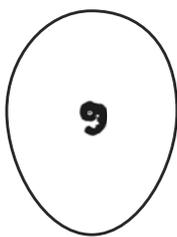


Chapter 1

Basic Aspects of Growth



Growth is a generic term that describes processes in which the mass of a body changes over time. In biology, the problem of growth is fundamental to all aspects of life, with realizations as diverse as cell division, morphogenesis, development, maintenance, cancer, and aging. All life forms experience growth to some appreciable degree and one of the ultimate challenges of modern biology is to understand the role of the genetic code in transforming cells into fully mature organisms and explaining how these organisms manage to regulate shape and function through growth and remodeling.

Growth processes also appear in some physical processes where new material is added to an evolving system. For instance, in epitaxial growth, a thin layer of crystal is produced by depositing raw material on an existing crystalline substrate. Growth is also associated with phase transition phenomena, where an interface evolves in time to produce new structures such as crystals [81, 687, 765]. These free boundary problems are controlled by diffusion and, unlike biological systems, the interface is a line of discontinuity with no particular material property. The swelling of gels is arguably the closest nonbiological process that mimics growth as it is non-diffusive and occurs in the bulk of the material. It can be used as a physical analog to gain insight into the role of mechanics in biological pattern formation [116, 663, 904].

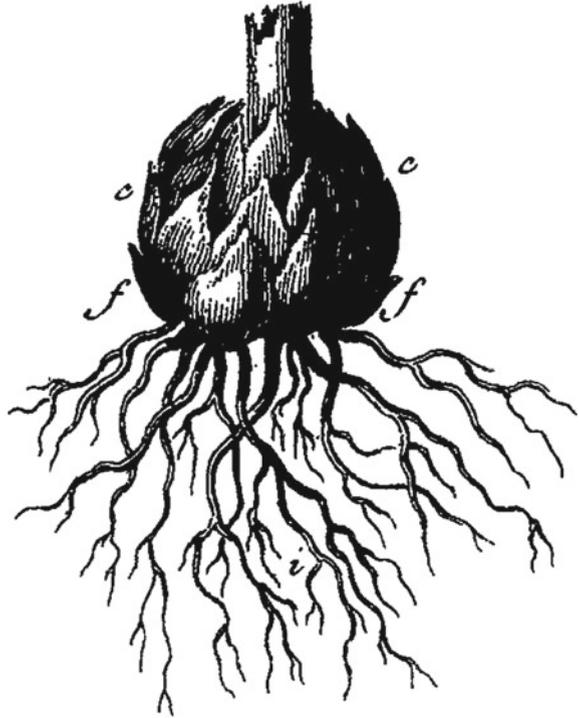
Our study of growth will mostly be limited to non-diffusive processes relevant to biological systems.

1.1 Classification

Aspects of growth and remodeling occur during the entire life of an organism. Therefore, growth fulfills many purposes and, accordingly, is associated with qualitatively different processes. Traditionally, a first classification is obtained by considering the way growth alters a body, either by changing its volume, its material properties, or by rearranging the relative position of material points. The three main growth processes are:

- **Growth.** The term *growth* by itself refers to a change in mass. It is colloquially understood as an increase in mass, but the concept extends naturally to describe mass reduction or shrinking. Change in mass can be created either by addition of mass at constant density, as found in the development of soft tissues, a change in density at constant volume, as in the case of bone densification, or both as found in a developing bone. Mathematically, a theory of growth must allow for changes in mass, volume, and density and must be flexible to account for mass permeating through the boundary of the body, accumulating at the boundary, or occurring within the body itself.
- **Remodeling.** It is well known that in the process of aging, tissues may become stiffer or softer. The term *remodeling* refers to an evolution of material properties in a system without change of mass such as stiffness, fiber orientation, fiber strength, and so forth. These remodeling processes are due to a change in the microstructure that determines the overall behavior of the tissue. For instance, the typical composition of soft tissues in many animals is a mixture of collagen fibers within an elastin matrix. Whereas elastin content remains mostly unchanged over many years, there is a continuous turnover of collagen that depends on the local biochemical and mechanical stimuli acting on the cells. The relative content of different types of collagen fibers and elastin determines the overall response of the tissue [635]. This process can occur without a change of mass, but it is crucial to understand the response of a tissue under mechanical loads. From a mathematical perspective, the variation of material properties can either be modeled by considering a separate evolution of the material parameters of a system or, at a lower scale, by taking into account the evolution of separate tissue components.
- **Morphogenesis.** Early in embryonic life, new tissues and organs are formed. In this process, major reorganization and differentiation of cells take place after cell division, and, importantly, there is a restructuring of material elements. This reorganization process can only happen if the adhesion between different components is weak enough so that they can separate and reattach. This simple observation has important consequences for modeling as tissues undergoing morphogenesis exhibit rapid elastic stress relaxation and plastic-like flow. Mathematically, this

Figure 1.1 Growing root as depicted by Duhamel in 1758 [898].



evolution is often described by modeling tissues as fluid or viscoelastic rather than elastic, even though these two points of views are equivalent, as we will show.

Growth can be further classified by the location of material addition. It can occur at the tip, on the surface, or in the bulk. We consider these processes in more detail next.

1.1.1 Tip Growth

In his book, “The Physics of Trees” published in 1758, Duhamel du Monceau describes the following discovery: “*The observations that I made in plants that grow in water helped me discover another peculiar phenomenon; that is, roots only grow at the tip.*” [898, p. 83] (see Figure 1.1). *Tip* or *apical growth* describes growth processes that take place in a small region at the tip of a filamentary structure. As shown in Figure 1.2, it is the main growth mechanism used by many microbial organisms and plant systems such as fungi, filamentary bacteria, pollen tubes, and root hair [431, 457, 479, 480, 482, 541, 625, 714, 715, 899, 1073]. In these organisms, there is a small active growing zone located near the tip where the outer shell is constantly remodeled and new material is consistently added.

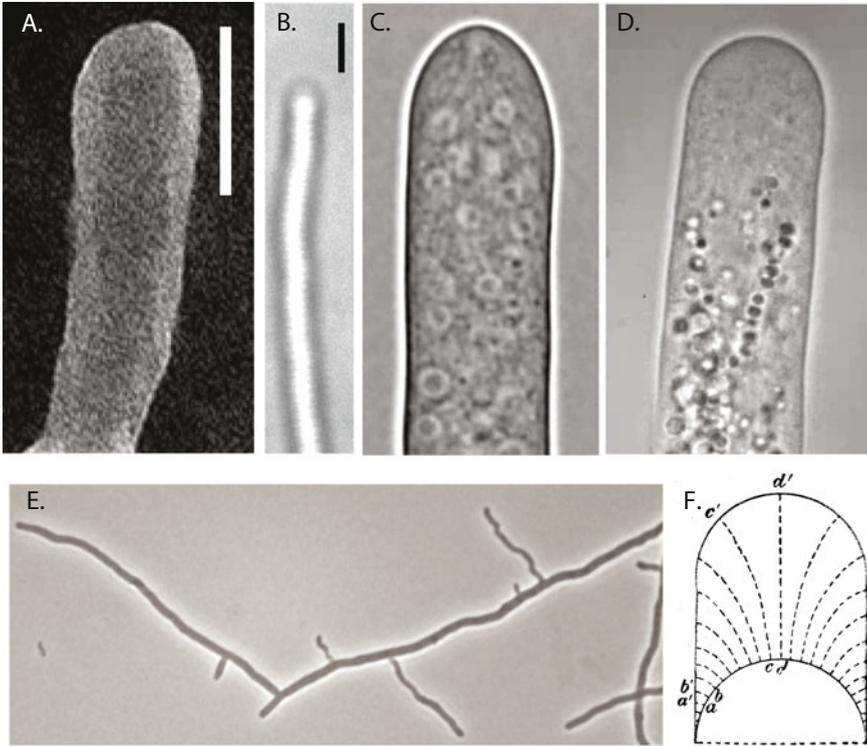


Figure 1.2 Tip growth. A. microbacterial filament, (bar is $1\ \mu\text{m}$) (*Kitasatospora setae* source: Society for Actinomycetes Japan, photograph by Y. Takahashi and Y. Iwai); B. microbacterial filament (*Streptomyces coelicolor* A3(2)), (bar is $1\ \mu\text{m}$); C. *Allomyces*; D. lily root hair (typical diameter $15\text{--}20\ \mu\text{m}$) (images courtesy of Jacques Dumais). E. Branching in *streptomyces* A3(2). F. First theoretical description of tip growth by Reinhardt in 1892 for the growth of fungus [1073].

