

Growth curve: an intelligent life history described by a mathematical model using the Practical Program for Forces Modeling spreadsheet

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ABSTRACT

The Practical Program for Forces Modeling (PPFM) spreadsheet is an innovative tool that analyzes the growth process and its history (phases and strategies). The biggest differential is in unfolding the evaluation according to the Newtonian point of view. To do so, the PPFM begins its process in a traditional way, by adjusting growth curves using the least square method, with subsequent unfolding of derivatives. The first derivative represents velocity and the second derivative characterizes acceleration. From this, its prerogative arises, the Newtonian phase of the evaluation, through the well-known formula $F = m \times a$ allows to define with great precision the transition between eight possible phases (lag, log up, linear, log down, plateau, death, spurt and resilience), which represent the most favorable strategies to follow this path. Finally, the spreadsheet calculates another novelty, the useful work (action = energy \times time) necessary to promote the growth process according to the period of time evaluated.

1. INTRODUCTION

A mystery! This is a classic answer to define what growth is (von Bertalanffy, 1952 p. 136). The growth process is probably the most common occurrence and observed in several systems, biological or not (Burkhart & Tomé, 2012; Dadson et al., 2017; Parker, 2012). How does it occur? It is easily observable with the naked eye. So, it is feasible to certify that growth generally follows a sigmoid curve (S-shaped), this being a universal characteristic. Still, visually it is allowed to contemplate different phases in its path (Bertin, 2014; Pommerening & Grabarnik, 2019).

The typical sigmoid growth behavior is well known and studied, generally including three defined stages: lag, log or exponential and stationary phase. However, other phases are still possible: death, spurts, increasing exponential, quasi-linear phase, decreasing exponential and resilience phases (Dandurand & Shultz, 2010; Legan et al., 2002; Meredith et al., 2018). Thus, the most

important thing is not only to characterize the geometric trend of growth, but to define the various phases and different strategies that describe its trajectory (Levert & Xia, 2001).

Therefore, in order to delve deeper into the essence of this enigma and contribute to answering other challenge, it is essential to understand why several stages in the growth process are necessary, this question actually represents the essence of the mystery (Grimm et al., 2011). This mystery presents strategies and optimizations (Karkach, 2006). The most common procedure for describing growth proposes to adjust the data in a mathematical model with few interpretable parameters, and the higher the complexity of the growth curve, the greater the number of parameters required. Because of that, the ideal model should predict the experimental values with the minimum number of parameters and still offer a good prediction of growth behavior (Ricklefs, 1983).

2. A STATE OF ART

2.1 THE ACTION PRINCIPLE

The dynamics of growth in biological (or not) structures, although complex, follow basic physical laws, allowing the approximation of Mathematics and Biology (Penna & Oliveira, 2008). Action, in physics, is an attribute of the dynamics that presents the scalar dimension: energy \times time. That is, the integral of the whole process, from the beginning to the end, that in biology would be the study of the growth of an organism (birth to maturation). In this way, biology resembles, but it does not equate to physics, because its flexibility allows and desires vitality and quality of life (Grandpierre, 2011a).

Power is a measure of how fast a job is done (J / s). The action, on the other hand, clarifies how great the performance of work is in a given period of time ($J \times s$) (Girtler, 2011a). Thus, the action presents as quantitative base the dimension energy \times time, integrating the evaluation of the entire interval of the event under consideration, from the beginning until its end endpoint (Grandpierre, 2011b). The growth equation could be described as an integral, by describing what was accumulated to form an organism during its developmental path (Zeide, 1993). Then, the Action is the sum of the energy changes observed at each time interval and can be considered as a cost function that aims to optimize a problem, which is very coherent in biological terms. From this fact, the sum of all energy changes in consecutive time intervals in relation to the total period, biologically, can be considered as the product of energy investment \times time investment (Grandpierre, 2013).

Thereby, action defines a numerical unit that affects both vitality (as high as possible) and longevity (as long as possible), a fact naturally desired by all living beings (Grandpierre, 2007). Such a procedure is compatible with being considered as a function of optimizing the most valuable resources for life (energy and time), paving the way to enter quantum biology (Grandpierre, 2013). But what is so beautiful about the principle of action? Perhaps it is because it has a compact structure, which allows measuring not a fixed moment in time. But since it is associated with the whole, it measures change. Thus, a history is summarized only in a single value, which offers perfect lucidity of an event (Grandpierre, 2008). Now, for that reason, action allows us to describe the whole path of an object whose historical events is summarized in a single number, flexible and dependent on challenges and new circumstances. Really, magical and admirable (Nagao & Nielsen, 2017; Zee, 1999).

Therefore, the fascination and grandeur of the action lies in its ability to describe a history with a number, which considers not only all possible paths between two points, but also all the ways to travel them, even so which at the end of the history only the one who optimizes resources is the one who defines action (energy \times time) (Johnson, 1992; Nagao & Nielsen, 2017). During the growth process, each organism has the opportunity to show its ability to capture and store energy. Thus, acquiring, concentrating, and conserving energy is called more action, and is expressed in energy multiplied by time, and the most efficient will occupy the highest hierarchy level (Vanriël & Johnson, 1995; Owen-Smith, 2005).

Consequently, when one wishes to study relationships and the path from an initial state to its end, the principle of the action of physics shares and clarifies events of biology in a very timely manner. It is possible to generalize that in biology, this concept could be defined as greatest action principle (Johnson, 2006; Grandpierre, 2007). As a result, in biology the study of action affects the growth trajectory of an organism, according to the accumulation of new biomass (kinetic energy), which is finalized when reaching the maximum level in accumulated biomass (potential energy), characterizing the well-known asymptote of the curve (Johnson, 1992). The principle of action presents itself as the most powerful tool in physics that accommodates itself elegantly and harmoniously with biology, and even more can be considered as the "first principle of biology", and thus allow, also, that all the fundamental laws of biology can be derived from the action dimension (Grandpierre, 2008). Therefore, energy is continuously transformed from kinetic (new biomass) to potential (biomass), until it reaches its state of maturity (growth saturation) (Hutzinger, 1989; Jorgensen, 2000).

Action allows a new growth criterion to promote a better evaluation by incorporating not only mass (m), but mainly the effect of velocity (v) and its quadratic attribute (Kinetic energy = $KE = \frac{m \cdot v^2}{2}$) (Kanski et al., 2015). Action is thus the fundamental tool when one wants to study the conditions from the beginning to the end of a growth, development or expansion trajectory (Hanc, 2006; Grandpierre, 2011c). When comparing the action to a cost function, the most fundamental is the optimization of the invested energy and the invested time, being an intelligent process (Grandpierre, 2008). This better quality of life combined with the longest possible duration involves applying useful work that will oppose balance to allow as far and as long as possible. By this procedure, living organisms, through their autonomy, maximize their survival with quality of life by intelligently investing useful work to optimize energy and time (Grandpierre & Kafatos, 2012, 2013). Thereby, the principle of action provides an excellent way to analyze the energy efficiency involved in the intelligent decisions of biological systems. This allows new insights to understand why the route chosen is the most efficient, opening up a new area to apply sustainability by maximizing energy potentials while minimizing negative impacts (Rosen et al., 2008). Therefore, the action principle is the key to assessing growth to its fullest, as it evaluates time and energy investment simultaneously. That is, an organism to grow requires optimizing the time and energy received in life (Bridson & Gould, 2000; Wolynes, 2009), evaluated as the integral of kinetic energy ($KE = \frac{m \cdot v^2}{2}$) in relation to time (Rudnicki, 2009). This results in the history of all useful work and its changes over time, which allows us to characterize the growth of a living organism and its actions to define the best path by being subjected to unexpected and continuous challenges, defining its growth curve (Grandpierre & Kafatos, 2012, 2013; Owen-Smith, 2005).

The better characterized the life span of a living organism and its different phases, the better the action analysis will be (Baty & Delignette-Muller, 2004; Lambertini et al., 2010; Zwietering et al., 1990). In other words, the more precise the definition of the trajectory (curve), the more appropriate is the value obtained for the action, which provides a powerful tool for condensing information about dynamic systems and their whole, and most importantly, which path was chosen in infinite possibilities to reach the endpoint (Grandpierre, 2008). This privilege is now offered by the spreadsheet PPFM, which unfolds the growth curve in its derivatives, with graphical and numerical visualization of the different phases of the path taken, culminating in the action energy-time dimension, which in short defines the history of a system, and not just a fixed moment of time, allowing to incorporate alternative units to characterize growth (height, length, mass, individuals, volume,

density, etc.) and time (seconds, minutes, hours, days, years etc.), that is, biological autonomy (Grandpierre, 2012).

2.2 DERIVATIVES

The derivative of a growth function allows to obtain the absolute growth rate (velocity), and deriving again the curve of the velocity obtains the curve of the acceleration of the growth (Bentea et al., 2017; Szparaga & Kocira, 2018). Jerk represents the derivative of acceleration, that is, three times the derivative of the position (Bentea et al., 2017; Kyriakopoulos & Saridis, 1988). This strange measure is useful in engineering, because when it manifests itself indicating discomfort in relation to passengers in a vehicle (Macfarlane & Croft, 2003; Eager et al., 2016). In amusement parks, Jerk is even appreciated, but on a daily basis it is a reason for liquids to be thrown out of its container, or damage to fragile structures such as egg transport (Jazar, 2011 p.53). In other words, Jerk allows to measure the “vibration” of acceleration (Eager, 2018; Sandin, 1990; Shimojo, 2006), that is, a sudden change in acceleration (Altintas & Erkorkmaz, 2003; Biral et al., 2010; Dong et al., 2007; Schot, 1978). For this reason, the third derivative of the position shows its importance when measuring abrupt changes (Kyriakopoulos & Saridis, 1988).

3 PRACTICAL PROGRAM FOR FORCES MODELING

In order to contribute in a practical way to measure the different stages of growth, we now have a new tool called Practical Program for Forces Modeling (PPFM; <https://sites.google.com/view/ppfm-spreadsheet/>). The PPFM spreadsheet is a user-friendly software that facilitates curve fitting without the need for a thorough knowledge of math (Fujikawa, 2011; Kemmer & Keller, 2010). The PPFM spreadsheet was developed in the 2016 version of Excel. Therefore, it is also compatible for versions higher than 2016. Excel is used worldwide, and is found in most personal computers. Among the several favorable attributes of Excel, macros and VBA (Visual Basic for Applications) facilitate the automation of calculations, it has several graphical facilities, and easy to manipulate data (John, 1998; Kazakis, 2019; Kemmer & Keller, 2010).

