Exploring the Accuracy of Isotopic Analyses in Atom Probe Mass Spectrometry

Frederick Meisenkothen^a, Daniel V. Samarov^b, Irina Kalish^{a,c}, and Eric B. Steel^a

^aMaterials Measurement Science Division, National Institute of Standards and Technology, Gaithersburg, MD 20899 U.S.A.

^bStatistical Engineering Division, National Institute of Standards and Technology, Gaithersburg, MD 20899 U.S.A.

^cMATSYS, Inc., Sterling, VA 20164 U.S.A.

<u>Corresponding Author</u>: Frederick Meisenkothen <u>Address</u>: National Institute of Standards and Technology 100 Bureau Drive, MS-8372 Gaithersburg, MD 20899 U.S.A. <u>Email</u>: <u>frederick.meisenkothen@nist.gov</u> <u>Phone Number</u>: 301-975-5181

Abstract

Atom probe tomography (APT) can theoretically deliver accurate chemical and isotopic analyses at a high level of sensitivity, precision, and spatial resolution. However, empirical APT data often contain significant biases that lead to erroneous chemical concentration and isotopic abundance measurements. The present study explores the accuracy of quantitative isotopic analyses performed via atom probe mass spectrometry. A machine learning-based adaptive peak fitting algorithm was developed to provide a reproducible and mathematically defensible means to determine peak shapes and intensities in the mass spectrum for specific ion species. The isotopic abundance measurements made with the atom probe are compared directly with the known isotopic abundance values for each of the materials. Even in the presence of exceedingly high numbers of multi-hit detection events (up to 80 %), and in the absence of any deadtime corrections, our approach produced isotopic abundance measurements having an accuracy consistent with values limited predominantly by counting statistics.

Keywords

atom probe, mass spectrometry, isotopic analysis, peak fitting, multi-hit detection events

Highlights

- APT isotopic measurement accuracy was explored.
- Isotopic analysis accuracy was limited predominantly by counting statistics.
- Machine learning-based peak fitting can improve accuracy and reproducibility.
- Analyses using timing-signal-only-based single-hit data greatly improved accuracy.
- IVAS corrected TOF data appears to contain little or no bias from pulse pile-up.

1.0 Introduction

Atom probe microscopy remains distinct among other forms of mass spectrometric analysis for solid-state specimens. The specimen atoms to be analyzed are field evaporated, not sputtered, ablated, or dissolved in liquid. Ideally, all elements are ionized with equal, and near 100 %, efficiency. The detection efficiency can approach 80 % and be independent of the ion species being detected. Hence, the atom probe can theoretically deliver accurate compositional analyses at a level of sensitivity and precision that would require an analysis volume roughly an order of magnitude larger when analyzed with other forms of mass spectrometry - all without the need for matrix correction algorithms or relative sensitivity factors to convert the ion counts to meaningful fractional abundances. However, the physics of an atom probe measurement can cause significant perturbations from the ideal. The causes for these perturbations can include differences in field ionization potential among elements and compounds; thermal dissipation; single or multiple ion emission by element and compound (on a per pulse basis); specimen shape; detection and analysis related artifacts; and more. Therefore, it can be a complex undertaking to understand chemical composition bias when it occurs. Further, the implication is that quantitative analyses in the atom probe can be trusted only if the chemical composition (or isotopic abundance) is known a-priori, or if additional information (e.g., correlative data from an independent analysis technique) is available to lend confidence to the results obtained via the atom probe [1-11].

Accurate quantitative analyses using atom probe tomography (APT) are hindered by the lack of community-wide accepted procedures for determining the number of ions in any given peak of a mass spectrum, i.e., "ranging," or assigning regions of interest in the mass spectrum to specific ion species. Since the peak form is governed by evaporation physics, material properties, and detector system response, the peak form (including the leading edge and trailing tail of the peak and the peak resolution) varies between different ion species in atom probe spectra, so no single model peak form can be universally applied to all peaks within a single spectrum or between data sets of a given material. Figure 1 illustrates this point by superimposing the various peak forms observed in a single mass spectrum, and the corresponding corrected time-of-flight (TOF) spectrum, from a natural mineral specimen of uraninite. The varying peak resolution means the peak shapes, or forms, must be taken into account (e.g., by using integrated peak intensities) to obtain the most accurate chemical analysis, as demonstrated by Figure 2. Figure 2 shows a hypothetical mass spectrum consisting of three Gaussian peaks. The three peaks each have an identical integrated peak intensity (i.e., area), but a different resolution (i.e., standard deviation). If each peak were to represent a different element, the true concentration of each component would be about 0.333. However, quantification using only the peak maxima will yield erroneous concentration results – blue (left) = 0.57, black (middle) = 0.29, red (right) = 0.14). Since all the peak forms are Gaussian, using the integrated peak intensity at the full width at half maximum (FWHM) would account for the change in resolution and produce accurate quantitative analysis results. However, had each of the three peak forms been different, as often occurs in APT, evaluation using the FWHM would have failed to produce the most accurate analysis result. A quantification strategy that accounts for peak shape is therefore the best option when performing quantitative analyses involving different ion species or the decomposition of overlapping peaks. However, as mentioned above, there is currently no community-wide consensus on how best to address this problem. A few methods have been proposed to decompose atom probe mass spectrum peaks [12-14], including blind deconvolution [15]; however, two approaches are used most often. The analyst either manually selects a region of interest on the mass spectrum to assign to a specific ion species, or a Gaussian or exponentially modified Gaussian function is fit to the peaks. The peak tails are usually modeled as exponential functions [16, 17]. Regardless of the methods used to define regions of interest, for either inter-element or isotopic quantitative analyses, the results often significantly exceed 10 % relative error (We define percent relative error as 100 % × (measured value - accepted value) / accepted value.), and the accuracy may not be reproducible between replicate measurements on the same material [10, 11]. Further, atom probe mass

spectrum peaks are not always well fit by a Gaussian or exponentially modified Gaussian function, and the form of peak tails can be complicated and not well modeled by a single exponential function. Knowledge of the true peak form would be required to assess the integrated peak intensity or to perform an accurate peak decomposition. When working with natural materials, the known isotope abundances are often used to guide the peak decomposition process and remove the contribution of one peak from another in an isobaric peak overlap. Isotopic abundance analysis is, therefore, thought to be fairly accurate in the atom probe. However, in an earlier paper on boron analysis, we found large discrepancies in isotopic abundance measurements could occur [18].

Isotopic abundance measurements in the atom probe are, in many ways, the simplest form of analysis we can perform. For isotopic variants of a single ion species (e.g., ²⁰⁴Pb²⁺, ²⁰⁶Pb²⁺, ²⁰⁷Pb²⁺, ²⁰⁸Pb²⁺), the peaks should be nearly identical in form, since only the mass (number of neutrons) differs between isotopes of the same element. Further, isotopes are chemically and physically alike, within slight variations. Therefore, in absence of deadtime effects, we expect any variations in peak intensity to be solely due to differences in isotopic abundance. Isotopic abundance measurement is, therefore, a way of testing some of the basic assumptions used for quantitative analysis in the atom probe. Indeed, accurate isotopic analysis is a prerequisite for accurate chemical quantification - i.e., if we cannot accurately measure isotopic abundance, we have no hope of accurately measuring complex multi-element and multi-compound chemical compositions. Isotopic abundance measurements, therefore, provide a basis for assessing the ultimate accuracy of atom probe mass spectrometry. Moreover, atom probe-based isotopic abundance measurements have become increasingly common in applications requiring high spatial resolution analyses on inherently nano-scale volumes of material, e.g., nuclear fuels [10, 19], geological materials [20, 21], semiconductor materials [22-26], and meteoritic materials [27-31]. For perspective, the mass of material included in an APT analysis often ranges from a few hundred femtograms down to tens of attograms.

We explore the empirical accuracy of quantitative isotopic abundance measurements via atom probe mass spectrometry to better understand the causes of some limited sources of bias. While the commercial atom probe instrument can deliver 3-dimensional (3-D) chemically resolved images, we will largely ignore the imaging capabilities of the instrument and focus on mass spectrometry. We hypothesize that the peaks of an isotopic series (same charge state and molecular form) have nominally identical peak shapes [15]. While this assumption generally will not hold for inter-element analyses and analyses involving different ions species, it has proved accurate for isotopic variants of a single ion species. The specimen materials used in this study were nominally pure materials having known "natural" isotopic abundances that could be readily compared to measurements made with the atom probe. Different methods for assigning mass spectrum regions to specific ion species are discussed. A machine learning-based adaptive peak fitting algorithm was developed to provide a reproducible and mathematically defensible means for determining peak shapes and intensities for specific ion species. The accuracy of isotopic abundance measurements was evaluated for a wide range of elements, including: lead (Pb), boron (B), tungsten (W), and uranium (U). Even in the presence of exceedingly high numbers of multi-hit detection events (> 80 %), and in absence of any deadtime corrections, accurate isotopic abundance measurements were possible.

2.0 Experiment

2.1 Data Acquisition

A CAMECA, Inc. Local Electrode Atom Probe (LEAP[®]) 4000Si instrument¹ was used for all data acquisition in this study. The instrument is equipped with a UV laser (355 nm) and a straight flight path

¹ Disclaimer

length of 90 mm was employed. The laser polarization direction was fixed parallel to the long axis of the specimen in an effort to maximize the efficiency with which the specimen was heated [32]. The detection efficiency of the ion detection system is approximately 50 % [33].

Specimen materials and data acquisition conditions are provided in Table 1. All the materials are available as nominally pure materials, National Institute of Standards and Technology (NIST) Standard Reference Materials (SRMs®), or Certified Reference Materials (CRMs) - SRM 981 (common lead, isotopic standard), CRM 129-A (triuranium octoxide, natural uranium isotopic standard), natural tungsten, natural boron, and cubic boron nitride (CBN). The materials were of natural origin or designed specifically to mimic natural materials, so the isotopic abundance was known or assumed. Natural boron can have a wide range of isotopic abundance values that depend on the source of the natural boron. The abundance of ¹⁰B has been observed to vary from 0.189 to 0.204. We have elected to use a ¹⁰B abundance of 0.199, since this was listed as the IUPAC representative isotopic composition [34], and it is the abundance NIST has deemed to be most commonly encountered in the laboratory². The atom probe specimens were prepared using conventional lift-out techniques and ion milling techniques in a FEI Nova NanoLab 600 and a FEI Helios NanoLab 660 FIB-SEM [35-37]. The Nova instrument was equipped with an OmniProbe 200 micromanipulator. The Helios instrument was equipped with a FEI EasyLift micromanipulator. The liftout specimens were placed on commercially available flat-top-post silicon atom probe specimen support coupons. The final ion milling step was often done at 5 keV to reduce the amount of ion beam damage and gallium or platinum (in-situ deposited) contamination on the surface of the specimen. The specimen materials and acquisition conditions were specifically chosen to span most of the periodic table and to provide a wide range of values for the fraction of multi-hit detection events - tungsten at the low end of this range (approx. 0.04) and CBN at the high end (approx. 0.8) (Table1).

2.2 Data Analysis

2.2.1 IVAS Analysis

The CAMECA Integrated Visualization and Analysis Software (IVAS[®]) (v3.6.14, v3.8.2) was used to create a 3-D spatial reconstruction of the ions for each data set, using standard procedures discussed in the literature [38-41]. A voltage evolved tip radius and default reconstruction parameters were used for each reconstruction, since the spatial reconstruction was not critical for this work. IVAS was also used to generate corrected TOF and mass spectra for some analyses. Since timing resolution varies with position on a 2-dimensional (2-D) position sensitive detector, peak shape may vary locally within a 3-D reconstruction, even for the same ion species. To reduce this effect, we chose to work with portions of the ion data pattern that were nominally centered on the ion detector and approximately similar in diameter between data sets (approx. $\phi = 50$ mm). The spectra were exported as *.csv files. The ion information was exported to *.ePOS files [42, 43] to permit additional analyses not possible in IVAS. Specialized custom scripts were used to read the *.ePOS files, create additional spectra, range spectra, filter the data by multiplicity, fit peaks, and perform peak decomposition. Using these scripts, it was also possible to remove detection events designated as multi-hit from the 3-D reconstruction data stored in an *.ePOS file. The remaining single-hit-only reconstruction data could then be saved as a *.csv file which was converted into

Certain commercial equipment, instruments, or materials are identified in this paper in order to specify the experimental procedure adequately. Such identification is not intended to imply recommendation or endorsement by the National Institute of Standards and Technology, nor is it intended to imply that the materials or equipment identified are necessarily the best available for the purpose.

