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A MATHEMATICAL APPROACH TO OPTIMAL SELECTION OF DOSE VALUES IN THE ADDITIVE DOSE METHOD OF EPR DOSIMETRY

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Abstract - Additive dose methods commonly used in Electron Paramagnetic Resonance (EPR) dosimetry are time consuming and labor intensive. We have developed a mathematical approach for determining optimal spacing of applied doses and the number of spectra which should be taken at each dose level. Expected uncertainties in the data points are assumed to be normally distributed with a fixed standard deviation and linearity of dose response is also assumed. The optimum spacing and number of points necessary for minimal error can be estimated, as can the likely error in the resulting dose estimate. When low doses are being estimated for enamel samples the optimal spacing is shown to be a concentration of points near the zero dose value with fewer spectra taken at a single high dose value within the range of known linearity. Optimization of the analytical process results in increased accuracy and sample throughput.

1. INTRODUCTION

Radiation dosimetry using electron paramagnetic resonance spectroscopy (EPR) relies heavily on the use of samples which show a linear response to additive irradiation's at dose levels of biological significance. The laboratory irradiation's are usually of equal size and least squares fitting methods are employed for dose estimation.

The major problem with a constant distribution of points along the dose axis is that it is not optimal for extrapolation when linearity of dose response can be assumed and when the expected errors of the individual points can be shown to be constant. The even spacing results in increased analytical time and greater errors in the extrapolated dose estimate than would be obtained with other sampling distributions. This is especially true for EPR measurements of enamel and bone where each additional irradiation can also require a lengthy annealing treatment to remove transient radicals (Oduwole and Sales, 1994).

One possible method of optimizing analysis comes by choosing individualized weights to associate with each datum (Hamilton, 1964). This has no application when the errors are known to have the same value. For such cases it may be possible to optimize results through altering the distribution if certain constraints can be imposed as described by Montgomery and Peck (1992). They also cite valuable references for those wishing to investigate this topic further.

From linear maximum likelihood methods, the dose distribution is shown to be a significant factor in the error estimation of the unknown dose. We have developed a systematic method for optimizing the spacing of the irradiation's. The application is for the common case where each individual

point has an expected error that can be shown to be constant and where relative error is negligible over the range of the doses applied. This approach also allows a researcher to estimate the expected error for a given dose distribution before an experiment is carried out and therefore design the experiment within acceptable error limits.

2. EXPERIMENTAL

2.1. Negligible relative errors at intermediate doses

Figure 1 shows an EPR dose response curve for human enamel with signal intensity graphed as a function of laboratory applied dose. The y-intercept is the EPR intensity prior to laboratory irradiation, the x-intercept is the estimate of the unknown dose of interest and the slope is a measure of the sample's relative sensitivity to radiation. The errors in the data points are the standard deviations of three spectra taken at each dose level with reorientation (shaking) of the sample grains between each spectral measurement. Note that the errors tend to be randomly distributed such that the relative error is negligible. Figure 2 is a dose response curve from an enamel sample used in a study (Haskell et. al., this volume, a) where individual errors are not shown and were not used for dose optimization. The clusters are superposition's of all the points taken. There are 35, 13 and 5 data points at 0, 1.05 and 10.5 Gy respectively. One outlier was removed at the 10.5 Gy dose level. Again we cannot discern the presence of any relative errors.

Figures 1 & 2 only suggest that the expected errors in the dose points are constant with negligible relative error. To fully validate such a claim we need to investigate the actual functional dependence of the errors on the signal size.

In Table 1, we see this dependency for samples given the same dose distribution shown in Figure 2 (where the sample T2E is graphed). The errors given in Table 1 are standard errors of the mean, $\hat{\sigma}$. The uncertainty in these error estimations were calculated using

$$\sigma(\hat{\sigma}) = \frac{\hat{\sigma}}{\sqrt{2(N-1)}} \quad (1)$$

from Leo (1994) for the standard deviation of $\hat{\sigma}$. The increasing value of the uncertainties in the error are due to decreasing numbers of points at higher dose values.

