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## CHAPTER 3

## VERIFICATION OF THE ETS LINKS

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*In order to verify the ets concept presented in the previous chapter, two links with ets are investigated. These are the links with insulin response prediction as well as with endurance energy expenditure. It is shown that with both these links linear relationships provide a good approximation of empirical data. It is also shown that individualised characterisation of different people is only dependent on a single measurable variable for each link.*

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### 3.1 Introduction

Establishing the ets concept in the previous chapter was the first step towards developing a comprehensive and integrated energy simulation model for the human body. In following sections the link between ets and insulin as well as the link between ets and exercise energy expenditure will be discussed. The links will later be used to quantify energy flow in terms of blood sugar and insulin for a person experiencing different situations. A better understanding of the basic energy principals, necessitated by simulation modelling can also help in making new discoveries as well as to speed up clinical trials.

In this chapter two applications of the ets concept are discussed. The first is the link between the ets value of ingested food and insulin response (or requirement). It will be shown that the ets concept is a better predictor of insulin response to ingested carbohydrates (CHO) for healthy people than the conventional methods of CHO counting and GI.

Secondly, the link between ets and exercise energy expenditure will be established. This link is important for the development of the simulation model of the glycaemic subsystem of the human energy system. Similar to food ingestion being the energy input for the system, exercise is the energy output of the system and needs to be quantified accordingly.

### 3.2 Insulin response to ingested carbohydrates

Among other things, insulin response is primarily influenced by ingested food containing carbohydrates (CHO) [28]. The amount of insulin that is secreted for ingested CHO is however not well understood. As mentioned in Section 1.2.2, a practical relationship between insulin response and food is important for diabetics as they either do not produce enough insulin or cannot utilise it efficiently [29].

Furthermore, endurance athletes prefer a minimal insulin secretion when consuming carbohydrates during endurance events. While competing, the switching from blood sugar utilisation to storage mode due to high insulin levels may induce a condition called hypoglycaemia (or low blood sugar levels) [30].

When viewed from a health consideration point of view high insulin concentrations and resulting insulin resistance increase the risk of certain cancers, cardiovascular diseases (CVD) and also

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obesity [31],[32],[33]. Since a sufficient amount of insulin in the bloodstream is vitally important and the only regulation hormone used for energy storage, it may be wise to reduce the strain on the only organ capable of producing insulin, the pancreas. Therefore, food choices leading to less insulin secretion are important for everyone.

The most well known methods for predicting insulin response due to food ingestion are CHO counting and the glycaemic index (GI) [34],[35]. However, as discussed in Chapter 2, these methods do not always give the correct response and many people find them difficult to use [36],[37],[38]. Furthermore, these methods assume a one-size-fits-all approach and therefore do not specifically account for differences between people.

In this section a user-friendly method for predicting insulin response due to carbohydrate ingestion is theoretically derived. The method uses the easy-to-understand measuring unit of equivalent teaspoons sugar or ets as derived in Section 2.4. It is shown that ets predicts insulin response more accurately than the other two well-known methods.

Furthermore, an equation for the relationship between insulin response and ets is also derived. The equation for the insulin / ets relationship also includes an efficiency factor called  $f_{AUCI}$  which accounts for physiological differences between people.  $f_{AUCI}$  could help explain why some people are more prone to Type 2 diabetes or find it difficult to loose weight. It could also explain why some athletes become hypoglycaemic while others do not.

### **3.2.1 Derivation of the link between insulin response and ets**

The following procedure is presented for the derivation of the equations necessary to calculated insulin response due to ingested carbohydrates. It follows from the derivation of the ets concept performed in Section 2.4.

The first important assumption is that only carbohydrates (CHO) in a meal are directly converted into blood sugar during digestion [39]. (The validity of this assumption was explained earlier.) The “conversion potential” of CHO, approximated by GI, estimates the amount of energy that is converted into blood sugar by a typical person. All losses, including energy needed for digestion, incomplete digestion, etc. are accounted for in  $GI_{CHO}$ . This value can be measured (as discussed in Section 2.3) and is a property of the meal. It depends on many factors including the content of dietary fibre, fat and protein in the meal [40].

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Energy from CHO that can be utilised by a person ( $E_{CHO}$ ) in the form of blood sugar is then a function of the mass of CHO in the meal ( $m_{CHO}$ ), the full energy content per mass of the CHO ( $k_{CHO}$ ) measured outside the body by means of a bomb calorimeter, and  $GI_{CHO}$  of the meal which accounts for how efficient the energy can be extracted inside the body.

Note that historically it was incorrectly assumed in diet planning that the energy content ( $k_{CHO}$ ) of CHO measured outside the body by a different process (bomb calorimeter) was fully utilised inside the body through another process, namely digestion and absorption. This was explained in more detail in Section 2.4. (The same mistake is probably also made with protein and fat.) The correct equation for CHO energy in a meal which can be utilised inside the body ( $E_{CHO}$ ) is therefore shown by:

$$E_{CHO} = GI_{CHO} m_{CHO} k_{CHO}. \quad (3.1)$$

The efficiency towards converting the effective CHO from a meal (Equation (3.1)) into blood sugar varies between different people [29]. A personalised CHO efficiency can be represented by the variable  $f_{CHO}$ . (It is important to note that  $f_{CHO}$  is a function of a specific person while  $GI_{CHO}$  is a function of a meal.) The total energy absorbed in the blood for a specific person is then given by

$$E_{Absorb} = f_{CHO} E_{CHO} = f_{CHO} GI_{CHO} m_{CHO} k_{CHO}. \quad (3.2)$$

Since  $E_{Absorb}$  is the CHO energy converted into blood sugar for a specific person,  $E_{Absorb}$  can also be found by means of blood sugar measurements for that specific person. First the response curve for blood sugar concentration ( $\int BS(t)dt$ ) above basal level from time of consumption back to basal level has to be integrated. The time elapsed is described by  $\Delta t$ . The elapsed time is specific to a person's blood sugar response and is inter alia dependent on a person's insulin secretion rate and sensitivity.