For sufficiently small organisms, such as filamentary bacteria, the newly added material is transported to the tip by diffusion processes whereas for larger organisms, such as fungi and pollen tubes, active transport processes which require a complex internal structure are required for propagation.

Typically growth occurs in a region that maintains a constant size. Therefore, the typical scaling of mass with time is linear, as shown in Section 4.3. However, many filamentary structures also undergo repeated branching as shown in Figure 1.2E. These branches allow for one-dimensional structures to explore three-dimensional volume for nutrients. This branching process transforms the scaling of mass from being linear to exponential with respect to time since each new branch adds mass linearly and can branch again, leading to an intricate, fractal-like, geometry.

Tip growth is sometimes referred to as *primary growth* in plants. Once a stem or root is large enough, it may also undergo *secondary growth*, sometimes referred to as *growth in the cambium*, by the addition of external layers to thicken itself.

Cambial growth in trees takes place between the old wood and the bark of the tree, and seasonal variations lead to the formation of tree rings.

Mechanically, the main issue is to understand the interaction of the tip with its environment and to determine its shape, internal stresses, and how a filamentary structure evolves based on different laws for material addition.

1.1.2 Accretive Growth

Accretive, surface, or appositional growth describe mechanisms, such as deposition in hard tissues, where new material is added to the boundary of an existing body. It is the typical mechanism responsible for the formation of teeth, seashells, horns, and corals [4, 914, 915, 1173]. At the microscopic level, surface growth is also found in bones where changes in bone density occur by deposition or resorption of new material on the surface of trabeculae, or the walls of canals excavated by osteoclasts [1230].

Mathematically, many problems in accretive growth can be modeled geometrically by studying the evolution of the boundary as a function of accreted mass. For instance, the shell of the ammonite in Figure 1.3 is the result of material being accreted with different velocities at different points of the opening. This velocity gradient is necessary for coiling since the outer ridge requires more material than the inner ridge. In general, if the boundary is known at time t , an accretion vector, giving the local velocity of material accretion, can be defined at each point on the boundary as shown in Figure 1.4D. The new boundary is then obtained after a small incremental time Δt .

Figure 1.3 The fossil shell of an ammonite of the genus *Promicroceras* [916]. Arrows denote the accretion vectors.



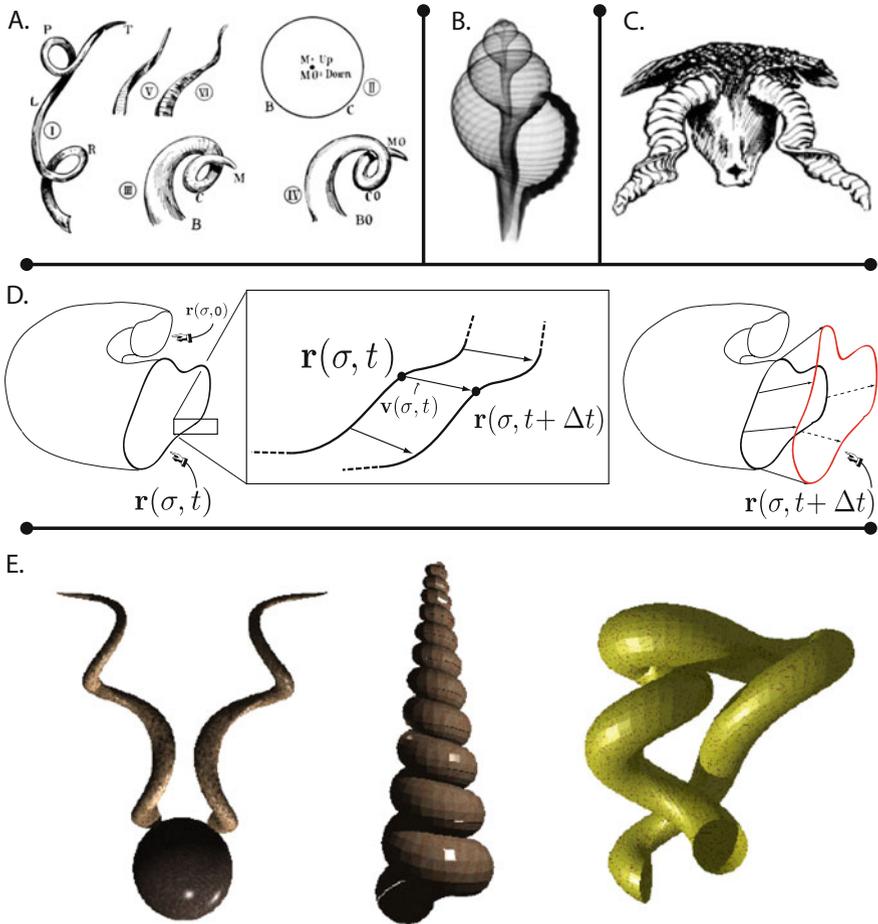


Figure 1.4 Accretive growth. ABC. Growth of horns and seashells as described by D'Arcy Thompson [1230]. D. The theoretical basis of accretive growth. For a given body at time t , a growth vector is defined at the active growth boundary. At time $t + \Delta t$ a new surface is created. E. Different body forms obtained by different choices for the growth vector (adapted from [914]).

The key question from a modeling point of view is to derive an accretion law based on the interaction between the soft part of the animal and the new hard accreted part. Mathematically, the main problem is to understand and classify the shapes and patterns that emerge through this process [202].

1.1.3 Volumetric Growth

Bulk, *volumetric* or *interstitial* growth all refer to processes in which local volume elements in the body change over time rather than on its boundary as in accretive or tip growth. Bulk growth is typical of many developmental, physiological, and pathological processes and has been particularly well documented in arteries, muscles, solid tumors, and the heart [242, 636, 1206].

Bulk growth encompasses *hyperplasia*, the increase of volume due to cell proliferation which is typical of many developmental systems; *hypertrophy*, the change of volume due to enlargement of its constituents, typical of many physiological processes; and *neoplasia*, the abnormal and often unregulated growth or division of cells found in cancer.

Mathematically, bulk growth offers many outstanding challenges. First, a local volume element may not remain isotropic during growth which implies that a tensorial description of the deformation is needed. Consider an infinitesimal spherical volume element extracted from a tissue, as shown in Figure 1.5. In volumetric growth, this sphere is transformed into an ellipsoid. This deformation is fully captured by the transformation of three orthogonal vectors into three new vectors along the principal directions of the ellipsoid. Mathematically, this local mapping is described by a tensor. Accordingly, the process of volumetric growth assigns a tensor, the *growth tensor* \mathbf{G} , at each point of the body, describing the change of a local volume element. A theory of growth is therefore intrinsically rooted in the theory of tensors.

