WHITE PAPER

Single Particle Inductively Coupled Plasma Mass Spectrometry: Understanding How and Why

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Introduction

Nanotechnology is an emerging and rapidly growing field whose dynamics and prospects pose many great challenges to scientists and engineers. Nanoparticles are being used in many materials and products, including coatings (on plastic, glass and clothing), sunscreen, antimicrobial bandages and clothing, MRI contrast agents, biomedical elemental tags and fuel additives, only to name few. However, rapid, simultaneous characterization of their elemental composition, number of particles, size, and size distribution is challenging. For inorganic nanoparticles, the technique best suited to provide the above-mentioned characteristics is inductively coupled plasma mass spectrometry (ICP-MS) operated in so-called single particle mode. Analyzing single nanoparticles with ICP-MS requires a different approach than measuring dissolved elements. This work describes the theory behind single-particle ICP-MS measurements, drawing comparisons and differences with analyzing dissolved elements.

Understanding Single Particle ICP-MS Analysis

Effectively detecting and measuring single, individual nanoparticles with ICP-MS requires operating the instrumentation in a different manner than when analyzing dissolved samples. Figure 1 shows traces from both dissolved and single nanoparticle analyses. In Figure 1a, a steady state signal results from measuring dissolved elements; the output when detecting single particles is quite different, as illustrated for 60 nm silver particles in Figure 1b. Each spike in Figure 1b represents a particle. The differences in the way these data are acquired are the key to understanding single particle analysis. The easiest way to gain this understanding is to review and compare the processes involved when both dissolved elements and particles are measured.

Dissolved Analyses with ICP-MS

When dissolved elements are measured, aerosols enter the plasma, where the droplets are desolvated and ionized. The resulting ions enter the quadrupole to be sorted by their mass-to-charge ratios (m/z). The quadrupole spends a certain amount of time at each m/z before moving to the next m/z; the time spent analyzing each m/z is called "dwell time". After each dwell time measurement, a certain amount of time is spent for the electronics to stabilize before the next measurement is performed. This stabilization time is called "settling time", i.e. overhead and processing time. When analyzing dissolved elements, the resulting signal is essentially a steady-state signal, as shown in Figure 2a. However, considering the dwell and settling times, a significant amount of the signal is not measured due to the settling time of the electronics, a critical aspect when analyzing nanoparticles (Figure 2b).

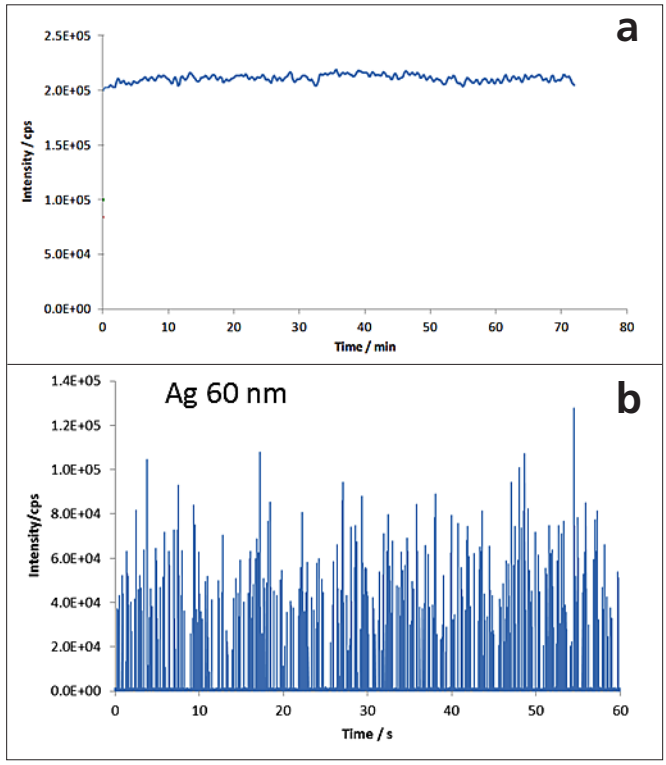

Figure 1. a) A continuous signal from measuring a dissolved analyte; b) A signal from measuring 60 nm silver nanoparticles.