The integral divided by  $\Delta t$  then describes the average concentration of blood sugar. The concentration has to be multiplied by the total volume of blood of the person ( $V_{Blood}$ ) to find the

total amount of glucose (or energy) in the blood. Finally,  $E_{Absorb}$  is then found by multiplying with  $k_{CHO}$ , the maximum energy value of CHO.

$$E_{Absorb} = \frac{\int_{t=ingestion}^{t=basal} BS(t)dt}{\Delta t} V_{Blood} \cdot k_{CHO} \quad (3.3)$$

If Equation (3.3) is substituted back into Equation (3.2), Equation (3.4) is the result.

$$\frac{\int_{t=ingestion}^{t=basal} BS(t)dt}{\Delta t} = \frac{f_{CHO} GI_{CHO} m_{CHO} k_{CHO}}{V_{Blood} k_{CHO}} \quad (3.4)$$

Studies have shown that for a typical balanced meal containing CHO there is a direct relationship between blood sugar response ( $\int BS(t)dt$ ) and the insulin response ( $\int BI(t)dt$ ) [41]. Although the best fit to this relationship is not linear, a linear relationship with an  $R^2$ -value of 0.963 was found through measurements by Lee and Wolever using meals consisting of mostly CHO [42]. This is deemed acceptable, especially if equations have to be made practical for everyday use. Equation (3.5) shows this assumed linear relationship.

$$\int_{t=ingestion}^{t=basal} BI(t)dt = f_{IBS} \int_{t=ingestion}^{t=basal} BS(t)dt \quad (3.5)$$

The insulin / blood sugar relationship varies from one person to the next and this person specific characteristic can be described with the blood insulin factor,  $f_{IBS}$ . (“IBS” in  $f_{IBS}$  is an abbreviation for “Insulin / Blood Sugar” relationship.)

If Equation (3.5) is substituted into Equation (3.4) the result is Equation (3.6), which describes the person specific insulin response to ingested food. (The  $k_{CHO}$  values are cancelled and therefore not present in Equation (3.4).)

$$\frac{\int_{t=\text{ingestion}}^{t=\text{basal}} BI(t)dt}{\Delta t} = \frac{f_{IBS} f_{CHO} GI_{CHO} m_{CHO}}{V_{Blood}} \quad (3.6)$$

However, due to the complexity of Equation (3.6), it cannot easily be used for everyday use. The following procedure is performed in order to simplify it. Instead of using  $m_{CHO}$  and  $GI_{CHO}$  in Equation (3.6) for the meals, it is proposed that effective CHO in foods and meals can be expressed in terms of equivalent teaspoons sugar (ets).

In Section 2.4 the ets concept was derived from first order energy principals. It was shown that the GI value of a meal and the mass of the carbohydrates present in the meal can be expressed in terms of ets to quantify the total amount of energy available from ingested carbohydrates. The equation for calculating ets (Equation (2.6)) is repeated here:

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

Interestingly, it can be shown that  $GI_{CHO}$  can be substituted with the insulin index ( $II_{CHO}$ ) to arrive at a more accurate value of ets [28]. The assumptions of linearity between insulin and blood sugar response as well as high CHO content are then not needed. It should also be noted that the ets / insulin relationship is linear for much higher ets values (approximately three time higher) than the ets / blood sugar relationship. Glycaemic index (GI) values are however used because they are more readily available and also easier to measure.

With the ets concept Equation (3.6) can further be simplified. If Equation (2.6) is substituted into Equation (3.6) and the term Area Under the Curve of Insulin ( $AUC_I$ ) is substituted for the integral, the following equations are found.

$$\frac{\int_{t=\text{ingestion}}^{t=\text{basal}} BI(t)dt}{\Delta t} = \frac{AUC_I}{\Delta t} = \frac{f_{IBS} f_{CHO}}{V_{Blood}} GI_{CHO} m_{CHO} = \frac{f_{IBS} f_{CHO}}{V_{Blood}} 325\text{ets} \quad (3.7a)$$

$$\therefore \frac{AUC_I}{\Delta t} = \frac{325 f_{IBS} f_{CHO}}{V_{Blood}} ets \quad (3.7b)$$

Equation (3.7b) can be simplified even further by defining a new person specific factor called  $f_{AUCI}$ . The factor  $f_{AUCI}$  accounts for all the person specific factors  $f_{CHO}$ ,  $f_{IBS}$ ,  $V_{Blood}$  and  $\Delta t$  in Equation (3.7b). (The notation, “ $AUCI$ ”, in  $f_{AUCI}$  is an abbreviation for “Area Under the Curve of Insulin” response.)

Among others, the factor,  $f_{AUCI}$ , of a person is a function of CHO metabolic efficiency, size, insulin resistance (which depends on fitness), body mass index (BMI), age, etc. For the sake of completeness the equation for  $f_{AUCI}$  is given in Equation (3.8) below. Measuring the individual variable is however difficult, so it is easier to measure the whole  $f_{AUCI}$  by simply using Equation (3.9).

$$f_{AUCI} = \frac{325 f_{IBS} f_{CHO} \Delta t}{V_{Blood}} \quad (3.8)$$

Substituting Equations (3.8) into (3.7b) yields the relationship between measured insulin response ( $AUC_I$ ) and ingested food represented by ets. This is shown in Equation (3.9).

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

In Equation (3.9)  $AUC_I$  is the integrated insulin response,  $f_{AUCI}$  is a measurable function of the individual person and ets is a measurable function of the meal. Values for ets can be found in published sources for most foods or it can be calculated by using Equation (2.6).

### 3.2.2 Verification of the equations

In order to verify the quality of Equations (3.9) as an insulin response predictor, the quality of the two current methods of insulin predictions should first be examined in more detail. These current methods are the CHO counting and the GI methods. For the verification purpose measurements

performed by Lee and Wolever will be used [42]. These measurements give insulin response curves for different healthy test subjects ingesting different amounts of CHO (0 to 100 grams) with varying GI values (23 to 100) [40].

Time integrals ( $\int BI(t)dt$  or  $AUC_I$ ) of the Lee and Wolever blood insulin ( $BI$ ) response measurements were calculated for all the test subjects. The  $AUC_I$  values were then normalised to a value of 10 and plotted against the amount of CHO consumed as well as against the GI values of the ingested foods. As an example, the CHO and GI plots for one test subject are shown in Figure 3.1 and Figure 3.2 respectively.