A second challenge in bulk growth is that it is relevant for soft tissues that are elastic and can also be deformed by the application of loads. When observing the deformation of a body from an initial state, we must determine whether it is due to the growth or elastic response of the material, or even a combination of the two processes. This problem, which will be discussed at length in further chapters, was

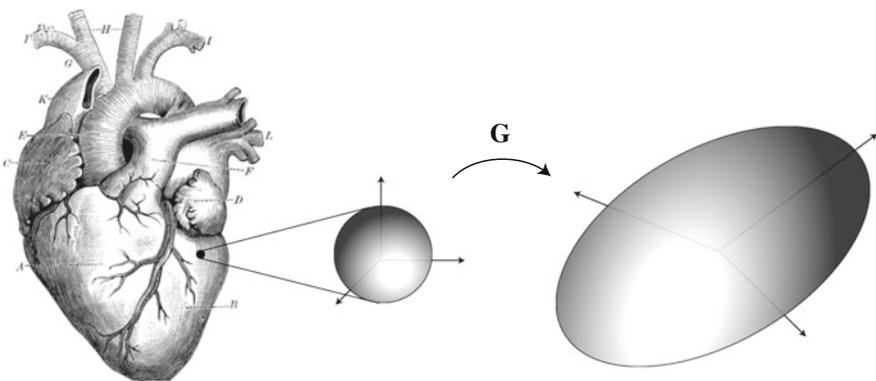


Figure 1.5 Volumetric growth. During growth, a local element inside the tissue can expand or shrink anisotropically. The description of such a process requires the definition of a growth tensor \mathbf{G} , locally transforming an infinitesimal sphere to an infinitesimal ellipsoid.

first formulated by Hsu in 1968, arguably the first work to address the fundamental problem of mechanical growth modeling: “*If the form to which a body grows under no applied loads is known, what will be the form of the body if some mechanical loads are applied during its growth?*” [627].

From a modeling perspective, bulk growth can also be used to describe the growth of filamentary objects, such as neurons or plant stems that have distributed growth, or surfaces, such as epidermal layers of cells that do not change their thickness.

The classification of growth as tip, accretive, or bulk is descriptive but not formal. It depends on the scale at which the problem is being studied. Indeed, both tip and accretive growth can be modeled as bulk growth processes where a thin soft layer, close to the boundary, expands and stiffens in time. Essentially, tip growth is a bulk process that is localized at the apical part of the filament. A detailed analysis of this process requires an understanding of areal growth due to the insertion of new material. Similarly, bone growth and wound healing can be modeled either as an accretive process or a localized bulk process where density evolves.

1.2 The Scaling of Growth

The first question about growth is one that is shared by most parents: How does the size of an organism change in time? The first historical records of growth were on the height of human beings. In 1759, Count Philibert Gueneau de Montbeillard started to record the height of his first son on his birth and he continued to do so every six months until his son reached the age of 18. This record, shown in Figure 1.6, was published in the fourth volume of the supplement to Buffon’s “Histoire

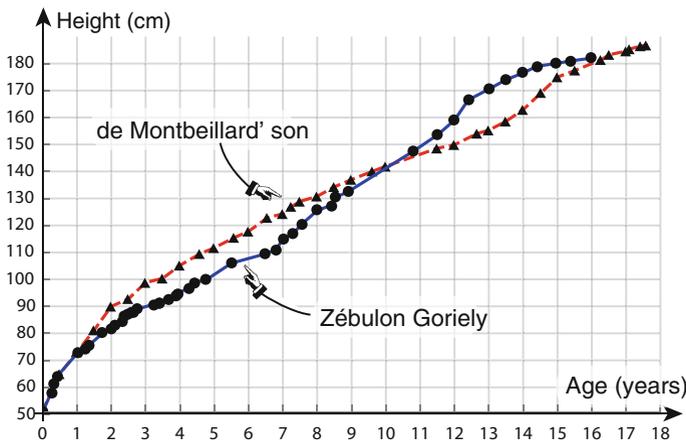


Figure 1.6 Record of longitudinal growth done by Count Montbeillard from 1759 (data from [1123]), compared to the height of Zébulon, the author’s first son.

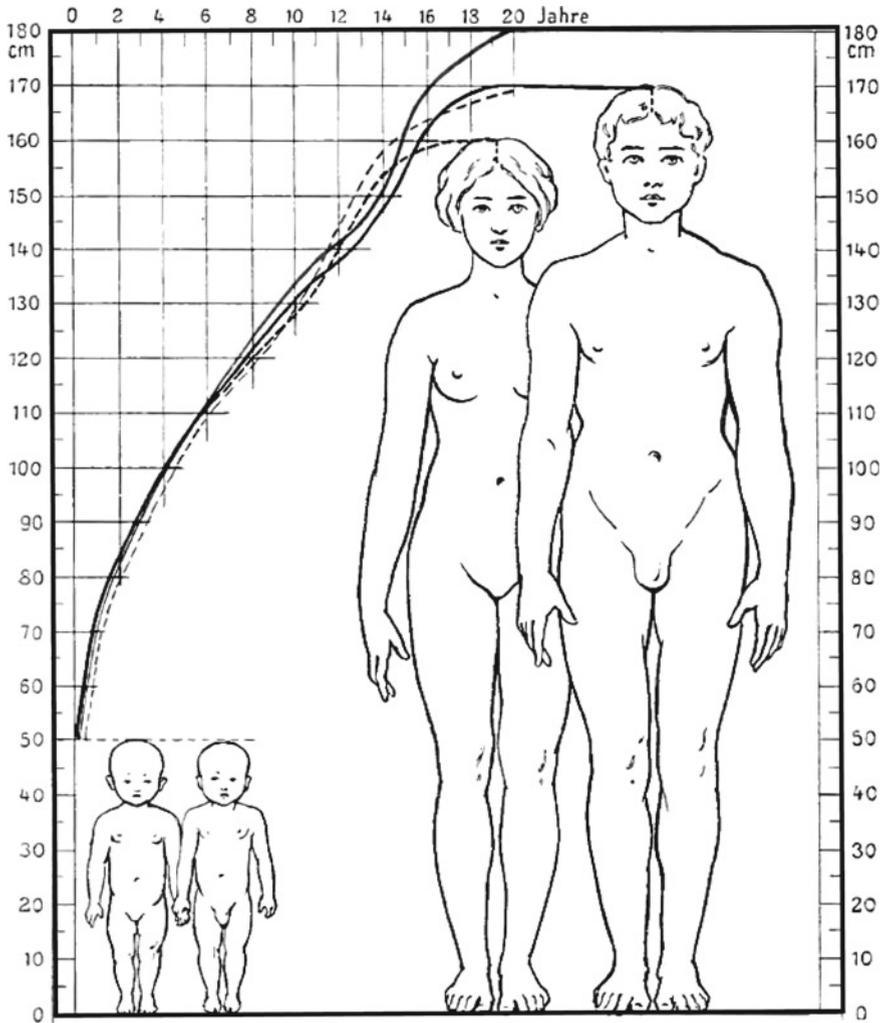


Figure 1.7 Growth curves obtained from statistical averages (from Stratz’s book published in 1904 [1200]).

Naturelle” [1123]. A quarter of a millennium later, it still captures the essence of human development from birth to adulthood. Its gross features are similar to the growth curve of the author’s first son as well as the curves found in modern medical growth charts, shown in Figure 1.7. These curves are the result of statistical averages over large populations and show variations over different geographic regions.

The first complete statistical study of the evolution of weight and height in human beings was conducted by the Belgian polymath, Adolphe Quetelet, and published in his “Treatise on Man” in 1835 [1053]. In this remarkable book, Quetelet pooled

and analyzed data from the Belgian population. He considered both general trends and deviations around the average using the Gaussian distribution. This work is considered to be the first application of the Gaussian distribution in a statistical study. Quetelet also suggested a law of growth by fitting the data of height $H(t)$ against time t

$$H(t) = at + \frac{b + t}{1 + \frac{4}{3}t}. \quad (1.1)$$

If both mass $M(t)$ and height $H(t)$ are known, one can speculate on how these two quantities might be related to each other. It was again Quetelet who proposed that, independent of time, weight is related to height by a scaling law of the form $M = cH^\alpha$, where $\alpha = 5/2$ during childhood and $\alpha = 2$ for adults. For $\alpha = 2$, the *Quetelet coefficient* c becomes the infamous *Body Mass Index* (BMI), which remains a critical estimate of fitness and obesity despite its obvious shortcomings and many criticisms [283]. Historically, Quetelet's proposal that height scales with respect to weight is the first case of an *allometric law*, that is, a power law between a given physical quantity and the total mass of the organism [649, 816, 1126, 1147] (see Section 1.3).