² The reader is referred to <u>https://physics.nist.gov/cgi-bin/Compositions/stand_alone.pl?ele=B</u> and <u>https://www.nist.gov/pml/atomic-weights-and-isotopic-compositions-column-descriptions#comp</u>.

a *.POS file using the FileConvert Utility in IVAS, so the native IVAS local range assisted background (LRAB) method could be used on the single-hit reconstructions and mass spectra. The scripts were written in R, a programming language for statistical computing, using the free and open-source integrated development environment, RStudio³.

2.2.2 Ion Ranging Strategies

We compared four different methods for assigning regions of the mass spectrum, or TOF spectrum, to specific ion species (i.e., isotopic variants with the same charge state and molecular form) for quantification. Each charge state was treated as a separate measurement when determining isotopic abundance. The abundance measurements made for each charge state were averaged together to produce the overall abundance measurement that was reported for each sample. In addition to the following four ranging strategies, some analyses used filtered data sets wherein detection events designated as multi-hit had been removed. These analyses are identified as "Filtered", "Singles," or "Single-Hit." The source of the spectrum used for the analysis is indicated as the *.ePOS file (ePOS) or the Cal/Recon Wizard (CRW), since this has a significant impact on the analysis results, as will be discussed below. Various combinations of these analyses to compare with our proposed method.

Local Range Assisted Background Method (LRAB)

LRAB analyses were performed in IVAS using the integrated peak intensities within ion ranges defined by the analyst in the mass spectrum (ePOS). The LRAB model uses a power law extrapolation to estimate peak tail contributions under each adjacent peak and includes a TOF-independent background contribution. Details of the LRAB can be found in the IVAS User Guide. Within the isotopic variants of a given ion species, care was exercised to ensure corresponding regions were selected for each peak and the width of each ion range was identical, under the assumption that all isotopic variants of a given ion species have nominally the same peak form (see section 3.1). Since the choice of the ion range associated with a given isotopic peak is a subjective decision made by the IVAS user, some variability in analysis results can arise from the analyst's decisions. The LRAB analyses were compared under two different data conditions – all ion detection events and single-hit ion detection events.

Maximum Channel Method (Max Channel)

Max Channel analyses use only the channel with the highest ion count for each peak in a family of peaks, i.e., the isotopic variants of a given ion species, in the mass spectrum (ePOS). A constant local background approximation was used under each family of peaks. This background estimate was determined by averaging a collection of spectrum bins immediately to the left of the family of peaks. The number of bins used was dependent upon the bin width in the spectrum, but generally numbered in the tens to hundreds of bins. Since the mass spectrum is a binned histogram, each channel is subject to statistical fluctuations due to counting statistics. The Max Channel method, as defined here, does not compensate for contributions from overlapping peaks. All ion detection events were used in the Max Channel analyses, except where noted otherwise.

Full Width at Half Maximum Method (FWHM)

The FWHM analyses used the integrated peak intensity under the mass spectrum (ePOS) region spanned by the FWHM for each isotope peak in the family of peaks. The channel with the highest ion count for each peak was used to designate the maximum value for that peak. Since the mass spectrum is a binned histogram, each channel is subject to fluctuations due to counting statistics and it is unlikely any single channel will have a count exactly half that of the maximum channel. Therefore, criteria must be established for determining which two channels - one on the leading side of the peak and one on the trailing side of the

³ The reader is referred to <u>https://www.r-project.org/</u> and <u>https://www.rstudio.com/</u>.

peak - define the range of channels spanned at the half maximum. Generally, these two channels were chosen such that the channels themselves had a count above the calculated half maximum, as did all channels between them. For low-count peaks (e.g., ¹⁸⁰W), two channels having a count below the calculated half maximum value could be included in the channels lying between the two channels designating the half maximum positions. The FWHM method used the constant local background approximation under each family of peaks, as defined above for the Max Channel method. Also, the FWHM method, as defined here, does not compensate for contributions from overlapping peaks. All ion detection events were used in the FWHM analyses, except where noted otherwise.

Adaptive Peak Fitting

A machine learning-based adaptive peak fitting algorithm was developed to provide a reproducible and mathematically defensible means to determine peak shapes and intensities for specific ion species in the corrected TOF spectrum (or mass spectrum) and to use this information to calculate isotopic abundances. The algorithm uses a gradient descent approach [44] to minimize the sum of squared residuals (SSR) to find an optimum peak form, subject to the constraints that all isotopic variants of a given ion species will have the same peak form and the spectrum is a linear combination of these component peak spectra. Additional information, including a detailed outline of the code, is provided in the Supplementary Materials for the interested reader. In contrast to the algorithm proposed by Johnson, et al. [15], our algorithm does not perform a true deconvolution in the mathematical sense. Rather, the algorithm decomposes the spectrum into component peaks, each having the same form, that when added together will produce a "best fit" to the empirical spectrum. The peak form is not assumed *a priori*, but rather is determined iteratively and channel-by-channel from the corrected TOF spectrum (or mass spectrum). Another advantage of this method is that it allows contributions from partially overlapping adjacent peaks to be separated from one another without having to make assumptions about isotopic abundance - which is commonly how the peak decomposition problem is handled, but useless when trying to *measure* the isotopic abundance.

Generally, we chose to work with the corrected TOF spectrum exported from the IVAS (CRW) when peak fitting, since TOF is the native domain of the atom probe [15]. Moreover, we might expect adjacent isotopic variant peaks in the corrected TOF spectrum to have less difference between them (at FWHM) than in the corresponding mass spectrum. Therefore, using the corrected TOF spectrum can theoretically reduce fitting errors associated with our assumption that isotopic variants of the same ion species share a common peak form. For example, Figure 1 shows the mass peaks, and their corresponding corrected TOF peaks, for a natural mineral specimen of uraninite. The mass peaks included in Figure 1 span the range from 1 Da to 286 Da. If the mass peak FWHM values are plotted against mass-to-charge state ratio (m/n), a nominally linear plot is the result. Likewise, a plot of the corrected TOF peak FWHM values versus the corrected TOF produces a nominally linear plot. Using a linear least squares approximation, the slope of the corrected TOF peak plot was found to be about half that for the mass peak plot, indicating isotopic variants of a single ion species will have less FWHM variation between them in the corrected TOF spectrum.

Due to the constantly varying standing voltage applied during atom probe data acquisition, the TOF for a given ion (e.g. ¹⁰B²⁺) will vary throughout acquisition. A voltage correction must be applied to the raw data, to in effect, refer all ion flight times to a single reference voltage. Without the voltage correction and a flight path length correction, sharp, clearly defined peaks would not be observed in the TOF spectrum, or the mass spectrum. The parameterized voltage correction used in IVAS calculates a different "optimal" reference voltage for each data set. Therefore, the peak positions observed in the corrected TOF spectra, as reported/exported by IVAS, can vary from data set to data set, even for spectra collected from different samples of the same material. This contrasts with the calibrated peak positions in the mass spectrum reported by IVAS. Direct use of the IVAS corrected TOF spectra are thus less conducive to batch processing because our current adaptive peak fitting algorithms require that the peak positions (and number of isotopes) be entered manually prior to an analysis. Further, the IVAS software has traditionally provided no means

to directly output the corrected TOF information specific to each ion through the *.ePOS file or another file format. As suggested by Johnson, et al. [15], it is possible to transform the calibrated mass peaks to corrected TOF peaks by taking the square root of the (m/n) values and applying a scaling factor. The (m/n)to-corrected TOF conversion relies on the expression, $(t = C * \operatorname{sqrt}(m/n))$, where t is the corrected TOF and C is a constant scaling factor equal to $sqrt((d^2)/2eV)$, where d = flight path length, V = reference voltage, and e = unit electron charge. A reference voltage must be chosen to calculate the scaling factor. It is not clear, which reference voltage should be chosen. However, if the IVAS-calculated "optimal" voltage is used, the corrected TOF peak positions will vary from spectrum to spectrum, as in IVAS. It is also important to mention, the instrument manufacturer has defined the multi-hit detection events in the ion data used by the IVAS (CRW) in a manner different than that used for the ion data reported in the *.ePOS file. The ion detection event information in the IVAS (CRW) is "raw", i.e. timing-signal-based only, and not further defined by the hit finding algorithm. The ion information in the *.ePOS file is recorded after hit finding, ion feedback (IFB) filtering, and other data processing has been applied to the data set. For example, some raw multi-hit events are redefined as single-hit events due to: (1) the prompt IFB software filter or (2) the hit-finding algorithm only resolving one ion from more than six timing signals. Likewise, some raw partialhit events are also redefined as single-hit events. As a result, it is generally not possible to reproduce the unsampled single-hit corrected TOF spectrum reported/exported by IVAS from the (m/n) information provided in the *.ePOS file. The difference in data after the hit-finding treatments can be significant (Table S 1). For example, in our CBN data set, the *.ePOS file recorded almost twice as many single-hit events as were observed in the unsampled single-hit corrected TOF spectrum of the IVAS (CRW). (Table and Figure labels designated with an "S" can be found in the Supplementary Materials.) Interestingly, we found the unsampled single-hit corrected TOF spectrum of the IVAS (CRW), i.e. timing-signal-only-based single-hit detection events, yielded the most accurate isotopic analysis results, not the *.ePOS data (see section 3.3.5 CBN Results and Discussion, below).

The adaptive peak fitting analyses were compared under two different data conditions – all ion detection events and single-hit ion detection events. The method used a constant local background approximation under each family of peaks, as defined above for the Max Channel method. A 0.01 ns bin width was generally used for peak fitting TOF spectra, except where noted otherwise, since this provided both efficient run time and acceptable accuracy. Using too coarse of a bin size (e.g., 0.1 ns) can make it impossible to properly position the peaks to yield an accurate quantitative result, as was also experienced by Johnson, et al. [15] with their blind deconvolution strategy. Using a finer bin size, 0.001 ns, did not yield an accuracy improvement sufficient to justify the additional run time.

3.0 Results and Discussion

3.1 Finding a Common Peak Form

Figure 1 demonstrates how the peak form (including the leading edge and trailing tail of the peak) and peak resolution can vary between different ion species in atom probe spectra. The problem is further illustrated by the portions of the TOF spectra shown in Figure 3 (Figure S 3), Figure 5 (Figure S 4), Figure 7 (Figure S 5, Figure S 6), Figure 9 (Figure S 7), Figure 11 (Figure S 8) for the specimen materials reported in Table 1. The families of peaks have a wide variety of forms with varying degrees of asymmetry. Generally, no single model peak form can be universally applied to all peaks within a single spectrum, or between different spectra collected from the same specimen material. Further, while a component of the resolution varies as a function of (m/n), the peak form does not vary as a systematic and predictable function of (m/n). This can be a problem for quantitative analyses involving inter-element comparisons or analyses between multiple and different ions species. Fortunately, for isotopic analyses within a single spectrum, we have no reason to believe the isotopic variants of a single ion species will have significantly different peak forms. It is for this reason the main constraint imposed by the adaptive peak fitting algorithm is the

requirement that there be a shared peak form between isotopic variants within a single ion species. Likewise, we used corresponding and identically sized regions of interest for the LRAB analyses. Determining a common peak form permits peak decomposition between isotopic variants of an ion species and accurate isotopic analyses, in the presence of complicated tail structures, without *a priori* knowledge of the isotopic abundance.

