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Attom Note **NA24**

Detecting <7 nm nanoparticles using a nebuliser with a desolvation system on Attom ES

- Improved signal to background
- Low carry over
- Simple operation

Introduction

The detection of nanoparticles which are small enough to penetrate cell walls and cause damage to proteins is of critical interest to researchers in the field of environmental toxicology and the biological impact of nanotechnology. Such nanoparticles are generally accepted to be those less than 10 nm in size (Xia Q, et al. J Biomed Mater Res Part A: 105A: 710-719, 2017). The detection of these small nanoparticles is made more problematic when dissolved ionic concentrations for the element of interest elevate the background signals in the sample making it more difficult to distinguish particle signals. This work will describe how a nebuliser with a desolvation system can be used with Attom to improve the size detection limit through an increase in the ion transmission and particle signal to ionic background ratio.

Instrumental setup

A desolvating nebuliser, in this case a Cetac Aridus II as shown schematically in Figure 1, uses a pneumatic nebuliser in the same way as conventional sample introduction except the spray chamber is heated at 110° C to increase the aerosol generation rather than cooled. As well as increasing the amount of aerosol, a significant amount of water vapour is generated which would normally create higher levels of oxides and hydrides in the ions being measured, even causing instability in some cases. The output from the heated spray chamber is passed through a porous membrane at a higher temperature (160° C) with a counter flow of argon gas passed on the outside of the membrane. In this manner the water vapour is removed from the aerosol stream and a greater portion of the analytes of interest remain in the argon flow passing to the plasma after the droplets have evaporated compared to conventional nebuliser and spray chamber arrangements. The instrument conditions for conventional “wet” and Aridus II “dry” sample introduction are shown in Table 1.

Aridus II™ Schematic, Figure 1

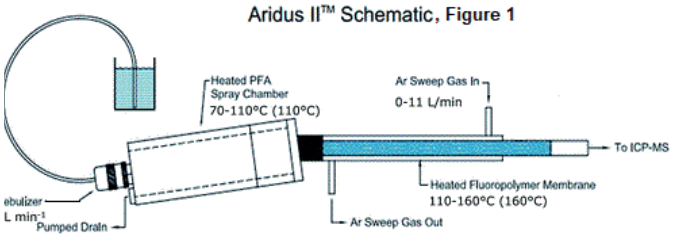

Table 1. Instrument setup conditions for Attom	
Conventional sample introduction:	Dry sample introduction:
200 µL/min glass concentric nebuliser Glass Expansion Twister cyclonic chamber Peltier cooled to 4° C Nebuliser pressure 28-30 psi No additional gas 1.5 mm ID injector one-piece torch 1.15 mm ID wet sample cone 0.7 mm ID wet skimmer cone	200 µL/min glass concentric nebuliser Aridus II heated spraychamber (110° C) Aridus II heated desolvation membrane (160° C) Nebuliser pressure 28-30 psi Membrane sweep gas 5-6 lpm 1.5 mm ID injector one-piece torch 0.9 mm ID dry sample cone 0.7 mm ID ES dry skimmer cone

Table 1: Shows a comparison of the instrumental conditions for conventional and dry sample introduction on the Attom.

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Single Particle ICP-MS (spICP-MS)

The technique of spICP-MS is recently introduced and used for the detection of individual metallic nanoparticles in solutions. The principle of operation is that for ionic solutions, the signal measured at the detector is generated by predominantly individual atoms or molecules passing as a continuous stream through the plasma creating a steady state signal. However, for nanoparticles, larger packets of ions are generated at the same point in the plasma and pass through to the detector within a few tens of microseconds.

The signal from a nanoparticle will generally last for 150-800 µs with the variation in peak width dependant on the sample introduction system as the packet of ions can diffuse as it passes through the ICP torch and the interface to the mass spectrometer. It is now well known in spICP-MS that the data acquisition dwell times need to be significantly shorter than the time taken for a particle signal to rise and fall for accurate measurements to be taken. To obtain accurate dead time correction for larger particle signals and improve signal to background detection when ionic signals are present, the shortest possible dwell times should be used, of the order of 20-50 µs.

