
CHAPTER 9

CLOSURE

A short discussion on the important aspects of this study is provided in this chapter, together with some recommendations for future work.

9.1 Introduction

This chapter provides a short discussion on the major contributions that were made by this study. Firstly, a summary of the important aspects that were discussed in the previous chapters is provided. Secondly, the main recommendations for future work are also listed.

9.2 Summary of the contributions

In this section a short summary of the preceding chapters is provided. It is divided into two distinct parts of which Chapters 2 through 4 are grouped as the first, and Chapters 5 through 8 are grouped as the second. (See Section 1.6.)

Chapter 1 serves as an introduction of this study where a brief background regarding simulation of biotechnological systems was presented. The goals and objectives of this study were outlined. It was mentioned that a quantification method for energy was necessary to construct a simulation model of the human energy system. This method was developed first.

9.2.1 New concept: equivalent teaspoons sugar (ets)

In Chapter 2 two major contributions were made. The first is a realisation that the available amount of energy from carbohydrates (CHO) in food is less than commonly accepted. It was shown that the glycaemic index (GI) provides a good approximation of the fractional amount of energy that is actually available. Therefore, it was proposed that the current definition of the GI concept, which is “rate of absorption”, should be redefined as the “fractional amount of available energy” or “energy conversion potential”.

The second major contribution in Chapter 2 was the development of a novel new concept, namely Equivalent Teaspoons Sugar (ets). The ets concept provides the quantity of the amount of glucose energy that can be extracted from ingested food. Other than the current methods of evaluating foods, the ets concept is a function of both the amount of CHO in the food (mass) and the effectiveness of the CHO in the food, provided by the new definition of GI. A method for calculating ets is provided by Equation (2.6).

$$ets = \frac{GI_{CHO}m_{CHO}}{325} \quad (2.6)$$

The purpose of the next chapter (Chapter 3) was to verify the ets concept as a quantification method of blood sugar energy. For this purpose two applications of the ets concept were proposed, for which comparisons with current quantification methods were drawn.

The first verification study involved the evaluation of the application of ets as a predictor for insulin response in healthy individuals. A linearised equation for the calculation of integral insulin response due to ingested food was provided in Equation (3.9).

$$AUC_I = f_{AUCI}ets \quad (3.9)$$

It is important to note that the linearised relationship in Equation (3.9) is described by a constant characterisation factor, namely f_{AUCI} . Unlike ets, which is a property of the ingested food, f_{AUCI} is a property that characterises the person ingesting the food. It is unique to one person and has to be measured prior to implementation of Equation (3.9).

When predictions with the ets concepts were compared to predictions of the two current predictors used by researchers, CHO counting and the GI method, the ets concept proved to be the method of choice [1],[2].

In Section 3.3 the second application of ets was presented for verification of the concept. The application involves a procedure for calculating the optimum ets ingestion while performing endurance exercise. This was shown in Equation (3.20).

$$E_{Expended} = f_{Expended}ets \quad (3.20)$$

Again the linear relationship is described by a characterisation factor, $f_{Expended}$ in this case. This factor is also a property of the person for which a measurement procedure is provided in Chapter 3.

The verification of the equation consists of a comparison between suggestions made with Equation (3.20) and other suggestions available in the literature. Currently a one-size-fits-all approach is used for suggestions, not an individualised one with a characterisation factor like $f_{Expended}$. The measured results from other researchers revealed that Equation (3.20) might indeed provide better suggestions than current methods [3],[4].

After the ets concept was empirically validated in Chapter 3, two new applications of the concept were discussed in Chapter 4. These applications are, firstly, the use of ets as a method for calculating insulin dosages for Type 1 diabetics and secondly, the use of ets as a unit for quantifying the effect of stress and illness on the human energy system.

