MATHEMATICAL MODELING OF THE TEMPERATURE-DEPENDENT GROWTH OF LIVING SYSTEMS

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(**Received: November 15, 2007 - Accepted in Revised Form: May 9, 2008)**

Abstract In this investigation a non-equilibrium thermodynamic model of the temperature dependent biological growth of a living systems has been analyzed. The results are derived on the basis of Gompertzian growth equation. In this model, we have considered the temperature dependent growth rate and development parameter. The non-equilibrium thermodynamic model is also considered for exploring the variation of growth rate with temperature. The biological growth process of a living system near the threshold temperature has been studied. The growth rate has been taken as general function of temperature. The analytical solution has been obtained by solving differential equation governing the model. The solution of non linear equation provides an expression for biomass of the living systems at a time t, which is valid for a temperature near the threshold temperature. The numerical experiment has been conducted to exhibit the effects of various parameters on growth. The physical conditions of a living systems for different value of activated constant energy and gas, has been examined.

Keywords Temperature Dependent Growth, Threshold Temperature, Gompertz Growth, Non-Equilibrium Thermodynamic Model, Living Systems

چکیده در این تحقیق، یک مدل ترمودینامیکی غیر تعادلی برای رشد بیولوژیکی وابسته به دمای سامانه زنده تحلیل شده است. نتایج براساس معادله رشد گمپرزین بدست آمده است. در طراحی مدل، نرخ رشد وابسته به دما و پارامتر توسعه در نظر گرفته شده است. مدل ترمودینامیکی غیر تعادلی همچنین برای تعیین تغییر نرخ رشد براثر دما در نظر گرفته شده است. فرایند رشد بیولوژیکی سامانه زنده نزدیک دمای حدی در نظر گرفته شده است. نرخ رشد تابع کلی دما انگاشته شده است. پاسخ تحلیلی از طریق حل معادله دیفرانسیل حاکم بدست آمده است. حل معادله غیر خطی رابطه ای برای "جرم ریستی" سامانه زنده در زمان t نتیجه می‌دهد که در نزدیکی دمای حدی معتبر است. آزمایش عددی برای نمایش تاثیر عوامل مختلف بر رشد انجام شده است. شرایط فیزیکی سامانه زنده برای مقادیر متفاوت انرژی تحریک ثابت و گاز، امتحان شده است.

1. INTRODUCTION

As per physiology, the specific characteristics and mechanisms of a human body is called a living system. The basic living unit of a body is a cell. Each organ is an aggregate of many different cells held together by intercellular supporting structures. Each type of cell is specially adapted to perform one or few particular functions. Furthermore, the general chemical mechanisms for changing nutrients into energy are the same in all cells. Almost all cells have ability to reproduce new cell of particular type. From the nutrient distributions it is possible to model different types of growth processes, which are driven by the local amount of available nutrients. Biological growth is represented by additional layers of material on top of the previous growth stages. The biological growth is being used to assess the state of the physical environment. The development of a higher organism is controlled by a complex network of biochemical reactions.

The study of biological growth of living organism is one of the fundamental problems of biological

sciences. There are some studies describing the growth processes. Modern theories concerning growth equation in thermodynamics of biological processes have been given by Walter, et al [1]. Zotin, et al [2] suggested thermodynamics of biological processes. Non-equilibrium thermodynamics and biological growth and development were discussed by Lurrie, et al [3]. Thermodynamic and kinetics of biological processes was given by Zotin, et al [4]. These studies are quite important for motivating research workers to work in this direction. There hasn't been much work done in this particular area. Terranova, et al [5] illustrated that human endothelial cells maintained in the absence of fibroblast growth factor undergo structural and functional alterations which are incompatible with their in vivo differentiated properties. Kooijman [6] presented the growth rate as a function of physiological parameters of comparative analysis in mathematical ecology. Sporn, et al [7] proposed, peptide growth factors are multifunctional. Spatial and spatio-temporal patterns in a cell-haptotaxis model have been given by Maini [8]. A simple model for the effects of receptor-mediated cell-substratum adhesion on cell migration has been considered by Lauffenburger [9].