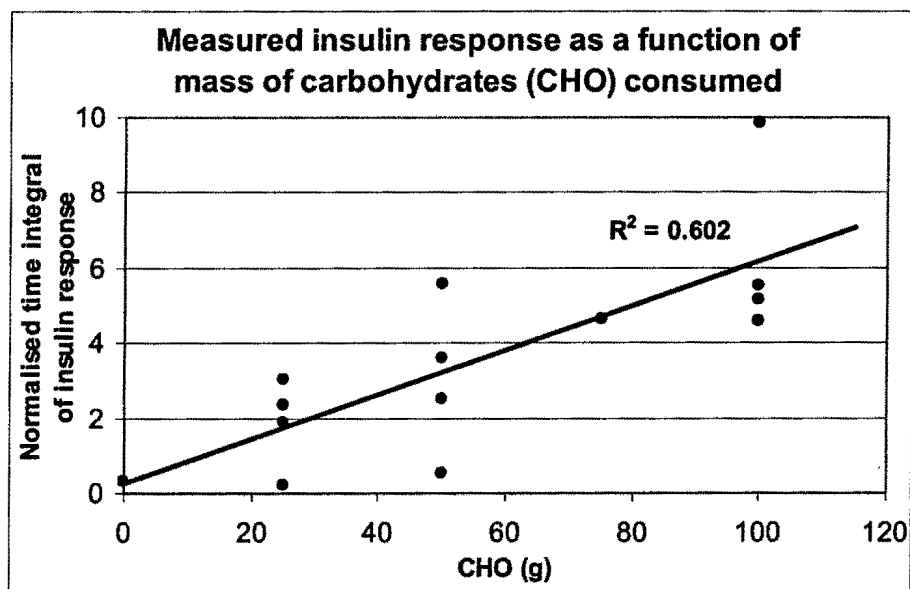


Figure 3.1 – Linear best fit trend line and corresponding  $R^2$ -value for normalised  $AUC_I$  values against CHO ingestion (one test subject).

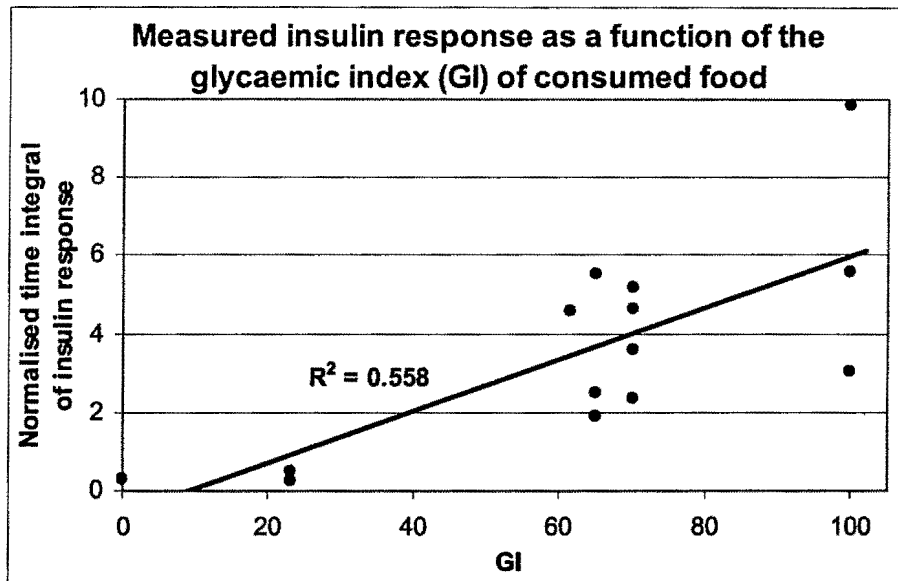


Figure 3.2 – Linear best fit trend line and corresponding  $R^2$ -value for normalised  $AUC_1$  values against GI values of ingested food (one test subject).

Pearson's  $R^2$ -values were calculated for linearised trend fits through the plotted data [43]. The  $R^2$ -values for the CHO and the GI methods were 0.603 and 0.558 respectively for the example test subject. For the CHO method the worst spread was found at 50 g of CHO, namely a factor of 12, while for a GI at 65 the spread factor was close to 3.

From the above figures the need for a better insulin prediction method according to ingested carbohydrates is obvious. A relatively successful attempt was presented by Wolever and Bolognesi [37]. They developed an empirical model based on measurements in seven healthy subjects. Unfortunately the resulting non-linear empirical equations have not found popular use because they are very difficult to use for everyday application.

Therefore, the ets method presented in the previous section (Section 3.2.1) is proposed instead. The method is theoretically derived from energy principals. Normally a theoretical approach is preferred to an empirical one since theory often leads to better insight. The simple linear link between insulin response and ets was given by Equation (3.9).

The quality of insulin predictions according to the ets method is investigated again by using the Lee and Wolever measurements for the same test subject as in Figure 3.1 and Figure 3.2 [42]. The results are given in Figure 3.3. The linear trend line for the ets method (Equation (3.9)) yields an  $R^2$ -value of 0.929 for this test subject. The value is significantly higher than those calculated for the

other two methods and therefore indicates that the ets predictor is better than both CHO counting and the GI method.

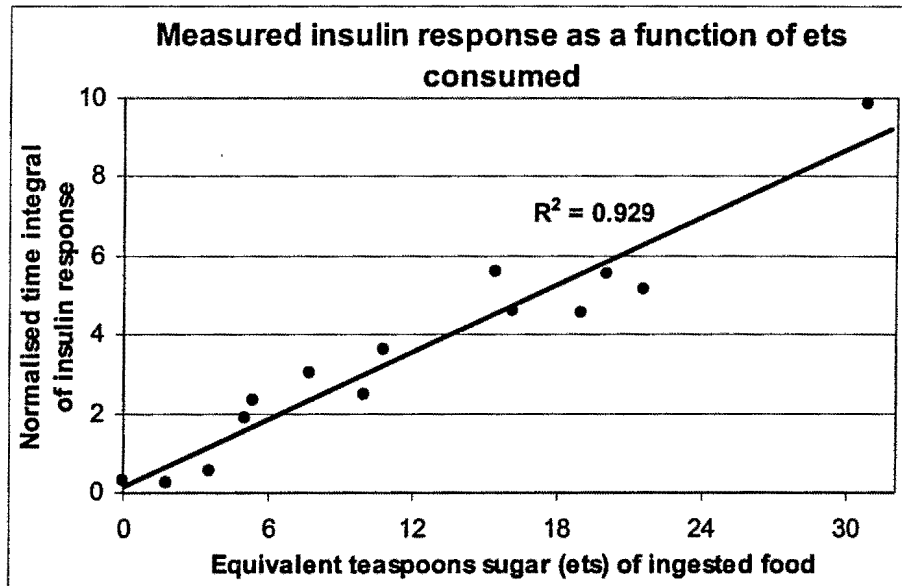


Figure 3.3 – Linear best fit trend line and corresponding  $R^2$ -value for normalised  $AUC_1$  values against ets values of ingested food (one test subject).

