J. Math. Biol. (2007) 54:27–43
DOI 10.1007/s00285-006-0037-7

Mathematical Biology

Dynamics of starvation in humans

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Received: 29 August 2005 / Revised: 9 March 2006 /
Published online: 8 September 2006

Abstract A differential equation model describing the dynamics of stored energy in the form of fat mass, lean body mass and ketone body mass during prolonged starvation is developed. The parameters of the model are estimated using available data for 7 days into starvation. A simulation of energy stores for a normal individual with body mass index between 19 and 24 and an obese individual with body mass index over 30 are calculated. The length of time the obese subject can survive during prolonged starvation is estimated using the model.

Keywords Differential equations · Starvation · Ketone bodies · Energy balance · Mathematical model

Mathematics Subject Classification (2000) 92C30 · 92C40

1 Introduction

In developed industrialized nations, food resources have become readily available and starvation is rare. The recent abundant food supply has been a principal cause of the overweight and obesity problems, with two-thirds of all Americans

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estimated as overweight [32]. As a response to this growing crisis, much of the current nutrition research focuses on obesity issues (see for example Ref. [10]). The considerable attention given to health problems due to being overweight has led to fat reserves being viewed as an undesirable product of eating. However, storage of fat was an evolutionary response to the inconsistent availability of food throughout most of human history [16]. As a result our bodies have a very adept and fascinating survival response to prolonged starvation.

Due to stricter governmental regulations on experiments involving human subjects, most direct controlled starvation investigations took place prior to the 1960s [1,2,14]. Because experimentation on humans is not a safe and viable option, a mathematical model that simulates the dynamics of starvation would be beneficial to understand how the body metabolizes energy in the absence of food. Many parts of the world are still exposed to starvation due to wars and famines and such a model would give insight to resulting health problems. In addition, a model can provide delicate information such as the length of time an individual can survive during prolonged fasting.

Based on the energy balance equation derived from the first law of thermodynamics, it is our goal to carefully model how stored energy in the body is transferred and expended during prolonged starvation. This paper develops a system of differential equations that describes the interactions of the three energy sources during starvation: stored fat mass, lean body mass and ketone body mass. The next section will explain the concept of an energy balance along with a description of the body's energy expenditures. This foundation is then used to determine a model of long-term starvation in Sect. 3. Section 4 provides a theoretical analysis of the model. In Sect. 5, we use data from [8,12,26] to determine the parameters in the model for the cases of a normal average human with body mass index between 19 and 24 and an obese individual with body mass over 30. The model is simulated to predict how long an individual could survive under prolonged starvation. Finally, we summarize the results and provide suggestions for future work.

2 Energy requirements during prolonged starvation

Measurements of energy used by the human body are typically reported in kilocalories (kcal) [7]. A *calorie* is defined to be the amount of energy required to raise the temperature of 1 g of water from 14.5 to 15.5°C at 1 atm of pressure [18]. The amount of energy in a gram of food is determined using a *bomb calorimeter* (for specifics see [18]). Bomb calorimeters determine the total energy in a given quantity of food by measuring the heat released upon oxidization (heat of combustion). Not all of this energy is available for use by the body. For example, the body cannot oxidize the nitrogen component of protein and as a result almost 19% of the total energy in protein is excreted through urine [18]. Energy obtained from food that can be digested and absorbed by the body is referred to as *net energy* or *available energy*. The energy values that appear on food labels consist of the net energy content of the food in kilocalories

per gram. We caution that although food energy is measured in kilocalories, nutrition information on food packaging refers to 1 kcal as 1 Calorie (using a capital C).

The amount of energy expended by the body can be estimated by measuring the dissipation of heat from the body using an *isothermal calorimeter* [7]. The rate of energy expenditure is more commonly measured by the rate of oxygen consumption. The process of measuring the body's loss of heat is called *direct calorimetry*.

The next section applies these measurements to the first law of thermodynamics to develop an energy balance equation during prolonged starvation.

3 The energy balance equation

The energy balance principle discussed in physiology and nutrition literature is based on the application of the *first law of thermodynamics* to an open system [4]. The human body is considered an open system because energy is continually lost and intermittently added to the system by input of mass flow in the form of food. In general, the first law of thermodynamics applied to an open system is

$$\frac{\mathrm{d}E_{\mathrm{sys}}}{\mathrm{d}t} = \frac{\mathrm{d}Q}{\mathrm{d}t} - \frac{\mathrm{d}W_{\mathrm{o}}}{\mathrm{d}t} + E_{\mathrm{in}} - E_{\mathrm{out}},$$

where $(\mathrm{d}E_{\mathrm{sys}}/\mathrm{d}t)$ is the rate of accumulated energy within the system, $\mathrm{d}Q/\mathrm{d}t$ is the rate at which heat flows into the system, $\mathrm{d}W_{\mathrm{o}}/\mathrm{d}t$ is the rate of work done by the system on its surroundings, E_{in} is the rate of energy added to the system by mass flow into the system, and E_{out} is the rate of energy leaving the system through outward mass flow.