Another way to evaluate this claim is to do a simple analysis of the residuals from a least squares fit (Netter and Wasserman, 1974). In Table 2 we show the vertical distance of the dose points from the curve representing their least squares fit, this distance or error is known as a residual. When this data is plotted on normal probability paper (where a cumulative normal distribution plots as a straight line), each set gives excellent linearity demonstrating that only normally distributed errors exist. The data comes from Polyakov *et al* (1995). Each data point came from a single measurement and so no individual errors can be estimated aside from the curve fit itself.

What we see is that the error is dominated by "radiation insensitive" error terms. We believe that a large portion of this is anisotropic inhomogeneities that can be effectively suppressed by taking many spectra in which the granular samples have been shaken between successive spectra. Another way to suppress this anisotropy is the use of a constant slow rotation goniometer where many spectra are taken and averaged over the angular range (Haskell *et. al.*, this volume, b).

Similar results are obtained from Soxhleted dentine up to 1.5 Gy. The dose response found by Haskell *et al.* (1994) shows the same distribution

about the curve fit as that found in Figure 1. It also gives similar error forms as those found in Table 2.

Pass and Aldrich (1985) show that above 1.5 Gy in dentine, the errors do appear to be dominated by relative values through a log-log plot. Each point in their dose response comes from a different sample and so could obscure this inference. This potential finding contrasts with the results found by Brady *et al.* (1968) who showed that for a rat femur, the relative errors do not appear to dominate until there has been 150 Gy or more of applied laboratory dose.

2.2. Linearity

Certain signals in quartz have been demonstrated to be linear up to 1 kGy (Toyoda and Ikeya 1994) and in burnt flints to around 200 Gy (Walther and Zilles, 1994).

Linearity has also been shown in the literature for many forms of hydroxyapatite, many of which were archeological samples. Animal bones were found to have a linear response to laboratory applied doses of 40 Gy (Ikeya and Miki, 1980; Oduwole *et al.*, 1993). Ostrich shells have given linearity beyond 60 Gy (Kai *et al.*, 1988). Enamel from a mammoth tooth was shown to be linear up to 200 Gy of laboratory applied dose (Wieser *et al.*, 1988). Aquatic shells and corals have varying linearity of typically more than 10 Gy.

Human bone has been shown to be linear up to at least 100 Gy (Schauer *et al.*, 1994). Certain preparations of synthetic calcium carbonates have only displayed linearity up to a region on the order of 10 Gy (Jacobs *et al.*, 1989). Grun (1989) showed human tooth enamel has a linear response at least up to 200 Gy.

The spin density (and therefore sensitivity and implied linearity) of many other potential radiation accident dosimeters are reviewed by Dalgarno and McClymont (1989).

3. RESULTS

In general, the dose estimate error $|\delta X_{int}|$, can be estimated using equation 2 which was derived in Appendix A;

$$|\delta X_{int}| = \sqrt{E[x^2] + (X_{int})^2} \frac{\tilde{\sigma}}{m \sigma(x)} \quad (2)$$

Here $|\delta X_{int}|$ is the error in the x-intercept (dose estimate), $E[x^2]$ is the expectation value of x^2 for discrete values, X_{int} is the value of the x-intercept found from least squares analysis, $\tilde{\sigma}$ is the error in a weighted average of the dose points and is defined here by equation a16, m is the slope of the least squares fit and $\sigma(x)$ is the numerical calculation for one standard deviation in the dose distribution.

Because $\sigma(x) \leq \sqrt{E[x^2]}$, minimizing the error in X_{int} as a function of the distribution is not an easily visualized task. In fact, the optimum distribution for low level dosimetry turns out to be a function of the fixed parameters in equation 2, namely m , X_{int} and σ .

Typically, a researcher has little or no control over m or σ as they are determined by optimum spectrometer parameters, configuration and sample preparation etc. One can then only optimize the other parameters (i.e. $E[x^2]$ and $\sigma(x)$) to achieve acceptable error in the dose estimate (X_{int}).

