

Chapter 7

Optimisation Techniques for Computer-Aided Quench Correction

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In liquid scintillation counting as practiced in today's laboratories the reliability and accuracy of the machines is commonly assumed to be a negligible factor when compared with the accuracy of the measurement being performed. Fortunately, for the majority of cases this is correct. The user of scintillation counters is allowed the luxury of some powerful simplifications. He can decide how long to count any specific sample based on Poisson statistics. He ignores the machine drift, sample asymmetries, position errors, sample inhomogeneities and most of the other pitfalls in the path of righteous counting. By controlling sample composition he will even often be able to ignore variable quenching.

All of these problems, however, become manifest for computer programs with the ultimate goal of on-line data capture and reduction. The most important design requirement for such a package is that the programs be written for the most sophisticated user to be encountered. With today's high speed computers, the storage space and management which would be required to hold a series of programs of various levels of sophistication are much more expensive than would be the saving in computer time realised by most of the users being content with simple algorithms.

Thus, it becomes incumbent on the systems analyst to find the limits of the system and those factors contributing to error. Using such a systems approach leads, in turn, to optimisation of the data handling, the machine design, and finally (and most difficult in many cases) education of the user in proper machine utilisation and sample preparation.

The goal is a good estimator of the disintegration rate D . This rate is observed indirectly by counting and adjusting for the efficiency, $D = C/E$ where C is the counting rate, E the efficiency of the channel. Goodness is not a subtle concept in this case. A good estimator should be sufficient, be consistent, have minimum variance, and perhaps be unbiased. We want to know its sampling distribution, or at least its variance so as to

set sample sizes and confidence limits and devise hypothesis tests. A standard procedure for deriving a good estimator is the maximum likelihood method. Maximum likelihood estimators are commonly used since they inherently have the desirable qualities listed above, with the possible exception of bias in the particular case. This method is based upon the concept of the likelihood, which is a function relating the set of observations to the parameter to be estimated. Maximum likelihood estimator means that value of the parameter for which this function achieves its maximum.

Automatic external standard will be treated first and channels ratio quench correction later. Other forms of quench correction, e.g., internal standardisation, do not lend themselves as readily to on-line computation and will not be considered here.

The sample efficiency is a known function (e.g. a cubic is commonly fitted) of the true AES (i.e. the count rate of one channel or ratio of two channels of automatic external standard) which is estimated by observing a variable, S , AES counts or ratio. We know that the average of observations on S is the maximum likelihood estimator of the true AES and therefore the sample efficiency at this average, $E[\text{ave}(S)]$, is the maximum likelihood estimator of E .

To show this, let L represent the likelihood and recall that the maximum of a function is achieved where its derivative vanishes. Because of the chain rule of calculus,

$$\frac{\partial L(E(\text{AES}))}{\partial \text{AES}} = \frac{\partial L(E(\text{AES}))}{\partial E} \cdot \frac{\partial E(\text{AES})}{\partial \text{AES}},$$

we see that

$$\frac{\partial L}{\partial \text{AES}} = 0 \text{ where } \frac{\partial L}{\partial E} = 0.$$

Secondly, C is estimated by observing the variable X , the number of sample counts. The maximum likelihood estimator of C is the average, $\text{ave}(X)$. Our goal, however, is neither C nor AES, but rather $D=C/E(\text{AES})$ where C and AES are nuisance parameters to the estimation problem.

Although X and S are statistically independent, we must solve for both simultaneously. The distribution of X is a function of the unknown AES which is estimated by S . Consider the likelihood function: $L(X, S \text{ given } D \text{ and AES})$.

