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Mathematical Modeling of Behavior-Induced Body Weight Changes

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Abstract

We formulate a short-term (minutes) stochastic model of the factors affecting food intake. The model incorporates the interplay of glycemia, insulinemia and appetite to determine the size of meals and the probability of snacking. Simulations show the plausibility of the described food intake dynamics over the course of several years. Using the model, we showcase two main situations: maintenance of a constant (lean) body habit, given healthy food choices; and rapid increase in body weight if sugary snacks and drinks are preferred, even when all other model parameters are kept unchanged (appetite, meal caloric offering etc.). The model is able to link minute-by-minute behavior with long-term changes in body weight and metabolic compensation, including increasing insulin resistance and increased variability of glycemia. Model simulations support quantitalively the hypothesis of a possible mechanistic pathway from alimentary lifestyle to Impaired Fasting Glucose and Impaired Glucose Tolerance and eventually to overt Type 2 Diabetes Mellitus.

Keywords: Body weight; mathematical modeling; glycemia; insulin resistance; obesity; energy expenditure; metabolism; ordinary differential equations; food intake

1. Introduction

1.1. Overweight and obesity

It is by now well established that overweight and obesity represent a world-wide health crisis. Characterized by excess body fat, these conditions have significant medical, social, and economic consequences. Body Mass Index (BMI) is used by the World Health Organization (WHO) to classify adults as overweight (BMI exceeding 25 kg/m^2) or frankly obese (BMI exceeding 30 kg/m^2). In 2022, over 2.5 billion adults were overweight, with over 890 million falling into the obese category. Even more alarmingly, global obesity rates have nearly quadrupled since 1990.

Obesity significantly increases the risk of developing a range of serious diseases. It is a major contributor to non-communicable diseases like heart disease, stroke (Gu et al., 2019; Cheng, 2020), and diabetes, which were the leading causes of death in 2019 (Mc Namara et al., 2019).

The idea that what we eat affects Body Mass Index (BMI) seems so obvious as to need little scientific support. What is less obvious is that while well-identified eating disorders significantly impact weight, so too can cultural habits, social norms and downright food preference.

Elucidating the actual, quantitative relationship between alimentary behavior and weight increase would help understand the failure of dieting regimens and inform social awareness campaigns. In fact, a mathematical model

linking eating behavior and long-term weight changes is not yet available.

1.2. Models for body weight changes

A host of models have addressed body weight changes.

In 2002 Christiansen and Garby (2002) used the law of energy conservation, data on energy expenditure of fat and lean tissues, and data on the composition of added/removed tissue during weight change to derive a mathematical model describing the development of body weight over time, with energy intake and energy expenditure as control variables.

Chow and Hall (2008) proposed a mathematical model of macronutrient flux balances, which could capture the long-term dynamics of human weight change. They divided the dynamic behavior of body composition for a clamped diet into two classes. In the first class, body composition and mass are determined uniquely; in the second class, body composition can only exist at an infinite number of possible states. Interestingly, perturbations of dietary energy intake or energy expenditure can yield identical responses in both model classes. Existing data are not sufficient to distinguish between these two possibilities. Ogwumu et al. (2015) estimated the body weight of human beings in relation to some of their anthropometric parameters (height and waist sizes) and showed that there was no specific body weight that could be identified as a maximum or minimum.

1.3. Models for energy expenditure

Another class of models, which are relevant to the present study, concerns attempts at quantifying the energy expenditure of a given individual, in particular as it relates to changes in body weight.

Kozusko (2001) developed a setpoint mathematical model for calculating daily energy requirements incorporating the metabolic response to weight loss. The model was designed to predict energy expenditure during weight loss as a function of the setpoint fat-free mass ratio and setpoint energy expenditure, disregarding characteristics such as age, gender and heredity.

Li et al. (2020) proposed a metabolic regulation model of the body during weight loss: they used time-varying differential equations to simulate how the body regulates metabolism during weight loss from dieting, exercise, or medication, focusing on changes in three major nutrients and ketone bodies. By analyzing the model qualitatively (through the theory of time-varying differential equations) they provided sufficient conditions for safe weight loss during dieting, exercise, and drug treatment.