Although the PPFM spreadsheet is robust, in order to obtain a reliable return, it is necessary to offer well-distributed data, which allow to describe and adequately represent all the phases contained in the growth behavior. Therefore, to avoid compromise and serious reservations about the quality of adjustments, all regions of the growth curve should have representative data (Barany &

Roberts, 1995), characterizing the entire period evaluated very well. The ideal is to offer at least 10 to 12 points, and also appropriate initial values (guess), to avoid mathematical solutions without biological coherence (Legan et al., 2002; McClure et al., 1994). The adjustment of a model, in relation to the growth data, must be necessary to accurately describe the entire course of the event, being the responsibility of the modeler to determine which is the most appropriate function, among the candidates, to better represent the adjustment, depending on of the data offered (Brisbin et al., 1987; López et al., 2004). Therefore, the PPFM spreadsheet provides models with 4 to 9 parameters.

The PPFM spreadsheet is based on Microsoft-Excel-Solver, which facilitates the understanding and application of the necessary operations, since it has a simple interface (Nemestóthy et al., 2018). Thus, the Excel Solver supplement, in a friendly and dynamic way, requiring the minimum of interventions, due to the fact that the functions are already inserted and the derivatives implemented, all simultaneously and automatically, with visual updated data and graph adjustments (Kemmer & Keller, 2010). In addition, the PPFM spreadsheet results, provided by the Excel editor and their graphs, are straightforward and easy to understand, making adjustments practical and clearly interpreted (Tjørve & Tjørve, 2010; Archontoulis & Miguez, 2015).

Solver is an Excel add-in that enables nonlinear optimization. The PPFM spreadsheet uses the Generalized Reduced Gradient (GRG) option to adjust growth models. For the Solver to operate properly, it is essential to provide coherent and appropriate initial values (guess) to the parameters that define the model (Archontoulis & Miguez, 2015; Strathe et al., 2010). The quality of this procedure is visually confirmed by the immediate graphical adjustment and observation of the residual analysis, predicting possible model fit violations (Strathe et al., 2010), and to compare the performance of models in terms of goodness-of-fit indicator: residual standard deviation, adjusted coefficient of determination (R^2_{adj}), proximity to the truth (Akaike information criterion / AIC) or probability of truth (Bayesian information criterion / BIC) (Wit et al., 2012). For some estimates, a longer time (5-10 minutes) may be required for Solver to finish interactions. Despite this inconvenience, the PPFM spreadsheet solves adjustments for complex growth curves with unfolding phases of the growth process and finalizes the calculation by determining the area (energy × time) that represents the useful work (action) applied in the growth process, and all these steps with graphical visualization of these analyzes (Girtler, 2009ab, 2011; Rudnicki, 2009). Sometimes the model shows itself to be very sensitive to the suggested initial values (guess), which impair or make it impossible to adjust by the Solver. In this case, the appropriate and prudent option would be to change the initial values and proceed with a new optimization (Zach et al. 1984), aiming at good starting parameter values.

VBA macros and codes have been included in the PPFM spreadsheet to facilitate and streamline its use, making it possible to automatically invoke the add-in Solver to minimize the sum of error squares, from iterations that adjust the initial parameters provided by the user, ending with the parameters estimated by the optimizer (Solver) in a simple, precise and somewhat fast way (Zhu & Chen, 2015). However, a criterion is needed to choose the initial starting parameters, so as not to induce the spreadsheet to violate biology (Kebreab et al., 2010), even with an apparent mathematical success provided by the Solver. Therefore, a coherent biological interpretation is required, which must be done with responsibility by the user. Thus, using the facilitating attributes of the Excel PPFM spreadsheet, the period studied can be subdivided into 3000 equidistant parts. This procedure makes it possible to calculate the area over or under the kinetic energy curve as a function of the evaluated time (Girtler, 2011ab).

At that moment, it highlights another great virtue of this calculation, the possibility of measuring up to the unfavorable moment (area over the kinetic energy curve), in which the value is negative, that is, one can now also know and measure the moment of stress or death, which it allows a new approach to this history, by characterizing its different phases and strategies (Firsov et al, 2001). In this way, this negative value, represented by the area over the kinetic energy curve, becomes a sensitive indicator for being precise to monitor the stress period very well (Fekedulegn et al., 2007; Vo et al., 2017). So, the action is an excellent indicator to monitor environmental stress, as it is flexible enough in characterizing and responding to this unfavorable effect at any time during the interval.

4 GROWTH CURVES

Sigmoid curves are often used to describe growth dynamics, and the most widely used models are: Gompertz, Logistic, Richards and Weibull (Beiki et al., 2013; Birch, 1999; Hernandez-Llamas & Kaplan, 2018; Panik, 2013; Tjørve & Tjørve, 2017; Yang et al., 1978; Zullinger et al., 1984). For a better understanding of this form of analysis it is possible to derive the curve to characterize velocity (1st derivative) and acceleration (2nd derivative) (Bentea et al., 2017; Buchanan & Cygnarowicz, 1990; Lambertini et al., 2010; Shahin et al., 2013; Szparaga & Czerwińska, 2017; Szparaga & Kocira, 2018). Up to this point, we are still in classical biology that fits in very well with classical physics, defining the different phases of a curve when evaluating the force involved in growth ($F = m \times a$) (Shimojo et al., 2006).

The mechanistic model and its derivatives (1st velocity; 2nd acceleration) should represent the growth process at the core of its mechanism (Eby et al., 2010; Tabatabai et al., 2005, 2013a; West et al., 2001). Therefore, among the candidate models to compose the PPFM spreadsheet, the function should be explicitly defined. Also, to allow for greater flexibility, the function should have a free inflection point (Cai et al., 2016; Vrána et al., 2019; Zeng & Wan, 2000), or even more inflection points (Ali et al., 2004; Bock et al., 1973; El-Lozy, 1978; Narushin & Takma, 2003; Shahin et al., 2013). To this end, alternative models are offered, allowing to capture the dynamics of growth, which involves its complexity and peculiarity (Bebbington et al., 2009; Cao et al. 2019; Chakraborty et al., 2019; Di Crescenzo & Spina, 2016; Ji & Fang, 2015; Koya & Goshu, 2013; Tjørve & Tjørve, 2010; Windarto et al., 2018).

The adjustment of non-linear models requires iterations (recalculation), taking as reference the suggestions of initial values, even for specialized and sophisticated programs such as SAS (Sauerbrei et al., 2006). Some of these programs are commercial; require a complex knowledge of commands, a lot of training and skill for correct handling (Ozgun et al., 2015). However, the PPFM spreadsheet presents a simple and practical form of use, with automated calculations and a numerical and graphical presentation of its results.

The data from the inputs (time) to outputs (expansion measures) must always be paired and preferably ordered, with or without repetitions (Vedenov & Pesti, 2008). There are several possibilities for measuring time (inputs): seconds, minutes, hours, days, months, years, etc. The important thing is that the time is characterized in the best possible way to accommodate the response data evaluated in the experiment (outputs). Thus, the outputs can be represented by several measurement options: height, width, diameter, volume, mass, optical density, etc.

One of the great virtues of the PPFM spreadsheet is to allow the use of any form of measuring time, as well as the multiple measures of the expansion of a body. This is a virtue of biology's flexibility, which should not necessarily be cast in an international standard or system like physics (Grandpierre, 2011ab). The most relevant is that the principle of action is an area measurement and, therefore, a neutral and unique measure (Girtler, 2011ab). This relevant detail is the greatest virtue presented by the PPFM spreadsheet.

The PPFM spreadsheet, as it presents eight model options for curve fitting, favors the possibility of good fits. However, depending on the complexity of the curve and the number of data pairs, more computational time, dedication and user patience may be necessary in order to obtain an appropriate model conversion, which is always dependent on minimizing the sum of squares of errors

(SSE). This last procedure occurs through the intervention of the Excel Solver and its iterations that allow the optimization of the algorithms (Fujikawa, 2011).

Excel, in addition to the Solver supplement, allows easy manipulation of the data (copy and paste), with immediate ease of numerical and graphical visualization of the results, favoring the necessary adjustments of the initial values that influence the success of the model conversion or not (Kemmer & Keller, 2010). The PPFM spreadsheet incorporates and uses both the Solver and other attributes that facilitate Excel, being offered a tutorial for better handling of the spreadsheet (https://drive.google.com/file/d/1yi9OZeP9q75Uan_BSJhLNqAObhokncLG/view?usp=download).

5 ONTOGENETIC GROWTH FORCE CURVE

The ontogenetic growth force curve represents an innovative basis (Garcia-Neto et al., 2018), of great efficiency to evaluate a biological system or not, since it allows to measure very accurately the addition of new material (interest) continuously during the growth period, offering an economic measure finished in useful work (action) (Girtler et al., 2011ab; Gleiss et al., 2011). Thus, it makes it possible to define the real efficiency of the organism in relation to the production of the new biomass or material, that is, representing the efficiency index of the growth curve. Consequently, the ontogenetic growth force curve is much more sensitive and appropriate to define the transition points of the phases of a growth curve, being automatically determined, making it possible to establish and quantify at least eight phases of the growth curve (Sibly et al., 2015).

In order to measure abrupt changes in the ontogenetic growth force curve (Garcia-Neto et al., 2018), the PPFM spreadsheet proposes to use the resources of the third derivative of that ontogenetic growth force curve, the Snatch or Snap (Davidson & Ringwood, 2017; Mann et al., 2014; Palm et al., 2016; Potvin et al., 2001). It is then possible to define the sudden change that occurs in the ontogenetic growth force curve, precisely in the transition from the Lag phase to the exponential phase (point F0). And also, between the exponential deceleration phase and the saturation phase (point F3). In this way, the Snatch is similar to Jerk in that it has the same ability to measure abrupt changes, being calculated by the force derivative (Easwaran, 2014). Thus, the PPFM spreadsheet automatically calculates Snatch, using the same concept to calculate Tug (T) and Yank (Y) (Lin et al., 2019), from the ontogenetic growth force.