3.2 Multi-hit Event Artifacts – Using Filtered Data

The atom probe has been described as a point projection microscope merged with a TOF mass spectrometer [16]. In APT, the TOF measurement is initiated by a laser pulse, or a voltage pulse, that is used to promote the field evaporation of, ideally, one ion from the specimen surface – i.e., a single-hit detection event. However, multi-hit detection events are also possible, in which multiple ions are detected in association with a single pulse. Multi-hit events, also referred to as "multiples", are classified according to the number of constituent ions detected in association with a single pulse event, e.g., multiplicity-2 consists of two detected ions on a single pulse [45, 46]. The detected ions can be further classified by the order of arrival, e.g., first-of-multiples (FOM), second-of-multiples (SOM), and third-of-multiples (TOM).

Several mechanisms have been proposed to explain the field evaporation of multiple ions from a specimen during a pulse [46-49], and some elements can be preferentially field evaporated in multi-hit events [46, 49-52]. The constituent ions in multi-hit detection events are often closely correlated in space and time [53, 54], making it difficult for the ion detection system to identify the number of individual ions that impact the detector. The effect is due to detector deadtime and is also known as ion pile-up [55-57]. When pile-up occurs, multiple ion impacts on the detector can be perceived as a single ion by the detection system [18]. It is also possible that no ions will be resolved by the hit finding algorithm. Therefore, ions can be lost in the detection process due to the detector dead-time and different ion species can suffer different degrees of loss. Due to both the detection efficiency being below 100 %, and the effects of detector dead-time, the true multiplicity of a multi-hit event is not known [58].

Multi-hit ion detection events in APT can experience significant signal loss as a result of detector dead time. The signal loss produces bias in the concentration values determined from the mass spectrum [46, 49, 51, 59-61]. Major constituents in the mass spectrum, as well as elements preferentially field evaporated in multi-hit events, will be the most affected [18]. Ideally, a mathematical deadtime correction could be applied to the data set to compensate for this bias. However, the problem of fully correcting for deadtime effects in an atom probe tomography data set is significantly more complex than with other spectrometry methods [62, 63]. Several such deadtime correction algorithms have been proposed in the literature [59, 61, 63, 64]; however, none have seen widespread use. Further, there has been no systematic study to compare the effectiveness of these algorithms on known, or well characterized, reference materials.

IFB is a well-known signal artifact associated with the micro-channel plates (MCPs) used in the single ion detection systems employed in atom probe tomography [65-69]. IFB can produce artifact peaks in the mass spectrum and raise the background signal in regions of the mass spectrum adjacent to major peaks [66, 67]. Each artifact peak is separated from its parent peak by a specific mean TOF difference. The effects of IFB are most pronounced when operating the MCP at a high gain, as is required in APT for single ion detection, or under poor vacuum conditions. Operating the MCP assembly below the saturation mode is generally not recommended for mass spectrometry applications, since this may introduce a relative difference in the detection efficiencies for different (m/n) ions [66]. Therefore, instrument manufacturers employ several strategies to reduce IFB in detection systems, e.g., using multi-stage MCP assemblies with opposing bias angles (i.e., the chevron configuration) [69, 70], applying input surface coatings to the MCP, or employing a software-based IFB filter. IFB is commonly observed in silicon mass spectra. Figure S 1 compares the multi-hit mass spectra for three different multiplicity values in the mass spectrum of a commercially available silicon pre-sharp specimen. In the multiplicity-1 (single-hit) mass spectrum, the Si²⁺ isotope peaks lie in the correct positions and no artifact peaks are apparent. However, the multiplicity-2 mass spectrum contains a significant artifact peak on the high (m/n) side of the ²⁹Si²⁺ peak. The TOF difference between the artifact peak and the parent ²⁸Si²⁺ peak is approximately 5 ns, indicating that the artifact peak is due to IFB. The magnitude of the artifact peak is observed on the high (m/n) side of the ³⁰Si²⁺ peak in the multiplicity-2 spectrum. A second IFB peak is observed on the high (m/n) side of the ³⁰Si²⁺ peak in the multiplicity-3 spectrum. Ion correlation analysis indicates that this second artifact peak is associated with the first artifact peak on the ²⁹Si²⁺ peak and lies at approximately 5 ns from the first artifact peak. The LEAP data acquisition software applies a filter to the raw ion data that removes much of IFB signal from the mass spectrum. Under most circumstances, the IFB filter can work well; however, as demonstrated, the IFB filter can fail under certain circumstances which are not fully understood. The IFB signal can contribute significant false intensity to regions of interest in the multi-hit mass spectrum adding an unquantifiable bias to any measurement that includes a contribution from this artifact.

Peak position shift and loss of resolution are two other artifacts that can be encountered in multi-hit spectra. Figure S 2 shows sections of multiplicity-2 spectra for the natural tungsten specimen, as an example. The W^{2+} ions are properly positioned in the mass spectrum for both the FOM and the SOM. Further, the mass resolution is similar between the FOM and the SOM. Similar behavior was not observed for the W^{3+} ions. A significant peak position shift has occurred between the FOM and SOM ions (+0.07 Da). Also, the mass resolution has significantly degraded between the FOM and SOM spectra. While the reason for the shift and resolution loss in the SOM spectrum is not understood, the implication is clear. Any mass spectrum that includes multi-hit data can suffer some degradation of resolution.

Reducing the number of multi-hit events in a data set, either through data acquisition conditions [18], or through reduction of ion detection efficiency [71] has been shown to improve isotopic abundance and elemental composition measurements. Given the number of artifacts present in the multi-hit spectrum, the multi-hit signal is a major source of bias in quantitative analyses. Therefore, the highest accuracy isotopic analysis measurements are achieved when as much as possible of the multi-hit contribution is removed from the mass spectrum (or TOF spectrum). Unfortunately, this can result in considerable ion signal loss when the fraction of multi-hit detection events is high. However, these ion losses can be tolerated for our experiments in which single-phase reference materials are used.

3.3 Testing Isotopic Analysis Approaches

The accuracy of the isotopic abundance measurement was found to be largely dependent upon the amount of multi-hit detection events in the spectrum and on the ranging strategy employed. We give five examples here, with varying complexity in terms of number of multi-hit ions, peak shape, and peak overlap. Further examples are given in the supplementary materials.

3.3.1 Tungsten (natural, 4 % multi-hits)

The initial testing and evaluation of the adaptive peak fitting algorithm was accomplished with the natural tungsten corrected TOF spectrum. As discussed earlier, we chose to work with the corrected TOF spectrum (CRW) for all adaptive peak fitting analyses. Using the corrected TOF spectrum can reduce the fitting errors associated with our assumption that isotopic variants of the same ion species share a common peak form. Since the tungsten data set has a low fraction of multi-hit detection events, approx. 0.04, the quantitative analysis is expected to have little bias introduced by the multi-hit data. The tungsten spectrum contains five isotopes that are well separated for W^{2+} (Figure S 3) but overlap with one another at W^{3+}

(Figure 3). Even if the overlap is not accounted for when measuring peak intensities, the isotopic abundance should be within a few percent relative error on the expected value. We used the W^{2+} and the W^{3+} peak families in the quantitative analysis. The peak forms of the two tungsten charge states are quite different from one another (Figure 3 and Figure S 3) yet the adaptive peak fitting algorithm successfully discerned the peak shape and decomposed the overlapping peaks. The SSR is based on the fit to the normalized spectrum and provides a measure of the amount of error between the fit and the empirical data. For an exact fit to the empirical data, the SSR will be zero. The SSR values were 1.5 (W^{2+}) and 0.1 (W^{3+}).

Figure 4 shows the results of the isotopic analyses in the form of a radar plot. The axes indicate the percent relative error observed for each of five different measurement methods. The isotopic abundance measurements are tabulated in Table S 2, with the associated percent relative errors reported in Table S 3. The number of single-hit ions recorded for each isotope is reported in Table S 4, for reference. All measurement methods performed well for the four major isotopes, with the relative error < 1.5 % on the accepted value. Comparing the two peak fitting analyses provided in Table S 3 indicates filtering the data to remove multi-hit events did not enhance the accuracy – not surprising, since the data set contained few multi-hit events. The results are supported by the two IVAS analyses provided. Using the ion counts reported in Table S 4, and assuming the number of counts in each bin is Poisson distributed, we can roughly estimate the 1- σ percent relative errors expected on each abundance through counting statistics alone (i.e., $^{180}W = \pm 3.8$ %, $^{182}W = \pm 0.3$ %, $^{183}W = \pm 0.4$ %, $^{184}W = \pm 0.3$ %, $^{186}W = \pm 0.3$ %). Comparing the counting-statistics-related errors with the relative errors reported in Table S 3 shows our Filtered Fit results are consistent with an experiment in which the accuracy is largely limited by the number of ions collected.

Throughout this work, we will refer to isotopes as being arbitrarily major (> 0.1), minor (0.1 – 0.01), or trace (< 0.01) for the abundance range specified in parentheses. Tungsten displays four major isotopes (^{182}W , ^{183}W , ^{184}W , ^{186}W) and one trace isotope (^{180}W). The results for the trace isotope, ^{180}W , showed a lot of variation, due to the low number of counts recorded for the peak, as compared to the four major peaks. Consistent with the other specimen data sets and analyses included in this study, the Max Channel method yielded the least accurate results for minor and trace isotopes.

3.3.2 SRM981 (natural, 16 % multi-hits)

SRM981 is a common-lead isotopic abundance reference material. The corrected TOF spectrum (CRW) was used as the input for the adaptive peak fitting algorithm. The four isotopes observed in the lead spectrum (204 Pb, 206 Pb, 207 Pb, 208 Pb) overlap with one another, as shown in Figure 5 (Pb¹⁺) and Figure S 4 (Pb²⁺). Even if the overlap is not accounted for when measuring peak intensities, the isotopic abundance is expected to be within a few percent relative error on the expected value. We used the Pb¹⁺ and the Pb²⁺ peak families in the quantitative analysis. As with the tungsten, the adaptive peak fitting algorithm successfully discerned the peak shape and decomposed the overlapping peaks in each case. The SSR values, based on the fit to the normalized spectrum, were 0.05 (Pb²⁺) and 0.03 (Pb⁺).

Figure 6 summarizes the results of the SRM981 isotopic analyses. The axes indicate the percent relative error observed for each of five different measurement methods. The isotopic abundance measurements are tabulated in Table S 2, with the associated percent relative errors reported in Table S 3. For reference, the number of ions for each recorded isotope is provided under three different analysis conditions (Table S 5).

The fraction of multi-hit detection events, approx. 0.16, is four times higher than for the tungsten data set. The quantitative analysis results are therefore expected to show some evidence of bias that can be attributed to the multi-hit data. Comparing the two peak fitting analyses in Table S 3 shows better than a factor of 2x improvement in accuracy is observed for all four isotopes after the multi-hit data is removed from the analysis. The results are supported by the two IVAS analyses provided. Filtering out the multi-hit

data and using adaptive peak fitting delivered a relative error < 0.5 % on all four isotopes. Using the ion counts reported in Table S 5, and assuming the number of counts in each bin is Poisson distributed, we can roughly estimate the 1- σ percent relative errors expected on each abundance through counting statistics alone (i.e., $^{204}Pb = \pm 5.9$ %, $^{206}Pb = \pm 1.6$ %, $^{207}Pb = \pm 1.6$ %, $^{208}Pb = \pm 1.2$ %). Comparing the counting-statistics-related errors with the relative errors reported in Table S 3 shows our Filtered Fit results are again well within the range of values expected for an experiment in which the accuracy is mainly limited by the number of ions collected.

Table 2 summarizes the results obtained with the peak fitting algorithm when different bin widths are used in the corrected TOF spectrum. Reducing the bin width from 0.1 ns to 0.01 ns provided > 2x improvement in accuracy – comparable to the accuracy gained by using the 0.01 ns bin size and filtering out the multi-hit events. This improvement in accuracy can be achieved without incurring a prohibitively long run time. The reduction in relative error observed with the finer bin size is attributed to the fitting algorithm being able to better position the peaks in the discrete binned histogram that comprises the spectrum. A peak positioning error of 0.01 ns will inherently provide a better fit, i.e., smaller residual, than a peak positioning error of 0.1 ns.