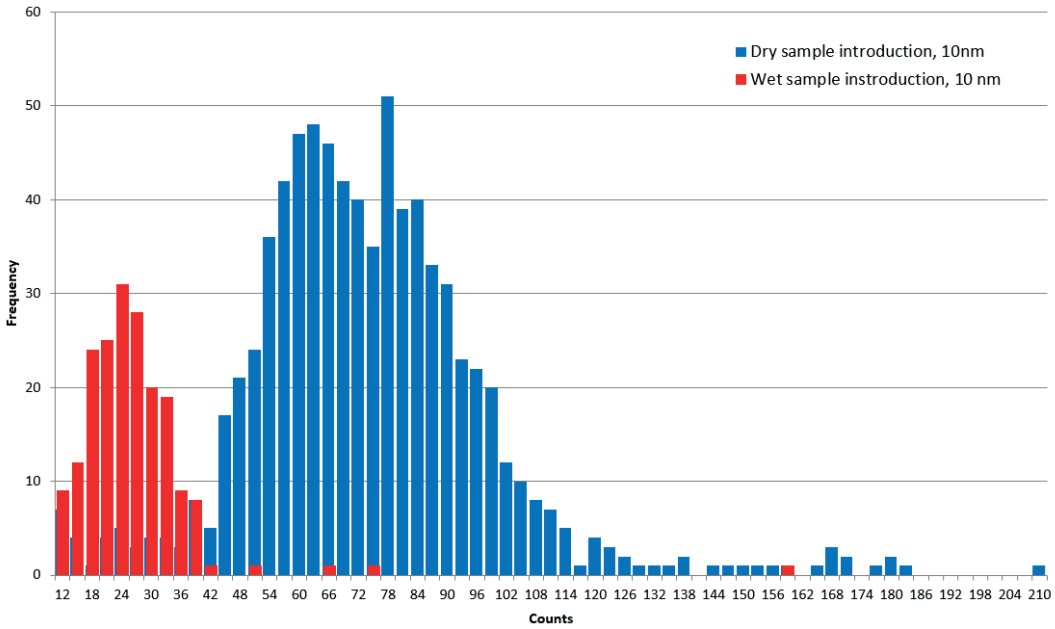
Performance of the desolvating nebuliser

The sample uptake rate was determined by aspirating a known nanoparticle standard, NIST 8012 30 nm gold, and then calibrating for gold with ionic standards. Knowing then the average counts measured for a reference particle size (counts/ng gold when converted to mass) and the ionic sensitivity (counts per second/ng per mL) allows the sample transport to the plasma to be calculated (mL/s). Table 2 shows the performance for conventional and dry sample introduction for gold:

Table 2. Performance comparison for both nebuliser systems.	Ionic sensitivity, cps/ng per mL	Sample transport rate, µL/s
Wet sample introduction, standard cones	330,000	0.124
Dry Aridus II, ES interface	3,180,000	0.434
Enhancement	9.6	3.5

As can be seen, the desolvating nebuliser increases the overall sensitivity of the ICP-MS by a factor of 10 but when sample transport is considered, the enhancement is only a factor of 3.5. This suggests that there must also be an enhancement in the ionisation and/or ion transport for a dry aerosol compared to conventional sample introduction. Figure 2 shows the count distributions for the same 10 nm gold nanoparticle standard for wet and dry sample introduction systems and Figure 3 and 4 show multi-standard calibrations using 10, 20 and 40 nm gold particles for wet sample introduction and 5, 10 and 20 nm gold particles for dry sample introduction respectively.

Figure 2: Particle count distributions for 10nm standard using wet and dry sample introduction systems on Nu Attom



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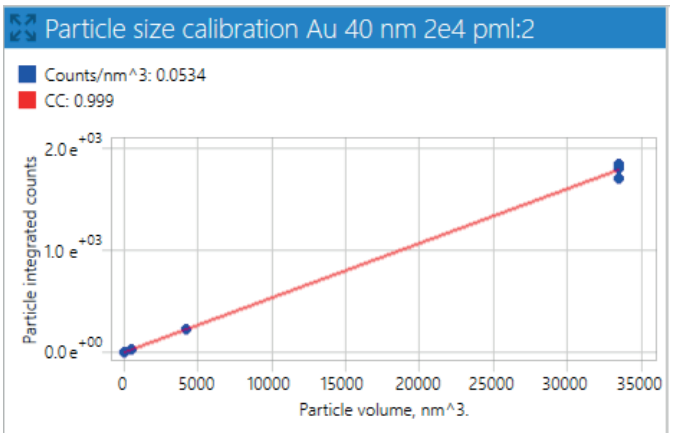


Figure 3: Wet calibration with 10, 20 and 40 nm gold nanoparticle standards.