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For dissolved ions, the part of the signal which is missed is not critical since the elements are dissolved and produce a continuous signal.

Single Particle Analyses with ICP-MS

Particles present in an aqueous solution are introduced to the plasma the same way as dissolved solutions. As the droplets are desolvated in the plasma, the resulting particles are ionized producing a burst of ions (one ion cloud per particle). The ions then pass into the quadrupole. However, using conventional ICP-MS data collection, alternating between dwell time and settling time, ion clouds are not always detected. If, for example, the ion cloud happens to fall within the dwell time window, it will be detected. Otherwise, if it passes into the quadrupole or reaches the detector during the settling time, it will not be detected, leading to an inaccurate counting efficiency. Figure 3a shows that an ion cloud from a single particle (the "Signal" peak) can be missed if it falls outside of the dwell time window. When the ion cloud from a single particle falls within the dwell time window, it is detected, as represented in Figure 3b. When multiple particles are detected in rapid succession, the resulting signal is a series of peaks, each one originating from a particle, as shown in Figure 3c.

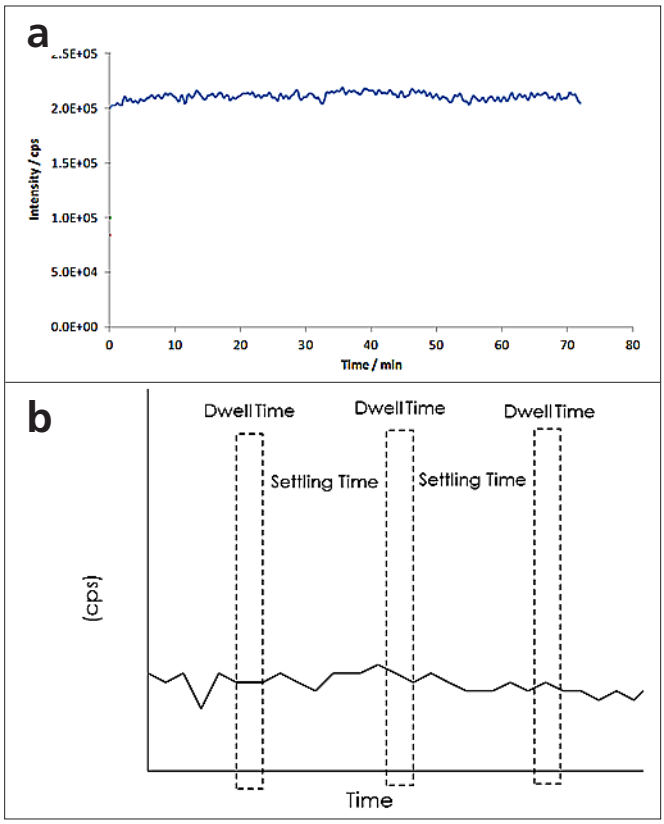

Figure 2. a) A continuous signal from measuring a dissolved element; b) A continuous signal, with the dwell and settling times overlaid – data is only collected during the dwell time.

The Timing Parameters of Single Particle ICP-MS

Figure 4 is a representation of the timing parameters involved in ICP-MS analysis. The three axes represent signal intensity, mass (m/z), and time. With conventional/dissolved analyses, the mass and intensity axes are the most important: resulting spectra are plots of m/z vs. intensity. The time axis is important when considering how fast the quadrupole can move from mass-to-mass – this parameter is called "quadrupole scan speed". The quadrupole scan speed is important when measuring multiple elements in a transient signal, such as for laser ablation and multielement speciation analyses.

