Relation of physiological variables and health by physics approach

Feng Lin [1]

Institute of blood transfusion,
Chinese academy of medical science and Peking union medical college
Huacai Road No.26, Chengdu, 610053, People's Republic of China

Abstract

Based on the non-equilibrium thermodynamics point of view that a biological system is sustained by a local potential provided by stable entropy production, we construct a mathematical model to describe the metabolism of human body system. According to the stable and periodic property of human body system, the embryonic form of the model is constructed by dimensional analysis. Based on the mathematical model, stability analysis is used to discuss the response to perturbation which corresponds to the influence on human health. With the help of physiology and medical science, the parameters in the model are determined by empirical formulas in physiology. The correspondence of parameters and the observable variables such as body temperature, body weight, heart rate etc is found out. As an example, an interesting result obtained from our model is that overweight adults, even though healthy in the medical examination reports, faces the risk of being sick, because overweight decreases the metabolic frequency, however, it drives the human body system "farther" from equilibrium (death). This result shows that the body weight of over weighted ones will gradually increase rather than staying at a stable interval. Our method provides a new approach of predicting human health according to the observable vital signs.

KEYWORDS: Non-equilibrium thermodynamics, Vital signs, Energy metabolism, Energy expenditure

[1] E-mail: linfeng_ibt@163.com

Contents

1 Introduction

Vital signs are important to clinic doctors[1]. Heart rate, respiration, blood pressure often changes when one is doing physical exercise, while body temperature is relatively stable. If one's body temperature is not normal, it is no doubt that this one is sick[2, 3]. In medical science, vital signs have already been used to estimate whether patients are critical condition. But seldom doctors pay attention to the vital signs of healthy individuals. Physiological variables, including vital signs are some index which reflects the property of an non-equilibrium system. Only physicists or mathematicians take non-equilibrium thermodynamics into consideration while studying the biological system[4–7]. In view of non-equilibrium thermodynamics, a live human body is a system far from equilibrium, with stable entropy production which serves as a local potential, that sustains life[8–13]. While hardly any physicists study human body system by vital signs. It may stem from the reason that human body system is too complex to study by using thermodynamics. In this paper we tried a way to construct a mathematical model to describe the metabolism of human body system, according to the feature that this kind of system has stable entropy production.

Human body can be regarded as a complex network consists of several subnetworks. All of these networks are in fact based on chemical reactions. If we exactly divide the complex network into limited subnetworks, each of the complex network represents a function of the system[14–17].

In this paper we just divide the system into 2 subnetworks to study the metabolism of the human body by mathematical model with the help of medical science and physiology. In section 2 the metabolism of human body is regarded as the decomposition of macro molecules and reconstruction of new macro molecules process. The mathematical model is constructed according to the process. In section 3 we give the exact mathematical model of human body according to the analysis in section 2. In section 3.2, we use the mathematical model obtained in section 3.1 to discuss the stability of human body system from the aspect of physics. In section 4, we use the empirical formulas constructed by physiologists to evaluate the parameters in the model we constructed in section 3, to find out the relation between the the vital signs and the parameters.

2 Phenomenological picture of energy-material metabolism

Even though energy metabolism is very complicated, still there is some way to understand this process. Physiology shows that human body system take materials from the outside. Some of the material is changed into energy and some of the material is changed into the substances which is used to construct the organs of the human body[4]. This phenomenon gives the clue that human body at least has 2 subsystems, the function of one system is to obtain materials from outside, the function of the other is to construct the organs by using the materials obtained from outside[18].

The other phenomenon from physiology is that the human body system is a periodic system and it is stable to the perturbation from outside[4], because of the fact that the total number of the cells in any time interval does not have significant difference. From the knowledge of physiology that the cells which construct our organs dies every day, and new cells will be produced to supplement the cells died. From our deduction of the clue, we define the 2 labels to represent the human body subsystem:

q_1: obtain the materials from outside, i.e. change macromolecules materials into molecules. For instance, starch is changed into glucose and protein is changed into amino acid.

$$macro \quad molecules \xrightarrow{q_1} micro \quad molecules \tag{1}$$

q_2': change the molecules into organs which sustain our lives. i.e. construct the 2 subsystems q_1 and q_2'.

$$micro \quad molecules \xrightarrow{q_2'} organs \quad (q_1 \quad and \quad q_2') \tag{2}$$

From the above phenomenon, a schematic map is described below:

At certain time t, $q_1(t)$ maps macromolecules into molecules, and it dies out after this process. At this time we can only observe $q_2'(t)$, then $q_2'(t)$ maps the molecules into new $q_1(t')$ and $q_2'(t')$, and $q_2'(t)$ dies out during this process.

$$\begin{aligned} q_1(t) &\xrightarrow{\Delta t} q_2'(t+\Delta t) \\ q_2'(t+\Delta t) &\xrightarrow{\Delta t} q_1(t+2\Delta t), q_2'(t+2\Delta t) \end{aligned} \tag{3}$$

Phenomenologically speaking under the time translation operation subsystem q_1 is changes into q_2', and the following time translation operation maps q_2' into q_1 and q_2'. One may notice that the time scale of the function of q_1 and q_2' are different. For instance, the recovery of a hurt lasts for several days while feeling not hungry lasts for several minutes. In section 3, we will solve this flaw.