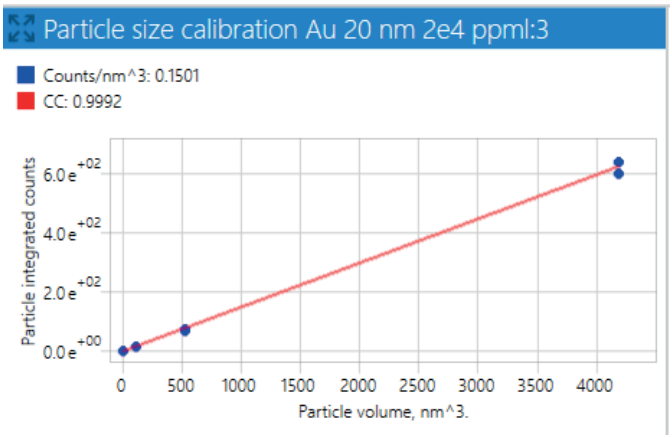


Figure 4: Dry calibration with 5, 10, and 20nm gold nanoparticle standards.

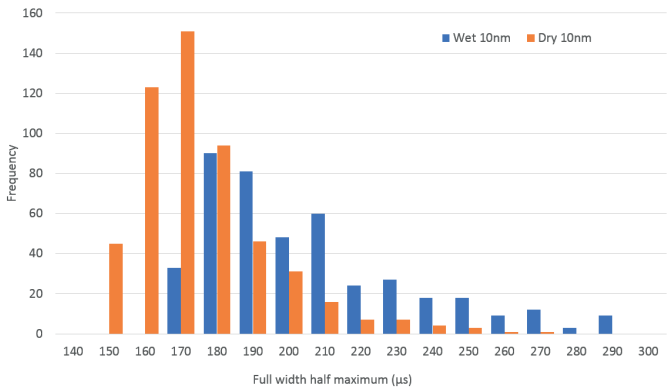
The sensitivity enhancement in terms of counts/nm^3 (or counts/ng) for dry aerosol sample introduction is 2.81. The value expected from the ratio between the overall enhancement of using the desolvation system for an ionic standard (9.6 times more cps/ng per mL) and the increase in particles counted in a given time for a nanoparticle standard (3.5 times more particles per second measured) would have meant that the enhancement in ion transmission would be 2.74.

Improvement in particle detection

The improvement in particle sensitivity makes small particles very easy to detect when the background levels are negligible. When measuring with dwell times of 50 µs, 1 count measured is equivalent to 2x10^4 cps. However, the desolvating nebuliser has a 10x enhancement for ionic signal so this could be the equivalent of as little as 2 ng/L (ppt) of an element. For the use of a desolvating nebuliser to improve the real-world detection of nanoparticles, the overall signal to background needs to increase.

As mentioned previously, with conventional sample introduction, the signal from a nanoparticle is 150-800 µs in duration. As particles volatilise and then ionise in different parts of the plasma and the cloud of ions can diffuse laterally in the central channel, it is typical to see a range of peak widths. The Nu Quant software measures the peak width as full width at half maximum (FWHM) for all detected particles and this can then be plotted to show the distribution of widths. When using a desolvating nebuliser, the peak widths are noticeably more narrow as can be seen in Figure 5 and the example 20 nm nanoparticle gold peaks for the mean width for wet (Figure 6) and dry (Figure 7).

Figure 5. Nanoparticle peak widths (FWHM) for wet and dry sample introduction.



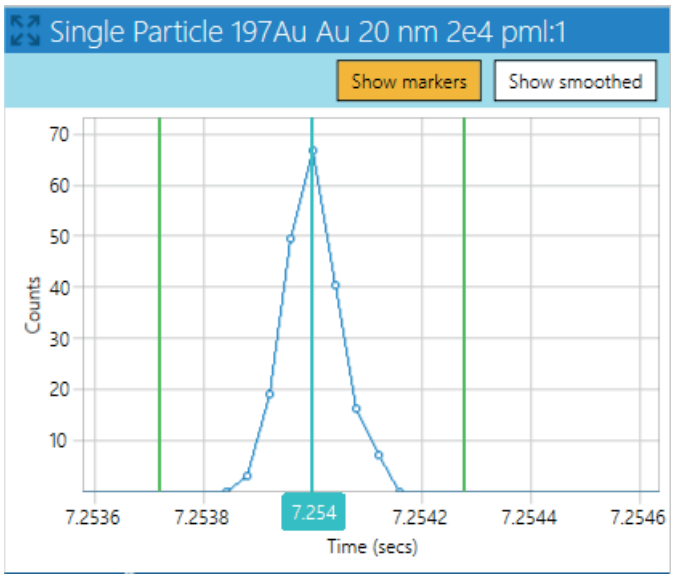


Figure 6: Typical peak shape for a 20 nm gold nanoparticle with wet sample introduction, 40 µs dwell.