DiMilla, et al [10] gave mathematical model for the effects of adhesion and mechanics on cell migration speed. Plata-Salaman [11] suggested a model dependent on epidermal growth factor and the nervous system. Paul, et al [12] illustrated a bone tissue growth enhancement by calcium phosphate coatings on porous titanium alloys. Variation in growth, sources of nitrogen and N-use efficiency by provenances of Gliricidia sepium have been given by Sanginga, et al [13]. Gompertz survival kinetics in case of fall in number of lives has been dicussed by Euston [14]. Chakrabarti, et al [15] proposed the non-equilibrium thermodynamics and stochastic model of Gompertzian growth. Noble, et al [16] analysed the growth factors glia and gliomas. Maheshwari, et al [17] explained scientifically the deconstructing and reconstructing cell migration. Miklos [18] presented the analysis of methylglyoxal in living organisms considering the chemical, biochemical, toxicological and biological implications. Daniela, et al [19] analysed the visualization of caveolin-1, a caveolar marker protein, in living cell. They modulated the subcellular distribution of caveolin-1 by cell-cell contact. Tachibana, et al [20] studied the up-regulation of nuclear protein import by nuclear localization signal sequences in living cells.

Huang, et al [21] investigated the shape-dependent control of cell growth, differentiation, and apoptosis. Gerhard, et al [22] differentiated between domain growth and interfacial melting. International standards for hepatocyte growth factor/scatter factor, initial assessment of materials and their evaluation were studied by Rafferty, et al [23]. Vascular endothelial growth factor and other biological predictors related to the postoperative survival rate on non-small cell lung cancer have been given by Liao, et al [24]. Cornel, et al [25] discussed the caenorhabditis elegans receptors related to mammalian vascular endothelial growth factor. Jean-Christophe, et al [26] studied mesenchymal cells potentiate vascular endothelial growth factor-induced angiogenesis in vitro. Elizabeth, et al [27] discussed the differential growth rates of tongue regions in humans. Ingolf [28] gave a coherent account of calorimetry and thermodynamics of living systems. Holly, et al [29] worked on the growth of hormone administration to long-living dwarf mice alters multiple components of the antioxidative defense system. New detection system for toxic agents based on continuous spectroscopic monitoring of living cells was developed by Ioan, et al [30]. The unique exponential growth of life powered by anaerobic glycolysis has been considered by John [31]. Robert, et al [32] proposed a forest growth and biomass module for a landscape simulation model wherein design, validation, and application have been ensured. Nicola, et al [33] discussed the growth and characterization of a cell culture model of the feline blood–brain barrier. Pescheck, et al [34] explained the novel electrochemical sensor system for monitoring metabolic activity during the growth and cultivation of prokaryotic and eukaryotic cells. Brownlee, et al [35] considered the prorocentrum minimum blooms and potential impacts on dissolved oxygen and chesapeake bay oyster settlement and growth. Lisbeth, et al [36] suggested the real-time measurement in living cells of insulin-like growth factor activity using bioluminescence resonance energy transfer. Roles of insulin-like growth factor (IGF) binding proteins in

regulating IGF actions were discussed by Cunming, et al [37]. Suzuki, et al [38] found that single protein production in living cells is facilitated by an mRNA interferase. Protein transduction therapy for anti-cancer effect on the growth of human malignant glioma cells has been considered by Michiue, et al [39]. Pavel, et al [40] presented a review of dietary polyamines. This study included the formation, implications for growth and health and occurrence in foods. Maria, et al [41] illustrated that the biologic substances present in human colostrums and demonstrated the evolution of essential nutrient for growth and development.

In most existing models, the parameters are taken either constant or independent of temperature. But, it is found that every living organism survives within a certain temperature range. When the temperature crosses the boundary or tolerance limit, the living organism dies. So far a realistic picture of biological growth process is concerned, the growth rate should be temperature dependent. The present study deals with a model of temperature dependent growth process by assuming growth rate as general function of temperature. A particular case is considered for exploring the effect of temperature on growth. The rest of the paper is organized in various sections as follows. In Section 2, we describe the basic model with assumed notations, which are used in this model for growth process. In Section 3, we explore the system parameters for numerical illustration. The effect of temperature is also explained in descriptive form as well as graphically. Finally, the conclusions are drawn in the Section 4.