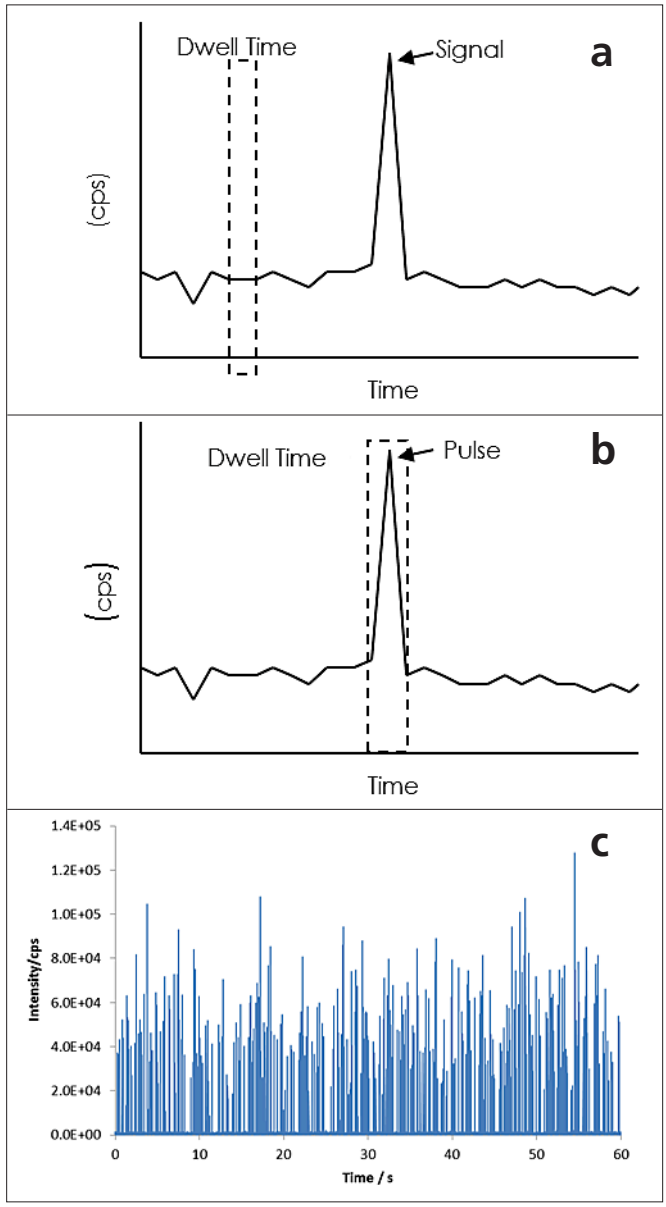

Figure 3. a) Signal from a single nanoparticle falling outside of the dwell time/measurement window, and, therefore, not detected; b) Signal from a single nanoparticle falling within the dwell time/measurement window, and, therefore, detected; c) Signals from multiple nanoparticles falling within dwell time/measurement windows and detected.

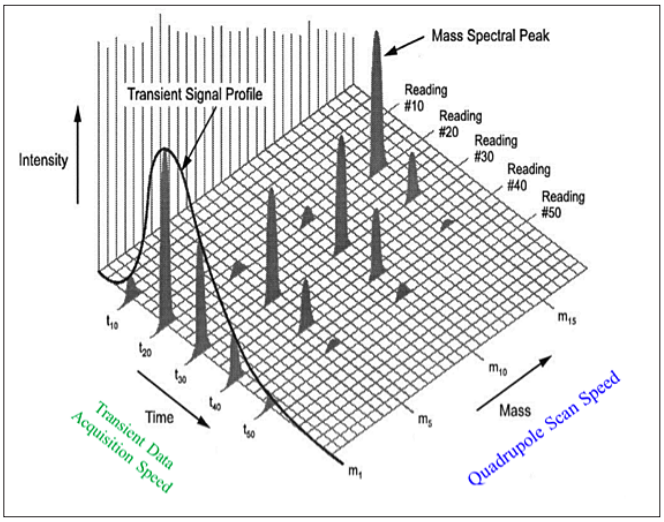

Figure 4. The timing parameters of ICP-MS analyses.

When measuring transient signals for a single m/z, the time axis becomes important, since enough data points must be acquired to define the peak. For example, with HPLC/ICP-MS, usually 4-10 points/second are enough to define a peak. Comparing HPLC peaks to single particle signals, the ion packets from each particle are typically 1000 times narrower than peaks produced by HPLC. Therefore, data must be acquired significantly faster for single particle analysis. Since only a single mass is being measured for single particle analysis, the quadrupole scan speed is not important, and the time axis becomes the "transient data acquisition speed", which encompasses both the dwell and settling times. The faster the transient data acquisition speed, the better suited the system is for single particle analysis.

