Estimation of the Short-Term Fluctuation from a Single Determination of the Visual Field

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The short-term fluctuation in regular grid threshold static fields is commonly determined from repeated observations of a number of threshold points. In this study we estimated the short-term fluctuation from a single determination of the field. Sixty-two eyes of 62 patients were tested, using three consecutive repetitions of a Humphrey 24-2 full threshold program. The resulting grid patterns were examined using a modified version of the statistical technique of trend-surface analysis. Polynomial surfaces of increasing degree were fitted to the data over the grid. The residual variances after detrending the surface correlated very well with the direct estimates based on the triple observations at each point (correlation coefficients of log-transforms of 0.8 and better). We conclude that short-term fluctuation (the square root of the variance) can be estimated with good reliability from grids of single threshold determinations. Invest Ophthalmol Vis Sci 31:730–735, 1990

Computerized threshold static visual field tests use spatial arrays of points in a regular lattice, each point representing a local threshold determination. Neighboring points in the array may be expected to have correlated threshold values. The statistical treatment of visual field data may therefore benefit from methods of analysis of spatial processes, an extension of the one-dimensional time series analysis.

In previous work (Mills et al),¹ we applied a variety of one-dimensional time-series analyses to meridional visual field data. We developed a modification of the Holt-Winters forecasting algorithm which produced variance estimates that correlated well with standard mean square calculations. Because of this success using linear visual field data arrays, we decided to apply spatial processes to two-dimensional visual field data to achieve a similar result.

In this work, regression methods of trend-surface analysis are applied to regular grid threshold visual field data. They provide an approximate model description of the individual tested visual field, and permit fairly precise estimation of the short-term fluctuation based on a single determination of the field.

The short-term fluctuation (SF) defines the "noise" level inherent in visual field data at a given time. It is commonly evaluated by replicating the threshold readings at a number of points in the visual field, calculating the threshold variances at each of those points, and averaging those values to obtain an estimate of the overall field variances. The square root of this estimate (root mean square or RMS) is used as a measure of the short-term fluctuation. It has been shown by Bebie et al² that the RMS calculated on the basis of ten doubly determined points lies within 44% of the true SF at a 95% confidence level. The precision of the RMS as an estimate of the SF depends on the number of points replicated and on the number of replications at those points. Specifically, it depends on n(k − 1), where n is the number of points replicated and k, the number of replications of each point. The estimation of the SF by the RMS is based on the implicit assumption that the short-term fluctuation is the same at the different points in the visual field; in reality, the variance differs among regions of the field.³ Nevertheless, the RMS may be thought of as reflecting the overall average variability of the visual field. The short-term fluctuation is abnormal in early chronic open-angle glaucoma. It can be used in qualifying the significance of observed field changes and in correcting the "loss variation," to estimate the clinically commonly used "corrected loss variation."⁴

The challenge of estimating the SF from a single threshold determination of the visual field, without
any point replication, arises since the replication of measurements at a sufficient number of points for a reasonably precise RMS estimate is a time-consuming and tedious process. Mathematically, the problem becomes that of estimating the variance of a spatial process from a single realization of that process.

Materials and Methods

Sixty-eight unselected patients referred to our visual field service, from whom informed consent was obtained, comprised our study group. On even dates, right eyes were tested with three consecutive determinations of the visual field using the 24-2 program of the Humphrey Field Analyzer; on odd dates, left eyes were tested with the same protocol (Fig. 1). All subjects had at least one prior experience with automated perimetry. Eight patients were unable to complete testing, had unacceptably high fixation losses (>33%), false positive (>33%), or false negative (>50%) responses, or had severe field loss which included some points with absolute field loss. The sample consisted of 27 glaucoma patients, 12 glaucoma suspects, four patients with CNS disease, three nonglaucomatous optic neuropathies, one person with retinal disease, and 15 normal patients with headache, transient visual blur, or other symptom with a normal examination.

Statistical Methods

A mirror-image reversal of left eye data across the vertical axis was applied to convert all data into a right eye format. The coordinates of the standard 52 points in the visual fields studied were expressed in Table 1.

Table 1. Geometric means and standard deviations of root mean squares (replicated estimates) and trend-surface estimates

<table>
<thead>
<tr>
<th>RMS</th>
<th>SF estimates (single determinations)</th>
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<tbody>
<tr>
<td>S11* 2.45(1.58)</td>
<td>D11 3.80(1.64) D12 3.66(1.68) D13 3.62(1.67)</td>
</tr>
<tr>
<td>S13 2.48(1.57)</td>
<td>D13 2.99(1.66) D14 2.80(1.64) D15 2.80(1.67)</td>
</tr>
<tr>
<td>S23 2.35(1.57)</td>
<td>D23 2.83(1.63) D24 2.68(1.64) D25 2.66(1.66)</td>
</tr>
<tr>
<td>S25 2.45(1.55)</td>
<td>D25 2.67(1.63) D26 2.53(1.63) D27 2.54(1.64)</td>
</tr>
</tbody>
</table>

* S: based on i” and j” determinations.  
† D: based on i” and j” determinations.  
‡ D: degree polynomial trend-surface.  
In parentheses: standard deviation.