Because S is not a function of D we have:

$$L = L(S \text{ given AES}) L(X \text{ given } D \text{ and AES}).$$

$L(X \text{ given } D \text{ and AES})$ is simply the Poisson distribution with parameter D times AES. $L(S)$ is not a common form, however recall that we know that the maximum likelihood estimator for AES is $\text{ave}(S)$, the average of the observations S . Therefore by the same argument as above we also have

$$\frac{\partial L(S \text{ given AES})}{\partial \text{AES}} = 0 \text{ at AES} = \text{ave}(S)$$

Moreover:

$$\frac{\partial L(X \text{ and } S \text{ given } D \text{ and AES})}{\partial D} \text{ is proportional to}$$

$$\frac{\partial L(X \text{ given } D \text{ and AES})}{\partial D}$$

so that the simultaneous solution will have

$$\frac{\partial L(X \text{ given } D \text{ and ave}(S))}{\partial D} = 0$$

This is easily seen to be satisfied by

$$G = \frac{\text{ave}(X)}{E(\text{ave}(S))}$$

We therefore use G as the maximum likelihood estimator for D .

Since X and S are independent variables, we can derive a good first order estimate of the variance of the maximum likelihood estimator of D as follows:

$$\begin{aligned} \text{var}(G) &= \left[\frac{\partial D}{\partial E} \cdot \frac{\partial E}{\partial S} \right]^2 \cdot \text{var}(S) + \left[\frac{\partial D}{\partial C} \right]^2 \cdot \text{var}(X) \\ &= \left[\frac{\text{ave}(X)}{E(\text{ave}(S))} \right]^2 \cdot \left[\frac{\partial E}{\partial S} \right]^2 \cdot \text{var}(S) + \frac{\text{var}(X)}{E(\text{ave}(S))} \end{aligned}$$

Since X is a Poisson variable its variance equals its mean. We can therefore estimate the variance with the same mean as estimates $\text{ave}(X)$. If we also use a Poisson count as the AES reading, then $\text{var}(S) = \text{ave}(S)$ and the form reduces to

$$\text{var}(G) = \left[\frac{\text{ave}(X)}{E(\text{ave}(S))} \right]^2 \cdot \left[\frac{\partial E/\partial S \text{ ave}(S)}{E^2(\text{ave}(S))} + \frac{1}{\text{ave}(X)} \right]$$

When a ratio is used for AES, this makes the calculation of its variance more difficult, and the easiest solution is just to estimate $\text{var}(S)$ from the sample of S .

In channels ratio counting, the efficiency estimator and the sample count rate estimator are not independent since the efficiency estimator (the observed ratio) is derived from the observed sample count rate estimator plus the count rate in a second channel. This makes the derivation of maximum likelihood estimator of the disintegration rate more complicated but still quite analogous to that described above for AES quench correction. The channels ratio counting maximum likelihood estimator, V , is:

$$V = \frac{1}{n} \sum_{i=1}^n X_i / E \left(\sum_{j=1}^n W_j / \sum_{k=1}^n X_k \right)$$

In this case W and X are naturally not independent, the parameter estimated is

$$D = C_x/E \left(\frac{C_w}{C_x} \right), \text{ and } X \text{ is the larger channel and } W \text{ the smaller.}$$

The variance of the channels ratio estimate is calculated essentially in the same way as for the AES method, except the counts and efficiency estimates are not independent. Therefore, their covariance must be included.

Given the form:

$$S = \frac{\text{ave}(X)}{E(\text{ave}(W) / \text{ave}(X))},$$

we approximate the variance:

$$\begin{aligned} \text{var}(S) = & \left[\frac{\partial S}{\partial C_x} \right]^2 \cdot \text{var}(X) + \left[\frac{\partial S}{\partial C_w} \right]^2 \cdot \text{var}(W) \\ & + \left[\frac{\partial S}{\partial C_x} \right] \cdot \left[\frac{\partial S}{\partial C_w} \right] \cdot 2 \text{cov}(X, W) \end{aligned}$$

