SIMULATION OF THE HUMAN ENERGY SYSTEM

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ABSTRACT

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Key terms: Simulation; Human energy system; CHO counting; GI; ets; Equivalent teaspoons sugar; Blood sugar response prediction; Insulin response prediction; Exercise energy requirement; Insulin requirement calculation; Stress and illness quantification; Dynamic integrated simulation; Energy pathways; Human energy system control; Blood glucose simulation

Preface

Biotechnology is generally accepted to be the next economical wave of the future. In order to attain the many benefits associated with this growing industry simulation modelling techniques have to be implemented successfully. One of the simulations that need to be performed is that of the human energy system.

Pharmaceutical companies are currently pouring vast amounts of capital into research regarding simulation of bodily processes. Their aim is to develop cures, treatments, medication, etc. for major diseases. These diseases include epidemics like diabetes, cancer, cardiovascular diseases, obesity, stress, hypertension, etc. One of the most important driving forces behind these diseases is poor blood sugar control.

The blood glucose system is one of the major subsystems of the complete human energy system. In this study a simulation model and procedure for simulating blood glucose response due to various external influences on the human body is presented.

The study is presented in two parts. The first is the development of a novel concept for quantifying glucose energy flow into, within and out of the human energy system. The new quantification unit is called ets (equivalent teaspoons sugar). The second part of the study is the implementation of the ets concept in order to develop the simulation model.

Development of the ets concept

In the first part of the study the ets concept, used for predicting glycaemic response, is developed and presented.

The two current methods for predicting glycaemic response due to ingestion of food are discussed, namely carbohydrate counting and the glycaemic index. Furthermore, it is shown that it is currently incorrectly assumed that 100% of the chemical energy contained in food is available to the human energy system after consumption. The ets concept is derived to provide a better measure of available energy from food.

In order to verify the ets concept, 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.

Lastly, two novel applications of the ets concept are considered. The first is a new method to use the ets values associated with food and energy expenditure in order to calculate both short-acting and long-acting insulin dosages for Type 1 diabetics. The second application entails a new quantification method for describing the effects of stress and illness in terms of ets.

Development of the blood glucose simulation model

The second part of the study presents a literature study regarding human physiology, the development for the blood glucose simulation model as well as a verification study of the simulation model.

Firstly, a brief overview is given for the need and motivation behind simulation is given. A discussion on the implementation of the techniques for construction of the model is also shown. The procedure for solving the model is then outlined.

During the literature study regarding human physiology two detailed schematic layouts are presented and discussed. The first layout involves the complex flow pathways of energy through the human energy system. The second layout presents a detailed discussion on the control system involved with the glucose energy pathway.

Following the literature review the model for predicting glycaemic response is proposed. The design of the component models used for the simulations of the internal processes are developed in detail as well as the control strategies implemented for the control system of the simulation model.

Lastly, the simulation model is applied for glycaemic response prediction of actual test subjects and the quality of the predictions are evaluated. The verification of the model and the procedure is performed by comparing simulated results to measured data. Two evaluations were considered, namely long-term and short-term trials. The quality of both are determined according to certain evaluation criteria and it is found that the model is more than 70% accurate for long-term simulations and more than 80% accurate for short-term simulations.

Conclusion

In conclusion, it is shown that simplified simulation of the human energy system is not only possible but also relatively accurate. However, in order to accomplish the simulations a simple quantification method is required and this is provided by the ets concept developed in the first part of this study. Some recommendations are also made for future research regarding both the ets concept and the simulation model.

Finally, as an initial endeavour the simulation model and the ets concept proposed in this study may provide the necessary edge for groundbreaking biotechnological discoveries.

SAMEVATTING

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Inleiding

Daar word algemeen aanvaar dat biotegnologie die volgende ekonomiese golf sal wees. Om al die voordele van hierdie groeiende industrie te benut sal suksesvolle implementering van simulasietegnieke nodig wees. Die simulasie van die menslike energiestelsel is een van die simulasies wat benodig word.

Farmaseutiese maatskappye is tans besig om groot bedrae geld te belê in navorsing wat die simulasie van liggaamsprosesse behels. Hulle doel is om genesing, behadeling, medikasie, ens. te vind vir belangrike siektes. Hierdie siektes sluit epidemies soos diabetes, kanker, hartsiektes, vetsug, stress, bloeddrukprobleme, ens. in. Een van die belangrikste oorsake van hierdie siektes is swak beheer van bloedsuikervlakke.

Die bloedglukosestelsel is een van die hoof substelsels van die totale menslike energiestelsel. In hierdie studie word 'n simulasiemodel en -prosedure vir die simulasie van bloedglukoserespons as gevolg van eksterne invloede op die menslike energiestelsel voorgestel.

