

Accuracy and Uncertainty in Radiochemical Measurements: Learning from Errors in Nuclear Analytical Chemistry

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Received: November 2, 2001

A characteristic that sets radioactivity measurements apart from most spectrometries is that the precision of a single determination can be estimated from Poisson statistics. This easily calculated counting uncertainty permits the detection of other sources of uncertainty by comparing observed with a priori precision. A good way to test the many underlying assumptions in radiochemical measurements is to strive for high accuracy. For example, a measurement by instrumental neutron activation analysis (INAA) of gold film thickness in our laboratory revealed the need for pulse pileup correction even at modest dead times.

Recently, the International Organization for Standardization (ISO) and other international bodies have formalized the quantitative determination and statement of uncertainty so that the weaknesses of each measurement are exposed for improvement. In the INAA certification measurement of ion-implanted arsenic in silicon (Standard Reference Material 2134), we recently achieved an expanded (95 % confidence) relative uncertainty of 0.38 % for 90 ng of arsenic per sample. A complete quantitative error analysis was performed. This measurement meets the CCQM definition of a primary ratio method.

Knowledge increases...not by the direct perception of truth but by a relentless bias toward the perception of error.

- K. E. Boulding, *Science* **207**, 831 (1980).

Introduction

Information is essentially surprise, something that was not previously known. Occasionally an analytical chemist can tell the person who submitted the samples something that he did not expect, or even does not believe. For instance, in our laboratory a sample of superconducting graphite intercalated with rubidium was found to contain potassium instead. When a customer is presented with an unforeseen result, it is sometimes comforting for him to decide that the analyst has made a blunder such as mixing up the samples. It is the analyst's responsibility to design her procedure and write her report so clearly that the customer must be convinced that the analysis was done without mistakes (which is not, of course, without error or uncertainty). It is this integrity of the chemical measurement process that quality systems, audits, and interlaboratory comparisons attempt to insure. Beyond this basic assurance of reproducibility and reliability, accuracy is improved and we become more confident of the results if our procedures are tested by stress.

Error Detection and Minimization

Quality management systems require a complete and detailed written procedure, which ensures that the measurement will be done reproducibly. However, aside from the impossibility of repeating a measurement every time under exactly the same conditions it is not always desirable to try to do so. For example, because one activation analyst always carefully duplicated his irradiation and decay parameters, a decaying interference could not be found until another person repeated the measurement with less rigorous reproducibility.

For robustness, it is desirable to vary parameters to test the sensitivity of the result to the variables, and build that requirement for variation into the protocol. The way to confidence is through demonstrated accuracy.

You never know what is enough until you know what is more than enough - William Blake

These points are illustrated by several attempts in our laboratory to perform neutron activation analysis (NAA) with better than usual accuracy.

1. A set of gold films of different thicknesses were evaporated on a silicon substrate to provide working standards for Rutherford backscattering. Instrumental neutron activation analysis (INAA) was used to measure the quantity of gold on the wafer.¹ In a blind comparison, INAA agreed with independent gravimetric measurements to within 0.3 % on average. In order to obtain such agreement, several potential sources of bias were tested. To examine the effect of resonance neutron self-shielding, a sandwich was made of a 5-mm diameter gold foil between two 10-mm foils. The package was irradiated and the foils counted individually. Surprisingly, the apparent specific activity of the inner foil was larger than the outer foils. Because the outer foil had four times the mass of the inner, the counting rate was four times higher, and the random coincidence (pulse pileup) correction² correspondingly more important. This experience led to the routine incorporation of pileup correction for all NAA counting at NIST.

Neglect of pileup at low count rates was not confined to our laboratory. At about the same time, the International Atomic Energy Agency (IAEA) organized the G2 intercomparison exercise to test the adequacy of dead time and pileup corrections.³ The task of the participants was the simplest metrology: to determine the activity, relative to a reference source counted at 1000 counts/s, of four radioactive sources up to 15 times the activity of the reference. Ninety-eight sets of results were submitted by laboratories in 24 countries. The results were sobering: for the most active source the median

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error was 6 % and the maximum error was 36 %.