The next step is to proceed to investigate more test subjects using the same procedure as for the single example subject. The full dataset of Lee and Wolever as well as another dataset from Wolever and Bolognesi are used [42],[37]. Correlation coefficients for data of 15 test subjects are presented in Table 3.1. The average  $R^2$ -values for the different methods decisively show ets to be the preferred insulin predictor.

Test subject	Mass of carbohydrates (CHO)	Glycaemic index (GI)	Equivalent teaspoons sugar (ets)
1	0.345	0.451	0.734
2	0.380	0.395	0.803
3	0.408	0.506	0.805
4	0.456	0.521	0.882
5	0.430	0.398	0.710
6	0.226	0.718	0.631
7	0.628	0.237	0.745
8	0.624	0.355	0.877
9	0.792	0.378	0.874
10	0.603	0.558	0.929
11	0.718	0.377	0.915
12	0.834	0.228	0.848
13	0.745	0.186	0.736
14	0.622	0.403	0.826
15	0.614	0.226	0.784
<b>Average R<sup>2</sup></b>	<b>0.562</b>	<b>0.396</b>	<b>0.807</b>
<b>% standard deviation / average R<sup>2</sup></b>	<b>32</b>	<b>36</b>	<b>10</b>

Table 3.1 – Pearson's  $R^2$ -values for correlations between normalised insulin response integrals ( $AUC_I$ ) and CHO, GI and ets values.

It should be noted that had the equations been derived in a different fashion using the Insulin Index (II) instead of the GI of the foods, even better accuracies could have been expected. This is especially true for mixed meals containing a high percentage of protein and / or fat. GI was however used due to a larger availability of published values. By employing GI the initial usefulness of the ets concept for everyday application will be enhanced.

### 3.2.3 Discussion of the results

The exact relationship between ets and insulin is dependent on the physiological characteristics of a person ( $f_{AUCI}$  in Equation (3.9)). However, if  $AUC_I$  is converted into insulin units it is found that for many diabetics the relevant average factor is close to one. This results in an easy-to-remember one unit of short-acting insulin required for one ets ingested. Equation (3.9) therefore makes diabetic glycaemic management easier than before. Better accuracy, as previously described, as well as easier application can have an important impact on diabetics.

The importance of the sensitivity factor,  $f_{AUCI}$ , for endurance events can be illustrated by the world's most consistently fast marathoner of all times, Gert Thys. Measurements performed by Noakes can be interpreted to suggest that Thys has a very high  $f_{AUCI}$  [30]. According to Equation (3.9) this high factor results in high insulin secretion after large CHO ingestion.

It is hypothesised that this leads to a switch from blood sugar utilisation to storage with resulting hypoglycaemia. According to Noakes, Gert Thys only became very successful after he started to consume small amounts of ets throughout the race with resulting small insulin response [30]. It might be that many people today have a similar problem as Gert Thys. It is commonly found that blood sugar levels are low after a large CHO ingestion, a condition called hyperinsulinemia. The reason could also be a high  $f_{AUCI}$ . More detail on this subject will be given in Section 3.3.

Furthermore, the  $f_{AUCI}$  sensitivity is very important for weight watchers, those having CVD and certain cancers because high insulin concentrations and resulting insulin resistance are prevalent in these people [31],[32]. By accounting for  $f_{AUCI}$  (and similar factors for the protein and fat cycles) more correct diets can be designed for specific patients. It is further hypothesised that through "self preservation"  $f_{AUCI}$  will increase when a person is on a "fasting" diet. This is the body's method to ensure maximum energy storage. It can also make weight loss a little more difficult than would be expected.

It is interesting to note that  $f_{AUCI}$  could additionally help explain why people from poor developing nations are prone to Type 2 diabetes when they change over to high caloric western diets with high ets values (both high CHO and high GI). With an evolutionary high  $f_{AUCI}$  to ensure maximum storing efficiency for low ets diets their bodies "over react" to the introduction of high ets diets, resulting in hyperinsulinemia, weight gain, insulin resistance and eventually Type 2 diabetes [44].

The impact of the link between ets and insulin response on diabetics, endurance sportspeople, weight watchers and those with CVD and certain cancers or those who want to live a healthy life is therefore obvious. In general all these interest groups strive to minimise insulin response.

Ongoing and as of yet unpublished clinical trials performed for this study show that the linearity of Equation (3.9) holds true for typical portion sizes of well-balanced meals. The application of Equation (3.9) by anyone who wants to minimise insulin response is now a straightforward

calculation. The consequence of Equation (3.9) is that the food with the lowest ets value will always lead to the smallest insulin response.

### 3.3 Exercise energy expenditure

As was shown in Section 2.4 the ets concept is originally based on the amount of energy that is available from ingested carbohydrates. This logic can now be extended further in order to express energy utilisation by the human energy system in terms of ets. The resolution is that the energy expenditure a person experiences during exercise can then directly be related to the required amount of ets that has to be consumed.

As mentioned earlier, hypoglycaemia (also referred to as a “hypo”) is the result of low blood glucose concentrations [29]. Since the brain and nervous system’s only source of fuel is blood glucose it becomes disoriented when it reaches a state of hypoglycaemia [45].

This often happens to athletes during endurance events where their liver stores become depleted of blood sugar energy (or glycogen) [30]. It is believed that it can also occur when a person is under high stress situations such as during a long examination, because these events also require abnormal amounts of glucose energy. This is a persisting problem with many endurance events, even though liver depletion and resulting low blood sugar can easily be countered through carbohydrates (CHO) ingestion [46].