Die studie word aangebied in twee dele. Die eerste deel behels die ontwikkeling van 'n nuwe konsep vir die kwantifisering van energie wat na binne, binnein en vanaf die menslike energiestelsel vloei. Die nuwe kwantifiseringseenheid word "ets" genoem. Die tweede deel van die studie behels die implementasie van die ets-konsep ten einde die simulasiemodel te ontwikkel.

Onwikkeling van die ets-konsep

In die eerste deel van die studie word die ets-konsep, wat gebruik word vir glukose-responsvoorspelling, ontwikkel en aangebied.

Die twee huidige metodes vir die bogenoemde voorspellings, naamlik koolhidraattelling en die glisemiese index, word bespreek. Verder word daar aangedui dat dit huidiglik verkeerdelik aanvaar word dat 100% van die chemiese energie wat in kos opgesluit is beskikbaar gestel word vir die menslike energiestelsel. Dit word gewys dat die ets-konsep 'n beter metode is om die beskikbare energy van kos te meet.

Om die ets-konsep te verifieer word twee skakels met ets bestudeer. Hierdie skakels is die met insulien-responsvoorspelling asook met voortdurige energiebenutting. Daar word aangewys dat vir beide skakels daar liniêre verwantskappe bestaan met goeie korrolasies teen empiriese data. Dit word ook aangetoon dat faktore vir persoonlike karakteriserings vir verskillinde mense slegs afhang van een meetbare veranderlike vir elke skakel.

Uiteindelik word twee nuwe toepassings van die ets-konsep ondersoek. Die eerste is 'n nuwe metode om ets-waardes vir kos en oefening te gebruik ten einde beide kort- en lang-werkende insulienbehoeftes vir Tipe 1 diabete te bepaal. Die tweede toepassing behels 'n nuwe kwantifiseringsmetode om die effek van stress en siekte in terme van ets te beskryf.

Ontwikkeling van die bloedglukose-simulasiemodel

Die tweede deel van die studie behels 'n literatuurstudie wat handel oor die menslike fisiologie, die ontwikkeling van die bloedsuiker-simulasiemodel asook 'n verifieringstudie met betrekking tot die bloesuiker-simulsiemodel.

Eerstens word 'n kort oorsig gegee ten opsigte van die motivering en die noodsaaklikheid agter die simulasies.'n Bespreking oor die implementering van die tegnieke vir die modelkonstruksie word dan aangewys waarna die prosedure vir oplossing van die model ook aangetoon word.

Gedurende die literatuurstudie wat handel oor die menslike fisiologie behels twee detail skematiese uitlegte voorgestel en bespreek. Die eerste uitleg dui die ingewikkelde energiebane van die energiestelsel aan. Die tweede uitleg bied 'n gedetaileerde bespreking oor die beheerstelsel wat met die energiebaan van glukose verband hou.

Gevolglik word die literatuurstudie van die model vir die voorspelling van glisemiese respons voorgelê. Die ontwerp van komponentmodelle, wat benodig word vir die interne prosesse, word ontwikkel asook die beheerstrategië wat op die beheerstelsel van die simulasiemodel van toepassing is.

Laastens word die simulasiemodel vir bloedglukose aangewend tot werklike toetsgevalle en die kwaliteit van die voorspellings word beoordeel. Die verifiering van die model en die simulasie-prosedure behels 'n vergelyking tussen gesimuleerde en gemete data. Twee verifieringstudies was gedoen, naamlik lang- en korttermyn toetse. Die kwaliteit van beide is bepaal deur sekere beoordelingskriteria. Daar is gevind dat die model meer as 70% akkuraat vir die langtermyn toetse is en meer as 80% akkuraat vir die korttermyn toetse is.

Gevolgtrekking

Ten einde word daar gewys dat simulasie van 'n vereenvoudigde menslike energiestelsel nie slegs moontlik is nie, maar ook relatief akkuraat is. Hierdie simulasies word moontlik gemaak deur 'n eenvoudige kwantifiseringsmetode. Die metode word voorsien deur die ets-konsep wat in die eerste deel van die studie ontwikkel is. Sekere voorstelle word ook gemaak vir toekomstige navorsing aangaande beide die ets-konsep en die simulasiemodel.

Ter afsluiting kan hierdie eerste en nuwe poging van die simulasiemodel en ets-konsep wat in hierdie studie voorgelê word ook gebruik word as 'n nodige voorsprong vir nuwe biotegnologiese ontdekkings.