To evaluate this, we see that dS/dC is estimated by:

$$\begin{aligned} \frac{\partial S}{\partial \text{ave}(X)} &= \frac{E(\text{ave}(W) / \text{ave}(X)) - \text{ave}(X) \cdot \left[\frac{\partial E}{\partial \text{ave}(X)} \right] \cdot \left[-\text{ave}(W) / \text{ave}^2(X) \right]}{E^2(\text{ave}(W) / \text{ave}(X))} \\ &= \frac{E(\text{ave}(W) / \text{ave}(X)) + \left[\frac{\partial E}{\partial \text{ave}(X)} \right] \cdot \left[\frac{\text{ave}(W)}{\text{ave}(X)} \right]}{E^2(\text{ave}(W) / \text{ave}(X))} \end{aligned}$$

and similarly:

$$\frac{\partial S}{\partial \text{ave}(W)} = - \frac{\partial E / \partial \text{ave}(W)}{E^2(\text{ave}(W) / \text{ave}(X))}$$

Therefore we have:

$$\begin{aligned} \text{var}(S) = & \frac{1}{E^4} \cdot \left[\left[E + \frac{\partial E}{\partial \text{ave}(X)} \cdot \frac{\text{ave}(W)}{\text{ave}(X)} \right]^2 \cdot \text{var}(X) + \left[\frac{\partial E}{\partial \text{ave}(W)} \right]^2 \cdot \text{var}(W) \right. \\ & \left. + 2 \left[E + \frac{\partial E}{\partial \text{ave}(X)} \cdot \left[\frac{W}{X} \right] \right] \cdot \left[\frac{\partial E}{\partial W} \right] \cdot \text{cov}(X, W) \right] \end{aligned}$$

In the Poisson process, the variance is equal to the mean. Therefore, we can estimate

$$\text{var}(X) = \text{ave}(X)$$

and

$$\text{var}(W) = \text{ave}(W)$$

Moreover, the covariance between Poisson counts when one window is entirely within the other is the mean of the smaller.

$$\text{cov}(X, W) = \text{ave}(W)$$

So that, finally:

$$\begin{aligned} \text{var}(S) = & \frac{1}{E^4} \cdot \left[\left[E + \frac{\partial E}{\partial \text{ave}(X)} \cdot \left[\frac{\text{ave}(W)}{\text{ave}(X)} \right] \right]^2 \cdot \text{ave}(X) \right. \\ & \left. + \left[\frac{\partial E}{\partial \text{ave}(W)} + 2E + \frac{\partial E}{\partial \text{ave}(X)} \cdot \left[\frac{\text{ave}(W)}{\text{ave}(X)} \right] \right] \cdot \left[\frac{\partial E}{\partial \text{ave}(W)} \right] \cdot \text{ave}(W) \right] \end{aligned}$$

The derivatives of E with respect to the windows depends on the functional form. It can be easily evaluated in any particular case.

Propagation of error through calculations. In the discussion to follow all arguments apply both to AES and channels ratio quench correction.

The maximum likelihood is one of the statistics currently used, however it is not the only common one.

Perhaps the most subtle of all error sources (except for the statistician or numerical analyst) to cope with is the propagation of error by the calculations themselves. An example (1) will illustrate the proposition.

Example 1 Let $y = [(x-9) \times 10] - 9$

Then if $x = 10$ and is error free

$$y = 1.0$$

However, if x has an error of -0.1 (i.e., -1%) then

$$x = 9.9 \text{ and}$$

$$y = 0. \text{ Thus, this simple series of mathematical manipulations has}$$

magnified the error 10 fold and reduced the calculation to nonsense.

In order to apply the latter considerations to liquid scintillation counting we began by asking a deceptively simple question. If one assumed a perfect counter with no drift or other sources of error, how should one calculate the results of a series of repeat counts? The existence of a polynomial (e.g. a cubic equation) which describes the relationship between absolute efficiency and the AES is also assumed. That is, should one total the observed counts and divide by the total time counted, thus calculating d.p.m. once only? Or is it equivalent to calculate the d.p.m. for each time the sample is counted and average the calculated d.p.m. figures?

