TUTORIAL

A Beginner's Guide to ICP-MS

Part XI — Peak Measurement Protocol

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With its multielement capability, superb detection limits, wide dynamic range, and high sample throughput, inductively coupled plasma–mass spectrometry (ICP-MS) is proving to be a compelling technique for more and more diverse application areas. However, no two application areas have the same analytical requirements. For example, environmental and clinical contract laboratories — although requiring reasonably low detection limits — do not really push the technique to its extreme detection capability. Their main requirement is usually high sample throughput because the number of samples these laboratories can analyze in a day directly impacts their revenue. On the other hand, a semiconductor fabrication plant or a supplier of high-purity chemicals to the electronics industry is interested in the lowest detection limits the technique can offer because of the contamination problems associated with manufacturing high performance electronic devices.

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Modern ICP-MS must be very flexible to meet such diverse application needs and keep up with the increasing demands of its users. Nowhere is this more important than in the area of peak integration and measurement protocol. The way the analytical signal is managed in ICP-MS directly impacts its multielement capability, detection limits, dynamic range, and sample throughput — the four major strengths that attracted the trace element community to the technique almost 20 years ago. To understand signal management and its implications on data quality in greater detail, this installment of this series will discuss how measurement protocol is optimized based on the application's analytical requirements. I will discuss its impact on both continuous signals generated by traditional nebulization devices and transient signals produced by alternative sample introduction techniques such as flow injection and laser ablation.

Measurement Variables

Many variables affect the quality of the analytical signal in ICP-MS. The analytical requirements of the application will often dictate this factor, but instrumental detection and measurement parameters can have a significant impact on the quality of data in ICP-MS. Some of the variables that can affect the quality of your data, particularly when carrying out multielement analysis, include

- whether the signal is continuous or transient
- the temporal length of the sampling event
- the volume of sample available
- the number of samples being analyzed
- the number of replicates per sample
- the number of elements being determined
- the detection limits required
- the precision and accuracy expected
- the dynamic range needed
- the integration time used
- the peak quantitation routines.

Before discussing these factors in greater detail, and how they affect data quality, it is important to remember how a scanning device such as a quadrupole mass analyzer works (1). Although we will focus on quadrupole technology, the fundamental principles of measurement protocol will be very similar for all types of mass spectrometers that use a scanning approach for multielement peak quantitation.

Measurement Protocol

Figure 1 shows the principles of scanning with a quadrupole mass analyzer. In this simplified example, the analyte ion (black) and four other ions (colored) have arrived at the entrance to the four rods of the quadrupole. When a particular rf/dc voltage is applied to the rods, the positive or negative bias on the rods will electrostatically steer the analyte ion of interest down the middle of the four rods to the end, where it will emerge and be converted to an electrical pulse by the detector. The other ions of different mass-to-charge ratios will pass through the spaces between the rods and be ejected from the quadrupole. This scanning process is then repeated for another analyte at a completely different mass-to-charge ratio

until all the analytes in a multielement analysis have been measured.

The process for detecting one particular mass in a multielement run is represented in Figure 2, which shows a ^{63}Cu ion emerging from the quadrupole and being converted to an electrical pulse by the detector. As the rf/dc voltage of the quadrupole — corresponding to ^{63}Cu — is repeatedly scanned, the ions as electrical pulses are stored and counted by a multichannel analyzer. This multichannel data-acquisition system typically has 20 channels per mass and as the electrical pulses are counted in each channel, a profile of the mass is built-up over the 20 channels, corresponding to the spectral peak of ^{63}Cu. In a multielement run, repeated scans are made over the entire suite of analyte masses, as opposed to just one mass represented in this example.

The principles of multielement peak acquisition are shown in Figure 3. In this example (showing two masses), signal pulses are continually collected as the quadrupole is swept across the mass spectrum (in this case three times). After a given number sweeps, the total number of signal pulses in each channel are counted.

When it comes to quantifying an isotopic signal in ICP-MS, there are basically two approaches to consider (2). One is the multichannel ramp scanning approach, which uses a continuous smooth ramp of 1 to *n* channels (where *n* is typically 20) per mass across the peak profile. This approach is shown in Figure 4.