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NOMENCLATURE

ABBREVIATIONS

ACSL	Advanced Continuous Systems Language
ACTH	Adrenocorticotropic Hormone
ADH	Antidiuretic Hormone
ARSC	Arctic Region Supercomputing Centre
AUC	Area Under the Curve
BMI	Body Mass Index
CHO	Carbohydrate(s)
CVD	Cardiovascular Disease
DARPA	Defence Advanced Research Projects Agency
ets	Equivalent Teaspoons Sugar
FSH	Follicle Stimulating Hormone
GI	Glycaemic Index
GIP	Glucose Dependent Insulinotropic Peptide
GL	Glycaemic Load
IBM	International Business Machines
IGF-1	Insulin-like Growth Factor-1
II	Insulin Index
ISB	Institute for Systems Biology
LH	Luteinising Hormone
MSC	Materials and Process Simulation Centre
PID	Proportional Integral Differential
RDA	Recommended Daily Allowance
RQ	Respiratory Quotient
TSH	Thyroid Stimulating Hormone

USA	United States of America
XML	Extended Mark-up Language

SYMBOLS

AUC_{BS}	Area under the curve of blood sugar response.
AUC_{Food}	Area under the curve of the food being tested.
AUC_{I}	Area under the curve of insulin response.
$AUC_{Ingested}$	Area of the blood glucose response curve of ingested glucose.
$AUC_{Injected}$	Area of the blood glucose response curve of injected glucose.
$AUC_{Reference}$	Area under the curve of the reference food in the test.
ΔBS_{Rise}	Absolute rise in blood sugar concentration due to an ingested meal.
ΔBS_{Fall}	Absolute drop in blood sugar concentration due to injected (or secreted) insulin.
$BI(t)$	Blood insulin response.
$BS(t)$	Blood sugar response.
$BS_{Blood(t)}$	Blood sugar concentration at a specific time.
$C_{Control}$	Amount of counter regulation hormone in the system.
$\dot{C}_{Control}$	Change in the amount of counter regulation hormone in the system.
$C_{Control(t)}$	Amount of counter regulation hormone in the system at a specific time step.
$C_{Control(t-1)}$	Amount of counter regulation hormone in the system at the previous time step.
$\dot{C}_{Control-Min}$	Minimum amount of counter regulation hormone that is released.
CF_{Dose}	Correction factor for the ets dose of a meal.
$CF_{Elapsed}$	Correction factor for the elapsed time from a previous meal.
$CF_{Exercise}$	Relationship between energy expended and insulin consumed for exercise.
CF_{GI}	Correction factor for the glycaemic index of a previous meal.
CF_{SM}	Second meal correction factor.
$CF_{Storage}$	Relationship between glucose change and hormones consumed during change.
$\dot{E}$	Energy flow.

E_{Absorb}	Total amount of energy absorbed into the bloodstream.
E_{CHO}	Converted carbohydrate energy potential.
E_{ets}	Total amount of blood glucose energy available from ingested ets.
$E_{Expended}$	Total amount of energy expended by the body.
$E_{Expended(RDA)}$	Total recommended amount of energy to be expended daily.
$\dot{E}_{in}$	Energy flowing into a component.
$E_{Ingested}$	Energy extracted from ingested food.
E_{Liver}	Energy extracted from the liver store.
$\dot{E}_{out}$	Energy flowing out of a component.
$\dot{E}_{released}$	Energy released by a storage component.
E_{RDA}	Total amount of daily energy required.
E_{Stored}	Energy retrieved from glucose energy stores.
$\dot{E}_{stored}$	Energy stored in a storage component.
$E_{teaspoon\ \ sugar}$	Energy available from a teaspoon of sugar.
$\dot{E}_{used}$	Energy utilised by a system component.
ets	Equivalent teaspoons sugar.
ets_{Actual}	Actual amount of ets consumed in a meal.
$ets_{Effective}$	Effective amount of ets consumed in a meal.
ets_{Max}	Maximum ets dose available from a meal.
ets_{RDA}	Recommended daily allowance of equivalent teaspoons sugar.
ets_{Stress}	Maximum amount of ets secreted due to stress or illness.
ets_{Total}	Total amount of ets for which long-acting insulin has to be injected.
f_{AUCI}	Insulin response area / ets relationship efficiency factor.
$f_{C-Control}$	Gradient of the PID counter regulation control strategy for regulation hormones.
f_{CHO}	Efficiency factor for converting ingested carbohydrates into blood sugar energy.
$f_{Expended}$	Efficiency factor for converting ingested ets into expendable blood glucose energy.

