

Discussion

Dr. L.I. Wiebe - University of Alberta (CAN)

Dr. Stanley, you stated earlier that many people only need CPM because they want only relative values. I can appreciate that DPM are seldom required but it would seem to me that most procedures at least in their initial stages require at least corrected CPM to get meaningful relative values. Would you care to comment on that?

Dr. P.E. Stanley - Queen Elizabeth Hospital (AUS)

Yes, I would agree with that. I think that probably the best thing to do is to check the sample channels ratio (SCR) or the external standard of all your samples if you have a well behaved cocktail system. Then you might check that all your samples lie within some channels ratio range that you consider to be acceptable. In this way you need only to examine more closely those samples that lie outside that range.

I think it is a realistic factor that most people do only want CPM. I think that provided there is some flag which will alert them to a problem in a sample, if something is wrong with that sample, this is all that is often required. This is especially true when routinely counting large numbers of samples.

I know this is horrifying to a lot of people but this is a real life situation.

Dr. W. Reid - Saskatoon Cancer Clinic (CAN)

I noticed that Dr. Noakes did not mention electrical interference as being a problem (with low level counting). Is that because of the scintillation counter you had, or were you working in a special lab?

Dr. J.E. Noakes - University of Georgia (US)

This problem did exist in our lab for a long time. What we finally did to resolve the problem was to design our own power system where we have a battery pack which operates under continuous charging from the A.C. current and can hold five counters up to twenty-four hours in case there is an outage.

Dr. W. Reid

So you kill two birds with one stone, you get rid of the power failure problem and the electrical interference.

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Dr. J. E. Noakes

We have an isolated power supply system.

Dr. W. Reid

The second question I would like to ask along that line is have you ever used counters with a sort of variable dead time? A long time ago I did this, intentionally made the dead time of the order of one-hundred microseconds to one millisecond, because often noise of the nature we are discussing and even some of the background is kind of time correlated. I have never actually studied this. Have you studied it?

Dr. J.E. Noakes

You have to incorporate a delay line into your electronics when using a sodium iodide anticoincidence shield. This is necessary because of the slow scintillation response of sodium iodide as compared to the liquid scintillators.

Dr. W. Reid

I mean long dead times like one millisecond. In fact, five-hundred times longer than the response time of sodium iodide.

Dr. J.E. Noakes

No, we have not extended it out that long. When you do that of course, you reduce your counting efficiency.

Dr. W. Reid

Not really if we are talking about low level counting.

Dr. J.E. Noakes

For low level counting that is true, but you are reducing it somewhat. We tried this idea out to extended times, but not to the degree you suggest, and we did not see any advantage in extending it out that far.

Dr. H.H. Ross - Oak Ridge National Laboratory (US)

Dr. Noakes, I wanted to ask you if my memory serves me correctly. Was there not a commercial liquid scintillation counter that had the phototubes at ninety degrees. It would seem that this orientation would severely cut down the crosstalk between photomultiplier tubes.

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Dr. J.E. Noakes

Yes, Tracerlab had one early in the game and the idea was to place one photomultiplier tube (PMT) so it would not directly view the other PMT and thereby reduce crosstalk. But in order to obtain good counting efficiency they put a mirror at the right angle, and the photons generated from the corona of one PMT would then be reflected to the second PMT and the net effect was the same as the one-hundred and eighty degree geometry.

Dr. D.L. Horrocks - Beckman Instruments (US)

I would like to make a couple of comments and then listen to Dr. Noakes' reply.

We investigated the distribution of background pulses as a function of the pulse height and we found that we could quench the liquid scintillator very drastically without affecting the distribution of the pulse heights that were coming just from background. Our conclusions from this was that most of the background was coming from cosmic events that were interacting with the phototubes and giving crosstalk between the two phototubes, rather than cosmic events interacting in the liquid scintillator. This idea may be reinforced by remembering that the liquid scintillator is a very low density medium. Some of it may be due to different cosmic events occurring in the glass but again those that occur in the glass are not affected by the quenching that occurs in the liquid scintillation cocktail itself. That is one point. I wanted to ask if you had looked at that and what your conclusions were on that.

The second point I would like to bring up and ask for your comment on was have you ever tried to change the high voltage on your phototubes? One of the things we found was that we could take a commercial instrument and by decreasing the high voltage on the phototubes we could, particularly for ^{14}C carbon counting (for tritium it is almost impossible to do because efficiency falls off too rapidly with high voltage) get backgrounds of around four counts per minute with counting efficiencies of sixty percent. This gives a figure of merit (E^2/B) of around nine hundred. I am sure with a little extra shielding and a few things as you suggested earlier, it could be improved even further.