3 Mathematical model of metabolism based of healthy individuals

We will finish constructing of the mathematical model by 2 steps. The first step follows the phenomenon and the logic of physics. The second step follows the knowledge from medical science and physiology.

3.1 Construction of model by physics picture

Time translation operation is the difference of time. From the periodic phenomenon, we can deduce that the model is like this

$$\begin{aligned} \dot{q}_1 &= -q_2' \\ \dot{q}_2' &= \omega^2 q_1 + f(q_1, q_2') \end{aligned} \tag{4}$$

in which ω is the angular frequency of the system. When $f(q_1, q_2') = 0$, (4) is a harmonic oscillator, which satisfies the periodic condition. But it is obvious that $f(q_1, q_2') \neq 0$, because harmonic oscillator describes a conservative system, while human body is a dissipative system. By dimensional analysis, the dimension of ω is $[t]^{-1}$, and $[f(q_1, q_2')]$ must have the same dimension as $[\dot{q}_2']$. In order to determine the exact information of $[f(q_1, q_2')]$, we have to turn to the function of the network q_1 and q_2'. One of these 2 networks maps macro molecules into micro molecules, and the other maps micro molecules into organs. This means that both of the networks have the dimension which equals to 0. The 1st equation in (4) means that the dimension of q_1 and q_2' are different, which means that (4) is not the model which we are looking for. Because of this, we have to return to the picture of the 2 networks' function.

We know that q_2' maps the molecules into a higher level (organs rather than macro molecules) than the reverse process of q_1 (if q_1 had the function of mapping micro molecules into macro molecules). The fact is that the time scale of changing food into energy and amino acid is much more shorter than the time scale of changing amino acid into some organ. For instance, the recovery of a hurt lasts for several days while feeling not hungry lasts for several minutes. One can easily imagine that the oscillation frequency tends to 0, if we set the model like (4). This means that in model (4), it is almost impossible to observe the oscillation between q_1 and q_2'. This picture does not satisfy the phenomenon that the oscillation frequency of q_1 and q_2' is able to be observed, which stems from the knowledge of physiology that the cells which consists our organs dies every day, while new cells will be produced to supplement those died. As the time scale of function q_2' is much larger than that of q_1, rescale q_2' i.e. $q_2 \equiv \frac{q_2'}{\omega}$. Rewrite the model (4) we get:

$$\begin{aligned} \dot{q}_1 &= -\omega \frac{q_2'}{\omega} \\ \frac{\dot{q_2'}}{\omega} &= \omega q_1 + f(q_1, \frac{q_2'}{\omega}) \end{aligned} \tag{5}$$

or more exactly:

$$\begin{aligned} \dot{q}_1 &= -\omega q_2 \\ \dot{q}_2 &= \omega q_1 + f(q_1, q_2) \end{aligned} \tag{6}$$

Our rescaling guarantees q_1 and $q_2 \equiv \frac{q_2'}{\omega}$ have the same dimension. This information shows that what we macroscopically observe is the network q_2 though we intuitively imagine the network is q_2'. The next step is to determine $f(q_1, q_2)$ which has the dimension $[t]^{-1}$. Since q_1 and q_2 are dimensionless, there must be some coefficient which has the dimension $[t]^{-1}$ in $f(q_1, q_2)$.

Try the simplest case: $f(q_1, q_2) \equiv \mu$ in which $\mu \neq 0$ is the coefficient with the dimension $[t]^{-1}$. Plug μ into $f(q_1, q_2)$, one can immediately find that (6) is periodic however it is still conservative.

Try the second simplest case: $f(q_1, q_2) \equiv \mu q_1$ or $f(q_1, q_2) \equiv \mu q_2$. The former leads to the same result as $f(q_1, q_2) = \mu$, the latter leads to the result that the system is not periodic. This way of finding $f(q_1, q_2)$ does not work. We must turn to other ways.

Notice that network q_1 only change some number of macro molecules to other number of micro molecules, that is why q_1 is dimensionless. However $\dot{q}_1$ has the dimension of $[t]^{-1}$, which is exactly the dimension of energy. This means that the tangent space of the solution of (6) in the phase space consists of q_1 and q_2 carries energy. As (6) describes a dissipative system, at almost all the tangent space of the solution, there is energy absorbing or releasing. So the divergence of (6) in phase space (q_1, q_2), div is defined as

$$div \equiv \frac{\partial f(q_1, q_2)}{\partial q_2} \tag{7}$$

Along the solution orbit of (6) if $div \equiv 0$ then (6) describes a conservative system, with closed orbit. We need the solution orbit to be closed, and $div \neq 0$ at most of the orbit. To guarantee the condition that the solution orbit is close and at most of the orbit $div \neq 0$, div must satisfy that along part of the solution orbit of (6) $div \leq 0$ and part of the orbit $div \geq 0$, and at some points on the orbit $div = 0$[19]. This leads to the result that the power of div consists of polynomials of q_1 and q_2 at least have the power of 2, and there must be some dimensionless number a added in div like $a + q_1^2$ or $a + q_2^2$ (the form like $a + q_1 q_2$ is not welcome, because it leads to the linear dependence of the 2 variables), so as to guarantee the condition above. So the result below gives us the general idea of div and $f(q_1, q_2)$