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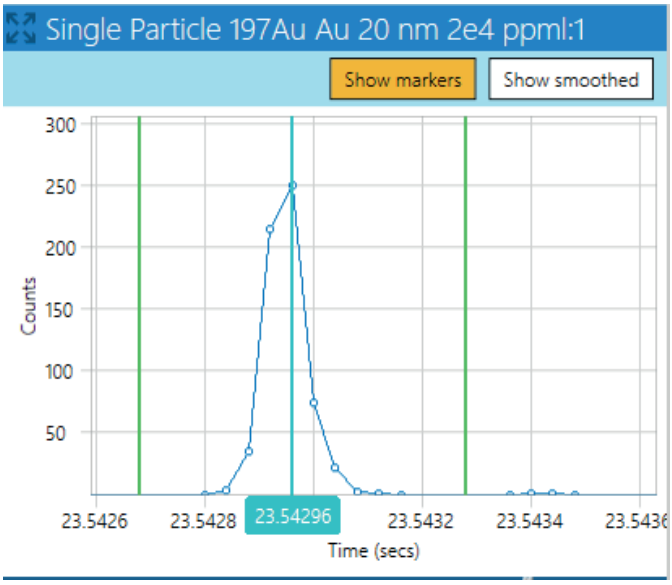

Figure 7: Typical peak shape for a 20 nm gold nanoparticle with dry sample introduction, 40 µs dwell.

The improvement in overall signal and the compression of the signal into a shorter time allows for sub-10nm particles to be fully characterised for many elements with size detection limits below 5 nm. Figures 8-10 show distributions for small particles of gold, platinum and manganese with the raw data display of an identified individual particle at the lower end of the distribution.

