

Scales Bridging in the Model of Growth of Animals, a Holistic Slant

V. L. Stass

Correspondence: Author V. L. Stass. Institute of animal husbandry and veterinary science. Latvia.

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Abstract

Scales bridging problem has been studied in mathematics and the natural sciences for decades. In this study we concentrate on a model of growth of animals. The model of growth of pigs was built in two different techniques continuum, and non-local. The both techniques model the same process and use the same variables. However, the outcomes that one can acquire from them are different. In this study, in this model, the problem how to bridge scales between genotype, and phenotypes of ontogenetic growth remain intact; it has not been considered. We narrowed the gap instead and discussed scales bridging problem between biochemistry of digestion, and the growth of animals. This range of scales the model potentially can bridge. In this study we discuss what does it mean bridge a scale. How to identify the scale to bridge. What means one has, to perform it. In this research non-local modelling technique was used. It was shown that this technique has sufficient power to make known emergent events in animals' growth. The use of the non-local modelling technique to bridge the scale was discussed.

Keywords: non-local technique, hybrid model, dynamic system, phase transition, emergent trajectory, integrated line

1 Introduction

In biology the problem of how to bridge scales between genotype, and phenotype has been discussed for a long time. In genetics, logical efforts in the form of verbal reasoning to solve the problem have failed thus far. It seems that time for analytical efforts in this field has probably come. In the life sciences modelling a biological function, in this study the growth of animals, would be supposed to deal with a reverse problem. In spite of the opinion that this is the reverse problem which allegedly is impossible to solve (Brenner, 2010) in this field of research some efforts may be taken. This opinion is based on experience; it suggests that the scales to bridge must be studied simultaneously by different methods with coherent progression on each scale. Then, at a point on this way, one naturally arrives at a scale to bridge. Which approach reductionism or holism will bridge the scale is of no importance; the both slants are complementary. The task of research is identify the scale, work on it, and bridge it.

If science is to progress, what we need is the ability to experiment and the intelligence to interpret the results. In fact it is necessary for the very existence of science that minds exist which do not allow that nature must satisfy some preconceived conditions.

Richard P. Feynman, a distinguished physicist

1.1 Scales in the Model of Growth of Animals

Growth of animals is a process observed on organism scale. In this instance the widest range of scales is probably from genotype to phenotype. One can take a rational line and narrow this range; in this research, from digestion biochemistry to animal ontogeny. In this study we followed this line. In an organism, it is possible conceive many scales between digestion biochemistry, and an animal ontogeny. Which of them are real and which are thoughts is impossible to tell a priori; research is needed. In addition, under the above conditions the scales may be object dependant or methods dependant. This is to say the scale to bridge ought to be identified. In the life sciences there are a few classifications of possible biological scales (Bardini et al., 2017). Living beings is possible to consider from different viewpoints. Conventionally, it is thought animals have been formed as a hierarchy in which some levels of organisation are proposed. In an organism one can propose molecular, cellular, tissue, organs, systems of organs, physiological, and organismal levels organised as a hierarchy. In living beings alongside the levels or scales of biological hierarchy physical scales have been considered. The physical scale is defined by a distinct set of mechanisms and constraints (Bershtein et al., 2017). Which of the scales to study is a research-dependant question.

1.2 Scales Bridging Problem

Reportedly, in biology models of multiscale systems have been produced. The models can capture interactions across different spatial and temporal scales (Anderson and Quaranta, 2008). However, it is not obvious that the interactions are in

a form of molecular reactions. Even if they are while modelling the growth of an animal this aspect has not been considered. This means that there is a scale on which a biological function begins. Which scale is it? Is growth of an animal seen on molecular scale? Before bridge a scale, it is rationally identify it. Abstract scales bridging methods are viable only in mathematics. While in physics or biology it is a problem or object related task. There are some ways to approach the problem. The analysis of the problem highlights the need of a modelling technique with causal explanatory power. How automatically in a machine-driven manner discover the relevant features is unclear. Another way to solve the problem is to ask which variables are the relevant order parameters in the problem at hand? (Tegnér et al., 2016). It follows that deterministic, analytical models are the main tools in this field of research. Which mathematical technique is right to use to solve the problem is unclear. In this study we discuss two techniques; a non-local hybrid, and continuum deterministic models. The dynamics of biological systems have usually been modelled by differential equations. It is known that biological systems are heterogeneous objects. Differential equation models though fail to account for the emergence of inhomogeneities, and for the influence of inhomogeneity on the general dynamics of biological systems (Louzoun et al., 2001); hybrid models are more suitable for this task.