3.3.3 CRM 129-A (triuranium octoxide, 34 % multi-hits)

CRM 129-A is an uranium oxide (U_3O_8) isotopic reference material synthesized to mimic natural uranium abundance. The corrected TOF spectrum (CRW) was used as the input for the adaptive peak fitting algorithm. A 0.01 ns bin width was used for analysis. We used the UO_2^{1+} , UO_2^{2+} , and the UO_3^{1+} peak families in the quantitative analysis. The two main isotopes observed in the spectrum (²³⁵U, ²³⁸U) overlap with one another, as shown in Figure 7 (UO_2^{2+}), Figure S 5 (UO_2^+) and Figure S 6 (UO_3^+). The fitting of the trace isotope peak proved challenging for the adaptive peak fitting algorithm, since the two isotopes differ in abundance by a factor of 138x. However, the adaptive peak fitting algorithm was able to successfully discern the peak shape and decompose the overlapping peaks for each ion species. The complicated tail structures, including buried hydride peaks, were successfully captured by the fit. The hydride peaks could thus be properly attributed to the respective parent isotope peaks during quantification. The quality of the fit was excellent with the SSR values 0.0002 (UO_2^{2+}), 0.00003 (UO_2^+), and 0.00003 (UO_3^+). The SSR is based on the fit of the normalized spectrum. The sum of squared residual values reported for this material are notably smaller than those found for the other materials in this study. The reason is the large abundance difference between the ²³⁵U and the ²³⁸U, so the fitting result is heavily influenced by the ²³⁸U peak. Natural uranium also has a 234 isotope that we can see a hint of in Figure 7 (approx. 780 ns).

Figure 8 summarizes the results of the CRM 129-A isotopic analyses. The axes indicate the percent relative error observed for each of five different measurement methods. The isotopic abundance measurements are tabulated in Table S 2, with the associated percent relative errors reported in Table S 3. The number of ions associated with each recorded isotope in the single hit spectrum is provided in Table S 6. Using the ion counts reported in Table S 6, and assuming the number of counts in each bin is Poisson distributed, we can roughly estimate the 1- σ percent relative errors expected on each abundance through counting statistics alone (i.e., ²³⁵U = ± 3.0 %, ²³⁸U = ± 0.4 %). Comparing the counting-statistics-related errors with the relative errors reported in Table S 3 shows our Filtered Fit results are again well within the range of values expected for an experiment in which the accuracy is predominantly limited by the number of ions collected.

The fraction of multi-hit detection events, approx. 0.34, is eight times higher than for the tungsten data set. The quantitative analysis results are therefore expected to show evidence of bias that can be attributed to the multi-hit data. Comparing the two peak fitting analyses in Table S 3 shows approx. a 4-fold improvement in accuracy on the trace isotope after the multi-hit data is removed from the analysis. Similarly, the two IVAS analyses show approx. a 4-fold improvement in accuracy for both isotopes after

the multi-hit data is removed from the analysis. Filtering out the multi-hit data and using adaptive peak fitting delivered a relative error < 2 % on both isotopes. The anomalous accuracy reported here for the FWHM method appears to be merely fortuitous. The average of the abundance measurements made on the three different ion species (UO₂²⁺, UO₂¹⁺, and UO₃¹⁺) happened to reduce the relative error. This behavior is not consistent when taken in the company of all other FWHM results shown in Table S 3.

3.3.4 Boron (natural, 64 % multi-hits)

Natural boron provides an interesting test case for performing accurate isotopic analyses. We have chosen to use a ¹⁰B abundance of 0.199, since this is the IUPAC representative isotopic composition and is the value NIST has reported as typically encountered in laboratory environments. We used the B¹⁺ and the B²⁺ peak families in the quantitative analysis. Two boron isotope peaks (¹⁰B, ¹¹B) are observed in the spectrum (Figure 9 and Figure S 7). The peaks tend to have a complicated tail structure, not easily modeled with a single exponential function. Further, the ¹⁰B tail often extends well underneath the ¹¹B peak (Figure 9), making it important to accurately fit and remove the ¹⁰B tail contribution from the ¹¹B peak for accurate quantitative analyses.

The corrected TOF spectrum (CRW) was used in the adaptive peak fitting algorithm, and three bin widths, spanning 3 orders of magnitude, were compared on filtered (single-hit) data (Table 3). An approx. 5-fold improvement in relative error was observed upon switching from a 0.1 ns bin width to a 0.01 ns bin width. However, no significant difference in accuracy was achieved by using a 0.001 ns bin width. A similar trend was observed for the lead analysis above. Therefore, in the interest of maximizing accuracy and minimizing analysis time, the 0.01 ns bin width seems to offer the optimal results – equivalent accuracy and 10x faster processing time over the 0.001 ns bin width.

The fraction of multi-hit detection events, approx. 0.64, is sixteen times higher than for the tungsten data set. The quantitative analysis results are therefore expected to show significant evidence of bias that can be attributed to the multi-hit data. Comparing the two IVAS analyses in Table S 3, a factor of 3x improvement in accuracy is observed for both isotopes after the multi-hit data is removed from the analysis. The difference in results reported for the single-hit and all-event analyses using peak fitting was even more striking, showing an approx. 20-fold improvement in accuracy when the multi-hit data is removed. Filtering out the multi-hit data and using adaptive peak fitting delivers a relative error < 2 % on both isotopes - a huge improvement over the approx. 30 % relative error observed for 10 B in a conventional analysis that includes all detection events.

The adaptive peak fitting algorithm did an excellent job at fitting the peak and tail structure in the TOF spectrum (Figure 9 and Figure S 7). The SSR values, based on the fit to the normalized spectrum, were 0.02 (B²⁺) and 0.004 (B⁺). Figure 10 summarizes the results of the boron isotopic analyses. The axes indicate the percent relative error observed for each of five different measurement methods. The isotopic abundance measurements are tabulated in Table S 2, with the associated percent relative errors reported in Table S 3. For reference, the number of ions for each recorded isotope is provided under four different analysis conditions (Table S 7). Using the ion counts reported in Table S 7, and assuming the number of counts in each bin is Poisson distributed, we can roughly estimate the 1- σ percent relative errors expected on each abundance through counting statistics alone (i.e., ${}^{10}B = \pm 1.3 \%$, ${}^{11}B = \pm 0.8 \%$). Comparing the counting-statistics-related errors with the relative errors reported in Table S 3 shows our Filtered Fit results are consistent with an experiment in which the accuracy is largely limited by the number of ions collected.

In section 2.2.2, Ion Ranging Strategies, we explained that the FWHM for peaks in the corrected TOF spectrum can roughly follow a linear relationship with respect to the corrected TOF (ignoring other aspects of peak shape and determining FWHM per the criteria in section 2.2.2). Defining the percent relative difference between two adjacent peaks as $100 \% \times (FWHM_2 - FWHM_1)/FWHM_1$, where the subscripts

indicate the isotopic variant peak, we can expect the percent relative difference to be larger at lower TOF values. For example, the relative difference in FWHM between ${}^{10}B^{2+}$ and ${}^{11}B^{2+}$ was estimated to be 2 % for corrected TOF (4 % for (m/n)), while the relative difference in FWHM between ${}^{207}Pb^{1+}$ and ${}^{208}Pb^{1+}$ was estimated to be 0.2 % for corrected TOF (0.5 % for (m/n)). Therefore, the accuracy of boron analyses may suffer slightly, since we have assumed isotopic variants within a single ion species have nominally the same peak shape. However, in practice, we did not observe a significant difference in the FWHM values between the isotopic variants of boron within the families of peaks for either the boron or the CBN materials. Any differences were easily accommodated by the "best fit" determined by the peak fitting algorithm, and the resulting accuracy significantly outperformed all other methods tested.

As mentioned above, boron is not an ideal known reference material, since relative to the other elements discussed so far, natural boron can have a wide range of isotopic abundance values that depend on the source of the natural boron. However, boron is useful as a case study to show the utility and validity of the approach used in this manuscript. Boron presents one of the worst cases for multi-hit detection events, and it can also have a complicated peak tail structure. While we do not know the precise isotopic abundance for boron in the natural boron material, it is not crucial for the purposes of this manuscript. Regardless of which natural abundance is chosen here as the reference value, within the specified IUPAC ranges, an analysis using "Singles (CRW) + Fitting" produces the least relative error for both ^{10}B (< 4 % rel. error) and ^{11}B (< 1 % rel. error).

3.3.5 CBN (natural boron, 80 % multi-hits)

CBN provides another interesting boron-based test case for performing accurate isotopic analyses. As with the natural boron sample, we will use a ¹⁰B abundance of 0.199. We used the B^{1+} and the B^{2+} peak families in the quantitative analysis. Two boron isotope peaks (¹⁰B, ¹¹B) are observed in the spectrum (Figure 11 and Figure S 8).

The corrected TOF spectrum (CRW) was used in the adaptive peak fitting algorithm, with a 0.01 ns bin width. The adaptive peak fitting algorithm did an excellent job at fitting the peak and tail structure in the TOF spectrum (Figure 11 and Figure S 8). The SSR values, based on the fit to the normalized spectrum, were 0.02 (B²⁺) and 0.01 (B⁺). Figure 12 summarizes the results of the boron isotopic analyses in the CBN material. The axes indicate the percent relative error observed for each of five different measurement methods. The isotopic abundance measurements are tabulated in Table S 2, with the associated percent relative errors reported in Table S 3. For reference, the number of ions for each recorded isotope is provided under two different analysis conditions (Table S 8). As discussed above for boron, it is worth noting the difference in FWHM between isotopic variants of boron ion species can potentially be significant. However, we did not observe a significant difference in the FWHM values between the isotopic variants of boron within the families of peaks for either the boron or the CBN materials. Using the ion counts reported in Table S 8, and assuming the number of counts in each bin is Poisson distributed, we can roughly estimate the 1- σ percent relative errors expected on each abundance through counting statistics alone (i.e., ${}^{10}B = \pm 4.7 \%$, ${}^{11}B = \pm 2.9 \%$). Comparing the counting-statistics-related errors with the relative errors reported in Table S 3 shows our Filtered Fit results are consistent with an experiment in which the accuracy is limited mainly by the number of ions collected.

The fraction of multi-hit detection events, approx. 0.80, is twenty times higher than for the tungsten data set. The quantitative analysis results are therefore expected to show severe bias that can be attributed to the multi-hit data. Comparing the two peak fitting analyses in Table S 3, shows an approx. 16-fold improvement in accuracy for both isotopes, after the multi-hit data is filtered from the spectrum. Similarly, comparing the two IVAS analyses in Table S 3, an approx. 1.5x improvement in accuracy is observed for both isotopes after the multi-hit data is Filtering out the multi-hit data and using

adaptive peak fitting delivers a relative error < 3 % on both isotopes - a huge improvement over the approx. 45 % to 50 % relative error observed for ¹⁰B in a conventional analysis that includes all detection events.

As mentioned above, natural boron is not an ideal known reference material, as it can have a wide range of isotopic abundance values that depend on the source of the boron. While we do not know the precise isotopic abundance for boron in the CBN material, it is not crucial for the purposes of this manuscript. Regardless of which natural abundance is chosen as the reference value, within the specified IUPAC ranges, an analysis using "Singles (CRW) + Fitting" produces the least relative error for both ¹⁰B and ¹¹B.

Table S 9 and Table S 10 provide the results of "Filtered (ePOS) + Max Channel" and "Filtered (ePOS) + FWHM" analyses for the three data sets that yielded the highest number of multi-hit detection events, i.e., CRM 129-A, boron, and CBN. Comparing the unfiltered Max Channel and FWHM results in Table S 2 and Table S 3 with the corresponding Filtered results in Table S 9 and Table S 10, further demonstrates how filtering out the multi-hit data improves accuracy. However, filtering out the multi-hit data does not alone provide optimal accuracy. Filtering plus accurate peak fitting are, together, required to consistently achieve maximum accuracy. These results are consistent with the hypothesis that the peak shape of all isotopic variants of an ion species are nominally the same. Close examination of Figure 3 (Figure S 3), Figure 5 (Figure S 4), Figure 7 (Figure S 5, Figure S 6), Figure 9 (Figure S 7), Figure 11 (Figure S 8) and the peak fitting results recorded in Table S 2 (Table S 3) and Table S 9 (Table S 10) confirms this assumption is generally applicable.