For illustration, in Figure 3 we set $\tilde{\sigma}/m = 1$, substituted this into equation 2 and then graphed the functional dependence of δX_{int} on X_{int} . We

used six different kinds of distributions to initially address the problem. Each distribution had 10 points total, the maximum x-value of each being 1000. Because the slope was fixed by the normalization, the y-intercept was varied to give the X_{int} variations.

From figure 3, one can immediately see that when the dose being estimated is less than 35% of the maximum dose, then the single high point distribution is the best shown for dose estimation. Above that, the 1/2 & 1/2 distribution becomes optimal. This is important because the most common distribution in use is the constant distribution and it never is optimal for extrapolation. Beyond the range shown in figure 3, the X_{int} errors tend to go off linearly with the last few points shown (as required by equation 2 when X_{int} becomes arbitrarily large).

The results from figure 3 suggest that optimum distributions will only have points at their extrema. In figure 4, we have graphed the effect of 10 points distributed only at the ends as previously done in two cases. Here we start off with 5 points at zero and 5 at 1000 (this distribution we term "1/2 & 1/2"). We then shift to 4 points at 1000 and 6 at zero and so on until we have only one point at 1000 and nine at zero (in figure 3 referred to as "Single high point distribution").

Figure 4 tells us that besides the region where X_{int} is less than 100% of the maximum dose Ω , the 1/2 & 1/2 distribution can be considered to always be close to optimal. In the transition region where $|X_{int}| < \Omega$, one favors "bottom heavy" distributions for smaller and smaller extrapolations.

Due to the simplicity of the form, it is worth noting that using the same assumptions used in deriving equation 2, we can write the y-intercept error as: $\sigma_b = \sqrt{S_{xx} / \Delta} = \sqrt{E[x^2]} \tilde{\sigma} / \sigma(x)$ and also the ratio of y-intercept error to

slope error as $\sigma_b/\sigma_m = \sqrt{E[x^2]}$. These can be applied to related applications as those described in this paper.

The question still remains as to how small the error must be for these approximations to be valid at higher doses as in archeological dating. If the minimum value of the error datum is α , we can write $\sigma_i^2 = (\alpha + f(y))^2$ so the approximation is valid only when $|f(y)| \ll |\alpha|$. If this is not the case, we will have to substitute $\sigma_i^2 = (\alpha + f(y))^2$ into all the corresponding appendix formulae. This will prevent much of the simplification thus prohibiting us from using these derivations.

4. APPLICATION

4.1. In general

Figures 3 and 4 were made with sufficient generality to insure ease of application to most situations. We use Ω as the maximum dose we can apply to a sample. This could be the lowest value where errors are constant or simply the largest dose one can give quickly due to time constraints or negligibility of transient components etc. We will further consider only those cases similar to those shown in figure 4, i.e. we will only have points located at the extrema of the distribution

We begin by obtaining estimates for X_{int} , ϕ , m and the number of data points N that we would like to use. We decide on the maximum dose Ω we will apply. We then take the initial estimate of the X_{int} and find what percentage of Ω it is. This determines which distribution to use. The optimal distributions as a function of X_{int} 's percentage of maximum dose are approximated in figure 5. A distribution with a ratio of high points to total points of 0.5 is equivalent to half the points at zero added dose and half at the

maximum dose level. A ratio of 0.1 has one at the high dose value and nine at the zero, etc. Once the optimal distribution is determined, further decrease in error can only be achieved by increasing the number of points taken at the two dose locations, while maintaining the ratios determined from Figure 5.

With the distribution now chosen, its $E[x^2]$ and $\sigma(x)$ are fixed and can be calculated. Note that these two values are the same for all distributions with the same ratio of high to total points. This can be verified by using equations a13 and a14 (which is equivalent to using the last row in table 3). Table 3 lists these values for the five distributions given in Figure 4. We then solve for these constants in terms of Ω and use them in equation 2. Assuming we have an estimate of the expected error for the individual points, we now have all the terms for use in equation 2. If the error is not small enough for the number of points we are using then we can scale it down by increasing the number of points. The error is inversely proportional to the square root of N through the $\bar{\sigma}$ term in equation 2.