Hypoglycaemia is further very relevant to diabetic patients. Exercise may induce a hypo much quicker in a diabetic athlete than in a healthy athlete because glucose released from liver stores of long-suffering diabetics can be up to four times smaller than those of healthy subjects. (This is based on some preliminary unpublished measurements.) The challenge is to find out how much CHO and of what type should be ingested by a healthy and diabetic person to prevent hypoglycaemic situations due to liver depletion.

Currently, empirical suggestions for CHO ingestion are published in sports and diabetic books [30],[47]. However, these results do not account for personalised characteristics such as fitness, efficiency in absorbing CHO into the blood, the type of CHO, etc. Because people differ this often leads to incorrect CHO dosages and more harm is done than good.

In the following sections a theoretical (in contrast to an empirical) approach is used to develop an easy-to-use analytical function in which the correct links between carbohydrate type and all the

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relevant elements for a specific individual are considered. It is shown that the results obtained from the application of the function are similar to those found by current empirical methods for the “average” person. A practical way to utilise the function for a specific sportsperson or diabetic using any type of CHO is also suggested.

Section 3.3.1 discusses methods currently used by researchers while in Section 3.3.2 the new method (link with ets) is derived. (Measurement procedures for determining the respective variables are presented in Section 3.3.3.) The new method is then implemented in Section 3.3.4 and verified in Section 3.3.5.

### **3.3.1 Current methods**

This section is a short investigation into some of the most successful empirical methods currently employed. During the discussion the specific shortfalls of these methods are also mentioned.

For endurance sport (like running and cycling), Noakes and co-workers did comprehensive literature reviews and extensive research on the subject of liver store depletion [30],[48]. To prevent liver depletion and possible resulting hypoglycaemic episodes they suggested an empirical one-size-fits-all 1 g of CHO per minute for an endurance event at marathon running pace. Noakes however did not provide other suggestions for CHO dosages with events at higher or lower exertions rates.

In the previous chapter it was proposed that both the glycaemic index (GI) and the ingested CHO amount must always be taken into account when calculating energy balance since it influences the amount of blood sugar energy that is available to the athlete. If the type of ingested CHO (GI) is not specified the 1 g of CHO per minute suggested by Noakes et al may be inadequate because not all the available energy can be utilised by the body. To illustrate this point, Noakes acknowledges in his book that fructose (which has a very low GI of only 23) should not be used as a CHO for endurance events. He however does not provide a reason [30].

Furthermore, the empirical one-size-fits-all value also does not account for the athlete’s size, event fitness and CHO metabolic efficiency. In his book Noakes states the need for an individualised approach to account for such factors. In this study a new approach using any type of carbohydrate for any endurance event, including such diverse activities as climbing mountains to writing long examinations, is suggested.

For Type 1 diabetics, the correct amount (mass measured in grams) and energy conversion potential (GI, see Section 2.4.1) of a specific CHO are even more important than for healthy athletes. If diabetics ingest too much CHO their blood sugar concentrations can rise to dangerously high levels, a condition called “hyperglycaemia”. On the other hand, if they ingest too little energy through CHO, a hypo can also be the result because blood glucose release from liver stores for a diabetic person can be up to four times smaller than for a healthy person [29].

The new approach suggested here is that liver depletion should be taken out of consideration by not utilising the liver glycogen stores at all during exercise. If diabetics ingest the correct amount ( $m_{CHO}$ ) as well as the correct type ( $GI_{CHO}$ ) of CHO, two conditions will be the result. Firstly, the liver stores will not be used and secondly, there will be a negligible rise in blood sugar concentration. If these conditions hold true, the same equation used to calculate the dosage for the diabetics can be applied to healthy subjects.

Walsh et al published empirical values of preferred CHO ingestion for athletes diagnosed with Type 1 diabetes mellitus [47]. However, in their suggestions they did not account for the type (GI) of the CHO, the CHO metabolic efficiency or even the specific event fitness level of the person under investigation. According to their own acknowledgement the suggestion therefore does not satisfy every situation or every person. The need for an easy-to-use, more accurate CHO ingestion suggestion method, which also accounts for the individual physiology, is evident.

In the following section a new method is theoretically derived using the technique of solving an energy balance equation. It is imperative for the derivation that the ets principle, which not only describes the amount, but also the energy conversion potential ( $GI_{CHO}$ ) is used. For more detail refer back to Section 2.4. In most cases a theoretical approach is preferred to an empirical one since theory usually leads to better understanding of the underlying principles.

### **3.3.2 Derivation of the link between exercise and ets**

A simplified version of the human energy system is considered. In this simplified system, when exercising, the total amount of energy expended by the body ( $E_{Expended}$ ) is obtained from two sources namely from the body’s energy stores and from food ingested during the endurance event [29],[30],[46].

Furthermore, because all people are different physiologically, each person has a specific extraction factor ( $f_{Ingest}$ ) for extracting energy ( $E_{Ingested}$ ) from ingested food as well as a specific retrieval efficiency ( $f_{Store}$ ) for retrieving energy ( $E_{Stored}$ ) from stores in the body. This energy balance is shown by Equation (3.10).

$$E_{Expended} = f_{Ingest} E_{Ingested} + f_{Store} E_{Stored} \quad (3.10)$$

The aim of this derivation is to prevent low levels of blood glucose energy, because these lows can lead to hypoglycaemia. Therefore, when Equation (3.10) is examined only the energy related to blood sugar control is considered.

In the process of blood glucose control only the liver controls the raising of blood sugar levels through glycogen release [30],[49]. Studies have shown that between 15% and 25% of the energy expended during exercise events ( $E_{Expended}$ ) is replenished from the liver stores in the form of blood sugar [48],[50]. For the sake of simplifying the problem an average factor of 20% is assumed.

In order for Equation (3.10) to only describe the energy that is available in the form of blood sugar (BS) the notation  $|_{BS}$  is used. This is shown in Equation (3.11). This equation describes the portion of the exercise energy that affects blood sugar levels as well as the sources of this energy.

$$0.2E_{Expended} = f_{Ingest} E_{Ingested} |_{BS} + f_{Store} E_{Stored} |_{BS} \quad (3.11)$$

(In order to simplify the equations that follow, the notation " $|_{BS}$ " throughout the rest of this section will not be shown, although it will implicitly be implied.)