As mentioned earlier, the multi-hit events in the ion data used by the IVAS (CRW) are defined in a manner different than that used for the ion data reported in the *.ePOS file. We have performed adaptive peak fitting analyses using both the IVAS-generated unsampled corrected TOF spectrum (CRW) and the back-calculated corrected TOF spectrum created from the (m/n) values in the *.ePOS data. The isotopic analysis results employing the IVAS-generated corrected TOF spectrum (CRW) were generally found to be more accurate than the results obtained from the back-calculated single-hit corrected TOF spectrum derived from the *.ePOS data (Table S 11). For B analysis in boron and CBN, the results showed a > 7-fold gain in accuracy by using the unsampled corrected TOF spectrum (CRW). The discrepancy between the single-hit IVAS corrected TOF spectrum (CRW) and the multiplicity information in the *.ePOS file is also expected to adversely impact the accuracy of any quantification method that relies on the *.ePOS data, for example "Filtered (ePOS) +LRAB" analyses.

Our observation, that filtering out as much of the multi-hit signal as possible from the corrected TOF (or mass) spectrum produces inherently accurate results, for all materials studied thus far, is somewhat surprising. Based on our understanding of how the LEAP-4000Si ion detection system works, when pileup occurs, multiple ion impacts on the detector can be perceived as a single ion by the detection system. Therefore, we expect a fraction of the multi-hit signal will be undetected. Similarly, another fraction of the multi-hit signal will contribute to the recorded single-hit spectrum. The contribution of these apparent single-hit detection events cannot be separated from the true single-hit detection events. Further, we expect major constituents in the mass spectrum, as well as elements preferentially field evaporated in multi-hit events, will be the most affected by these pile-up-related effects. As a result, in recorded spectra containing all ion detection events, the major isotopes will be under-reported and minor-to-trace isotopes will appear more abundant. This effect is observed in our results. However, we would expect the opposite to be true for the recorded single-hit spectra, since the ion species most affected by pile-up will contribute most of the apparent single-hit events. Further, we might expect a systematic variation in bias on different ion species (or charge states) based on the relative number of counts associated with each one. However, no such consistent biases were observed in this study. The implication is, for reasons we do not yet understand, isotopic analyses using the IVAS-reported unsampled single-hit corrected TOF spectrum (CRW) are largely unaffected by pulse pile-up contributions. It may be that the contribution of apparent single-hit detection

events to the recorded single-hit spectrum is much lower than anticipated, or perhaps, the ion detection system is doing a very good job at identifying multi-hit detection events, using solely timing signal-based information, even under pile-up situations. It is important to note, the greatest accuracy gains are achieved simply by filtering the data to remove as much of the multi-hit signal as possible, as evidenced by comparing the "All Events (CRW) + Peak Fitting" results to the "Singles (CRW) + Peak Fitting" results in Table S 2 and Table S 3. While the adaptive peak fitting algorithm does contribute to accuracy, the related gains are mostly realized in situations involving complicated tail structures and overlapping peaks.

4.0 Conclusions

We have demonstrated an APT analysis methodology that consistently delivers accurate isotopic analysis results for a variety of elements (boron, tungsten, lead, uranium). The accuracy achieved is within the range of what would be expected for measurements limited predominantly by counting statistics. Accurate results were achieved even in the presence of exceedingly high fractions of multi-hit detection events (> 80 %), and in the absence of any mathematical deadtime correction.

Empirical APT data often contains significant biases that lead to erroneous isotopic abundance measurements. We found a major component of this bias is associated with multi-hit detection events. The greatest accuracy gains are achieved by filtering the data set to remove as much of the multi-hit signal as possible. The more multi-hit detection events in a data set, the greater the observed measurement bias prior to filtering out the multi-hit signal, regardless of the ion ranging strategy employed. However, the ranging strategy does play a role in accuracy, particularly when peak overlaps and complicated peak tail structures are involved in the analysis. Adaptive peak fitting consistently delivers the most accurate results on filtered single-hit data. Specifically, we found using the unsampled single-hit corrected TOF spectrum exported by IVAS (CRW) provided the most accurate analysis results. Generating a single-hit corrected TOF spectrum from the *.ePOS file did not, due, at least in part, to a difference in how the multi-hit events are defined in the file. Currently, this dramatically limits the application of our approach to single phase samples or easily parsed data sets, since the 3-D reconstructed data (*.ePOS data) cannot be used to perform the most accurate analyses. The Max Channel (ePOS) method consistently yields the least accurate results. The FWHM (ePOS) method can deliver high accuracy results, but it is inconsistent - delivering highly accurate results on one data set, but poorly accurate results on another. The IVAS-LRAB (ePOS) solutions generally provide measurement accuracies somewhere in the middle of the measured accuracy ranges. Where the IVAS-LRAB method fails, it is usually because of a mismatch between the actual form of the peak tail and the mathematical model employed by the software to fit the tail. The Singles (ePOS) + IVAS-LRAB analyses also suffer an accuracy loss, because this method relies on the *.ePOS file for single-hit information.

We offer the following guidelines for making accurate isotopic abundance measurements: (1) Work with the IVAS-generated unsampled corrected TOF spectrum (CRW), with a bin width of 0.01 ns or shorter, when possible. (2) Filter the data set to remove the detection events designated as multi-hit. (3) Treat each ion species as a separate measurement for isotopic abundance. (4) Assume all isotopic variants of a given ion species have the same peak form. (5) Use an optimization algorithm to determine an estimate of the common peak form shared by the isotopic variants of a given ion species. (6) Pool the isotopic abundance measurements obtained from each ion species to report the isotopic abundance for the specimen (We used simple averaging with excellent results.). The proposed analysis methodology is only applicable to isotopic analyses, not inter-element analyses. Completely different ion species lying at different positions in the corrected TOF spectrum cannot be relied upon to have the same peak form. Therefore, a fundamental assumption in our methodology would be violated. Further, some elements are preferentially detected in multi-hit detection events and so can be preferentially lost to deadtime effects. Pulse pile-up from multi-hit detection events is expected to contribute to the recorded single-hit spectrum. However, for reasons we do not yet understand, the unsampled single-hit corrected TOF spectrum exported by IVAS appears to contain little or no bias as a result of pulse pile-up contributions when used to perform isotopic analyses – even for analyses with multi-hit fractions as high as 80 %. Further, we observed no systematic variation in bias on different ion species (or charge states), or relative to the number of counts associated with each ion species. Hopefully, the publication of this manuscript will generate some discussion within the community on this topic and yield new insights into the phenomenon behind our observations. Increased access to raw ion data, and a better understanding of the raw data, might enable the development of better approaches to interpretation of the detection events and potentially lead to more accurate and precise analyses.

Acknowledgements

The authors are grateful to Ed Oltman of CAMECA, Inc. for helpful discussions and for suggesting IFB as an explanation for the artifact peak that had been observed in the silicon mass spectra. We would also like to thank Ty Prosa and Robert Ulfig of CAMECA for providing information to explain the detection event discrepancy observed between the IVAS Cal/Recon Wizard corrected TOF spectrum and the *.ePOS data.

Funding Sources

This work was supported by the National Institute of Standards and Technology, Gaithersburg, MD, U.S.A.

References

[1] D.R. Diercks, B.P. Gorman, Nanoscale Measurement of Laser-Induced Temperature Rise and Field Evaporation Effects in CdTe and GaN, The Journal of Physical Chemistry C, 119 (2015) 20623-20631.

[2] D.R. Diercks, B.P. Gorman, R. Kirchhofer, N. Sanford, K. Bertness, M. Brubaker, Atom probe tomography evaporation behavior of C-axis GaN nanowires: Crystallographic, stoichiometric, and detection efficiency aspects, Journal of Applied Physics, 114 (2013) -.

[3] F. Exertier, A. La Fontaine, C. Corcoran, S. Piazolo, E. Belousova, Z. Peng, B. Gault, D.W. Saxey, D. Fougerouse, S.M. Reddy, S. Pedrazzini, P.A.J. Bagot, M.P. Moody, B. Langelier, D.E. Moser, G.A. Botton, F. Vogel, G.B. Thompson, P.T. Blanchard, A.N. Chiaramonti, D.A. Reinhard, K.P. Rice, D.K. Schreiber, K. Kruska, J. Wang, J.M. Cairney, Atom probe tomography analysis of the reference zircon gj-1: An interlaboratory study, Chemical Geology, 495 (2018) 27-35.

[4] H.S. Kitaguchi, S. Lozano-Perez, M.P. Moody, Quantitative analysis of carbon in cementite using pulsed laser atom probe, Ultramicroscopy, 147 (2014) 51-60.

[5] F.A. Laiginhas, A. Perez-Huerta, R.L. Martens, T.J. Prosa, D. Reinhard, Atom Probe Tomography Analysis of Bulk Chemistry in Mineral Standards, Microscopy and Microanalysis, 21 (2015) 843-844.

[6] G.R. Lomboy, D. Isheim, S.P. Shah, Atom probe tomography for Nanomodified Portland cement, in: K. Sobolev, S.P. Shah (Eds.) Nanotechnology in Construction, Springer International Publishing, Switzerland, 2015, pp. 79-85.

[7] A. Pérez-Huerta, F. Laiginhas, D.A. Reinhard, T.J. Prosa, R.L. Martens, Atom probe tomography (APT) of carbonate minerals, Micron, 80 (2016) 83-89.

[8] J.R. Riley, R.A. Bernal, Q. Li, H.D. Espinosa, G.T. Wang, L.J. Lauhon, Atom Probe Tomography of a-Axis GaN Nanowires: Analysis of Nonstoichiometric Evaporation Behavior, ACS Nano, 6 (2012) 3898-3906.

[9] A. Devaraj, R. Colby, W.P. Hess, D.E. Perea, S. Thevuthasan, Role of Photoexcitation and Field Ionization in the Measurement of Accurate Oxide Stoichiometry by Laser-Assisted Atom Probe Tomography, The Journal of Physical Chemistry Letters, 4 (2013) 993-998.

[10] A.J. Fahey, D.E. Perea, J. Bartrand, B.W. Arey, S. Thevuthasan, Uranium isotopic ratio measurements of U 3 O 8 reference materials by atom probe tomography, Journal of Environmental Radioactivity, 153 (2016) 206-213.

[11] D. Hudson, G.D.W. Smith, B. Gault, Optimisation of mass ranging for atom probe microanalysis and application to the corrosion processes in Zr alloys, Ultramicroscopy, 111 (2011) 480-486.

[12] J.M. Cairney, K. Rajan, D. Haley, B. Gault, P.A.J. Bagot, P.-P. Choi, P.J. Felfer, S.P. Ringer, R.K.W. Marceau, M.P. Moody, Mining information from atom probe data, Ultramicroscopy, 159 (2015) 324-337.
[13] D. Haley, P. Choi, D. Raabe, Guided mass spectrum labelling in atom probe tomography, Ultramicroscopy, 159 (2015) 338-345.

[14] A.J. London, D. Haley, M.P. Moody, Single-Ion Deconvolution of Mass Peak Overlaps for Atom Probe Microscopy, Microscopy and Microanalysis, 23 (2017) 300-306.

[15] L.J.S. Johnson, M. Thuvander, K. Stiller, M. Odén, L. Hultman, Blind deconvolution of time-of-flight mass spectra from atom probe tomography, Ultramicroscopy, 132 (2013) 60-64.

[16] G.D.W. Smith, Field Ion Microscopy and Atom Probe Microanalysis, in: ASM Handbook, ASM International, 1986, pp. 583-602.

[17] A. Vella, B. Mazumder, G. Da Costa, B. Deconihout, Field evaporation mechanism of bulk oxides under ultra fast laser illumination, Journal of Applied Physics, 110 (2011) 044321.