The peak-hopping approach is where the quadrupole power supply is driven to a discrete position on the peak (normally the peak point) and allowed to settle; a measurement is then taken for a fixed amount of time. This approach is represented in Figure 5.

The multipoint scanning approach is best for accumulating spectral and peak shape information when doing mass scans. It is normally used for doing mass calibration and resolution checks, and as a classical qualitative method development tool to find out what elements are present in the sample, as well as to assess their spectral implications

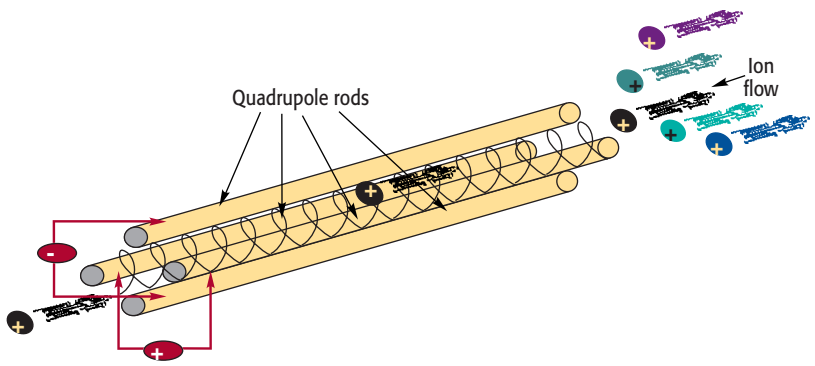


Figure 1. Principles of mass selection with a quadrupole mass filter.

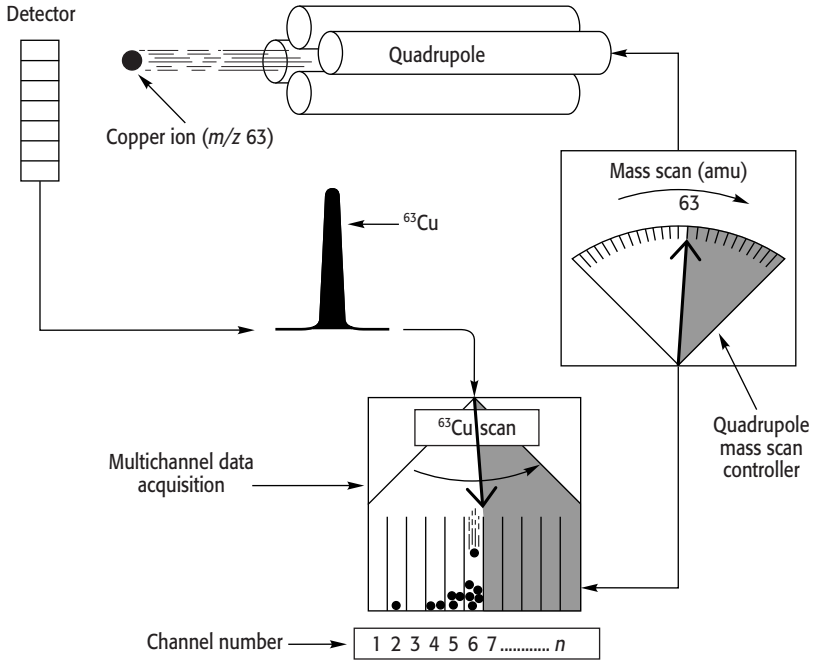
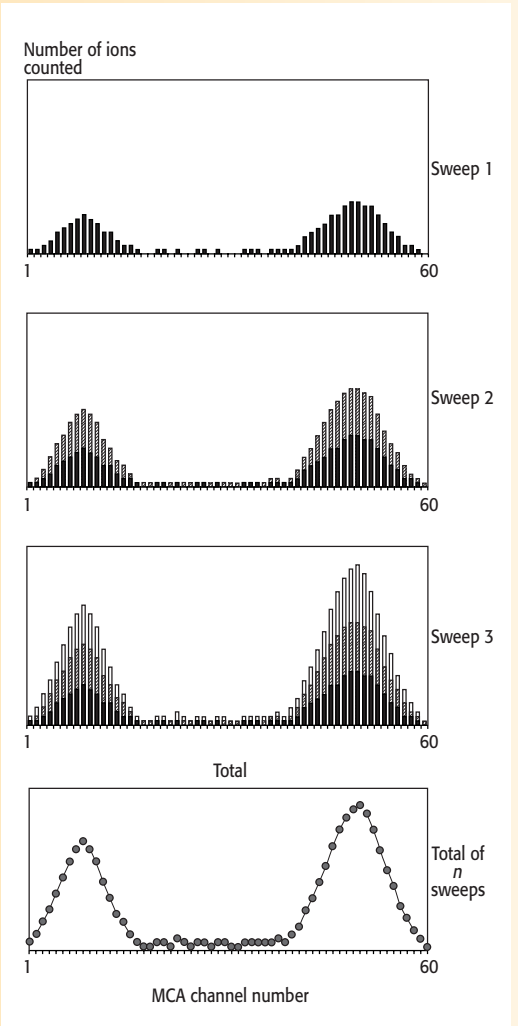
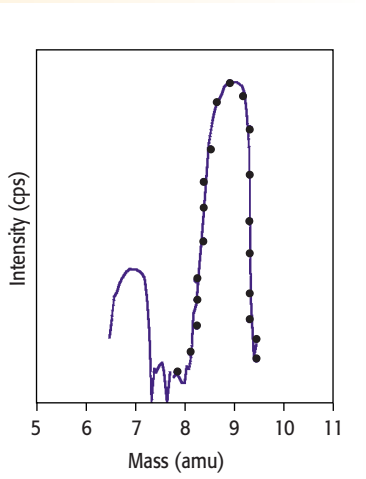


