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An Efficient Method for Smoothing Indicator–Dilution and Other Unimodal Curves¹

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Abstract

A mathematical function has been developed for approximating unimodal functions, particularly those which are non-Gaussian, skewed, and incomplete. It is useful as an alternative to cubic splines in smoothing noisy experimental data. Particular applications are to indicator–dilution curves and probability density functions of varied form. In its Fortran implementation, SMOEX, it is computationally inexpensive compared to standard cubic spline smoothing routines and requires less storage to preserve the smoothed function for retrieval or interpolation.

1. Introduction

Mathematical functions describing the primary portions of indicator–dilution curves have been the random walk (1), the lag normal curve (2), the singly or multiply lagged normal density function (3), and the gamma variate function (4). All are unimodal right-skewed density functions with shapes governed by three or four parameters. Many others are available. None have the flexibility of form to describe strikingly skewed functions; thus none of these particular ones can be fitted to functions which do not return to the baseline within a range of a few times the mode. For such reasons, cubic spline routines have been used to fit functions of more general shape.

The general question is how to provide, quickly, an accurate but parsimonious description of a noisy but fundamentally simply shaped unimodal positive function whose tail may or may not return to baseline within the range of the observations. Indicator–dilution curves in a recirculating system provide a particular challenge because the concentration–time curve does not return to zero, but rather flattens out with time at a positive value. These provide one extreme of a right-skewed function.

At another extreme are highly symmetrical but non-Gaussian probability density functions. Examples are in the distribution of regional flows within an organ such as the heart (5) where the fundamental function to produce contraction is not complicated by other functions and other requirements for blood flow which might skew the distribution.

For describing such functions, derived from noisy data, smoothing functions are invaluable for display, summarizing description, interpolation, integration, or differentiation for other operations. They must also reduce the extraneous frequency content of the function while

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preserving the inherent frequency content and peculiarities of shape of the underlying function. Smoothing splines are used with varying degrees of “tensioning” (higher tension reduces local curvature) and numbers of “knots” (nodes at which the derivatives between cubic expressions are continuous). Splines are fitted at the ends of functions, or around a sharp peak, only with difficulty, requiring more “knots” or special treatment in some way, and are no panacea for generalized smoothing. Even when they are adequate descriptions, they require substantial storage, namely four parameters per “knot” for cubic splines.

Herein we propose a hitherto undeveloped smoothing function, the rational exponential, and demonstrate its application to various positive unimodal functions.

2. The Rational Exponential Function

We define this in the form of a univariate function, $\hat{h}(t)$ with independent variable t :

$$\hat{h}(t) = A \exp \left(- \left(\frac{\left| \sum_{i=0}^I a_i t^i \right|}{\left| 1 + \sum_{j=1}^J b_j t^j \right|} \right)^p \right), \quad [1]$$

where A is the amplitude, having the dimensionality of the $\hat{h}(t)$; the exponent is dimensionless; a_i is the shaping coefficient in the numerator of the rational; b_j is the shaping coefficient in the denominator; I and J are the highest degrees of polynomial to be used in the numerator and denominator, respectively (J is usually less than or equal to 3 and I is usually less than or equal to 10); and p is an arbitrary positive power, usually $1 \leq p \leq 2$ (in the examples below, we set $p = 1.25$). This value, found by trial, influences the fit at large t ; other values may suit other problems better. To fit $h(t)$ to noisy unimodal functions is a non-linear optimization problem. The fitting can however be done in linear fashion by a logarithmic transformation followed by taking a p th root. In the Appendix it is shown that the error is not greatly different in the transformed space.

3. A Smoother for Indicator–Dilution Curves

Consider the application of the exponential rational function to the smoothing of the recorded indicator–dilution curve $h(t)$ shown in Fig. 1. The curve with open circles is a pulmonary thermal dilution curve of a lung-injured dog recorded at the common iliac after injection into the left atrium. Although there was dispersion at the injection site and through the sampling system, the circulatory dispersion is much diminished by the proximity of the injection and sampling sites. Therefore the curves have rapid time components.