4.2. A step by step approach

- 1) Obtain estimates of m , X_{int} and $\bar{\sigma}$.
- 2) Decide on the maximum dose Ω to be given to the sample.
- 3) Determine what percentage X_{int} is of Ω .
- 4) Using figure 5 estimate which distribution is optimal using the value found in step 3.

(Please insert Figure 5 here)

- 5) Choose a convenient number, N , of data points to start with.
- 6) Having found your distribution type and number of points, look up in table 3 and calculate your $E[x^2]$ and $\sigma(x)$ terms.

(Please insert Table 3 here)

- 7) Substitute all the variables into equation 2 to get an estimate of your expected error.
- 8) If the error is too large then increase the number of data points until acceptable error is achieved. The error is scaled by $1/\sqrt{N}$.

4.3. A simple example

We take some initial scans for a sample whose dose is to be determined and then assume that the error to be encountered for the individual dose points is equal to the uncertainty found in these measurements. We use the mean of the initial points to estimate X_{int} from a previously derived calibration curve. The value of m is then the slope of this calibration curve.

Assume that it is convenient for us to have a maximum dose of 640 mGy due to arbitrary constraints. In particular we will use the data shown in figure 1 and make a comparison of an optimal distribution with its linear dose distribution using only 8 points (note that a linear distribution will always give better results than a constant distribution but worse than an optimal distribution). The error in the first point from figure 1 is 235 (a.u.) whereas the average of all the errors in the points is 197 (a.u.). From this we can say that if we had taken say 9 spectra, we should have gotten the correct estimate. We will go ahead with the assumed correct averaged value. We will also use the median of the three unirradiated sample spectra for the y-intercept which is 814 (a.u.) and not the actual intercept of the linear regression. Using the least squares fit shown in figure 1 as our calibration curve gives a slope of $m = 11.06$ (a.u.)/mGy. Using this with the y-intercept we get an estimate of $X_{int} = 74$ mGy.

Because 74 mGy is 11.5% of the maximum dose 640 mGy, figure 5 tells us that the distribution ratio of 0.09 will be optimal i.e.; we will use 1 point for the high dose value and 7 at the zero level. Looking up the necessary values in table 3, we calculate the expected errors in the dose estimates (using $N = 8$). The expected error using the optimal distribution would be 7.41 mGy. The expected x-intercept error using the linear distribution shown in figure 1 (not the actual error from the least squares fit) is 8.84 mGy, we have therefore reduced our error by 16% while reducing our dose applications from 7 to 1.

If this expected error is not small enough, we can decrease it through the proportionality factor $1/\sqrt{N}$ in the σ term from equation 2 i.e.; we can increase N until the error is acceptable, or alternatively, we can chose a larger additive dose and repeat the optimization calculation.

5. DISCUSSION

If the uncertainties in the data points are dominated by relative errors then the dose distributions presented here cannot presently be justified in the form given. In this case the form of equation 2 can be understood to be unchanged by switching to the convention that $\sigma_i = \text{constant} \cdot y_i$ with a similar rule for Poisson errors.

In human tooth enamel, linearity normally continues up to near 200 Gy. Negligibility of relative errors is believed to continue up to the same range. This is so significant that even if relative errors are only negligible for doses near 10 Gy, constant distribution least squares fitting for extrapolation purposes is still not optimal for minimizing errors in this range (which is below

the typical maximum used). It also seems that this is likely true for obtaining larger dose estimates including those encountered in archeological dating.

In cases where nonlinearity is occasionally observed at low doses (Haskell et al., this volume b), it may be possible to apply a relatively small dose to the sample following the zero dose measurements and then test linearity against a calibration curve derived for the type of material under investigation. If the slope of the sample matches that of the calibration curve then linearity may be assumed and the technique described here applied. If the slope differs significantly from that of the calibration curve then a different distribution, appropriate for revealing the shape of the dose response curve, may be applied.

6. CONCLUSIONS

The optimal dose distribution is a function of the size of the unknown dose and the dose distribution itself. The optimal distribution will have points located at the extremities of the distribution.

Caution is warranted when the range of the distribution may overlap nonlinear regions where altered techniques (Barabas *et al.*, 1992) would be required to optimize the distribution. The methods described here should only be routinely applied over regions previously known to be linear where relative errors are negligible.

