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Analytical Solutions to a Generalized Growth Equation

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Systems of the form

$$\dot{X}_i = \alpha_i \prod_{j=1}^{n} X_j^{g_{ij}} - \beta_i \prod_{j=1}^{n} X_j^{h_{ij}} \qquad i = 1,..., n$$

occur in the analysis of biological networks. They also include as special cases the known growth laws and probability functions, famous differential equations like those of Bessel, Chebyshev, and Laguerre, and solutions to important physical problems. These systems have no known analytical solution. However, an important subclass comprising many of the special cases mentioned above is solved. © 1984 Academic Press, Inc.

1. INTRODUCTION

Sets of ordinary nonlinear differential equations of the form

$$\dot{X}_i = \alpha_i \prod_{j=1}^{n} X_j^{g_{ij}} - \beta_i \prod_{j=1}^{n} X_j^{h_{ij}} \qquad i = 1,..., n \tag{1}$$

have previously been called "synergistic" systems (S-systems) [5, 6]. They represent an enormous range of mathematical and physiological problems. It has been shown, in particular, that Eq. (1) can be used efficiently to analyze biochemical networks [4, 9, 11, 12] and genetic regulatory systems [4]. Furthermore, all of the well-known growth laws found in the literature are special cases of Eq. (1) [7], and almost all probability distribution functions are represented by Eq. (1) [8]. Because the known growth laws and probability functions correspond to only a few combinations of the α, β, g and h parameters in Eq. (1), it can be considered as a "suprasystem" for

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both classes of functions [7, 8]. Many physical laws, for instance those describing electrical circuits, gravitation, unforced vibrations, cooling, and dilution problems, that are formulated as differential equations [1], also can be shown to have an equivalent representation in Eq. (1). Finally, many famous differential equations like those of Bessel, Chebyshev, Hermite, Laguerre, and Legendre [10] are readily rewritten as a system of the form in Eq. (1) by defining suitable new variables.

Most of these special cases of Eq. (1) were solved earlier, but no analytical solution to Eq. (1) in its general form is known. Many of the examples mentioned above, for instance the growth laws and probability functions, can be shown to belong to an important subclass of Eq. (1) that is defined by two equations. One equation contains a single variable and has an explicit solution; the other equation is "separable" in the sense that $g_{12} = h_{12}$:

$$\dot{X}_1 = \alpha_1 X_1^{g_{11}} X_2^{g_{12}} - \beta_1 X_1^{h_{11}} X_2^{g_{12}} \tag{2a}$$

$$\dot{X}_2 = \alpha_2 X_2^{g_{22}} - \beta_2 X_2. \tag{2b}$$

In this paper we show that Eq. (2) can be solved analytically.

2. Formulation of the Problem

It is convenient to eliminate some of the parameters by choosing suitable scaling factors for X_1, X_2, and t. If $\alpha_1, \alpha_2, \beta_1$, and $\beta_2 \neq 0$, $g_{11} \neq h_{11}$, and $g_{22} \neq 1$, Eq. (2) can be simplified by replacing X_1/X_{1s} by X_1, X_2/X_{2s} by X_2, and γt by t, where

$$\begin{aligned} X_{1s} &= (\beta_1/\alpha_1)^{1/[g_{11}-h_{11}]} \\ X_{2s} &= (\beta_2/\alpha_2)^{1/[g_{22}-1]} \end{aligned} \tag{3}$$

are the non-trivial steady-state solutions of X_1 and X_2, respectively, and $\gamma = \alpha_1 X_{1s}^{g_{11}-1} X_{2s}^{g_{12}}$ is a scaling factor of time. With these substitutions and upon renaming $g_{12} = a$, $g_{11} = b$, $h_{11} = c$, $g_{22} = d$, and $\beta_2/\gamma = \beta$, Eq. (2) becomes

$$\dot{X}_1 = X_2^a (X_1^b - X_1^c) \tag{4a}$$

$$\dot{X}_2 = \beta (X_2^d - X_2). \tag{4b}$$

Equation (4b) is a Bernoulli differential equation with time-invariant coefficients. Its solution, also referred to as the Bertalanffy growth law [7], is

$$X_2(t) = (1 - (1 - X_{20}^{1-d})(\exp((d-1)\beta t)))^{1/[1-d]} \tag{5}$$

where X_{20} is the value of X_2 at $t = 0$.