Quetelet's book prompted similar studies and, by the end of the nineteenth century, there was a flurry of activity dedicated to understanding growth in humans, animals, and plants [292]. The idea emerged that growth in different biological organisms could follow some universal laws that would determine sizes and forms. This research program was presented in the seminal book "On Growth and Form" by D'Arcy Thompson, first published in 1917 [1230]. This monumental book remains a reference and a source of inspiration for many researchers to this day.

Bogin reports that, by 1972, no less than 200 different models or fitting functions had been proposed to describe the evolution of human growth [110]. The modeling of growth as a slow continuous process is only valid on the long-time scale of months or years. A detailed daily recording and analysis of height in infants between the age of one and two shows that growth mostly occurs through discontinuous aperiodic *saltatory spurts* [759, 760] of about 0.5 to 2.5 centimeters separated by long intervals typically lasting between 2 to 63 days, where no growth takes place as shown in Figure 1.8. Jumps and oscillations during growth are also encountered in other biological systems including fungi [799], pollen tubes [188, 360, 590], plants [354, 728], and invertebrates [78].

The first attempt to model the evolution of the total mass from physical principles was based on an idea by Pütter, first published in 1920 [1048]. Pütter proposed that animal growth can be seen as a balance between addition and removal of building materials in the body. Growth proceeds as long as new material is added faster than it is removed, and stops when both processes are balanced.

Typically, in such models, the rate of material removal is assumed to be proportional to the mass $M(t)$ itself, as in a standard exponential decay problem, whereas the rate of addition of new material is proportional to a power of the mass. Combining these two effects leads to [1285]

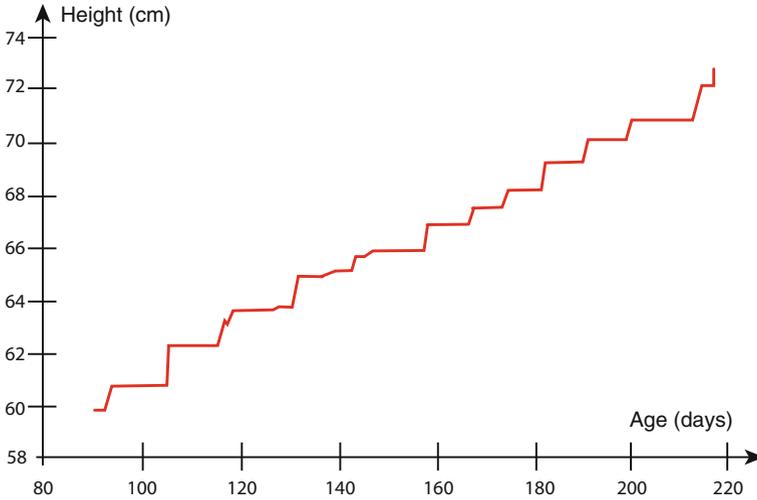


Figure 1.8 Daily measurements of the height in a boy between the age of 90 to 218 days show discontinuous growth spurts separated by periods of no growth (data from [760]).

$$\dot{M} = M(aM^{-p} - b), \quad (1.2)$$

where $\dot{M} \equiv dM/dt$ denotes the time derivative of $M(t)$ and $ab > 0$. The solution of this equation for $p = 0$ describes a simple exponential process

$$M(t) = M_0 e^{(a-b)t}, \quad (1.3)$$

where $M_0 = M(t = 0)$ is the mass at birth.

For $p \neq 0$, Equation (1.2) is a Bernoulli equation [460, p. 232] whose general solution is given by

$$\left(\frac{M(t)}{M_\infty}\right)^p = 1 - \left[1 - \left(\frac{M_0}{M_\infty}\right)^p\right] e^{-bpt}, \quad (1.4)$$

where $M_\infty = (a/b)^{1/p}$ is the asymptotic mass. Figure 1.9 shows examples of mass evolution as a function of time for various values of the parameters.

Equation (1.2) also contains the classic *logistic model* [1255] obtained for $p = -1$ with a and b negative, and the *Richards model* [1078], defined by $p < -1$, used to model the growth of plants.

While this general approach is appealing, the choice for the exponent p is problematic. A typical argument is to assume that the addition of new material is limited by energy input and metabolic rates. If the energy intake and growth rate are directly proportional to the weight itself, we have $\dot{M} = \alpha M$ for a certain $\alpha \neq 0$. This behavior is recovered with $a > b > 0$, $p = 0$, and exponential unlimited growth is observed.

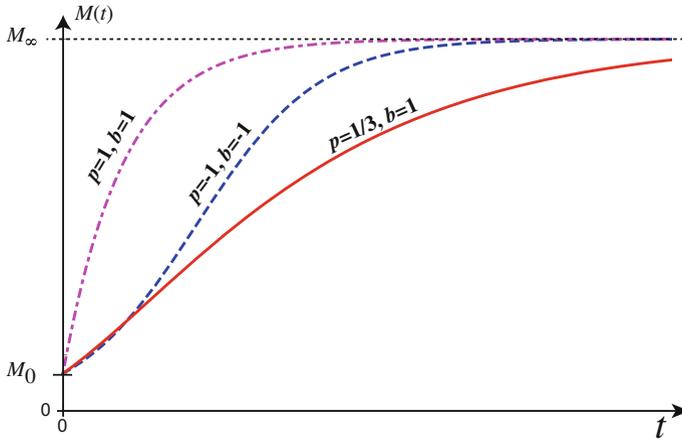
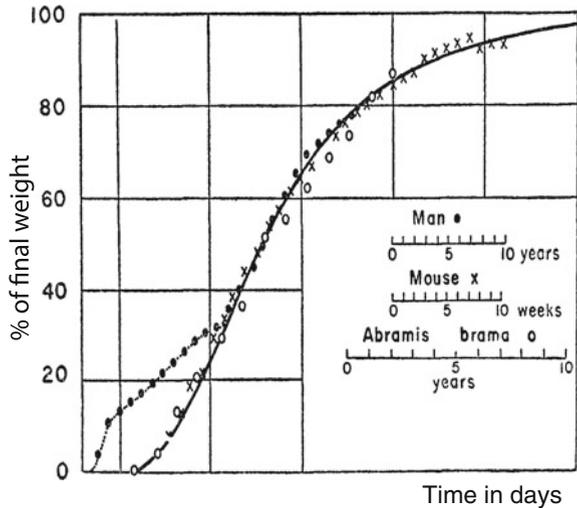


Figure 1.9 Examples of growth curves given by Equation (1.4) for various values of the exponent p .

Figure 1.10 Example of data fitting with $p = 1/4$ by von Bertalanffy [1285] (*Abramis brama* is the common bream).



This behavior, observed in the early developmental stages of insects, is only valid until a new phase of growth takes place.

If we assume that the metabolic rate follows a scaling law based on geometry by postulating that energy intake is proportional to surface area, we have $\dot{M} = \alpha M^{2/3}$, which corresponds to the choice $p = 1/3$. This power law was originally proposed in 1839 by Sarrus and Rameaux [1118]. Based on the same general ideas, Ludwig von Bertalanffy [1285] suggested that most biological systems grow in an intermediate regime with exponent $0 < p < 1/3$ and suggested $p = 1/4$ as suitable to fit different data sets, as shown in Figure 1.10.