Stated another way, if a radioactive sample is counted a number of times, there are at least three ways a computer program may be written to perform the estimation of the disintegration rate. First, in the maximum likelihood estimation described above, the

observed counts are accumulated over the total observations and divided by the total time counted and the final calculation performed only once. Second, the disintegration rates could be calculated for each observation and these averaged at the end. Third and intermediate between the other two, is the possibility of averaging the count rates and averaging the efficiencies separately and then dividing. The difference in computer time for the alternatives is negligible, but there are other important differences.

One of the important considerations of a statistic is the limiting value it has when the sample consists a very large number of observations. The idea is that you should get the 'true' value if you sample enough. It happens that the results are not the same if the order of operations is reversed. All maximum likelihood estimations, ours included, converges on the true values. Consider the second estimator for D

$$Y = \frac{1}{n} \sum_{i=1}^n \frac{X_i}{E(S_i)}$$

where as above n is the number of observations, E is the efficiency, S is the observed AES and X is the sample count. As n is increased the value of Y will be distributed more and more tightly around the mean

$$Y \rightarrow \text{ave} \left[\frac{X}{E(S)} \right]$$

Since X and S are independent, the mean of their ratio is the ratio of their means

$$Y \rightarrow \text{ave}(X) \text{ ave} \left[\frac{1}{E(S)} \right]$$

However the second term, the mean of the inverse of the efficiency, is not the value we need which is the inverse of the mean efficiency. Therefore, as sample size is increased the value Y will differ from D more and more certainly. Thus, the more the sample is counted and calculated by this method the surer it is that the answer converged upon will be wrong. The third common alternative estimator (T) above is

$$T = \sum_{i=1}^n X_i / \sum_{j=1}^n E(S_j)$$

The same problem occurs again because the limit of the denominator is the mean of efficiency and not the efficiency of the mean of S , which is what we want.

Sources of error and minimisation of their effect. Table 1 presents major categories of input to the scintillation counting system as contributing error and some means of minimising the error due to each of the categories. Errors inherent in the sample itself can only be minimised by careful sample preparation (including container selection). The one exception to this is the detection and recovery of error due to inhomogeneous samples, as will be discussed later.

Three classes of machine error exist: (a) additive (e.g. background); (b) subtractive (e.g. coincidence loss); and (c) spectral distortion resulting a drifting response to pulse height (e.g. drift in photomultiplier gain). Additive errors such as 'background' are normally minimised by the approximation of determining its magnitude in each counting

Table 1. Methods of recovery from error in liquid scintillation counting.

| | |
|---------------------------|--|
| Sample | |
| Preparation | Accurate, multiple measurements Homogeneous distribution in vial |
| Container | Accurate manufacture Selection by user |
| Position | Recounting after rotation of vial |
| Machine | |
| Electronics | Preventive maintenance Stable design |
| Photomultipliers | Cooling Periodic drift correction Short counts, multiple cycles Intersperse standards |
| Data reduction | |
| Calibration for quenching | |
| AES | Many standard vials |
| Channels ratio | High count rates in each channel |
| Calculations | Test method for minimal error propagation |

channel on an 'unquenched' sample and subtracting these figures from all other determinations. This method ignores the fact that 'background' pulses have two main sources, i.e. extraneous radiation in the vial and machine generated pulses. The approximation is valid only for the machine generated pulses. Extraneous pulses due to radioactive events must be treated by a quench correction algorithm since their magnitude changes with quenching in a manner analogous to the isotope(s) being determined.

Subtractive loss, most commonly coincidence loss, are simply avoided by keeping the sample count rate below levels at which the losses become discernible. Due to the high speed electronics in modern counters this imposes essentially no restriction and hence requires no further treatment in this discussion.

Drift in response is the most serious of the machine generated errors. It is most commonly due to changing response in the photomultiplier tubes. Thus, it leads to 'unique' errors which depend on the nature of the sample and the window settings. Recovery from this type of error requires a combination of proper counting procedures and a computational method designed to minimise error propagation.

The most obvious source of increased error in data reduction is the use of inaccurate methods for calibration curve fitting. For example, Wampler² has evaluated a great variety of polynomial least squares methods and found enormous variation in their results.

