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Allometric morphogenesis of complex systems: Derivation of the basic equations from first principles*

(organismal biology/population biology/social systems/economics/organization)

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ABSTRACT Allometric morphogenesis is the generation of form or pattern as a result of differential growth according to power-law relationships among the elements of a complex system. This phenomenon has been noted in a variety of fields for many years, in some cases for centuries, and yet it has never been related to the underlying determinants of the systems. By starting with fundamental properties of the component mechanisms in such systems, one can derive a basic growth equation from which the well-known law of allometric morphogenesis follows naturally.

The development of form or pattern by differential growth among the component parts of a complex system appears to follow relatively simple rules in spite of what is known about the enormous complexity of such systems. Julian Huxley was the first to treat this subject in depth, which he did within the context of growing biological organisms, in his book *Problems in Relative Growth* (1). He used the empirical formula $y = bx^k$ to describe his observations. The parameters b and k are constants, x is the amount or size of some part of the organism (or the entire organism), and y is the amount or size of another part. Growth according to this relationship is called allometric.

The astonishing fact is not that it fits in many cases, but that a wide variety of phenomena is described by this simple law.† Numerous examples can be found in the original work of Huxley (1), and since that time additional examples have been found among all the major groups of animals (3) and higher plants (4, 5). Allometry has been found in studies of morphology, physiology, pharmacology, biochemistry, cytology, and evolution (see ref. 6). Allometry also has been found in the etiology of certain diseases; e.g., coronary disease is related allometrically to the concentration of serum cholesterol (7).

Joseph Needham (8) has presented numerous examples of the relative change of one chemical substance with respect to another that conform to the allometric law. In addition, his finding the same constant, relative growth patterns for substances in a wide range of organisms led Needham to suggest the existence of a common "chemical groundplan." Needless to say, the broad aspects of such a common chemical plan have been dramatically revealed by molecular biologists in recent years.

According to Adolph (9), we should expect future observations of this kind to conform to the allometric relationship because there are now so many confirmed examples in any given organism. Any new finding that did not conform would be inconsistent with the harmony among the component parts of the growing organism, as expressed by the allometric relationships.

Allometry is not confined to examples within biological organisms. Other types of complex phenomena that exhibit this law are the distribution of income within an economic system (10), the process of urbanization (11), social differentiation and division of labor in primitive societies (11), relative growth of staff within industrial firms (12), and the change of proportions in technological design (13). There is no doubt as to the widespread occurrence of allometry in complex systems.

Allometry is a purely empirical law, but there have been several attempts to provide it with a theoretical basis and thereby relate it to other well-established principles (see ref. 14). Early attempts to derive the allometric law used dimensional analysis or various similarity rules based on physical considerations. This approach has been used repeatedly for such derivations and in some cases to predict the numerical values of the parameters in the allometric equation (see refs. 15 and 16). Derome (17) has suggested that group theory is the most appropriate formalism underlying this approach. Bertalanffy (18) provided a derivation of allometry based on competition or partitioning among the parts within an organism or system (see also ref. 14). Rosen (13) has shown that the allometric law can be derived from the principle of optimality in biological design. Although these approaches have met with some success, they are all formal approaches that do not address the questions of underlying mechanisms and causation. Because of this and contemporary emphasis on the analytic experimental sciences, allometry has failed to be incorporated into the mainstream.

The power-law approach presented earlier (19) allows yet another derivation of the allometric law, but one that provides an important link between the underlying molecular determinants and the well-established allometric properties of the intact system.

System description

The derivation of the fundamental equations describing complex systems is given in detail elsewhere (19); it will be outlined here only in brief.

For purposes of analysis, spatially distributed systems can be conceptually subdivided into compartments sufficiently small that within them the system may be considered spatially homogeneous. The concentration or amount of an element within such a compartment will be represented by the symbol X_i, where the subscript i signifies both the name (type) and the location (compartment) of the element.

For a general system of n elements, one can define additional variables X_{n+l} as aggregate measures of the entire system and of particular subsystems within the system. For example, these could be the total weight of an organism or a particular organ of the organism; the total population of a society or a particular group within the society; the capital accumulation of an economy or of a particular sector of the economy, etc. Each

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† Even complex biological shapes and shape changes, which may not immediately suggest allometry, exhibit regular patterns of allometric growth when appropriate measurements are made and then transformed according to the general methods recently developed by Bookstein (2).

X_{n+l} is the sum of all the relevant elements of the system or subsystem.

The functional equations describing a general system of n elements different in kind or location or both and $(s - n)$ aggregate measures can be written in the form

$$\dot{X}_i = V_i(X_1, X_2, \ldots, X_n) - V_{-i}(X_1, X_2, \ldots, X_n) \qquad i = 1, 2, \ldots, s \qquad [1]$$

and

$$X_i = \sum_{\substack{\text{relevant} \\ j \text{ from } 1}}^{n} X_j \qquad i = n + 1, n + 2, \ldots, s \qquad [2]$$

in which V_i is a polynomial (or rational) function representing the composite rate of increase in X_i and, similarly, V_{-i} is a polynomial (or rational) function representing the composite rate of decrease in X_i. $\dot{X}_i$ is the time derivative of X_i.