1.4. Models for food intake

There is a common saying, "We are what we eat". Food intake is the first step toward body weight modelling, since it plays a major role in weight management.

Extensive research exists on the mathematical modeling of digestion, absorption, and metabolism (gastric emptying being a prime example). On the contrary, the act of eating itself has received much less attention. Boston et al. (2008) modeled the eating rate during a meal as a normal distribution. They then used this model to investigate differences in eating patterns between healthy individuals and those with night eating syndrome. Cameron et al. (2009) focused on developing a system to detect meals and estimate portion sizes. This would eliminate the need for patients to input data for calculating insulin dosages. Interestingly, their model employs a Bayesian approach assuming a uniform prior probability for each meal. Chudtong and De Gaetano (2021) proposed a first complete mathematical meal model, incorporating stomach distension, glycemic variations, ghrelin dynamics, cultural habits and influences on the initiation and continuation of meals, reflecting a combination of hedonic and appetite components. Such a detailed model could be used as entry point in full-scale simulations of food absorption and metabolism, both in health and disease.

1.5. Models for glucose-induced satiety

Feeding behavior is clearly linked to glucose concentration in blood. Hyperglycemia (high blood-glucose concentration) from eating high-sugar diets is effective in reducing food intake, even if it is not clear how much of this effect is mediated by the inhibition of ghrelin production due to rising glycemia (Vartiainen, 2009). There is evidence linking the satiety induced by hyperglycemia with its effect in increasing insulin serum concentrations: rising insulinemia in fact inhibits dopamine signaling and interrupts feeding (Palmiter, 2007; Figlewicz et al., 2003, 1994). For the present work we may take glycemia as a single representative signal determining appetite. The ingestion of carbohydrates,in terms of their glucose equivalent (McMillin, 1990), and the absorption of glucose into the circulation should thus be considered as determinants of (the decrease of) appetite through the increase in glycemia they produce.

1.6. Models for glycemic control

Since a key determinant of feeding behavior is glycemia, it is useful to study glucose homeostasis. Many mathematical models have been developed in this area, considering different aspects of this complicated physiological control mechanism.

Close control of glycemia is important for preventing morbidity and mortality (Russell et al., 2014). Dated short-term glucose-insulin models, even if they have been proven to exhibit implausible qualitative properties (De Gaetano and Arino, 2000) are still used in the medical community, together with extensions including gastrointestinal absorption (Dalla Man et al., 2007).

1.7. Aim of the present work

It can be appreciated that, to the best of our knowledge of the existing literature, no model has yet been proposed to link body weight dynamics with alimentary choices determining food intake. The aim of the present work is therefore to develop a first such model and show how this model is consistent with the clinical, empirical observation that mere choice of food types, *ceteris paribus*, may determine substantial changes in body weight over the span of few years.

2. Materials and methods

2.1. The mathematical model

In the following the most relevant model variables are presented and discussed in turn.

λ_{CG} **Probability rate of assuming a snack given the current glycemia (/min)**

λ_{CG} indicates the probability rate or propensity of assuming a food snack, given the current glycemic level. It is assumed to follow a decaying sigmoid attaining a maximum at zero glycemia and falling off to zero with increasing glycemias:

$$\lambda_{CG}(G) = 1 - \frac{G^{\gamma_{CG}}}{G_{C50}^{\gamma_{CG}} + G^{\gamma_{CG}}} \tag{1}$$

P_{CG} **Probability of assuming a snack during the next time interval (#)**

P_C indicates the actual probability of assuming a food snack over the next discretization time interval, and depends both on the above-defined propensity and on the length of the interval:

$$P_C(G, \Delta t) = 1 - e^{-\lambda_{CG}(G)\Delta t} \tag{2}$$

S **Stomach food content (kcal)**

S is the energy in *kcal* obtained from food in stomach, or the stomach food content expressed in *kcal*:

$$\begin{aligned} \frac{dS}{dt} = & -k_{OS}\,S(t) \\ & + A(t)\sum_{D=1}^{N_D}\sum_{m=1}^{3} M_{m,D}\,\delta(t - t_{m,D}) \\ & + A(t)(C^{min} + U(C^{max} - C^{min}))\chi_G, \\ & S(0) = S_0 \end{aligned} \tag{3}$$

where

$m \in \{1, 2, 3\}$ indicates the standard meal (1 breakfast, 2 lunch, 3 dinner),