1.3 Hybrid Piecewise Smooth Models

Hybrid modelling is defined as the coupling of a continuous approach with a discrete one to model a complex phenomenon which is hardly possible to model in a standard homogeneous way mainly due to its inherent multiscale nature (Stéphanou and Volpert, 2016). Well known is the discrete-time version of the continuous-time piecewise smooth system. These systems can be described as hybrid dynamic systems with continuous and discrete variables. An important class of autonomous hybrid dynamic systems is a piecewise smooth system. Hybrid dynamic systems are particularly important for understanding the nonlinear dynamics of biological and medical systems as they have many discontinuities (Aihara and Suzuki, 2010).

2. Methods

In this study methods of mathematical modelling and analyses were used. The model was built based on experimental data and field observations. The data set was obtained in the experiments with pigs (Stass, 2020). The model was built as an extension of an earlier created model (Stass, 2022). In the study both continuum and hybrid techniques were used. In the model the hybrid method treats time as a discrete variable. In the hybrid model minimal time span Δt is one day. This time span corresponds to one cycle of the circadian rhythm. In animals during this time processes of growth and development go through one cycle. The growth of animals was modelled by a dynamic system. In the model the same processes of growth of animals were modelled by two techniques continuum, and non-local. The both techniques use the same set of data and the same set of variables.

2.1 Methodological Aspects

The problem this study deals with is ontogenetic growth of animals. The aim of this research was to acquire new facts about ontogenetic growth from analyses of the model. The dynamics of the growth of pigs was modelled from the beginning of rapid growth up to maximum weight. The task was to model some aspects in the growth dynamics to reveal qualitative, emergent events. A more general task was to think about scales bridging problems in this field. In the study, the scales span a range of processes from biochemistry of digestion up to growth of an organism. How to bridge the scales is theme for discussion. In biology, to build a meaningful mathematical model of a process one must have a concept of the process, and theoretical framework of the concept (Hyman, 2011). Besides, one must find a mathematical technique to implement the concept in a model (Stass, 2022). This scheme is valid also for scales bridging models. What concept of scales bridging may be? (Bardini et al., 2017). In the field of scales bridging many models exist or are under development. Yet a methodology of the modelling seems to be missing (Sloot and Hoekstra, 2009). From the standpoint of mathematics, alignment of maps on low-dimensional manifold is a feasible if not the only option for bridging scales (Harrison and Yates, 2016). This is to say to bridge a scale on a manifold overlap of maps is needed.

2.2 The Concept of the Model

The concept of the model is as follows. Animals to sustain life and grow need a feed. The feed is environmental factor. For a growing animal feed is needed in sufficient quantity and quality. Feed or food, let F denote it, has been converted to current weight M by an organism. It takes place after digestion. During digestion feed or food has been reduced to simpler compounds and absorbed by an organism for metabolism. One cycle of this process takes one day. Feed or food has been converted to the current weight M with efficiency Z . Feed or food conversion coefficient, let Z denote it, is the variable which describes how efficient conversion of food F to weight M was. In the model, a growth invariant K has been used. The growth invariant K is a species-specific parameter. In the study the parameter K makes the model species-specific and imposes functional constraints on other variables. The growth of animals was modelled by an autonomous dynamic system.

2.3 The Model's Variables

Let M denote an animal current weight, measured in kilograms.

$M = \{M \in \mathbb{R}_+ \mid 30 \leq M \leq 600\}$, an animal individual maximum weight $M_x = 600$ kg.

Let m denote an animal initial considered weight, measured in kilograms, $m \leq M$, $m_0 = 30$ kg.

Let t denote the chronological current time, measured in days from an animal's birth.

$t = \{t \in \mathbb{N} \mid 0 \leq t < \infty\}$, $\Delta t = 1, 2, 3, \dots, n$. $n \in \mathbb{N}$. t_0 denotes time corresponds to m_0 , $t_0 = 90$ days.