Polynomial and rational functions can be approximated over a wide range of values for the variables by a linear relationship in a space with logarithmic coordinates (20, 21); this approximation corresponds to a product of power-law functions in the conventional space with cartesian coordinates (21). Thus, Eqs. **1** and **2** can be written

$$\dot{X}_i = \alpha_i \prod_{j=1}^{n} X_j^{g_{ij}} - \beta_i \prod_{j=1}^{n} X_j^{h_{ij}} \qquad i = 1, 2, \ldots, s \qquad [3]$$

and

$$X_i = \gamma_i \prod_{j=1}^{n} X_j^{f_{ij}} \qquad i = n + 1, n + 2, \ldots, s. \qquad [4]$$

This approximation applies to a large class of systems that have been called synergistic (19); its validity is discussed in detail elsewhere (19, 21).

Allometric growth

Only one assumption is necessary to derive the allometric relationships from Eqs. **3** and **4**; namely, there is a single, temporally dominant process in the growing system. This assumption implies that a single equation in **3**, representing the slowest phenomenon of interest, determines the temporal behavior of the entire system; all other equations, representing the faster phenomena, can be assumed to have reached a quasi-steady state with time derivatives equal to zero (see ref. 19).

Eqs. **3** and **4** then can be rewritten as

$$\dot{X}_1 = \alpha_1 X_1^{g_{11}} - \beta_1 X_1^{h_{11}}$$
$$X_i = \delta_i X_1^{e_{i1}} \qquad i = 2, 3, \ldots, s, \qquad [5]$$

in which the parameters g_{11}, h_{11}, and e_{i1} are functions of the original fs, gs, and hs and the parameters α_1, β_1, and δ_i are functions of all the original parameters in Eqs. **3** and **4**. By suitably renumbering the variables, one can have X_1 represent any of the basic variables or any of the aggregate measures of the system. Thus, each of the variables in the system is related to each of the other variables by means of the allometric relation (Eq. **5**). Simple allometry follows naturally from the power-law formalism and the assumption of a single, temporally dominant process.

Anomalous allometric growth

Although simple allometric growth as described in the previous section is the rule (i.e., there is usually a good fit of experimental data to a straight-line relation between the variables expressed logarithmically), exceptions are recognized (see refs. 1, 6, and 14). In this section I shall show that these anomalous forms of allometric growth can be accounted for by relaxing the assumptions of the preceding section.

Sharp Breaks in Allometry. At critical times of reorganization (metamorphosis, puberty, the managerial revolution) a sharp break in an allometric growth relationship can occur with simple allometric growth exhibited before and after the break. Mathematically, this anomalous growth behavior can be accounted for by allowing two of Eqs. **3** to be temporally dominant. If the relaxation times for these two equations are sufficiently different, there will be two zones in which the represented growth is governed by simple allometric relations and these zones will be separated by a relatively sharp break.

In the first zone, the more slowly varying of the two temporally dominant components (say X_1) may be considered essentially a constant, whereas the other (say X_2) governs simple allometric growth. After X_2 has reached quasi-steady state, the behavior is again simple allometric growth in a zone governed by X_1. In the first zone, X_1 is constant, X_2 is governed by the equation

$$\dot{X}_2 = \alpha_2 X_2^{g_{22}} - \beta_2 X_2^{h_{22}},$$

and each of the remaining $(s - 2)$ variables is in quasi-steady state and related to X_2 as follows:

$$X_i = \delta_{i2} X_2^{e_{i2}} \qquad i = 3, 4, \ldots, s.$$

In the second zone, X_1 is governed by the equation

$$\dot{X}_1 = \alpha_1 X_1^{g_{11}} - \beta_1 X_1^{h_{11}},$$

and all the remaining $(s - 1)$ variables are in quasi-steady state and related to X_1 as follows:

$$X_i = \delta_{i1} X_1^{e_{i1}} \qquad i = 2, 3, \ldots, s.$$

In general, $e_{i1} \neq e_{i2}$ and $\delta_{i1} \neq \delta_{i2}$, so the allometric relations will be different in the two zones.

Continuously Changing Allometry. In a log–log plot of relative growth the slope changes continuously in a few well-documented cases. This behavior can be represented mathematically when the two temporally dominant processes of the last subsection have comparable relaxation times. Under these conditions X_1 and X_2 are governed by equations of the form:

$$\dot{X}_1 = \alpha_1 X_1^{g_{11}} X_2^{g_{12}} - \beta_1 X_1^{h_{11}} X_2^{h_{12}}$$
$$\dot{X}_2 = \alpha_2 X_1^{g_{21}} X_2^{g_{22}} - \beta_2 X_1^{h_{21}} X_2^{h_{22}}.$$

The remaining $(s - 2)$ variables are in quasi-steady state and related to X_1 and X_2 as follows:

$$X_i = (\delta_i X_2^{e_{i2}}) X_1^{e_{i1}} \qquad i = 3, 4, \ldots, s.$$

Thus, a log–log plot of X_i against X_1 continuously changes because the instantaneous value of the intercept—indicated within the parentheses—is a function of X_2 and continuously changing. This is the simplest explanation for continuously changing allometry. However, there could be cases in which more than two processes have relaxation times within the relevant range.