$$div \propto \mu(a + q_1^2) \tag{8}$$

or

$$div \propto \mu(a + q_2^2) \tag{9}$$

integrate div by q_2, we get $f(q_1, q_2)$. One can try very limited times to find that $f(q_1, q_2) = -\mu(q_1^2 - a)q_2$ with $\mu > 0$, so as to guarantee the solution of (6) is a closed orbit in phase space of (q_1, q_2) with $div \neq 0$ at most of the orbit. By physics and mathematics, the simplest model of the material-energy metabolism we can get is:

$$\begin{aligned} \dot{q}_1 &= -\omega q_2 \\ \dot{q}_2 &= \omega q_1 + \mu(a - q_1^2)q_2 \end{aligned} \tag{10}$$

surprisingly what we construct (10) is in fact the famous Van der Pol model[20]. When the parameters in Van der Pol model satisfies $\mu > 0$,$\omega > 0$, $a > 0$ and $a >> \frac{\mu}{\omega}$, the its solution is a limit cycle. Its limit cycle solution satisfies periodicity and stability which are the conditions we need. $\frac{\mu}{\omega}$ describes the "distance" to equilibrium. Because when $\frac{\mu}{\omega} = 0$, the system returns to equilibrium. Once the parameters are set, they reflect the intrinsic property of the system.

3.2 Information from non-equilibrium thermodynamics and medical science

In section 3.1, we get a general picture of what this model looks like, however, there still remains some problems to be solved which can not be answered by physics: what do those coefficients in (10) mean? and what do they numerically equal to?

Let us first rescale the parameter $t \to t' \equiv t\omega$. This rescaling makes the parameter t' dimensionless. Rewrite (10) in the dimensionless form:

$$\begin{aligned} \frac{d}{dt'}q_1 &= -q_2 \\ \frac{d}{dt'}q_2 &= q_1 + \frac{\mu}{\omega}(a - q_1^2)q_2 \end{aligned} \tag{11}$$

The approximate solution of (11) to the order of $\frac{\mu}{\omega}$ is[21, 22]:

$$\sqrt{q_1^2 + q_2^2} = 2a - 8\frac{\mu}{\omega}\cos\theta \sin^3\theta \tag{12}$$

in which $q_1 \equiv \sqrt{q_1^2 + q_2^2}\cos\theta$ and $q_2 \equiv \sqrt{q_1^2 + q_2^2}\sin\theta$. This solution is a limit cycle represented by polar coordinates in phase space.

We have already mentioned in section3.1 that the divergence at most points of the orbit are non-zero. This means that at most of the points on the solution in phase space, there is energy absorbing or releasing. Summing up div at each point on the orbit, the result is negative. Mathematically it confirms that system (10) or (11) is stable. In physiology, it is the steady energy divergence div in each period that sustains life. $div < 0$ corresponds to energy absorbing and $div > 0$ corresponds to energy releasing.

Define 2 symbols div_+ and div_- which are corresponds to energy absorbing and releasing in an oscillation period, i.e. summing up all the $div > 0$ terms in an oscillation period we get div_+, so on and so forth.

$$div_+ = 2\int_{q_1=-\sqrt{a},q_2(q_1=-\sqrt{a})}^{q_1=\sqrt{a},q_2(q_1=\sqrt{a})} ds \quad div(s) \tag{13}$$

$$div_- = 2(\int_{q_2=0,q_1(q_2=0)>0}^{q_1=\sqrt{a},q_2(q_1=\sqrt{a})} ds \quad div(s) + \int_{q_1=-\sqrt{a},q_2(q_1=-\sqrt{a})}^{q_2=0,q_1(q_2=0)<0} ds \quad div(s)) \tag{14}$$

the integration ranges are on the limit cycle solution (12). It is not difficult to figure out when $q_1 = \pm\sqrt{a}$, $div = 0$. This "stable energy dissipation" in an oscillation period τ exactly corresponds to the "negative entropy" that sustains life. We define it by E_D which is proportional to:

$$E_D \propto \frac{1}{\tau}(|div_-| - |div_+|) = \frac{\pi}{2\tau}[3(\frac{\mu}{\omega})^2 + 8a^2 - 4a]\frac{\mu}{\omega} \tag{15}$$

