WHY WE STOP GROWING

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CONTENT

PREFACE

In 2013 Paige Williams asked, “Why do we stop growing?” In her answer she noted, “It’s in our genes, but how they exert this control is a mystery”.

In the report, which appeared on NBC News, Williams acknowledged that Dr Scott A. Rivkees, a professor of paediatric endocrinology at Yale school of Medicine, had come to the conclusion that we were “just starting to understand the growth-promoting and growth-inhibiting factors of organs”.

Earlier findings by Slack (1999), as detailed in his book “On Growth and Form: Spatio-temporal Pattern formation in Biology”, led to three very interesting questions associated with growth:

(1) What controls the absolute size of the whole, or why are we bigger than mice? (2) Within a whole, what maintains the constancy of proportions of individual parts? (3) How is a possible change of relative proportions (allometry) produced?

In Geraert (2004) several answers are given in an article titled, “Constant and continuous growth reduction as a possible cause of ageing”. In another article called, “A quadratic approach to allometry yields promising results for the study of growth”, Geraert (2016) reflects on the mathematics of differential growth. A study on human growth based on data obtained in Belgium from the XIXth century was subsequently added to the literature (Geraert, 2018). These articles together with selected papers written on the growth of nematodes form the basis of this book.

The aim is to show the reader that the growth questions above have been answered. Studies of various animals (worms, arthropods, vertebrates) have showed one and the same phenomenon – and the human being presents no exception. As Needham (1964) already concluded, “It may be taken as established that growth is fundamentally similar in all organisms”.

Simple mathematics explain and predict growth – not only growth, but also the entire life cycle.

Some of the working titles of this book included “Ageing starts at birth”, “Constant and continuous growth reduction is the cause of ageing”, “Growth is never exponential” and “The Laws of Growth”.

In general, growth is not well understood. Having studied this complex phenomenon for years, I have come to the conclusion that growth is not time-dependent but relation-dependent. In other words, growth depends on the relationship between several parts of an organism.

I would like to thank Dr G. Packard (Colorado, USA) for mentioning Needham (1957) and the anonymous reviewer of Geraert (2018) for his interesting remarks.

Cited in Needham (1964) “The Growth Process in Animals”

“… our birth is nothing but our death begun …”

(From the poet Edward Young in “Night Thoughts”).

INTRODUCTION

Growth occurs equally well in unicellular and multicellular organisms. It is only in multicellular organisms that growth can be considerable; these organisms die, so multicellularity is only temporarily an advantage. The general idea is that growth starts exponentially (Huxley, 1924) until adulthood, and then unicellular offspring are made and only afterwards, ageing starts. Some presume that ageing is caused by the activity of special genes that were not active during growth. If these ageing genes were to be stopped, the adult would remain young and vigorous. Exponential growth means growth without restrictions. If, however, we consider that multicellularity in itself could cause problems, we might as well assume that the restrictions start at the very beginning. When a zygote divides, the many cells become slightly different. Every cell has its own metabolism: some products of each cell positively or negatively influence the metabolism of each other cell. As a consequence, a multicellular organism produces various growth-promoting and growth-inhibiting substances influencing the growth patterns.

To simplify the study of the three-dimensional and complicated growth patterns, it is customary to measure only some distances (or other data) and to compare the measurements. By putting observed values of a growth pattern in an arithmetic graph, curved lines are often found. The nature of the curve has been a subject of controversy for years. Huxley (1924) proposed a power curve. As this curve was not able to explain why growth stops, several other curves and variants have been introduced (see the review in Zeger and Harlow, 1987 for the curves known then). Some of the curves describe growth patterns that differ from what is studied here. For example, West *et al. (*1997, 2001) argued for fractional power laws on the basis that the limiting factor in growth was the formation of branching trees of the circulatory system and that this had an essentially fractal dimensionality.

MATHEMATICAL APPROACHES TO DIFFERENTIAL GROWTH

When growth is studied by comparing the measurements of two body parts over time a curved line is usually observed.

To decide which curve should be used, it has been found helpful to obtain scatter diagrams of transformed variables. To facilitate this, researchers use special graph paper for which one or both scales are calibrated logarithmically, referred to as semi-log or log-log graph paper, respectively.

One can also use arithmetic graph paper and untransformed variables.

The process of curve fitting has the disadvantage that different observers present different curves and equations, so there is a need for a theoretical understanding of growth.