The dashed line is the fit by the exponential rational function with $I = 3$ and $J = 3$. The coefficients of the exponential rational function were obtained by solving the following overdetermined linear equations:

$$a_0 + a_1 t + \cdots + a_I t^I - b_1 \theta(t) t - \cdots - b_J \theta(t) t^J = \theta(t), \quad [2]$$

where $\theta(t) = \sqrt[P]{\log A - \log h(t)}$, $h(t)$ is the recorded indicator–dilution time curve, A is the peak value of $h(t)$, and t ranges over the set $\{t_k: 1 \leq k \leq K\}$. As long as the total order of the polynomial to be determined is less than the data points K , the coefficients are well defined in the least-squares sense. We may improve the fitting by using the following iterative scheme.

Let a and b specify a vector of dimension $I + 1$ and J , respectively. Define polynomials P and Q by the formulas

$$P(t) = \sum_{i=0}^I a_i t^i \quad \text{and} \quad Q(t) = 1 + \sum_{j=1}^J b_j t^j, \quad [2a]$$

where t ranges over the set $\{t_k: 1 \leq k \leq K\}$. We seek (a^*, b^*) to minimize

$$\sum_{k=1}^K \left[\frac{P(t_k)}{Q(t_k)} - \theta(t_k) \right]^2 = \sum_{k=1}^K Q(t_k)^{-2} [P(t_k) - Q(t_k)\theta(t_k)]^2, \quad [2b]$$

subject to $Q(t_k) > 0$, $k = 1, \dots, K$. The linear least-squares problem

$$\text{minimize} \sum_{k=1}^K [P(t_k) - Q(t_k)\theta(t_k)]^2 \quad [2c]$$

yields a solution close to (a^*, b^*) if $Q(t)$ changes little over the set $\{t_k: 1 \leq k \leq K\}$. This process is called stage 1.

If, however, $Q(t)$ changes rapidly a few iterations of the following formula are suggested. Let (a^s, b^s) be the result from the s th iteration. Let $Q^s(t_k) = Q(b^s, t_k)$. Choose (a^{s+1}, b^{s+1}) to minimize

$$\sum_{k=1}^K [(P(t_k) - Q(t_k)\theta(t_k))/Q^s(t_k)]^2. \quad [2d]$$

This is called stage 2. In Fig. 1, the solid line is the fit improved by the iteration method, which solved a weighted linear least-squares equation expanded from [2d], after one

iteration. The fitting error of the rational, $\sum_{k=1}^K [(P(t_k)/Q(t_k)) - \theta(t_k)]^2$, decreased from 0.3832 to 0.03623.

In order to assess the goodness of fit of the stage 2, we used a weighted nonlinear least-squares solver, SENSOP (6), to further improve the fit. We find A, a_i, b_j to minimize

$$\sum_{k=1}^K w_k (\hat{h}(t_k) - h(t_k))^2, \quad [3]$$

where $\hat{h}(t_k)$ is an exponential rational function defined in [1], $h(t_k)$ is the data, and w_k is the weighting function determined by SENSOP. This process is called stage 3. It is computationally very intensive, so it is used only for testing the excellence of the stage 2 procedure and not for data smoothing since stage 2 is very satisfactory in all problems we tried.

4. Comparison with a Smoothing Spline Routine

For comparison of the smoothing by the exponential rational function (SMOEX) with an alternative smoothing technique, we chose a standard IMSL library routine,² ICSVKU (8), which gives a least-squares approximation to a function with cubic splines having variable knots (the routine determines the optimal locations of the knots). The data, a pulmonary dye dilution curve, used in the comparison were from the same experiment as in Fig. 1, but with 5% uniformly random noise added to the original curve of 104 points over 52 sec. We used the dye curve, which has a sharper peak than the thermal curve, to show the flexibility of the exponential rational function.