f_{FAT}	Efficiency factor for converting ingested fat into blood sugar energy.
f_{Fat}	Efficiency factor for retrieving blood glucose energy from fat stores.
f_{I}	Insulin response / ets relationship efficiency factor.
f_{IBS}	Insulin / blood sugar relationship efficiency factor.
$f_{I-Control}$	Gradient of the PID regulation control strategy for regulation hormones.
f_{Ingest}	Efficiency factor for extracting energy from ingested food.
f_{Liver}	Efficiency factor for retrieving blood glucose energy from the liver store.
$f_{Muscles}$	Efficiency factor for retrieving blood glucose energy from muscle stores.
$f_{PROTEIN}$	Efficiency factor for converting ingested protein into blood sugar energy.
f_{Store}	Efficiency factor for retrieving energy from glucose energy stores.
f_{Stress}	Ability factor to secrete ets due to stress or illness.
$\dot{G}$	Glucose energy flow.
$\dot{G}_{Basal}$	Glucose energy required for everyday living.
G_{Basal}	Amount of basal energy required.
G_{Blood}	Blood glucose concentration.
$G_{Blood(t)}$	Blood glucose concentration at a specific time step.
$G_{Blood(t-1)}$	Blood glucose concentration at the previous time step.
$G_{Blood-C-Setpoint}$	Blood glucose energy setpoint for counter regulation hormones.
$G_{Blood-I-Setpoint}$	Blood glucose energy setpoint for regulation hormones.
$\dot{G}_{Digest}$	Glucose energy flow from the digestion system to the bloodstream.
$\dot{G}_{Exercise}$	Glucose energy flow from the bloodstream to the energy expenditure.
$\dot{G}_{Exercise-Min}$	Minimum value of $\dot{G}_{Exercise}$.
G_{Liver}	Capacity of an average person's liver storage.
$\dot{G}_{Movement}$	Glucose energy required for movements.
$G_{Movement}$	Total amount of glucose energy required for movements.
$\dot{G}_{RDA(t)}$	Glucose energy required per day at a specific time step.

$\dot{G}_{Storage}$	Glucose energy flow between the primary storage and secondary storage.
$G_{Storage(t)}$	Glucose energy storage flow at a specific time step.
$G_{Storage(t-1)}$	Glucose energy storage flow at the previous time step.
$\dot{G}_{Storage-Max}$	Maximum glucose energy flow rate between storage components.
$\dot{G}_{Storage-Min}$	Minimum glucose energy flow rate between storage components.
$\dot{G}_{Store-IN}$	Glucose energy flow from the bloodstream to the primary storage.
$\dot{G}_{Store-OUT}$	Glucose energy flow from the primary storage to the bloodstream.
GI_{CHO}	Conversion potential of energy from ingested food (approximated with GI).
$GI_{previous}$	Glycaemic index of a previous meal.
GI_{sugar}	Conversion potential of energy from sugar.
I_{Basal}	Basal insulin level.
$I_{Control}$	Amount of regulation hormone in the system.
$\dot{I}_{Control}$	Change in the amount of regulation hormone in the system.
$I_{Control(t)}$	Amount of regulation hormone in the system at a specific time step.
$I_{Control(t-1)}$	Amount of regulation hormone in the system at the previous time step.
$\dot{I}_{Control-Min}$	Minimum amount of regulation hormone that is released.
$\dot{I}_{Exercise}$	Insulin consumed from the blood when exercising.
$I_{Injected}$	Short-acting insulin requirement.
$I_{Injected(Long)}$	Long-acting insulin requirement.
$I_{Secreted}$	Amount of insulin secreted.
K	Blood sugar / ets conversion factor.
k_{CHO}	Maximum amount of energy available from carbohydrates.
L	Length.
m_{CHO}	Mass of carbohydrates contained in the food.
$m_{teaspoon\ sugar}$	Mass of carbohydrates contained in a teaspoon of sugar.
Δt	Time elapsed between consumption and restoration of basal level.

t	Time.
$t_{Current}$	Current time in the simulation process.
t_{Digest}	Total digestion time of the specific meal.
$t_{Elapsed}$	Time elapsed up to current time.
t_{Event}	Duration of an exercise.
$t_{Exercise}$	Duration of the exercise.
$t_{Exhaustion}$	Duration of exercise until exhausted.
$t_{Glucose}$	Elapsed time of digestion of pure glucose.
t_{Meal}	Time of day a meal is taken.
$t_{Movement}$	Time of day an exercise is performed.
t_{Total}	Duration of the release function.
V_{Blood}	Volume of blood of a person.
VO_2	Amount of oxygen consumed by the body.
VO_{Max}	Maximum amount of oxygen the body can consume.
W	Weight.

UNITS

ets	Equivalent Teaspoons Sugar
g	Grams
h	Hours
kCal	Kilocalories
kg	Kilograms
l	Litre
m	Meters
min	Minutes
mmol	Milli-mol
unit(s)	Insulin units
W	Watt

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