The power curve theory

Huxley's (1924) assumption was that for a theoretical small amount of growth there was a constant ratio between the two growth rates of body part y and body part x.

$$dy/dx = \text{constant } k \qquad (1)$$

This resulted in the formula of allometric growth, first used by Snell (1891)

$$y = bx^k \qquad (2)$$

b and k being constant factors. This formula can also be written

$$\log y = \log b + k \log x \qquad (3)$$

The curvilinear relationship (2) is linearised when the data are plotted on a log-log scale. The slope of that line is represented by the power factor k (known as the allometric coefficient) and log b is the intercept of the line on the y-axis.

The study of growth has been greatly influenced by Huxley's proposal, although doubts have also been expressed. The results on log-log graph paper often show not one single straight line, but two to three consecutive straight lines. These observations have been explained by "sudden changes" in the allometric constant k, which have casted some doubt on the allometric formula (Ford & Horn, 1959 considered them as "methodological artefacts"). Several other formulas have been proposed, a review of which can be found in Zeger & Harlow (1987). The main point is that Huxley's curve did not consider that differential growth was size related.

As Kidwell & Williams (1956) noted: "Huxley (1924) suggested that this equation might express a general law of differential growth. Later (Huxley, 1932), in an attempt to establish a theoretical basis for the equation as a biological law, he derived the formula on the basis of assumptions about growth in general. A number of investigators have postulated different hypotheses to account for the allometric equation as a fundamental biological law of growth, but none has withstood critical analysis. It must be concluded that no satisfactory theoretical basis has yet been found for simple allometry."

Recent publications on that matter are for example, Stern & Emlen (1999), Gayon (2000), Knell *et al.* (2004), Shingleton (2010) and Packard (2012).

The parabola theory

In 1978 and 1979 I published several articles on growth and form in nematodes. I realised that the curves I obtained (when differential growth was studied) fitted best with parabolic curves. No theoretical explanation was given at that time, but I revisited my findings later on in Geraert (2004).

When we compare the growth of one body part in relation to another body part, we have to take into account that the growth of these two body parts is mutually controlled (the more so if the two body parts are functionally related to each other). This means that each additional amount of growth of one body part depends on the additional amount of growth of another body part with which it can be compared.

When we express the additional amount of growth in body part x as Δx and in body part y as Δy, we can translate the slight and gradual changes in shape during growth into slight and gradual changes in Δx and Δy. When these changes have a regular character, as they usually do, we can suppose that a constant Δx provokes a constantly smaller or larger Δy or for each $\Delta x = 1$, $\Delta y2 - \Delta y1 = 2a$ (a = constant factor). The resulting growth relation between x and y will be a quadratic parabola because for this curve “the second differences remain constant” (Batschelet, 1975). This curve can be written as

$$y = a.x^2$$

when the vertex is at the origin, or as

$$y = a.x^2 + b.x + c$$

when the vertex is not at the origin

The values b and c in this formula have a mathematical meaning, not a biological one; they are needed to position the curve in a diagram. The important factor is the quadratic factor a. It can have a positive or negative sign. When the sign is negative it shows that the increase in the y-value decreases and its size shows exactly the degree of change in the growth of body part y relative to x (multiplied by two it gives the exact value of the second growth difference in y for one unit of x). When, during growth, factor a is very low, the curves approach a straight line.

By using this formula, we assume that measurement y is the dependent variable and x the independent variable, but growth in general is more complicated. Moreover, the given measurements are probably not taken along the important growth axes. Nevertheless, the negative sign of a in various comparisons indicates why growth stops, namely, because the growth of one body part is constantly and negatively influenced by the growth of another body part. This does not happen suddenly or after some growth has occurred – it starts from the very beginning. Therefore, I hypothesise that when growth starts, a very precise growth pattern ensues that cannot be changed.

