

# Functional Renal Imaging Through Factor Analysis

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**Functional images tend to be noisy, since they are formed from parameter values estimated from noisy time-activity curves. Factor analysis provides a rapid method for fitting smooth curves to these noisy curves. Noise in functional images is reduced by estimating parameter values from the smooth curves. The method is illustrated for three parameters: TMAX (time to maximum value), RISE (increase from first to maximum value), and RISMV (maximum increase between successive values). When curve-fitting through factor analysis is used to generate functional renal images from clinical studies or to estimate parameter values for simulated noisy renogram curves, noise is reduced for the TMAX and RISMV parameters and accuracy is improved for the RISE parameter.**

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A dynamic process is usually displayed in nuclear medicine as a series of images obtained at fixed times following the injection of the radiopharmaceutical. Such images are adequate for demonstrating gross functional abnormalities, but subtle abnormalities may be missed, since the eye cannot readily detect slight differences in regional brightness between one image and the next. An alternative approach is to generate images of various measures of the changes that occur over time, commonly referred to as functional images. These demonstrate time-related information together with spatial information, and are potentially better than the standard series of images in revealing subtle asymmetries and regional abnormalities in function.

To generate a functional image, the study is stored in the computer as a sequence of digital images, and for each pixel (picture element) a time-activity curve is constructed representing the sequence of counts detected within the region of the camera's crystal corresponding to that pixel. Some parameter of curve shape is evaluated for each curve, and that value is assigned to the pixel. The resulting digital image is the functional image of that parameter.

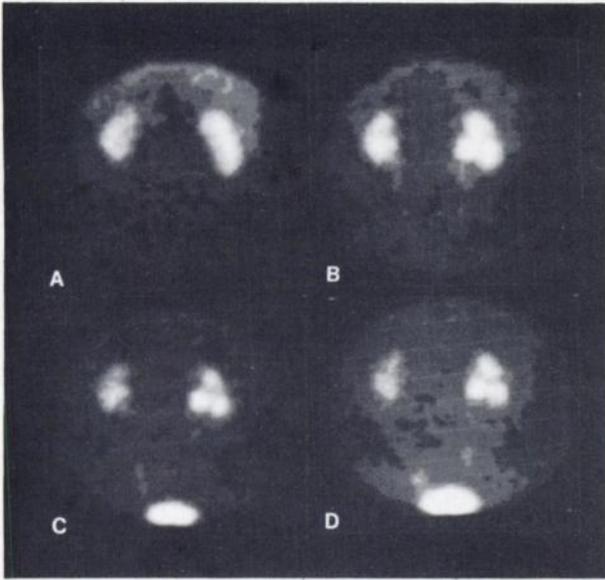
Despite several enthusiastic reports (1-3), functional images have gained very limited acceptance. A major reason is that the time-activity curves for individual pixels are usually very noisy, and parameter values estimated from such curves may be quite inaccurate. Better functional images should be obtained by fitting a smooth curve to each of the noisy time-activity curves, but most methods for curve fitting are too time-consuming to be practical for this application. We have developed a rapid yet reasonably accurate method for curve fitting based on factor analysis. Estimation of parameter values from the smooth curves obtained through this method leads to improved functional images.

## METHOD

Dynamic renal scintigraphy with [<sup>123</sup>I]orthiodohippurate was carried out in 13 subjects. Following the injection of 1 mCi of the tracer, the kidneys were imaged in the posterior projection and the data were stored in a computer as a series of 64 × 64 digital images. These were compressed into 16 images, each of 40-sec duration, spanning the first 11 min of the study (Fig. 1). The images were smoothed once using a nine-point smoothing procedure. For each pixel a 16-value time-activity curve was constructed, consisting of the values of the corresponding pixels in the 16 images. This curve was nor-

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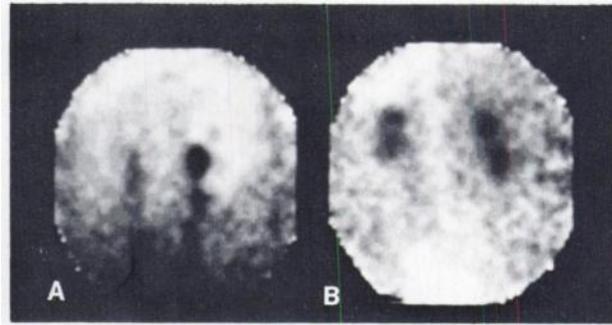
**FIG. 1.** Dynamic renal scan (posterior view) for  $[^{123}\text{I}]$ orthiodohippurate study in patient with stenosis of left renal artery. Four of 16 40-sec views are shown. A, 1 min; B, 4 min; C, 7 min; and D, 10 min.

malized to unit area to avoid undue influence of high-activity regions of the image. Twenty-four parameters were evaluated for each curve, but only three will be discussed in this communication: TMAX, time to maximum value; RISE, increase from first value to maximum value; and RISMV, maximum increase between any two successive values.