[18] F. Meisenkothen, E.B. Steel, T.J. Prosa, K.T. Henry, R. Prakash Kolli, Effects of detector dead-time on quantitative analyses involving boron and multi-hit detection events in atom probe tomography, Ultramicroscopy, 159, Part 1 (2015) 101-111.

[19] B. Valderrama, H.B. Henderson, J. Gan, M.V. Manuel, Influence of instrument conditions on the evaporation behavior of uranium dioxide with UV laser-assisted atom probe tomography, Journal of Nuclear Materials, 459 (2015) 37-43.

[20] J.W. Valley, A.J. Cavosie, T. Ushikubo, D.A. Reinhard, D.F. Lawrence, D.J. Larson, P.H. Clifton, T.F. Kelly, S.A. Wilde, D.E. Moser, M.J. Spicuzza, Hadean age for a post-magma-ocean zircon confirmed by atomprobe tomography, Nature Geosci, 7 (2014) 219-223.

[21] J.W. Valley, D.A. Reinhard, A.J. Cavosie, T. Ushikubo, D.F. Lawrence, D.J. Larson, T.F. Kelly, D.R. Snoeyenbos, A. Strickland, Nano-and micro-geochronology in Hadean and Archean zircons by atom-probe tomography and SIMS: New tools for old minerals⁺ k, American Mineralogist, 100 (2015) 1355-1377.

[22] C.N. Ironside, D.W. Saxey, W.D.A. Rickard, C. Gray, E. McGlynn, S.M. Reddy, N.A. Marks, Atom probe microscopy of zinc isotopic enrichment in ZnO nanorods, AIP Advances, 7 (2017) 025004.

[23] A. Menand, D.R. Kingham, Isotopic variations in field evaporation charge-state of boron ions, Journal of Physics D: Applied Physics, 17 (1984) 203.

[24] O. Moutanabbir, D. Isheim, D.N. Seidman, Y. Kawamura, K.M. Itoh, Ultraviolet-laser atom-probe tomographic three-dimensional atom-by-atom mapping of isotopically modulated Si nanoscopic layers, Applied Physics Letters, 98 (2011) 013111.

[25] Y. Shimizu, Y. Kawamura, M. Uematsu, K.M. Itoh, M. Tomita, M. Sasaki, H. Uchida, M. Takahashi, Atom probe microscopy of three-dimensional distribution of silicon isotopes in [sup 28]Si/[sup 30]Si isotope superlattices with sub-nanometer spatial resolution, Journal of Applied Physics, 106 (2009) 076102.

[26] Y. Shimizu, Y. Kawamura, M. Uematsu, M. Tomita, T. Kinno, N. Okada, M. Kato, H. Uchida, M. Takahashi, H. Ito, H. Ishikawa, Y. Ohji, H. Takamizawa, Y. Nagai, K.M. Itoh, Depth and lateral resolution of laser-assisted atom probe microscopy of silicon revealed by isotopic heterostructures, Journal of Applied Physics, 109 (2011) 036102.

[27] J. Lewis, D. Isheim, C. Floss, T. Daulton, D. Seidman, Atom-Probe Tomography Measurements of Isotopic Ratios of High-field Materials with Corrections and Standardization: a Case Study of the 12 C/13 C of Meteoritic Nanodiamonds, Microscopy and Microanalysis, 21 (2015) 39-40.

[28] J.B. Lewis, D. Isheim, C. Floss, D.N. Seidman, 12C/13C ratio determination in nanodiamonds by atomprobe tomography, Ultramicroscopy, (2015).

[29] J.B.I. Lewis, D.; Floss, C.; Daulton, T.; Seidman, D. N.; Heck, P. R.; Davis, A. M.; Pellin, M. J.; Savina, M. R.; Hiller, J.; Mane, A.; Elam, J.; Auciello, O.; Stephan, T., Meteoritic Nanodiamond Analysis by Atom-Probe Tomography, 43rd Lunar and Planetary Science Conference, held March 19–23, 2012 at The Woodlands, Texas. LPI Contribution No. 1659, id.2192, (2012).

[30] J.I. Lewis, D; Floss, C; Daulton, TL; Seidman, DN; Heck, PR; Davis, AM; Pellin, MJ; Savina, MR; Hiller, J; Mane, A; Elam, JW, Stephan, T Atom-Probe Measurements of Meteoritic Nanodiamonds and Terrestrial Standards, Meteoritic and Planetary Science, (2013) 5296.

[31] P.R.P. Heck, M. J.; Davis, A. M.; Isheim, D.; Seidman, D. N.; Hiller, J.; Mane, A.; Elam, J.; Savina, M. R.;
Auciello, O.; Stephan, T.; Larson, D. J.; Lewis, J.; Floss, C.; Daulton, T. L., Atom-Probe Tomographic Analysis:
Towards Carbon Isotope Ratios in Individual Nanodiamonds, 43rd Lunar and Planetary Science
Conference, held March 19–23, 2012 at The Woodlands, Texas. LPI Contribution No. 1659, id.1790, (2012).
[32] A. Cerezo, G.D.W. Smith, P.H. Clifton, Measurement of temperature rises in the femtosecond laser
pulsed three-dimensional atom probe, Applied Physics Letters, 88 (2006) 154103.

[33] D.J. Larson, T.J. Prosa, R.M. Ulfig, B.P. Geiser, T.F. Kelly, 5.6.1.1 Parameter #1: Efficiency, in: Local Electrode Atom Probe Tomography; A Users Guide, Springer, New York, 2013, pp. 146.

[34] M. Berglund, M.E. Wieser, Isotopic compositions of the elements 2009 (IUPAC Technical Report), Pure Appl. Chem., 83 (2011) 397-410.

[35] M.K. Miller, K.F. Russell, G.B. Thompson, Strategies for Fabricating Atom Probe Specimens With a Dual Beam FIB, Ultramicroscopy, 102 (2005) 287-298.

[36] K. Thompson, B. Gorman, D.J. Larson, B. van Leer, L. Hong, Minimization of Ga Induced FIB Damage Using Low Energy Clean-up, Microscopy and Microanalysis, 12 (2006) 1736-1737.

[37] K. Thompson, D. Lawrence, D.J. Larson, J.D. Olson, T.F. Kelly, B. Gorman, In Situ Site-Specific Specimen Preparation for Atom Probe Tomography, Ultramicroscopy, 107 (2007) 131-139.

[38] P. Bas, A. Bostel, B. Deconihout, D. Blavette, A General Protocol for the Reconstruction of 3D Atom Probe Data, Applied Surface Science, 87-88 (1995) 298-304.

[39] D. Blavette, J.M. Sarrau, A. Bostel, J. Gallot, Direction et Distance d'Analyse a' la Sonde Atomique, Revue de Physique Appliquée, 17 (1982) 435-440.

[40] B.P. Geiser, D.J. Larson, E. Oltman, S. Gerstl, D. Reinhard, T.F. Kelly, T.J. Prosa, Wide-Field-of-View Atom Probe Reconstruction, Microscopy and Microanalysis, 15 (2009) 292-293.

[41] D.J. Larson, T.J. Prosa, R.M. Ulfig, B.P. Geiser, T.F. Kelly, Data Processing and Reconstruction, in: Local Electrode Atom Probe Tomography, Springer, 2013, pp. 109–162.

[42] B. Gault, M.P. Moody, J.M. Cairney, S.P. Ringer, C. Appendix: File Formats Used in APT, in: Atom Probe Microscopy, Springer, New York, 2012, pp. 322-329.

[43] D.J. Larson, T.J. Prosa, R.M. Ulfig, B.P. Geiser, T.F. Kelly, Appendix A: Data File Formats, in: Local Electrode Atom Probe Tomography; A Users Guide, Springer, New York, 2013, pp. 249-256.

[44] A. Cauchy, Méthode générale pour la résolution des systemes d'équations simultanées, Comptes Rendus Hebd. Seances Acad. Sci., 25 (1847) 536-538.

[45] F. Tang, B. Gault, S.P. Ringer, J.M. Cairney, Optimization of pulsed laser atom probe (PLAP) for the analysis of nanocomposite Ti–Si–N films, Ultramicroscopy, 110 (2010) 836-843.

[46] L. Yao, B. Gault, J.M. Cairney, S.P. Ringer, On the multiplicity of field evaporation events in atom probe: A new dimension to the analysis of mass spectra, Philosophical Magazine Letters, 90 (2010) 121-129.

[47] F. De Geuser, B. Gault, A. Bostel, F. Vurpillot, Correlated field evaporation as seen by atom probe tomography, Surface Science, 601 (2007) 536-543.

[48] M. Gruber, F. Vurpillot, A. Bostel, B. Deconihout, Field Evaporation: A Kinetic Monte Carlo Approach on the Influence of Temperature, Surface Science, 605 (2011) 2025-2031.

[49] E.A. Marquis, J.M. Hyde, Applications of atom-probe tomography to the characterisation of solute behaviours, Materials Science and Engineering: R: Reports, 69 (2010) 37-62.

[50] B. Gault, M.P. Moody, J.M. Cairney, S.P. Ringer, 8.1.4 Analyses of Multi-hit Detector Events, in: Atom Probe Microscopy, Springer, New York, 2012, pp. 222-225.

[51] T. Kinno, H. Akutsu, M. Tomita, S. Kawanaka, T. Sonehara, A. Hokazono, L. Renaud, I. Martin, R. Benbalagh, B. Sallé, S. Takeno, Influence of Multi-Hit Capability on Quantitative Measurement of NiPtSi Thin Film with Laser-Assisted Atom Probe Tomography, Applied Surface Science, (2012).

[52] P. Ronsheim, P. Flaitz, M. Hatzistergos, C. Molella, K. Thompson, R. Alvis, Impurity measurements in silicon with D-SIMS and atom probe tomography, Applied Surface Science, 255 (2008) 1547-1550.

[53] M.K. Miller, Appendix C Predictions of Low Temperature Evaporation Fields and Charge States for the Elements, in: Atom Probe Tomography Analysis at the Atomic Level, Kluwer Academic/Plenum Publishers, New York, 2000, pp. 222-223.

[54] M.K. Miller, 5.3 Preferential Retention and Evaporation, in: Atom Probe Tomography Analysis at the Atomic Level, Kluwer Academic/Plenum Publishers, New York, 2000, pp. 127-129.

[55] B. Gault, M.P. Moody, J.M. Cairney, S.P. Ringer, 3.2.1 Experimental Setup, in: Atom Probe Microscopy, Springer, New York, 2012, pp. 43-47.

[56] M.K. Miller, 5.4.3 Ion Pile Up, in: Atom Probe Tomography Analysis at the Atomic Level, Kluwer Academic/Plenum Publishers, New York, 2000, pp. 134.

[57] M.K. Miller, A. Cerezo, M.G. Hetherington, G.D.W. Smith, 5.1.3 Pile-up Correction, in: Atom Probe Field Ion Microscopy, Oxford University Press, 1996, pp. 277-281.

[58] F. Meisenkothen, T.J. Prosa, E.B. Steel, R.P. Kolli, The role of multi-hit detection events on the accurate measurement of boron in atom probe tomography, Microscopy and Microanalysis, 20 (2014) 1962-1963.
[59] A. Cerezo, G. Smith, A. Waugh, The FIM100 - Performance of a Commercial Atom Probe System, Journal de Physique Collogues, 45 (1984) 329-335.

[60] U. Rolander, H.O. Andren, Statistical Correction for Pile-Up in the Atom-Probe Detector System, Journal de Physique Colloques, 50 (1989) 529-534.

[61] T.T. Tsong, Y.S. Ng, S.V. Krishnaswamy, Quantification of Atom-Probe FIM Data and an Application to the Investigation of Surface Segregation of Alloys, Applied Physics Letters, 32 (1978) 778-780.

[62] Z. Peng, F. Vurpillot, P.-P. Choi, Y. Li, D. Raabe, B. Gault, On the detection of multiple events in atom probe tomography, Ultramicroscopy, 189 (2018) 54-60.