$D \in \{1, \ldots, N_D\}$ indicates the day

$M_{m,D} = M_m^{min} + U(M_m^{max} - M_m^{min}), U \sim \mathcal{U}[0, 1]$, indicates the random size of the meal, uniformly distributed between limits pertaining to the corresponding standard meal,

C^{min} and C^{max} are the standard minimum and maximum snack sizes, $U \sim \mathcal{U}[0, 1]$, so that $(C^{min} + U(C^{max} - C^{min}))$ is a uniformly distributed random snack size between C^{min} and C^{max} *kcal*,

$$\chi_G = \begin{cases} 1 & \text{if } U < P_C(G(t), \Delta t) \\ 0 & \text{otherwise} \end{cases}, \text{ with } U \sim \mathcal{U}[0, 1],$$

indicates the actual consumption of a snack at time t depending on its probability as a function of glycemia and of the time discretization interval.

Within the framework of a relatively complex representation of the factors influencing food intake, the submodel concerned with gastrointestinal absorption of nutrients has been kept relatively simple.

Z **Relative insulin sensitivity (#)**

$Z(W)$ is the level of insulin sensitivity, relative to baseline value, as determined by the current body weight. It is in fact assumed (as clinically observed) that increased body weight is associated with progressively more severe degrees of insulin resistance:

$$Z(W) = 1 - \frac{W^{\gamma_{GIW}}}{W_{GI50}^{\gamma_{GIW}} + W^{\gamma_{GIW}}} \tag{4}$$

G **Glycemia (mM)**

G is the current glycemia:

$$\frac{dG}{dt} = -Zk_{OGI}IG + k_G + \frac{\rho_{GS}}{V_G}k_{OS}S\,, \quad G(t_0) = G_0 \tag{5}$$

where ρ_{GS} is the conversion factor between absorbed glucose-equivalent food *kcal* and *mmol* of glucose absorbed into the bloodstream.

I **Insulin plasma concentration (pM)**

I is the current insulinemia. Insulin secretion by the pancreas is here assumed to depend on glycemia nonlinearly (higher glycemic peaks determining proportionally greater insulin secretion):

$$\frac{dI}{dt} = -k_{OI}I + k_{IG}G^2\,, \quad I(t_0) = I_0 \tag{6}$$

W Body weight (kg)

W is the current body weight. Its variation is determined by the balance between (a fraction of) what is absorbed from the stomach and current energy expenditure (converted from kcal/day to kcal/min):

$$\frac{dW}{dt} = \rho_{WS}\left(k_{OS}S - \frac{Y}{1440}\right), \quad W(t_0) = W_0 \tag{7}$$

Y Energy expenditure (kcal/day)

$Y(W)$ is the daily energy expenditure, as determined by the current body weight. It is in fact assumed that an increase in body weight determines, by itself, an increase in daily energy expenditure (related to the heavier mass to move, to possibly increased metabolism etc.):

$$Y(W) = Y^{max}\frac{W^{\gamma_{YW}}}{W_{Y50}^{\gamma_{YW}} + W^{\gamma_{YW}}}$$

A Appetite (#)

A is the appetite level, which, for the purpose of the present model, is assumed to depend on glycemia:

$$A(G) = A^{max}e^{-\lambda_{AG}G} \tag{8}$$

A schematic diagram of the relationships among the state variables is shown in Figure 1.

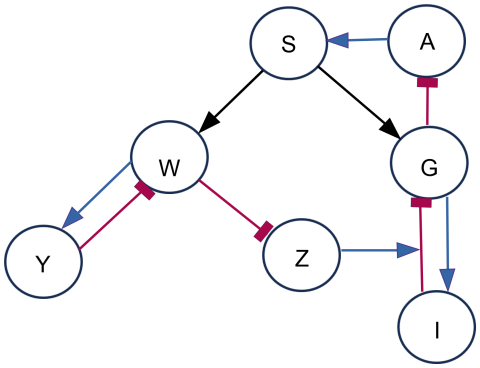

Figure 1. Block diagram of the WeightGain model. Labeled circles correspond to the state variables as defined in the text. Black arrows represent transfer of substance. Blue arrows represent stimulation or excitation, while red (block) arrows represent inhibion or repression.