The functional image of a parameter was obtained by assigning the value of the parameter for each time-activity curve to the corresponding pixel of a digital image.

Functional images of each parameter were generated by the direct method and the factor-table method. In the direct method a parameter value is determined by direct inspection of the noisy time-activity curve. For example, the maximum value is defined as the greatest of the sixteen values comprising the curve.

The factor-table method uses factor analysis for curve fitting and locates parameter values in a look-up table. (We discuss the method briefly here. For a full mathematical description, the reader is referred to the Appendix.) Any noisy renogram curve,  $r(t)$ , can be associated with a pair of numbers,  $f_1$  and  $f_2$ , which we call the factor weights for that curve. This pair of factor weights identifies a specific smooth curve,  $r^*(t)$  (this curve has only as many points as  $r(t)$ , but can be converted into a continuous curve by spline interpolation). It will generally be found that  $r^*(t)$  is a good fit for  $r(t)$ . Thus the noisy renogram curve,  $r(t)$ , can be fitted by computing its factor weights,  $f_1$  and  $f_2$ , and then computing the fitting curve,  $r^*(t)$ , from the factor weights. We find it convenient to store all  $f_1$  and  $f_2$  values as two images, F1 and F2 (Fig. 2).



**FIG. 2.** Factor images representing first two factor weights. A = F1 image. B = F2 image.

To estimate some parameter for curve  $r(t)$ , one can generate the fitting curve,  $r^*(t)$ , and then evaluate the parameter from that curve, using spline interpolation to evaluate intermediate points of the curve. Considerable time can be saved by taking advantage of the fact that  $r^*(t)$  is uniquely identified by  $f_1$  and  $f_2$ , the factor weights for  $r(t)$ . We can construct, ahead of time, a table containing the values of the desired parameter corresponding to an appropriate sampling of pairs of numbers  $f_1$  and  $f_2$ . This is accomplished by generating the curve identified by each pair of numbers, evaluating the parameter from this curve, and inserting the parameter value in the appropriate location in the table. We call this table the *factor table* for the parameter.

The procedure for generating a functional image of some parameter by the factor-table method is as follows:

1. The time-activity curve for each pixel is formed and normalized to unit area.
2. The values of  $f_1$  and  $f_2$  are determined for each curve and are stored as F1 and F2 images (Fig. 2).
3. The value of the parameter is looked up in the appropriate factor table using the numbers  $f_1$  and  $f_2$  as entries, and using linear interpolation to find values between those in the table.
4. A digital image is formed of the parameter values found in this manner.

To generate images of additional parameters, only Steps 3 and 4 need be repeated, since the same  $f_1$  and  $f_2$  values are used to enter the factor table for each parameter.

Computer simulations were carried out to determine the amount of noise reduction that could be achieved in parameter estimation using the factor-table method. We studied eight typical curves (two for blood pool, six for renogram, Fig. 3) generated from a four-compartment renal model (4). For each curve, 1000 noisy curves were simulated for  $N = 200$  and  $N = 1000$  total counts per curve (assuming Poisson statistics), the values of the TMAX, RISE, and RISMV parameters were determined from these curves using the direct and factor-table methods, and the means and standard deviations of these values were computed. The true values of the parameters