The theoretical distribution of the variables involved in scintillation counting are quite simple. Exponential decay generates data distributed according to the Poisson Law. When two channels are used the smaller channel usually is completely inside of the larger channel which is therefore made up of counts in two channels which are independent. When AES is used it is independent of the number of counts in the channels.

(Because the channels ratio estimator is derived directly from the sample counts it is affected by inhomogeneity in the sample. The AES estimator, being independent, is largely unaffected by non-uniform samples. Thus major discrepancies in calculated disintegration rates using the two efficiency estimators would indicate biphasic or inhomogeneous samples. Provided the count rates are high enough to give satisfactory estimates of quenching, the channels ratio results should be used and will largely be valid).

Now all the distributions depend heavily upon these assumptions. All the expectations and particularly the covariances would be affected by deviations of the data from these theoretical qualities. Many tests of repeated counting were performed over long periods and it was easy to trace the deviations from the values expected due to very large drift of the counts over time. Although there are several hypotheses for explanation of this drift, no one has proved the cause definitely.

Table 2 is a summary of the correlation analysis performed on the output of two experiments which were originally run without concern for time trends. They were run rather as a verification of the theoretical distributions with no expectation of what actually occurred. They were for that reason, not truly experiments in the sense that they were designed to optimise any sort of an observation. Several vials with different quenchings and different radioactivities were just mixed together in the automatic machine which ran them interleaved. They ran in order 1 to 6 and 1 to 4 respectively.

The vials 0-1 and $N-1$ listed in Table 2 had no radioactivity in them at all and so the correlations are not very meaningful. The 24 counts and 17 counts in the wide channels are simply background.

In all the other runs the correlations and variances are quite outside of the values which would have been obtained if the theoretical model were in fact operating. First of all the theoretical correlation between the AES and the sample counts is zero. They are independent events, being quite different measurements of exponential decay in completely different windows and at different times. There should be no correlation at all. Although the correlations obtained are not consistent they are often quite significant. The AES, in this case, is a ratio between two channels in the range induced by gamma radiation. The correlation between AES and the channels ratio of the wide and narrow windows in the beta range is often around 40 to 50%. This could lead to an explanation that the same phenomenon is taking place all along the energy spectrum throughout time. For example, if the overall gain of the photomultipliers were changing over a period of time, and if the two pairs of windows of the AES and the channels had the same relationship to each other, then a downward shift in both cases would have a correlated effect over a period of time. Another problem is the correlation between the wide and narrow channels. The correlation between the two Poisson variables, one inside of the other, as is the case here (where the narrow channel is a part of the wide channel) should be the square root of the ratio of the two channel means. Taking the average for each channel as a estimate of the mean, the correlations actually obtained are much too low in every case. In addition, the variance of a Poisson variable is equal to the mean of that variable. Taking the averages and standard deviations of the values obtained, the standard deviation of the channels are much too high for them possibly to have come from a Poisson distribution.

The experiment number 36, the last one in Table 2, is a test of the first hypothesis brought forth to explain the correlations observed. The hypothesis was that the move-

Table 2. Statistical analysis of repetitive counting.