In the case of the human body, the energy accumulations are in the form of caloric values of grams of lipids (fats), proteins and glucose. During long-term exercise or starvation, glycogen stores are depleted. The body begins to transform stored fatty acids into molecules called *ketone bodies* which are then used as an alternative to glucose as an energy source for the brain [11]. Ketone bodies consist of the molecules β-hydroxybutyric acid (BHB), acetoacetic acid (AcAc) and acetone and are produced from fatty acids in the liver through a process called *ketogenesis* [11].

Most proteins that are used for energy can be found in the muscle. Although muscle is largely composed of protein, it also contains glucose and fat in obese individuals. Proteins can also be broken down and transformed to glucose to be used for energy and in the case of short-term starvation (less than 1 week) the body begins to metabolize proteins from muscle mass [6]. However, producing the glucose required by the brain alone would result in the metabolization of 172–259 g/day of protein [26]. At this rate, death would occur in approximately 2 weeks. In order to prolong life, ketones become the brain's energy

source in the absence of glucose, which was a landmark result discovered by Cahill [2].

Ketone bodies (an aggregate of BHB, AcAc and acetone) are found in low concentrations during normal non-fasting states (0.03–0.7 mmol/l [12]). After a week or more of fasting, higher concentrations of ketones are found in non-obese individuals (4.4–5.5 mmol/l [12]). On 1-week fasting, ketone body concentrations were seen to increase up to 20 times higher than the normal individuals in untreated Type 1 diabetic patients [28]. Obese individuals were observed to have 60 times higher concentrations of ketone bodies compared to normal individuals after 1 week of fasting [8].

If R is the rate of energy accumulation/loss obtained from lipids (stored fat) and proteins then

$$R = \frac{\mathrm{d}E_{\mathrm{sys}}}{\mathrm{d}t}.$$

Because glucose/glycogen stores are depleted during starvation, R consists of two terms: the rate of energy obtained from stored fat and the rate of energy obtained from stored protein. If we let $F(t)$ be the kilogram of stored fat (adipose tissue) and $M(t)$ be the kilogram of muscle mass (protein) where t is measured in days, then

$$R = \lambda_{\mathrm{F}} \frac{\mathrm{d}F}{\mathrm{d}t} + \lambda_{\mathrm{M}} \frac{\mathrm{d}M}{\mathrm{d}t},$$

where λ_{F} and λ_{M} are the caloric values of 1 kg of stored fat and stored protein, respectively. Estimates for λ_{F} and λ_{M} appear in [18] as 7,777.78 and 1,400 kcal/kg, respectively. Heat flow does not enter the body from surroundings. In fact, the body maintains constant temperature and expends energy to cool itself when the surrounding environment is too warm (sweating) and heat itself when the surrounding area is too cold (heat can be generated by shivering or enhanced oxidation of carbohydrates and brown fat). Because heat flows out of the system, $\mathrm{d}Q/\mathrm{d}t$ is negative. Therefore, the body needs to expend energy to maintain body temperature. The work done by the body is in the form of energy expenditures which will be dissected in detail during specific model formulation. At this time, we represent the rate of body energy expenditures as E and therefore $E = \mathrm{d}W_{\mathrm{o}}/\mathrm{d}t - \mathrm{d}Q/\mathrm{d}t$.

As described earlier, energy measurements of food are labeled in terms of net energy. Therefore, $E_{\mathrm{in}} - E_{\mathrm{out}}$ is equal to I where I is the rate of usable food energy intake by the human body. Combining all terms in the energy balance equation, we arrive at

$$R = I - E, \tag{1}$$

which appears as the standard human energy balance equation [18]. Because starvation is the condition of the body in the absence of energy intake, $I = 0$.

Energy expenditure in the body consists of four different quantities: dietary induced thermogenesis (DIT), physical activity (PA), adaptive thermogenesis (AT) and basal metabolic rate (BMR) [7]:

$$E = \mathrm{DIT} + \mathrm{PA} + \mathrm{AT} + \mathrm{BMR}. \tag{2}$$

DIT is the work involved in processing food. This consists of digestion, absorption, metabolization, storage and transport of ingested food and is estimated to account for 5–15% of total energy expenditures [7]. Because there is no digestion during starvation, DIT = 0. With the exception of eating disorders, most cases of starvation involve little or no physical activity. Therefore, we assume that PA = 0. AT is the change in metabolism due to environmental, psychological or other influences and is often referred to as the shiver factor [7]. We assume the environmental and psychological factors remain constant and as a result AT = 0.

An individual's BMR is the rate of energy required to sustain life. BMR is measured in a very controlled manner. The subject must be in a relaxed (preferably just having awakened), postabsorptive state (12 h or more of fasting) [7]. Thus, the direct determination of BMR is not simple. There exist several simple estimates of BMR depending on sex, total body mass, height and age. These correlations are based on extensive experimental data.