Comparison of vertical and horizontal degrees of eccentricity (range vertically: ±3° to ±21°; horizontally: ±3° to ±21°–27°). Two points overlapping the area of the physiological blind spot were deleted from the study to reduce uninformative data variability. Four RMS values were calculated for each eye, one based on all three determinations and three additional ones based on all pairs of determinations.

Trend-surface analysis was applied to each visual field determination. This is a regression technique which fits a polynomial surface of arbitrary degree to the data. Coefficients are tested for significance, a coefficient of determination (R²) is calculated and the calculated surface is then subtracted, or “detrended,” from the data. The residual deviations of each point from the estimated surface are used to assess the variance of the process. These residuals tend to be considerably less correlated with one another than the original measurements; they may therefore serve to calculate a more precise and less biased estimate of the SF of the field. Polynomial surfaces of linear, quadratic, cubic and quartic degree were fitted successively to the data for each visual field determination. With X and Y denoting horizontal and vertical eccentricities, respectively, and Z representing threshold values, the surfaces had the following general expressions:

Bilinear:

$$Z = a_1 + b_1X + c_1Y$$

Biquadratic:

$$Z = a_2 + b_2X + c_2Y + d_2X^2 + e_2XY + f_2Y^2$$

Bicubic:

$$Z = a_3 + b_3X + c_3Y + d_3X^2 + e_3XY + f_3Y^2 + g_3X^3 + h_3X^2Y + i_3XY^2 + j_3Y^3$$

Biquartic:

$$Z = a_4 + b_4X + c_4Y + d_4X^2 + e_4XY + f_4Y^2 + g_4X^3 + h_4X^2Y + i_4XY^2 + j_4Y^3 + k_4X^4 + l_4X^3Y + m_4X^2Y^2 + n_4XY^3 + o_4Y^4$$

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In general, surfaces of higher degree become increasingly "wiggly", reflecting greater irregularities in the data: bilinear surfaces slope flatly across the field, biquadratic ones have sufficient curvature to allow for one peak (or one trough), bicubics permit the surface to have both a peak and a trough, and bi-quartics accommodate up to two troughs and a peak (or two peaks with a trough).

While a surface of higher degree provides an increasingly better fit by matching the variation in the observed data more closely, it ultimately models more and more of the random variation in the data rather than the shape of the visual field. Various guides to choosing among fits have been proposed. Since the thrust of this study was to provide a precise estimate of the residual variance, the principle of parsimony was adopted with regard to model selection: the surface of lowest degree providing a significant fit to the data ($P < 0.05$) was chosen. Higher degree polynomials no longer gave significant improvement to the fit, and could be regarded as absorbing more of the random variation, thus leading to underestimation of the SF.

The residual variances obtained from these regressions were compared with the four estimated RMS values calculated directly. Correlation analysis on the

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Fig. 2. (A) Bilinear trend-surface: normal eye data. ® = above surface, X = below surface. (B) Biquadratic trend-surface: same normal eye. © = above surface, O = below surface. (C) Gray Scale printout of 24-2 program, same normal eye.
logarithmically transformed values was carried out. The log transform was applied to bring about variance stability and normality in the data.

Results

The 62 study patients ranged in age from 18 to 86 (mean = 52.3 ± 17.5 years), and there were 34 right and 28 left eyes included in the analysis. Table 1 shows the geometric means (all eyes) of the root mean squares calculated from each pair of determinations as well as from all three determinations combined. It also gives the geometric mean (all eyes) of the estimates of the SF from each separate determination based on bi-linear, -quadratic, -cubic and -quartic trend surfaces fitted to each individual field. Figure 2A, B shows a bilinear and a statistically better-fitting biquadratic trend surface applied to the visual field data of a normal eye ($R^2 = 0.059$ and 0.819, respectively). The gray scale printout of the corresponding field is shown in Figure 2C. Two views of a bicubic trend surface of a glaucomatous eye are shown in Figure 3A,B ($R^2 = 0.783$), corresponding to the gray scale of Figure 3C.