Perhaps you would make some comments on your experiences on these two points.

Dr. J.E. Noakes

Yes, there has been some work published on this interaction with the glass, and we did look at this. However, since we got such a definite response from just diminishing the volume of our cocktail from say twenty through to five millilitres while keeping all other variables stable, we felt that the volume sensitivity was much more a factor. This was also a factor which we could influence more readily rather than trying to alter any of the glass components or trying to get RCA to do something with their phototubes. Actually we would like to have, instead of RCA's two inch diameter tube, a one inch diameter tube that would have the fast response of a RCA 4501-V4.

Now concerning the other point of adjustment of the high voltage. I should have mentioned earlier that the phototubes we use are the RCA 4501-V4 tubes with the gallium phosphide first dynode. These can go up to twenty-four hundred volts and perhaps even a little more than that. Most commercial counters today are designed to get as high a tritium efficiency as is possible, and ^{14}C is of little concern. However, when you are counting ^{14}C you can gain a lot by lowering the voltage, which does then diminish the crosstalk and hence the background.

Dr. D.L. Horrocks

I would like to bring out another point. When you reduce the volume of your sample but contain it in the same size of glass vial, you reduce the ability of light to be transmitted through it because you are introducing a second and third glass-air interface. Just reducing the volume may very well reduce the ability of crosstalk to go from one tube to the other. We took a vial and filled it up with water and the background was not reduced in going from the liquid scintillation cocktail to just water. I do not think just the volume reduction of the scintillator is the complete answer.

Mr. B.H. Laney - Searle Analytic (US)

We have examined the pulse height spectrum of background using a dual parameter multichannel analyzer¹. For the range of pulse heights corresponding to ^{14}C in fifteen millilitres of scintillator we have identified which portion of the spectrum is due to crosstalk. We note that for crosstalk events one of the phototube signals is always quite small. This is because that light produced within one of the phototubes behind its faceplate, is attenuated by the photocathode before it is transmitted to the other phototube.

Thus, there is a high probability that the light detected by one phototube is much lower than that from the other for crosstalk events. This pulse height difference is sufficient to discriminate crosstalk events from scintillation in the sample².

As Dr. Noakes pointed out this crosstalk may be reduced by masking off the outer edge of the phototube faces or by tightening up the coincidence resolving time, or by electronic discrimination.

If you employ lesser pulse height analysis in which only the smaller of the two phototube signals is used, these crosstalk events can be eliminated by simply raising the lower level discriminator. However, if the two phototube signals are summed then we cannot discriminate against crosstalk in this way.

¹ B.H. Laney *in* Liquid Scintillation Counting, Vol. IV, p. 74, M.A. Crook and P. Johnson (Eds.), Heyden and Son, London (1976).

² B.H. Laney *in* Organic Scintillators and Liquid Scintillation Counting, p. 991, D.L. Horrocks and C.T. Peng (Eds.) Academic Press (1971).

Dr. B.E. Gordon - Lawrence Radiation Laboratory (US)

When employing the lesser pulse height approach one observes that a quench curve is valid for samples that are both chemically and colour quenched. I would like a rather exact explanation on why it is that Beer's Law overlaps with all the quenching kinetics that govern chemical quenching.

Mr. B.H. Laney

There are several references to describe why the method works^{1,2}. I want to make it clear that I have never made a claim that both coloured and chemically quenched samples fall on the same quench curve; it depends on the range of quenching that you consider. Dr. Noujaim, Mr. Ediss and Dr. Wiebe³ showed that a much higher level of quenching is required to cause divergence of the quench curves when using lesser pulse height analysis when compared to pulse summation.

In simple terms, we are familiar with the idea that loss in counting efficiency is generally associated with a shift in pulse height spectra to regions of smaller pulse heights. Essentially the problem with pulse summation in this regard is that for samples that are coloured we get a distribution of pulse heights that are spread over a wider range than that expected for that observed counting

efficiency. Actually, in Baillie's⁴ original article he pointed this out. He suspected that the divergence between the chemical and colour quenched curves is probably due to the fact that we are dealing with a coincidence system, and not a single tube counter. That is what is really happening here.

When we have a heavily coloured sample (and hence a low counting efficiency) then using the pulse summation method we get a much wider range of pulse heights than that obtained for a sample chemically quenched to the same degree. For the coloured sample those events that take place at the edge of the vial close to one phototube will give rise to a large pulse in one phototube and a small one in the other. If these two pulses are now added together the resulting pulse height may well be as large as those pulses obtained from an unquenched sample. By taking only the lesser of the two pulses we get a pulse height distribution that is more representative of the observed counting efficiency.