2. THE MODEL DESCRIPTION

For the modelling purpose, let us consider the mass m as a function of time t i.e. m(t). Let μ be the growth rate at t = 0, and δ be the development parameter. When m is not dependent on temperature, it depends only on time t, and then the Gompertz growth equation of the living systems is described as follows:

$$\frac{dm(t)}{dt} = \mu e^{-\delta t} m \tag{1}$$

Where, μ and δ are greater than zero. Equation 1 is the basic growth equation, which is time dependent and independent of temperature. The solution of this equation with conditions

$$m(0) = m_0 > 0,\ m(\infty) = M > m_0 \tag{2}$$

is as follows

$$m(t) = m_0 e^{-\frac{\mu}{\delta}(1-e^{-\delta t})} \tag{3}$$

Here m_0 is the initial mass of an organism at time t = 0 and M is the final mass at time $t = \infty$. Again let T_c be the threshold temperature, E activated constant energy and R gas constant. Let us now suppose that the growth rate μ depends on temperature T, defined by general function as follows:

$$\mu = \mu_0 \frac{E}{R} f\left(\frac{1}{T} - \frac{1}{T_c}\right) = \mu(T) \tag{4}$$

With conditions

$$\mu_0 = \mu(T_c) > 0,\ T \geq T_c = \frac{E}{4R} \tag{5}$$

Now, substituting the value of μ in Equation 1, we get the modified growth equation as follows:

$$\frac{dm}{dt} = \mu_0 \frac{E}{R} f\left(\frac{1}{T} - \frac{1}{T_c}\right) e^{-\delta t} m \equiv \psi(T,t)\text{, (say)} \tag{6}$$

Above Equation 6 is the tempreture dependent general growth equation.

2.1. Special Case I

Let

$$f\left(\frac{1}{T} - \frac{1}{T_c}\right) = \cos\left(\frac{1}{T} - \frac{1}{T_c}\right) \tag{7}$$

Then the particular temperature growth rate is

$$\mu = \mu_0 \frac{E}{R}\cos\left(\frac{1}{T} - \frac{1}{T_c}\right) = \mu(T) \quad (8)$$

Using Equation 8, Equation 1 can be written as

$$\frac{dm}{dt} = \mu_0 \frac{E}{R}\cos\left(\frac{1}{T} - \frac{1}{T_c}\right)e^{-\delta t}\ m \equiv \phi(T,t)\ , \text{(say)} \quad (9)$$

With initial conditions

$$\mu_0 > 0,\ T \geq T_c \quad (10)$$

Now the solution of Equation 10 can be obtained as

$$m = m\exp\left\{\frac{\mu_0}{\delta}\frac{E}{R}\cos\left(\frac{1}{T} - \frac{1}{T_c}\right)(1 - e^{-\delta t})\right\} = m(T, t) \quad (11)$$

Let the temperature be equal to the threshold temperature i.e. at $T = T_c$ and mass equals to the initial mass i.e. $m = m_0$, then the above Equation 11 yields

$$m = m_0 \exp\left\{\frac{\mu_0}{\delta}\frac{E}{R}(1 - e^{-\delta t})\right\} = m(T,t) \quad (12)$$

Equation 9 describes a temperature dependent Gompertzian growth and it is the first order non-homogeneous differential equation. But, Equation 12 does not contain any term of temperature at $T = T_c$. That is why, we are interested for solution near the threshold temperature (T_c).

We proceed for the approximate solution for T sufficiently near the threshold temperature (T_c). This can be done by Taylor's series expansion, with the initial condition

$$m(T,0) = m(T_c,0) = m_0 > 0 \quad (13)$$

Which is as follows:

$$m(T,t) = m(T_c,t) + (T - T_c)\frac{\partial m}{\partial T} + \frac{(T - T_c)^2}{2!}\frac{\partial^2 m}{\partial T^2} + \frac{(T - T_c)^3}{3!}\frac{\partial^3 m}{\partial T^3} \quad (14)$$

At T near T_c, and after neglecting the higher power derivatives, we have

$$m(T) = m_0\left[1 + \frac{(T - T_c)^2}{2!}\frac{\mu_0}{\delta}\frac{E}{R}\frac{1}{T^4}\right] \quad (15)$$

Equation 15 determines the mass of an organism at a time t for temperature T near the threshold value T_c. In this solution we see that the total mass of an organism basically depends on two components. First one is initial mass and second one is temperature. It is zero, if we take the temperature equal to the threshold temperature T_c.

In this case, the example of periodic cell growth with respect to temperature can be realized in case of Malaria patients.