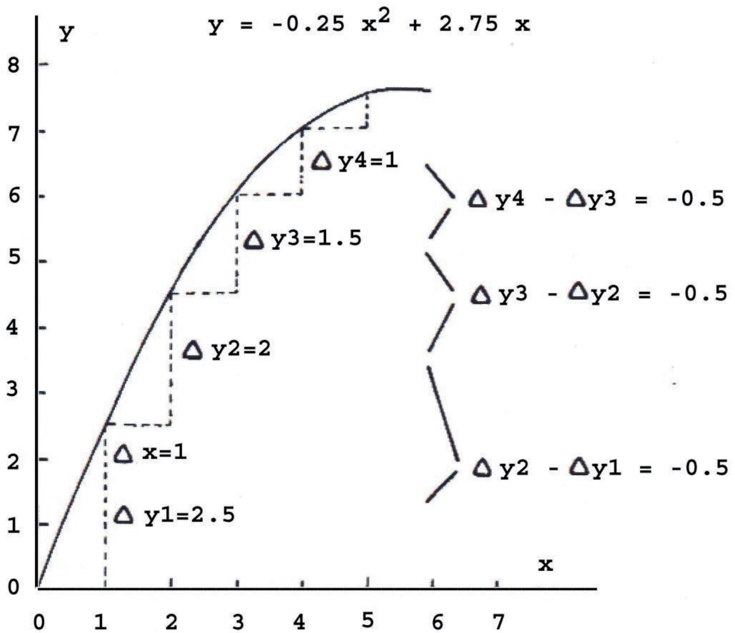


Fig. 1. *When the growth relation between y and x is of the form* $y = -0.25\, x^2 + 2.75\, x$ *then for a constant difference of x = 1 the second difference in y = -0.5. This is twice the quadratic factor of -0.25. In this theoretical example, factor c = 0 and so the parabolic curve goes through the origin (courtesy of* Biologisch Jaarboek Dodonaea).

MATHEMATICS OF THE QUADRATIC EQUATION

For the values x_1 and y_1 the quadratic equation reads as follows

$$y_1 = a.x_1^2 + b.x_1 + c$$

When one unit is added to x_1, the result is y_2.

$$y_2 = a.(x_1 + 1)^2 + b.(x_1 + 1) + c$$

$$y_2 = a.(x_1^2 + 2.x_1 + 1) + b.(x_1 + 1) + c$$

$$y_2 = a.x_1^2 + a.2.x_1 + a + b.x_1 + b + c$$

The difference between y_2 and y_1 is Δy_1.

$$\Delta y_1 = y_2 - y_1 = a.x_1^2 + a.2.x_1 + a + b.x_1 + b + c - a.x_1^2 - b.x_1 - c$$

$$\Delta y_1 = a.2.x_1 + a + b$$

When 2 units are added to x_1, the result is y_3.

$$y_3 = a.(x_1 + 2)^2 + b.(x_1 + 2) + c$$

$$y_3 = a.x_1^2 + a.4.x_1 + a.4 + b.x_1 + b.2 + c$$

The difference between y_3 and y_2 is Δy_2.

$$\Delta y_2 = y_3 - y_2 = a.x_1^2 + a.4.x_1 + a.4 + b.x_1 + b.2 + c - a.x_1^2 - a.2.x_1 - a - b.x_1 - b - c$$

$$\Delta y_2 = a.3 + a.2.x_1 + b$$

The second difference is between Δy_2 and Δy_1.

$$\Delta y_2 - \Delta y_1 = a.3 + a.2.x_1 + b - a.2.x_1 - a - b$$

$$\Delta y_2 - \Delta y_1 = 2.a$$

EARLIER DISCOVERIES

The study of differential growth in the abdomen of the female pea-crab, *Pinnotheres pisum* Leach, brought Needham (1950, 1957) to the conclusion that “For purely empirical purposes a general polynomial relation was fitted to the measurements, but the quadratic proved a very good fit”. Later, in his book on growth (Needham, 1964) he interpreted his discovery thus: “For simple comparative purposes, without theoretical implications, the fitting of the best polynomial relation has been advocated, largely because it is mathematically easy to manipulate”.

The arithmetic parabola was also used by Kidwell & Howard (1970), Martin (1960) and Walker & Kowalski (1971), whereas Cuzin-Roudy & Laval (1975) adopted the logarithmic parabola for their findings. It is interesting to know that every one of these authors stressed that his discovery was arbitrary and had no biological meaning.

Conclusion

The quadratic equation provides the most suitable answer to questions about several differential growth processes because the curve reflects the result of mutually controlled growth processes. Depending on size and function, mutual control creates a gradual change in shape; the more constant these changes between body parts are, the more the observed measurements will match a calculated parabola.

Huxley’s allometric growth formula (the expression of a non-size-related change in shape) was not suitable for the differential growth studies I checked.