In single particle ICP-MS, transient data acquisition speed consists of two parameters: dwell time (reading time) and settling time (overhead and processing time). It is very important that the ICP-MS is able to acquire signals at a dwell time that is shorter than the particle transient time, thus avoiding false signals generated from partial particle integration, particle coincidence and agglomerates/aggregates. The shorter the settling time, the less chance there is of missing a particle. Figure 5 demonstrates the importance of settling time using a constant 100 µs dwell time and a constant time window. In Figure 5a, there are only two 100 µs windows to detect particles; the rest of the time is overhead, where data cannot be acquired. In this case, there are only about 100 measurements made in one second. Therefore, most of the time is wasted. Figure 5b is the same time scale, but with a settling time of 100 µs. Therefore, more time is spent measuring and looking for nanoparticles – about 5000 measurements in one second. However, still half of the time is wasted. Figure 5c represents the ideal situation with no settling time. This allows for 10,000 measurements per second, with no wasted time: all the time is spent looking for particles, the ideal situation for single particle ICP-MS.

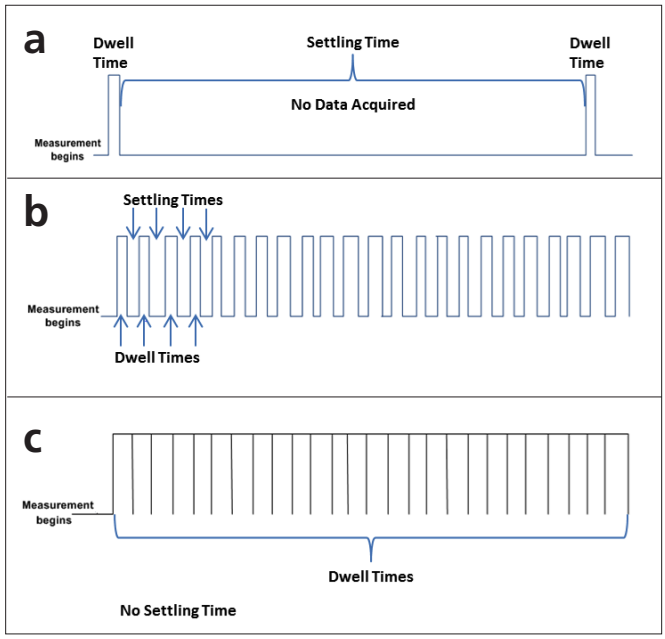

Figure 5. Effect of settling time and dwell time on ICP-MS measurements: a) Settling time is much longer than the dwell time; b) Settling time is equal to the dwell time; c) Settling time is eliminated.

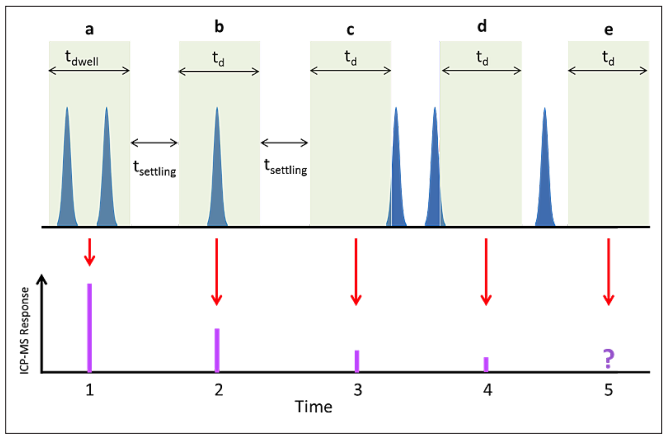

Figure 6. Effect of dwell and settling times on single nanoparticle measurements: a) Two particles detected; b) One particle detected; c) The leading edge of one particle detected; d) The trailing edge of one particle detected; e) No particles detected.