For the calculation of insulin dosages two equations were derived. The equations were Equation (4.4) for short-acting insulin and Equation (4.7) for long-acting insulin. Both are shown here.

$$I_{Injected} = f_I ets \quad (4.4)$$

$$I_{Injected(Long)} = \frac{f_I}{f_{Expended}} E_{Expended(RDA)} \quad (4.7)$$

Similar to the previous derivations, a characterisation factor was again defined to equate the linear relationship between the short-acting insulin injection and the ets ingested as well as the relationship between the required long-acting injection and the total amount of daily energy expended. This factor is f_I .

A measurement procedure for f_I was presented together with a brief validation of both the equations. An interesting observation was that, according to assumptions based on the current literature, the value of f_I has a spread of up to 75% [4]. This indicates that the need for an accurate suggestion for insulin dosages, especially long-acting insulin, is very relevant. Equations (4.4) and (4.7) can therefore have a large impact on improving the lives of Type 1 diabetics.

The second new application discussed in Chapter 4 was the implementation of the ets concept as a quantification method for the effects of stress and illness on the human energy system. It was shown that the effects of a certain level of stress can be mimicked in the body by ingesting a certain

amount of ets. With the aid of simulation of the human energy system this amount of ets could be estimated.

The maximum estimated virtual ets values that can effectively be secreted by an average healthy human subject during times of stress or illness (ets_{Stress}) were listed in Table 4.3. These values are for a person weighing 65 kg. If the table is to be used for a person of another weight, the values should simply be scaled linearly.

It was further mentioned that not all people experience stress and illness in the same magnitude. For this reason a characterisation factor describing the “effectiveness” of the stress in a person was introduced. This factor is f_{Stress} . With f_{Stress} Equation (4.11) could be derived which can be employed to calculate the amount of long acting insulin a Type 1 diabetic should inject during times of long-term stress or illness.

$$I_{Injected(Long)} = f_I (ets_{RDA} + f_{Stress} ets_{Stress}) \quad (4.11)$$

And so, in Chapters 2 through 4, the novel new ets concept was derived, verified and applied. In the following chapters the concept was used as the quantification unit for describing all the energy flow in the human energy system. The next four chapters (5 through 8) involved the simulation model used for glycaemic response prediction.

9.2.2 Simulation of the human energy system

In Chapter 5 a brief description of the simulation methods used in this study was outlined. The mathematical methods used are however well researched and widely used in numerous other studies. Unnecessary details were therefore omitted from this text.

In Chapter 6 the necessary background literature regarding the physiology of the human energy system was summarised. That chapter was subdivided into two sub-issues. The first was the background required for understanding the flow of energy in the human body. A schematic diagram of the major energy pathways was constructed and presented in Figure 6.2.

The second sub-issue of the chapter was the control system of the human energy system. The control system is responsible for regulating flow, storage, retrieval and utilisation of the glucose

energy along the major energy pathways. A schematic layout of the control system involved with glycaemic control was developed and shown in Figure 6.3.

In the conclusion of Chapter 6 it was pointed out that the flows of energy between the human energy system components are very complex processes. A simple quantification method was therefore necessary for successful simulation. This is the reason why the ets concept was developed in the earlier chapters.

The following chapter, Chapter 7, was the part of the study in which the design of the glycaemic response simulation model was described. A detailed description of each of the system components used in this simplified version of the human energy system was provided. Since the model is a generic design, an individualised model has to be constructed for each individual person that is simulated.

Similar to the background study of the human energy system (Chapter 6), Chapter 7 was also divided into two parts. The first part described the system components through which the glucose energy flow was simulated. A schematic layout of the proposed system was provided in Figure 7.1. The second part was a discussion on the control system implemented on the simulation model. Again a schematic layout was shown (Figure 7.8).

Finally the verification study of the simulation model and simulation procedure was discussed in Chapter 8. The study involved an evaluation into the accuracy of the simulation results in comparison to measured glycaemic responses. For the study two different types of trials were considered.

On the one side were the short-term simulations in which isolated influences on the human energy system were simulated. For this study glycaemic response to certain influences like food, exercise, insulin, etc. was simulated separately and the results were compared to measured data. The purpose of these trials was to evaluate the accuracy of the simulations for each individual input as well as to discover new applications of the ets concept like for instance the “amount” of stress a person experiences. This is described in more detail in Section 4.3.