Since the variables in (4a) are separable, it can be integrated to yield

$$\int (X_1^b - X_1^c)^{-1}\, dX_1 = \int X_2^a\, dt. \tag{6}$$

By substituting

$$v = -(1 - X_{20}^{1-d}) \exp[(d-1)\beta t)] \tag{7}$$

the integral on the right side of Eq. (6) is transformed into

$$\beta^{-1}(d-1)^{-1} \int (v+1)^{-\rho} v^{-1}\, dv \tag{8}$$

where $\rho = a/(d-1)$. By substituting

$$u = X_1^{b-c} - 1 \tag{9}$$

the integral on the left side of Eq. (6) can be transformed into

$$(b-c)^{-1} \int (u+1)^{-\sigma} u^{-1}\, du \tag{10}$$

where $\sigma = (b-1)/(b-c)$.

If $\alpha_1 = 0$ or $\beta_1 = 0$ or $g_{11} = h_{11}$, then Eq. (2a) reduces to the form

$$\dot{X}_1 = (\alpha_1 - \beta_1) X_1^{g_{11}} X_2^{g_{12}} \tag{11}$$

which upon separation yields

$$(\alpha_1 - \beta_1)^{-1} \int X_1^{-g_{11}}\, dX_1 = \int X_2^{g_{12}}\, dt \tag{12}$$

rather than Eq. (6). The left side is a simple integration and the right side reduces to integral (8).

3. Solution

By transforming equations and substituting variables as described in Section 2, the problem of solving Eq. (2) is reduced to the solution of the known integral [2]

$$\int (u+1)^{-\sigma} u^{-1}\, du. \tag{13}$$

We will call σ the "characteristic parameter."

If σ is a positive integer, the integral (13) can be reduced through recursive integration:

$$\int (u+1)^{-\sigma}u^{-1}\,du = (u+1)^{1-\sigma}(\sigma-1)^{-1} + \int (u+1)^{1-\sigma}u^{-1}\,du. \tag{14}$$

The last integral in this series can be solved explicitly:

$$\int (u+1)^{-1}u^{-1}\,du = \ln|u(u+1)^{-1}|. \tag{15}$$

Hence, the complete solution to the integral (13) when the characteristic parameter is a positive integer is

$$\sum_{i=1}^{\sigma-1} (u+1)^{i-\sigma}(\sigma-i)^{-1} + \ln|u(u+1)^{-1}|. \tag{16}$$

Similarly, if σ is a negative integer the integral (13) can be reduced using

$$\int (u+1)^{-\sigma}u^{-1}\,du = -(u+1)^{-\sigma}\sigma^{-1} + \int (u+1)^{-\sigma-1}u^{-1}\,du. \tag{17}$$

The remaining integral has the solution

$$\int (u+1)\,u^{-1}\,du = u + \ln|u|. \tag{18}$$

The complete solution to the integral (13) when the characteristic parameter σ is a negative integer is therefore

$$-\sum_{i=0}^{-\sigma-2} (u+1)^{-\sigma-i}(\sigma+i)^{-1} + u + \ln|u|. \tag{19}$$

If the characteristic parameter σ is a rational number, the integral (13) can be reduced successively until σ is between 0 and 1. For $\sigma > 1$, a reduction according to Eq. (14) yields

$$\int \frac{du}{(u+1)^{\sigma}u} = \sum_{i=1}^{[\sigma]} \frac{(u+1)^{i-\sigma}}{\sigma-i} + q\int \frac{w^{q[\sigma]-s+q-1}}{w^{q}-1}\,dw \tag{20}$$

where $\sigma = s/q$, $s, q \in \mathbb{N}$, $s > q$, $[\sigma]$ is the greatest integer less than σ, and $w = (u+1)^{1/q}$. For $\sigma < 0$, a reduction according to Eq. (17) yields

$$\int \frac{du}{(u+1)^{\sigma}u} = -\sum_{i=0}^{[-\sigma]} \frac{(u+1)^{-\sigma-i}}{\sigma+i} + q\int \frac{w^{-q[-\sigma]+s-1}}{w^{q}-1}\,dw \tag{21}$$

where $\sigma = -s/q$ and $s, q \in \mathbb{N}$.