Correlation coefficients were calculated between the log estimates of the SF based on the residuals of
each trend-surface fit and the corresponding log RMS calculated directly from the various pairs and triples of repeated determinations. By example, Figure 4 shows a scatterplot of the fourth-order (quartic) trend-surface log SF estimates (first field determination) against the log RMS in the corresponding eyes based on the first and third replicated fields. Table 2 shows the correlation coefficients between the log SF estimated from the lowest degree significant \((P < 0.05)\) polynomial trend-surface fit and the various corresponding direct log RMS estimates. These correlations ranged from 0.73 to 0.86 (median 0.81). Lower-order surfaces generally sufficed for detrending normal or nearly normal fields, and higher-order surfaces were needed to detrend the more irregular fields. However, the correlation coefficients calculated for normal and for glaucomatous eyes showed no systematic differences from the pooled sample correlations.

### Discussion

The problem of estimation of the short-term fluctuation from a single determination of the visual field is complicated by the presence of the underlying “hill of vision,” which consists of a variable trend surface of threshold values over the field, as well as by correlations between values of neighboring points. The method of trend-surface analysis provides an effective solution to these difficulties. In addition to giving a mathematical description of the field, it reduces the field data to a roughly stationary process. The method calculates a polynomial regression surface of adequate degree (bilinear, biquadratic, bicubic or higher). It tests the significance of the successively higher-order coefficients and of the corresponding coefficients of determination \((R^2)\), and estimates the residual mean square error. The square root of the latter quantity provides a very good estimate of the short-term fluctuation of the visual field and is based on the “detrended” observations or residuals after the estimated surface has been subtracted from the data. The precision of estimation is usually of the order of \(\pm 6.5\%\) of the RMS (as calculated by repeated observations of the visual field) at a 95% confidence level.

This value can be considered in the context of the precision of various RMS estimates. As Bebie et al\(^2\) have calculated, at a 95% confidence level, the RMS estimate obtained from ten doubly determined points lies within 44% of the true SF. Using similar calculations, the RMS estimate calculated on the basis of double determinations of all 52 points in the 24-2 program lies within 19% of the true SF at a 95% confidence level. With the method described in this study, the SF estimate from trend surface analysis is therefore likely to be within 25% of the true SF of the visual field at a 95% confidence level.

This suggests that the SF estimate from trend surface analysis is likely to be more precise than that obtained from the standard method of double determinations at ten preselected points. Not only is the estimate more precise, but it is also likely to be more robust, so that aberrant findings at one or two points will not unduly affect the estimate.

Normal visual fields were easier to detrend using lower-order polynomial surfaces because they had a reasonably predictable and smooth decrement of sensitivity with increasing eccentricity. More abnormal visual fields required higher-order polynomials to describe a good surface fit. No eyes with severe field loss were included because surfaces are harder to fit to such fields, and because SF estimates are of less clinical value in such eyes.

### Table 2. Correlations between trend-surface log SF estimates (highest-order significant fit) and log RMS (replicated measurements)

<table>
<thead>
<tr>
<th></th>
<th>(D_1)*</th>
<th>(D_2)</th>
<th>(D_3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(S_{12})†</td>
<td>0.75</td>
<td>0.75</td>
<td>0.76</td>
</tr>
<tr>
<td>(S_{13})</td>
<td>0.86</td>
<td>0.75</td>
<td>0.81</td>
</tr>
<tr>
<td>(S_{23})</td>
<td>0.73</td>
<td>0.82</td>
<td>0.84</td>
</tr>
<tr>
<td>(S_{123})‡</td>
<td>0.81</td>
<td>0.80</td>
<td>0.83</td>
</tr>
</tbody>
</table>

* \(D_n\): \(n^{th}\) determination, trend-surface fit.
† \(S_{1n}\): Log RMS estimated from \(1^{st}\) and \(n^{th}\) determinations.
‡ \(S_{123}\): Log RMS estimated from first, second and third determinations.

![Fig. 4. Scatterplot of log SF estimates from biquartic trend-surface based on first field determination (vertical) against direct estimates of log RMS from first and third determinations (horizontal).](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933579/ on 09/23/2017)
We used three repetitions of the 24-2 program as the data base for our statistical manipulations because the test session for each patient was of acceptable duration (less than 1 hr, including routine testing on the fellow eye). This should not be construed as a recommendation that one 24-2 test should be used in routine testing. There is no mathematical or theoretical reason why this method of surface trend analysis cannot be applied to any regular grid of visual field data (eg, programs 30-1, 30-2 or 10-2), as clinical validation is obtained. Presumably, inclusion of more peripheral test locations, in the absence of weighting, would be associated both with increased estimates of SF and with decreased precision of those estimates. If the method is validated by future research, it could be applied to resident software of automated perimeters since the method is simple to program and automate, and can be applied with equal success to normal and to glaucomatous eyes.

Key words: short-term fluctuation, spatial processes, correlation, trend-surface analysis, residuals

References