REFERENCES

- Brady J. M., Aarestad N. O. and Swartz H. M. (1968) In Vivo Dosimetry By Electron Spin Resonance Spectroscopy. *Health Phys.* **15**. 43-47.
- Barabas M., Mudelsee M., Walther R. and Mangini A., (1992) Dose-response and thermal behavior of the ESR signal at $g=2.0006$ in carbonates. *Quat. Sci. Rev.* **111**. 173-179.
- Dalgarno B. G. and McClymont J. D. (1989) Evaluation of ESR as a Radiation Accident Dosimetry Technique. *Appl. Radiat. Isot.* **40**. 1013-1020.
- Grun R. (1989) Present Status of ESR-Dating. *Appl. Radiat. Isot.* **40**. 1045-1055.
- Hamilton W. (1964) Statistics In Physical Science - Estimation, Hypothesis Testing and Least Squares. pp. 146-148. The Ronald Press Company, New York
- Haskell E., Kenner G. and Hayes R. (1995) Electron paramagnetic resonance dosimetry of dentine following removal of organic material. *Health Phys.* **68**(4):579-584
- Haskell E., Kenner G., Hayes R., Sholom S. and Chumak V. (in press) An EPR intercomparison using teeth irradiated prior to crushing. *Radiat. Meas.* (this volume)
- Haskell E., Hayes R. and Kenner G. (in press) Improved accuracy of EPR dosimetry using a constant rotation goniometer. *Radiat. Meas.* (this volume)
- Ikeya M. and Miki T., (1980) Electron Spin Resonance Dating of Animal and Human Bones. *Science*. **207**, 977-979.
- Jacobs C., De Canniere P., Debuyst R., Dejehet F. and Apers D. (1989) ESR Study of Gamma-ray Irradiated Synthetic Calcium Carbonates. *Appl. Radiat. Isot.* **40**, 1147-1152.

- Kai A., Miki T. and Ikeya M. (1988) ESR dating of teeth, bones and eggshells excavated at a paleolithic site of Douara Cave, Syria. *Quat. Sci. Rev.* **7**, 503-508.
- Leo W. (1994) Techniques for nuclear and particle physics experiments. eqns. (4.52), (4.54) & (4.56) pp. 96. Springer-Verlag, New York.
- Montgomery D. and Peck E. (1992) Introduction to linear Regression Analysis, 2nd Ed. pp. 409-411. John Wiley & Sons, Inc. New York.
- Neter J. and Wasserman W. (1974) Applied Linear Statistical Models - Regression, Analysis of Variance and Experimental Designs. pp. 97-111. Richard D. Irwin, Inc. Homewood, Il.
- Oduwole A. D. and Sales K. D. (1994) Transient ESR signals induced by γ -irradiation in tooth enamel and bone. *Quat. Sci. Rev.* **13**, 647-650.
- Oduwole A. D., Sales K. D. and Dennison K. J. (1993) Some ESR Observations on Bone, Tooth Enamel and Eggshell. *Appl. Radiat. Isot.* **44**, 261-266.
- Pass B. and Aldrich J. E. (1985) Dental Enamel as an In Vivo Dosimeter. *Med. Phys.* **12** (3), 305-307.
- Polyakov V., Haskell E., Kenner G., Huett G. and Hayes R. (1995) Effect of mechanically induced background signal on EPR dosimetry of tooth enamel. *Radiat. Meas.* **24**:249-254.
- Press W., Teukolsky S., Vetterling W. and Flannery B. (1992) Numerical recipes in C 2nd Ed. pp. 662-663. Cambridge University Press, New York.
- Schauer D. A., Desrosiers M. F., Le F.G., Seltzer S. M. and Links J. M. (1994) EPR Dosimetry of Cortical Bone and Tooth Enamel Irradiated with X and Gamma Rays: Study of Energy Dependence. *Rad. Res.* **138**, 1-8.
- Toyoda S. and Ikeya M., (1994) ESR Dating of Quartz with Stable Component of Impurity Centers *Quat. Sci. Rev.* **13**, 625-628