3. Results

In the following the model has been used to investigate quantitatively the effect of merely changing food preferences on the long term development of obesity.

3.1. Scenario 1

The baseline scenario portrays an individual of 70*kg* weight, with a normal baseline appetite, following a normal (healthy) diet, defined as a diet consisting of such varied and fiber-rich foods as to determine a stomach emptying half-life of 60 minutes. All other parameters of the simulation have been calibrated so as to reflect common medical consensus and to determine a stable weight over the course of four years. In this simulation, offered meal sizes and meal times are uniformly, randomly distributed within usual limits (say between 6 AM and 9 AM for an offered breakfast containing between 450 and 650 *kcal*), and snacking is not assumed to happen between 2 AM and 1 hour after breakfast.

Figure 2 shows the time course of stomach contents, glycemia, appetite and daily total food intake over the course of four years of simulation. Notably, glycemia peaks (post-prandially) at around 12 mM, total daily food intake averages around 2600 *kcal*, of which around 400 derive from snacking.

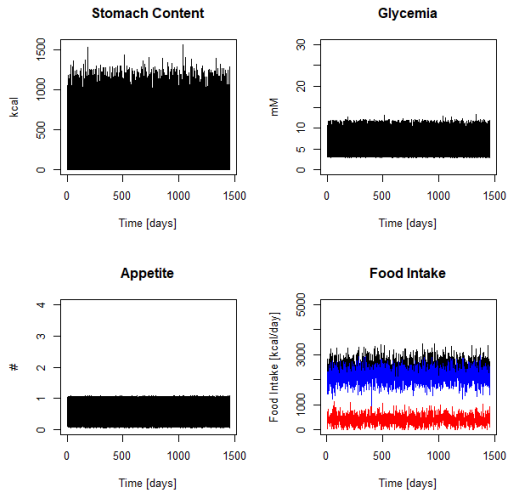

Figure 2. Maintenance of normal body weight: stomach contents (top left), glycemia (top right), appetite (bottom left) and daily food intake (bottom right: daily kcal from snacking in red, from regular meals in blue and total in black).

Figure 3 shows the time course of body weight, daily energy expenditure, fasting glycemia and relative insulin sensitivity, none of which change appreciably over four years. In particular, weight is maintained around 70*kg* throughout, and fasting glycemia (the average glycemia

in the early hours of the morning, before breakfast) is stable at values around 3.7*mM* (66*mg*/*dl*).

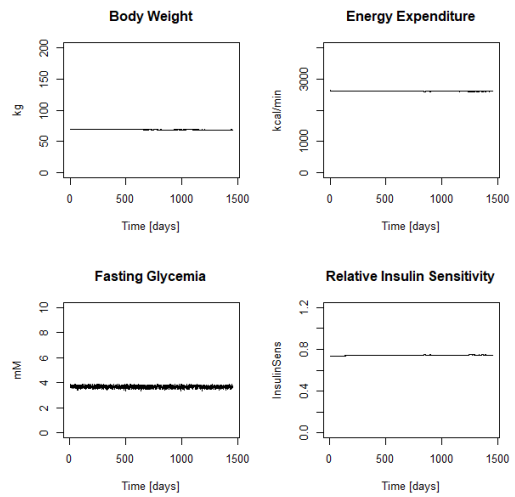

Figure 3. Maintenance of normal body weight: body weight (top left), daily energy expenditure (top right), fasting glycemia (bottom left) and relative insulin sensitivity (bottom right).

Figure 4 shows the time course of stomach content, glycemia, insulinemia and appetite over the course of four days: in this stable situation, at normal body weight, glycemic excursions, the corresponding insulinemic peaks and appetite oscillations are limited.