THE RESTUDY OF HUXLEY'S MATERIAL

1. The case of *Carcinus maenas*

Huxley & Richards (1931) compared the increase in the width of the abdomen with the increase in carapace length of the shore crab *Carcinus maenas*. The sample was split into three categories: unsexables, females and males. Huxley (1932) gave the measurements for the unsexables and the females using abdomen breadth for y and carapace length for x (both in mm).

I calculated the quadratic equation between both (Fig. 2) thus

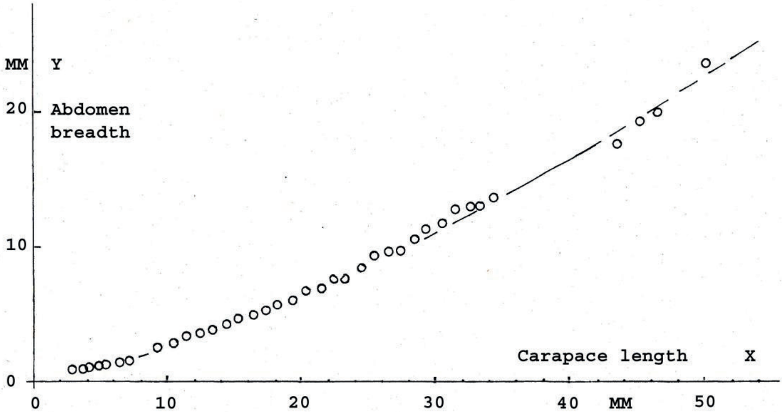
$$y = 0.0039\,x^2 + 0.2685\,x - 0.467$$

For each 10 mm increase in carapace length (= x) the abdomen breadth (= y) shows a constant secondary increase of 0.78 mm (this is twice the quadratic factor).

Huxley (1932) did not find the single straight line needed to support his theory in the case restudied here. The logarithmic plotting showed a kink in the observations for females as well as for males, so different growth coefficients were observed for younger and older specimens. Huxley (1932) gave several k-values (added on Fig. 3) that he experimentally derived from his figure. Moreover, the constant b was not given. Therefore, it is not possible to compare his (several) equations with the single quadratic equation I obtained. The straight lines found by Huxley (1932) in his log-log diagram (Fig. 3) can be interpreted as mathematical accidents. However, Fig. 2 suggests another three consecutive straight lines, which are also mathematical accidents but on an arithmetic diagram.

Fig. 2. *Comparison of carapace length to abdomen breadth in the shore crab* Carcinus maenas. *The measurements given in Huxley (1932) are represented on a double arithmetic scale (and not on a log-log scale). The open circles are the measurements for*

the unsexed specimens and for the adult females of the shore crab. The calculated quadratic parabola is added. (courtesy of Belgian Journal of Zoology).



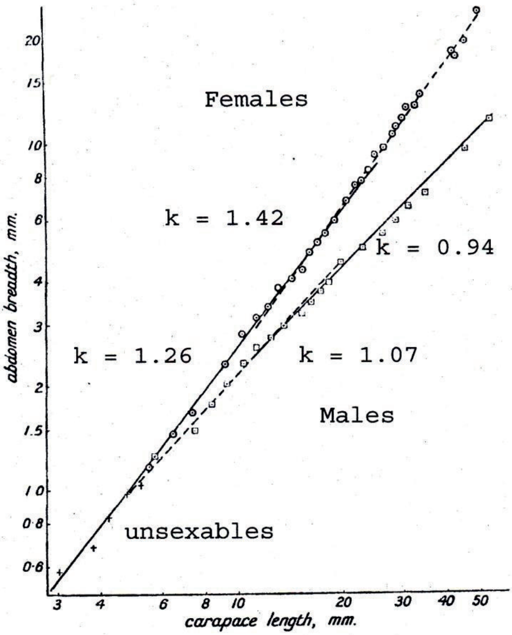


Fig. 3. *Figure taken from Huxley (1932) with the following explanation: "Increase of width of abdomen with increase of carapace length in the shore crab,* Carcinus maenas, *logarithmic plotting". The signs for unsexables, males and females are explained on the graph. The growth coefficients given by Huxley (1932) were also added. (courtesy of* Belgian Journal of Zoology).