For a better understanding of Equation (3.11),  $E_{Ingested}$  first needs to be expanded. Of the food ingested during the endurance event only the carbohydrates (CHO) has a significant and immediate effect on blood sugar concentrations [39]. The CHO extraction factor,  $f_{CHO}$ , is defined to describe the athlete's ability to convert CHO into blood sugar energy. On the other hand  $f_{PROTEIN}$  and  $f_{FAT}$  are defined as similar factors for protein and fat respectively.

Conversion of ingested fat and protein into blood sugar is too slow to aid in blood sugar control during the endurance exercise [30]. These two terms are therefore negligible and can be taken out of the equation as shown in Equation (3.12). The total amount of energy available for blood glucose from the ingested food is therefore given by Equation (3.12).

$$f_{Ingest} E_{Ingested} = f_{CHO} E_{CHO} + f_{PROTEIN} E_{PROTEIN} + f_{FAT} E_{FAT} \quad (3.12)$$

The second part of Equation (3.11), namely  $E_{Stored}$ , can now also be expanded. Of the three major energy stores in the body (fat, muscles and liver), only the liver store influences blood sugar concentrations during exercise [30]. (The energy provided by the muscles and fat stores are not converted into blood glucose for the purpose of blood glucose control.) The muscle and fat stores will therefore not be considered.

The retrieval factor,  $f_{Liver}$ , describes the athlete's ability to convert stored energy in the liver into expendable exercise energy within a certain time frame. (Note that, as already mentioned, the term  $f_{Liver} E_{Liver}$  can vary by up to 400% between different Type 1 diabetics and can be a complicating factor in the final equations.)  $f_{Muscles}$  and  $f_{Fat}$  are similar retrieval factors for muscle and fat energy stores respectively. The energy flow from the energy stores to the bloodstream in the form of blood glucose (from Equation (3.11)) can now be written as shown in Equation (3.13).

$$f_{Store} E_{Stored} = f_{Liver} E_{Liver} + f_{Muscles} E_{Muscles} + f_{Fat} E_{Fat} \quad (3.13)$$

Equations (3.12) and (3.13) can now be substituted back into Equation (3.11) to arrive at Equation (3.14). This equation describes the link between expended energy and the two different energy sources for blood sugar control.

$$0.2E_{Expended} = f_{CHO} E_{CHO} + f_{Liver} E_{Liver} \quad (3.14)$$

A healthy athlete will become hypoglycaemic when the energy store in the liver is depleted [30]. One way to prevent this depletion from occurring is by preventing the out-flow of stored energy

from the liver ( $E_{Liver}$ ) completely through ingestion of just enough CHO ( $E_{CHO}$ ) [46]. If the term  $f_{CHO}E_{CHO}$  equals  $0.2E_{Expended}$ , the term  $f_{Liver}E_{Liver}$  can be taken out of Equation (3.14) because the flow of energy from the liver ( $E_{Liver}$ ) will equal zero. This also eliminates the complication for Type 1 diabetics with their large variation in liver function ( $f_{Liver}E_{Liver}$ ). If  $f_{CHO}E_{CHO}$  is correct their liver stores will not be utilised at all.

The suggested amount of energy from CHO ingestion, which will restrict  $E_{Liver}$  from the liver stores to zero, is henceforth given by Equation (3.15).

$$0.2E_{Expended} = f_{CHO}E_{CHO} \quad (3.15)$$

where  $E_{CHO}$  is the “effective” CHO energy available from pure glucose ( $GI_{CHO} = 100$ ). In Section 2.4 it was shown that ingesting other types of CHO (with a different GI than glucose) large errors in energy calculations might result. For instance, an error of more than 70% will be made if the apparent CHO energy of fructose is used without accounting for its GI of only 23. (This fact was also empirically established by Noakes [30].)

To take mixed meal and GI effects into account the “effective amount of CHO energy” ingested has to be considered. As discussed in Section 2.4, this is described by the amount of ets contained in the ingested food.

From the derivation of ets (Section 2.4.2), 1 ets contains 5 g of sugar ( $m_{CHO} = 5$  g), which has a GI (or  $GI_{CHO}$ ) of 65. Also, there are ideally 4 kCal of energy in 1 g of carbohydrate ( $k_{CHO} = 4$  kCal). Due to the fact that GI represents the conversion potential of the energy contained in the sugar the energy content available to the human energy system from 1 ets ( $E_{ets}$ ) is therefore 13 kCal. This is shown in Equation (3.16).

$$E_{ets} = GI_{CHO} \cdot m_{CHO} \cdot k_{CHO} = (65\%)(5)(4) = 13 \text{ kCal} \quad (3.16)$$

Now the equivalence between  $E_{CHO}$  and ets can be expressed in terms of available energy, measured in kCal. This is represented by Equation (3.17).

$$E_{CHO} \text{ (kCal)} = 13ets \text{ (kCal)} \quad (3.17)$$

If Equation (3.17) is substituted into Equation (3.15) the following equation is found.

$$E_{Expended} = \frac{f_{CHO} 13}{0.2} ets = 65 f_{CHO} ets \quad (3.18)$$

The “65” and “ $f_{CHO}$ ” in Equation (3.18) can then be incorporated into one conversion factor called  $f_{Expended}$  as shown by Equation (3.19).

$$f_{Expended} = 65 f_{CHO} \quad (3.19)$$

Preliminary unpublished measurements done for this study show that typical values of  $f_{CHO}$  are between 0.8 and 0.9. As a first approximation, an easy-to-use value of 55 can therefore be assumed for  $f_{Expended}$ .

If Equation (3.19) is substituted into Equation (3.18) the amount of CHO (measured in ets) that should be ingested during exercise is found. This amount of ingested CHO will restrict blood sugar energy flow from the liver to zero for a person with an energy expended factor of  $f_{Expended}$ . It is presented in Equation (3.20).

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

$E_{Expended}$  in Equation (3.20) is the total amount of energy expended during the endurance event and it is measured in kCal. It can be measured for any specific person participating in any specific event or an approximated value can be found from published exercise tables. (Importantly, these tables are developed for the “average” athlete and do not account for the event fitness level of the specific person performing the exercise.) Furthermore,  $f_{Expended}$  for the specific person can also be measured. This measurement procedure will be discussed later in this section.