[63] T. Stephan, P.R. Heck, D. Isheim, J.B. Lewis, Correction of dead time effects in laser-induced desorption time-of-flight mass spectrometry: Applications in atom probe tomography, International Journal of Mass Spectrometry, (2015).

[64] A. Menand, T. Al Kassab, S. Chambreland, J. Sarrau, Atom-Probe Study of Aluminum-Lithium Alloys, Journal de Physique Colloques, 49 (C6) (1988) C6-353-C356-358.

[65] M. Liptak, W.G. Sandie, E.G. Shelley, D.A. Simpson, Microchannel plate electron multiplier for mass spectrometer applications, IEEE Transactions on Nuclear Science, NS-31 (1984) 780-785.

[66] M. Muller, T. Mikoviny, A. Wisthaler, Detector aging induced mass discrimination and non-linearity effects in PTR-ToF-MS, International Journal of Mass Spectrometry, 365-366 (2014) 93-97.

[67] D.M. Murphy, K. Mauersberger, Operation of a microchannel plate counting system in a mass spectrometer, Review of Scientific Instruments, 56 (1985) 220-226.

[68] K. Oba, P. Rehak, Studies of high-gain micro-channel plate photomultipliers, IEEE Transactions on Nuclear Science, NS-28 (1981) 683-688.

[69] J.L. Wiza, Microchannel Plate Detectors, Nuclear Instruments and Methods, 162 (1979) 587-601.

[70] M. Hellsing, L. Karlsson, H.O. Andren, H. Norden, Performance of a microchannel plate ion detector in the energy range 3-25 keV, J. Phys. E: Sci Instrum., 18 (1985) 920-925.

[71] M. Thuvander, A. Kvist, L.J.S. Johnson, J. Weidow, H.-O. Andrén, Reduction of multiple hits in atom probe tomography, Ultramicroscopy, 132 (2013) 81-85.

Tables and Figures for

Exploring the Accuracy of Isotopic Analyses in Atom Probe Mass Spectrometry

	Temperature	Detection Rate	Pulse Energy	Pulse Frequency	Multiples	Pressure
	(К)	(%)	(Ld)	(kHz)	(%)	(Pa)
CBN	25	0.1-1.0	45-700	500	80	4.7E-09
В	44	0.5	20	500	64	1.1E-08
CRM 129-A (U)	57	1	2	250	34	6.5E-08
SRM981 (Pb)	44	1	40	160	16	1.9E-08
Si	44	0.5	0.058	500	19	1.3E-08
w	25	1	200	250	4	1.5E-08

Frederick Meisenkothen, Daniel V. Samarov, Irina Kalish, and Eric B. Steel

Table 1: Specimen acquisition conditions.

SRM981			Measured	Abundance	9
Bin Size (ns)	Detection Events	208	207	206	204
0.1	Single-Hit	0.516	0.223	0.245	0.015
0.01	All	0.516	0.223	0.245	0.015
0.01	Single-Hit	0.522	0.222	0.242	0.014
Reference		0.524	0.221	0.241	0.014
SRM981			Polativa	$E_{rror}(9/)$	
			Relative	EITOI (%)	
Bin Size	Detection		Relative		
Bin Size (ns)	Detection Events	208	207	206	204
Bin Size (ns) 0.1	Detection Events Single-Hit	208 -1.39	207 1.11	206 1.51	204 8.26
Bin Size (ns) 0.1 0.01	Detection Events Single-Hit All	208 -1.39 -1.34	207 1.11 1.05	206 1.51 1.61	204 8.26 5.67

Table 2: Isotopic abundance measurements (CRW, peak fitting) for Pb in common lead isotopic standard, SRM981.

Boron		Measured	Abundance
Bin Size	Detection		
(ns)	Events	11	10
0.01	All	0.743	0.257
0.1	Single-Hit	0.816	0.184
0.01	Single-Hit	0.804	0.196
0.001	Single-Hit	0.803	0.197
Reference		0.801	0.199
Boron		Relative	Error (%)
Bin Size	Detection		
(ns)	Events	11	10
0.01	All	-7.27	29.27
0.1	Single-Hit	1.84	-7.42
0.01	Single-Hit	0.38	-1.55
0.001	Single-Hit	0.28	-1.13

Table 3: Isotopic abundance measurements (CRW, peak fitting) for B in natural boron.



Figure 1: Comparison of spectrum peak forms encountered for a geological specimen - (a) Mass spectrum (ePOS), (b) Corrected TOF spectrum (ePOS). The peak maxima have been brought into coincidence with one another and the ion count for each peak has been normalized to its maximum channel.



Figure 2: Hypothetical mass spectrum consisting of three model Gaussian peaks each having an identical integrated peak intensity, but a different resolution (i.e., standard deviation). The true concentration of each component is therefore about 0.33. Quantification using only the peak maxima will yield erroneous concentration results, i.e., blue (left) = 0.57, black (middle) = 0.29 and red (right) = 0.14.



Figure 3: Tungsten, corrected TOF spectrum (CRW) showing the isotopic variants of the W^{3+} ion species (black dots = empirical data). (a) Blue hollow circles indicate the total result of the adaptive peak fitting algorithm. (b) The individual peaks determined by the adaptive peak fitting algorithm - red triangles (A = 186), green stars (A = 184), magenta inverted triangles (A = 183), cyan asterisks (A = 182), and orange squares (A = 180).



Figure 4: Tungsten percent relative error, comparison of isotopic abundance measurements by different methods – cyan diamonds (A = 186), blue inverted triangles (A = 184), green triangles (A = 183), red circles (A = 182), and black squares (A = 180).



Figure 5: SRM981, corrected TOF spectrum (CRW) showing the isotopic variants of the Pb¹⁺ ion species (black dots = empirical data). (a) Blue hollow circles indicate the total result of the adaptive peak fitting algorithm. (b) The individual peaks determined by the adaptive peak fitting algorithm - red triangles (A = 208), green stars (A = 207), cyan triangles (A = 206), and magenta asterisks (A = 204).



Figure 6: SRM981 percent relative error, comparison of isotopic abundance measurements by different measurement methods – inverted blue triangles (A = 208), green triangles (A = 207), red circles (A = 206), and black squares (A = 204).



Figure 7: CRM 129-A, corrected TOF spectrum (CRW) showing the isotopic variants of the $UO_2^{2^+}$ ion species (black dots = empirical data). (a) Blue hollow circles indicate the total result of the adaptive peak fitting algorithm. (b) The individual peaks determined by the adaptive peak fitting algorithm - red triangles (A = 238) and green stars (A = 235). Note the hydride-related peaks on the trailing tail for each peak.



Figure 8: CRM 129-A, U percent relative error, comparison of isotopic abundance measurements by different methods - - red circles (A = 238) and black squares (A = 235).



Figure 9: Boron, corrected TOF spectrum (CRW) showing the isotopic variants of the B^{2+} ion species (black dots = empirical data). (a) Blue hollow circles indicate the total result of the adaptive peak fitting algorithm. (b) The individual peaks determined by the adaptive peak fitting algorithm – green stars (A = 11) and red triangles (A = 10).



Figure 10: Boron percent relative error, comparison of isotopic abundance measurements by different methods – red circles (A = 11) and black squares (A = 10).



Figure 11: CBN, corrected TOF spectrum (CRW) showing the isotopic variants of the B²⁺ ion species (black dots = empirical data). (a) Blue hollow circles indicate the total result of the adaptive peak fitting algorithm. (b) The individual peaks determined by the adaptive peak fitting algorithm - green stars (A = 11) and red triangles (A = 10).



Figure 12: CBN percent relative error, comparison of isotopic abundance measurements by different methods – red circles (A = 11) and black squares (A = 10).

Supplementary Material for

Exploring the Accuracy of Isotopic Analyses in Atom Probe Mass Spectrometry

Frederick Meisenkothen, Daniel V. Samarov, Irina Kalish, and Eric B. Steel

S2.2.2 Adaptive Peak Fitting Algorithm Outline

The adaptive peak fitting algorithm uses a gradient descent approach to minimize the sum of squared residuals (SSR) to find an optimum peak form, subject to the constraints that all isotopic variants of a given ion species will have the same peak form and the spectrum is a linear combination of these component spectra. The isotopic peak with the highest intensity (highest isotopic abundance) is chosen as the reference component spectrum. Each other component spectrum is generated by creating a copy of the reference component spectrum at the user-defined peak positions and scaling the channel intensities. Therefore, the reference spectrum channel intensities and the scaling factors (one for each component peak spectrum) are the parameters to be optimized by the gradient descent algorithm.

The SSR, is a defined and differentiable multi-variate function, $SSR = f(x_m)$, in which x_m is a point in multi-dimensional space comprised of the scaling factors, B_i , and the n channel intensities in the reference spectrum, S_1 . The gradient descent optimization algorithm seeks to find a local minimum in the function, based on the premise that the SSR at the point, x_m , will decrease with steepest descent in the direction of the negative gradient of the SSR. Therefore, as the algorithm proceeds through each iteration, a sequence of points, $x_m = (x_0, x_1, x_2, ...)$, is generated according to the expression, $x_{m+1} = x_m - \gamma \nabla SSR(x_m)$. Ideally, the sequence of x_m converges to the local minimum.

- I. Import the empirical spectrum data as a vector, E.
 - a. Subset E to limit the analysis to a single family of peaks.
 - b. Save the subset of E as a new vector, R.
 - c. Normalize each channel in R to the maximum channel intensity within R.
 - d. Perform Savitzky-Golay smoothing (optional).
 - e. Determine the number of channels, n, in R.
- II. Enter the user defined parameters.
 - a. Specify the number of isotopes (i.e. peaks) to include in the analysis, p.
 - b. Specify the position of each peak used in the analysis.
 - c. Provide initial estimates for the fitting parameters, $x_0 = (B_i, S_1)$.
 - i. Scaling factors, B_i
 - ii. Reference spectrum channel intensities (the component spectrum corresponding to the most intense peak), S₁
 - d. Set the number of iterations for the gradient descent optimization.
 - e. Specify the step size, γ , for each iteration of the gradient descent.
- III. Initialize the parameters for gradient descent optimization.
 - a. Use the peak positions to determine the corresponding channels between the component spectra (The channel intensities in each component spectrum are

dependent upon the corresponding channel intensities in the other component spectra.).

- b. Generate each component spectrum $(S_2, ..., S_p)$ using peak position, scaling factor, and reference spectrum intensities.
- c. Sum the component spectra $(S_1 + S_2 + ... S_p)$ to produce the first estimate of the empirical spectrum, H.
- d. Calculate the residual vector, r = R H.
- IV. Employ gradient descent optimization to minimize the cost function.
 - a. Calculate the residual using the results of the previous iteration.
 - b. Calculate the gradient of the cost function. The SSR is defined as $SSR = \sum_{i=1}^{n} (R_i H_i)^2$.
 - c. Revise the estimates of the fitting parameters, $x = (B_i, S_1)$.

$$x_{m+1} = x_m - \gamma \nabla SSR(x_m)$$

- d. Revise each component spectrum (S₂, ..., S_p) using the new scaling factors, new reference spectrum channel intensities, and the stored corresponding channel information.
- e. Enforce non-negative solutions and remove fitting artifacts.
 - i. The intensity in all channels below the first left-hand zero crossing point are set to zero.
 - ii. The intensity in all channels above the first right-hand zero crossing point are set to zero.
- f. Sum the component spectra $(S_1 + S_2 + ... S_p)$ to produce a revised estimate of the empirical spectrum, H.
- g. Repeat steps a f for the specified number of iterations.
- V. Assess results
 - a. Plot the total fit and the component spectra superimposed on the empirical spectrum.
 - b. Plot the residual spectrum.
 - i. Identify any characteristic features in the residual spectrum indicating peak position errors or scaling errors (e.g., not enough iterations).
 - ii. Adjust the peak positions accordingly and re-run the program.
 - c. Calculate the isotopic abundance from the final optimized scaling factors. Abundance_i = $B_i / \sum_{i=1}^p B_i$

	Number of S	Number of Single-Hit Events		
	*.ePOS	Cal/Recon Wizard	(%)	
CBN	679420	383009	77	
Boron	2685241	2066655	30	
CRM 129-A	20811870	18777040	11	
SRM981	1652788	1591915	4	
Tungsten	28742177	26569700	8	

Table S 1: Comparing the number of single-hit events recorded in the *.ePOS file vs. the unsampled IVAS (CRW) corrected TOF spectrum. The manufacturer uses different multi-hit event definitions in the two files.