The most commonly used of these formulas is the Harris–Benedict equation [9]. The form of the Harris–Benedict equation for both men and women is

$$\mathrm{BMR} = b_i + p_i W + c_i H_i - \delta_i A_g \tag{3}$$

where the index i equals 1 and 2 representing male and female, respectively, H_i represents the height (in cm), A_g the age of the individual (in years) and W total body mass (in kg). The parameters to obtain BMR (in kcal/day) are estimated as $b_1 = 66$, $b_2 = 655$, $p_1 = 13.7$, $p_2 = 9.6$, $c_1 = 5$, $c_2 = 1.7$, $\delta_1 = 6.8$ and $\delta_2 = 4.7$.

Total mass, often referred as weight, W, is the sum of two components: lean body mass and stored fat mass. The lean body mass, $L(t)$, is the sum of two terms: total muscle mass from which stored protein is derived, $M(t)$, and the remaining essential fats, organs and skeletal mass, L_0. If we assign the function $F(t)$ to be the kilogram of fat mass on day t, we have weight or total body mass as $W = M(t) + L_0 + F(t)$. Although age and height appear in Eq. (3), since we are interested on the impacts of energy storage over a period of about a year, age and height remain relatively constant. Thus, similar to the concept of the Harris–Benedict formula we model BMR as the sum of a constant, C, and a direct proportion of W,

$$\mathrm{BMR} = C + \kappa(L(t) + F(t)).$$

Combining each term in (2) yields

$$E = C + \kappa(L(t) + F(t)), \tag{4}$$

which leads to the energy balance equation during starvation

$$\lambda_F \frac{\mathrm{d}F}{\mathrm{d}t} + \lambda_M \frac{\mathrm{d}M}{\mathrm{d}t} = -[C + \kappa(L + F)]. \tag{5}$$

At this time, we apply the energy balance equation to derive a mass balance system to describe the loss of stored fat and protein during prolonged starvation.

4 The model

Starvation is formally defined as the condition of the human body in the absence of energy intake [2]. In this paper we assume that starvation does not include water deprivation.

During short-term starvation (3–4 days), glycogen stores are depleted and the brain obtains glucose which is synthesized from protein in the muscle mass [29]. This fact is determined through an observed decrease in insulin production (a hormone that stimulates the storage of blood glucose to glycogen) and an increase in the release of amino acids from muscle tissue [2,5,21]. Due to the increased metabolism of proteins, BMR was found to increase during short-term starvation [15,22,27,30]. After the initial starvation period of 3–4 days, BMR begins to decrease. In fact, after 1 month of total starvation, BMR can decrease up to 30% due to a slow down of cellular metabolism and a reduction in the amount of metabolically active cells [1]. Because we are interested in modelling the effects of long-term starvation we will assume that initial time ($t = 0$) represents the energy levels and metabolic state of the body after short-term starvation (approximately 1 week). The model is developed using a mass balance equation. Energy utilized during starvation is obtained from two sources: stored fat mass and muscle mass. Recall that although muscle mass is mostly composed of protein, it does contain glucose and fat in obese individuals. We are assuming that the supply of glucose is exhausted during short-term starvation and that the amount of fat in the muscle is negligible. Therefore, energy from protein is obtained from the muscle. The brain exclusively uses ketone bodies derived from fat mass. We assume here that the three types of ketone bodies are combined in total.

To organize our discussion, we compile a complete list of assumptions at this point.

1. The body's supply of protein is contained exclusively in the muscle mass. Although muscle contains some glucose and fat, the amount is small and we ignore it as a significant energy source during starvation.

2. The start of evolution of the model occurs after glucose reserves are depleted (3–4 days of fasting). The remaining energy sources available are fat and protein.
3. The individual undergoing starvation is not deprived of water or vitamins. As a result, blood volume remains constant and stresses on the body occur exclusively from energy deprivation.
4. All energy to sustain life during starvation with the exception of the brain function comes from a proportion of fat and protein. During starvation, the brain obtains its energy exclusively from ketone bodies. The three different ketone bodies are aggregated as one for the purposes of this model.
5. The brain requires a constant rate of energy until death occurs.
6. Death due to starvation can occur in two different manners. Either the supply of ketone bodies are depleted or lean body mass reaches a critical value. This critical value is estimated to be half of the original lean body mass [1,18]. When death occurs, the model ceases to have meaning.

Based on our assumptions, our state variables are

$$\begin{aligned} F(t) &= \text{total kg of stored fat mass on day } t \\ M(t) &= \text{total kg of muscle mass on day } t \\ K(t) &= \text{total kg of ketone bodies on day } t \end{aligned}$$

Ketone bodies are conventionally measured in concentrations of millimole per litre of blood, however, we may convert this unit to kilogram. Because there is no energy intake during starvation, all terms in the rate equation appear as losses except for the conversion of fat to ketone bodies. Specifically,

$$\begin{aligned} \frac{\mathrm{d}F}{\mathrm{d}t} &= -F_{\mathrm{K}} - F_{\mathrm{B}} \\ \frac{\mathrm{d}M}{\mathrm{d}t} &= -M_{\mathrm{B}} \\ \frac{\mathrm{d}K}{\mathrm{d}t} &= VF_{\mathrm{K}} - K_{\mathrm{B}} \end{aligned}$$

where F_{K} is the rate of conversion from fat mass to ketone bodies, F_{B} and M_{B} are the rate of fat mass and muscle mass used to support all organs excluding the brain, respectively, and K_{B} is the rate of ketone requirements by the brain. The constant, V, represents the conversion of 1 kg of fat mass to 1 kg of ketone body mass.