E_D is intrinsic and stable as long as the parameters μ, ω, a are given. The given parameters corresponds to a definitely given individual. The oscillation period is relevant to the angular frequency ω, i.e. $\tau\omega = 2\pi$. (10) or (11) describes the energy metabolism in molecular reaction level, which is much faster than that in macroscopic level. So τ goes to 0 in macroscopic world. And these 2 models have already reduced the dimension, so

$$\begin{aligned} E_D &= \frac{k_B < T_b >}{\tau}(|div_-| - |div_+|) = \frac{k_B < T_b > \omega}{2\pi}(|div_-| - |div_+|) \\ &= \frac{k_B < T_b > \mu}{4}[3(\frac{\mu}{\omega})^2 + 8a^2 - 4a] \end{aligned} \tag{16}$$

in which k_B is the Boltzmann constant, and $< T_b >$ is the average body temperature. Since the time scale is on the molecular level i.e. $\tau \to 0$ on macroscopic level, E_D is the macroscopic minimum energy dissipation rate of the system, which is proportional to the "negative" entropy that sustains life. Because of the stability property of the system, the parameters must satisfy:

$$3(\frac{\mu}{\omega})^2 + 8a^2 - 4a > 0 \tag{17}$$

The parameters satisfy:

$$a > \frac{1}{4} + \frac{1}{4}\sqrt{1 - 6\frac{\mu^2}{\omega^2}}$$

and

$$\sqrt{\frac{1}{6}} > \frac{\mu}{\omega} > 0$$

Macroscopically, the minimum dissipation of energy can be observed either by body temperature or basal metabolic rate. Both of them are intrinsic for a definitely given individual. That is why most of the times body temperature at the same place of the body remains the same. The former directly related to entropy production rate:

$$\begin{aligned} E_D &= \beta \sum_{T_b} T_b \frac{d_i s}{dt} \sigma(T_b) \\ &= -\beta \sum_{T_b} T_b \frac{T_{en} - T_b}{T_{en} T_b} \kappa \frac{T_b - T_{en}}{\Delta r} \sigma(T_b) \end{aligned} \tag{18}$$

In which β is a dimensionless parameter which builds the bridge between microscopic world and macroscopic world. $\sigma(T_b)$ is the body surface area where the temperature is T_b. This term is added because the body temperature is different at different part of the body. T_{en} is the temperature of the enviroment at the distance Δr from the surface of body in which $\Delta r \to 0$, and $d_i s$ is the inertial entropy. $\kappa > 0$ is thermal conductivity constant. In differential form, the entropy production rate is

$$\frac{d_i s}{dt} = -\kappa \bigtriangledown T (T_b^{-1} - T_{en}^{-1}) \tag{19}$$

It is hard to collect the body temperature at every point of the body surface. σ directly multiplied by energy dissipation at certain part of body is not accurate. Summing up each part of body area with different temperature is more accurate but more difficult. Moreover, T_{en} is hard to get to some extent. To get the intrinsic energy dissipation of an individual, we can turn to the basal metabolic rate, which is estimated by empirical formulas from the medical science. This index exactly corresponds to the minimum entropy production of the system[11]. We estimate the basal metabolic rate of healthy individuals suggested by [23]. For males the basal metabolic rate B_m

$$\begin{aligned} B_m &= \frac{10.0m}{1kg} + \frac{6.25h}{1cm} - \frac{5.0ag}{1year} + 5 \\ B_f &= \frac{10.0m}{1kg} + \frac{6.25h}{1cm} - \frac{5.0ag}{1year} - 161 \end{aligned} \tag{20}$$

The subscript m denotes males and f denotes females. m is the mass with dimension kg. h is the height with dimension cm and ag is the age with dimension $year$. The basal metabolic rate has the dimension $kcal.day^{-1}.m^{-2}$, that is, $\frac{4.2\times10^3}{24\times3600} J.s^{-1}.m^{-2}$. According to the literature report[23], the healthy individuals' basal metabolic rate do not have significant difference. This implies that 2 healthy individuals with the same gender, at the same age, with similar height have similar weight. That is why their body surface area are the same.

The definition of basal metabolic rate is the thermal energy detected at unit time at unit body usrface area. This is in fact the energy dissipation at unit time at unit body surface area. So total energy dissipation of human body E_D and basal metabolic rate have the relation below:

$$\frac{E_D}{\sigma} = \beta B_{m(f)} \tag{21}$$

in which σ is the body surface area with dimension m^2 calculated by the formula give below[24]

$$\sigma = 0.007184 m^{0.425} h^{0.725} \tag{22}$$

m and h have the same meaning as in (20). Plug (16) into (21), we get:

$$\frac{k_B < T_b > \mu}{4}[3(\frac{\mu}{\omega})^2 + 8a^2 - 4a] = \beta B_{m(f)}\sigma \tag{23}$$

equation (23) gives constraint for the parameters which reflects the intrinsic state of the energy-material metabolism. The solution of (11) is at the lowest "energy level", which corresponds to the basal metabolism.

Daily exercise or physical exercises can not last for infinite long time. Anyone feels tired after long time exercises, and needs rest. During this process, one can observe the thermal energy increases at unit area of body surface at unit time, but when he or she is at rest at $293K$ (20 centigrade), the thermal energy at unit area of body surface at unit time returns to basal metabolic rate $B_{m(f)}$. This means that daily exercise is just the perturbation to the basal metabolism, in language of physics, basal metabolic rate is a potential well in phase space (q_1, q_2).