Figure 2. Detection and measurement protocol using a quadrupole mass analyzer.

on the masses of interest. Full peak profiling is not normally used for doing rapid quantitative analysis because valuable analytical time is wasted taking data on the wings and valleys of the peak, where the signal-to-noise ratio is poorest.

When the best possible detection limits are required, the peak-hopping approach is best. It is important to understand that, to get the full benefit of peak hopping, the best detection limits are achieved when single-point peak hopping at the peak maximum is chosen. However, to carry out single-point peak hopping, it is essential that the mass stability is good enough to reproducibly go to the same mass point every time. If good mass stability can be guaranteed (usually by thermostating the quadrupole power supply), measuring the signal at the peak maximum will always give the best detection limits for a given integration time. It is well documented that there is no benefit to spreading the chosen integration time over more than one measurement point per mass. If time is a major consideration in the analysis, then using multiple points is wasting valuable time on the wings and valleys of the peak, which contribute less to the analytical signal





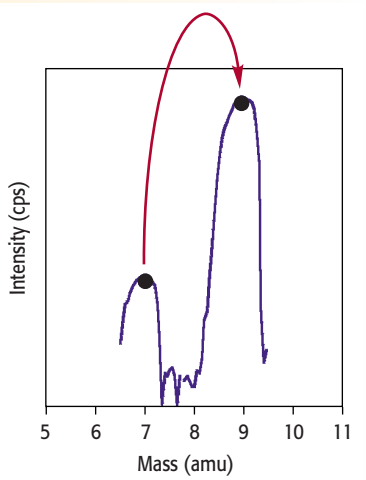


Figure 3 (above left). A profile of the peak is built up by continually sweeping the quadrupole across the mass spectrum.

Figure 4 (above right). Multichannel ramp scanning approach using 20 channels per amu.

Figure 5 (below right). Peak-hopping approach.

and more to the background noise. Figure 6 shows the degradation in signal-to-background noise ratio of 10 ppb Rh with an increase in the number of points per peak, spread over the same total integration time. Detection limit improvement for a selected group of elements using 1 point/peak, rather than 20 points/peak, is shown in Figure 7.