We begin by developing the formulation of F_{B}. Both F_{B} and M_{B} must satisfy the energy balance equation (5) developed in the previous section. Thus, we know that F_{B} must be some fraction of

$$\frac{1}{\lambda_{\mathrm{F}}}(C + \kappa(L(t) + F(t)).$$

After short-term starvation, the body attempts to draw more energy from fat stores. Fat is directly used to support the energy needs of the body. Although muscle is degraded, the body minimizes the breakdown of muscle protein because most protein in the body performs other operational functions. For example, proteins are used as enzymes. Thus, BMR should obtain more of its energy from fat reserves when stored fat is abundant. Applying this concept, a simple fraction that can be used is $F(t)/(F(t) + M(t))$ and so we formulate F_{B} as,

$$F_{\mathrm{B}} = \frac{1}{\lambda_{\mathrm{F}}} \frac{F}{(F+M)} (C + \kappa(L+F)).$$

The energy balance equation forces M_{B} to be

$$M_{\mathrm{B}} = \frac{1}{\lambda_{M}} \frac{M}{(F+M)} (C + \kappa(L+F)).$$

Notice that as fat reserves decrease, more energy is obtained from muscle mass.

As depicted in Fig. 1, fat mass is turned over to produce ketone bodies. This rate of loss, F_{K} is modelled by $r(K)F$, where $r(K)$ is decreasing as a function of K and the limit of $r(K)$ as K goes to infinity is constant (saturation).

Finally, K_{B} is the rate of loss of ketone body mass required for the brain. Regardless of the amount of ketone bodies available, the rate of energy needs

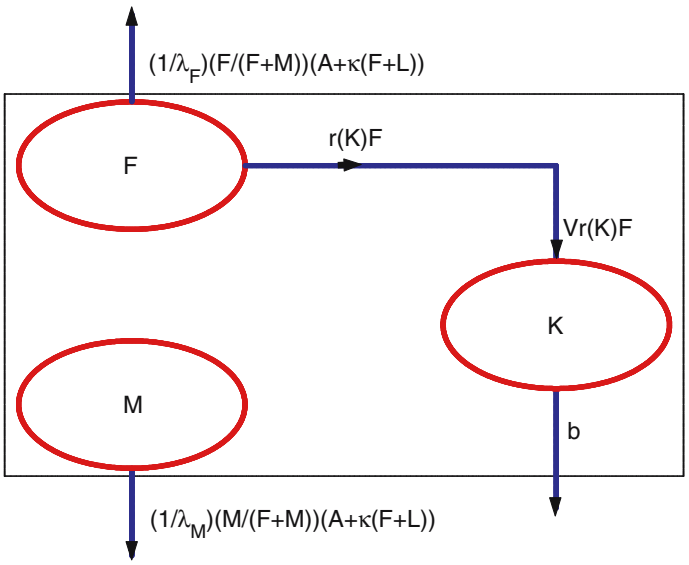

Fig. 1 Depiction of the model of body components during long-term starvation in humans. F is mass of lipids, M is mass of muscle, and K is mass of ketone bodies. The flow rate out of F compartment to K is $r(K)F$. As an inflow rate into compartment K, we need to adjust by a conversion parameter, V

by the brain do not change. Therefore, we model K_B by a constant, b. Thus, the full system is

$$\frac{dF}{dt} = -r(K)F - \frac{1}{\lambda_F}\frac{F}{F+M}(C + \kappa(L+F)) \tag{6}$$

$$\frac{dM}{dt} = -\frac{1}{\lambda_M}\frac{M}{F+M}(C + \kappa(L+F)) \tag{7}$$

$$\frac{dK}{dt} = Vr(K)F - b \tag{8}$$

The value V is a conversion constant that computes how much ketone body mass can be generated when 1 kg of fat mass is oxidized in the β-oxidation. If $F(0), M(0)$ and $K(0)$ are positive then $F(t)$ and $M(t)$ initially decrease. If $F(t)$ decreases to zero, the supply of ketone bodies will decrease to zero and the brain will not meet its energy requirements, resulting in death. Similarly, if $M(t) = 0$, death will result and the model ceases to make sense. In fact, because of the multi-function of proteins, death is observed before all muscle mass is depleted. In the case of a normal man, estimates of the critical lean body mass, $L_c > L_0$ appear in the literature [1,18]. Death can occur if $L(t) = L_c$ (a lack of protein requirements to support the body), or $K(t) = 0$ (lack of energy sources for the brain's requirements). As a result, $F(t)$ and $L(t)$ decrease until death occurs. Because the model will cease to make sense at the point of death, a traditional stability analysis of equilibria do not apply to this model. However, in the next section we provide some monotone properties of the model that relate to the physical dynamics of starvation.