Wieser A., Goksu H.Y., Regulla D.F. and Vogenauer A. (1988) Dose Rate Assessment in Tooth Enamel *Quat. Sci. Rev.* **7**, 491-495

Walther R. and Zilles D., ESR Studies on Flint With a Difference Spectrum Method *Quat. Sci. Rev.* **13**, 635-639

APPENDIX A

A.1. Review of weighted least squares fitting

We follow the same pattern as Press *et al.* (1992). Define chi-squared as;

$$\chi^2 = \sum_{i=1}^N \frac{(y_i - b - m x_i)^2}{\sigma_i^2} \quad (\text{a1}).$$

The maximum likelihood estimates of b and m come from the global minimum of equation a1 in the b and m parameter space. In order to do this minimization, we set

$$0 = \frac{\partial \chi^2}{\partial b} = -2 \sum_{i=1}^N \frac{(y_i - b - m x_i)}{\sigma_i^2} \quad (\text{a2})$$

$$0 = \frac{\partial \chi^2}{\partial m} = -2 \sum_{i=1}^N \frac{x_i (y_i - b - m x_i)}{\sigma_i^2} \quad (\text{a3})$$

This results in a system of equations in b and m , to solve these we use the notation;

$$S_1 = \sum_{i=1}^N \frac{1}{\sigma_i^2}, \quad S_x = \sum_{i=1}^N \frac{x_i}{\sigma_i^2}, \quad S_y = \sum_{i=1}^N \frac{y_i}{\sigma_i^2}, \quad S_{xx} = \sum_{i=1}^N \frac{x_i^2}{\sigma_i^2}, \quad S_{yy} = \sum_{i=1}^N \frac{y_i^2}{\sigma_i^2} \quad \text{and}$$

$$S_{xy} = \sum_{i=1}^N \frac{x_i y_i}{\sigma_i^2}. \quad \text{This allows us to rewrite equations a2 and a3 as}$$

$$b S_1 + m S_x = S_y \quad (\text{a4})$$

$$b S_x + m S_{xx} = S_{xy} \quad (\text{a5})$$

respectively. Using further the notation that $\Delta = S_1 S_{xx} - S_x^2$ allows us to write for the solution of equations a4 and a5;

$$b = \frac{(S_{xx} S_y - S_x S_{xy})}{\Delta} \quad \& \quad m = \frac{(S_1 S_{xy} - S_x S_y)}{\Delta}.$$

To obtain the errors in these estimates we use the applicable error propagation formulae i.e.;

$$\sigma_f^2 = \sum_{i=1}^N \sigma_i^2 \left(\frac{\partial f}{\partial y_i} \right)^2 \quad (\text{a6}).$$

Continue by substituting $\frac{\partial b}{\partial y_i} = \frac{(S_{xx} - S_x x_i)}{\sigma_i^2 \Delta}$ and $\frac{\partial m}{\partial y_i} = \frac{(S_1 x_i - S_x)}{\sigma_i^2 \Delta}$

into equation a6 and doing the summations. Skipping four or five steps of cancellations and simplifications one arrives at both the variance in the y-intercept

$$\sigma_b^2 = \frac{S_{xx}}{\Delta} \quad (\text{a7})$$

and the variance in the slope

$$\sigma_m^2 = \frac{S_1}{\Delta} \quad (\text{a8}).$$

A.2. Error dependency on distribution

From standard error propagation (equation a6), we can also obtain the error in the x-intercept (δX_{int}) allowing us to write (using here δ symbols in place of σ 's)

$$X_{int} \pm \delta X_{int} = -\frac{b}{m} \pm \left\{ \left(\frac{\delta b}{m} \right)^2 + \left(\frac{b \delta m}{m^2} \right)^2 \right\}^{\frac{1}{2}} \quad (\text{a9}).$$