Optimization of Measurement Protocol

Now that the fundamentals of the quadrupole measuring electronics have been described, let us now go into more detail on the impact of optimizing the measurement protocol based on the requirement of the application. When multielement analysis is being carried out by ICP-MS, a number of decisions need to be made. First, we need to know if we are dealing with a continuous signal from a nebulizer or a transient signal from an alternative sampling accessory. If it is a transient event, how long will the signal last? Another question that needs to be addressed is, how many elements are going to be determined? With a continuous signal, this isn't such a major problem, but it could be an issue if we are dealing with a transient signal that lasts a few seconds. We also need to be aware of the level of detection capability required. This is a major consideration with a single-shot laser pulse that lasts 5–10 s. Also with a continuous signal produced by a concentric nebulizer, we might have to accept a compromise of detection limit based on the speed of analysis requirements or amount of sample available. What analytical precision is expected? If it's isotope ratio/
dilution work, how many ions do we have to count to guarantee good precision? Does increasing the integration time of the measurement help the precision? Finally, is there a time constraint on the analysis? A high-throughput laboratory might not be able to afford to use the optimum sampling time to get the ultimate in detection limit. In other words, what compromises need to be made between detection limit, precision, and sample throughput? Clearly, before the measurement protocol can be optimized, the major analytical requirements of the application need to be defined. Let's take a look at this process in greater detail.

Multielement Data Quality Objectives

Because multielement detection capability is probably the major reason why most laboratories invest in ICP-MS, it is important to understand the impact of measurement criteria on detection limits. We know that in a multielement analysis, the quadrupole's rf/dc ratio is scanned to mass regions or *driven,* which represent the elements of interest. The electronics are allowed to settle

Table I. Precision of Pb isotope ratio measurement as a function of dwell time using a total integration time of 5.5 s.

Dwell time (ms)	%RSD, $^{207}Pb/^{206}Pb$	%RSD, $^{208}Pb/^{206}Pb$
2	0.40	0.36
5	0.38	0.36
10	0.23	0.22
25	0.24	0.25
50	0.38	0.33
100	0.41	0.38

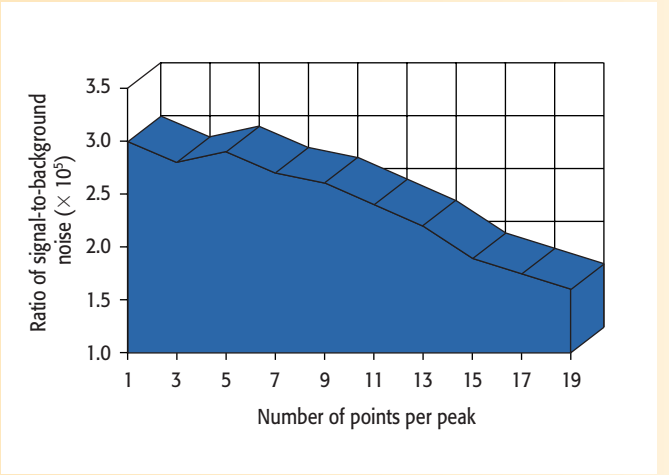


Figure 6. Signal-to-background noise ratio degrades when more than one point, spread over the same integration time, is used for peak quantitation.

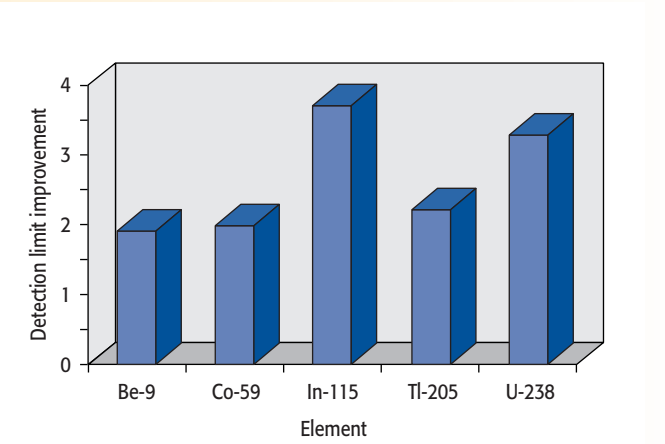


Figure 7. Detection limit improvement using 1 point/peak rather than 20 points/peak over the mass range.

and then dwell on the peak, or *sit*, and take measurements for a fixed period of time. This step is usually performed a number of times until the total integration time is fulfilled. For example, if a dwell time of 50 ms is selected for all masses and the total integration time is 1 s, then the quadrupole will carry out 20 complete sweeps per mass, per replicate. It will then repeat the same routine for as many replicates that have been built into the method. This process is illustrated very simplistically in Figure 8, which shows the scanning protocol of a multielement scan of three different masses.