Let K denote the invariant of growth, nondimensional. $K = \{K \in \mathbb{R}_+ \mid 1 \leq K < 11\}$, $K_0 = 1$.

Let Z denote the current feed conversion coefficient, nondimensional.

$Z = \{Z \in \mathbb{R}_+ \mid Z_0 \leq Z \leq \infty\}$, $(Z = \infty) \rightarrow (M = M_x) \vee (M = M_{xx})$, where M_{xx} denotes species maximum weight.

Let F denote consumed food or feed, measured in kilograms. $F = \{F \in \mathbb{R}_+ \mid 0 < F < \infty\}$.

3. Results

The model of growth of animals was built in the two techniques continuum, and non-local. The both techniques use the same set of data and the same set of variables. In the both techniques the models were built as autonomous dynamic systems. The both models do not have unknown, speculative parameters. It follows that in this research the problem of identification of the parameters does not exist.

3.1 Non-local Model of Animal Growth

The analysis of the experimental data led to the following set of equations.

$$\begin{cases} \frac{M}{m_0} = 2K - 1 + \frac{(Z-2K)(K-1)}{ZK} \\ \frac{t-Kt_0}{t} = \frac{(Z-2K)(K-1)}{ZK} \\ K = \frac{Mt}{m_0(2t-t_0)} \end{cases}, \tag{1}$$

where K denotes the invariant of growth; K is the same value in the same weight animals. From (1) it follows

$$\frac{1}{m_0} \cdot \frac{\Delta M}{\Delta t} = \frac{K}{t} \cdot \frac{Z(2K+1)-2K}{Z(K+1)-2K}, \quad Z > 0, Z \neq 1. \tag{2}$$

$$\frac{\Delta K}{\Delta t} = \frac{1}{t} \cdot \frac{ZK^2}{Z(K+1)-2K}, \quad Z > 0, Z \neq 1. \tag{3}$$

From (2) and (3), by eliminating time t , we get

$$\frac{1}{m_0} \cdot \frac{\Delta M}{\Delta K} = \frac{2K+1}{K} - \frac{2}{Z}, \quad Z > 0. \tag{4}$$

And, considering (1) and (4) we have

$$\frac{\Delta Z}{\Delta K} = \frac{2K(3Z-2)}{9Z}, \quad Z > 0. \tag{5}$$

In the model, equations (4) and (5) are autonomous dynamic system. The system has been used to analyse growth of animals. It follows from (4) and (5) that $Z > 0$; this has a clear biological meaning. Equations (2), (3), (4) and (5) are meaningful relations; they may be used for calculation.

To carry out analyses of the model one need some additional facts. The facts one can derive considering the concept of the model. At a point in ontogeny a growing animal reaches its individual maximum weight; let M_x denote this weight. Under the model's condition $M_x = 600$ kg. Let us find K_x , $K_{|M=M_x} = K_x$. It follows from the experimental results that the limit ($M \rightarrow M_x$) below holds.

$$\lim_{M \rightarrow M_x} \frac{2K-1}{K+1} = \sqrt{3}. \tag{6}$$

From (6) we get $K_x = 5 + 3\sqrt{3}$, where $K_{|M=M_x} = K_x$. Z_x , $Z_{|M=M_x} = Z_x$ is given by

$$Z_x = \frac{2K_x(K_x-1)}{3}. \tag{7}$$

When an animal reaches its individual maximum weight M_x its growth stops. In this weight, in this point, Z grows into

infinity $Z_x \rightarrow \infty$. In this point the first-order phase transition $Z_x \rightarrow \infty \rightarrow Z_{xv}$ with subsequent bifurcation develops. Z_{xv} is given below.

$$Z_{xv} = \frac{2K_x^2}{3} . \tag{8}$$

In the point (M_x, K_x, Z_x) the following equation holds.

$$K_x^2 - K_x \cdot \frac{M_x}{2m_o} - 2 = 0 . \tag{9}$$

Analyses of (9) shows that there is an inflection point. Let M_{IP} denote the inflection point; $M_{IP} = 2m_oK_x$. In the model the first-order phase transition develops as follows $Z_x \rightarrow \infty \rightarrow Z_{xv}$. In this model variable Z is the order parameter. Analyses in detail is found in Stass (2022). The result of the analyses is shown in figure 1.