2.2. Special Case II In this case, we choose the growth rate as exponential function which is given by:

$$\mu = \mu_0 \exp\left\{-\frac{E}{R}\left(\frac{1}{T} - \frac{1}{T_c}\right)\right\} \equiv \mu(T) \quad (16)$$

The final solution of Equation 1 with the initial condition

$$\text{at } T = T_c,\ (T,0) = m(T_c,0) = m_0 > 0,\ a = \mu_0/\delta \quad (17)$$

is as follows:

$$m(T,t) = m_0 e^{-a(1 - e^{-\delta t})} + \frac{m_0(T - T_c)Ea}{RT_c^2}(1 - e^{-\delta t})e^{-a(1 - e^{-\delta t})} \quad (18)$$

Where

$$a = \frac{m_0 \mu_0 E}{R\,T_c^2} \quad (19)$$

Here, Equation 18 determines the mass of organism at any time t and near the threshold temperature T_c. In this solution, we see that the total mass of an organism is the addition of two components. First one is time dependent and second one is both time and temperature

dependent. If we choose, the temperature T equal to the threshold temperature T_c, then it is zero and mass is same as in Equation 2. So the time dependent growth rate gives additional contribution to the biomass production.

In case of non-equilibrium thermodynamic temperature dependent growth, it is worthwhile to mention that the biological growth is the consequence of the process of complex chemical reactions. So, this theory of biological growth is based on the process of metabolism. The flux can be obtained by using the following formula:

$$J = \frac{1}{m}\frac{dm}{dt} \tag{20}$$

For the biological growth and development there are some restrictions, mathematically one of which is as follows:

$$|\delta.t| << 1 \tag{21}$$

Above equation shows that, either the time t or the value of development parameter δ must be very small. For maximum growth of the living system we assume the time $t_m = 1/\delta$.

The linear approximation between development parameter δ and time t can be taken as follows:

$$e^{-\delta t} = 1 - \delta.t = \delta(t_m - t) \tag{22}$$

Also the thermodynamic force can be taken as follow:

$$X = k(t_m - t) \tag{23}$$

Here, the thermodynamic force X is proportional to $(t_m - t)$, k being constant to adjust the dimension of force X. Using Equations 22 and 23, we get:

$$e^{-\delta t} = \delta X / k \tag{24}$$

Now using Equation 17, mass is thermodynamically as follows:

$$m(T,t) = m_0 e^{-a(1-e^{-\delta t})} + m_0 \beta (1-e^{-\delta t}) e^{-a(1-e^{-\delta t})} \tag{25}$$

Where,

$$\beta = \frac{(T - T_c) E a}{R T_c^2} \geq 0, \quad a = \mu_0 / \delta \tag{26}$$

In terms of thermodynamic force, the flux can be expressed as follows:

$$J(X) = L(X) X \tag{27}$$

Where, L(X) is the phenomenological coefficient and is given by:

$$L(X) = \frac{a\delta^2}{k}\frac{(X - b)}{X - C} \tag{28}$$

The coefficient b and C are obtained using

$$b = \frac{k(a + \beta + \beta a)}{a \beta \delta}, \quad C = \frac{k(1 + \beta)}{\delta \beta} \tag{29}$$

Here, we see that the thermodynamic flux J(X) is a non-linear function of thermodynamic force X. It is also seen that the flux J(x) and the phenomenological coefficient L(X) both are the non-linear functions of temperature T. It tends to zero, if X tends to zero.

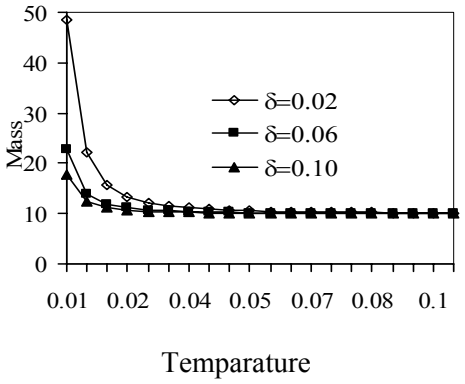
In case of HIV-2 patients, the cell growth can be realized exponential with respect to the temperature.