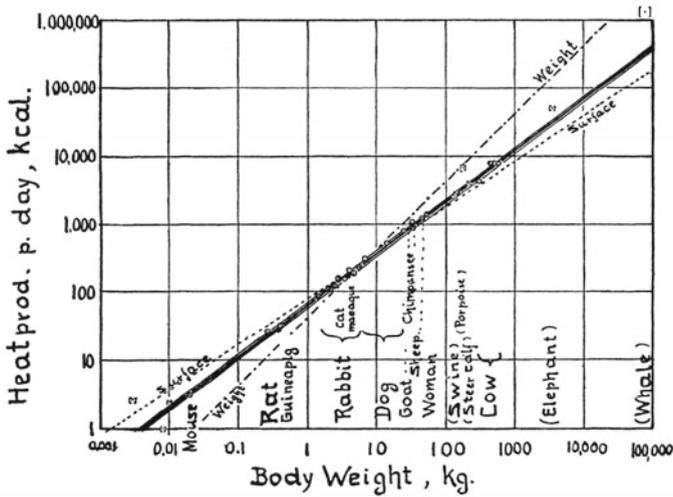


Figure 1.11 Kleiber’s law: metabolic rate as a function of mass [704]. The experimental data for the variation shows a 3/4 power law. It is compared with a scaling with respect to surface area (2/3) and weight (1).

More recently, it was proposed [1316] that the production of new material should be related to *Kleiber’s law* [704], which states that the metabolic rate of an organism, defined as the energy expended by an organism per unit time, scales as the three-fourth power of the total mass as shown in Figures 1.11 and 1.12. This assumption also leads to von Bertalanffy’s choice of $p = 1/4$.

It has been argued that this power law for the metabolic rate is widely applicable to biological systems from bacteria to whales and even plants and forests [957], spanning 27 orders of magnitude in mass. However, some authors have criticized the validity of this statistical analysis and have argued for exponents closer to two-third [572, 1126]. The problem is that the arguments used to derive such laws are inevitably vague and based on a number of simplifying assumptions that neglect many well-established physiological processes. Unfortunately, the absence of a theory for growth linking mass to size leaves room for endless discussions, controversies, and grandiose teleological theories with very little scientific content and no mathematical foundation. As a result, the general field of scaling laws for growth remains in its infancy [287, 1315].

For any choice of exponent $p \in (0, 1]$, the growth curves show a sigmoidal behavior observed in many organisms as shown in Figure 1.9. A slow initial phase is followed by quick maturation, that slows down after the reproductive age, eventually reaching an asymptotic limit.

Humans have evolved and adapted in such a way that they cannot be simply described by many of the power laws applicable to other species. However, these animal models can still be used to describe human growth if pre- and post-pubertal periods are considered independently [106].

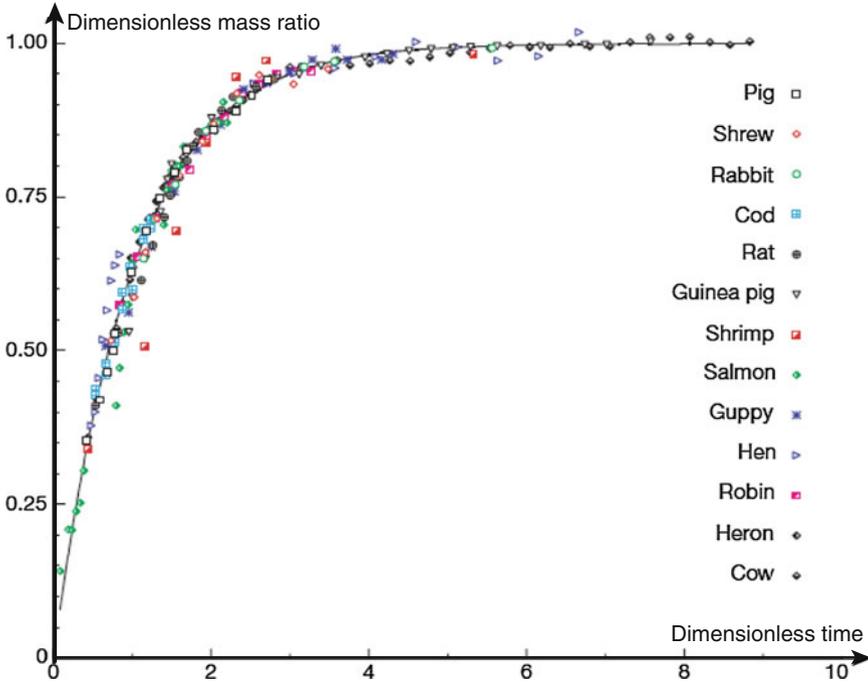


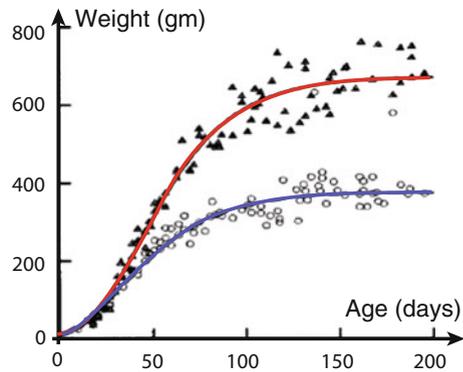
Figure 1.12 Scaling and data analysis based on Kleiber’s law [1316]. Here M/M_∞ is plotted against the dimensionless time $\tau = bpt - \ln(1 - (M_0/M_\infty)^p)$ as described by Equation (1.4) with $p = 1/4$.

The key feature of this simple power-law model is that it identifies the *specific growth rate*, defined as the growth rate per unit mass, \dot{M}/M , as a central quantity. The basic idea in all models showing a sigmoidal behavior is that a proportion of new tissue generated by growth is capable of growing itself, but as time goes by, this ability is reduced. These two typical trends were first presented as fundamental principles for growth by Peter Medawar in 1941 [856] when he wrote: “*What results from biological growth is itself, capable, of growing*” and “*Under the actual conditions of development, the specific acceleration of growth is always negative.*”

Another model that has been used in the context of growth is the so-called *Gompertz’ law*, first introduced in 1825 [455] for the evolution of human populations. It was subsequently used in actuarial sciences as a modified compound law, then rediscovered as a suitable growth law for organisms [244, 1329]. The Gompertz law is obtained as the solution of a Malthusian equation of growth, $\dot{M} = KM$, with a growth rate K decaying exponentially in time, following Medawar’s principles. Choosing $K = a \exp(-kt)$ with $a, k > 0$, we have

$$\dot{M} = ae^{-kt} M, \quad a = k \ln \left(\frac{M_\infty}{M_0} \right), \quad (1.5)$$

Figure 1.13 Gompertz' law. Growth curves for male (triangles) and female (circles) rats (*Rattus norvegicus*) fitted by a Gompertz law (adapted from [1195]).



which leads to

$$M(t) = M_{\infty} \left(\frac{M_{\infty}}{M_0} \right)^{-e^{-kt}}. \quad (1.6)$$

This equation, whose solution contains the exponential of an exponential and two characteristic time scales ($1/a$ and $1/k$), has been shown to be a particularly good fit for bacterial and tumor growth, among others [37, 965, 1090, 1341, 1369], and remains widely used for the purpose of fitting experimental growth data as illustrated in Figure 1.13.

1.3 Relative Growth

Extensive psychological studies have demonstrated that children and puppies are cute and lovable [20, 727]. It has been argued that this *cuteness factor*, a propensity or desire to cuddle or defend a person, is due in part to our perception of the relative size of body and facial features in children versus adults [110, 803]. As shown in Figure 1.14, the skull of babies is proportionally larger than those of adults [159]. Further, the relative dimensions of the skull, such as height versus diameter or roundness, are also different. Our ability to distinguish almost instantaneously children from adults independently of their size implies that no adult organism is simply a pure dilation of itself at birth.

The pure dilation of an organ or organism from birth to adult life, is referred to as *isometric growth*, as shown in Figure 1.15, whereas the relative growth of an organ with respect to the total weight of the organism is known as *allometric growth*. Therefore, the second fundamental problem of growth is to understand how organs, limbs, or tissues grow with respect to the total body mass. This is the general topic of the theory of *relative growth* [648, 649, 857].