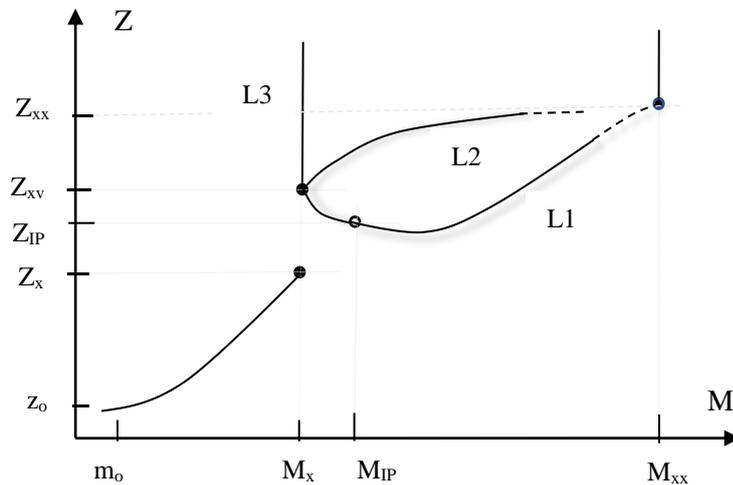


Figure 1. The trajectory of growth of animals

After the first-order phase transition ($Z_x \rightarrow \infty \rightarrow Z_{xv}$) trifurcation of the growth trajectory takes place. In the model, the trifurcation is an emergent event. In the point (M_x, Z_{xv}) new growth trajectories emerge, see figure 1. The cause for this emergent event was the dynamics of variable Z . Initially stable growth trajectory $m_o \rightarrow M$ in the point (M_x, Z_x) loses its stability as Z grows into infinity $Z \rightarrow \infty$. As a result, the first-order phase transition with following bifurcation develops (Stass, 2022). As a result, new growth trajectories emerge. In this model the new growth trajectories are new growth phenotypes. One can distinct the following three growth phenotypes. Phenotypes L1 and L2, figure 1, are considered homozygotes. Phenotype L12 is considered as a heterozygote; on figure 1 it is not shown. It is thought that the phenotype L12 emerges in the form of the Hopf bifurcation as a coherent whole of L1, and L2. On trajectory L3 animals do not grow; on this trajectory animals continue to live in the constant weight M_x and $Z = \infty$.

3.2 Continuum Model of Animal Growth

If in the non-local model we considered time t as a discrete variable $t \in \mathbb{N}$ then in continuum model $t \in \mathbb{R}_+$. From (1) one can derive autonomous dynamic system, given below.

$$\frac{1}{m_o} \cdot \frac{dM}{dK} = \frac{2K^2+1}{K^2} - \frac{2}{Z} + \frac{dZ}{dK} \cdot \frac{2(K-1)}{Z^2} , Z > 0 . \tag{10}$$

$$\frac{1}{m_o} \cdot \frac{dM}{dZ} = \frac{dK}{dZ} \cdot \left[\frac{2K^2+1}{K^2} - \frac{2}{Z} \right] + \frac{2(K-1)}{Z^2} , Z > 0 . \tag{11}$$

$$\frac{dZ}{dK} = \frac{2Z(3Z-2)(2K-1)}{9Z^2-4K(K-1)} , Z > 0 . \tag{12}$$

If set of equations (10), (11), and (12) consider as the starting point for the analyses then it is feasible only on a computer. I can remind the interested reader that in this set of equations there are not unknown, speculative parameters. It means that in this model the problem of identification of the parameters does not exist. In this favorable situation how to deliver the description of the qualitative events in the normal form is unclear. In this model, whether continuum methods can provide more details is unclear. The hybrid technique proved effective due to two reasons; the facts of the

growth process were acquired in the experiments and the model was well posed. There is one more advantage; the results obtained by the hybrid model have a clear biological reading.