2. Perhaps the most precise and accurate gamma-ray spectrometry ever published was performed in the calibration of reference materials for nuclear safeguards, certified for ^{235}U enrichment.⁴ The sample-to-sample variations in gamma assays within each of five sets of 25 samples was 0.06 % - 0.13 % relative standard deviation (rsd), and the uncertainty of relative measurements was comparable with the best mass spectrometry. A significant source of uncertainty was the variation in the peak area as detected by the peak search program. In order to obtain this precision, a fixed-boundary summation⁵ was used in preference to a Gaussian fit to the spectral peaks. In this work the pileup correction algorithm was shown to be adequate at this degree of precision over a wide range of counting rate, from 4 % to 22 % dead time.

Spectrum analysis programs are an often-overlooked source of uncertainty in gamma spectrometry.⁶ Intercomparisons of different algorithms have always shown differences in peak detection capability and net area determination, and reveal the importance of user-selected parameters.^{7,8-10} Overlapping peaks present a particularly rich field for errors and choices of algorithm.^{11,12}

3. The publication of a high-precision value for the half-life of ^{28}Al (Ref. 13) permitted a high-accuracy INAA determination of aluminum as a major element in coal fly ash. Because the half-life is only 2.2 minutes, precise timing and correct calculation of the combined effects of pileup in the amplifier, dead time in the multichannel analyzer, and radioactive decay in the source were crucial.^{14,15} The method was tested by analyzing single-crystal sapphire (Al_2O_3); the measured aluminum concentration was within 0.2 % of the theoretical stoichiometry.

Later examination revealed a pattern in the results. When the sapphire sample was irradiated between two standard Al foils the apparent concentration was slightly higher than if the inverse sandwich was irradiated. Experiments designed to test the idea that neutron scattering was important in this well-thermalized, near-isotropic neutron irradiation, as it certainly is for neutron beam experiments,¹⁶ have made this explanation unlikely.¹⁷

4. INAA was used for certification of NIST Standard Reference Material (SRM) 2134, consisting of 90 ng of arsenic implanted in 1-cm² silicon samples. For this measurement a complete quantitative analysis of all components of uncertainty was done.¹⁸ The expanded relative uncertainty was $U = 0.38$ %, calculated using a coverage factor of 2, which gives a level of confidence of approximately 95 %. The largest single contributor to the overall uncertainty was the uncertainty of the concentration of the reference standards. As discussed below, this measurement can serve as a prototype for INAA as a primary method of analysis. The potential of NAA as a reference technique for As in Si has also been suggested by others.¹⁹

In the course of these arsenic measurements, an apparent systematic error was found in the most recently published value of the ^{76}As half-life, so an earlier consensus value was used for the computations in that work. In a subsequent re-determination of this half-life,²⁰ it was inferred that the author of the recent value may have used a biased procedure for fitting decay curves. From this we learned that even the most recently published and professionally evaluated nuclear data may still not be sufficiently reliable for the most accurate work.

Uncertainty Evaluation and Primary Methods

A growing influence on analytical chemistry is the *Guide to the Expression of Uncertainties in Measurement*, published by the International Organization for Standardization: the ISO

GUM.²¹ Written to facilitate legal metrology and trade, this standard requires that all sources of uncertainty be examined and quantitatively specified, as a consequence of which the greatest weaknesses of the procedure are exposed for improvement. Supplementary guides to the implementation have been written by Eurachem/CITAC²² and NIST.²³ A guide specifically directed toward nuclear methods is in preparation by the IAEA. The application of these principles to NAA²⁴ has been addressed, and to the k_0 standardization method in particular.²⁵ These guides give numerical examples of the application of the GUM principles to specific cases.

The algorithm for uncertainty assessment is easily described mathematically: simply determine the uncertainty in each parameter in the measurement equation and compute the degree to which that uncertainty affects the final result. In practice, of course, for most analytical methods it is tedious to compute the necessary partial derivatives analytically. However, a spreadsheet approach has been proposed^{25,26} that performs differentiation numerically, and displays the influence of each factor in an instructive way.

For the arsenic in silicon SRM described above,¹⁸ twenty-nine sources of uncertainty were quantitatively evaluated, as shown in Table 1. Of these, six (in bold) accounted for 95 % of the relative combined uncertainty and only two, the reproducibility of replicate samples and the concentration of the standards, accounted for 70 %.