| Experiment | 0-1 | 0-2 | 0-3 | 0-6 | N-1 | N-2 | N-3 | N-4 | 36 |
|--------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Average | | | | | | | | | |
| Wide (c.p.m.) | 24.6 | 32,400 | 32,600 | 27,800 | 17.2 | 32,600 | 28,600 | 15,600 | 31,000 |
| Narrow (c.p.m.) | 20 | 29,100 | 28,300 | 16,600 | 8.51 | 17,100 | 10,000 | 968 | 23,000 |
| AES (ratio) | 0.65 | 0.62 | 0.60 | 0.37 | 0.62 | 0.61 | 0.40 | 0.30 | 0.63 |
| Ratio (n/w) | 0.81 | 0.89 | 0.87 | 0.60 | 0.49 | 0.52 | 0.35 | 0.062 | 0.75 |
| Standard Deviation | | | | | | | | | |
| Wide | 5.22 | 179 | 174 | 193 | 4.26 | 189 | 160 | 151 | 192 |
| Narrow | 4.43 | 182 | 183 | 195 | 2.95 | 156 | 123 | 37 | 189 |
| AES | 0.0022 | 0.0022 | 0.0021 | 0.0021 | 0.0021 | 0.0023 | 0.0018 | 0.0018 | 0.0080 |
| Ratio | 0.26 | 0.0044 | 0.0044 | 0.0045 | 0.12 | 0.0037 | 0.0034 | 0.0022 | 0.0031 |
| Correlation | | | | | | | | | |
| AES, Wide | + 0.05 | - .09 | - 0.15 | + 0.37 | 0.00 | + 0.21 | + 0.22 | + 0.44 | - 0.29 |
| AES, Narrow | + 0.04 | + .27 | + 0.28 | + 0.58 | 0.00 | + 0.49 | + 0.43 | + 0.43 | + 0.16 |
| AES, Ratio | 0.00 | + .44 | + 0.52 | + 0.56 | + 0.03 | + 0.46 | + 0.43 | + 0.34 | + 0.12 |
| Wide, Narrow | + 0.54 | + .66 | + 0.64 | + 0.79 | + 0.71 | + 0.63 | + 0.63 | + 0.43 | + 0.87 |
| Wide, Ratio | - 0.50 | - .29 | - .24 | + 0.32 | 0.00 | 0.00 | + 0.22 | + 0.20 | + 0.19 |
| Narrow, Ratio | + 0.43 | + .53 | + .77 | + 0.83 | + 0.66 | + 0.67 | + 0.89 | + 0.96 | + 0.66 |

A series of vials used as calibration standards for carbon-14 were counted repetitively for approximately 2.5 days. The vials were counted for 1 min on each cycle. Thus, each vial was counted about once every 12 minutes. All data was taken from Packard 3375 Liquid Scintillation counters. (Comparable data however, was obtained using counters of other manufacture. Since it is not the purpose of this chapter to evaluate various brands or types of counters, comparison will be specifically avoided.)

The columns denoted: (0-n); (N-n) and 36 were each a separate series of determinations. All vials contained the same amount of isotope, except the non-radioactive vials 0-1 and N-1. The data are rounded to 3 significant figures in most cases.

ment of the vial and the positioning of the vial on each cycle induced the correlation. It was hypothesised that the measurement would be different depending upon the exact position or circular angle at which the bottle was placed in the receptacle for measurement. A test was made over about the same period of time in which the vial was not moved at all. The errors and correlations are approximately the same for that experiment, with the exception of the standard deviation of AES in which a mechanical failure was found. The data are still not in Poisson distribution and a plot of the data shows that the time trend is still in action at what would appear to be at the same level. The movement of the vials seems to have explained very little.

Plotting the data in a serial fashion led to a very clear picture of what was disturbing the theoretical distribution. The powerful time trend completely overwhelms the random deviation of the data in both cases being of a completely larger scale over the whole duration of the experiment. This can easily be seen in Fig. 1.

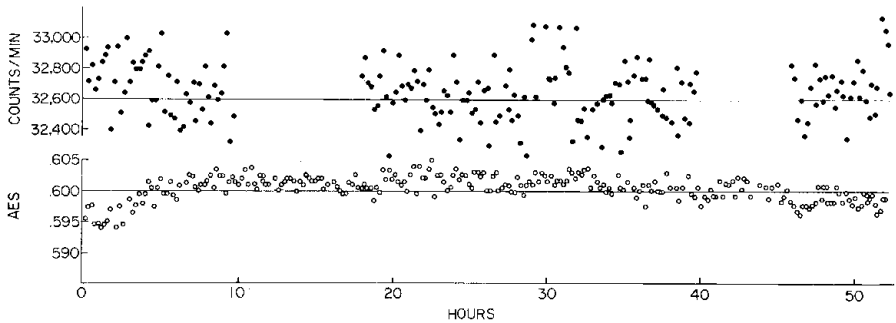


Fig. 1: Long Term Time Trends in Counting. This data is a plot of some of the actual observations from vial 0–3 in Table 2. The AES numbers are the ratios of two channels. The horizontal lines are the averages of the data. The gaps in the data have no significance other than the level of persistence of the authors in plotting data.