6 THE MECHANICS POINT OF VIEW TO THE BASES OF GROWTH ANALYSIS

From these two derivatives (velocity and acceleration) it is possible to apply the mechanics point of view to the bases of growth analysis, and it is possible to define the growth force ($F = m \times a$), where m = mass of the organism and a = acceleration (second derivative) of its growth (Shimojo et al., 2006). Therefore, using the mathematical properties of mechanics to evaluate the growth of an organism, according to Newton's laws, it is still possible to calculate the kinetic energy ($KE = \frac{m \cdot v^2}{2}$), where v = growth rate (first derivative) (Kanski et al., 2015).

The advantage of using kinetic energy ($KE = \frac{m \cdot v^2}{2}$) as a new way to evaluate the growth to measure different dimension with flexibility and autonomy, that is, one of the great virtues of biology (Kanski et al., 2015; Wong et al., 2018). All this is facilitated by the graphical feature that allows analysis of the area (action) that enables the evaluation of useful work at any point of the path (growth) (Grandpierre, 2014). Finally, the integral of the KE as a function of time yields the Action, which in a simple way would be the sum of all the useful work of the growth path (Girtler, 2011 ab). Despite being recognized for its importance, the principle of action in modern physics is considered as a difficult and obscure topic, and only addressed in very advanced courses and texts (Hanc & Safarik, 2006), and it is stated that even in physics, the potential of its application is still very far from its full potential of use (Grandpierre, 2008).

The unit expressed in $J \times s$ or $N \times m \times s$ is considered problematic to interpret by physics, and thus is very little used (Grandpierre, 2007; Hanc & Safarik, 2006). However, this attribute of physics applied to biology allows a clear interpretation of the principle of action (energy \times time) in biological phenomena. Another reason for the need to use area to measure the action is that at each instant of time changes in the value of kinetic energy, necessitating the use of the integral (Rosen, 2004), than, if energy is time dependent, action must be determined as integral (Dzida & Girtler, 2016).

The action is the investment in growth, that is, the product of the invested energy and the time invested in the evaluated process, and in this way can even be considered as a cost function (Rosen, 1986; Rosen et al., 2008). Therefore, it is again evident that action is not a moment of the trajectory, but always the whole of the trajectory (Gribbin, 1998; Johnson 2006). In this way, the principle of action is virtually universal in terms of application (Johnson, 2006). The principle of action applied to biology offers a great assistance in the understanding of useful work, which enables the expansion of an organism, until reaching its climax of development. The principle of action allows us to evaluate how much free energy was used to perform useful work (growth expansion), indeed, living organisms

have their limits of growth (endpoint), while biologically useful work (Grandpierre, 2014). This allows to evaluate the performance efficiency of the work carried out that makes possible the accumulation of biomass.

7 MEASURING THE PRINCIPLE OF ACTION BY SUMMATION AREA

Perhaps the most fascinating thing is to represent the entire growth process in just a single number, the action (energy × time). Action represents another mysterious topic, even for physics, but it applies perfectly to biology and the growth process (Grandpierre, 2009). Recalling that the first derivative makes it possible to define the velocity (v) at each moment of time. So, again, with the help of the laws of physics, the formula $KE = \frac{m \cdot v^2}{2}$ is applied (Kanski et al., 2015; Wong et al., 2018). Such a simple and majestic procedure now allows obtaining the kinetic energy (KE) required at each moment of the growth process. Hence the action (A = KE × time) that represents the summation area (A), that is, nothing more and nothing less than the useful work applied in the growth process (Girtler, 2011ab).

The area under or over the kinetic energy curve is obtained by adding the areas of the trapezoids, applying the Riemann sum principle (<http://mathworld.wolfram.com/RiemannSum.html>) (Shah et al., 2007). This procedure is performed automatically by PPFM spreadsheet (Excel), which subdivides the period evaluated in 3000 equidistant parts, being calculated the individual area of each trapezoid (<https://www.zweigmedia.com/RealWorld/Excel/tuts/RiemannSum.xls>), resulting in the end in the added area of all of them (Jeger & Viljanen-Rollinson, 2001; Sprouffske & Wagner, 2016).

8 OBJECTIVES

We aim to offer an innovative, useful and practical tool to evaluate the possible eight phases of a growth curve (Lag, increasing exponential, almost linear, decreasing exponential, saturation, death, resilience and spurts phase). In addition, biological parameters can be evaluated from a Newtonian point of view, by analyzing the forces, energy and finally, the useful work (action) that promotes growth, and not just details of its geometric location (displacement, velocity and acceleration) (Simeonov et al., 2012).

9 MODEL AND METHOD

The basic principle of most curve fitting programs for nonlinear models is to minimize the sum of squared errors (SSE) (Kemmer & Keller, 2010), which is also the criterion adopted by the PPFM spreadsheet. Other statistical supports can be seen in the PPFM spreadsheet, such as standard error (SE), confidence intervals and three options for assessing goodness-of-fit (BIC, AIC_c and R^2_{adj}). It is important to understand that the iterative principle is a repetitive procedure of recalculations, by "trials, successes and errors", which in turn is very sensitive to the initial values offered by the user (guess) (Vedenov & Pesti, 2008). Thus, a simple observation of the curve automatically adjusted by manually offered values can be revised to others that are more opportune, allowing to better accommodate the shape of the curve. All this care must always be taken before starting the Solver. Such procedure favors more correct estimates to evaluate the model parameters by the generalized reduced gradient method (Solver) (Fujikawa, 2011). However, there is no definitive and unique solution for a nonlinear model, but the most approximate ones. For this reason, it is prudent to activate the Solver more than once, and observe if the results have been stabilized or if it is possible to further improve the curve adjustment, which is why patience is fundamental in modeling (Vedenov & Pesti, 2008).

As facilitating resources, offers access to the eight models through a mobile menu. In addition, for each model, different spreadsheets are available with free access to the graphics and, if necessary, their copy or changes. Each model the PPFM spreadsheet has a limit of 1000 data pairs (inputs and outputs), allowing manual changes or via copy and paste data.

The essence of the optimization promoted by the Solver, when applying the principle of the generalized reduced gradient method (optimization process of the Solver supplement), is based on minimizing the value of the SSE, and for that purpose it changes automatically and successively all the values that were initially assigned by the user and their common sense. Several iterations will be performed until the best estimate is found. But, if Solver is triggered again, better adjustments can be obtained (Kemmer & Keller, 2010). We emphasize, again, the importance of the effort to offer good initial data (guess), as well as patience to run the Solver more than once. This is probably the cause of "failed to converge", even for more sophisticated programs like SAS (Vedenov & Pesti, 2008).

In this way, regardless of the program chosen to promote the optimization (e.g. SAS, R or PPFM), the algorithmic calculation will always be very sensitive to the values offered initially. Therefore, it is necessary to always observe the graph of the growth curve and make corrections for better guess, before activating the Solver supplement, all of this to favor both the velocity and the success of the model conversion. After the conversion, it is possible to evaluate the required time

(runtime), the standard error (SE), the confidence intervals (95%) in relation to the parameter estimates. Also, the quality of fit of the models, according to the criteria R^2_{adj} , BIC and AIC_c , which allow a better definition and comparison to decide which model is more appropriate to characterize the data of the experiment (Wit et al., 2012).

To demonstrate the robustness and applicability of this new proposal, the attributes and other novelties of the PPFM spreadsheet will be presented in a practical way, through two examples of adjustments. The first example consists of adjusting data with 13 data pairs (13 points) for a cancerous tumor curve [tumor volume/mm³ vs time after treatment (days)], which clearly shows a visible phase of resilience, (explicit copyright statement <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC539271/?report=reader#!po=43.3333>).

The second example describes the resistance of the bacterium *Pseudomonas aeruginosa* (PA14) and its growth curve when uninfected and infected by the phage alias Ab31, by adjusting 10 pairs of data (10 points) for each comparison (uninfected and infected) [OD (600nm) vs time (hours)], (explicit copyright statement <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3974807/figure/pone-0093777-g002/#>).

More details and methods of both examples are available on the website (<https://www.ncbi.nlm.nih.gov/pubmed/24699529> and <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC539271/>).

The values of both examples are approximate, since they were obtained through the free access program WebPlotDigitizer 4.2 (<https://apps.automeris.io/wpd/>), which makes it very practical and efficient to obtain the necessary values for be used in the simulations, by a simple copy and paste from the data obtained from WebPlotDigitizer 4.2 to the PPFM spreadsheet. The initial values assigned as guessed followed the previous recommendations that emphasize the need to observe the quality of the adjustment of the growth curve as the first criterion, before the activation of the Solver. After this care, proceed to optimization by activating the supplement Solver. Then evaluate the statistics available on the PPFM spreadsheet and decide to accept or restart the adjustments.

10 PROGRAM DESCRIPTION

The PPFM spreadsheet allows you to adjust eight (8) different mathematical models, with subsequent unfolding of their corresponding derivatives representing velocity and acceleration (Pommerening & Muszta, 2016). Thus, the definition of the model parameters is an attribute of the

Solver supplement, which is why Excel chose to offer the GRG method to make iteration calculations feasible. Automatically, after defining the best parameters for the model chosen from the 8 models available, the velocity (1st derivative) and acceleration (2nd derivative) curve are automatically generated (Swain et al., 2016).

From the velocity and the acceleration, at each moment of the evaluated period, it becomes possible to define the curve of the ontogenetic growth force, which acts and enables the growth (new biomass) that specific moment of time: $F = m_1 \times a$; where F = ontogenetic growth force, m_1 = new biomass (which represents the increase in size of the process per unit of time evaluated) and a = acceleration (2nd derivative) (Karkach, 2006). The PPFM spreadsheet will adjust the data offered, being of great responsibility that the values provided are accurate to represent the studied phenomenon reliably. It can compute the data, but it cannot correct its errors. Hence, the great importance of its accuracy, that is, doubtful data do not allow generating reliable curves.

11 RESULT AND DISCUSSION

The PPFM spreadsheet successfully converged for all models and examples analyzed. The time required varied from 4.02 to 11.47 minutes (Figures 1 and 2), using a laptop with an Intel (R) Core (TM) i3-7100U CPU @ 2.40GHz processor, with installed memory (RAM) of 8.00 GB and a 64-bit operating system.