Since most quench correction methods detect changes in counting efficiency by monitoring shifts in the pulse height distribution of either the sample or some external standard, the argument given above explains why one might expect lesser pulse height analysis to provide some improvement. I hope that answers the question.

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- ¹ B.H. Laney *in* Liquid Scintillation Counting: Recent Developments, p. 455, P.E. Stanley and B.A. Scoggins (Eds.) Academic Press (1973).
 - ² B.H. Laney *in* Liquid Scintillation Counting, Vol. IV, p. 74, M.A. Crook and P. Johnson (Eds.), Heyden and Son, London (1976).
 - ³ C. Ediss, A.A. Noujaim and L.I. Wiebe *in* Liquid Scintillation Counting: Recent Developments, p. 91, P.E. Stanley and B.A. Scoggins (Eds.), Academic Press (1973).
 - ⁴ L.I. Baillie, International Journal of Applied Radiation and Isotopes, 8, 1 (1960).

Mr. T. Carter - University of Birmingham (UK)

I'd like to ask Dr. Stanley whether he sees any advantages or disadvantages in fitting to a few points in a narrow range of interest, rather than fitting a whole quench correction curve, when using a computerized system.

Dr. P.E. Stanley

Are you trying to say that you should get the curve to pass through the points, or close to them?

Mr. T. Carter

No, instead of fitting say a fifteen or twenty point curve, fit a curve over say five or six points around the area of interest.

Dr. P.E. Stanley

No, I can't say that I do.

Mr. B.H. Laney

I would like to comment on that. Most of the curves plotting counting efficiency versus some type of quench parameter are dependent upon which quench parameter is used, and what the window settings are. There is really no physical reason why these curves should follow a polynomial function.

As more points are added to a curve, a higher order polynomial is required to fit that curve closely. The higher the order of the polynomial you use, the more careful the user must be in order to be sure that the curve does not pop out between the points. Force fitting at the data points (by using high order polynomials) can cause very large errors between those points.

I believe Mr. Carter is referring to a spline fit which we found to be very good.

Dr. S. Apelgot - Institut du Radium (F)

I would like to return to the problem of reporting experimental results in CPM as opposed to DPM. It is true that in biological laboratories people use CPM, but this is only correct if the counting efficiency from the different samples is about the same.

Also, I have observed errors due to the counting vials themselves. I work mostly with glass vials and I decided to screen them. I found that it was necessary to reject ten to fifteen percent of them because of their deviation from the norm.

Dr. P.E. Stanley

Yes, I would agree with that comment about glass vials. If you look at the transmission of light through them they are indeed quite variable and 15% would certainly be a number that I would agree with. There is a paper in the latest issue of Analytical Biochemistry which considers light transmission through scintillation vials. (Corredor et al. Anal. Biochem. 70, 624 (1976)). It was particularly about bioluminescence, and they used bioluminescence as a light source. They were getting (if my memory serves me correctly)

about $\pm 10\%$ variation within a batch and quite large differences from batch to batch. This is certainly an important problem. I know of several authors who go through their vials and select them in critical applications.

Dr. W. Reid

I would like to comment on some of Dr. Stanley's remarks concerning RIA. The sort of problems one gets clinically in radioimmunoassay are almost an order of magnitude more complicated than just quench corrections. However, in my experience the associated calibration curves deviate from a straight line by at most just a few percent. A second order polynomial fits very adequately over the entire range of concentrations we use.

We do have some problems, however, in estimating the errors in our results when using these calibration curves. By determining the variability in the calibration curves (by generating many of them); and by measuring replicates of our serum samples we can find that the variance is a function of the resulting concentrations. However, we need an off line computer, and an accumulation of these calibration curves for a year or so to be able to do it.

Dr. P.E. Stanley

The estimation of errors in radioimmunoassay curves is an ever present problem. It seems that there is a special breed of statisticians who make it their business to deal with problems such as this.

People doing RIA by liquid scintillation counting frequently fail to do quench correction on their samples. Whether they be urine or blood samples, they can contain all sorts of other odds and ends, especially if the patient is on one or more sorts of medication. So you can imagine the sort of problems they get. This may well be why you see a bigger variation in patient samples than that which you see on your standard curve.

Dr. E. Schram - University of Brussels (B)

My question has to do with the use of delay lines in coincidence circuits used to demonstrate the presence or absence of chemiluminescence. This system was used in at least one instrument more than fifteen years ago and has been reintroduced in recent instruments.

Is there any reason why it has not been used for many years, and how adequate is it for showing the presence of chemiluminescence?