This calls immediately for a new model to explain the variations of the data observed. The simplest model to appeal to one is the following:
 $Y = P + T$ where Y is the observation, the component P is distributed as a random Poisson random variable with parameter C , plus a component T which is the drift random variable. So far, we can put no conditions on the drift factor except that its mean value equals zero. By calculating the time trend and subtracting it out of the model (or subtracting an estimator of it out) this should leave the Poisson variable we had originally believed that we had. This procedure would be followed for the AES estimator and for every applicable sample channel. The exact nature of the time trend will vary with the particular variable being estimated.

Naturally the important question is how to obtain an estimate of the drift. A common method would be a running average of the data. For time trend component of observation j , take the average of all the values from $j-10$ to $j+10$ to be an estimator of the trend at time T_j . A standard error for that estimate can easily be obtained.

The time trend will be removed under the conditions that the expected value of X at any time T_1 equals the expected value of X at any other time T_2 , that those expected values over ranges of T must all be equal and finally that the autocorrelation between times with lag T must be zero for all time lags.

The foregoing discussion assumes that the half-life of the isotope is great enough to be a negligible part of the drift of the system. Counting of short half-life isotopes adds a complication to the search for better estimators of decay rate. On first consideration, it appears to us that the data should be corrected back to some arbitrary but common starting point in time as early as possible in the algorithm. This minimises weighting the answer obtained by the time at which the particular sample is counted. In counting of one isotope at a time, the correction back to 'zero time' thus should be done on the observed counts themselves.

In multiple isotope counting of short half-life isotopes, the half-life correction cannot be made on the raw counts since the ratio of counts due to each isotope in each window is unknown until the estimator of quenching for each observation is evaluated. The ratio of isotopes at the time of counting would then be evaluated for each sample and the counts due to each corrected back to the initial point before final calculation.

Evaluation of alternate algorithms for computing disintegration rates is made difficult due to the lack of a precise radiation standard. The most accurate standards currently available are stated to be $\pm 0.5\%$ with respect to disintegration rate. A further complication is introduced by the unknown error in sample preparation. Drift due to chemical instability versus machine is undefined.

It would be of advantage to develop sets of data simulating the various types of error that might be encountered in practice. Thus, the exact correct answer would be known. Various algorithms could then be tested empirically and directly for their ability to handle error and converge on the correct value.

To this end, we have built a simulator program which develops the requisite data. It allows up to twenty channels to be simulated with any degree of correlation.

The potential advantage of simulation becomes evident when one considers the complexity of the range of questions to be asked of a simulator. As mentioned above, various algorithms can be compared for their ability to converge on a correct solution. The theoretical derivation of a good estimator for each possible algorithm would not be a practical approach. Other possible algorithms being considered are interpolation after spline fitting or some form of linear interpolation using polygonal line segments.

The simulator generates counts similar to real data in that it is Poisson distributed, it may vary with time, and the various windows can be either independent or related. The value of such generated data over real data, in addition to convenience, is that the estimation procedures can be related to the true values and their performance thereby judged. With real data, when one estimates, there is no true value with which to compare.

In this simulator, the time trend is defined by the user through its expression by Fourier series coefficients. There are available standard computer programs which calculate these coefficients for any set of sample data, so that the user need only supply data having the characteristics he would like to test. It can be taken from real observed drift if appropriate. The entire energy spectrum being tested must be defined by the user, but only in terms of the desired covariance relationships among the windows used need be specified and this can be taken from observations. With the true decay rate calculated for each period, an 'experiment' is run by using random numbers to generate a count

which deviates from the expected value by a random amount. A set of these values are then subjected to the data analysing program to be evaluated by comparing the estimated values with the true input values. This method is referred to as a numerical experiment.