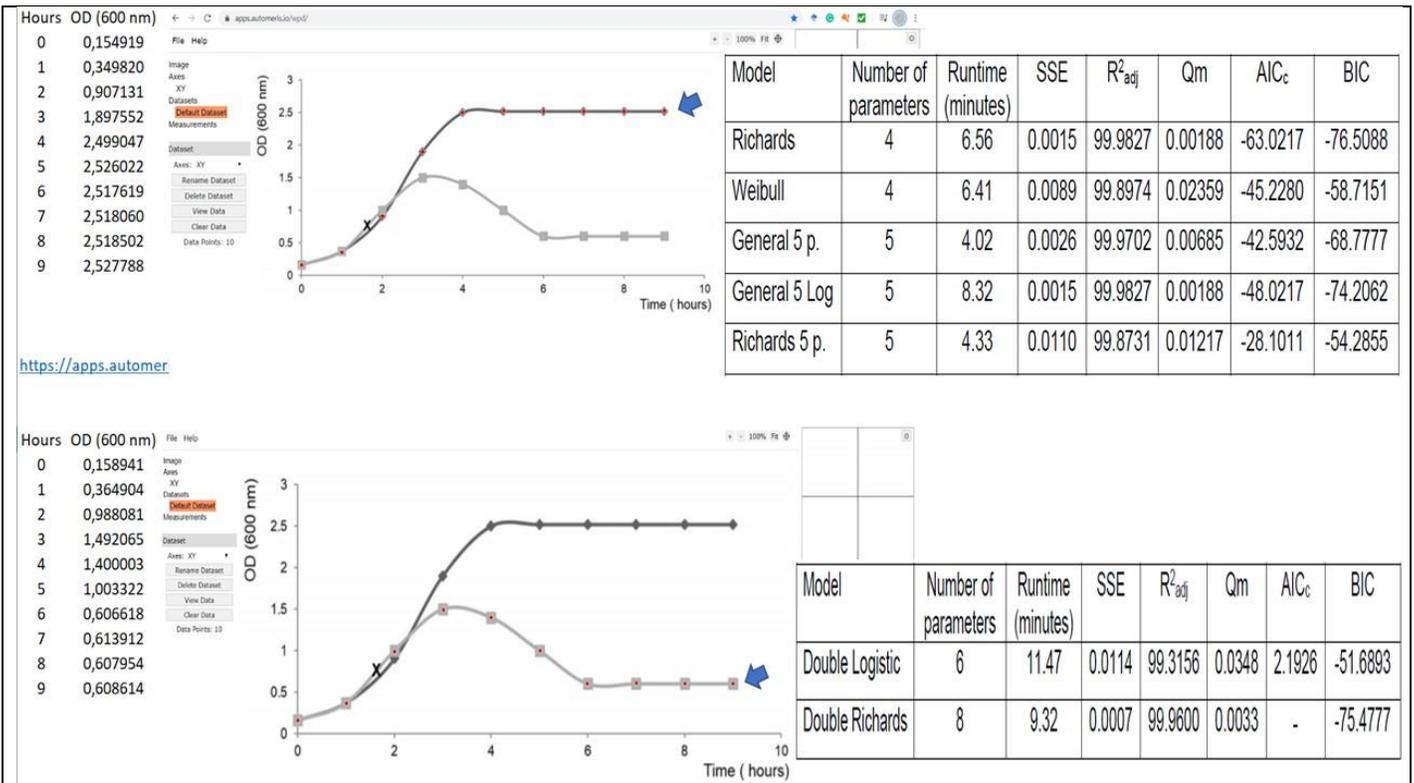


Figure 1. Example one: converged according to the models analyzed.

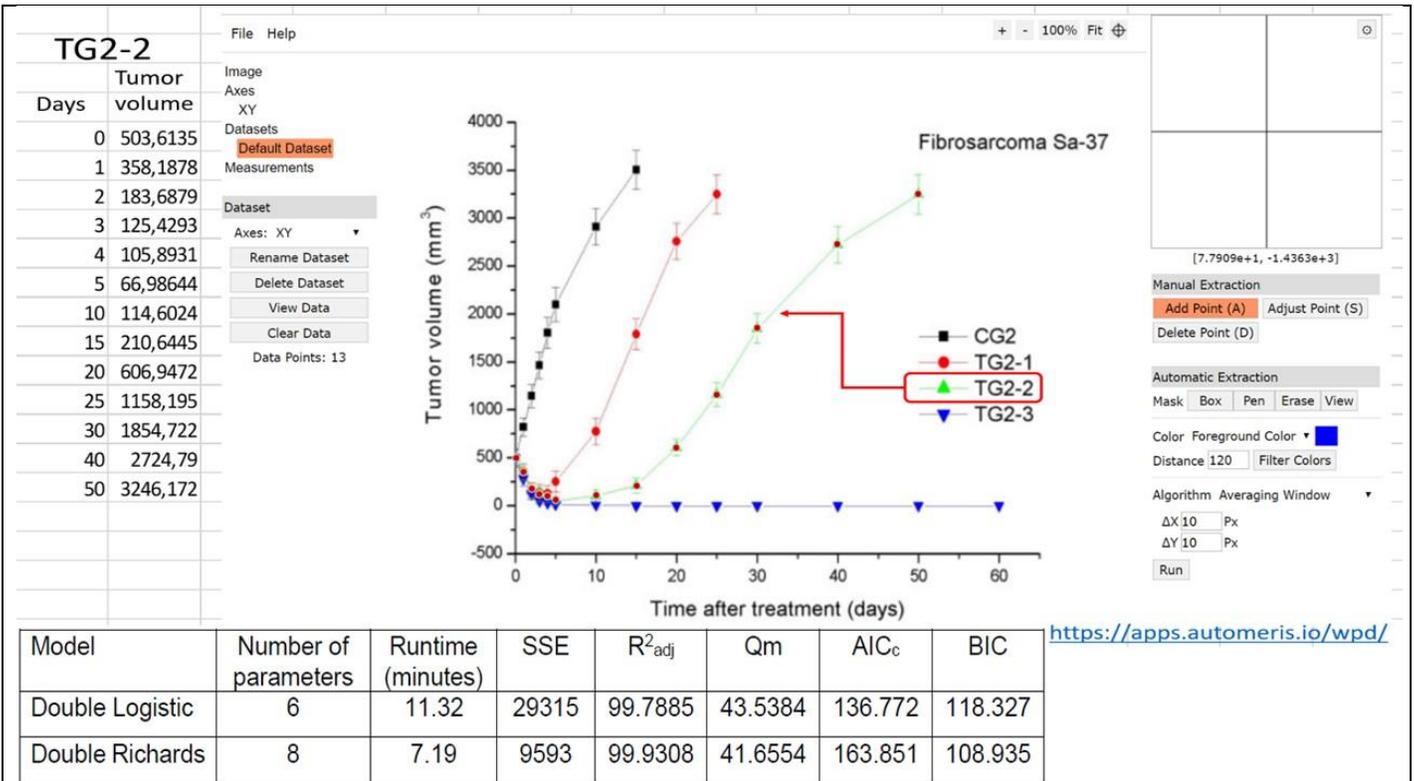


Figure 2. Example two: converged according to the models analyzed.

All the models analyzed converged, with the decision to define the most appropriate AIC_c and BIC, since for some models, both R²_{adj} and other adjustment criteria were identical (Figure 3).

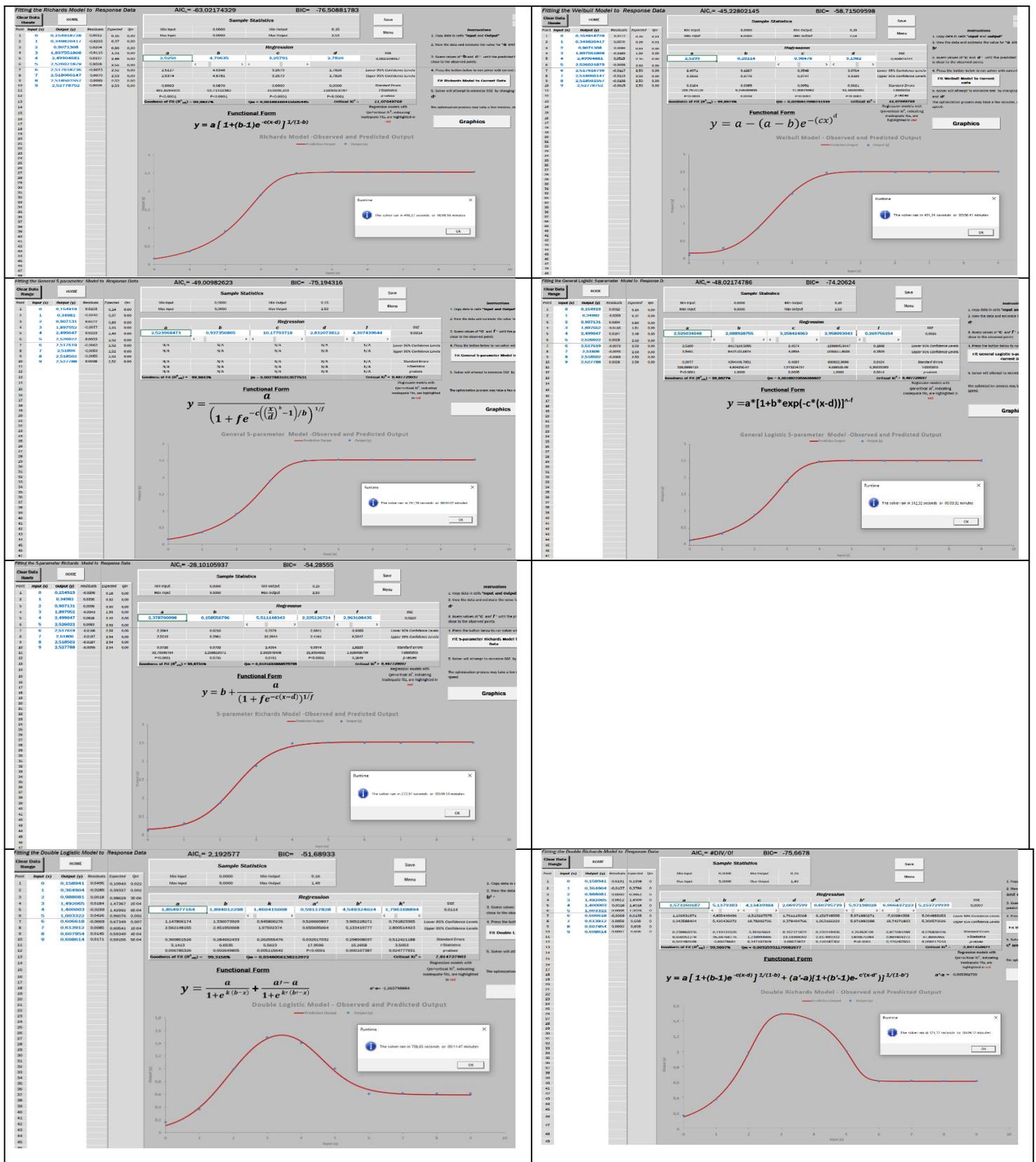


Figure 3. Models analyzed converged.