We start with

$$|\delta X_{int}| = \left(\frac{1}{m} \right) \sqrt{(\delta b)^2 + (X_{int})^2 (\delta m)^2} \quad (\text{a10})$$

which is a slightly modified version of equation a9. We now substitute back into equation a10 the S_i notations (from equations a7 and a8) and their explicit definitions when desired giving;

$$|\delta X_{int}| = \left(\frac{1}{m} \right) \sqrt{\frac{S_{xx}}{\Delta} + (X_{int})^2 \frac{S_1}{\Delta}} = \left\{ \frac{\sum_{i=1}^N x_i^2 / \sigma_i^2 + (X_{int})^2 \sum_{i=1}^N 1 / \sigma_i^2}{S_1 S_{xx} - (S_x)^2} \right\}^{\frac{1}{2}} \frac{1}{m} \quad (a11).$$

If the y errors (σ_i) can be approximated by a constant value such that

$$\sigma_i^2 \approx \text{constant} = \sigma^2 \quad \forall i \quad (a12)$$

then from

$$E[f] = \left(\sum_{i=1}^N f / \sigma_i^2 \right) / \left(\sum_{i=1}^N 1 / \sigma_i^2 \right) \quad (a13)$$

(which is the definition of an expectation value using discrete variables with known variances) we can see that even if all the σ_i^2 are equal to the same constant, then this formula is still valid. With this, we can start substituting expectation values from equation a13 into a11 when appropriate. Although the errors used here are for the y values, they are each by assumption the same constant and so can be used in this manner. Remember the x values are simply the laboratory applied doses (or any linearly dependent variable) having by assumption negligible error.

Utilizing this new notation, we can now rewrite the denominator term in equation a11 using;

$$\begin{aligned} & (S_1 S_{xx} - (S_x)^2) / \left(\sum_{i=1}^N 1 / \sigma_i^2 \right)^2 = \\ & = E[x^2] - E[x]^2 = \text{Var}[x] = \sigma^2(x) \end{aligned} \quad (a14)$$

All this gives us a new form for equation a11;

$$|\delta X_{int}| = \left\{ \frac{E[x^2] + (X_{int})^2}{\sum_{i=1}^N 1 / \sigma_i^2} \right\}^{\frac{1}{2}} \frac{1}{m \sigma(x)} \quad (a15)$$

where we have pulled out the standard deviation term from the variance. Note that this is not a standard error of the mean term as we have not scaled it by the square root of N-1.

If we further notice that the term $\sqrt{1 / \left(\sum_{i=1}^N 1 / \sigma_i^2 \right)}$ in equation a15 is just the error in a weighted average (Leo, 1994), we can pull this term out and call it

$$\bar{\sigma} = \sigma / \sqrt{N} \quad (\text{a16})$$

from which we can discern the direct dependence on the individual errors (from equation a12) and the statistical decrease in errors with increasing data points. Now we are left with

$$|\delta X_{\text{int}}| = \sqrt{E[x^2] + (X_{\text{int}})^2} \frac{\bar{\sigma}}{m \sigma(x)} \quad (2)$$

which is the proper general form for evaluating the dose distribution dependency of propagated errors in least squares fitting with constant errors.

It is unlikely that the error will indeed be a constant number, what is more likely (and agrees with figures 1 and 2) is a normally distributed error with a fixed standard deviation. If this is the case then nothing need be changed. Equation a12 can be considered unchanged where σ is the actual fixed standard deviation of the ordinates rather than the constant number previously used. In either case, we input a constant value. Because of this equations a13 and a14 are left untouched in form and meaning. From these we can see that equation 2 is unchanged without making any assumptions other than those already made.

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Table 1. Error dependency on signal size (dose)[†]

Dose (Gy)	T1E Error	T2E Error	T3E Error
0	11800 ± 1200	6310 ± 770	5020 ± 580
1.05	8600 ± 1800	5100 ± 1100	4150 ± 930
10.5	11800 ± 3700	7300 ± 2600	6800 ± 2200

[†]These values are the standard deviations of the individual distributions. The expected errors in the standard deviation estimator came from equation 1.

Table 2. Residuals from dose response curve for enamel[†]
taken from Polyakov et. al. (1995)

Dose (Gy)	d1 residuals	d2 residuals	d3 residuals
10	-94	63	-32
20	39	78	29
30	-95	67	57
40	-9	-185	-184
60	45	-109	-142
80	131	90	254
110	69	-44	275
140	-20	19	320
220	-66	21	-65

[†]The spectra from which these points came were recorded with different EPR parameters than those in table 1. Each column represents a different grain size.