The Consultative Committee on the Quantity of Material (CCQM) of the Bureau International des Poids et Mesures (BIPM) has described a primary method of measurement as "...

TABLE 1: Enumeration of Sources of Uncertainty for INAA Measurement of Arsenic in Silicon

Uncertainty Source	Relative standard uncertainty u
Concentration of standard solutions	0.106 %
Measurement precision for samples ($\nu = 9$)	0.081 %
Counting statistics for standards ($\nu = 10^5$)	0.073 %
Pulse pileup	0.066 %
Effects of half life	0.056 %
Amount of standard solutions deposited	0.041 %
Neutron fluence exposure - irradiation geometry	0.039 %
Neutron fluence exposure - self shielding	0.024 %
Peak integration	0.019 %
Neutron fluence exposure - scattering	0.015 %
Blank ($\nu = 100$)	0.013 %
Sample area - micrometer accuracy	0.012 %
Counting efficiency - geometry effects	0.009 %
Sample Area - Measurement Precision ($\nu = 26$)	0.009 %
Counting efficiency - gamma ray self absorption	0.004 %
Inadequacy of live-time extension	0.001 %
Fast neutron interferences	0.0003 %
Decay until start of count - accuracy	0.00007 %
Count intervals - live time	0.00003 %
Effective cross sections	0.000005 %
Gamma-ray interferences	0.000004 %
Decay until start of count - precision	0.000002 %
Irradiation timing	0 %
Count intervals - clock time	0 %
Fission interferences	0 %
Irradiation losses	0 %
Target isotope burn-up	0 %
Perturbed angular correlations	0 %
Isotopic abundances (unknown/standard)	0 %
Combined uncertainty u	0.188 %

Note: The six sources in bold type together accounted for 95 % of the relative combined uncertainty. ν denotes degrees of freedom

a method having the highest metrological properties, whose operation can be completely described and understood, for which a complete uncertainty statement can be written down in terms of SI units. A primary direct method: measures the value of an unknown without reference to a standard of the same quantity. A primary ratio method: measures the value of a ratio of an unknown to a standard of the same quantity; its operation must be completely described by a measurement equation.²⁷ If care is taken to document uncertainties, in many cases INAA can comply fully with the definition of a primary ratio method.²⁸ In particular, the NIST determination of arsenic in silicon meets all these criteria. The measurement and its corresponding relative expanded uncertainty of 0.38 % is of the highest metrological properties, since no other analytical method is able to provide a smaller uncertainty for trace levels of this element. In addition, equations describing the measurement process and its uncertainty can be written in terms of SI units, the well-understood equations of neutron activation and radioactive decay.

Why should we care about this definition? "Strictly, traceability to the SI in measurements of amount of substance – or of any other quantity – requires that the measurements be made using a primary method of measurement, which is correctly applied and stated with an evaluated uncertainty."²⁹ Nuclear methods in analytical chemistry are perceived, correctly, as being more tedious than methods that merely require that the sample be dissolved and aspirated into a plasma. Yet the dissolution step can lead to large errors from insoluble phases, reprecipitation, or volatilization even for simple biological materials.³⁰ Even if all the sample is in solution, differing response of the atomic and molecular analytical instruments to different analytes, and still different effects of the matrix on calibrations, make it clear that *easy* and *correct* do not necessarily go together.

Because most nuclear techniques are based on simple physical principles, many merely chemical obstacles to accurate analysis become more tractable. The fact that NAA has effectively zero blank has made it possible to measure ultratrace levels of essential and toxic trace elements in biological tissues with little concern for sample contamination during the analytical process. For example, using radiochemical NAA the natural levels of chromium in whole blood were shown to be more than an order of magnitude lower than previously believed.³¹ Values for other difficult elements (Mn, Mo, and V) in tissue have been established by NAA,³² and over half of the reference values in blood or serum selected in a critical review³³ were established by NAA. Results such as these have stimulated the development of ultrapure reagents, clean-room chemistry, and non-contaminating containers necessary for the application of non-nuclear techniques to reliable, routine trace analysis.