The possibility of manual alteration and the immediate visualization of the Excel dispersion graphs greatly favor the choice of the most appropriate initial values of the present work (Kemmer & Keller, 2010), which favor the adjustment of the nonlinear models evaluated by the PPFM spreadsheet. This procedure reinforces the need for good and convenient initial values (guess) for the velocity and success of conversions.

The sum of squared errors (SSE) which is also a good indicator to compare the quality of the adjustment, because this value is the objective of the Solver optimization. That is, the lower its value, this will signal that the model parameters were estimated with better fit quality (Fujikawa, 2011).

Discussing R^2_{adj} involves some controversy, which due to the non-linearity of the models induces that the values obtained for R^2 are generally very close, but even so it allows a useful and even efficient measure of comparison between the models, that is, it indicates which model it would be more appropriate to characterize the analyzed data (Vedenov & Pesti, 2008). However, it is the user's responsibility to maintain the objectives of the experiment (Baker, 1986).

11.1 GROWTH PHASES

The growth curve of the non-infected is visually a typical and traditional S-shaped curve. Thus, it presents its lag, exponential and saturation moment (Figure 4). However, when infected, the curve requires greater adjustment complexity (Figure 5).

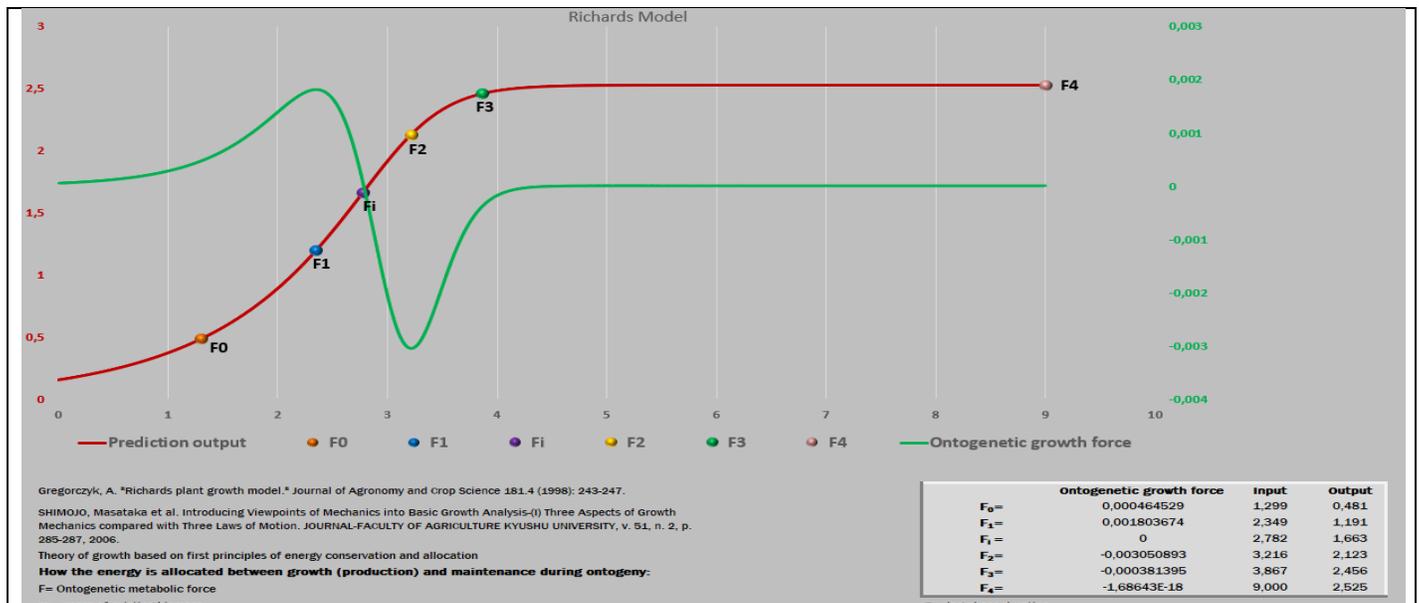


Figure 4. The growth curve of the non-infected with traditional S-shaped.

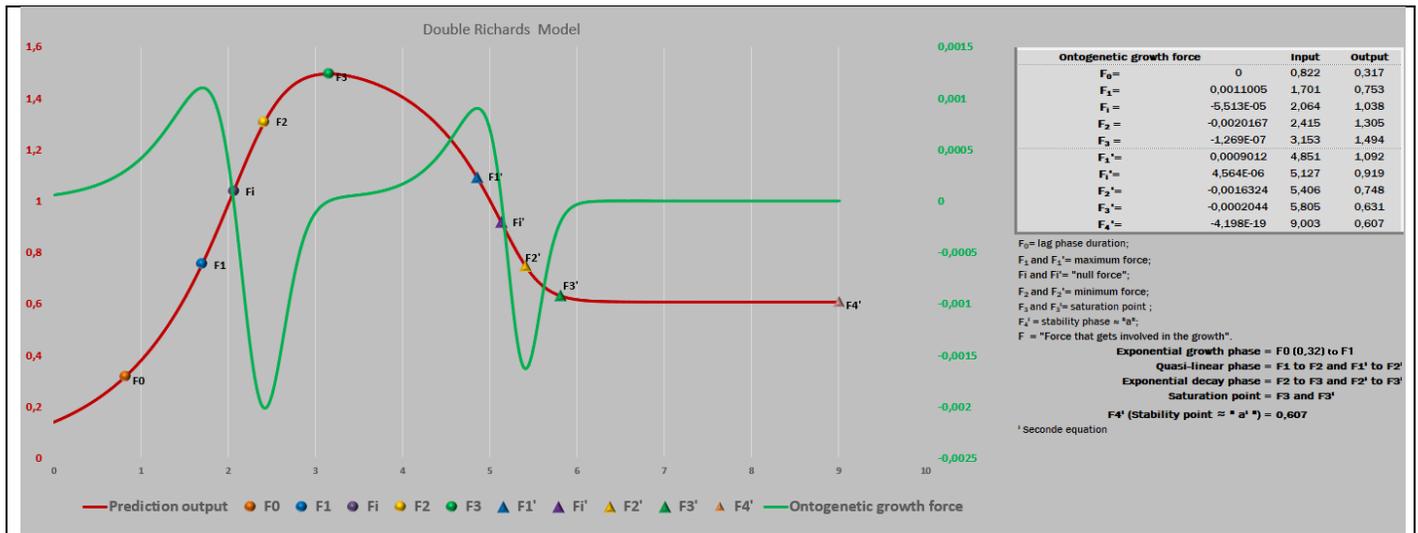


Figure 5. The growth curve of the infected with greater adjustment complexity.

The correct definition, both at the beginning and at the end, of the phases that characterize a growth curve are of great biological and economic importance (Passos et al. 2012; Strathe et al., 2010). There are several alternatives presented in the literature to measure the phases of a growth curve, they are not accurate (Cate Jr & Nelson 1971, Evans 2008), as tangent at the inflection point, segmented regression, 90 or 95% to upper limit and second derivative of growth function (Korndorfer et al. 2001).

The PPFM spreadsheet presents elegantly the eight possible phases of growth by the adjusts data for multiple equations, and providing a gradual transition between these phases more accurately. Among the several curves available, the Richards function is one of the most flexible, although it requires one more parameter when compared to logistic or Gompertz, both of which are intrinsically inflexible, or because of their symmetrical nature or because they overestimate the asymptote, respectively (Yin, 2003).

Many studies value biological interpretations for the parameters of the equations, being this one of the virtues pointed to indicate the logistic and Gompertz curve, and the reason of Richards to be criticized. However, the present proposal presents the adjustment of the equation as a first step, and not as the end of the analysis using the PPFM spreadsheet (Practical program for forces modeling). Reason not to require biological interpretations for all parameters, but flexibility (Kebreab et al., 2010).

The points of maximum and minimum acceleration (second derivative) are suggested, respectively, as the end of the lag phase and the end of the exponential growth phase (Buchanan & Cygnarowicz, 1990). And yet, being also considered the third derivative to characterize these end

points refinements in the prediction of microbial growth curves (Garthright, 1991). Death phase more cells die than are produced so even replacement to sustain the total produced is no longer viable. Motives like starvation, lack of oxygen, toxicity due to waste products (Figure 6).

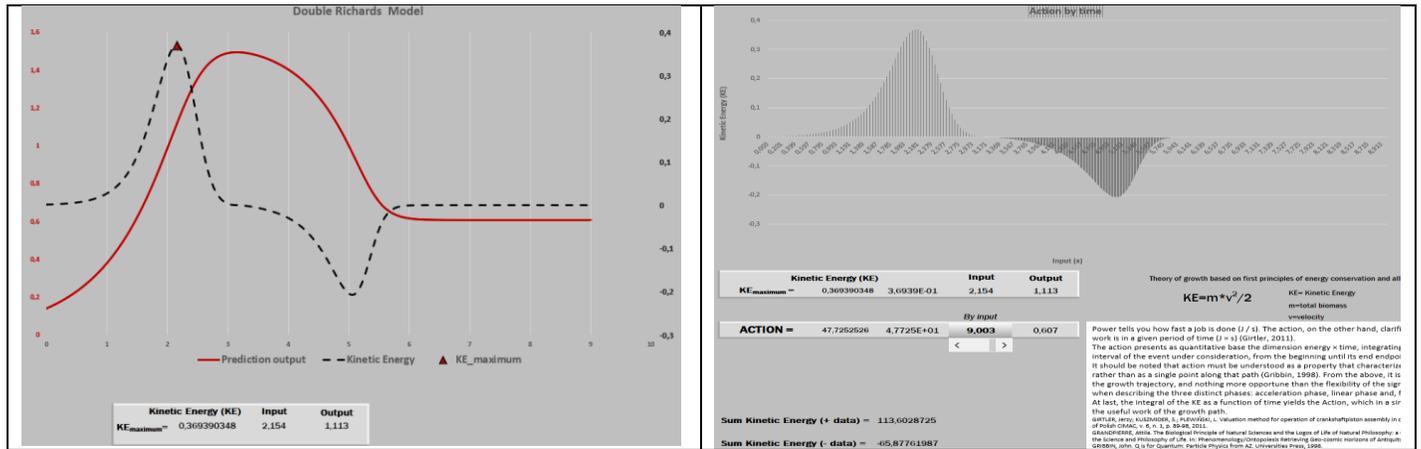


Figure 6. The death phase moment.