In this example, the quadrupole is scanned to mass A. The electronics are allowed to settle (settling time) and left to dwell for a fixed period of time at one or multiple points on the peak (dwell time); intensity measurements are then taken (based on the dwell time). The quadrupole is then scanned to masses B and C and the measurement protocol repeated. The complete multielement measurement cycle (sweep) is repeated as many times as needed to make up the total integration per peak. It should be emphasized that this example is a generalization of the measurement routine — management of peak integration by the software will vary slightly, based on different instrumentation.

It is clear from this information that, during a multielement analysis, a significant amount of time is spent scanning and settling the quadrupole, which doesn't contribute to the quality of the analytical signal. Therefore, if the measurement routine is not optimized carefully, it can have a negative impact on data quality. The dwell time can usually be selected on an individual mass basis, but the scanning and settling times are normally fixed because they are a function of the quadrupole and detector electronics. For this reason, it is essential that the dwell time — which ultimately affects detection limit and precision — must dominate the total measurement time, compared with the scanning and settling times. It follows, therefore, that the measurement duty cycle (percentage of actual measuring time compared with total integration time) is maximized when the quadrupole and detector electronics settling times are kept to an absolute minimum. Figure 9 shows a plot of percentage of measurement efficiency against dwell time for four different quadrupole settling times — 0.2, 1.0, 3.0, and 5.0 ms for one replicate of a multielement scan of five masses, using one point per peak. In this example, the total integration time for each mass was 1 s, with the number of sweeps varying, depending on the dwell time used. For this exercise, the percentage of measurement efficiency is defined by the following calculation:

$$\frac{\text{Dwell Time} \times \#\text{Sweeps} \times \#\text{Elements} \times \#\text{Replicates}}{\left(\text{Dwell Time} \times \#\text{Sweeps} \times \#\text{Elements} \times \#\text{Replicates}\right) + \left(\text{Scanning / Settling Time} \times \#\text{Sweeps} \times \#\text{Elements} \times \#\text{Replicates}\right)} \times 100$$

So to achieve the highest measurement efficiency, the nonanalytical time must be kept to an absolute minimum. This leads to more time being spent counting ions and less time scanning and settling, which does not contribute to the quality of the analytical signal. This factor becomes critically important when a rapid transient peak is being quantified, because the available measuring time is that much shorter (3). Generally speaking, peak quantitation using multiple points per peak and long settling times should be avoided in ICP-MS because it ultimately degrades the quality of the data for a given integration time.

Figure 9 also shows that shorter dwell times translate into a lower measurement efficiency. For this reason, it is probably desirable, for normal quantitative analysis work, to carry out multiple sweeps with longer dwell times (typically 50 ms) to get the best detection limits. So if an integration time of 1 s is used for each element, this would translate into 20 sweeps of 50 ms dwell time per mass. Although 1 s is long enough to achieve reasonably good detection limits, longer integration times generally have to be used to reach the

lowest possible detection limits. Figure 10 shows detection limit improvement as a function of integration time for ^{238}U. As would be expected, there is a fairly predictable improvement in the detection limit as the integration time is increased because more ions are being counted without an increase in the background noise. However, this only holds true up to the point where the pulse-counting detection system becomes saturated and no more ions can be counted. In the case of ^{238}U, this occurs around 25 s, because there is no obvious improvement in detection limit at a higher integration time. So from these data, we can say that there appears to be no real benefit in using an integration time longer than 7 s. When deciding the length of the integration time in ICP-MS, you have to weigh the detection limit improvement against the time taken to achieve that improvement. Is it worth spending 25 s measuring each mass to get a 0.02 ppt detection limit if 0.03 ppt can be achieved using a 7-s integration time? Alternatively, is it worth measuring for 7 s when 1 s will only degrade the performance by a factor of 3? It really depends on your data quality objectives.