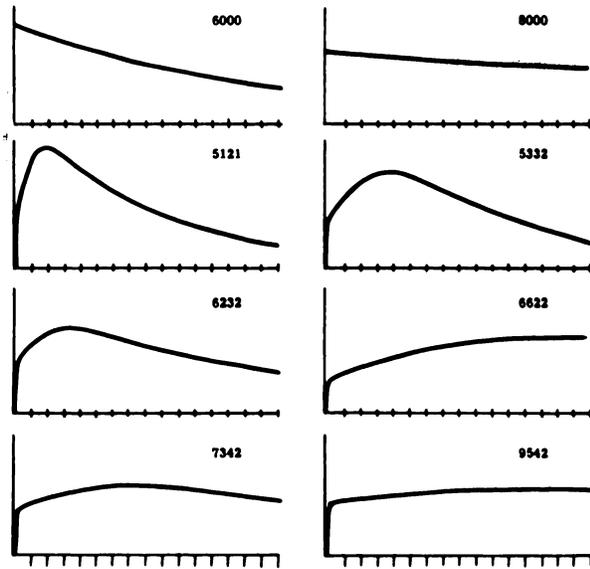


FIG. 3. Two typical blood-pool curves and six typical renogram curves generated by a four-compartment model, with identification numbers.

were determined analytically from the generating equations.

#### RESULTS

In each of the 13 studies the factor-table method produced a TMAX image that was much less noisy than the image obtained by the direct method, with far better preservation of anatomic relationships (Fig. 4). Table 1 demonstrates the results of estimation of the TMAX parameter for the simulated noisy curves. In most instances the statistical noise, represented by the standard deviation of the parameter estimates, was much lower when the factor-table method was used than when the

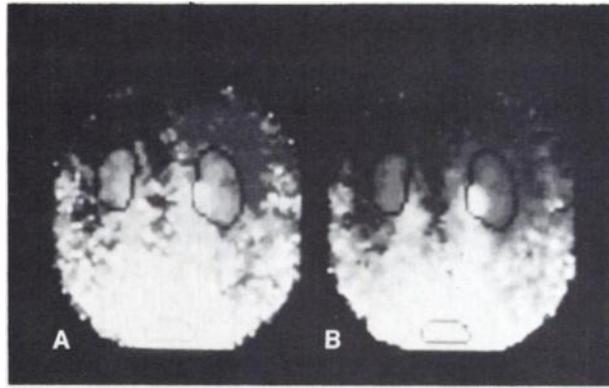


FIG. 4. Comparison of TMAX images produced by direct method (A) and factor-table method (B).

direct method was used. The estimates of the mean value of TMAX obtained by the former method were generally closer to the true value than estimates obtained by the latter method. The poorest results for both methods were obtained for curve 9542, a very flat curve with a very poorly defined peak, representing renal failure.

The RISE images obtained by both methods were comparable for all 13 studies, although the extrarenal regions were somewhat more prominent in the images produced by the direct method than in those produced by the factor-table method (Fig. 5). Results of estimation of the RISE parameter for the simulated noisy curves are given in Table 2. These values, as well as those for the RISM parameter in Table 3, are expressed as percentages of the expected average height of the curve, permitting comparison for different total counts. This is equivalent to the curve normalization that we use in functional imaging. Estimates of the mean value by the factor-table method were quite accurate in most instances, but when obtained by the direct method, they were consistently too high, especially for the curves

TABLE 1. TMAX PARAMETER ESTIMATED BY DIRECT AND FACTOR-TABLE METHODS

Curve no.*	True value (min)	N = 200 total counts		N = 1000 total counts	
		Direct† (min)	Factor-table† (min)	Direct† (min)	Factor-table† (min)
6000	0	1.8 ± 1.5	1.0 ± 0.8	1.2 ± 1.0	0.7 ± 0.4
8000	0	4.2 ± 3.5	2.1 ± 2.6	3.0 ± 2.7	1.3 ± 1.4
5121	1.7	2.3 ± 0.9	1.7 ± 0.5	2.0 ± 0.6	1.7 ± 0.3
5332	3.7	4.0 ± 1.5	2.7 ± 0.6	3.9 ± 1.1	2.7 ± 0.3
6232	3.2	4.3 ± 2.0	2.6 ± 0.8	3.6 ± 1.0	2.6 ± 0.4
6622	13.1	10.5 ± 3.1	11.8 ± 3.2	11.9 ± 2.5	12.3 ± 1.9
7342	6.3	8.1 ± 3.4	6.4 ± 3.2	7.4 ± 2.2	5.9 ± 1.4
9542	15.1	9.7 ± 4.1	8.6 ± 5.1	11.7 ± 2.7	10.3 ± 2.4

\* Typical curves (two blood-pool, six renogram) generated from four-compartment model. Each is identified by a four-digit number. See Fig. 3 and Ref. (4).