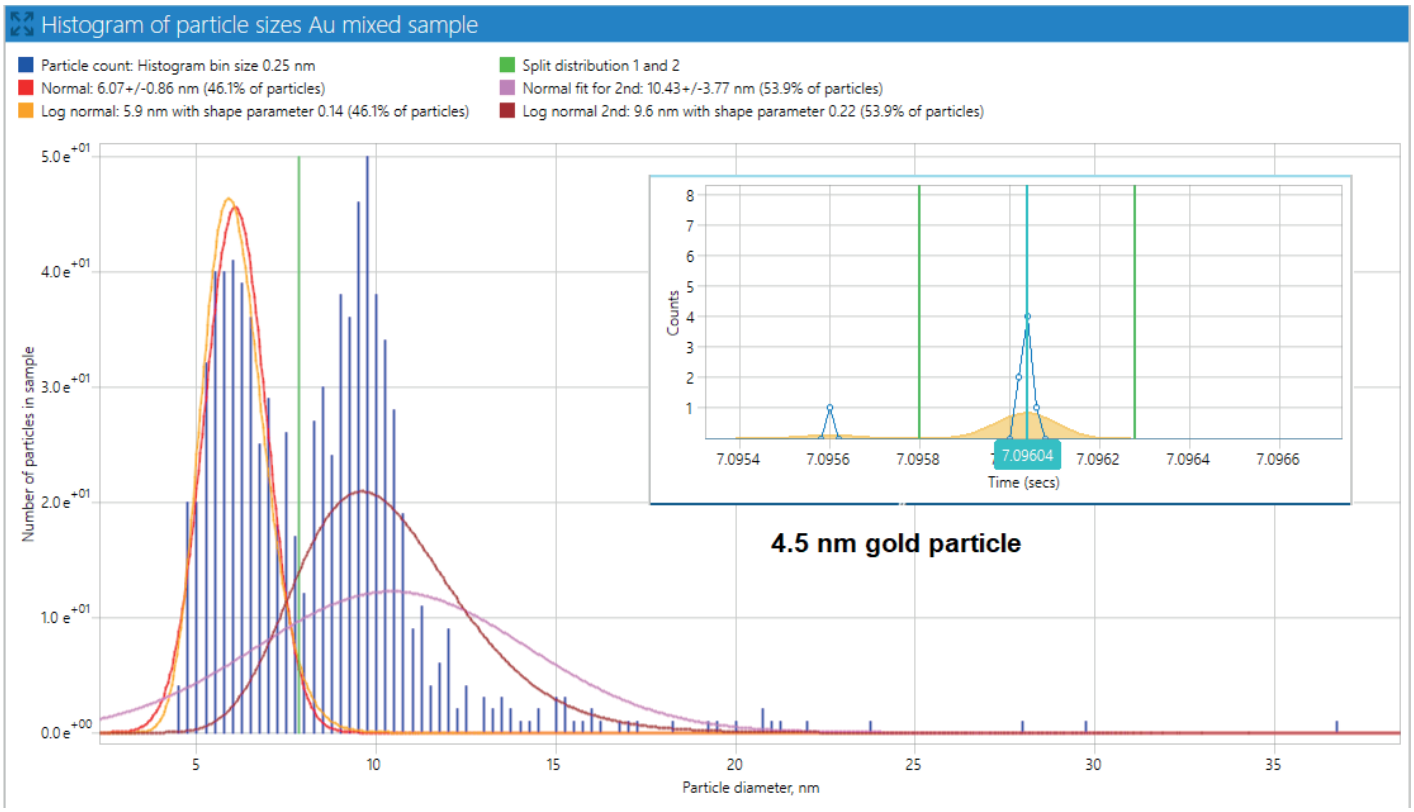

Figure 8: Bi-modal distribution of gold nanoparticles with well-defined measurement of a 4.5 nm particle using 20 µs dwell times.

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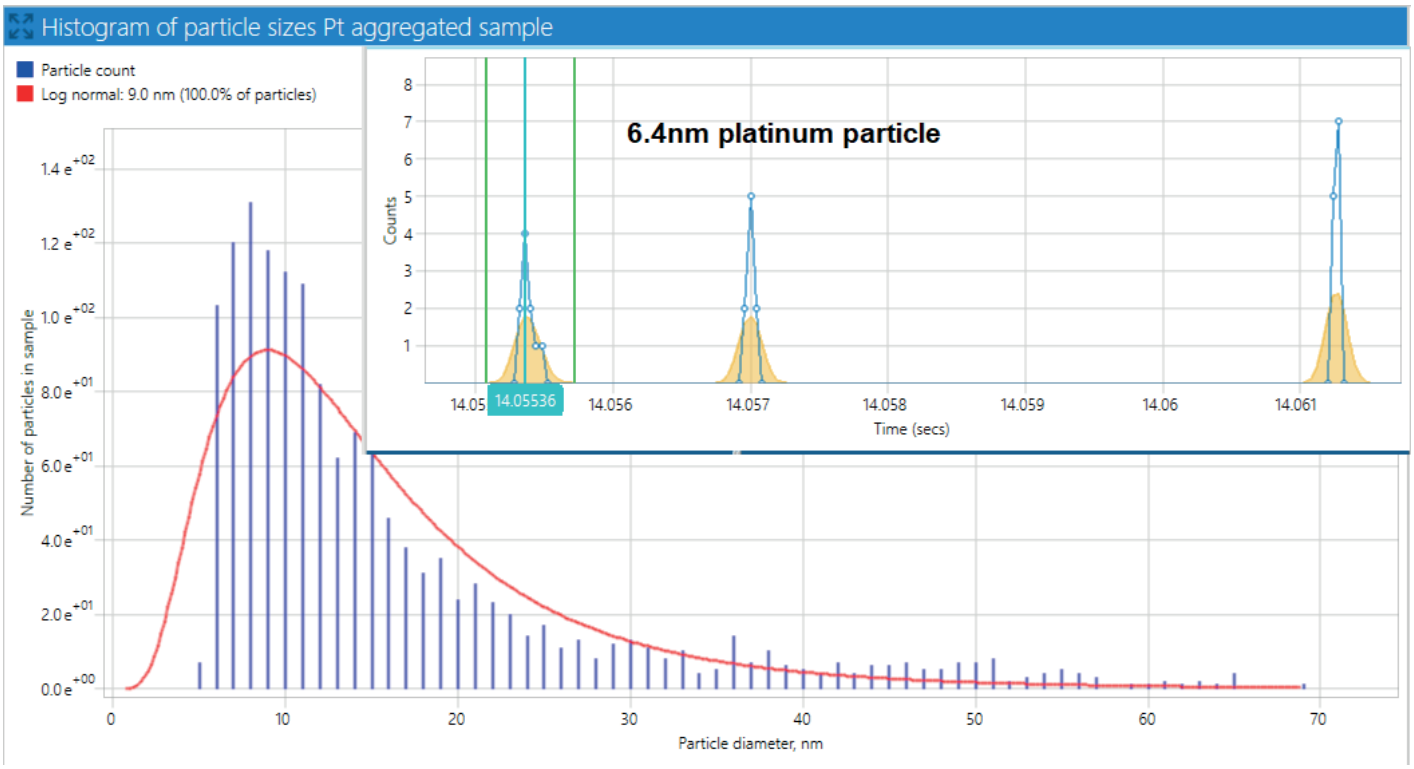