Other analytical problems are also best solved by nuclear methods. In particular, the use of radioactive tracers is underused, perhaps because the technique is "fictitiously difficult."³⁴ Because of the complications of chemical trace-element analyses of high-purity solids, "all reliable values for segregation coefficients for impurities in semiconductors have been determined by radiotracer methods."³⁵ Radiotracers can give exquisite sensitivity in studies of biochemical speciation,^{36, 37} and environmental transport processes.^{38, 39} In the analytical chemistry laboratory, radioactive tracers can often efficiently shed light on issues of homogeneity, contamination and losses, and the yield and purity of separation processes.⁴⁰ Bowen has written a thorough introduction to the virtues, applications, and practicalities of radiotracers.⁴¹

Conclusions

For analytical results to be demonstrably reliable, some believe that it is necessary to write and adhere to a detailed quality manual which sets out every step to be followed in every unit operation in every analytical procedure. Such rigidity can only guarantee reproducibility, not accuracy. It also guarantees scientific boredom. However, the ISO GUM can also be interpreted as a spur to improved analysis by encouraging the systematic examination of every significant source of error and uncertainty, and thus lead to improved accuracy through more complete understanding of the chemical measurement process. Nuclear methods, with their long history of attention to counting statistics and other uncertainties, can lead the way.

To the ignorant the great results alone are admirable; to the knowing, rather the infinite device and sleight of hand that made them possible. - Robert Louis Stevenson

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References

- (1) R. M. Lindstrom, S. H. Harrison, and J. M. Harris, *J. Appl. Phys.* **49**, 5903 (1978).
- (2) A. Wytttenbach, *J. Radioanal. Chem.* **8**, 335 (1971).
- (3) H. Houtermans, K. Schärf, F. Reichel, and K. Debertain, *Int. J. Appl. Radiat. Isot.* **34**, 487 (1983).
- (4) R. R. Greenberg and B. S. Carpenter, *J. Radioanal. Nucl. Chem.* **111**, 177 (1987).
- (5) R. M. Lindstrom, *Biol. Trace Elem. Res.* **43-45**, 597 (1994).
- (6) H. P. Yule, *Radioact. Radiochem.* **6** (4), 4 (1995).
- (7) R. M. Parr, H. Houtermans, and K. Schaerf, in *Computers in Activation Analysis and Gamma-Ray Spectroscopy (CONF-780421)*; B. S. Carpenter, M. D. D'Agostino, and H. P. Yule, Eds.; U. S. DOE: Springfield, Va. 544 (1979).
- (8) C. G. Sanderson, *Environ. Internat.* **14**, 379 (1988).
- (9) K. M. Decker and C. G. Sanderson, *Appl. Radiat. Isot.* **43**, 323 (1992).
- (10) M. Blaauw, V. Osorio Fernandez, P. Van Espen, G. Bernasconi, R. Capote Noy, H. Manh Dung, and N. I. Molla, *Nucl. Instrum. Methods* **A387**, 416 (1997).
- (11) G. L. Ritter and L. A. Currie, in *Computers in Activation Analysis and Gamma-Ray Spectroscopy (CONF-780421)*; B. S. Carpenter, M. D. D'Agostino, and H. P. Yule, Eds.; US Dept. of Energy: Springfield, VA. 39 (1979).
- (12) M. Blaauw, *Nucl. Instrum. Methods* **A333**, 548 (1993).
- (13) R. Van Schandevijl, R. Van Grieken, and J. Hoste, *J. Radioanal. Chem.* **9**, 55 (1971).
- (14) R. F. Fleming and R. M. Lindstrom, *J. Radioanal. Nucl. Chem.* **113**, 35 (1987).
- (15) R. M. Lindstrom and R. F. Fleming, *Radioact. Radiochem.* **6** (2), 20 (1995).
- (16) E. A. Mackey and J. R. D. Copley, *J. Radioanal. Nucl. Chem.* **167**, 127 (1993).
- (17) R. M. Lindstrom, R. R. Greenberg, D. F. R. Mildner, E. A. Mackey, and R. L. Paul, in *Second International k₀ Users Workshop*, Jozef Stefan Institute: Ljubljana, Slovenia, 50 (1997).
- (18) R. R. Greenberg, R. M. Lindstrom, and D. S. Simons, *J. Radioanal. Nucl. Chem.* **245**, 57 (2000).
- (19) M. Grasserbauer, *Pure & Appl. Chem.* **60**, 438 (1988).
- (20) R. M. Lindstrom, M. Blaauw, and R. F. Fleming, *J. Radioanal. Nucl. Chem.* 2001. (submitted).
- (21) ISO, *Guide to the Expression of Uncertainties in Measurement*, International Standards Organization,