† Estimate of parameter value (mean ± 1 s.d.) for 1,000 simulated noisy curves containing N expected total counts, assuming Poisson statistics.

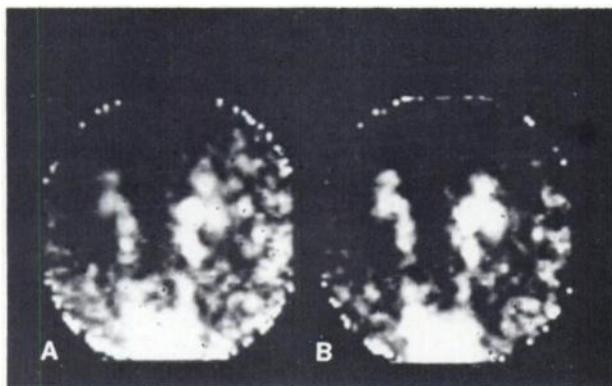


FIG 5. Comparison of RISE images produced by direct method (A) and factor-table method (B).

containing fewer total counts. This provides an explanation for the somewhat greater prominence of the extrarenal regions in the images of the RISE parameter obtained by the direct method, since those are the regions of fewest total counts. The factor-table method underestimated the value of the RISE parameter for curve 5121, since this curve has a very prominent upslope, which the curve-fitting process did not reproduce accurately (see Fig. 4 of (4)). Little noise reduction was achieved for the RISE parameter by using the factor-table method instead of the direct method, as indicated by the standard deviation values.

In every study the RISM image obtained by the factor-table method clearly demonstrated the renal structures, whereas the image obtained by the direct method was totally worthless, since the renal structures were unidentifiable or barely identifiable (Fig. 6). Table 3 gives the results of estimation of the RISM parameter for simulated noisy curves. Although estimates of the mean values obtained by the factor-table method were not very accurate, there was a fairly good correlation between these values and the true values for all curves, with the exception of curve 5121, as noted above.

For the direct method, on the other hand, there was only a very weak correlation between the estimated mean values and true values of RISM, but a very strong inverse correlation between these estimates and the total number of counts in the curves. Furthermore, the standard deviation was much larger for the curves with lower total counts. Thus the noise in low-total-count regions of the RISM image obtained by the direct method would be expected to obscure the structure in higher total-count regions, as was indeed observed in every study.

DISCUSSION

Factor analysis has been used to obtain image smoothing and data compression in scintigraphy (5,6) and in the analysis of individual renogram curves (7,8). We have shown that it provides an effective means for reducing noise in functional images. This is accomplished by fitting noisy time-activity curves with smooth curves. We have applied the factor-analysis approach to functional renal imaging in an efficient manner through the factor-table method.

The nature of the improvement obtained by this method differed for each of the parameters investigated. For TMAX there was considerable reduction in image noisiness attributable to a smaller standard deviation of parameter estimates, while improved accuracy of the mean estimates was not obtained consistently. For the RISE parameter, on the other hand, there was significant improvement in accuracy of the mean estimates but little reduction in image noisiness. Noise introduces an upward bias in values of the RISE parameter obtained by the direct method, which selects the largest of the random variables in the vicinity of the true peak as the maximum value. The factor-table method, by fitting a smooth curve in the region of the true peak, tends to average the values in this region and produces a relatively unbiased estimate of the maximum value.

TABLE 2. RISE PARAMETER ESTIMATED BY DIRECT AND FACTOR-TABLE METHODS

Curve no.*	True value (%)†	N = 200 total counts		N = 1000 total counts	
		Direct* (%)†	Factor-table* (%)†	Direct* (%)†	Factor-table* (%)†
6000	0	24 ± 31	10 ± 18	6 ± 10	3 ± 5
8000	0	19 ± 31	8 ± 14	13 ± 13	2 ± 5
5121	64	84 ± 33	32 ± 20	67 ± 17	30 ± 10
5332	64	94 ± 37	71 ± 35	73 ± 16	70 ± 15
6232	38	71 ± 35	39 ± 23	50 ± 16	37 ± 10
6622	60	103 ± 26	61 ± 19	78 ± 12	59 ± 9
7342	37	75 ± 21	41 ± 26	51 ± 11	38 ± 12
9542	20	62 ± 34	23 ± 23	37 ± 14	18 ± 11

\* See footnotes for Table 1.

† Expressed as percentage of expected average curve height.