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Mr. B.H. Laney

The delayed coincidence method of determining accidental coincidence has been around for a long time. It is only in recent years when the detection efficiency of a scintillation counter has become high enough for chemiluminescence to again be a problem. When phototubes had low quantum efficiency the problem was of no great concern. Now, especially with surfactant systems, chemiluminescence is an ever-increasing problem. The delayed coincidence method of monitoring or measuring accidentals is an old technique revitalized.

Dr. Horrocks was describing a new system that is included in recent Beckman instruments, and perhaps he would care to comment.

Dr. D.L. Horrocks

In the Beckman system we have tried to approach the problem of measuring the chance coincident rate employing a different technique than the use of a delay line. The reason why we avoided the delay line method is the fact that since radioactive decay events are random in themselves, delaying one signal relative to the other risks a certain probability of having chance coincidence between two different beta events. Thus, as the count rate goes up, the chance coincidence would be increasing only because the sample activity has gone up, not because of any single photon event.

The approach we take involves monitoring the sample prior to counting. After the vial goes down into the counting well, the first thing we do is to turn off the coincidence requirements and measure the count rate in a wide open window. In that wide open window we get a single photon count (SPC_1). That single photon count is going to be the sum of the singles from each phototube (S_1 and S_2), plus the sample activity (S_a) plus the chance coincidence rate (S_c).

$$SPC_1 = S_1 + S_2 + S_a + S_c$$

That rate (SPC_1) is usually a fairly high count rate so we can get good statistics on it in a very short time. When we then go into regular counting of the samples, we want to count in particular counting windows. While this normal counting is going on we have a coincidence pulse circuit which acts as a gate for the pulses coming from the pulse height analyzer before they go to the scaler. This coincidence gate provides a pulse whenever it detects a coincidence event. We count these pulses with a scaler to provide a measure (S_m) of the sample activity plus the chance coincidence.

$$S_m = S_a + S_c$$

If we take the single photon count (SPC_1) and subtract S_m from it we are left with $S_1 + S_2$. Now for the single photon rate to contribute to the chance coincidence rate it has got to be something that is occurring in the cocktail itself. The chances are that it is going to be seen equally by both phototubes.

$$\text{Thus, } S_1 \approx S_2 \approx \frac{(SPC_1 - S_m)}{2}$$

Now we have all the information we need to calculate the chance coincident rate.

$$S_c = 2 \cdot T_r \cdot S_1 \cdot S_2$$

Where T_r is the resolving time of the instrument and thus

$$S_c = 2 \cdot T_r \left(\frac{SPC_1 - S_m}{2} \right)^2$$

Since S_m is a measure of all coincidence events, and since our sample counting windows may accept only a portion of these events, our observed sample counts will be less than S_m . Thus, S_m will be known to equal or greater precision than the sample counts.

If we report $100 \cdot S_c / S_m$ then this factor gives the maximal percentage contribution of chance coincidence to the measured sample countrate.

Another feature of this technique is that the single photon count rate can be measured (SPC_1 and SPC_2) both before and after the sample counting period. In this way you can tell whether the chance coincidence rate has changed dramatically while counting, or whether it has remained constant.

We do not recommend this as a way of correcting for chemiluminescence because you do not know at what pulse height the chance coincidences occur. You could only use the factor given above to determine what correction should be made to your sample count rate if that sample count rate was accumulated using a wide open window. However, this technique is useful for screening samples that might have a high chance coincidence rate. Then problem samples could be recounted later, or some corrective action taken to remove the chemiluminescence.

Dr. A.A. Noujaim

I would like to ask two questions. Firstly, in view of the problems that have been mentioned with regard to photomultiplier tubes, can I have some estimate from the

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manufacturing industry as to how far away we are from seeing a liquid scintillation counter with a different light sensitive device?

Secondly, was Dr. Horrocks assuming that chemiluminescence is a single photon event or a multiple photon event in his calculations?

Dr. D.L. Horrocks

In answer to your first question, we really haven't seen anything that could replace phototubes at present.

We have been talking to the phototube manufacturers and we imply that the phototube is the weakest link in the liquid scintillation process. The quantum efficiency is only 28%. We keep saying we want more efficiency, but this development is at a standstill. What really has to happen is a total breakthrough. Maybe a new idea, a development of a new photocathode material just like when the bialkali system was discovered. I do not really see any big improvements at the present time.

Dr. A.A. Noujaim

What I had in mind was light sensitive diodes.

Dr. D.L. Horrocks

It is my understanding, I may be a little naive here, that the big push on these diodes has been into the infrared where they are much more sensitive rather than into the visible. Dr. Kelly is more of a spectroscopist, he might have some more comments on that.