For applications such as isotope dilution/ratio studies, high precision is also a very important data quality objective (4). However, to understand what is realistically achievable, we must be aware of the practical limitations of measuring a signal and counting ions in ICP-MS. Counting statistics tells us that the standard deviation of the ion signal is proportional to the square root of the signal. It follows, therefore, that the relative standard deviation (RSD), or precision, should improve with an increase in the number (N) of ions counted as shown by the following equation:

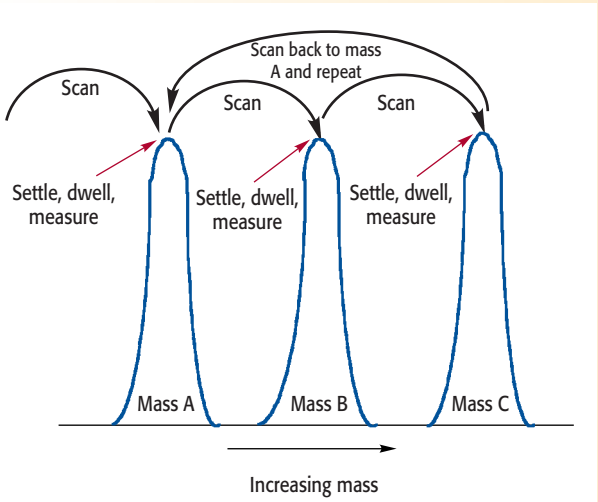
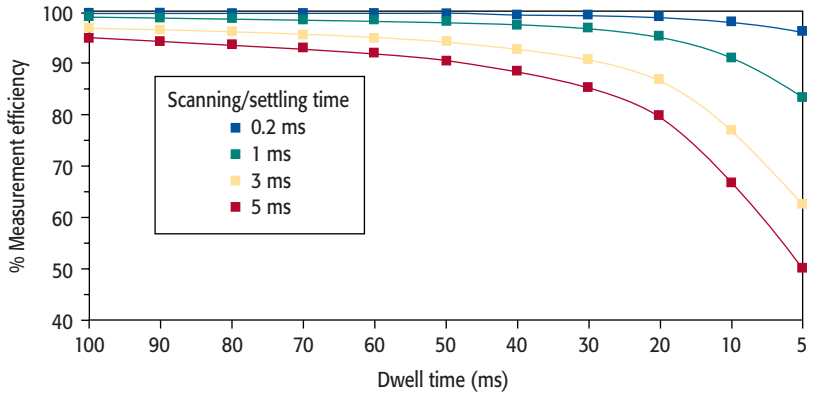


Figure 8 (left). Multielement scanning and measurement protocol of a quadrupole.

Figure 9 (below). Percent of measurement efficiency as a function of dwell time with varying scanning/settling times.



$$\%RSD = \frac{\sqrt{N}}{N} = 100$$

In practice this holds up very well, as shown in Figure 11. In this plot of standard deviation as a function of signal intensity for ^{208}Pb, the dots represent the theoretical relationship as predicted by counting statistics. It can be seen that the measured standard deviation (bars) follows theory very well up to about 100,000 cps. At that point, additional sources of noise (for example, sample introduction pulsations or plasma fluctuations) dominate the signal, which leads to poorer standard deviation values.

So based on counting statistics, it is logical to assume that the more ions that are counted, the better the precision will be. To put this in perspective, it means that at least 1 million ions need to be counted to achieve an RSD of 0.1%. In practice, of course, these kinds of precision values are very difficult to achieve with a scanning quadru-

Table II. Impact of integration time on the overall analysis time for Pb isotope ratios.