Multiple Measurements per Particle: The Ideal Situation

To understand the importance of fast sampling time for single particle measurements, consider the representation in Figure 6. In this figure, the upper portion represents pulses from single particles as they relate to dwell and settling times, while the lower portion shows the corresponding mass spectrometer response (intensity vs. time). In Figure 6a, two particles are detected in a single dwell time window, leading to a response twice as large as if one particle were detected, not a desirable situation and easily encountered if the instrument dwell time is longer than the nanoparticle transient pulse. In Figure 6b,

a single particle is detected in the dwell time window – the ideal situation, if fast continuous data acquisition was not available. The resulting signal is half the size of Figure 6a. Figures 6c and 6d represent undesirable situations where only a part of the ion pulse from particles is detected, leading to small signals, thus inaccurate particle sizing. Figure 6e represents the most undesirable situation, where the particle falls outside of the dwell time window and is not detected. These examples demonstrate the importance of having fast continuous data acquisition ability, where data is collected continuously without any settling time, ensuring accurate particle counting - every particle entering the plasma will be counted.

Another benefit of fast continuous data acquisition is that multiple points can be measured from a single particle, thus eliminating the chances that particles are missed or that only partial ion clouds from particles are detected. Figure 7 shows how this can be accomplished. In Figure 7a, the signal from a single particle is measured multiple times. The signal from each time slice is plotted, which defines the peak. When multiple particles are detected, the resulting peaks are a series of time slices, as shown in Figure 7b.

Figures 8a and 8b show how typical single particle responses can be converted into peaks which define a single particle. In Figure 8a, data was collected in fast continuous mode (no settling time)

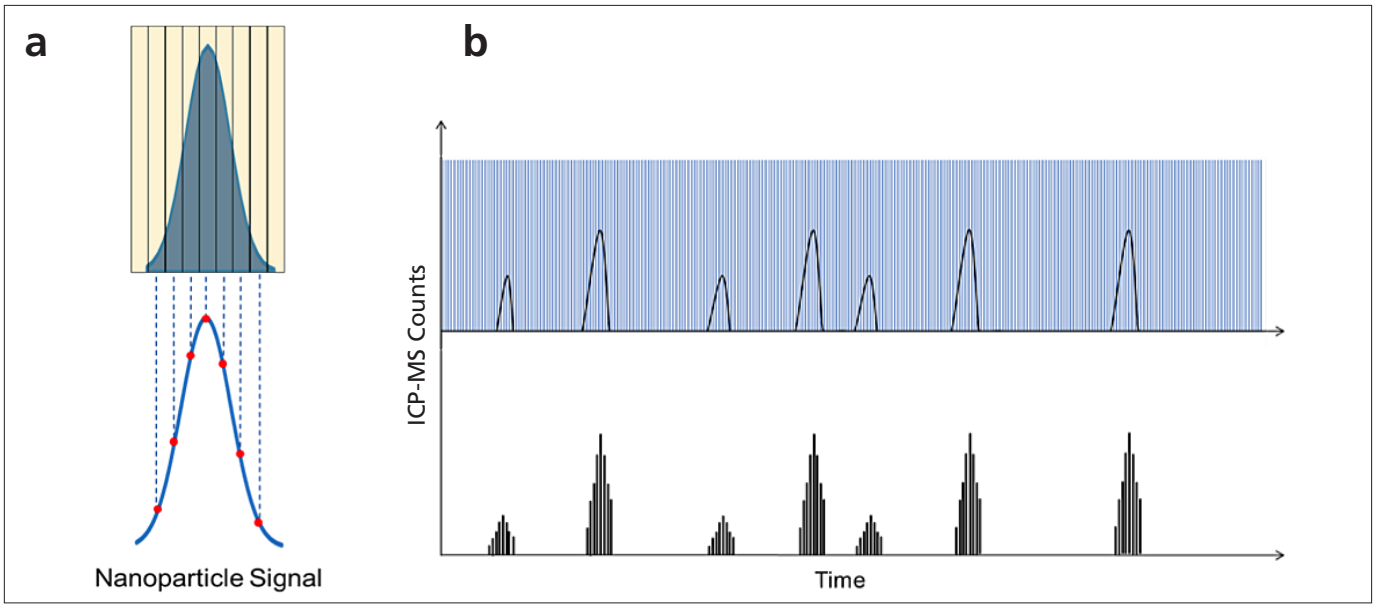

Figure 7. Effect of measuring multiple measurements per particle: a) For a single particle and b) For multiple particles detected in series.