Figure 9: Distribution of small platinum particles with well-defined measurement of ~6-7 nm particles using 40 µs dwell times.

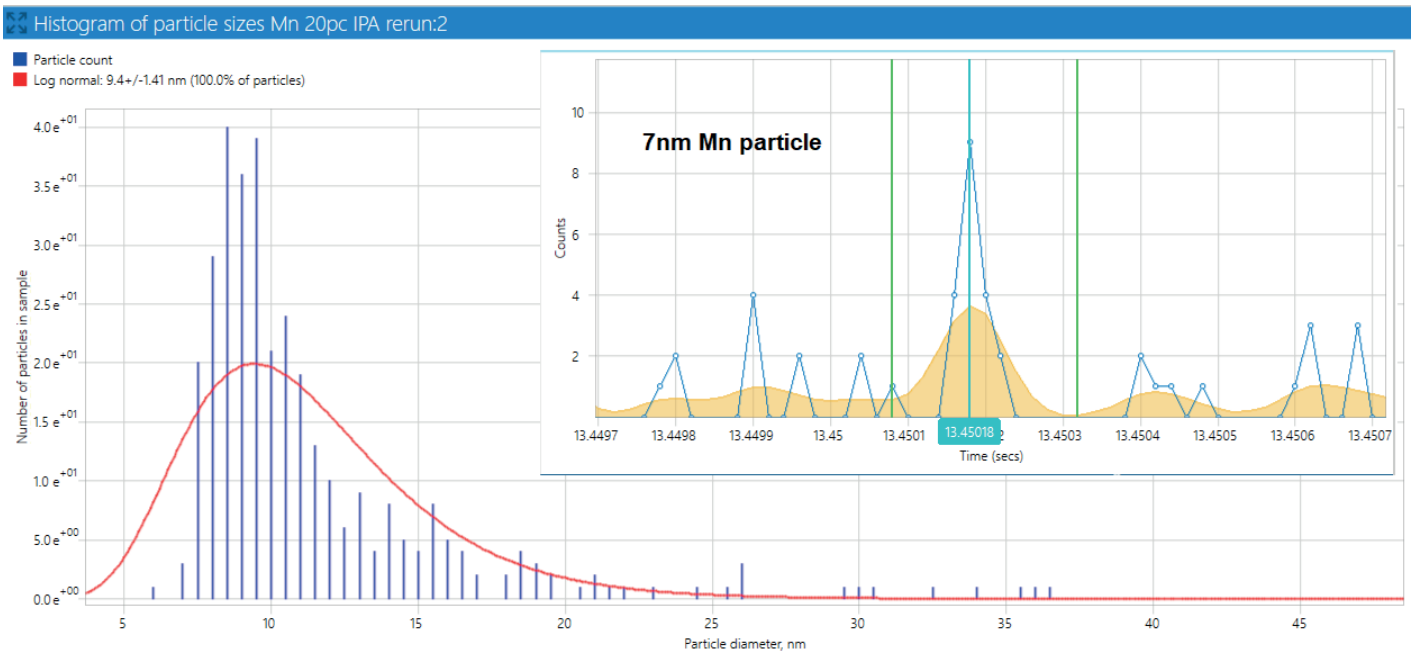

Figure 10: Distribution of manganese nanoparticles in 20% isopropyl alcohol with a well-defined 7 nm particle using 20 µs dwell (with an ionic background of 5.5 ppt, equivalent to 30,000 cps).