Dwell time (ms)	Number of sweeps	Integration time (s)/mass	%RSD, $^{207}Pb/^{206}Pb$	%RSD, $^{207}Pb/^{206}Pb$	Analysis time for 9 reps
25	220	5.5	0.24	0.25	2 min 29 s
25	500	12.5	0.21	0.19	6 min 12 s
25	700	17.5	0.20	0.17	8 min 29 s

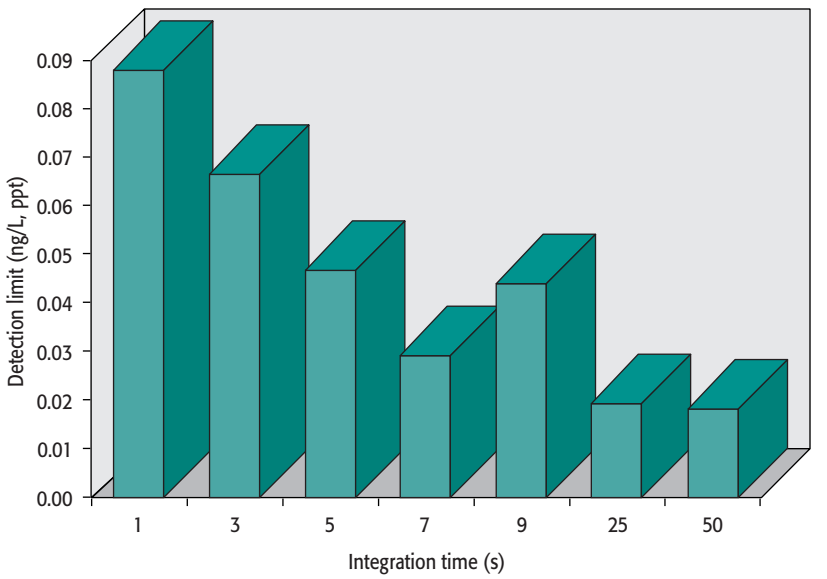


Figure 10. Plot of detection limit against integration time for ^{238}U.

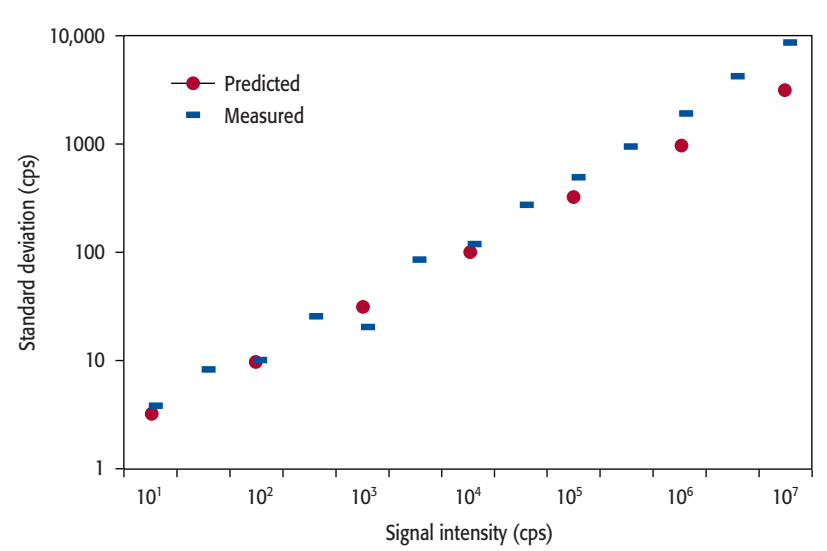


Figure 11. Comparison of measured standard deviation of a ^{208}Pb signal against that predicted by counting statistics.

pole system because of the additional sources of noise. If this information is combined with our knowledge of how the quadrupole is scanned, we begin to understand what is required to get the best precision. This is confirmed by the spectral scan in Figure 12, which shows the predicted precision at all 20 channels of a 5 ppb ^{208}Pb peak (2).

Therefore, the best precision is obtained at the channels where the signal is highest, which as we can see are the ones at or near the center of the peak. For this reason, if good precision is a fundamental requirement of your data quality objectives, it is best to use single-point peak hopping with integration times in the order of 5–10 s. On the other hand, if high-precision isotope ratio or isotope dilution work is being done — in which analysts would like to achieve precision values approaching counting statistics — then much longer measuring times are required. That is why integration times of 5–10 min are commonly used for determining isotope ratios with a quadrupole ICP-MS system (5, 6). For this type of analysis, when two or more isotopes are being measured and ratioed to each other, it follows that the more simultaneous the measurement, the better the precision becomes. Therefore, the ability to make the measurement as simultaneous as possible is considered more desirable than any other aspect of the measurement. This is supported by the fact that the best isotope ratio precision data are obtained with time-of-flight or multicollector, magnetic sector ICP-MS systems, which are both considered simultaneous in nature. So the best way to approximate simultaneous measurement with a rapid scanning device, such as a quadrupole, is to use shorter dwell and scanning/settling times, resulting in more sweeps for a given integration time. Table I shows precision of Pb isotope ratios at different dwell times carried out by researchers at the Geological Survey of Israel (7). The data are based on nine replicates of a NIST SRM-981 (75 ppb Pb) solution, using 5.5 s of integration time per isotope.