- Geneva, 1993.
- (22) S. L. R. Ellison, M. Rosslein, and A. Williams, Eds. *Quantifying Uncertainty in Analytical Measurements (2nd ed.; QUAM:2000. P1)*; Eurachem/CITAC, 2000.
- (23) B. N. Taylor and C. E. Kuyatt, *Guidelines for Evaluating and Expressing the Uncertainty of NIST Measurement Results*, NIST Tech. Note 1297 (National Institute of Standards and Technology, Gaithersburg, 1993).
- (24) J. Kucera, P. Bode, and V. Stepanek, *J. Radioanal. Nucl. Chem.* **245**, 115 (2000).
- (25) P. Robouch, G. Arana, M. Eguskiza, S. Pommé, and N. Etxebarria, *J. Radioanal. Nucl. Chem.* **245**, 195 (2000).
- (26) J. Kragten, *Analyst* **119**, 2161 (1994).
- (27) Minutes from *the Fifth Meeting (February 1998) of the Consultative Committee on the Quantity of Material (CCQM) of the Bureau International des Poids et Mesures (BIPM)* (Sevres, France, 1998).
- (28) P. Bode, E. A. De Nadai Fernandes, and R. R. Greenberg, *J. Radioanal. Nucl. Chem.* **245**, 109 (2000).
- (29) Report of the CCQM (2nd meeting), 1996.
- (30) R. R. Greenberg, H. M. Kingston, R. L. Watters Jr., and K. W. Pratt, *Fresen. J. Anal. Chem.* **338**, 394 (1990).
- (31) R. R. Greenberg, R. Zeisler, and S. Mazolowski, in *Trace Element Analytical Chemistry in Medicine and Biology* edited by P. Brätter and P. Schramel, (de Gruyter: Berlin, **5**, 220 (1988)).
- (32) J. Versieck, *Biol. Trace Elem. Res.* **43-45**, 407 (1994).
- (33) J. Versieck, *CRC Crit. Rev. Clin. Lab. Sci.* **22**, 97 (1985).
- (34) E. W. Haas and R. Hofmann, *Solid-State Electronics* **30**, 329 (1987).
- (35) P. F. Kane, G. B. Larrabee, *Characterization of Semiconductor Materials*, (McGraw-Hill: New York, 1970).
- (36) D. Behne, C. Weiss-Nowack, M. Kalcklösch, C. Westphal, H. Gessner, and A. Kyriakopoulos, *Biol. Trace Elem. Res.* **43-45**, 287 (1994).
- (37) R. Cornelis, *J. Radioanal. Nucl. Chem.* **244**, 255 (2000).
- (38) Y. Muramatsu, S. Uchida, M. Sumiya, Y. Ohmomo, and H. Obata, *Water, Air, and Soil Pollution* **45**, 151 (1989).
- (39) J. P. McKinley, C. J. Zeissler, J. M. Zachara, R. J. Serne, R. M. Lindstrom, H. T. Schaef, and R. D. Orr, *Environ. Sci. Technol.* **35**, 3433 (2001).
- (40) V. Krivan, in *Treatise on Analytical Chemistry, Part I: Theory and Practice*, 2nd ed., v. **14**, I. M. Kolthoff, P. J. Elving, and V. Krivan, Eds. (Wiley: New York, 1986), pp.339-417.
- (41) H. J. M. Bowen, in *Treatise on Analytical Chemistry, Part I: Theory and Practice*, 2nd ed., v. **14**, I. M. Kolthoff, P. J. Elving, and V. Krivan, Eds. (Wiley: New York, 1986), pp.193-240.