Table 1 provides a summary of the variables and parameters used to develop the model in this section and parameter estimates in Sect. 6.

Table 1 Table of symbols, meanings and units

Symbol	Meaning	Units
$F(t)$	kg of fat (adipose tissue)	kg
$M(t)$	kg of protein in the muscle mass	kg
$K(t)$	kg of ketone bodies available	kg
F_K	Rate of conversion of fat mass to ketone body mass	kg/t
F_B	Rate of fat mass used to support the body	kg/t
M_B	Rate of muscle mass used to support the body	kg/t
$r(K)$	Proportion at which fat mass is turned into ketone body mass	1/t
C	Term in Harris–Benedict BMR not dependent on body mass	kcal/t
κ	Proportion constant of body mass in BMR	kcal/(kg t)
λ_F	Caloric value of 1 kg of stored fat	kcal/kg
λ_M	Caloric value of 1 kg of muscle	kcal/kg
V	Conversion constant of 1 kg of fat mass to 1 kg of ketone body mass	kg/kg
b	Constant rate of ketone body use by the brain	kg/t
a	Conversion rate of fat mass to ketone body mass when $K = 0$	kg/t

5 Monotone property of the model

The model (6–8) is an example of a cooperative system (all off-diagonal entries in the Jacobian matrix are positive) [25]. As a result, the system preserves *regular order* in $\mathbb{R}^3_+$. Regular order is componentwise order; $P_1 \geq P_2 \in \mathbb{R}^3_+$ if $P_1(i) \geq P_2(i)$ for $i = 1, 2, 3$.

Because the system preserves regular order, if two initial vectors

$$\left(F^{\{1\}}(0), M^{\{1\}}(0), K^{\{1\}}(0)\right) \leq \left(F^{\{2\}}(0), M^{\{2\}}(0), K^{\{2\}}(0)\right),$$

then

$$\left(F^{\{1\}}(t), M^{\{1\}}(t), K^{\{1\}}(t)\right) \leq \left(F^{\{2\}}(t), M^{\{2\}}(t), K^{\{2\}}(t)\right)$$

for all $t > 0$.

The order-preservation property provides a mathematical explanation to why individuals with higher body mass index (BMI), which is total body mass divided by stature (height squared), can survive for a longer period of time under prolonged starvation. For example, if $F^{\{1\}}(0) \leq F^{\{2\}}(0)$, then $F^{\{1\}}(t) \leq F^{\{2\}}(t)$ for all $t > 0$ (see Fig. 2). The preservation of regular order also leads us to draw the similar conclusions on survival time regarding larger fat mass and ketone body mass (see Fig. 3). The numerical simulations in the next section illustrate this characteristic.

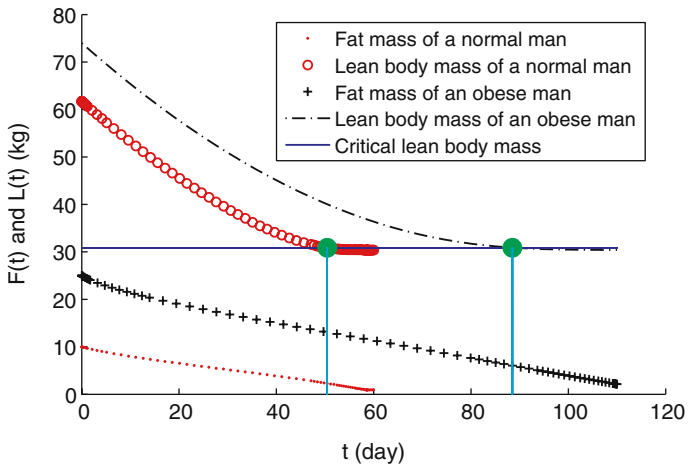

Fig. 2 The decline of fat and lean body mass for a normal man and an obese man during long-term starvation. For a normal man, death occurs in about 51 days. For an obese man, death occurs in about 90 days