The subject of relative growth was first discussed by Galileo in 1638 when he considered the relative size of bones in animals [414]. He writes: “*Nature cannot*

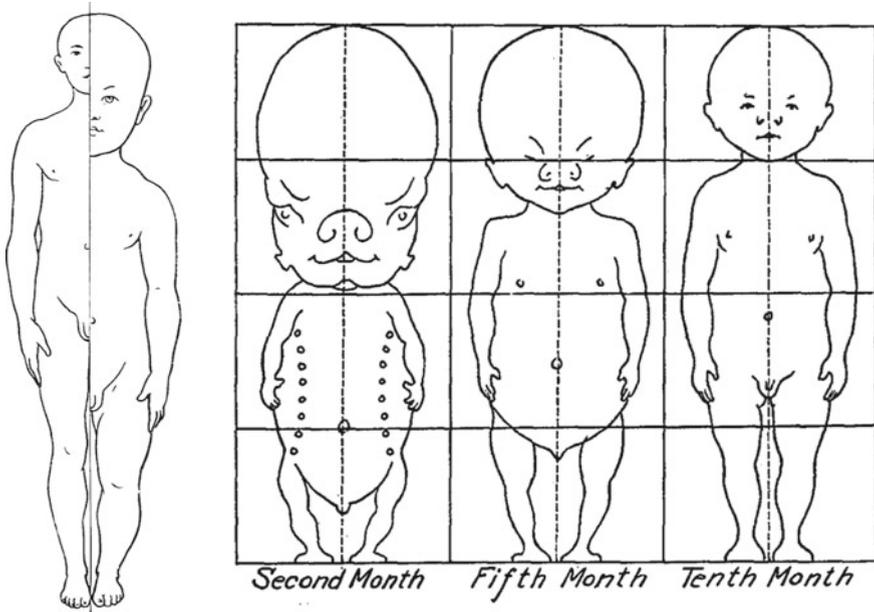
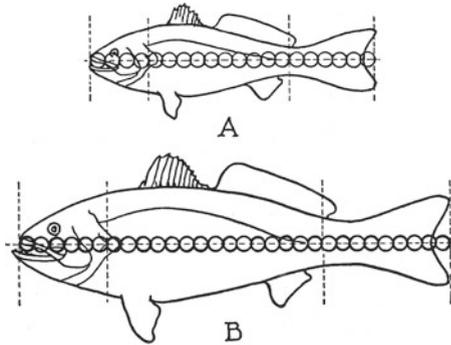


Figure 1.14 Relative proportion in the growth of man (adapted from Stratz [1200]).

Figure 1.15 Isometric growth. Hecht found in 1916 that the dogfish *Anchovia brownii* grows isometrically. Its adult form (B) is a uniform dilation of its infant form (A) [557].



produce a horse as large as twenty ordinary horses or a giant ten times taller than an ordinary man unless by miracle or by greatly altering the proportions of his limbs and especially of his bones.” That is, the same bones in larger animals are comparatively thicker than those in smaller animals, as illustrated in Figure 1.16B. The discussion on giants by Galileo is based on the common belief at the time that large fossil bones of dinosaurs or large mammals belonged to giants of the past. The biggest giant in Figure 1.16A, next to an “ordinary man”, is based on bones discovered in Sicily. Through simple scaling arguments, Galileo correctly concluded that if giants did exist they would not be a simple dilation of an ordinary man.

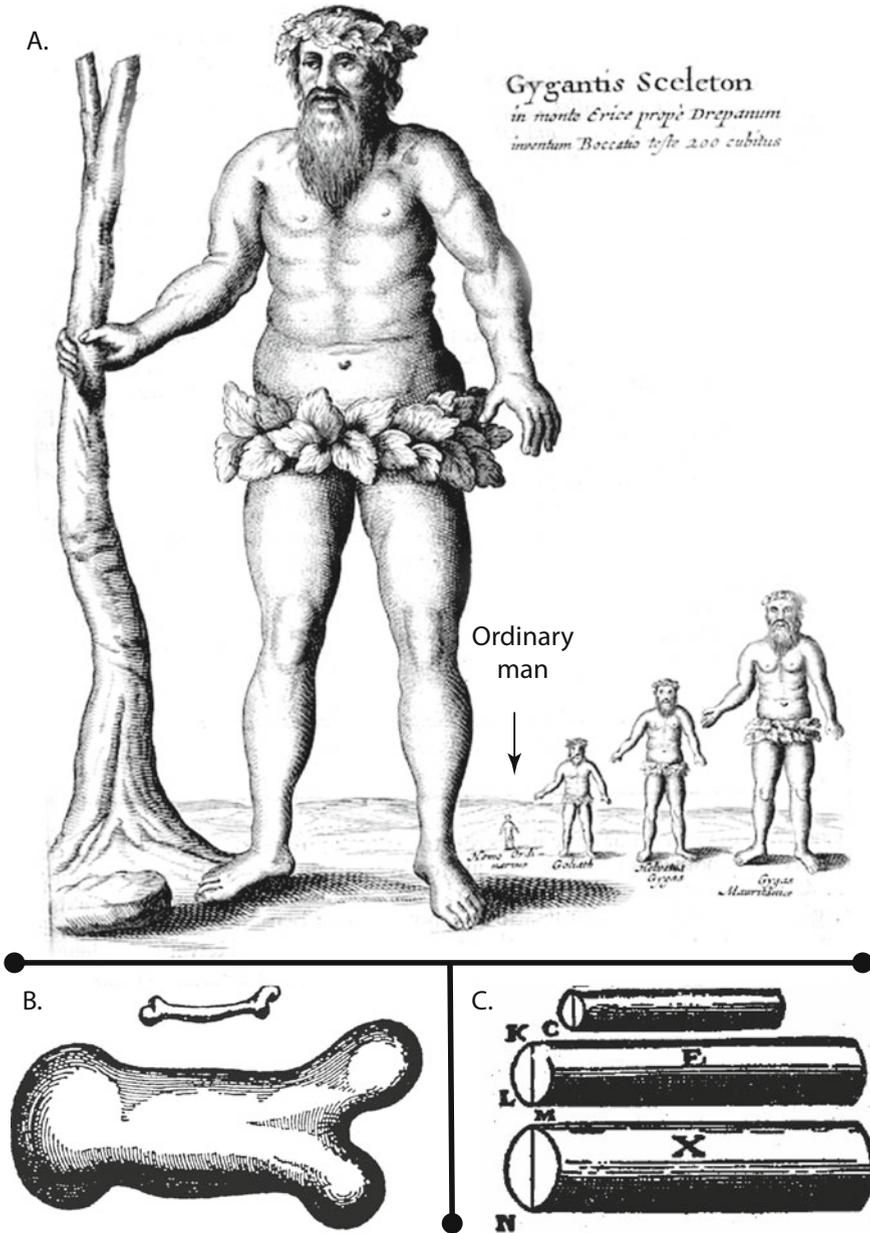


Figure 1.16 A. Improbable giants from “Mundus subterraneus” by Athanasius Kircher (1678) [697]. BC. In his “Discorsi”, published in 1638, Galileo noted that bones are subject to allometric growth and, therefore, giants could not have the same bones or proportions as ordinary humans. Galileo used the physical analogy that to support increasing loads, a column must grow thicker [414].

A systematic study of relative growth began at the end of the nineteenth century with the work of Dubois and Lapique, who compared brain sizes within and between species [308, 309, 770]. Their work follows an early observation from Cuvier that bigger mammals have relatively smaller brains [127, 141, 489]. Based on extensive research, D’Arcy Thompson reflected on the inevitability of differential growth in this passage [1230, p. 205]: “*An organism is so complex a thing, and growth so complex a phenomenon, that for growth to be so uniform and constant in all the parts as to keep the whole shape unchanged would indeed be an unlikely and an unusual circumstance. Rates vary, proportions change, and the whole configuration alters accordingly.*” The theory was further expanded on and applied to many different biological systems by Julian Huxley. In his book, “Problem of Relative Growth”, he coined the word *allometry* to describe relative growth that follows a power law with respect to mass [647].