TABLE 3. RISM X PARAMETER ESTIMATED BY DIRECT AND FACTOR-TABLE METHODS

Curve no.*	True value (%)†	N = 200 total counts		N = 1000 total counts	
		Direct* (%)†	Factor-table* (%)†	Direct* (%)†	Factor-table* (%)†
6000	0	65 ± 21	8 ± 12	25 ± 9	2 ± 5
8000	0	70 ± 23	5 ± 7	30 ± 10	1 ± 3
5121	60	79 ± 26	25 ± 14	60 ± 17	25 ± 7
5332	31	80 ± 27	46 ± 20	46 ± 14	46 ± 9
6232	20	73 ± 27	25 ± 13	36 ± 12	25 ± 6
6622	11	75 ± 24	14 ± 9	36 ± 10	11 ± 4
7342	9	75 ± 22	18 ± 13	35 ± 9	16 ± 7
9542	3	73 ± 23	7 ± 7	33 ± 10	4 ± 2

\* See footnotes for Table 1.

† Expressed as percentage of expected average curve height.

The prominent upslope of curve 5121 (Fig. 3) was not fitted accurately by factor analysis as we implemented it, which resulted in low estimates of the RISE parameter for this curve. On the whole, however, the factor-table method gave more accurate values for the RISE parameter than the direct method, and therefore appears preferable, although some suppression of the brightest regions might be expected in RISE images obtained by this method. It should be possible to improve the fit of curve 5121 by giving this and similar curves more weight in the data base used to implement factor analysis for curve fitting, as described in the Appendix.

Evaluation of the RISM X parameter involves taking first differences, and this, like differentiation, greatly increases noise. In the direct method this noise became so great that it totally dominated the value of the parameter, resulting in a worthless functional image. The factor-table method, by replacing the noisy curve with a smooth curve, permitted first differences to be taken without significant noise amplification.

Curve fitting by factor analysis is superior to curve fitting by smoothing (point averaging) because the former uses *a priori* information about the possible curve shapes that can occur in the given context. This information is supplied through the data base of representa-

tive curves with which the method begins (see Appendix). Given the values of a noisy curve, factor analysis identifies the smooth curve that fits these values best while preserving the features common to the curves in the data base. This curve will usually be closer to the "true" noiseless curve than the curve obtained by smoothing, since smoothing uses no information other than that contained in the values of the noisy curve. We have shown (4) that estimation of the TMAX parameter from curves fitted by factor analysis led to far greater noise reduction than estimation of this parameter from curves smoothed by weighted seven-point smoothing.

It may appear paradoxical that 16-value curves can be identified by only two numbers, the factor weights  $f_1$  and  $f_2$ . This can be attributed to the following reasons.

1. The "true" curves are smooth, so that the information carried by adjacent values is quite redundant.
2. Due to the underlying physiology, renogram curves can take on only a rather limited variety of shapes. Factor analysis identifies the most common shape characteristics of these curves.
3. The observed curves are very noisy, which further limits the variety of shapes that can be distinguished.
4. The curves have been normalized to unit area, so that curve amplitude is not a variable.
5. By subtracting an "average" curve before evaluating the factor weights (see Appendix) an additional variable is removed (4).

As noted in the Appendix, we have shown (4) that for noisy renogram curves of the type encountered in functional imaging, the optimal number of factor weights to be used for curve fitting is two.

One may also ask whether it is appropriate to represent a renogram curve by subdividing it into only 16 time intervals. We carried out parameter estimation by the factor-table method for simulated noisy curves containing 200 and 1,000 total counts, each of which was subdivided into 32 time intervals. The resulting param-

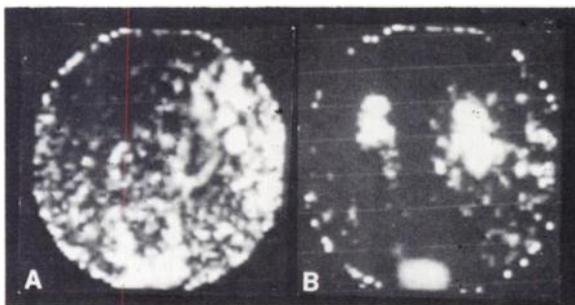


FIG. 6. Comparison of RISM X images produced by direct method (A) and factor-table method (B).

eter estimates had essentially the same means and standard deviations as the estimates obtained for the 16-interval curves. This confirmed our impression that coarse sampling is adequate for very noisy curves.