### 3.3.3 Measurement of the variables

Firstly, a possible procedure to measure  $E_{Expended}$  is suggested. The method involves finding the precise amount of chemical energy released by the process of carbohydrate oxidation in the body. This procedure requires measurement of both  $VO_2$  (the amount of oxygen utilised in the body) and RQ (the respiratory quotient) of the athlete while he or she is exercising [51]. The exercise should be performed at event pace, but in a laboratory under controlled circumstances.

The values obtained from the measurements can then be substituted into Equation (3.21). This Equation was developed by Nishi in order to find  $E_{Expended}$  and expressed it in Watt [51].

$$E_{Expended} = 352(0.23RQ + 0.77)VO_2 \text{ Watt} \quad (3.21)$$

However, it was mentioned earlier that it is preferred to express  $E_{Expended}$  in total amount of kCal expended during the exercise. To convert  $E_{Expended}$  (measured in Watt) in Equation (3.21) into kCal the answer needs to be multiplied with  $0.857t_{Exercise}$  kCal/Watt, where  $t_{Exercise}$  is the duration of the exercise measured in hours.

Secondly, now that a procedure for measuring  $E_{Expended}$  is known, another procedure, to measure  $f_{Expended}$  is suggested. The following reasoning is used: In Equation (3.19) it was shown that  $f_{Expended}$  is dependant on  $f_{CHO}$  which is the body's ability to extract energy from ingested CHO. From an energy balance point of view it can be assumed that ideally the maximum amount of energy that can be extracted is 100% of the CHO energy when it is injected directly into the bloodstream. Therefore a procedure to measure the fractional value of  $f_{CHO}$  in relation to this maximum is suggested.

An important assumption is that if glucose is injected directly into the bloodstream, the resulting blood glucose response will be the maximum possible response from that amount of carbohydrate. Therefore, the first step of the suggested method involves an adequate fasting period prior to the test. (A possible suggestion is performing the test early in the morning after a nightly fast.)

The next step is to inject a known amount of glucose. For this purpose 5 ets of glucose (i.e. 16.25 g) is sufficient. The injection should be directly into the athlete's bloodstream in order to measure the athlete's maximum possible blood glucose response over time back to basal level.

The following morning, after another nightly fast, the third step of the test is performed. The athlete should then eat the same amount of pure glucose than was injected the previous day. The glucose may be diluted in water for easier consumption. Again the blood glucose response is measured.

Finally,  $f_{CHO}$  is then defined as the fractional relationship of the areas under the curves ( $AUC$ ) of the two measured glucose responses. This calculation is presented in Equation (3.22).

$$f_{CHO} = \frac{AUC_{Ingested}}{AUC_{Injected}} \quad (3.22)$$

To find  $f_{Expended}$ ,  $f_{CHO}$  can then simply be substituted back into Equation (3.19). (For clarity Equation (3.19) is repeated here.)

$$f_{Expended} = 65f_{CHO} \quad (3.19)$$

### 3.3.4 Application of the equations

Equation (3.20) provides a method of calculating how much ets to ingest during exercise to prevent hypoglycaemia due to liver energy store depletion. Logic reasoning states that if less ets is consumed than that which is suggested by Equation (3.20), the liver stores will be required to provide energy to the bloodstream and will therefore get exhausted. The question however is: why can the athlete not simply ingest more ets than the amount suggested by Equation (3.20)?

The answer is that too high blood glucose levels will induce storage mode. This condition (often referred to as "hyperinsulinemia") also has to be prevented since it too can later result in hypoglycaemia [30].

If the athlete consumes a large amount of ets instantaneously, the regulatory control system of the body will secrete large amounts of insulin in order to store the excessive amounts of glucose energy

in the body (storage mode). Because of the high insulin secretion all the blood sugar is stored, leaving little in the blood to provide energy to the brain and nervous system. This often leads to a hypoglycaemia (also known as “hitting the wall”). A good example is that of Gert Thys mentioned in Section 3.2.3. According to Noakes he is the world’s most consistently fast marathoner of all times and he often “hit the wall” [30].

Therefore, eating too much as well as eating too little ets can lead to hypoglycaemia. This is the reason why Equation (3.20) is so important for endurance athletes. They need to determine how much ets to ingest during an event and they then have to consume the total amount evenly throughout the duration of the race. By following this ets ingestion regime their liver stores will most unlikely be used for blood sugar energy and they also will not induce storage mode.

Obviously the ideal would be to continuously ingest ets, thereby more closely mimicking the energy available from the liver stores. That is however impractical, so the following regime is suggested: Since the full cycle of digestion occurs over a 30 to 40-minute period after ingestion, a probable approach would be to consume the suggested fractional amount of ets (calculated with Equation (3.20)) in equal portions on 20-minute intervals.

In the following section the validity of applying Equation (3.20) is evaluated.

### 3.3.5 Verification of the equations

The simple linear link between energy expended, measured in kCal, and ets is derived in Section 3.3.2 and is given by Equation (3.20). The individualised “energy expended” factor,  $f_{Expended}$  in Equation (3.20), can be measured and accounts for the important individual characteristics of a person.

A preferred procedure to verify Equation (3.20) would be the following: Firstly measure the glucose oxidation of fasting athletes performing endurance exercises. Bosch et al describe this measurement procedure in more detail [46]. The athletes will only have the blood sugar energy from liver stores available for blood sugar control because they are fasting. The utilisation of this energy is called endogenous oxidation.

A second test can then be performed where the same athletes continuously ingest ets during the same exercise. The optimum amount of ets to ingest should be calculated using Equation (3.20). The measurement procedure now measures the exogenous utilisation (“burning” of ingested ets).

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If the amount of exogenous (ingested) utilisation from the second test and the endogenous (liver) utilisation from the first test are equal, Equation (3.20) will indeed suggest the optimum ets consumption during the event. The reason is that the endogenous utilisation during the second test will be zero and therefore the liver stores will not be utilised at all. It is then impossible to become hypoglycaemic.

Unfortunately the means to perform the clinical trials discussed above were beyond the scope of this study. Instead the Bosch et al measurement results for 17 test subjects performing endurance cycling were used [46]. With these findings only a qualitative investigation into the accuracy of Equation (3.20) could be assessed.