Studying the relationship between abdomen breadth and carapace length with a different approach yielded more interesting results (Fig.4), namely, by considering the carapace length (= y) as dependent on the abdomen breadth (= x). The formula is as follows

$$y = -0.0375\ x^2 + 2.917\ x + 2.483$$

For each 1 mm increase in the abdomen breadth (= x) there is a constant secondary decrease of 0.075 mm in the carapace length (this is twice the quadratic factor). Therefore, the growth in length of the carapace is negatively influenced by the growth in width of the abdomen.

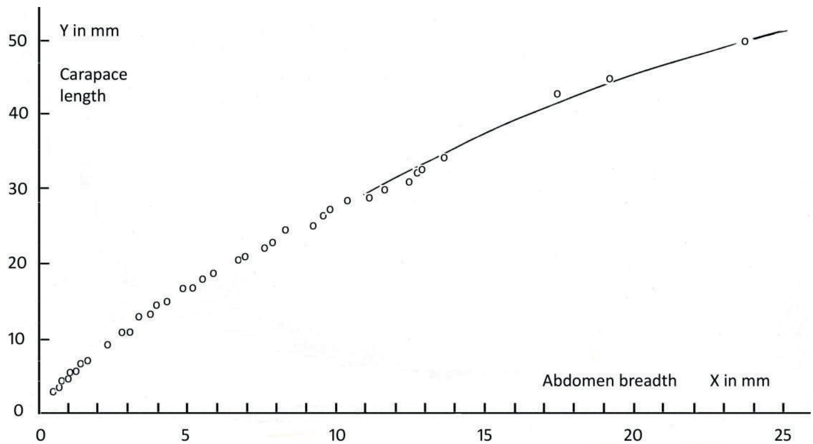


Fig. 4. *Comparison of carapace length and abdomen breadth in the shore crab* Carcinus maenas. *The measurements for the unsexed specimens and for the adult females are given. The calculated quadratic parabola is added.*

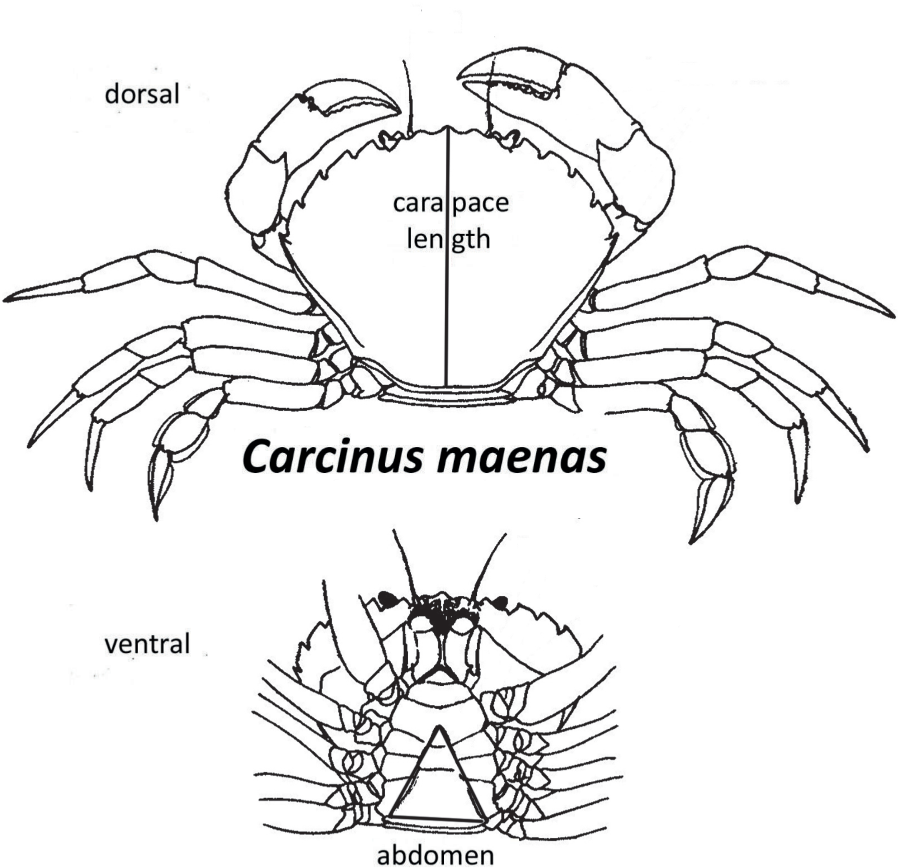


Fig. 5. *Dorsal and ventral view of the shore crab with indication of the carapace length and the shape of the abdomen.*