From these data, the researchers concluded that a dwell time of 10 or 25 ms offered the best isotope ratio precision measurement (quadrupole settling time was fixed at 0.2 ms). They also found that they could achieve slightly better precision by using a 17.5-s integration time (700 sweeps at a 25-ms dwell time), but felt the marginal improvement in precision for nine replicates was not worth spending the approximately 3.5-times-longer analysis time, as shown in Table II.

This work shows the benefit of optimizing the dwell time, settling time, and the number of sweeps to get the best isotope ratio precision data. The researchers were also very fortunate to be dealing with relatively healthy signals for the three Pb isotopes, ^{206}Pb, ^{207}Pb, and ^{208}Pb (24.1%, 22.1%, and 52.4% abundance, respectively). If the isotopic signals were dramatically different like in ^{235}U to ^{238}U (0.72 % and 99.2745% abundance, respectively), then the ability to optimize the measurement proto-

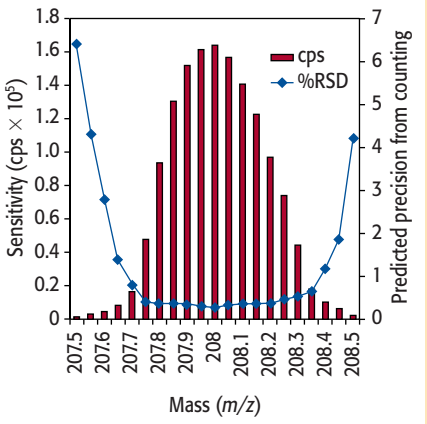


Figure 12. Comparison of % RSD with signal intensity across the mass profile of a ^{208}Pb peak.

col for individual isotopes becomes of even greater importance to guarantee precise data.

It is clear that the analytical demands put on ICP-MS are probably higher than any other trace element technique because it is continually being asked to solve a wide variety of application problems. However, by optimizing the measurement protocol to fit the analytical requirement, ICP-MS has shown that it has the capability to carry out rapid trace element analysis, with superb detection limits and good precision on both continuous and transient signals, and still meet the most stringent data quality objectives.

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applications and provides everything necessary for a typical x-ray detector, incorporating one DXP spectrometer channel, preamplifier power, and detector HV bias in one compact chassis. Its input is compatible with a wide range of common detectors, including pulsed optical reset, transistor reset, and RC feedback preamplifiers. The Saturn offers complete computer control over all amplifier and spectrometer functions including gain, filter peaking time, and pileup inspection criteria. Its DXP digital filters significantly increase throughput compared to typical analog systems.

The new X-Beam x-ray source from **X-Ray Optical Systems** (Albany, NY) delivers an intense, micrometer-sized focal spot. Designed for OEM use in micro-XRF instruments, the compact unit uses polycapillary focusing optics and 50 W of power to generate an extremely high flux-density gain, the company reports. Increased spatial resolution and beam stability are also promised. An integrated cooling system eliminates the need for a separate cooling unit.

Attendees can see many of these products, along with others not mentioned, at the 2002 Denver X-ray Conference — sponsored by the International Centre for Diffraction Data — at Antlers Adam's Mark Hotel (formerly Antlers Doubletree Hotel), Colorado Springs, Colorado, July 29–August 2, 2002. For more information, contact Denise Flaherty, DXC Conference Coordinator, 12 Campus Boulevard, Newtown Square, PA 19073-3273, (610) 325-9814, fax: (610) 325-9823, e-mail: flaherty@icdd.com, web site: www.dxcicdd.com. ■