During the Bosch et al trials the subjects were divided into two control groups. The one group ingested CHO and the other ingested a placebo (the “fasting” group) while cycling at approximately 70% of their  $VO_{Max}$  intensities. During the course of the exercise various measurements were taken [46]. These measurements can be used to compare their results to that of Equation (3.20).

The Bosch et al energy measurements showed an average volumetric oxygen consumption ( $VO_2$ ) of 2.58 l/min and an average respiratory quotient (RQ) of 0.892 for the athletes [46]. If these two values are used in Equation (3.21) it is found that the average amount of energy expended by these athletes during the three hours of exercise was 2273 kCal.

Unfortunately Bosch et al did not perform the measurements for  $f_{CHO}$  and therefore  $f_{Expended}$  is not known for these athletes [46]. However, preliminary unpublished measurements done on test subjects used for this study show a typical approximate value of 55 for an “average” person. This value will be assumed in the absence of more correct and detailed measurements. Substituting a value of 55 for  $f_{Expended}$  into Equation (3.20) leads to a suggested ingestion of 41 ets during the three-hour duration of the exercise.

Now the Bosch et al measurements can be investigated [46]. During the trials they provided the athletes with a mass ( $m_{CHO}$ ) of 50 g of CHO per hour. They however do not specify the type ( $GI_{CHO}$ ) of the carbohydrates that were used. It is therefore assumed to be glucose diluted in water which has a  $GI_{CHO}$  of 100. The amount of ets that represents this amount of glucose can then be calculated with the ets equation given in Section 2.4.2. Equation (2.6) is repeated here for clarity.

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

Applying Equation (2.6) to these results suggests that the athletes ingested

$$ets = \frac{GI_{CHO} \cdot m_{CHO}}{325} = \frac{(100)(50)}{325} = 15.38 \text{ ets/h} \quad (3.23)$$

This amounts to approximately 46 ets over the total three-hour duration of the exercises.

The 46 ets ingested is more than the 41 ets that would be suggested when using Equation (3.20). However, from the Bosch et al published results it can be deduced that the athletes ingested more ets than what was required to ensure that the liver stores were not used [46]. This statement can be explained with the following logic:

The experimental procedure of Bosch et al was very similar to that which was described as the ideal experiment earlier in this section [46]. However, their results showed that the exogenous oxidation (utilisation of ingested ets) was more than the endogenous oxidation (utilisation of the liver). This validates the fact that in practice the ingested 46 ets was more than the true optimum value. By estimated extrapolation it can be deduced that the suggested value of 41 ets using Equation (3.20) could be closer to the true optimum.

It is interesting to note that if 50 g/h of fructose (GI of 23) instead of glucose (GI of 100) were used, a hypoglycaemic event would have possibly resulted. Over the three hours exercise period, a 150 g of fructose would provide about 10 ets. If this total is added to the capacity of typical liver stores of approximately 30 ets, the total available energy would be 40 ets.

However, as shown, the athletes need at least 41 ets of energy to complete the exercises, which means that the liver stores would have been depleted at the end of the trials. This is the reason why Noakes, based on empirical findings, suggests not using fructose during an endurance race [30]. He does however not provide a scientific reason for the non-performance of fructose.

A further qualitative investigation into the application of Equation (3.20) leads to its relevance to Type 1 diabetics. Equation (3.20) can be compared to a method described by Walsh et al for

ingesting the optimum amount of energy through carbohydrates [47]. According to their exercise tables, the 2273 kCal expended during the exercise experiment of Bosch et al, constitute 94 g of extra, unspecified, CHO that need to be ingested per hour [46]. This amounts to 282 g of CHO in total over the three-hour duration of the experiments.

It could be assumed that the average GI of the CHO diabetic patients normally consume is close to 50. According to Equation (2.6) this results in 43 ets that should be consumed. The calculation is shown in Equation (3.24).

$$ets = \frac{GI \cdot m_{CHO}}{325} = \frac{(50)(282)}{325} = 43 \text{ ets} \quad (3.24)$$

Walsh et al therefore suggests that a Type 1 diabetic should ingest an extra 43 ets to perform the Bosch et al exercises [47], [46]. This is close to the predicted value of 41 ets found with Equation (3.20). However, if other types of CHO with higher GI values are ingested it is probable that empirical suggestions by Walsh et al will result in ets overdose and resulting high blood sugar [46].

In conclusion, Equation (3.20) provides athletes with the ability to calculate the correct amount of CHO (measured in ets) to adequately replenish liver stores while exercising at a specific energy output (measured in kCal). The equation also helps Type 1 diabetics while exercising. They should eat the calculated amount of ets from Equation (3.20) to prevent both unnecessarily high blood glucose levels as well as going into hypoglycaemia.

By consuming the optimum amount, their liver stores will never be utilised, which illuminates the uncertainty of ineffective liver action. (It has to be noted that Equation (3.20) only holds true if the diabetic patient uses the correct amount of long-acting insulin. Too little basal (long-acting) insulin will result in high blood sugar while exercising.)

### 3.4 Conclusion

In this chapter energy related links with the ets concept were investigated and quantified. The links were then used to verify the ets concept by means of comparing insulin response and exercise energy expenditure to ingested ets.

Insulin response curves proved that the ets concept is a better predictor of insulin response to ingested carbohydrates (CHO) than any one of the two methods currently used. (These are CHO counting and GI methods [34],[35].) The verification data that was used, is independent measurements performed by Lee and Wolever as well as Wolever and Bolognesi [37],[42].

Furthermore, it was shown that the ets concept could be used to predict the amount of CHO energy that should be ingested while a person is exercising. To date only empirical measurements have been used in a one-size-fit-all approach to prescribing CHO ingestion during endurance exercise. In the chapter a new method was derived, expressed in ets.

Two remarkable discoveries are that linear links could be established between ets and insulin response as well as between ets and exercise energy expenditure. The linear relationships, described by Equations (3.9) and (3.20), show that the links with the ets concept can easily be quantified with single person specific characterisation factors. These equations are repeated here.

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

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

The linear relationships make construction of a simulation model easier because individualised differences between people can now be accounted for much easier than previously assumed.

### 3.5 References

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