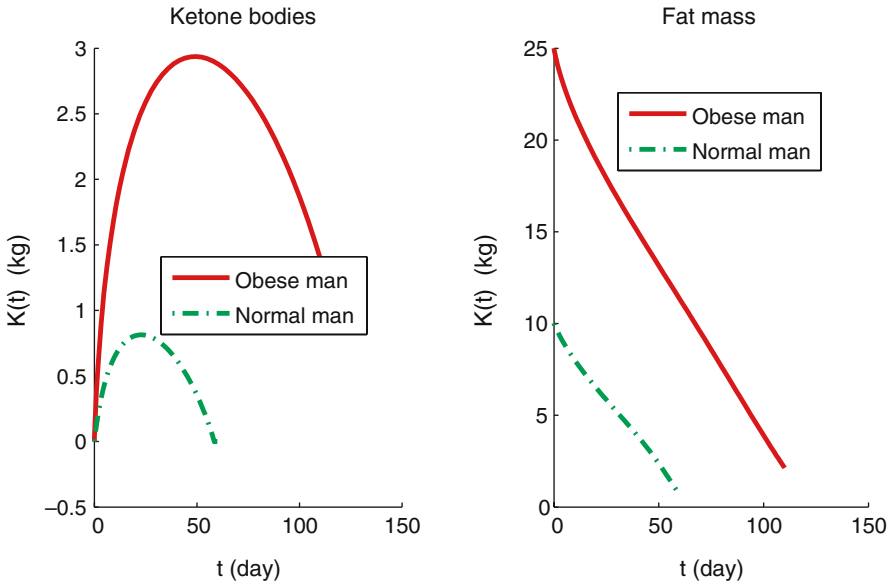

Fig. 3 Comparison of the decline in fat and ketone body mass for an obese individual with a BMI of 32 to a normal man

6 Parameter estimation and numerical simulations

Because parameter values will vary with individuals, it is important to view examples of how to run the model for specific cases. To this end, we will numerically compute two cases. The first case simulates the dynamics of starvation in a normal average man weighing 70 kg, with height 5 feet 9 in. (175.26 cm) and age 25 years. These conditions lead to a normal BMI of 22.7 kg/m^2. Recall that the BMI is defined as the ratio of weight in kg to stature [18]. Stature is defined as the square of the height measured in m^2. The second case considers a slightly obese man with the same height and age weighing 99 kg. This yields a body mass index of 32 kg/m^2 (over 30 kg/m^2 is considered obese) (Table 2).

The following list describes the estimation of the parameters and the initial conditions.

1. From the Harris–Benedict equation, we know $b_1 = 66$, $c_1 = 5$, $h_1 = 175.26$ cm, and $\delta_1 = 6.8$, which results in $\kappa = 13.7$ kcal/(kg day). With $Ag = 25$ years, we obtain the estimate for $C = b_1 + c_1 H_1 - \delta_1 Ag = 772.3$.

Table 2 Estimated parameters

a	b	C	κ	L_C	L_0	λ_F	λ_M	V
0.013	0.05–0.075	772.3	12.33	30.75	30.4	7,777.8	1,400	0.9

2. The caloric values of 1 kg of fat and muscle mass appear in [18] as $\lambda_F = 7,777.78$ kcal/kg, $\lambda_M = 1,400$ kcal/kg.
3. In the case of a normal man, total lean body mass is approximately 61.7 kg, muscle mass is 31.3 kg ($M(0) = 31.3$ kg), bone mass constitutes approximately 10.4 kg and essential fat is 2.1 kg [18]. Therefore, $L_0 = 61.7 - 31.3 = 30.4$ kg. We will assume that L_0 remains the same for the obese individual.
4. The critical lean body mass for a normal man is estimated as one half of the original lean body mass: critical lean body mass $L_C = 0.5(M(0) + L_0) \approx 30.75$ kg [1,18].
5. The parameter b in our model represents daily brain energy derived from the ketone bodies. The brain requires 100–145 g/day of glucose [20]. During starvation, two-thirds of the brain's energy is provided by ketone bodies [20]. The energy content in 1 g of glucose is 3.8 kcal [7] and the energy content of 1 g of ketone bodies is 4.92 kcal [33]. Applying these facts yields a range of parameter estimates for b: $\frac{2}{3}(100)\frac{3.8}{4.92} \times 10^{-3} = 0.0515\,\text{kg} \le b \le \frac{2}{3}(145)\frac{3.8}{4.92} \times 10^{-3} = 0.0747\,\text{kg}$.
6. The conversion constant V is around 0.9. We estimate this value by considering energy content in fatty acid and ketone bodies. The energy content of 1 g fatty acid is 9.3 kcal while 1 gram of ketone bodies contain 4.92 kcal [33]. That is, the energy content of fatty acid is 1.89 times than that of ketone bodies. However, because the β oxidation of fatty acid into ketone bodies includes a sequence of chemical reactions, not all energy stored in fatty acid can be carried out to ketone bodies. We use $V = 0.9$ based on our assumption that 50% of energy in fatty acid is kept.
7. A closed formulation for $r(K)$, the conversion rate of ketone bodies from fat mass, does not exist in the literature. For the purpose of numerical simulations, we take $r(K) = a/(1 + K)$. We chose this expression because we assumed that when K is small, more fat mass needs to be converted to ketone bodies and when K is large, less fat mass needs to be converted. Observe that when K is very small, the conversion rate is approximately directly proportional to F and when K is large, the conversion to ketone bodies is close to zero. The liver normally can produce as much as 185 grams of ketone bodies per day [17]. Therefore, we estimate $r(K(0))F(0) = 0.185$ kg/day. Applying this estimate and the initial data to the equation, $[aF(0)/(1 + K(0))] = 0.185$, we estimate $a \approx 0.013$ kg/day.
8. The Harris–Benedict equation is a statistically based formula and was derived using a large amount of data [9]. However, this data did not include extreme cases such as starvation. To adjust the proportionality constant, $\kappa = 13.7$ kcal/(kcal day), the simulations in Figs. 2 and 3 scale κ by 90%, that is, $\kappa = 13.7 \times 0.9 = 12.33$. In addition, in order to observe the impact of variations in κ on the dynamics, we allowed κ to vary with a normal distribution with mean being $13.7 \times 0.8 = 10.96$ kcal/(kcal day).
9. Initial values are, of course, different for obese and normal individuals. For the obese individual with a BMI of 32 kg/m^2, we assume $F(0) = 25$ kg, $M(0) = 74 - L_0 = 43.6$ kg, $K(0) = 0.02$ kg. For the normal average