To demonstrate our proposal, rewrite (11) in polar coordinate:

$$\begin{aligned} \frac{d}{dt'} r &= \frac{\mu}{\omega}(a - r^2\cos^2\theta) r \sin^2\theta \\ \frac{d}{dt'}\theta &= 1 - \frac{\mu}{\omega}(a - r^2\cos^2\theta)\sin\theta\cos\theta \end{aligned} \tag{24}$$

where $q_1 = \sqrt{q_1^2 + q_2^2}\cos\theta \equiv r\cos\theta$, similarly, $q_2 = r\sin\theta$. The angular speed does not contribute to radial direction, which corresponds to energy level in phase space. So suffice it to focus on the first equation (24). if there is a small deviation δr from the limit cycle solution (12) r_0:

$$\frac{d}{dt'}(r_0 + \delta r) = \frac{\mu}{\omega}[a - (r_0 + \delta r)^2\cos^2\theta](r_0 + \delta r)\sin^2\theta \tag{25}$$

Because r_0 is the limit cycle solution of (11), to the first order approximation, (25) becomes:

$$\frac{d}{dt'}\delta r = \frac{\mu}{\omega}(a - 3r_0^2\cos^2\theta)\sin^2\theta\delta r + O(\delta r^2) \tag{26}$$

the solution of (25) is:

$$\delta r = e^{\frac{1}{8}\frac{\mu}{\omega}[(4a - 3r_0^2 - 4a\cos 2\theta + 3r_0^2\cos 4\theta)t' - (4a - 3r_0^2 - 4a\cos 2\theta + 3r_0^2\cos 4\theta)t_0']} \tag{27}$$

where t_0' is the initial time. The leading term in the equation $a - 3r_0^2\cos^2\theta$ is negative definite[21, 22]. In its solution $4a - 3r_0^2$ is negative definite, and $e^{-4a\cos 2\theta + 3r_0^2\cos 4\theta}$ is bounded i.e. it does not change the result that δr goes to 0 when t goes to infinity. This result shows that the perturbation changes *div*, but at last *div* will tend to the relation (23).

4 Energy metabolism with daily exercise for healthy individuals and the determination of the parameters in mathematical model

Last section 3, we have already discussed the approach of constructing mathematical model describing the basal metabolic rate which is intrinsic for human body. In this subsection, we discuss the energy metabolism of healthy individuals when daily exercise is taken into consideration.

From the mathematic point of view, perturbation to the intrinsic state leads to the deviation of energy metabolism. In practice what we can detect is the perturbation to E_D, the "negative energy dissipation":

$$\begin{aligned}\Delta E_D &= k_B < T_b > \{-\frac{1}{\tau}\int_0^{2\pi} d\theta \frac{\mu}{\omega}[a-(2a-8\frac{\mu}{\omega}\cos\theta\sin^3\theta+\delta r)^2\cos^2\theta] \\ &\quad +\frac{1}{\tau}\int_0^{2\pi} d\theta\frac{\mu}{\omega}[a-(2a-8\frac{\mu}{\omega}\cos\theta\sin^3\theta)^2\cos^2\theta]\} \\ &= k_B < T_b > \{\frac{\mu}{4}[3(\frac{\mu}{\omega})^2+8a^2-4a]-\frac{\mu}{2}(2a\delta r+\delta r^2)-\frac{\mu}{4}[3(\frac{\mu}{\omega})^2+8a^2-4a]\} \\ &= -k_B < T_b > \frac{\mu}{2}(2a\delta r+\delta r^2)\end{aligned} \tag{28}$$

in which δr is the deviation from limit cycle solution. The deviation from the limit cycle solution changes the intrinsic dissipation, the "negative energy dissipation". If $\delta r > 0$, (28) shows that the intrinsic dissipation is decreased, but this decrease leads to the system nearer to equilibrium, because $\frac{d_i s}{dt} = 0$ corresponds to equilibrium[11]. As is known to all that the equilibrium means the end of life. This result implies that endless exercising (improper exercise) without rest leads to death. If $-2a < \delta r < 0$, (28) shows that the intrinsic dissipation is increased, which drives the system farther from equilibrium. No matter (28) is positive or negative, it will go to 0, when t' goes to infinity. Because $\delta r \to 0$, when $t' \to \infty$.

If we return to the way of understanding the energy metabolism of human body in section 3.2, one can notice that the activity like daily exercise is in fact perturbation to basal metabolism. The observable fact that one's energy expenditure always returns to the basal metabolic level and the result of (27) are one-to-one correspondent. (27) describes the phenomenon that the energy expenditure (dissipation rate) of a healthy individual who is at rest after some exercise will return to its basal metabolic rate i.e. the intrinsic energy metabolism. Take the result of (28) into consideration, which shows that positive perturbation to the human body is harmful, because it leads the system nearer to equilibrium, we can deduce that the types of unhealthy lifestyle (corresponding to (28) negative) is much more than that of healthy lifestyle, because the interval of δr that makes (28) to be positive is narrower than that makes (28) to be negative. No wonder healthy lifestyle is not easy to keep.

Daily exercises increases the energy expenditure of human body[25], and it is widely accepted that proper daily exercises does no harm to our health. From the view in our paper, continuous physical exercise gives initial condition of δr, the evolution of δr following (27) begins when the physical exercise stops. And the increase of energy expenditure means that (28) is positive. So we are to discuss the relation between daily exercises that increases energy expenditure and the perturbation to our mathematical model which makes $\Delta E_D > 0$.