The central idea in Huxley’s work is that the mass m or length l of an organ scales as a power of the total mass M of the organism, that is

$$m = kM^\alpha. \quad (1.7)$$

By expressing m as a function of M , the explicit dependence on time is removed enabling the comparison of the relative sizes of m and M at given points in development for different animals. The case $\alpha = 1$ corresponds to isometric growth, and any other value of α characterizes relative or allometric growth. If a fixed exponent α holds during growth (that is, when k and α are time-independent), allometry is equivalent to the statement that the specific growth rates of an organ and an organism are proportional:

$$m = kM^\alpha \iff \frac{\dot{m}}{m} = \alpha \frac{\dot{M}}{M}. \quad (1.8)$$

Starting in the 1920s, this simple, but fundamental, power law has played the role of an ordering principle in comparative biology and evolution [488–490, 1321]. The possibility for applications appears endless, as the size of any organ in a given species can be compared to any other species at any point in its development as illustrated in Figure 1.17. Generations after generations, students and researchers, ecologists and biologists, have combed the beaches, swept the forests, and fished the seas to gather data on size and weight in the hope of recovering existing laws or uncovering new ones. Depending on the data and the scientific question, one compares either the relative size of different organs in one species (*intraspecific allometry*), the relative sizes of one organ within different species (*interspecific allometry*), or the relative size of one organ to different organs, at different points in development for a given species (*dynamic allometry*).

A typical allometric study proceeds with the following steps [849, 958, 1037]:

- Gather experimental or bibliographic data on a given physical quantity q and the corresponding weight M of the animal. For instance, q can be the size or weight

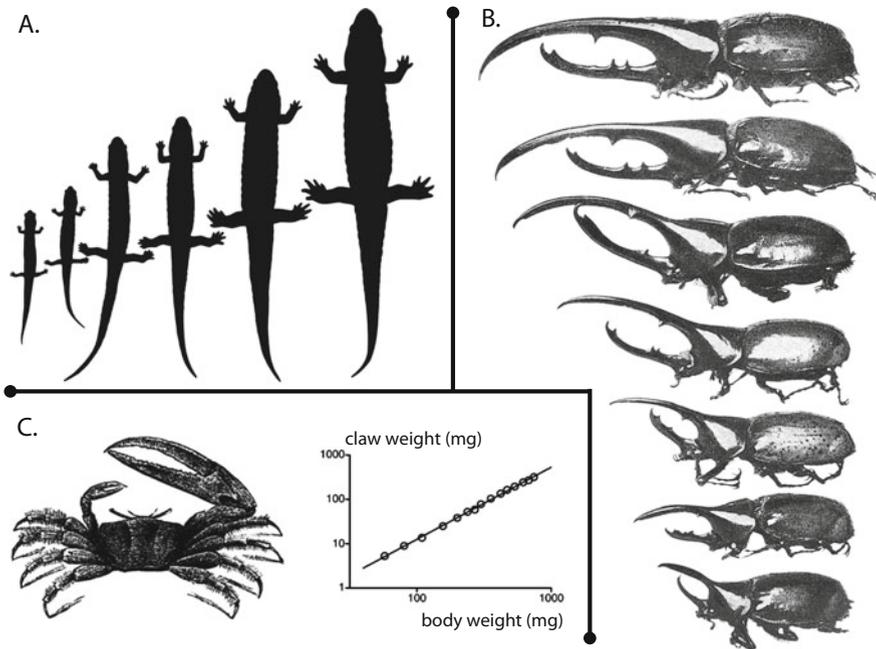


Figure 1.17 Isometric and allometric scaling. A. Six species of salamanders in the genus *Desmognathus* retain their proportions despite being of different sizes (reproduced from [681]). B. Different males in the beetles *Dynastes* showing the relative increase of horns as a function of size (1924 illustrations from Champy [182], reproduced from [427]). C. Allometric scaling for the claw of the fiddler crab in the genus *Uca* (adapted from [1192]).

of an organ, the metabolic rate of an organism, the growth rate, or the number of cells;

- Plot $\log(q)$ against $\log(M)$, so that a law of the form $q = kM^\beta$ would be represented as a line of slope β on this plot;
- From the plot, find the best linear fit and extract the slope β ;
- Find a rational number, α , preferably with a small denominator, close to β ;
- Justify, using arguments from geometry, physics, mechanics, or thermodynamics, that this exponent α can be obtained from first principles;
- Discuss the relevance of this law in the context of physiology, pathology, ecology, evolution, or optimal design;
- Discuss why some species or organs may not follow the expected law. This last step provides a falsidical justification of the law through its exceptions.

This approach is illustrated in Figure 1.18 which demonstrates allometric growth in plants. These studies, despite their obvious shortcomings from an epistemological point of view, have been extremely successful, as power laws have been shown to hold across diverse organisms [957, 1303]. As such, allometry remains a favorite tool and provides a methodological framework for comparative biology [136, 446,

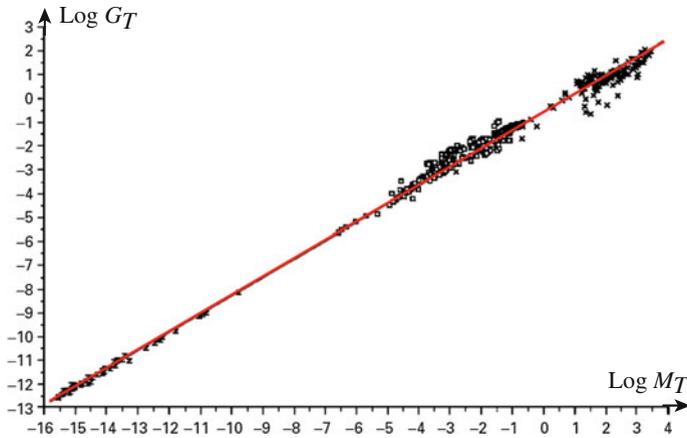


Figure 1.18 Allometry in plants. An interesting example of a possible allometric law for growth arises in plants when the growth rate G_T is plotted against the weight M_T in a log–log plot (adapted from [957]).

956, 1320]. These studies clearly demonstrated that aspects of sizes, growth rates, or metabolic rates tend to cluster in a linear fashion against total weight when expressed in log–log coordinates. Therefore, the mere existence of observed scaling laws suggests that critical aspects of size and growth rate are governed or constrained by geometry, mechanics, and physics. This fundamental observation was already put forward by Medawar in 1941 [856]. However, Medawar believed that growth is dominated and limited by diffusion, which turns out to be relevant only at the microscopic scale.

At the organ or body level, relative growth can be tracked by simple external measurements. However, different regions of an organ may experience different growth rates. The skull of mammals elongates after birth, brains in humans fold onto themselves during development [466], and roots tend to lengthen by limiting their expansion in a small region at the tip. Typically, growth is neither isometric nor homogeneous. Therefore, different points on the growing body may expand at different rates creating, in the words of Huxley, *growth gradients* and *growth sources* [647], or in the terminology preferred by nineteenth century plant physiologists, *differential growth* [1107]. Differential growth is central to all aspects of growth mechanics; it is responsible not only for shaping an organism, but also for creating stresses through geometric incompatibility. However, to capture its key features, new experimental and mathematical methods are needed.

1.4 The Kinematics of Growth

The third fundamental problem in the modeling of growth is to track growth processes both spatially and temporally. It implies that the expansion and relative deformation of different points in an organ must be followed during growth.

This idea can be illustrated in one dimension. Initially at time $t = 0$, we paint a number of marker points, say A_0 and B_0 , on a filament as shown in Figure 1.19. During growth, we record the position of these marks as a and b , respectively. The problem is then to extract information from the dynamics of these material points, such as the growth rate or the region where expansion takes place. For instance, the stretch of the initial segment from A_0 and B_0 is the ratio of the lengths $\Delta x / \Delta X_0$. In general, we want to define the stretch at a single point by taking the limit $\Delta X_0 \rightarrow 0$. To do so, we denote by S_0 the initial position of a material point from one end, labeled $S_0 = 0$ at time $t = 0$. The position of this point at time t is denoted $s = s(S_0, t)$. Then, assuming that there is no other stretching process, the local stretch at the material point S_0 and time t due to growth is given by

$$\gamma(S_0, t) = \frac{\partial s}{\partial S_0}. \tag{1.9}$$

In particular, if growth is taking place independently of the position, we would have simply $\gamma = l/L_0$, the ratio of the two lengths.