Carry-over

When measuring nanoparticles the solutions are very often ultrapure water or very low ionic strength so the particles are not degraded by acids. Care must always be taken to ensure that there is no carry-over in the sample introduction system so particular attention should be paid to use rinse between samples, even using a dilute acid as the rinse using a sequence of sample 1, dilute acid, deionised water, sample 2 etc, with monitoring of blanks periodically in the sample sequence. This was tested when using the Aridus II by running a blank deionised water (Figure 11) and even by aspirating air to check for particle signals (Figure 12). For some elements, particles were always present in the deionised water blank which can be explained by the elements forming particles from weak interactions between the solvated ions which break down with an increase in ionic strength or acid addition. The ionic background for silver when aspirating deionised water was equivalent to 0.2 ng/L and the particle background was 0.002 ng/L by mass – 5 particles in 40 seconds. When aspirating air with the Aridus II no particles were seen indicating that the membrane was not trapping particles causing a memory effect in later samples. The signal background when aspirating air was the equivalent of 0.2 ppt indicating that the background seen was instrument background from silver contamination on the cones.

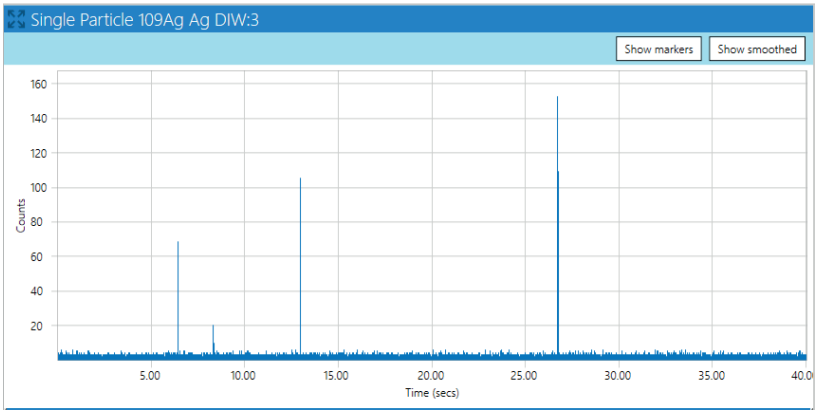

Figure 11: Silver nanoparticles in a deionised water blank after running a set of samples containing nanoparticles.

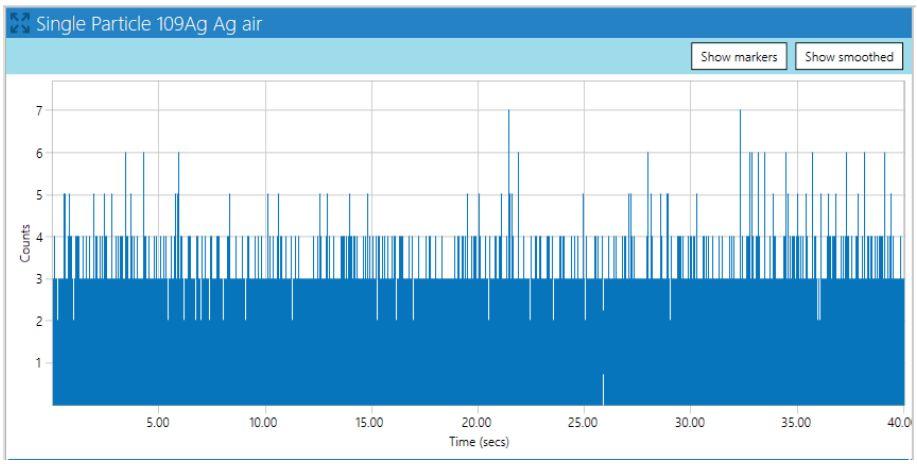

Figure 12: Shows the signal for silver over 40 seconds of aspirating air to show that no particles were captured by the membrane of the Aridus II.

Conclusion

The use of a desolvating nebuliser improves the sensitivity for nanoparticles by approximately 3 in terms of counts/ng of particle and reduces the duration of particle signals so there is significant improvement in the size detection limit. Particles in the range 4-10 nm can be fully distinguished from instrument background levels and the desolvating nebuliser does not show any measurable memory effect with careful use of rinsing between samples and checks with blanks and air aspiration.