On the other hand, long-term simulations were performed for verification in which simulation results were compared to measured blood sugar levels of test subjects for the duration of an entire test day. The purpose of this study was to investigate the ability of the simulation model to simulate integrated influences on the human energy system as they occur simultaneously.

The results of the verification study are shown in Table 8.3 for the whole-day simulations and Table 8.4 for the isolated simulations. According to predefined evaluation criteria the verification study revealed that both the whole-day simulations (more than 70% within 1 mmol/l) and the three isolated simulations (more than 80% within 1 mmol/l) were considered accurate. For the few simulations reflecting poor results a possible explanation for the inaccuracies was provided.

All things considered, the simulation model and procedure proposed in this study proved useful for most applications. Also, due to the unavailability of other models this model now provides good insight and a clearer understanding of the processes involved with the human energy system.

9.3 Recommendations for further work

In this study several new derivations and concepts were proposed. Most of these were also verified before being implemented for the development of the human energy system simulation model. However, due to the originality of the concepts many more studies will have to be conducted for further refining and verification of the ideas. In this section recommendations for some of these future studies are presented.

- The ets concept was derived only for the purpose of quantifying blood sugar energy flow in the human energy system. It was shown that less energy is available from CHO as was previously assumed. Logic suggests that the same principle should also apply to the energy available from the other macronutrients (protein and fat). Quantification concepts for these foods are therefore required.
- It was mentioned in Chapters 2 and 3 that the ets concept, which is a function of the glycaemic index (GI), may yield even more repeatable results if it is calculated as a function of the insulin index (II) [5]. However, due to the larger availability of the GI values, it was chosen for this study. In future studies the ets concept may be revised when more II values become available.
- In Section 3.3.5 the ideal method for the verification of the exercise equations was proposed. The resources for performing the trials were however not available within the scope of this study, so another, less precise method was used. For future research efforts the ideal verification is recommended.

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- In Chapter 4 the equations for Type 1 diabetic insulin dosage calculation were derived. The verification of both the long-acting and short-acting suggestions is so far only based on a number of assumptions. Due to the novelty of the equations some more verification is required.
 - Another recommendation is a more detailed study of the stress and illness quantification also proposed in Chapter 4. The method exposes a whole new field of research for which many studies can be performed.
 - Similar to the two new links presented in Chapter 4 many other possibilities also exist for the application of the concept. These include specialist diets, new medications, more involved diabetes management systems, etc. All of these possibilities will require some degree of research.
 - In Chapter 6 a detailed schematic layout of the human energy system was presented. The main objective of this study was however primarily to simulate glycaemic response. Therefore, the control system that was investigated was only relevant to the blood sugar concentrations. In the future the lipid and amino control systems also have to be investigated.
 - The new investigations will provide further insight into the simulation of the human energy system. It will enable the model to be extended for simulation of the entire human energy system, instead of only the glycaemic subsystem.
 - Finally, it is recommended that Type 2 diabetic test subjects are also used for further verification of the simulation system. In Chapter 8 only healthy people and Type 1 diabetics were used. If necessary the model design (Chapter 7) might also require some revision if the possible need for different model component properties is revealed.

9.4 Closure

In conclusion, the mission statement in Section 1.3, which was: *“To develop a simulation model and procedure to dynamically simulate the integrated energy processes of the blood sugar energy subsystem and its controls as part of the complete human energy system”*, was successfully accomplished. Furthermore, all the objectives of the study were reached to an acceptable degree.

Obviously, as mentioned in the introduction chapter, simulation of the human energy system now paves the way for faster, less expensive and more accurate medical advancement. The true recommendation for future work is therefore to implement the philosophy and basic ideas of this study for performing even more involved and complex simulations.

Because the biotechnology industry is at the brink of rapid expansion the simulation model and procedure presented in this study may prove to be one of the steps that are instrumental towards better living for all.

9.5 References

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