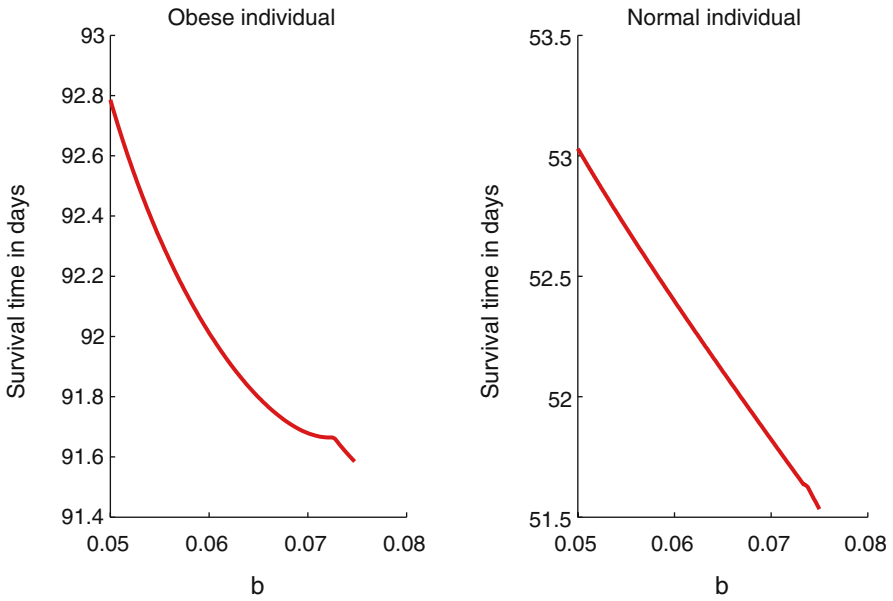

Fig. 4 Survival lengths as a function of parameter b for an obese man and a normal man during long-term starvation

man, we use the standard values that appear in the literature: $F(0) = 8.7$ kg, $M(0) = 61.3 - L_0 = 30.9$ kg, $K(0) = 0.02$ kg [18].

Recall that death occurs either when $L(t) = L_C = 30.85$ kg (death due to lack of proteins) or $K(t) = 0$ (death due to lack of brain energy requirements). A normal man can survive as long as 51 days, as is shown in Fig. 2. In Fig. 2, we see that an obese person with a BMI of 32 kg/m^2 may survive as long as 3 months (see also Fig. 2). These values correspond to theoretical estimates in [13,18]. In [11,13], it is estimated that a severely obese individual can survive up to 1 year without food!

Mass of ketone bodies has a large initial dramatic increase and then declines (see Fig. 3). A similar dynamic was observed experimentally in Cahill's original work and reproduced in later studies [20]. However, as expected, the ketone body mass was not allowed to decline for a prolonged amount of time while experimenting on human subjects.

Because we could only estimate a range for parameter b, we systematically varied the value over the interval [0.05, 0.075] and determined the effect on survival time. As shown in Fig. 4, for an obese individual the resulting survival times ranged from 91.6 to 92.8 days; for a normal individual the resulting survival times ranged from 51.5 to 53 days. The sharp drop seen in Fig. 4 near $b = 0.0725$ is due to numerical error. It is clear that the uncertainty of b does not have much impact on survival time. We also confirm this by a histogram in Fig. 5 that is drawn based on 10,000 runs. In each run, the value of b is randomly chosen from the uniform distribution over $[0.05, 0.075]$. This histogram