Dr. M.J. Kelly - Beckman Instruments (US)

At the present time, the photodiodes are just getting down into the UV visible regions, and at this stage we do not see that they will be sensitive enough for the liquid scintillation process. However, there may be some new developments fairly soon.

Dr. P.E. Stanley

I just wonder if anybody has tried using the 95% of the energy that is lost. After all, the scintillation process itself is only 5% efficient, the other 95% presumably goes away as heat or something along those lines. Really the scintillation efficiency is the weakest link in the chain.

Dr. D.L. Horrocks

The scintillation process is governed by the methods of radiation interaction with matter. I think those processes are pretty well controlled by the laws of physics, and I just do not see any way to get more energy to be converted into more excited molecules or ions.

Dr. P.E. Stanley

I was thinking of the other 95%. Can we measure that by some other means, not a light detector?

Dr. D.L. Horrocks

Well, one could always build a very sensitive calorimeter!

The second question Dr. Noujaim asked was whether I considered all the events as single photon events in calculating the random coincidence rate. The answer is that it does not make any difference as long as they are random events because we look in a wide open window. If it is a chance coincidence between a single event in one tube and a two or three photon event in another tube, it does not make any difference because it is just a chance coincident event. The important criterion is that they are chance events, and of course most of them will be single photon events.

Dr. H.H. Ross

I would just like to say that in spite of the difficulties there will be new photon detectors used very shortly. I am confident of that. If you observe what has happened to the calculator and digital watch industry you can surmise that photodiodes, charge coupled devices and charge injection devices are developing quickly. Right now there are some photodiodes that have sensitivities approaching those of photomultiplier tubes but the geometry is very small, and this of course is a limiting factor. I cannot predict exactly when it is going to happen, but every day I see new items becoming available that I would not have expected to be viable.

In my group, which is involved with new detectors, we purchased a charge coupled two dimensional array about a year ago for four-thousand dollars. This was a state of the art device; it was the hottest thing off the diffusion oven! Today that device is obsolete. So we are in a tremendous state of flux in that particular area

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and I think that perhaps in ten years you will find some things that you would not have thought possible.

Dr. E.I. Wallick - Alberta Research Council (CAN)

I would like to know if there is any control on the radioactivity of the materials used in manufacturing counting instruments.

Mr. B.H. Laney

At Searle there is a program of lot control on the metallic materials that go anywhere near the detectors used in the counting systems. A sample of each lot is evaluated before anything is fabricated from it, and only when it has been proved to have sufficiently low background is approval for its use given.

The answer is yes.

Mr. E. Polic

There is lot control on all materials used in the detector section. The materials of greatest concern are aluminum, stainless steel and lead. Yes, there is very good control over these materials, and I think all manufacturers do the same things we do.

Mr. J. Burnham - New Brunswick Power (CAN)

Dr. Noakes, with all the techniques you described for reducing background in commercial counters, if you go to your five millilitre lead shielded vial and you do all the other things you describe, how low a background can you get with a commercial machine?

Dr. J.E. Noakes

First of all we must specify which isotope we are considering. With a commercial instrument, if we are considering tritium the following steps will be required. Firstly, your sample must be prepared in such a form that it may be counted with high efficiency. Perhaps it might be converted to benzene or something of this sort. Then secondly, because of the high counting efficiency you can take advantage of going to smaller volumes. In this way you could probably maintain a counting efficiency for tritium of 60% with backgrounds for a five millilitre vial or three or four counts per minute, or maybe even less.

There may be some other tricks that could be worked out, but at present this is probably the best you could do.

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Dr. L.I. Wiebe

Our work reported at this conference on using methyl salicylate as a counting medium indicates that the external standard quench correction method (ESP) is not going to work very well for this system. From Dr. Horrock's description I suspect that the 'H' number will encounter similar problems when using this material. Should there not be some warning about this limitation in the respective operating manuals?

Dr. D.L. Horrocks

I am not sure I have a complete answer for you because I do not think that the 'H' number technique is applicable to Cerenkov counting or pseudo scintillation counting. The 'H' number technique requires that we be able to produce a Compton distribution that will be predictable, and give a nice sharp Compton edge that we can analyze. When you do Cerenkov counting you are dealing with a more complex situation. Only the most energetic Compton scattered electrons are going to give you any Cerenkov light. The distribution of those light pulses is going to be very markedly compromised by the fact that the resolution will be very poor. I would never recommend that the 'H' number be used as a parameter for monitoring quench, or determining efficiencies in other than the usual liquid scintillation systems.