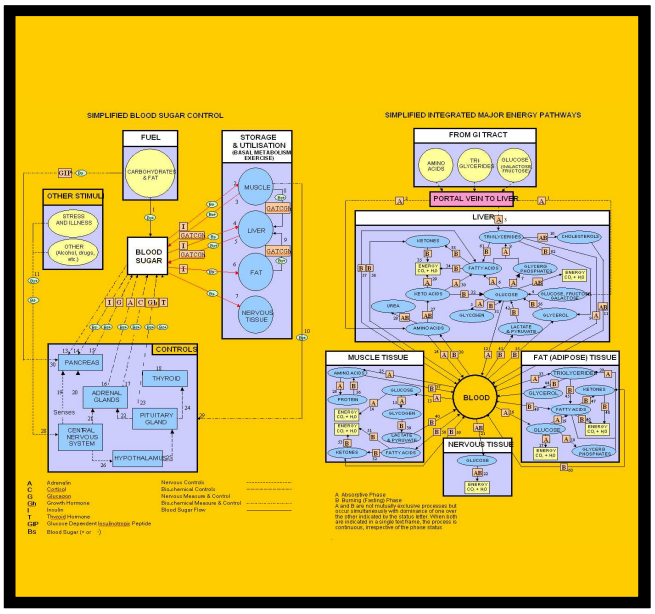

Figure 4: Human metabolic system

Important discoveries which resulted from the above-mentioned approach was that we can now show why, depending on the initial state, blood glucose of type 1 diabetics can either go up or down when the person is exercising. This is now accounted for and the results can be clearly seen in the human simulations.

6.5 Third engineering equivalent: Refrigeration plant system

The refrigeration plant is our engineering equivalent of the pancreas. If we understand how to sensibly control the refrigeration plant [45-47] we would also better understand how to control the pancreas. The varying refrigeration plant coefficients of performance (COP), for varying exterior conditions, lead us to understand the need to vary the efficiency of insulin usage for different 'operating conditions'. It is for example now easier to describe why we need less insulin during physical exercise. This effect was included in the human simulation model.

6.6 Fourth engineering equivalent: Processing systems

One of the most important drivers of our blood glucose levels is what we eat. Therefore, it is important to investigate the digestion system in our human simulation. Previously (over the past 100 years) it was popularly assumed that all carbohydrates will always present 4 kcal energy per gram of CHO during the conversion process. These values were measured in a bomb calorimeter.

However, our bodies do not use the same conversion process of full combustion. Our conversion process (metabolism) is more like a typical engineering processing plant. Investigation into plants shows that depending on the grade of the input product, different efficiencies for output extraction will result [48-50]. We have similar differences in metabolic efficiencies of different foodstuffs.

This engineering background enabled us to mathematically describe our most important insight, namely that all CHO's do not lead to the same amount of metabolized energy (or output, in engineering terms). Before the engineering work we (and the entire medical field during the past century) could not develop the ideas behind the mathematics. Detail of the derivations is given in sections 3 and 4 of this paper.

6.7 Fifth engineering equivalent: Material-handling systems

The handling of energy is an important element of the human simulation. To understand this better, you can look at an engineering materials handling process [51]. This led us to understand that there is not a linear relationship between food eaten and fat gain ability as currently used by all dieticians.

The human system also becomes overloaded during over production (over eating) similar to an engineering system. The ability to produce (gain fat) will be reduced in such cases. Another important impact is that weight loss primarily happens in the linear phase of the kcal vs. weight loss graph. All the above were not practically used before by dieticians. We correctly incorporated this factor into our prediction of CHO metabolism to blood sugar.

6.8 Sixth engineering equivalent: Storage systems

The storage and utilisation of blood glucose from the liver is similar to the charging and discharging of batteries. The important engineering equivalent was that the energy need for typical complex engineering systems is much less than anticipated [52]. (The baseline or true use is usually much lower than the installed capacity.)

By applying this insight to humans we realised that the baseline energy (RDA) is at present probably higher than necessary. Typical healthy diets (accounting for the metabolic efficiency mentioned in section 3) actually give lower energy values than previously thought.

This now makes sense to us if we compare it to the insight gained with the difference between the baseline and installed capacity for engineering storage systems.

6.9 Seventh engineering equivalent: Compressed air simulations

We also investigated industrial compressed air networks [53]. Here, similar to the pumping and refrigeration plants, the importance of characterisation of engineering equipment again became apparent. This led us to appreciate the need for detailed patient characterisation for efficiency of metabolism. This is important when looking at especially oral drugs and also insulin dosage.

Now that we understand this we realise why one shoe does not fit all in medicine. For example some people with high metabolic efficiencies will need fewer oral drugs and those with low efficiency will need more. Therefore with current drug prescriptions some people will develop allergic reactions because they need fewer oral drugs, while others will not heal as they actually need more.

This insight has an effect on the efficiency of all drugs, including ARV (antiretroviral) drugs for AIDS patients. The problem with AIDS patients is that for someone with low metabolic efficiency they will not get enough active drugs in their blood which would not only prevent them

from being protected, but the viruses would actually become resistant.

The value of 'letting off steam' (i.e. relieving stress) and its effect on metabolism also became apparent. For a compressor not to surge and break down it blows off gas into the atmosphere. The effect of stress in humans must be treated similarly. Various stress-relieving options were therefore investigated and developed.