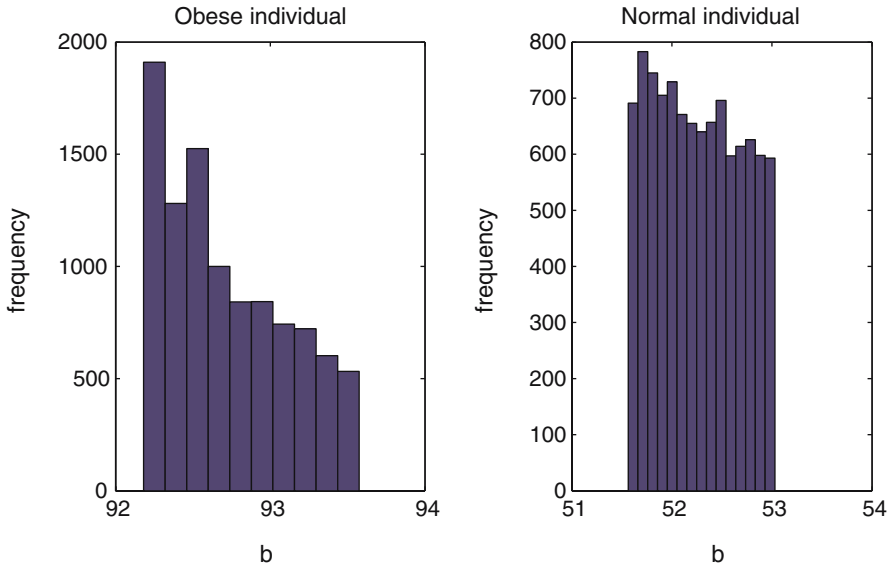

Fig. 5 Histogram of survival lengths as the parameter b varies. For each run of total 10,000 runs, the parameter value of b is randomly chosen from the uniform distribution over $[0.05, 0.75]$

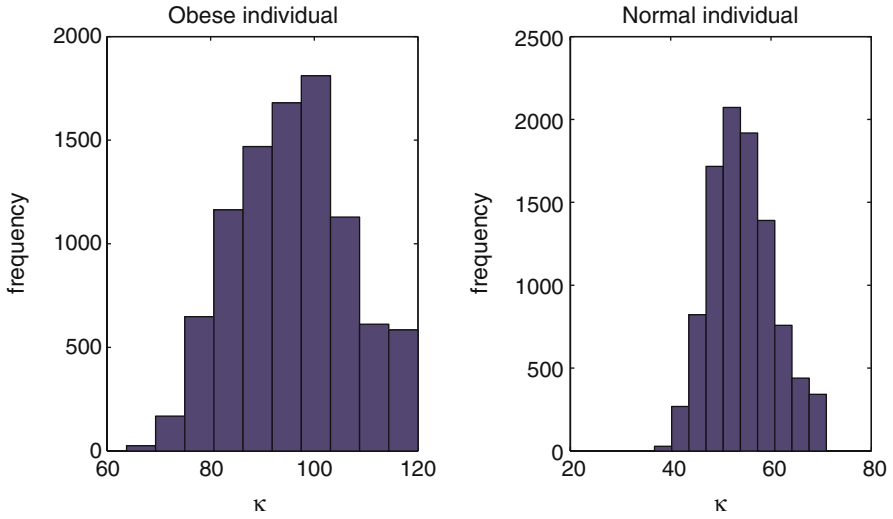

Fig. 6 Histogram of survival lengths as the parameter κ varies. The parameter κ was chosen randomly from the normal distribution $N(12.33, 2^2)$ for each of the 10,000 simulations

shows that for an obese individual, the survival time is between 91 and 94 days, while for a normal one, it is between 51 and 53 days. Both Figs. 4 and 5 show that the uncertainty of b does not have much impact on the survival time. On the other hand, the survival lengths are highly affected by the parameter κ. Figure 6 illustrates this fact for both the normal and obese cases. For the obese

case, death can occur between 60 and 120 days with mean 90 days, and for the normal case, the death occurs from 40 to 70 days with mean 55 days.

7 Conclusion

This paper developed a differential equation model describing an individual's energy usage in terms of stored fat mass, lean body mass, and ketone body mass during prolonged starvation. Parameters of the model were estimated using experimental data in [1,2,12,18,26]. The model can be used to estimate the number of days a human can survive during prolonged starvation. Clearly, experimental data on this length of time is scarce for a variety of obvious reasons and hence the model has important predictive value.

The model presented here has several limitations. First, the equations describe starvation in a controlled environment. Starvation external to a laboratory usually includes water and vitamin deprivation. Thus death can occur from a combination of factors long before critical lean body mass is reached [13]. Long-term starvation also causes negative neurological effects which would alter the assumption that AT = 0. The model is also not equipped to describe the benefits of starvation to treat diseases such as Parkinsons [13]. One of the recent fascinating aspects of fasting is its correlation to retarding aging. A model of starvation linked to recovery may capture mathematical explanations for the slowdown of the aging process.

For future work, one can build on the basic model presented here to explore several problems. The model can be adjusted to understand semi-starvation in eating disorders which are on the rise. To modify the model, I, the kilocalorie of food ingested should be taken to be small. In addition, the physical activity, PA, should be nonzero, accounting for the aerobic workouts that accompany some eating disorders.

The model can also be adjusted to understand starvation in a realistic setting. This would entail an addition of water and essential vitamin deprivation. Such a model could ascertain the impact of starvation related disease in famine stricken regions.

Finally, benefits of starvation can be explored by formulating a model to understand treatment of disease and slow down of aging.

Acknowledgements The authors would like to thank John Stevens and Jeffrey Toney for valuable suggestions and advice on the model. We would like to thank Dr. Peter Kerndt, Dr. Charles C. Ophardt and Dr. Oliver Owen for discussing their research on the chemistry of starvation with us. Finally, we would like to thank the two anonymous referees for their many suggestions which significantly improved the paper.

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