The prediction of energy expenditure in physical exercises has been studied since 1970s [26, 27]. Here we focus on walking which is the most general physical exercise that we face very day. The energy expenditure is related to oxygen uptake converted to energy used in metabolism. The formula of estimating energy expenditure is given in [25].

The metabolic equivalent task (MET) is related to basal metabolic rate, with the dimension $1MET = 1kcal.kg^{-1}.h^{-1} = \frac{4.2\times10^3}{3600}J.kg^{-1}.s^{-1}$. Converting to the oxygen demand of at unit time is $1MET = 3.5\dot{V}_{O_2}$, in which $\dot{V}_{O_2}$ is the oxygen demand unit mass unit time, with dimension $ml.kg^{-1}.min^{-1}$[25]. According to [25] the total energy expenditure measured in $\dot{V}_{O_2}$ is:

$$\dot{V}_{O_2}(ml.kg^{-1}.min^{-1}) = 3.5(ml.kg^{-1}.min^{-1}) + 0.1(ml.kg^{-1}.min^{-1}.(m.min^{-1})^{-1}) \times v(m.min^{-1}) \quad (29)$$

in which v is the speed of walking. Here we do not take graded walk into consideration, because we just consider the case of daily exercise. $3.5ml.kg^{-1}.\min^{-1}$ is just the basal metabolic rate per unit mass. The energy expenditure apart from basal metabolic rate is:

$$\Delta E_D = \frac{0.1v}{3.5}\frac{4.2\times10^3}{3600}m \quad (30)$$

in which m is just the mass in (20). The perturbation to E_D is explicitly related to the energy expenditure:

$$-k_B < T_b > \frac{\mu}{2}(2a\delta r + \delta r^2) = \beta\frac{0.1v}{3.5}\frac{4.2\times10^3}{3600}m \quad (31)$$

When $v = 0$, $\delta r = 0$. If v is some nonzero number, when it suddenly equals to 0, the response to the perturbation will last for some time. So this equation is only valid for the case when the individual is walking. The walking speed v gives initial condition of δr. The initial state of $\delta r = \delta r(t_0')$ are

$$\delta r(t_0') = -a \pm \sqrt{a^2 - \frac{1}{60}\frac{mv\beta}{\mu k_B < T_b >}} \quad (32)$$

consider the condition: if $v = 0$ then $\delta r = 0$, so we can only take the root with $+$:

$$\delta r(t_0') = -a + \sqrt{a^2 - \frac{1}{60}\frac{mv\beta}{\mu k_B < T_b >}} \quad (33)$$

It is known to all that anyone's walking speed is limited. Physiologist have already explained the reason: it is limited by our heart rate[28]. During physical exercise, heart rate, respiration and blood pressure will adjust to adapt to the oxygen demand of human body. 3 of the vital signs are changing except body temperature, which is relatively stable. So these 3 vital signs interdependent from one another. The maximum of the physical exercise is related to the cardiorespiratory fitness, suffice it to say that focus on the heart rate, as long as the individual is healthy. [28] gives the maximum of oxygen demand estimation $\dot{V}_{O_2max}$ during physical exercise:

$$\begin{aligned} \dot{V}_{O_2max} &= 111.33 - (0.42 \times hear \quad beat \quad min^{-1}) \quad (male) & (34) \\ \dot{V}_{O_2max} &= 65.81 - (0.1847 \times hear \quad beat \quad min^{-1}) \quad (female) & (35) \end{aligned}$$

The term $hear \quad beat \quad min^{-1}$ is the heart rate observed at the time that one is exhausted, rather than the rest heart rate. Convert the equation into energy-heart rate relation:

$$\Delta E_{Dmax} = \frac{\dot{V}_{O_2max} - 3.5}{3.5} \frac{4.2 \times 10^3}{3600} m \tag{36}$$

$\dot{V}_{O_2max}$ is a function of heart rate and gender. Plug ΔE_{Dmax} into the formula of $\delta r(t_0')$, it turns out to be

$$\delta r(t_0') = -a + \sqrt{a^2 - \frac{\dot{V}_{O_2max} - 3.5}{3.5} \frac{4.2 \times 10^3}{3600} \frac{m\beta}{\mu k_B < T_b >}} \tag{37}$$

$\delta r(t_0')$ must be real number, so when one's physical exercise reaches its limit, ΔE_D reaches its maximum, and $\delta r(t_0') = -a$, which implies:

$$a = \sqrt{\frac{\dot{V}_{O_2max} - 3.5}{3.5} \frac{4.2 \times 10^3}{3600} \frac{m\beta}{\mu k_B < T_b >}} \tag{38}$$

a in model (10) is a parameter concerned with the hear rate, gender and weight of a definite individual, with dependence on μ. In (23) the 3 parameters have only 1 constraint, now take (38) into consideration, we get the relation of μ and ω:

$$\frac{\mu}{4}[3(\frac{\mu}{\omega})^2 + 8a(\mu)^2 - 4a(\mu)] = \frac{\beta}{k_B < T_b >} B_{m(f)}\sigma \tag{39}$$