We chose 5, 10, 15, and 20 variable knots for ICSVKU to smooth the noisy data separately. The goodness of the fit is measured by the averaged percentage error (AE),

$$\frac{1}{104} \sum_{k=1}^{104} \frac{|\hat{h}(t_k) - h(t_k)|}{h(t_k)} \times 100, \quad [4]$$

where $\hat{h}(t_k)$ is the smoothing function. The quantity CPU, central processor unit time in seconds, is the measurement of the cost of the computation. Table 1 is the summary of the cubic spline fits with different knots.

In Fig. 2, the circles are noise-added data, the dotted line is the spline function with 5 knots, the dashed line is the spline function with 10 knots, the dash-dot line is the spline function with 15 knots, and the dash-dot-dot line is the spline function with 20 knots.

A similar table will now be constructed for the exponential rational function smoother (SMOEX). We varied I , the order of the polynomial in the numerator, while keeping $J=2$, the order of the polynomial in the denominator. As the order of the polynomial in the numerator increases, the fitting improves. Too many coefficients in the denominator should be avoided because this may create poles in the rational function. Table 2 summarizes the fits with $I = 4, 5, 6$, and 8 with $J = 2$ for all cases. The CPU for stage 3 includes the CPU for stages 1 and 2. Similarly, the CPU for stage 2 includes the CPU for stage 1.

²ICSSCV, a cubic spline data smoother, using statistical considerations to determine the amount of smoothing required, did not work well on our problems. The degree of the smoothing determined by the generalized cross-validation (7) was too small; the cubic spline curve followed the noisy data curve.

Figure 3a shows the data (open circles) fitted by stage 1 with different orders of polynomial in the numerator. Figure 3b shows the data (open circles) fitted by stage 2 with different I .

5. Tests on a Noisier Function

Spline smoothing deteriorated as the number of data points decreased and as the noise level increased. In Fig. 4, we added 20% uniformly random noise to the data and cut the number of data points to 27 (open circles). A reasonable number of knots, e.g., 5 knots, for the number of the data did not give a reasonable fit (dotted line) with AE = 1174%. A higher number of knots would make the spline function (dashed line) an interpolating spline, not a smoothing spline, which followed the noise (erroneous derivatives at the knots).

In Fig. 5, the open circles are noise-added data, the dashed line in stage 2 of SMOEX fit, and the solid line is the original data before adding any noise.

6. Tests on Leptokurtic Noisy Distribution

We used SMOEX and ICSVKU to fit a leptokurtic noisy data as shown in Fig. 6. The open circles represented the probability density functions of relative regional flows in the left ventricular myocardium in an awake baboon. The data, expressed as a probability density function, from King *et al.* (5) are irregular for an individual heart at a single observation, but are smooth when several sets of observations on one animal are combined. Therefore it seems logical to obtain a best estimate of the shape by smoothing.

We chose $I=3$ and $J=2$ for SMOEX fit and obtained a goodness of the fit (AE) of 27%. In Fig. 6, the dashed line is the fit by the exponential rational function. In fitting ICSVKU to data, we used five variable nodes. The goodness of the fit (AE) was 30%.

7. Discussion

The exponential rational function can be applied to any positive function, especially for unimodal curves where the data cover several orders of magnitude difference between the peak and the tail. The new smoothing procedure using an exponential rational function minimizes the relative errors, while the least-squares approximation by a cubic splines routine, ICSVKU, minimizes the sum square of the residuals. ICSVKU emphasizes the fit around the peak. As shown in the examples above, the routine fitted the data well around the peak and failed in the front end. A weighted least-squares fit by cubic splines will cure the problem of the ICSVKU.

ICSVKU works well for data having within one order of magnitude and for any kind of shape. The exponential rational function is a special kind of data smoother. It works only for the positive functions, especially the unimodal functions, and is therefore not as general as a spline routine.