Oscillations in Allometry. Cyclic changes in a log–log plot of relative growth are another anomalous form of allometric relation that has been recognized for some time in biological and economic systems. One of the simplest mathematical representations involves one temporally dominant equation [**6**] together with a pair of equations [**7** and **8**] coupled so as to produce oscillations (e.g., see ref. 22):

$$\dot{X}_1 = \alpha_1 X_1^{g_{11}} - \beta_1 X_1^{h_{11}} \qquad [6]$$

$$\dot{X}_2 = \alpha_2 X_2^{g_{22}} X_3^{g_{23}} - \beta_2 X_2^{h_{22}} X_3^{h_{23}} \qquad [7]$$

$$\dot{X}_3 = \alpha_3 X_2^{g_{32}} X_3^{g_{33}} - \beta_3 X_2^{h_{32}} X_3^{h_{33}}. \qquad [8]$$

These three equations then govern the growth behavior. All the remaining equations are in quasi-steady state and the corresponding variables are related to the first three as follows:

$$X_i = (\delta_i X_2^{e_{i2}} X_3^{e_{i3}}) X_1^{e_{i1}} \qquad i = 4, 5, \ldots, s.$$

A log–log plot of X_i against X_1 will show a simple allometric trend with an intercept given by the time-average of the quantity within the parentheses. Superimposed upon this trend will be oscillations due to changes in the instantaneous value of this intercept.

Thus, as in the case of the growth laws treated earlier (19), essentially all of the data can be accounted for, at least in principle, by synergistic systems in which one, two, or at most three variables play a dominant temporal role and all other variables are in a quasi-steady state.

Discussion

Most methods for the analysis of complex systems involve: (*i*) strictly linear models, which are inappropriate for most complex systems in biology and elsewhere; (*ii*) a detailed nonlinear model of a specific component of the system, yielding results that have a correspondingly restricted range of application; or (*iii*) arbitrary nonlinear models having little, if any, relationship to the actual system but chosen for their ability to mimic certain aspects of the complex system. The formalism that has been developed elsewhere (19, 21) and described briefly in earlier sections of this paper largely overcomes these difficulties. Considerable evidence has accumulated for the validity and utility of this approach.

To begin with, there is evidence that rests on first principles. The development of this formalism began with the basic nonlinear nature of the component mechanisms of complex synergistic systems. The most general set of equations describing such systems is insoluble, but the nonlinearities in these equations can be simplified by expanding them in a Taylor series and retaining the first two terms. However, the Taylor series expansion is performed in a logarithmic space, which yields power-law rather than linear equations in the corresponding cartesian space. Although the philosophy of approximation is much like that involved in the linearization of nonlinear systems, the resulting approximate equations are still nonlinear. Consequently, the resulting approximate equations are guaranteed to be an accurate representation of the original system so long as the excursions of the variables about their normal operating values are not excessive.

Second, there are experimental data in agreement with the theoretical results. Power-law relations are predicted for the variables of a system in quasi-steady state. Experimental evidence for this prediction can be found in many biological systems including hormone-mediated effects in various differentiated tissues (23–25) and gene dose–response relationships in microorganisms (25–27). There also is direct evidence from studies *in situ* showing that individual reactions are governed by power-law kinetics over a wide range of concentrations in living animal cells (28). Analogous examples for other types of complex systems can be found in ref. 19 and the refs. cited therein.

The results presented in the previous paper (19) and in the preceding sections lend further support to the validity and utility of the power-law formalism. We have seen that all the well-known laws of growth are special cases of a more general law of growth that can be derived in a straightforward manner by using this formalism (19). Furthermore, there are undoubtedly many examples of growth for which the well-known laws do not apply and for which the data are never reported or characterized. Such examples might well be characterized by this general growth equation. The preceding sections on allometric growth also show that essentially all of the phenomena can be accounted for, at least in principle, by this formalism.

It is important to reemphasize that the parameters in the growth law and the parameters in the allometric relationships can, in principle, be related to the parameters that characterize the component mechanisms of the intact system. Thus, a link between the level of the intact system and the level of the elemental components is provided.

Having provided such a link does not solve any of the currently outstanding problems of growth and morphogenesis. The study of these phenomena is still at the stage of trying to identify the underlying component mechanisms. Nevertheless, we have seen how the well-established laws of growth and allometry can ultimately be reconciled with molecular findings as they begin to emerge. This formalism also provides an important new tool for further theoretical investigation of these important phenomena.

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