Furthermore, describing and predicting this path only by means of kinematics, allows only to characterize geometric measurements (location, velocity and acceleration), but does not make it possible to reveal the wisdom and intelligence involved in this trajectory (Calvo & Baluška, 2015; Westerhoff et al., 2014). However, by the principle of action, it is possible to evaluate and compare performance on a common basis.

At each moment of time changes in the size of an individual or population occur, due to competition for energy and nutrients, which define the best strategy (survival, maintenance, growth or reproduction) (Burkhart & Tomé, 2012). In other words, the expansion of growth is nothing more than the integral of the adjusted model, which allows changes to represent either the phase of expansion or decline of the studied process. In this way, a history represents continuous challenges, successes and failures to enable growth, reproduction; or just maintenance, or just life, especially when resources are scarce.

It is desired that the equations accommodate time course data on the growth of an organism (Kebreab et al, 2010), and their interactions, to characterize the expansion of the organism throughout its growth path (Zeide, 1993). In this way, both the action principle and the growth curves are similar, since they represent or present the initial and final state as a basis, when integrating the whole process. Through this appreciation, both physics and biology become reciprocal (Woese, 2004). As for favorable conditions (abundance of nutrients, space, non-stressful conditions), expansion (success) occurs, but the decline in growth is a sign of competition, limited resources, stress or even

the internal mechanisms of the organism that limit growth (failures and challenges) (Burkhardt & Tomé, 2012).

Thus, penetrating this mystery of life and mainly why, nothing better than using bacterial growth curves as an example. The admirable thing is to know that there is an excellent communication between them, and also, that the colony always uses intelligent strategies (Bridson & Gould, 2000; Ben-Jacob et al., 2004, Ben-Jacob, 2009). Thus, in order to guarantee success and optimize growth, it is essential to maintain the same motto: “One for all and all for the colony”, resulting in success. Failure, in turn, is represented by the motto “Each one for herself”. Still, in relation to bacteria, probably the most crucial moment is in defining the end of the lag phase (Jiang et al., 2018). It takes a lot of conviction to get out of the lag phase and start the exponential phase, because success requires decision making to be very conducive (Ben-Jacob, 2009).

11.2 LAG PHASE

Defining the lag phase duration has been a great challenge (Baranyi et al, 1993, 1995; Fakruddin et al., 2011; Lambertini et al., 2010). The most classic definition of the end of the lag phase is the tangent that passes through the inflection point and cuts the lower asymptote, being attributed through the maximum second derivative of the growth curve, representing the maximum of the first derivative the inflection point (Baranyi & Pin, 1999; Buchanan & Cygnarowicz, 1990). Other alternatives would be the introduction of new parameters in the growth curve itself (Fujikawa et al, 2004; Huang, 2013).

Lag time duration is of great importance, especially for the food industry, which aims to extend this period indefinitely, avoiding or preventing possible contamination (Buchanan & Cygnarowicz, 1990; Gibson et al., 1987, 1988; Jiang et al., 2018). Such concern meets a growing appeal from the client that demands guarantees on the shelf life of the products consumed, for this it is extremely important to predict the end of the lag phase (Bath et al., 2002; Fukikawa & Kano, 2009).

The PPFM spreadsheet exhibit the point F0 that represents the moment that the lag phase ends and starts the exponential phase. This is a crucial moment, as it features an abrupt change in behavior, from static (lag phase) to exponential, being a new alternative to define the lag time end (Kyurkchiev & Iliev, 2016; Swinnen et al., 2004), allowing to measure the duration of this phase accurately. As an analogy, it recalls a 100m race, in which all athletes wait anxiously for the starting signal to pull out, in a sprint, as efficiently as possible. Interestingly, the bacteria exhibit the same behavior, and through communication, they wait for the signal to awaken, precisely at the moment

F0, thus beginning their exponential multiplication phase. Thus, the definition of this critical point by the PPFM spreadsheet offers a new indicator of the lag phase duration. On the other hand, it is essential that adequate data is ensured to characterize the referred phase (Baranyi et al 1993).

11.3 DEFINING OTHER GROWTH CURVE TRANSITION POINTS

The PPFM spreadsheet presents from the ontogenetic growth force curve and its derivatives, it is possible to define more precisely, beyond the point F0, the points F1, F2 and F3, with accuracy and applying robust principles of physics. It is clear that at the beginning and for a certain period the growth, represented by the sigmoid curve, "struggle" to maintain a "J" shape. At this first moment of the sigmoid curve the initial mass is favorable, as well as other resources (nutritional, space, body volume, etc.) (Burkhart & Tomé, 2012). This voltage is ruptured exactly at point F1. From this point on, it presents itself as a linear form and preserves its bravery in order to remain so, since there are opposing forces in order to, once again, de-characterize this format. The said resistance is overcome at point F2, whose shape passes a decreasing exponential.

In this last phase (exponential descending) the own mass acquired militates against. In other words, the nutritional requirements (maintenance) make the synthesis of new biomass unfeasible. Thus, all features are carried to "keep" the accumulated mass around the sigmoid path (Banavar et al., 2002; West et al., 2002; Cassiano et al 2018). Therefore, the larger the mass, the greater the resistance of the body to the change of its velocity. Growth can be limited by a simple essential factor that also justifies the plateau phase. In relation to the subsequent decline observed after the saturation phase (plateau), it is generally justified by the accumulation of waste excretory products and by the decrease in the supply of nutrients, that is, environmental stressors (physical, chemical or competitive) (Burkhart & Tomé, 2012; Zeide, 1993).

It is visually explicit that the point F1 represents exactly the beginning of the linear phase, and at the same time, the end of the exponential growth phase. Point F2 marks the exact moment at the end of the linear period and the beginning of the decreasing exponential phase. The points F0, F1, F2 and F3 are endpoints that allow to mark the end of each phase of the growth curve, and thus, it allows to define its duration. Then, also opportune for a better understanding of the growth process, are the beginning of the linear phase and its end (F1↔F2). Finally, point F3 corresponds to the moment when the decreasing exponential phase ends (F2↔F3) and starts the plateau phase (Bilge & Pekcan, 2013; Passos et al., 2012; Sedmák & Scheer, 2015). However, it was necessary to use

the derivatives of the ontogenetic growth force to find the points F0 and F3. Thus, the third derivative of the ontogenetic growth force curve (Snatch) was obtained.

The justification for using the third derivative is that the real moment when the lag phase ends and the phase of increasing exponential growth begins (point F0). Still, by Snatch it was possible to define the point F3, which marks the end of the phase of exponentially decreasing growth and the beginning of the plateau phase. Indeed, without the concepts of physics it would not be possible to find these points, which from now on are real and no longer mysterious, obscure or arbitrary (Bentea et al., 2017; Firsov et al 2001).

This path (growth) involves interactions with the environment (favorable or not), preventing the growth path from being kept identical for the same species. This implies that one should be dynamic to adjust to the new realities in each case, including the choice of the most suitable model for each new scenario, with comparisons between different models according to the criteria of information Bayesian (BIC) and corrected Akaike (AIC_c) (Wit et al., 2012), which allow the selection of a more adjusted model, by evaluating which one best explains the phenomenon studied (Motulsky & Cristopoulos, 2004). Therefore, it is clear and definite that there is to choose models with free inflection point for assessing the metabolic and catabolic more biological accuracy, not allowing "mathematical symmetries" (logistic and Gompertz curves) (Marinakis, 2012; Tjorve & Tjorve, 2017).

The growth process will really only be better understood if the different phases that characterize development are precisely estimated. Thus, defining the beginning and end of each phase is a very important key component for full understanding, not only of the growth trajectory, but mainly of the intelligent phase changes that occur in this period, allowing to adequately characterize the multiple moments of growth (Bukhman et al., 2015; Westerhoff et al., 2014). The estimated values of each parameter should be based on the best visual quality of the graph (curve) that represents the model (Heinen, 1999; Marušić et al., 1994; Strathe et al., 2010). Thus, these initial values (guess) should be as coherent as possible to promote convergence and will allow successful Solver adjustment by their successive iteration processes (Archontoulis & Miguez, 2015; Tsoularis & Wallace, 2002). More appropriate values can be obtained from previous studies (Narushin & Takma, 2003).

11.4 RESILIENCE PHASE

What characterizes the beginning of the resilience phase can be considered as the period of the growth curve in which survival is the priority and not the growth itself, requiring adaptations that focus on longevity, rather than growth (Mayne et al., 2015). Surviving implies resistance and refers to the ability to absorb a disturbance without a noticeable change (Jabr, 2012).

For this reason, resilience is the ability to recover to the pattern prior to the manifestation of a biological, chemical or physical disorder, and depending on the severity of the stress suffered (Juan-Garcia et al., 2017), the growth becomes negative, reflecting in the area over the kinetic energy curve, capturing quantitatively the effect of the stressful condition (Figure 7 and 8).