The smoothing procedure using an exponential rational function is computationally inexpensive; it solves a few overdetermined systems of linear equations, each with less than 10 coefficients. In addition to the high cost of computing the locations of the variable knots, the cubic spline must find 80 coefficients for a 20-knots situation.

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Appendix

How good is the regression in the transformed space? To answer this question, we need to determine the relationship between the error of the regression in the original space and the error of the regression in the transformed space.

We consider an approximation by a rational exponential function as defined in (1) (which can be rewritten in a simpler form $\hat{h}(t) = Ae^{-p(t)/Q(t)^p}$) to a positive unimodal function $h(t)$, with t ranging over the set $T = \{t_k: 1 \leq k \leq K\}$. For fixed values of I and J (the degrees of the numerator and the denominator of the rational function) choose $a_0, a_1, \dots, a_I, b_1, b_2, \dots, b_J$, and p so that $e^{-p(t)/Q(t)^p}$ best approximates $h(t)/A$ on the set T in the sense of least squares. This is an unfamiliar nonlinear problem.

However, a simple transformation leads to a rational approximation that is tractable and is reasonably accurate.

Taking logarithms and the p th root of both sides leads to the approximation $(-\ln(h(t)/A))^{1/p}$, which is positive, by $P(t)/Q(t)$. By increasing I and J , this approximation can be made more accurate. We assume that there is sufficient accuracy so that $P(t)/Q(t)$ is positive. Let

$$\varepsilon(t) = P(t)/Q(t) - [-\ln(h(t)/A)]^{1/p}, \quad [A1]$$

where $\varepsilon(t)$ is the error in the approximation at each t in the transformed space. We further increase the accuracy of our approximation, if this is necessary, to ensure that $P(t)/Q(t) - \varepsilon(t) > 0$ for all t in T .

Claim

Set $r = P(t)/Q(t)$ and $\eta = \varepsilon(t)/r$. Let e denote the base of natural logarithm. Assume [A1] with $p \geq 1$, then if $\max\{p|\eta|, p(e-1)|\eta|^p\} < 1$ for all t in T , we can calculate the relative error $\varepsilon_p(t)$ in the original time domain:

$$|\varepsilon_p(t)| = |[h(t)/A - e^{-r^p}]/e^{-r^p}| \leq (e-1)^2 r^{(p-1)p} |\varepsilon(t)|. \quad [A2]$$

Proof of the claim

We first observe that if $p \geq 1$ and $-1/p \leq \eta \leq 1/p$, then

$$1 - (e-1)|\eta|p \leq (1-\eta)^p \leq 1 + (e-1)|\eta|p. \quad [A3]$$

If $\eta > 0$, the right hand inequality is evident. For the left hand inequality let $\phi(\eta) = (1-\eta)^p - (1-\eta p)$ then $\phi(0) = 0$ and $\phi'(\eta) > 0$ whenever $0 < \eta < 1/p$. Whence $\phi(\eta) > 0$ for all η satisfying $0 < \eta \leq 1/p$ while $1 - (e-1)|\eta|p < 1 - \eta p$. If $\eta < 0$, the left hand inequality is trivial. For the right hand inequality, notice that if $0 \leq \theta \leq 1/p$ the function $(1+\theta)^p$ is convex in θ and that the function $(1+1/p)^p$ is increasing in p with supremum e . Since the graph of $1 + (e-1)\theta p$ contains the points $(0, 1)$ and $(1/p, e)$, $(1+\theta)^p \leq 1 + (e-1)\theta p$. Thus Eq. [A3] obtains.