From (38), $a(\mu) \sim \frac{1}{\sqrt{\mu}}$, ω is implicitly written as

$$\omega^{-2} = \frac{1}{3\mu^2}(\frac{4\beta}{\mu k_B < T_b >} B_{m(f)}\sigma + 4a(\mu) - 8a(\mu)^2) \tag{40}$$

Notice that $0 < \frac{\mu^2}{\omega^2} < \frac{1}{6}$ we get

$$0 < \frac{4\beta}{\mu k_B < T_b >} B_{m(f)}\sigma + 4a(\mu) - 8a(\mu)^2 < \frac{1}{2} \tag{41}$$

For a given individual, if we know the age, gender, and height, it is not difficult to estimate the interval of μ. Here, lack of detailed document of some healthy adult, we generally estimate an interval of μ, neglecting the age, gender and height, using $3.5\dot{V}_{O_2}m = \frac{7}{6}m \quad J.s^{-1}$ at rest state to substitute $B_{m(f)}\sigma$, the heart rate 170 per minute to substitute the maximum heart rate. Plug the maximum heart rate into (34) we get:

$$a = \sqrt{\frac{39.93 - 3.5}{3.5}\frac{4.2 \times 10^3}{3600}\frac{m\beta}{\mu k_B < T_b >}} \approx \sqrt{\frac{70}{6}\frac{m\beta}{\mu k_B < T_b >}} \tag{42}$$

after some calculation we get the interval of μ:

$$0 < \sqrt{\mu} < \frac{76\sqrt{\frac{7}{6}\frac{m\beta}{k_B<T_b>}}}{2\sqrt{10} + \sqrt{2}} \tag{43}$$

or

$$\sqrt{\mu} > \frac{76\sqrt{\frac{7}{6}\frac{m\beta}{k_B<T_b>}}}{2\sqrt{10} - \sqrt{2}} \tag{44}$$

We take the former condition and drop the latter, because in Van der Pol model, $\frac{\mu}{\omega}$ is a small parameter. Even though we can not get the explicit value of μ, we find out that μ is related to body weight and body temperature. Most of the time, the body temperature is stable, so μ will change after m. If some one suffers fever, μ will decrease.

The last task is to estimate the parameter ω. Use the relation (18):

$$\frac{k_B < T_b > \mu}{4}(3\frac{\mu^2}{\omega^2} + 8a^2 - 4a) = \beta \sum_{T_b} T_b \frac{d_i s}{dt}\sigma(T_b) \tag{45}$$

Take the largest μ:

$$\mu = \frac{76^2 \frac{7}{6}\frac{m\beta}{k_B<T_b>}}{(2\sqrt{10} + \sqrt{2})^2} \tag{46}$$

Still we use the relation $3.5\dot{V}_{O_2} m = \frac{7}{6}m \quad J.s^{-1}$ to substitute the entropy production rate on the right hand side of (45). Then the average entropy production is:

$$\beta \frac{\frac{7}{6}m}{< T_b >} J.K^{-1}.s^{-1} \tag{47}$$

plug it into (45) we get:

$$\omega^{-2} = \frac{4\sqrt{\frac{70}{6}\frac{m\beta}{\mu k_B<T_b>}} - 8\frac{70}{6}\frac{m\beta}{\mu k_B<T_b>} + \frac{\frac{7}{6}m\beta}{k_B<T_b>}}{3\mu^2} \tag{48}$$

So $\omega^{-2} \propto (\frac{k_B<T_b>}{m\beta})^3 + const \quad (\frac{k_B<T_b>}{m\beta})^2$, this means that the "distance" to equilibrium $\frac{\mu}{\omega}$ is related to the order like:

$$\frac{\mu}{\omega} \sim \sqrt{\frac{m\beta}{k_B < T_b >} + const} \tag{49}$$

const is some constant. For the qualitative estimation, we do not care the exact number of the constant. $\frac{\mu}{\omega}$ in our model is related to body temperature. So the increase of body temperature drives the system "nearer" from equilibrium.

This interesting result shows that the "distance" from equilibrium is related to body temperature and body weight. However, body temperature is stable quite often, so body weight is an important index. As we can see, $\frac{\mu}{\omega}$ is in roughly proportion to body weight. This means that the increasing of body weight drives the system "farther" from equilibrium. ω is reverse proportion to m. This means that overweight decreases the frequency of metabolism. So the cost of sustaining life when someone is overweight is established on decreasing the metabolism frequency. Low frequency of metabolism is harmful to our health. Surely high frequency of metabolism is also harmful, but in this paper we just discuss the case of healthy adults. The unhealthy case is to discuss in other paper.

5 Conclusion and remarks

So far we have established the mathematical model of healthy adults' energy metabolism. The parameter a in the model corresponds to the cardiorespiratory, which gives the limit of one's physical ability. μ and ω are mainly related to body temperature and body weight, which are important criterion to confirm whether the life will sustain or end. What is more, a depends on μ and ω which are all related to body temperature, body weight and heart rate etc, even though we have already used the simplest case to estimate these parameters. From this result , we have to conclude that every organ in human body is related to each other.