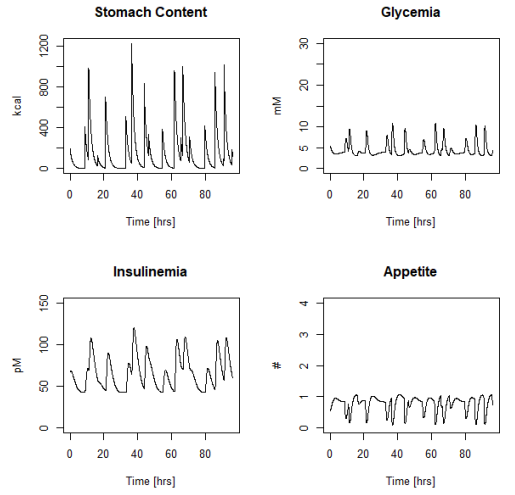

Figure 4. Maintenance of normal body weight: stomach content (top left), glycemia (top right), insulinemia (bottom left) and appetite levels (bottom right) over the course of four days.

3.2. Scenario 2

The second scenario refers to a subject starting out exactly as before, at 70*kg* body weight, with all of the same parameter values as in Scenario 1, except that the food preference is shifted towards foods richer in carbohydrates, in particular richer in sugars (e.g. from soft drinks, desserts and sugary snacks) and poorer in fibers, fats and protein, so that the stomach-emptying half-life is reduced from 60 to 20 minutes. Notice that the offered caloric content of meals and snacks is exactly the same as before (but if eating with increased appetite the subject will partake of a larger fraction of the offered meal, possibly greater than 1). In other words, nothing changes except digestion half-life.

Figure 5 shows once again the time course of stomach contents, glycemia, appetite and daily total food intake over the course of four years. Notice that stomach content peaks are only marginally larger than before. Conversely, glycemia peaks reach the 20*mM* mark, a substantial increase with respect to Scenario 1, due to the more rapid availability of ingested sugars in the circulation. Appetite peaks are increased, due to the fact that rebound hypoglycemias occur after the rapid elimination of peaking glucose loads (with persistent insulin concentrations). This is reflected in the much greater contribution of snacking to the total daily food intake: initially approximately 1700*kcal*/*day* out of a total of 3700*kcal*/*day*, eventually (at the end of the four years) 1000*kcal*/*day* out of a total of 2900*kcal*/*day*.

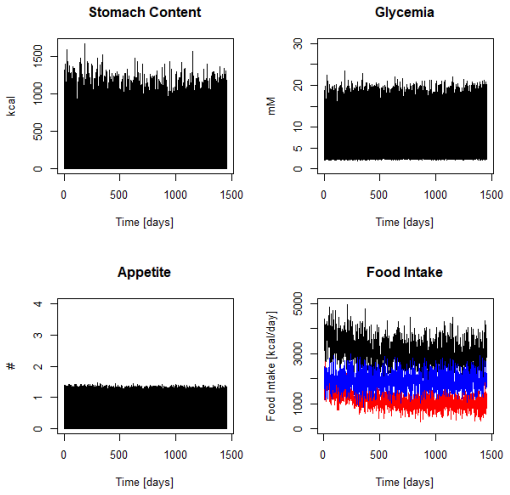

Figure 5. Consequences unhealthy diet choices: stomach contents (top left), glycemia (top right), appetite (bottom left) and daily food intake (bottom right: daily kcal from snacking in red, from regular meals in blue and total in black).

Figure 6 shows the time course of body weight, daily energy expenditure, fasting glycemia and relative insulin sensitivity. Weight increases from 70 to about 90*kg*, but it

should be noted that the greater proportion of this increase occurs within a couple of years, weight then stabilizing around its higher level. This is due to both an increase (and eventual stabilization) of energy expenditure as well as to a decrease of insulin sensitivity, leading to higher glycemias and thus to a decreased average appetite. Notice however that glycemias are more variable: not only post-prandial glycemic peaks are higher (Figure 5 top right panel), but fasting glycemias range from $3mM$ to $4.2mM$. In other words in this situation the subject is potentially exposed to both hyper- and hypo-glycemias. While quantitatively the clinical situation depicted in this scenario does not yet reach the severity of overt diabetes, the configuration of the abnormalities is very clear and coincides with the progressive development of Type 2 Diabetes Mellitus.