The noise reduction obtained in functional images through the use of factor analysis is accomplished at the expense of increased computation time. Our minicomputer, programmed in Fortran, requires about 6 min to generate the factor-weight images F1 and F2 (Fig. 2). Individual functional images are then generated at the rate of about 1 min each using the factor tables, which is about the time required by the direct method. Some reduction in computation time should be achievable by programming in assembler.

We are currently carrying out a clinical evaluation of functional images of a number of parameters of curve shape, including the three discussed in this paper, obtained from studies performed with  $[^{123}\text{I}]\text{orthoiodohippurate}$ . Results of this evaluation will be the subject of a future communication. Our preliminary results are highly encouraging, for the functional images appear to be quite sensitive in detecting subtle abnormalities that are not apparent on inspection of conventional images or renogram curves.

ACKNOWLEDGMENT

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APPENDIX

To accomplish curve fitting through factor analysis one begins with a large representative set of curves  $r_j = [r_{ij}]$  ( $i = 1, \dots, n; j = 1, \dots, m$ ), obtained either from clinical data or from a compartmental model of the process under investigation. For the present report we used 162 renal curves and 137 blood-pool curves generated from a four-compartment model of renal function and representing a wide variety of normal and abnormal curve shapes (4). Each curve was normalized to unit area, i.e.,  $\sum_i r_{ij} = 1$  for all values of  $j$ . We define  $r_{av} = (1/m)\sum_j r_j$  as the average curve. We form the set of shifted curves  $r'_j = r_j - r_{av}$  ( $j = 1, \dots, m$ ). The covariance matrix,  $C = [c_{ik}]$  ( $i, k = 1, \dots, n$ ), is formed, where  $c_{ik} = \sum_j r'_{ij}r'_{kj}$ . We compute the orthogonal eigenvectors  $e_l$  ( $l = 1, \dots, n$ ) of  $C$ , normalized to be unit vectors and ordered by decreasing magnitude of the corresponding eigenvalues.

Now let  $\tilde{r} = [\tilde{r}_i]$  represent any noisy curve normalized so that  $\sum_i \tilde{r}_i = 1$  (the tilde over a scalar indicates a random variable, and over a vector indicates a stochastic process). To fit a smooth curve to  $\tilde{r}$ , we identify the first  $p$  factor weights,  $\tilde{f}_l$ , of  $\tilde{r}$ :

$$\tilde{f}_l = (\tilde{r} - r_{av})^T e_l \quad (l = 1, \dots, p),$$

and then form the curve  $\tilde{r}_p$ :

$$\tilde{r}_p = r_{av} + \sum_l \tilde{f}_l e_l,$$

which is the fit for  $\tilde{r}$  generated from  $p$  eigenvectors. When  $p$  is small,  $\tilde{r}_p$  is smooth, but as  $p$  is increased,  $\tilde{r}_p$  begins to approach the noisy curve  $\tilde{r}$ , and becomes identical to it for  $p = n$ . This raises the question: how many eigenvectors should be used for curve fitting?

To answer this question we let  $r = [r_i] = [E\{\tilde{r}_i\}]$  be the noiseless

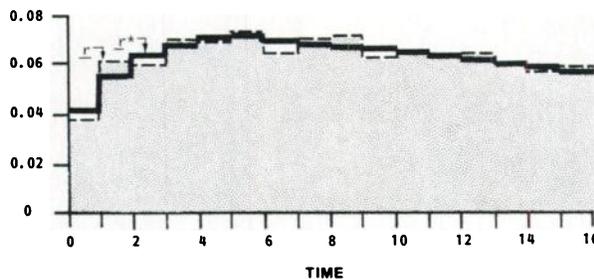


FIG. 7. Noisy curve,  $r$  (dashed line), and fitting smooth curve,  $r^*$  (heavy line), generated with two eigenvectors. The discrete curve  $r^*$  can be converted into a continuous curve by spline interpolation.

curve corresponding to  $\tilde{r}$ , where  $E\{\}$  is the expected value operator. We define the error in  $\tilde{r}_p$  as

$$\tilde{\delta}_p = \|\tilde{r}_p - r\|/\|r\|,$$

and let  $\delta_p = E\{\tilde{\delta}_p\}$ . The term  $\|r\|$  is the norm of  $r$ , which is a scalar having the value  $(r^T r)^{1/2}$ . Through computer simulation of renogram curves we have shown (4) that the value of  $p$  that minimizes  $\delta_p$  is dependent on the total counts per curve. For curves containing between 200 and 1,000 total counts,  $\delta_p$  was minimized when  $p = 2$ . For curves containing 10,000 total counts, a slight reduction in  $\delta_p$  was obtained by adding a third eigenvector. Since curves obtained in functional renal imaging contain on the order of 1,000 or fewer total counts, only two eigenvectors should be used, since the use of more will introduce more noise than structure into the fitting curve  $\tilde{r}_p$ .