Table 3. Factors for use in equation (2) when the optimum distribution ratio is chosen.

Distribution ratio of high points to total	$E[x^2]$	$\sigma(x)^\dagger$
1:10	$\Omega^2/10$	$3 \Omega/10$
1:5	$\Omega^2/5$	$2 \Omega/5$
3:10	$3 \Omega^2/10$	$(\Omega/10)\sqrt{21}$
2:5	$2 \Omega^2/5$	$(\Omega/5)\sqrt{6}$
1:2	$\Omega^2/2$	$\Omega/2$
in general	$h \Omega^2/N^*$	$\frac{\Omega h}{N} \sqrt{\frac{N}{h} - 1}$

[†]This is a standard deviation term and not a standard error of the mean.

*Here h is the number of high points and N is the total number of points.

FIGURE CAPTIONS

Fig. 1 - Reasonable enamel dose response. The curve fit gave the values for $Y = mX + b$ as $m = 11.06 \pm 0.34$, $b = 853 \pm 66$, $R = .997$ and chi-squared = 6.09. EPR parameters were 5 mT sweep width, 8 mW microwave power, 10 sweeps, 0.5 mT modulation amplitude, 20.4 ms conversion time and 164 ms time constant.

Fig. 2 - Enamel dose response using a semi-optimized dose distribution. The points at the 1 Gy level were to verify linearity. The curve fit gave the values for $Y = mX + b$ as $m = 46.19 \pm 0.13$, $b = 8130 \pm 430$ and $R = .9998$. EPR parameters were 3.5 mT sweep width, 2 mW microwave power, 50 sweeps, 0.5 mT modulation amplitude, 20.4 ms conversion time and 164 ms time constant.

Fig. 3 - Distribution error dependency. A somewhat ad-hoc choice of distributions to demonstrate the effect that a distribution choice has on the propagated error when individual points have a constant expected error. The $1/2$ & $1/2$ distribution is five points at the minimum ($x=0$) and five at the maximum. The constant distribution is the familiar distribution of equally spaced dose points. The linear distributions were linearly distributed from left to right to begin at zero and end at 1000 (figure 1 shows a linear distribution). The single high point distribution had nine points at the zero and only one at the 1000 (in figure 4 it is referred to as "1 point at the top"). The average difference between the quadratic distribution and the single high point distribution was less than 1% and so wasn't shown. The Gaussian neg distribution had one point in the center with the others pushed to the outside of the range (five up and four down) in a manner like an upside-down Gaussian

(hence the name). The Gaussian distribution was centered on the $x=500$ point. Each distribution used the value of $N=10$.

The units of the horizontal range are dimensionless and equal to $100 \cdot X_{int}/\Omega$ (in this case $\Omega=1000$ a.u.). This was done with such generality that scaling (both dimensions) to a particular application would be as straightforward as possible.

Fig. 4 - Optimum type distributions. All these distributions have points only at the distributions extrema. The maximum is at 1000 (a.u.) and the minimum is at 0. Each distribution has 10 points total. No distributions are shown that have more points at the top of the distribution than at the bottom.

The units of the horizontal range are in percent of the maximum distribution value. This was done with such generality that scaling (both dimensions) to a particular application would be as straightforward as possible.

Fig. 5 - Optimum distributions as a function of the estimate of the X_{int} 's percent of maximum dose. The vertical is the ratio of the number of points at the maximum dose to the total number of points N used. This graph is a cubic spline to 46 data points. These data points came from calculating the expected dose estimate error for 46 different optimal distributions. The distributions ranged from a high-to-total ratio of 0.01 to 0.46, they were also distributed in increments of 0.01 for different dose estimation values. It should also be noted that the curve is assumed to saturate to 0.50 at infinity and to go through the origin. A useful approximation to the graph over the region shown is given by the equation $y = 0.468 (1 - \exp[(0.363 - x)/47.4])$ which gives an average error of 0.455% to the curve.

Fig 1.

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

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