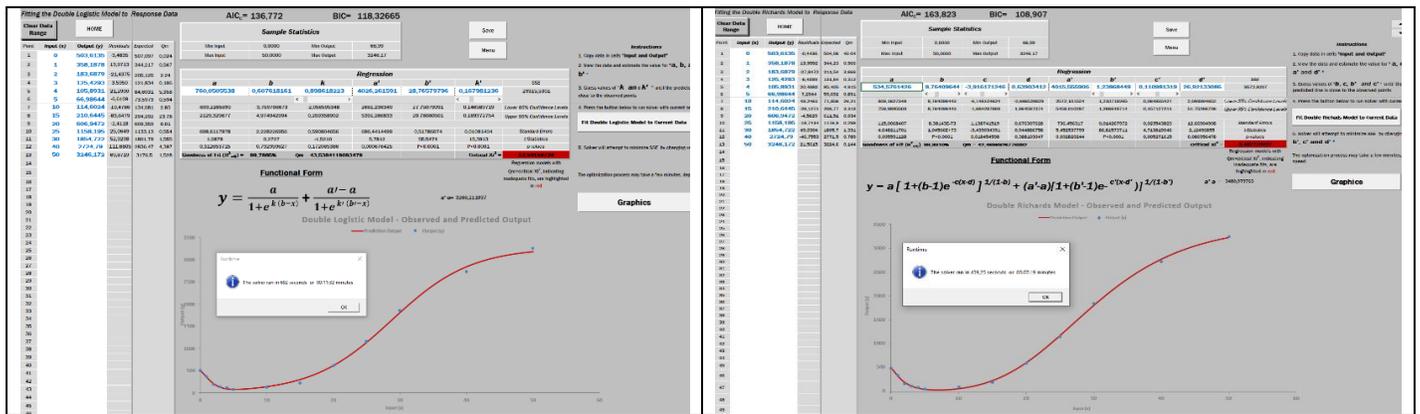


Figure 7. The resilience phase moment, capturing quantitatively the effect of the stressful condition.

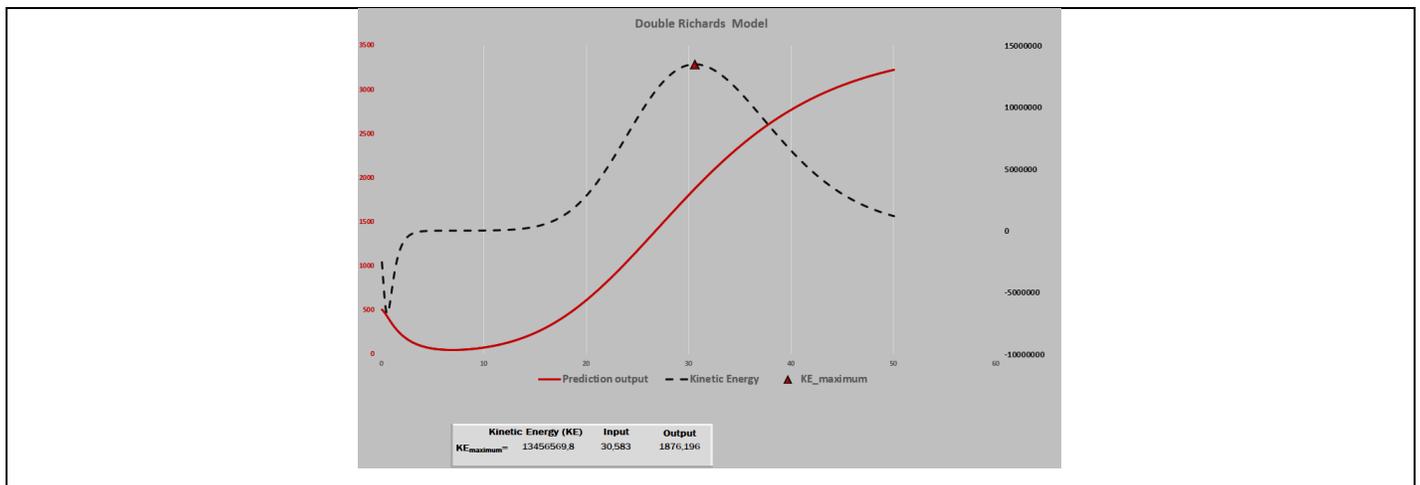


Figure 8. The resilience phase moment reflecting in the area over the kinetic energy curve.

Resistance is necessary, as well as smart strategies to promote growth, as there are always stressors opposing the journey (Ben-Jacob, 2009). But when the best strategy is to retreat, resilience manifests itself, characterizing the moment that the disturbance prevents the growth from continuing (Jabr, 2012; Mayne et al., 2015) (Figure 9).

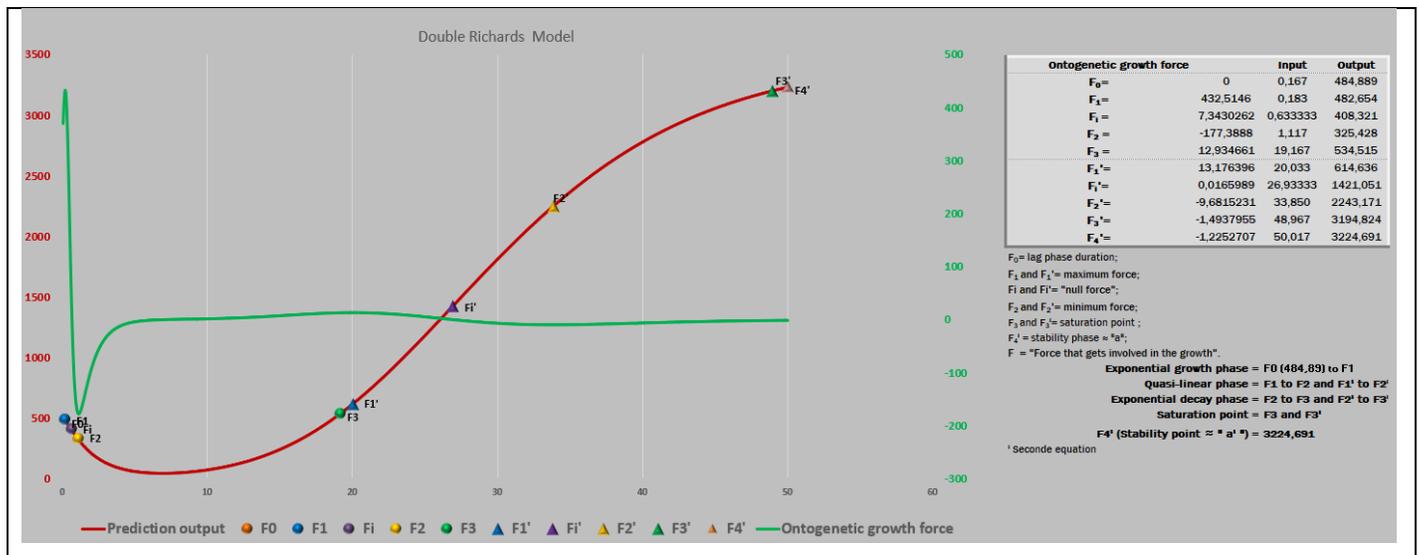


Figure 9. The resilience phase characterizing the moment that phases the disturbance.

The great importance of a system being resilient is to allow and guarantee its sustainability (Juan-Garcia et al. 2017), to minimize the magnitude and duration of the disturbance. And so, maintain the continuity of growth by returning to the condition immediately prior to the stress suffered (stress conditions).

The PPFM spreadsheet allows to evaluate and quantify the capacity of an organism or system to absorb and recover, from an overtime impact of a stressor, to these adverse stressors, showing the ability to reduce the magnitude (area over the kinetic energy curve) to disturbance. The measurement of stress for being across the area, allows the comparison between different models, as it represents a neutral measure (Myerson et al., 2001; Pruessner et al., 2003). The robustness of the resilience (the regions where the area is over the kinetic energy curve) allows estimating the impact, numerically quantified, characterizing the moments of recoil and recovery induced by a stressful event of great magnitude, being a flexible index to represent the moment of resilience in a growth curve (Fekedulegn et al., 2007).

The hatched area over the curve allows to represent the total loss of system performance, and the duration of this disturbance is the resilience time. Then, it is possible to know resilience and recovery, since the trajectory of recovery is known at every moment of time. The knowledge of the

impact of the resilience phase (duration of loss vs loss of performance) over the curve allows us to understand or describe the system's ability to retreat and then recover from a period of stress). F3 can represent the moment of transition between the setback and the recovery contained in the resilience phase (Figure 9). Then, resilience phase indicates the ability of a system to recover from a suffered disorder. Growth stability depends on resilience (setback and recovery) and resistance to stress factors inherent in the history of the evaluated processes, which are complementary and distinct to represent the intelligence and optimization necessary to ensure stability (Westerhoff et al., 2014).

Both concepts inherent in the resilience phase (setback and recovery) must be evaluated when analyzing a growth curve, whether in the ecological, socioeconomic or biological area. Thus, retreat and recovery represent different aspects to assess the resilience phase of a growth process. Therefore, the PPFM spreadsheet information is complementary and not conflicting. That is, the first measures the impact and the time needed to get around the disorder, while the second, the time needed to recover.

The PPFM spreadsheet allows to quantify resistance and resilience that occurs in response to disturbances that occur during the growth period. Thus, being able to measure a chronic or an acute stressor. The under the curve area is suggested as a way of assessing the resilience of a growth process. The action principle makes it possible to measure numerically the effects of both resistance and resilience against the growth process. Therefore, the action is also a relevant indicator to define the resilience phase, as it numerically defines the duration and intensity of this disturbance. Resistance and resilience are part of the concept of robustness, which would be the capacity of a biological system to maintain the rhythm of growth, even suffering stressful disorders. It is possible to specify resilience as the ability to recover and return to the growth process prior to the disturbance (Westerhoff et al., 2014).

The PPFM spreadsheet allows to evaluate and quantify the capacity of an organism or system to absorb and recover, from an overtime impact of a stressor, to these adverse stressors, showing the ability to reduce the magnitude (area over the curve) to disturbance. Resilience focuses on the ability to recover from stress and return to the point of growth immediately prior to the moment of the stressor's action, and this occurs from the beginning to the end of the period, with several phases manifesting in a period of growth. Resistance is needed, as well as smart strategies to promote growth, as there are always stressors opposing the journey (Ben-Jacob, 2009). But when the best

strategy is to retreat, resilience manifests itself, characterizing the moment that the disturbance prevents the growth from continuing (Jabr, 2012; Mayne et al., 2015).

The great importance of a system being resilient is to allow and guarantee its sustainability (Juan-Garcia et al. 2017), to minimize the magnitude and duration of the disturbance. And so, maintain the continuity of growth by returning to the condition immediately prior to the stress suffered (stress conditions). The PPFM spreadsheet makes it possible to monitor and identify the moment that the resilience phase starts and ends and its robustness (intensity \times time). Thus, it evaluates in a practical, understandable and directly applicable manner, quantifying both the moment of the impact of resilience.

11.5 ACTION PRINCIPLE

Energy cost is one of the most critical, reason for modulating the behavior of organisms (growth, survival or death phase) (Bejarano et al., 2017; Tomlinson et al., 2014; Wilson et al., 2006) (Figure 10). Another cost factor is time (Gleiss et al, 2011). Thus, the determination of the energy-time cost enables the definition of the action (Rosen, 1986; Grandpierre, 2011c).