Since by [A1]

$$h(t)/A - e^{-r^p} = e^{-(r-\varepsilon(t))^p} - e^{-r^p}, \quad [A4]$$

evidently

$$\varepsilon_p(t) e^{-r^p} = e^{-r^p(1-\eta)^p} - e^{-r^p}. \quad [A5]$$

By Eq. [A3]

$$e^{-r^p[1+(e-1)|\eta|p]} \leq e^{-r^p(1-\eta)^p} \leq e^{-r^p[1-(e-1)|\eta|p]}. \quad [A6]$$

Whence,

$$e^{-r^p p(e-1)|\eta|} - 1 \leq \varepsilon_p(t) \leq e^{r^p p(e-1)|\eta|} - 1. \quad [A7]$$

If $0 \leq x \leq 1$, then $e^x - 1 \leq (e-1)x$; while if $-1 \leq x \leq 0$, then $(e-1)x \leq e^x - 1$. Thus

$$|\varepsilon_p(t)| \leq (e-1)^2 [P(t)/Q(t)]^{p-1} p |\varepsilon(t)|. \quad [A8]$$

Thus if $p = 1$, and $|\varepsilon(t)|$ is sufficiently small, the function $P(t)/Q(t)$ that approximates $[-\ln(h(t)/A)]^{1/p}$ with an error of $\varepsilon(t)$ also approximates $h(t)/A$ using the form $e^{-[P(t)/Q(t)]^p}$ with a relative error of at most $(e-1)^2 |\varepsilon(t)|$. For $p > 1$, the relative error is at most $(e-1)^2 p [P(t)/Q(t)]^{p-1} |\varepsilon(t)|$.

Fig. 1. A dog pulmonary thermal dilution curve (open circles), the fit by the stage 1 of SMOEX (dashed line), and the fit by the stage 2 of SMOEX (solid line) with the order of the numerator and denominator both equal to 3.

Fig. 2.

A dog pulmonary dye dilution curve with 5% uniformly random noise added (open circles) and the fits by the cubic splines with 5 (dotted line), 10 (dashed line), 15 (dash-dot line), and 20 (dash-dot-dot line) variable knots.

Fig. 3.

(a) A dog pulmonary dye dilution curve with 5% uniformly random noise added (open circles) and the fits by the stage 1 of SMOEX with the order of the denominator equal to 2 and the orders of the numerator equal to 4 (dotted line), 5 (dashed line), 6 (dash-dot line), and 8 (dash-dot-dot-dot line). (b) A dog pulmonary dye dilution curve with 5% uniformly random noise added (open circles) and the fits by the stage 2 of SMOEX with the order of the denominator equal to 2 and the orders of the numerator equal to 4 (dotted line), 5 (dashed line), 6 (dash-dot line), and 8 (dash-dot-dot-dot line).

Fig. 4.

A reduced number of data points of a dog pulmonary dye dilution curve with 20% uniformly random noise added (open circles), the noise-free dye dilution curve (solid line), and the fits by the cubic splines with 5 (dotted line) and 8 (dashed line) variable knots.

Fig. 5.

A reduced number of data points of a dog pulmonary dye dilution curve with 20% uniformly random noise added (open circles), the noise-free dye dilution curve (solid line), and the fit (dashed line) by stage 2 of SMOEX with the order of the denominator equal to 2 and the numerator equal to 6.

Fig. 6. Probability density functions of relative regional flows in the left ventricular myocardium in an awake baboon (open circles), the fit by SMOEX (dashed line), and the fit by ICSVKU (dotted line).

TABLE 1

Results and Timings of the Cubic Spline Fits

Knots	AE	CPU
05	634	2.4
10	112	8.9
15	107	21.5
20	3.04	72.2

TABLE 2

Results and Timings of the Exponential Rational Function Fits

Stage	Case											
	I = 4			I = 5			I = 6			I = 8		
	AE	CPU		AE	CPU		AE	CPU		AE	CPU	
1	74.6	1.0		26.8	1.0		8.4	1.0		4.5	1.1	
2	4.2	1.4		3.0	1.4		2.8	1.4		2.7	1.6	
3	4.1	3.3		3.0	3.5		2.7	4.0		2.7	5.1	