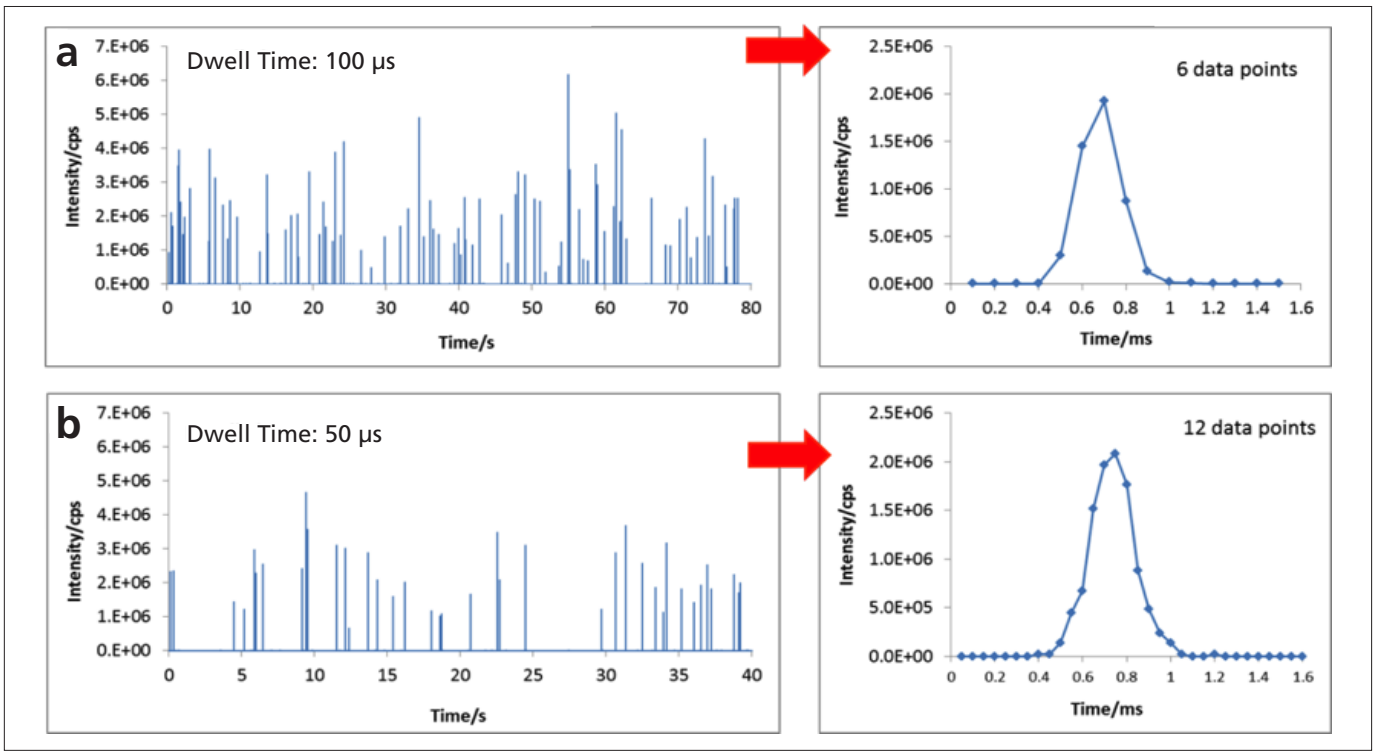

Figure 8. Ability to acquire multiple measurements per particle: a) 6 data points per particle; b) 12 data points per particle.

with a dwell time of 100 µs. When the intensities from the first 1.6 seconds are plotted, it is seen that 6 points define a peak. In Figure 8b, the dwell time was reduced to 50 µs, which leads to twice as many data points being acquired. As a result, the peak shape is defined by 12 points, leading to a different peak shape. These examples demonstrate the benefit of sampling multiple data points per particle.

Summary

As has been shown, measuring single particles with ICP-MS is quite different than measuring dissolved species. The most important factor when measuring single particles is the speed at which data can be acquired: since particle ionization events are on the order of microseconds, rapid data acquisition and elimination of the settling time between measurements are crucial. Continuous measurement allows multiple readings per particle ionization event, which results in more accurate size determinations. For single particle ICP-MS analysis, continuous data acquisition at a dwell time smaller than or equal to 100 µs is the most important instrumental requirement for precise nanoparticle counting and sizing.

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