For both positive and negative rational characteristic parameters, the remaining integral has the form

$$\int w^{p-1}(w^q - 1)^{-1}\, dw. \tag{22}$$

The same integral also is obtained from integral (13), if $0 < \sigma < 1$. $w^q - 1$ can be considered as a polynomial in w and, therefore, factored into

$$w^q - 1 = (w-1) \prod_{k=1}^{m} (w^2 - 2w \cos(2k\pi/(2m+1)) + 1) \quad \text{for} \quad q = 2m+1 \tag{23}$$

or

$$w^q - 1 = (w-1)(w+1) \prod_{k=1}^{m-1} (w^2 - 2w\cos(k\pi/m) + 1) \quad \text{for} \quad q = 2m. \tag{24}$$

The angles $2k\pi/(2m+1)$ and $k\pi/m$ in Eqs. (23) and (24), respectively, correspond to the complex conjugate roots of $w^q - 1$.

The integrand of (22) can be expressed as a sum of partial fractions, which can then be integrated. The solution to the integral (22) is then

$$\begin{aligned} \int \frac{w^{p-1}\, dw}{w^q - 1} &= \frac{1}{2m+1} \sum_{k=1}^{m} \cos\left(\frac{2kp\pi}{2m+1}\right) \ln\left[w^2 - 2w\cos\left(\frac{2k\pi}{2m+1}\right) + 1\right] \\ &\quad - \frac{2}{2m+1} \sum_{k=1}^{m} \sin\left(\frac{2kp\pi}{2m+1}\right) \tan^{-1}\left\{\frac{w - \cos[2k\pi/(2m+1)]}{\sin[2k\pi/(2m+1)]}\right\} \\ &\quad + \ln(w-1)/(2m+1) \qquad \text{for} \quad q = 2m+1; \end{aligned} \tag{25}$$

$$\begin{aligned} \int \frac{w^{p-1}\, dw}{w^q - 1} &= \frac{1}{2m} \sum_{k=1}^{m-1} \cos\left(\frac{kp\pi}{m}\right) \ln\left[w^2 - 2w\cos\left(\frac{k\pi}{m}\right) + 1\right] \\ &\quad - \frac{1}{m} \sum_{k=1}^{m-1} \sin\left(\frac{kp\pi}{m}\right) \tan^{-1}\left[\frac{w - \cos(k\pi/m)}{\sin(k\pi/m)}\right] \\ &\quad + [\ln(w-1) + (-1)^p \ln(w+1)]/(2m) \qquad \text{for} \quad q = 2m. \end{aligned} \tag{26}$$

With Eqs. (16), (19), (20), (21), (25), and (26) the differential equations in (2) are solved (at least implicitly) for all rational characteristic parameters.

If $g_{12} = 0$, then Eqs. (2a) and (2b) are uncoupled. This special case of Eq. (2) already contains many of the growth equations and the physical interpretations mentioned in the Introduction.

4. Discussion

The general synergistic system (1) has no known analytical solution. But because the system has many applications in mathematics and the sciences, it is desirable to develop analytical solutions at least for important subclasses, even if they cannot be extended to a general solution.

A solution to one important subclass is given in this paper. This subclass (2) is not only of academic interest, because it contains many equations with known interpretations, as mentioned before. The analysis of observed growth phenomena, for instance, is no longer restricted to the well-known growth laws, which correspond to but a few parameter combinations among the multitude defined by Eq. (1), but now can be approached easily in a more general and unbiased way. Furthermore, the estimation of parameter values yielding an optimal fit to observed data is now considerably simplified because Eq. (2) has an analytical solution. The parameter values can be found from the analytical solution with a standard searching routine. Without an analytical solution, they would have to be estimated by repeatedly solving the differential equations [3] with slightly changed parameter values, which is costly and time consuming [4], or by determining slopes from the empirical data [12], which tends to aggravate the errors inherent in the data.

Because Eq. (2) includes not only the known growth laws and probability functions, but defines a much more general class, Eq. (2) can serve as a tool for a "natural" classification of the known and the yet to be considered functions of this class. The n-variable system (1) provides an even more general underlying structure showing that there are fundamental principles that connect seemingly very different phenomena like biochemical networks, probability distributions, electrical circuits, gravitation and growth.

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