Borrowing basic concepts from continuum mechanics, we define the *Lagrangian growth velocity* $V(S_0, t)$ as the velocity of a material point and the *Eulerian growth velocity*, $v(s, t)$ as the velocity at a spatial point s as

$$V(S_0, t) = \frac{\partial s}{\partial t}(S_0, t), \quad v(s, t) = V(S_0(s, t), t). \tag{1.10}$$

Then, the *Lagrangian growth rate* $\dot{\gamma}$ defines a local growth rate in terms of the initial material coordinate S_0 , which is given by

$$\dot{\gamma} \equiv \frac{\partial V}{\partial S_0}(S_0, t) = \frac{\partial^2 s}{\partial t \partial S_0}(S_0, t). \tag{1.11}$$

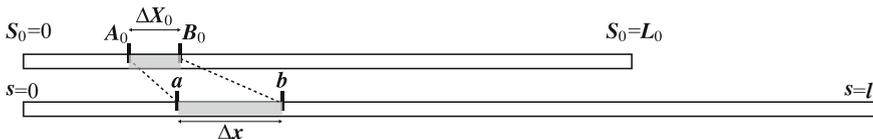


Figure 1.19 Kinematics of growth in one dimension. Two arbitrary points A_0 and B_0 are marked initially and tracked through growth. Of particular interest is the evolution of the relative distance between these points (the increments ΔX_0).

This approach was already used by plant physiologists of the nineteenth century to quantify the growth of stems [1159, 1182] and roots [187] and identify regions of active growth, as shown in Figure 1.20. The function γ is an important quantifier; it identifies spatial locations where growth takes place and is referred to as the *relative elemental growth rate* [193, 236, 444, 1158, 1181], a term coined by Erickson and Sax [344, 345]. To obtain this elemental growth rate in an experiment, the position of initial markers is followed over time and interpolated to obtain an estimate for both a discrete version of the Eulerian velocity and for its gradient [1157, 1302].

The analysis of growth kinematics in higher dimensions [1127, 1334] follows the same principle. In the case where growth is considered as the only possible deformation, we consider a body in an initial configuration $\mathcal{B}_0 \subset \mathbb{R}^3$ with coordinates \mathbf{X}_0 denoting the position of material points in the body. The same body at a later time t is in the current configuration, denoted \mathcal{B}_t . We will assume that the current configuration is related to the initial configuration by a smooth invertible map $\chi : \mathcal{B}_0 \rightarrow \mathcal{B}_t$ such that a material point located at \mathbf{X}_0 in \mathcal{B}_0 is mapped to a point $\mathbf{x}(t) = \chi(\mathbf{X}_0, t)$ in \mathcal{B}_t . In this case, the *Lagrangian* and *Eulerian growth vectors* are defined as

$$\mathbf{V}_g(\mathbf{X}_0, t) = \frac{\partial \chi(\mathbf{X}_0, t)}{\partial t}, \quad \mathbf{v}_g(\mathbf{x}, t) = \mathbf{V}_g(\mathbf{X}_0(\mathbf{x}, t), t). \quad (1.14)$$

The vector field defined by these growth vectors creates growth lines that indicate the direction in the body where expansion takes place, as shown in an experiment on rabbit ears in Figure 1.21.

Assuming that the density remains constant, the evolution of the mass density $\rho(\mathbf{X}, t)$ is governed by

$$\partial_t \rho + \rho \operatorname{div} \mathbf{v}_g(\mathbf{x}, t) = \rho \gamma, \quad (1.15)$$

where $\rho \gamma$ is the local growth rate (see Section 13.2 for a derivation). Therefore, once the growth vectors are known, the computation of the divergence provides information on the local growth rate through (1.15), as shown in Figure 1.22C.

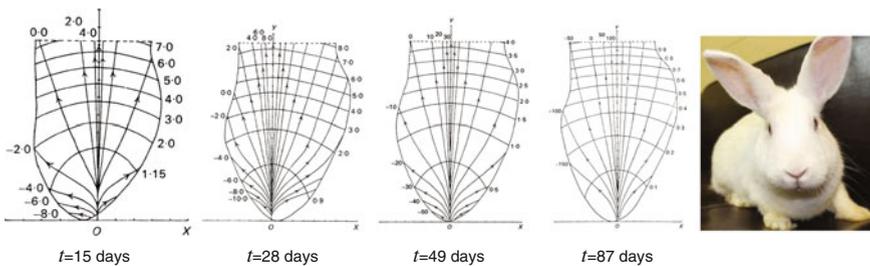


Figure 1.21 Tracking growth on rabbit ears. Streamlines and equipotential lines for the growth of a New Zealand white rabbit ear from day 15 to day 87 [249].

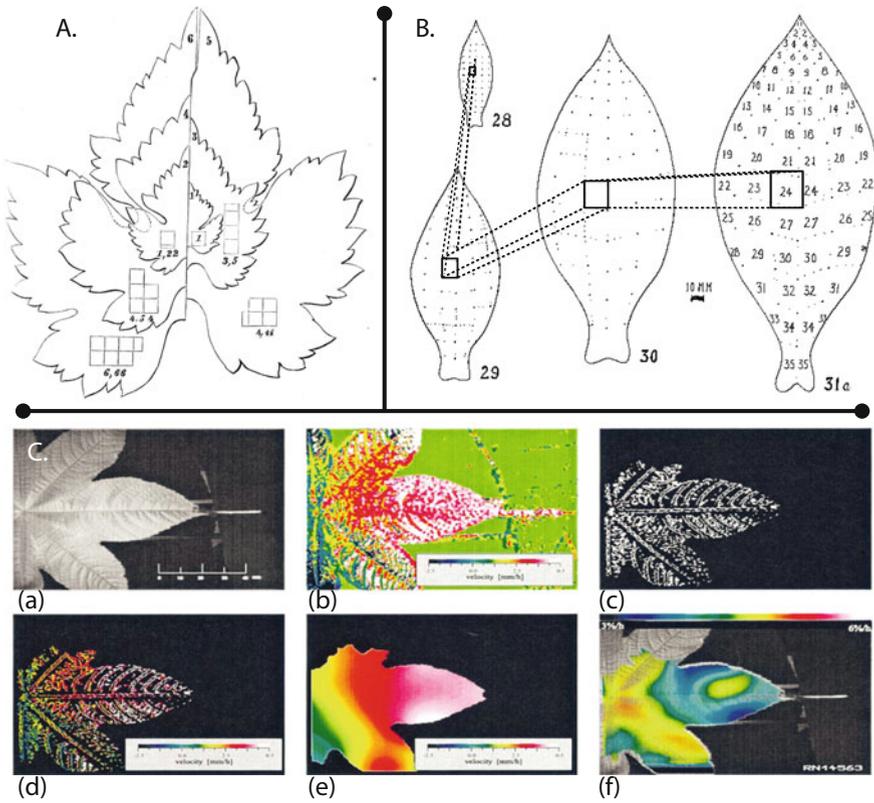


Figure 1.22 Tracking growth on leaves. A. Initial marker points are placed on the leaves and tracked through time (from Müller's textbook [924]). B. Tobacco leaves from Avery [48]. C. Digital analysis of growth. Starting from an original time lapse sequence (a), the displacement vectors are calculated (b), a mask of nonmoving points is evaluated (c), and used to correct the displacement vector (d). A smooth interpolation of the displacements (e) provides a way to compute the divergence of the displacement giving the local rates of growth (f) (reproduced from Schmundt et al. [1127]).

The local mass density ρ is only related to the volumetric change of a volume element, without giving any information on the local direction of the deformation; that is, the anisotropy of growth. This information is contained in the gradient of the deformation and will be discussed in Chapter 12.