4. Discussion

In this study we consider two scales to bridge. One scale to bridge is between digestion biochemistry, and feed conversion efficiency Z . The problem is how flows of metabolites formulate in terms of food conversion efficiency Z . Second scale that this model potentially can bridge as well is a scale between growth phenotypes. The problem is how to line up animals' growth phenotypes in weight M_x , and their phenotypes in the species maximum weight M_{xx} . Also, below we discuss the two modelling techniques continuum, and non-local, which were used in this study.

Considering a manifold it is known that two maps on the manifold is possible line up if the maps overlap. Is this approach relevant to the modelling of growth of animals? In general, this is a reasonable if not the only option for bridging scales (Harrison and Yates, 2016). For the above mentioned problem with the growth phenotypes this is a reasonable approach. Still, for some biological processes it is hardly the case. Linking a molecular level process to an organism scale physiology looks like a transition due to a qualitative change of variables rather than alignment of maps. Along with the above approach there is an opinion that the study of multiscale phenomena is nothing else as systems science in the domain of interest (Hoekstra et al., 2014).

4.1 Scales Bridging in the Model

Feed conversion coefficient Z in this research, in this model, is the order parameter; its dynamic and limits one can study only on organism scale. How on molecular scale see the growth of an animal and read its Z is unclear. This is the scales bridging problem in this model. In the model as the initial scale we considered digestion. Digestion takes place in all animals. During digestion feed or food has been reduced to simpler compounds which can be absorbed by an organism for metabolism. It is feasible to formulate flows of metabolites; still the flows are not conversion of food. What is? In this scheme it seems anabolism is missing. There is the hope that the better we understand food conversion on organism scale the sooner we comprehend its molecular bases; hardly otherwise, though. This is a holistic approach. If this logic is followed then some difficulties arise. If this logic is followed then macroscopic events, it is events on organism scale ought to have basis in biochemistry. Growth of animals is a process observed on organism scale. How to see, measure, and model the growth on molecular scale is unclear. In this model developments such as passage to the limit ($Z \rightarrow \infty$), the first-order phase transition ($Z_x \rightarrow Z_{xv}$), growth trajectory bifurcation are events brought about by the dynamics of variable Z . The variable Z in this model is the order parameter. What processes on molecular scale are right behind the dynamics of food conversion Z ? We expect to see the dynamics of flow of metabolites and anabolism expressed in units of weight and not in concentrations. Can this approach provide the scale bridging for the growth process? In an effort to perform a scale bridging one can come across logical difficulties and lack of knowledge of the biological process studied. It is feasible that logical difficulties may turn out to be harder than mathematical; as it is the case frequently in biology. In this case only a logical 'argument', a qualitative transition, can resolve the problem. And such logical 'argument', a phase transition, may make available a method of the scale bridging as well. Possibly unique for each case.

An inference from the model is that species maximum weight M_{xx} can reach only those phenotypes that can pass through the bifurcation point and then grow further. There are three phenotypes that can potentially reach the species maximum weight M_{xx} , they are L1, L12, and L2, see figure 1. It is unclear which phenotypes can actually reach weight M_{xx} . It is thought that phenotype L12, not shown in figure 1, emerges in the form of the Hopf bifurcation as a coherent whole of L1, and L2. There is temptation to identify phenotypes L1, L12, and L2 with species maximum weight phenotypes M_{xx1} , M_{xx2} , and M_{xx3} , respectively (Stass, 2019). Though, it is only a guess. There is no evidence for this statement to make. How to line up the three phenotypes? This is the scale bridging problem and potentially this model can solve it. In this case the considered scale is between growth phenotypes in the weight M_x , and M_{xx} . This scale it is feasible to bridge by alignment of maps.

4.2 Modelling Techniques

In this study both continuum and non-local techniques were used. There are considerable differences between them; if continuum technique has well developed theory and methods than non-local technique has no one. In this model though, biologically meaningful results were obtained by the use of the non-local technique. In this field however, there are many modelling techniques in use (Bardini et al., 2017). On the other hand, it turns out that only a very few types of multiscale couplings are possible (Hoekstra et al., 2014). For example, such coupling may be performed in two different ways, one can denote them hierarchical, and hybrid multiscale modelling (Coveney and Fowler, 2005).