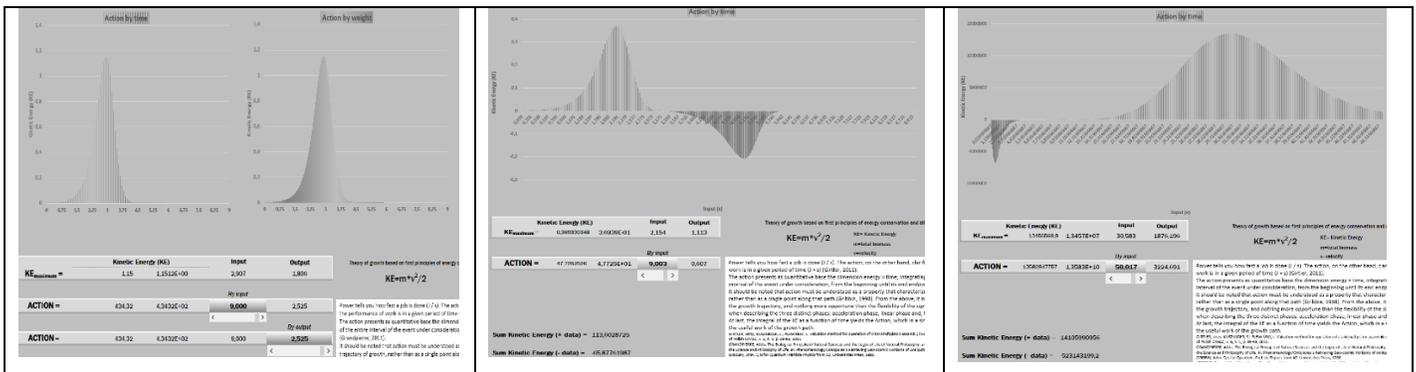


Figure 10. The action principle characterizing modulating the growth behavior of organisms.

This brings us back to optimization, which makes it possible to set the path by prioritizing efficiency, which minimizes energy and time costs (Rosen et al., 2008). Applying action allows measuring the magnitude of efficiency losses and their location in time, favoring better insights to define the cause or essence of the challenge or problem, minimizing negative impacts, either on the organism itself or on nature. Thus, the action promotes sustainability (Grandpierre, 2012) and allows to identify and predict the response to a disturbance that occurs in a period of growth, quantifying resistance and resilience.

Therefore, the principle of action allows and reveals the growth behavior of a living organism, summarizing a whole history that accommodates various interactions of favorable and unfavorable factors that always arise in life's journey of being alive (Johnson, 2006). Thus, the integral energy \times time (action) enables a better understanding of the forces that govern growth, and also, at each moment, to estimate the useful work applied to growth (Girtler, 2011ab).

The appreciable success for greatest happiness is precisely to maximize the return (profit) of the path (time), to be biologically as advantageous as possible from the beginning to the end of the sum of all energy investments made in this life history (Grandpierre 2011c; Rosen 1986; Zee, 1999). Such a procedure justifies the cost function being fully consistent with the biological pathway (Rosen 1986). Exactly the optimization of this product (energy \times time) is the whole essence of life (cost function), which in physical language would be the principle of greatest action, but in biological terms is defined as the principle of greatest happiness, being one of basis for unification (Grandpierre, 2007, 2011abc).

Although the first principle is valid for both sciences, the behavior is quite different, since physics is moving towards equilibrium (end point), whereas biology does not, reason for the latter to invest work (energy) against equilibrium (optimal end state) (Grandpierre, 2007). Therefore, what is evaluated is not only a growth curve that fits the data, but an optimized evaluation, expressed through a specific numerical value, such as the energy \times time dimension, which in turn is adopted in quantum mechanics and that characterizes Planck's constant (Girtler, 2009ab). Moreover, the system by presenting energy \times time coordinates, allows to be represented graphically, and its respective area represents the principle of action, that is, the integral of useful work at each moment of time (Girtler, 2008, 2009ab, 2011ab).

Since energy can only be evaluated at the moment it is transformed, it is at this very moment that useful work is measured that allows the growth of a living organism. Thus, this is the relationship between kinetic energy and work (Girtler et al., 2011ab). During the growth process of a living organism, through the principle of action, it is now possible not only to characterize its growth, but mainly to measure the energy conversion into the useful form of labor that was effectively destined for growth (Johnson, 1992). The biology version of the principle of action allows us to enter quantum biology in a practical and accurate way both numerically and graphically. From the data of the growth curve, the path of growth (action) is determined by quantum processes and decisions (Grandpierre, 2002). The principle of action allows a deeper meaning and better understanding of the growth process of living beings, not only in accommodating a curve, but now it is possible to numerically

evaluate the intelligent route that optimizes the development, or rather the strategy found in virtual interactions, and all this at the quantum level (Grandpierre, 2002; 2008).

From the above, applying the principle of action, it is possible to observe the quantum effect on a macroscopic scale, by adjusting the growth curves of living organisms, allowing the interface between quantum physics and biology (Arndt et al, 2009; Brookes, 2017). Thus, through quantum evaluation in biology, it is possible to find the route chosen to reach the final goal, among several possible paths, and all hidden within the growth curve (Brookes, 2017). The ideal would be the minimum to survive and the maximum to prosper, which is nothing but the most efficient way. The challenge of every living organism is considered a problem of optimizing all the energy invested in each consecutive time (Grandpierre & Kafatos, 2013; Bridson & Gould, 2000). Definitely, a living organism wisely selects the best endpoint through its activities and choices according to the greatest action principle (Grandpierre, 2009).

Recalling that action presents the energy x time dimension, summarizing comprehensively, but very profoundly, all the completeness to preserve and seize every opportunity in life. Action would be, consistently, the wisest way to preserve and energy available between the beginning and end time, which rules the path of every living organism (Grandpierre, 2002). This makes the reason for the term investment in biology coherent, because through action as the integral (sum) of all the energy invested at each moment of time, it seeks not only to prolong life, but also quality of existence, which is summarized in a single value (action) (Johnson, 1992; Grandpierre, 2008).

The PPFM worksheet is offered as a tool for assessing useful work (action) against the respective invested lifetime of a living organism, which in turn characterizes its most efficient journey (Johnson, 2006; Grandpierre, 2008). Thus, what we have then is the PPFM spreadsheet that allows validating data with biological interpretation, compatible with the cost function (time invested x energy invested = action) (Grandpierre & Kafatos, 2012; Rosen, 1986). When measuring the action by the PPFM spreadsheet, there is also the measurement of stress (challenges during the history of life), peculiar to all living organisms, which certainly always harms the maximum output but does not prevent it being optimized (Johnson, 2006).

The PPFM tool enables a broader understanding of the path chosen for a living organism to grow, allowing for a deeper, and especially, measurable assessment (Grandpierre & Kafatos, 2012). Thus, the spreadsheet offers a new insight into the interpretation of the time invested and the useful work applied at each moment of the life path of a living organism, in a compact, transparent and easy

to handle, favored by graphical and numerical visualizations, with possibility manual or automatic changes.

Here is a deeper understanding of the nature of the curve, not just a simple trajectory, but which from its inception represents phenomena (growth itself), laws (energy and time) and principles (doing everything possible to stay alive and flourish with quality) (Grandpierre, 2009; Grandpierre & Kafatos, 2012). From this, the PPFM spreadsheet goes far beyond allowing only a simple curve fitting and its derivatives (velocity and acceleration), but enters and accommodates the laws of physics ($F = m \times a$ and $KE = \frac{m \cdot v^2}{2}$), which allow us to evaluate the intelligence of living organisms in expressing the best energy and time investment, which is numerically represented by action (energy \times time integral).

This strong and mysterious link allows us to relate quantum physics to quantum biology, not only for presenting the same dimension (energy \times time), but for manifesting the same wise and intelligent behavioral optimization of the chosen path. Based on this new perspective, the proposal of the PPFM spreadsheet is to apply the principle of action in biology (Grandpierre, 2008). The point F3 is an excellent indicator to designate the end of exponential growth. Thus, the time used for the organism to actually grow will be between F0 and F3, that is, the beginning at the end of the period destined for growth that can now be evaluated with great accuracy of prediction, regardless of whether it is a short or long lag period.

That is, all the effort made that allowed the expansion or growth of an organism until reaching its F3 endpoint. Thus, the end of the trajectory of the growth that characterizes the plateau of the growth curve (asymptote) (Arons, 1999; Grandpierre et al., 2014). Therefore, more action: an organism's ability to acquire and convert energy into new biomass (Owen-Smith, 2005). It should be noted that action must be understood as a property that characterizes the whole trajectory of growth, rather than as a single point along that path (Gribbin, 1998; Johnson 2006). From the above, it is essential to determine precisely the growth trajectory, and nothing more opportune than the flexibility of the sigmoid curves (Yin et al., 2003, Kebreab et al., 2010), when describing the distinct phases. So, the action principle becomes an indispensable ally, allowing significant progress as a new modeling tool in curves evaluations, allowing a coherent and more complete, for improving and facilitating the biological interpretation of growth, with objectivity, simplicity and utility (Grandpierre, 2008).

The mystery of this history is that always the most advantageous one is the one chosen, giving an almost philosophical and almost theological connotation. This is the description of the growth path, which in an extraordinary and compact manner is summarized by the principle of action. Action is neither more nor less than Newton's laws more compactly (Zee, 1999).

12 CONCLUSION

The PPFM spreadsheet presents as a great novelty the improvement of the numerical definition of the critical points that make it possible to characterize up to eight growth phases, through the endpoints F0, F1, F2 and F3, that is, Lag phase, exponential increasing, almost linear, exponential decreasing, plateau, resilience, death and spurts phase. Another great originality is to be able to calculate the kinetic energy involved in the growth process, which allows to measure the useful work mobilized and used in the demand for growth and its strategies.

The action (energy \times time) allows to explore concepts of physics, to clarify biological phenomena, offering a common basis for theoretical biological physics in its most fundamental aspects. Thus, the PPFM worksheet allows to present in a practical way, the establishment of the first law of biology, contributing to the evaluation of growth expansion, allowing a new approach, which in a refined way unifies physics to biology, allowing more understanding of the most basic attributes of nature.

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