The parameters estimated in our model are all based on the healthy adults, so if the body weight is too light, it will of course cause some other illness. This needs discussing by the clinical data of from the patients.

6 Acknowledgement

The author would like to thank

This work is supported by...

References

[1] Lauralee Sherwood. *Human physiology: from cells to systems.* Cengage learning, 2015.

[2] Matthew J Kluger. *Fever: its biology, evolution, and function.* Princeton University Press, 2015.

[3] Anthony S Fauci et al. *Harrison's principles of internal medicine*, volume 2. McGraw-Hill Medical New York, 2008.

[4] James P Keener and James Sneyd. *Mathematical physiology*, volume 1. Springer, 1998.

[5] Stephanie E Pierce. Non-equilibrium thermodynamics. *Cross Bound–Interdis J*, 1:49–59, 2002.

[6] Leopoldo S García-Colín and Leonardo Dagdug. Non-equilibrium thermodynamics. In *The Kinetic Theory of a Dilute Ionized Plasma*, pages 5–11. Springer, 2009.

[7] T Chou, K Mallick, and RKP Zia. Non-equilibrium statistical mechanics: from a paradigmatic model to biological transport. *Reports on progress in physics*, 74(11):116601, 2011.

[8] Lars Onsager. Reciprocal relations in irreversible processes. i. *Physical Review*, 37(4):405, 1931.

[9] Lars Onsager. Reciprocal relations in irreversible processes. ii. *Physical Review*, 38(12):2265, 1931.

[10] Sybren Ruurds De Groot and Peter Mazur. *Non-equilibrium thermodynamics*. Courier Dover Publications, 2013.

[11] P Glansdorff and Ilya Prigogine. Structure, stability and fluctuations. *New York, NY: Interscience*, 1971.

[12] Ilya Prigogine. Introduction to thermodynamics of irreversible processes. *New York: Interscience, 1967, 3rd ed.*, 1, 1967.

[13] Gregoire Nicolis and Ilya Prigogine. *Self-organization in nonequilibrium systems*, volume 191977. Wiley, New York, 1977.

[14] Jia Shao, Sergey V Buldyrev, Lidia A Braunstein, Shlomo Havlin, and H Eugene Stanley. Structure of shells in complex networks. *Physical Review E*, 80(3):036105, 2009.

[15] Sergey V Buldyrev, Roni Parshani, Gerald Paul, H Eugene Stanley, and Shlomo Havlin. Catastrophic cascade of failures in interdependent networks. *Nature*, 464(7291):1025–1028, 2010.

[16] Jianxi Gao, Sergey V Buldyrev, Shlomo Havlin, and H Eugene Stanley. Robustness of a network of networks. *Physical Review Letters*, 107(19):195701, 2011.

[17] Jianxi Gao, Sergey V Buldyrev, H Eugene Stanley, and Shlomo Havlin. Networks formed from interdependent networks. *Nature physics*, 8(1):40–48, 2012.

[18] John E Hall. *Guyton and Hall textbook of medical physiology*. Elsevier Health Sciences, 2015.

[19] Zhifen Zhang, Tongren Ding, Wenzao Huang, and Zhenxi Dong. *Qualitative theory of differential equations*. Science Press, 1985.

[20] Balth Van der Pol. Lxxxviii. on relaxation-oscillations. *The London, Edinburgh, and Dublin Philosophical Magazine and Journal of Science*, 2(11):978–992, 1926.

[21] H Giacomini, J Llibre, and M Viano. On the nonexistence, existence and uniqueness of limit cycles. *Nonlinearity*, 9(2):501, 1996.

[22] Hector Giacomini, Jaume Llibre, and Mireille Viano. On the shape of limit cycles that bifurcate from hamiltonian centers. *Nonlinear Analysis: Theory, Methods & Applications*, 41(3):523–537, 2000.

[23] Mark D Mifflin, Sachiko T St Jeor, Lisa A Hill, Barbara J Scott, Sandra A Daugherty, and YO Koh. A new predictive equation for resting energy expenditure in healthy individuals. *The American journal of clinical nutrition*, 51(2):241–247, 1990.

[24] Luís B Sardinha, Analiza M Silva, Claudia S Minderico, and Pedro J Teixeira. Effect of body surface area calculations on body fat estimates in non-obese and obese subjects. *Physiological measurement*, 27(11):1197, 2006.

[25] American College of Sports Medicine et al. *ACSM's guidelines for exercise testing and prescription*. Lippincott Williams & Wilkins, 2013.

[26] WH Van der Walt and CH Wyndham. An equation for prediction of energy expenditure of walking and running. *Journal of Applied Physiology*, 34(5):559–563, 1973.

[27] Eric Ravussin and Clifton Bogardus. Relationship of genetics, age, and physical fitness to daily energy expenditure and fuel utilization. *The American Journal of Clinical Nutrition*, 49(5):968–975, 1989.

[28] David C Nieman. *Exercise testing and prescription: a health related approach*. McGraw-Hill Companies, 2003.