4.3 Synergy of the Modelling Techniques

In this section we compare results produced by the two modelling techniques. I can remind the interested reader that the both techniques use the same data set and the same variables. There are cases the both techniques deliver the same result.

For example, from the hybrid technique it follows that local minimum $Z = 2/3$. By the continuum method, considering (1) and solving the following system

$$\begin{cases} \frac{\partial M}{\partial K} = 0 \\ \frac{\partial M}{\partial Z} = 0, \end{cases}$$

one arrives at the same result, local minimum $Z = 2/3$. Though, $\frac{\Delta M}{\Delta K} \neq \frac{dM}{dK}$ as it should be.

In this model the transition from one technique to other is possible. For example, let us consider equation (7), it was obtained by non-local technique. From (7) it follows

$$\frac{dZ_x}{dK_x} = \frac{2(2K_x-1)}{3} . \tag{13}$$

Let us consider $\frac{dZ}{dK}$, equation (12), and its limit ($Z \rightarrow \infty$), given below.

$$\lim_{Z \rightarrow \infty} \frac{dZ}{dK} = \lim_{Z \rightarrow \infty} \frac{2Z(3Z-2)(2K-1)}{9Z^2-4K(K-1)} = \frac{2(2K-1)}{3} , \tag{14}$$

since $K \rightarrow K_x$ as $Z \rightarrow \infty$, equation (13) and limit (14) are the same.

In this section we show how in this model the both techniques continuum and non-local work together. Let us consider longevity of pigs. Applying non-local technique one can find age of pigs in weight M_x . It follows from (6) that in weight M_x , $K_x = 10, 19615$. Under condition $M_x = 600$ kg and $K_x = 10, 19615$ one can find $t_x = 6,40$ years. In analytical form t_x is given below.

$$\frac{t_x}{t_o} = \frac{K_x^2}{4} .$$

Let us find maximum theoretical longevity of pigs. To complete this task continuum technique was used. In this research maximum longevity we modelled by the limit ($t \rightarrow \infty$). Consider a well-known formula, given by

$$MK = \int M dK + \int K dM . \tag{15}$$

In the next stage let us find the limit ($t \rightarrow \infty$) of K , equation (1), given below.

$$\lim_{t \rightarrow \infty} K = \lim_{t \rightarrow \infty} \left(\frac{Mt}{m_o(2t-t_o)} \right) = \frac{M}{2m_o} . \tag{16}$$

And, by substitution (16) into (15) we have the following equation

$$K_2 = \frac{M_x}{2m_o} + \frac{m_o}{2M_x} , \tag{17}$$

where $K_2 = K_{|(t \rightarrow \infty) \wedge (M = M_x)}$. Numerically, $K_2 = 10, 0250$. Under condition $(K_2 = 10,0250) \wedge (M = M_x)$, $t_2 = 49,43$ years, where t_2 denotes maximum theoretical longevity of pigs. In analytical form t_2 is given below

$$\frac{t_2}{t_o} = 2K_2^2 - \frac{1}{2} . \tag{18}$$

In this part of the study the continuum method was essential. The synergy of the both techniques is notable. Though the contribution of the techniques to this model is not equal.

This research deals with a transition from one growth trajectory to other. Or, what is the same, from one growth phenotype to other. It follows from the model that this transition is a discontinuous event of the first-order phase transition form. The hybrid model explains this transition well. How to obtain the same or similar results by continuum methods is unclear. How to show the growth trajectory bifurcation in the normal form is unclear. Growth of animals is a process observed on organism scale. How to see, and model the growth on molecular scale is unclear. If these are persistent problems then one can suggest to model the growth of animals by a hybrid technique on organism scale.

Moreover, the problem of scales bridging in animals requires knowledge of subtle facts of the processes studied or of the scales to bridge. In this case as well the hybrid method has advantage. The advantage has been achieved through the synergy of the modelling technique and the experimental facts. In this scheme the new knowledge has been acquired in the experiments and models.

5. Conclusions

- In this study the hybrid technique has sufficient power to describe emergent events in the growth of animals.
- It is the hybrid technique that can potentially bridge the scales considered in this study.
- To build a hybrid model of a process the experimental results have to be transformed to the analytical form. This kind of transformation of the data is nothing else as interpretation of the results.

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