To illustrate the method of renogram curve fitting through factor analysis using two eigenvectors, say that we are given the noisy 16-valued renogram,  $r$ , normalized to unit area (Fig. 7):

$$r = [0.0380, 0.0611, 0.0591, 0.0689, 0.0681, 0.0728, 0.0639, 0.0702, 0.0712, 0.0619, 0.0650, 0.0631, 0.0647, 0.0594, 0.0549, 0.0578]^T,$$

where the superscript  $T$  (transpose) indicates that this is a column vector rather than a row vector. We wish to find a smooth curve  $r^*$  that fits  $r$ . We know in advance the average renogram,  $r_{av}$ , and the two orthonormal eigenvectors  $e_1$  and  $e_2$ :

$$r_{av} = [0.0676, 0.0723, 0.0738, 0.0731, 0.0716, 0.0694, 0.0671, 0.0648, 0.0624, 0.0601, 0.0579, 0.0558, 0.0538, 0.0519, 0.0501, 0.0484]^T,$$

$$e_1 = [0.4732, 0.4268, 0.3433, 0.2468, 0.1557, 0.0770, 0.0089, -0.0501, -0.1007, -0.1429, -0.1783, -0.2084, -0.2338, -0.2552, -0.2732, -0.2882]^T; \text{ and}$$

$$e_2 = [0.6842, 0.1292, -0.1701, -0.2823, -0.3072, -0.2814, -0.2311, -0.1705, -0.1073, -0.0461, -0.0116, 0.0652, 0.1142, 0.1586, 0.1986, 0.2343]^T.$$

We first find the factor weights  $f_i = (r - r_{av})^T e_i$  ( $i = 1, 2$ ):

$$f_1 = -0.0379; f_2 = -0.0131.$$

We can now form the renogram  $r^* = r_{av} + f_1 e_1 + f_2 e_2$ :

$$r^* = [0.0420, 0.0544, 0.0630, 0.0674, 0.0697, 0.0702, 0.0698, 0.0689, 0.0676, 0.0661, 0.0649, 0.0628, 0.0612, 0.0595, 0.0579, 0.0562]^T.$$

Figure 7 demonstrates that  $r^*$  is a good fit for  $r$ . The method is fast,

requiring only  $2n$  multiplications and  $3n$  additions to compute the values for  $f$ , and  $2n$  multiplications and additions to generate  $r^*$  for an  $n$ -valued noisy curve.

This method is derived from the principal-components method of factor analysis (9), also known as the Karhunen-Loève expansion (10).

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## THE HAWAII CHAPTER SOCIETY OF NUCLEAR MEDICINE 4TH ANNUAL MEETING

May 23-24, 1981

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The Hawaii Chapter of the Society of Nuclear Medicine will hold its Fourth Annual Memorial Day Weekend Meeting Saturday, May 23 and Sunday, May 24, 1981. The location for the meeting will be the Hyatt Kullima Resort Hotel on Oahu's beautiful north shore. The program will be divided into two segments with noted speakers from the Mainland presenting talks on Gastrointestinal Imaging and Nuclear Cardiology.

Due to the success of its previous annual meetings the Hawaii Chapter SNM is extending an invitation to all other chapters to join in an enjoyable and interesting weekend. For further information and registration please write:

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#### BOOKS RECEIVED

*Medical Physics Monograph No. 5. Biological Risks of Medical Irradiations*. Gary D. Fullerton, David T. Kopp, Robert G. Waggener, Edward W. Webster, Eds. New York, American Institute of Physics, 1980, 335 pp, illustrated

*Medical Physics Monograph No. 6. Medical Physics of CT and Ultrasound: Tissue Imaging and Characterization*. Gary D. Fullerton, James A. Zagzebski. New York, American Institute of Physics, 1980, 717 pp, illustrated

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