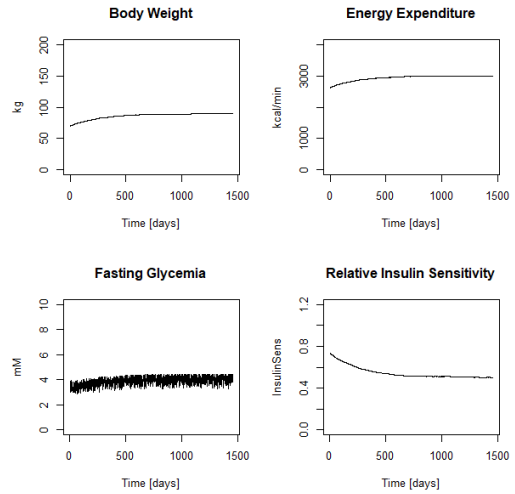

Figure 6. Consequences unhealthy diet choices: body weight (top left), daily energy expenditure (top right), fasting glycemia (bottom left) and relative insulin sensitivity (bottom right).

Figure 7 shows the time course of stomach content, glycemia, insulinemia and appetite over the course of four days at the stable regimen attained after four years of unhealthy eating habits: glycemic excursions are larger due to the increased proportion of (simple) carbohydrates in the diet, leading to higher insulinemic peaks, hence to rebound hypo-glycemias and more sustained appetite overall, with the consequence of more frequent, larger snacks and increased calorie intake.

4. Discussion

While it is common knowledge that overeating causes obesity, the causes of overeating itself are less well understood. One aspect that is examined in the present work relates to how dietary choices influence the development of obesity. The main effect which emerges from the numerical implementation of the current model confirms

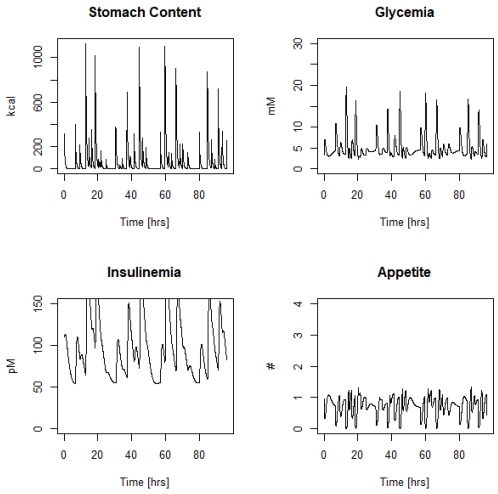

Figure 7. Consequences unhealthy diet choices: stomach content (top left), glycemia (top right), insulinemia (bottom left) and appetite levels (bottom right) over the course of four days.

the everyday observation that refined carbohydrates cause rapid spikes in glycemia, followed by rebound hypoglycemia ("crashes"), causing in turn craving for more (sugary) food thus repeating the cycle, eventually determining substantial increases in calorie intake.

There are as yet no models, to the best of our knowledge, that link minute-by-minute metabolism and food intake mechanisms with their long-term consequences: this work presents a first attempt to build such a model. It should be remarked that the significance of the conclusions that can be drawn from simulating this model goes beyond establishing quantitatively that a preference for sugary foods determines a very substantial weight increase over the span of a few years. We can in fact observe how the representation of the interplay of insulin, glucose and appetite in this situation gives rise to the hallmarks of prediabetes: variable glycemias with the possibility of dangerous hypo-glycemic episodes, spiking post-prandial hyperglycemias (Impaired Glucose Tolerance, IGT), increased fasting glycemias (Impaired Fasting Glucose, IFG), development of insulin resistance.
As such, the present model represents a first step towards the quantitative understanding of the development of Type 2 Diabetes Mellitus on the basis of unhealthy lifestyles, clearly more dangerous when accompanied by genetic predisposition.

5. Conclusions

It is clearly not necessary to use mathematical modeling to support the concept that overeating causes obesity. However, mathematical modeling can offer useful quantitative insights as to how and why this happens.

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