3. NUMERICAL ILLUSTRATION

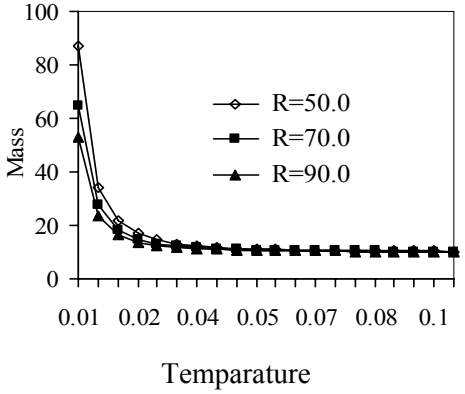
In this section, we present the numerical results to explore the effect of temperature on flux, the phenomenological coefficient and different parameters on the growth of mass. For this purpose, we use Equations 11, 14 and 17 for temperature dependent mass of living system. Computer program is developed in software MATLAB and run on Pentium IV.

In special case I, the growth of mass for different values of parameters, is examined and shown in figure 1, taking threshold temperature Tc = 0.001 unit and time t = 10.0 units. Figure 1a shows the growth of an organism with temperature

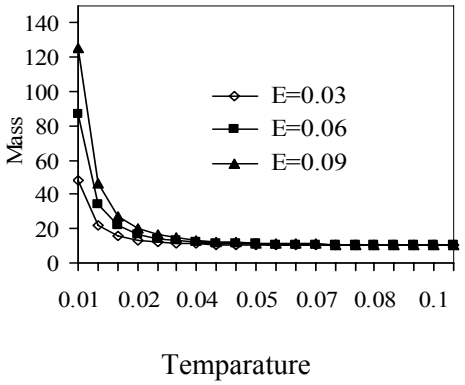
for different values of δ taking R = 100 and E = 0.03. It is observed that the mass decreases upto 0.03 unit temperature very rapidly after that it is almost constant. Figure 1b depicts the growth in mass for different values of R, and δ = 0.020 and E = 0.03. In this case decrease in mass growth is sharp upto T = 0.02 and then, it tends to be constant. In Figure 1c mass growth is shown by



(a)



(b)



(c)

Figure 1. Mass growth vs. temperature for special case-I by varying (a) δ, (b) R, (c) E.

varying E and taking δ = 0.020 and R = 100. We notice that the trend of mass growth in this case is also the same as in case 1b. The mass growth of an organism is shown in Figure 2 for special case II taking threshold temperature Tc = 0.001 unit and time t = 10.0 units.

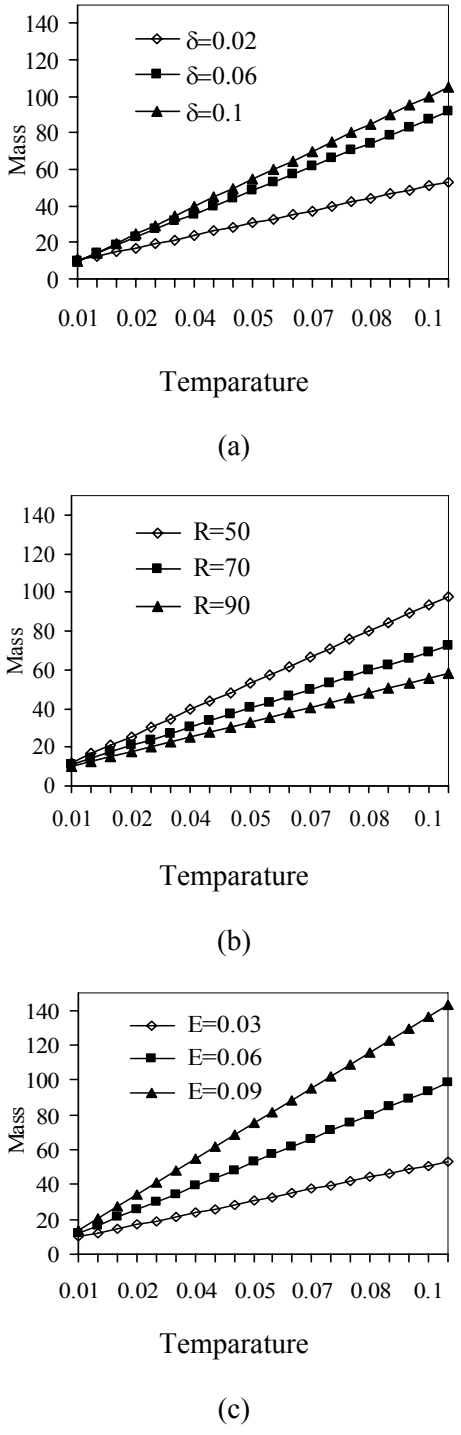
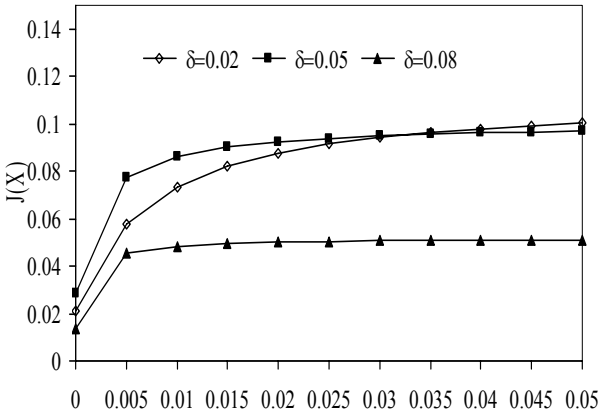