We have also done work on the effects of stress on blood sugar. This is especially important for diabetics and for our blood sugar simulation. A summary of this work was published elsewhere [54].

6.10 Eighth engineering equivalent: Energy system control

The importance of the control of engineering energy systems cannot be over estimated. If you investigate the human metabolic cycle you will see that it is very closely controlled.

A real time energy management (or control) system (REMS) is therefore needed for simulating and later mimicking (for artificial pancreas) the human metabolic system. This is similar to the REMS which we have developed for engineering systems [55].

In the process of developing the human REMS we have attempted to simplify the simulations but to still ensure good control. With engineering experience gained we have reduced the control simulation from initially only running on a personal computer to later on a PDA (personal digital assistant) and now finally we do a full control simulation of the metabolic control on a cell phone.

This makes it practical and easy to use by our client market. It took quite a while to reach this stage and would not have been possible without the lessons learnt from engineering.

6.11 Ninth engineering equivalent: Information management system

The ultimate diabetic product is an artificial blood glucose controller which takes over the function of the pancreas and the liver. Although this may sound futuristic there are numerous examples of engineering systems and their controls which are far more involved.

Similar to an engineering system we not only need a REMS (as discussed in section 6.10) but also an on site information management system (OSIMS*)* to ensure that the control is not only correct, but fail-safe. If something catastrophic happens (e.g., insulin pump fails or not functioning correctly) the user must be immediately notified.

This is similar to engineering systems where the operator is informed of potential problems, based on site information [56]. We believe that with our engineering background we can achieve this artificial blood glucose controller which will be of great value to type 1 diabetics.

7. Simulation Model, Results and Applications

The engineering experience and all the lessons learned from the previous discussion were integrated to develop the simulation model. It is not the purpose of this paper to discuss the detail of the model, only the underlying philosophy used to accomplish the simulations.

Blood glucose measurements were taken for non-diabetics and type 1 diabetics, under typical conditions, i.e. before and after meals, before and after exercise, at bedtime, after waking up, before and after insulin injections for type 1 diabetics, etc.. Our system and control simulation model provided good answers to the typical blood glucose energy questions. Figure 5 shows a comparison between the simulated and measured blood glucose data. The data are statistically analysed in table 1. It can be seen that for more than 80 % of the time the predictions were within 1 mmol/L from the measurements.

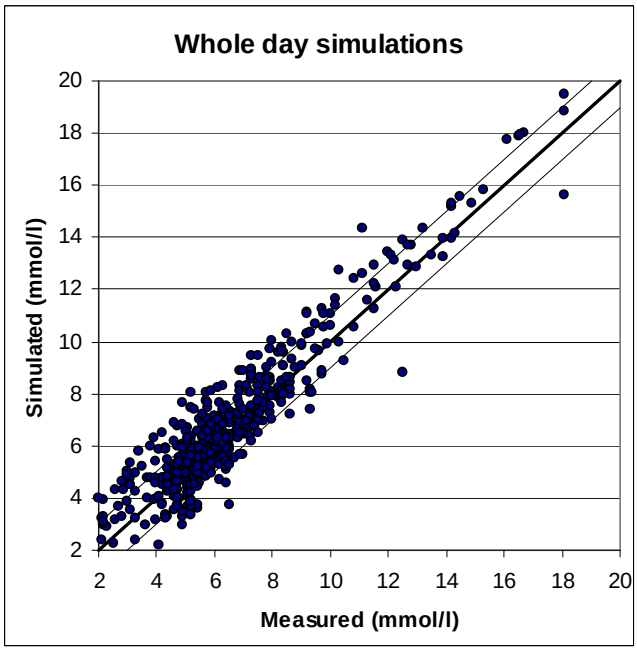

Figure 5: Measured versus predicted data points

Trial	Number of data points	Error bands and fractions of the data points that fall within the specific error bands		
		0.5 mmol/L	1.0 mmol/L	2.0 mmol/L
Food ingestion	454	45.6%	81.5%	98.9%
Exercise	109	74.3%	96.3%	100.0%
Insulin injections	66	40.9%	81.8%	95.5%

Table 1: Accuracy of the blood glucose simulations

Errors are mainly attributed to phase differences between the measured and simulated data as the time feedback of the subjects was proven to be inaccurate. We might argue that the phase difference presents a false perception of inaccurate simulation. Even though the results reflect badly in terms of falling within or outside the acceptable error band, the trends and significant influences on the blood glucose levels were nevertheless indicated quite well. The simulations can therefore be applied to suggesting insulin dosages for diabetics. After all, the absolute drop in blood glucose concentration due to injected insulin is still correct.

Despite all this, the results are far better than what is currently available. The accuracy of all the simulations suggests that the simulation model and its results may yet be implemented in various applications. Albeit drug discovery,

clinical testing or artificial blood sugar controller for type 1 diabetics, the proposed simulation and modeling of the human energy system is successful enough for further development and implementation.

Various applications already resulted from the simulation model. These are described elsewhere [57-59].

8. Conclusion

The medical discoveries presented in this paper would not have been made without underlying knowledge of engineering principles and vast experience in the engineering field. In the process of gaining more experience, we have actually made more discoveries regarding peripheral issues not set out in our initial vision. We believe that we have shown the value that knowledge and experience in engineering can bring to the field of medicine.

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