Another aspect of the use of simulation, in addition to comparing alternative algorithms, is the ability to assess the contribution to final error of various sources of error. It would be most difficult to calculate the contribution of drift, for example, in a given counting window to the overall error in multiple isotope counting. With cubic polynomials fitted to the efficiency function for each isotope in each counting window,³ the two isotope case leads to evaluation of a sixth degree polynomial.

Some interim conclusions can be reached at this writing. Because of machine drift and half-life considerations, counting of high precision should not be attempted using any method in which the decay rate is observed directly. This admonition holds whether the decay rate is derived from a special purpose computer installed on the counter itself, by an on-line general-purpose computer, or any other method of computation.

Throughout, we have assumed that, at any given level of quenching, all similar samples in a given counting window will exhibit similar drift characteristics. While the assumption has not been tested *per se*, it is related to the principle underlying quench correction by both AES and channels ratio. Recovery from drift errors is possible by including quench standards with the unknowns. The whole series is counted for a short time on each sample. The whole procedure is repeated for as many observations on the series as is required to accumulate the total time period desired. The raw data is averaged and the quench correction done but once. The curve fitting should then correct for drift as well as quenching.

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DISCUSSION

B. Scales: Are you suggesting that a single 10 min count is inherently more inaccurate than the sum of 10 x 1 min counts for simple non-computerised work, especially when samples are being analysed which are close to background?

M. I. Krichevsky: Yes. In a drifting system one must calibrate and count at the 'same' time. Additionally, if one is close to background, it is essential to calibrate quenching of the background itself.

G. G. J. Boswell: Is your computer for the exclusive use of the five liquid scintillation counters?

M. I. Krichevsky: No, amino acid analysers, neurophysiology laboratories, a gas chromatograph, a u.v.-visible recording spectrophotometer and some fermentation equipment are in various stages of being interfaced with our process-control computer. Five counters on one computer is a trivial use of any computer having the capacity to handle the computations on-line because of the extremely slow data rate.

G. A. Buckley: Could you put the right perspective by telling us the error when one has chosen the method of calculation which 'converges on the wrong answer'?

M. I. Krichevsky: The error is obviously small (usually less than a few percent for singly labelled counting). By simulation we hope to give a more intelligent answer to this question in the future.

D. S. Glass: (i) How accurate do you consider you can make your liquid scintillation counter operate—as an intrinsic property of the machine and the calibration method? (ii) Do you consider a twenty channel (hypothetically) machine would overcome drift problems by comparing results in each channel? (iii) How many liquid scintillation counters do you need to justify an on-line system (as a question of cost)?

M. I. Krichevsky: (i) Certainly better than $\pm 1\%$ if all pains are taken. How much better I cannot say; in fact, it becomes a matter of definition since the best standards are not as good. Thus we can only talk in relative terms. (ii) No. Machine drift is inseparable from spectral shift due to quenching or chemical instability if one considers only the sample data. Only recalibration (either mechanically or by computation) against a stable standard can do this. (iii) If the central computer exists and will accept teletype or equivalent input in its operating system then 2 to 4 should do as most interfaces for computers to accept such data can handle multiple 10 to 15 characters per second data rates. Such an interface can be obtained for less than \$10,000. If the computer is doing nothing else but processing this kind of data, then one would presumably need 10 or more to justify the expense. The realistic answer is conditioned however, more by the particular administrative environment one is in and one's station within it—coupled to the persistence of the request rather than the number of counters.

K. L. Evans: Could you provide information on the selection of polynomials as models for quench correction curves, i.e. the basis upon which the polynomial order is selected?

M. I. Krichevsky: If polynomials are used for calibration, the order should be increased until the standard error is within acceptable limits. This assumes that the data is well-behaved. I would suggest that most quench curves that have been obtained can be fitted to a cubic with a degree of accuracy that makes it non-limiting in terms of overall error.