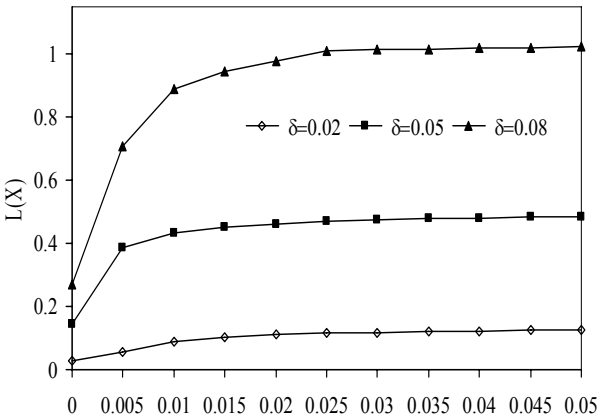
Figure 2. Mass growth vs. temperature for special case II by varying (a) δ, (b) R, (c) E.

From Figure 2a, we see that the mass increases with the increase in the temperature for various values of δ by fixing R = 100 and E = 0.03. The increase in all the three cases is sharp and linear, then δ has a positive effect on growth of mass. The mass growth with temperature is shown in Figure 2b. The linear increasing trend for fixed parameters value δ = 0.020 and E = 0.03 is similar as in Figure 2a, but growth decreases with the increase in R. Figure 2c also depicts the same linear trend, for different values of E, when parameters are set as δ = 0.020 and R = 100. Furthermore the increasing value of E reduces the growth.

The thermodynamic flux J(x) and phenomenological coefficient L(X) are evaluated and shown by the Figure 3a,b respectively for different values of δ and fixed parameter values R = 100, E = 0.03, threshold temperature Tc = 0.001 unit and time t = 10.0 units. The flux J(X) initially increases sharply and then after becomes almost constant. With regards to the effect of development parameter δ, J(X) increases for δ = 0.05 in comparison to δ = 0.02 upto temperature = 0.035. However beyond temperature = 0.035, J(X) is higher for δ = 0.02 in comparison to δ = 0.05. For δ = 0.08, J(X) much lower than the above values. Regarding, phenomenological coefficient L(X), Figuer 3b shows that for δ = 0.08, it rises very sharply for lower value of T, then after all three cases the trend is almost constant value. Figure 3a,b shows that the effect of temperature is prominent initially for the growth of mass. It is concluded that the non-equilibrium thermodynamic model leads to a non-linear phenomenological relation with its coefficient and force.



(a)



(b)

Figure 3. Effect of temperature for different value of δ on (a) flux {J(X)} (b) phenomenological coefficient {L(X)}.

4. CONCLUSION

By analysing the growth process of a living systems, it became apparent that, animals die at higher temperature, also biomass decreases with increasing temperature special case-I, biomass increases with increasing temperature special case-II. Some times growth pattern due to complexity of the medium, is impractical to measure cell mass. In these cases growth can be measured by determining the amount of mass. Such measurements are often the most practical way to determine the microbial mass and growth in a natural environment. It is known that, living organisms could survive up to a tolerance limit of temperature but they die excceding the tolerance limit. The tolerance range varies form species to species. We hope that our study will be helpful in providing insights of non-linear thermodynamic growth of living organisms, which may be the cause of different diseases such as influenza, smallpox and etc.

5. ACKNOWLEDGEMENTS

The authors are thankful to the learned referees for their fruitful suggestions for improving the presentation of this work.

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