	Measured Abundance				
CBN	¹⁰ B	¹¹ B			
All Events (ePOS), Max. Channel	0.287	0.713			
All Events (ePOS), FWHM	0.287	0.713			
All Events (ePOS), IVAS (LRAB)	0.299	0.701			
All Events (CRW), Peak Fitting	0.280	0.720			
Singles (ePOS), IVAS (LRAB)	0.272	0.728			
Singles (CRW), Peak Fitting	0.204	0.796			
Accepted Value	0.199	0.801			
Boron	¹⁰ B	¹¹ B			
All Events (ePOS), Max. Channel	0.269	0.731			
All Events (ePOS), FWHM	0.256	0.744			
All Events (ePOS), IVAS (LRAB)	0.263	0.737			
All Events (CRW), Peak Fitting	0.257	0.743			
Singles (ePOS), IVAS (LRAB)	0.220	0.780			
Singles (CRW), Peak Fitting	0.196	0.804			
Accepted Value	0.199	0.801			
	²⁰⁴ Pb	²⁰⁶ Pb	²⁰⁷ Pb	²⁰⁸ Pb	
All Events (ePOS), Max. Channel	0.018	0.240	0.230	0.511	
All Events (ePOS), FWHM	0.014	0.242	0.226	0.518	
All Events (ePOS), IVAS (LRAB)	0.016	0.249	0.226	0.510	
All Events (CRW), Peak Fitting	0.015	0.245	0.223	0.516	
Singles (ePOS), IVAS (LRAB)	0.015	0.245	0.223	0.516	
Singles (CRW), Peak Fitting	0.014	0.242	0.222	0.522	
Accepted Value	0.014	0.241	0.221	0.523	
CRM 129-A	²³⁵ U	²³⁸ U			
All Events (ePOS), Max. Channel	0.0102	0.9898			
All Events (ePOS), FWHM	0.0072	0.9928			
All Events (ePOS), IVAS (LRAB)	0.0094	0.9906			
All Events (CRW), Peak Fitting	0.0077	0.9923			
Singles (ePOS), IVAS (LRAB)	0.0078	0.9922			
Singles (CRW), Peak Fitting	0.0071	0.9929			
Accepted Value	0.0072	0.9927			
Tungsten	¹⁸⁰ W	¹⁸² W	¹⁸³ W	¹⁸⁴ W	¹⁸⁶ W
All Events (ePOS), Max. Channel	0.0014	0.2667	0.1445	0.3066	0.2808
All Events (ePOS), FWHM	0.0011	0.2648	0.1440	0.3069	0.2833
All Events (ePOS), IVAS (LRAB)	0.0012	0.2675	0.1412	0.3061	0.2841
All Events (CRW), Peak Fitting	0.0012	0.2657	0.1431	0.3063	0.2837
Singles (ePOS), IVAS (LRAB)	0.0012	0.2674	0.1412	0.3061	0.2841
Singles (CRW), Peak Fitting	0.0012	0.2640	0.1430	0.3063	0.2856
Accepted Value	0.0012	0.2650	0.1431	0.3064	0.2843

 Table S 2: Comparison of isotopic abundance measurements using different measurement methods.

	Relative Deviation From Accepted Value (%)				ıe (%)
CBN	¹⁰ B	¹¹ B			
All Events (ePOS), Max. Channel	44.09	-10.95			
All Events (ePOS), FWHM	44.11	-10.96			
All Events (ePOS), IVAS (LRAB)	50.50	-12.55			
All Events (CRW), Peak Fitting	40.93	-10.17			
Singles (ePOS), IVAS (LRAB)	36.72	-9.12			
Singles (CRW), Peak Fitting	2.55	-0.63			
Boron	¹⁰ B	¹¹ B			
All Events (ePOS), Max. Channel	35.27	-8.76			
All Events (ePOS), FWHM	28.68	-7.13			
All Events (ePOS), IVAS (LRAB)	32.22	-8.00			
All Events (CRW), Peak Fitting	29.27	-7.27			
Singles (ePOS), IVAS (LRAB)	10.33	-2.57			
Singles (CRW), Peak Fitting	-1.55	0.38			
SRM981	²⁰⁴ Ph	²⁰⁶ Ph	²⁰⁷ Ph	²⁰⁸ Ph	
All Events (ePOS), Max. Channel	27.30	-0.51	4.32	-2.33	
All Events (ePOS), FWHM	0.20	0.06	2.22	-0.97	
All Events (ePOS), IVAS (LRAB)	13.59	2.99	2.13	-2.65	
All Events (CRW), Peak Fitting	7.59	1.80	0.97	-1.44	
Singles (ePOS), IVAS (LRAB)	6.87	1.55	1.03	-1.34	
Singles (CRW), Peak Fitting	-0.23	0.11	0.48	-0.25	
 CRM 129-Δ	235	²³⁸ 11			
All Events (ePOS), Max, Channel	42.06	-0.30			
All Events (ePOS), FWHM	0.16	0.00			
All Events (ePOS), IVAS (LRAB)	30.39	-0.21			
All Events (CRW). Peak Fitting	6.83	-0.04			
Singles (ePOS), IVAS (LRAB)	8.14	-0.05			
Singles (CRW), Peak Fitting	-1.71	0.02			
	100	100	102	104	100
Tungsten	W	¹⁰² W	¹⁰⁵ W	¹⁶⁴ W	W
All Events (ePOS), Max. Channel	12.42	0.63	0.96	0.06	-1.23
All Events (ePOS), FWHM	-11.85	-0.09	0.59	0.16	-0.37
All Events (ePOS), IVAS (LRAB)	0.07	0.93	-1.39	-0.12	-0.08
All Events (CRW), Peak Fitting	-0.96	0.26	-0.01	-0.03	-0.21
Singles (ePOS), IVAS (LRAB)	-0.31	0.91	-1.36	-0.10	-0.09
Singles (CRW), Peak Fitting	-2.81	-0.38	-0.12	-0.04	0.44

Table S 3: Percent relative error for values in Table S 2.

Tungsten		Number of lons					
Bin Size (ns)	Detection Events	186	184	183	182	180	Total
0.01	Single-Hit	172316	185134	86228	159599	711	603988

Table S 4: Total number of ions recorded in the peak maxima (CRW, peak fitting) for W in natural tungsten.

SRM981		Number of lons				
Bin Size (ns)	Detection Events	208	207	206	204	Total
0.1	Single-Hit	268007	114767	126339	7735	516848
0.01	All	11646	5007	5498	333	22484
0.01	Single-Hit	10777	4581	4998	294	20650

Table S 5: Total number of ions recorded in the peak maxima (CRW, peak fitting) for Pb in common lead, SRM981.

CRM 129-A		Number of lons		
Bin Size (ns)	Detection Events	238	235	Total
0.01	Single-Hit	162392	1143	163535

Table S 6: Total number of ions recorded in the peak maxima (CRW, peak fitting) for U in natural uranium, CRM 129-A.

Boron		Nu	umber of Ic	ons
Bin Size (ns)	Detection Events	11	10	Total
0.01	All	64968	22564	87532
0.1	Single-Hit	247533	58017	305550
0.01	Single-Hit	30183	7454	37637
0.001	Single-Hit	3149	780	3929

Table S 7: Total number of ions recorded in the peak maxima (CRW, peak fitting) for B in natural boron.

CBN		N	umber of Io	ons
Bin Size (ns)	Detection Events	11	10	Total
0.01	All	6532	2660	9192
0.01	Single-Hit	2129	550	2679

Table S 8: Total number of ions recorded in the peak maxima (CRW, peak fitting) for B in CBN.

Measured Abundance ¹¹ B
¹¹ B
-
0.746
0.752
0.801
¹¹ B
0.770
0.776
0.801
²³⁸ U
0.9910
0.9933
0.9927

Table S 9: Comparison of isotopic abundance measurements using different measurement methods on filtered single-hit data (ePOS, mass spectrum).

	Relative Deviation From Accepted Value (%)				
CBN	¹⁰ B	¹¹ B			
Singles (Max. Channel)	27.54	-6.84			
Singles (FWHM)	24.40	-6.06			
Boron	¹⁰ B	¹¹ B			
Singles (Max. Channel)	15.70	-3.90			
Singles (FWHM)	12.60	-3.13			
CRM 129-A	²³⁵ U	²³⁸ U			
Singles (Max. Channel)	25.63	-0.18			
Singles (FWHM)	-7.10	0.06			

Table S 10: Percent relative error for values in Table S 9.

Single-hit Corrected	% Relative Error							
TOF Spectrum	¹⁰ B	¹¹ B						
CBN								
ePOS	22.87	-5.68						
CRW	2.55	-0.63						
	¹⁰ B	¹¹ B						
Boron								
ePOS	10.90	-2.71						
CRW	-1.55	0.38						
	²³⁵ U	²³⁸ U						
CRM 129A								
ePOS	-2.80	0.03						
CRW	-1.71	0.02						
	²⁰⁴ Pb	²⁰⁶ Pb	²⁰⁷ Pb	²⁰⁸ Pb				
SRM 981								
ePOS	3.24	0.84	0.70	-0.77				
CRW	-0.23	0.11	0.48	-0.25				
	¹⁸⁰ W	¹⁸² W	¹⁸³ W	¹⁸⁴ W	¹⁸⁶ W			
Tungsten								
ePOS	-2.01	0.24	-0.04	-0.03	-0.20			
CRW	-2.81	-0.38	-0.12	-0.04	0.44			

Table S 11: Comparing the accuracy of isotopic analyses (Singles + Peak Fitting) performed using the single-hit events contained in the *.ePOS file vs. the unsampled IVAS (CRW) corrected TOF spectrum. Isotopic analyses using the CRW corrected TOF spectrum tend to be significantly more accurate for data sets containing a large number of multi-hit detection events.



Figure S 1: Mass spectra extracted at different multiplicity values for the silicon specimen: multiplicity-1 (blue/solid), multiplicity-2 (black/dots), multiplicity-3 (red/50% transparent). The bins in each mass spectrum have been normalized to the height of the ${}^{28}Si^{2+}$ peak. The IFB-related artifact peaks are visible on the high (m/n) side of the ${}^{29}Si^{2+}$ and ${}^{30}Si^{2+}$ peaks.



Figure S 2: Tungsten, multiplicity-2 mass spectra (ePOS, FOM = black/dots, SOM = red/solid). (a) W^{2+} charge state ions. (b) W^{3+} charge state ions. Note that the peaks in the SOM mass spectrum are inexplicably shifted to higher (m/n) values by about 0.07 Da for the W^{3+} charge state.



Figure S 3: Tungsten, corrected TOF spectrum (CRW) showing the isotopic variants of the W^{2+} ion species (black dots = empirical data). (a) Blue hollow circles indicate the total result of the adaptive peak fitting algorithm. (b) The individual peaks determined by the adaptive peak fitting algorithm - red triangles (A = 186), green stars (A = 184), magenta inverted triangles (A = 183), cyan asterisks (A = 182), and orange squares (A = 180).



Figure S 4: SRM981, corrected TOF spectrum (CRW) showing the isotopic variants of the Pb^{2+} ion species (black dots = empirical data). (a) Blue hollow circles indicate the total result of the adaptive peak fitting algorithm. (b) The individual peaks determined by the adaptive peak fitting algorithm - red triangles (A = 208), green stars (A = 207), magenta inverted triangles (A = 206), and cyan asterisks (A = 204).



Figure S 5: CRM 129-A, corrected TOF spectrum (CRW) showing the isotopic variants of the UO_2^{1+} ion species (black dots = empirical data). (a) Blue hollow circles indicate the total result of the adaptive peak fitting algorithm. (b) The individual peaks determined by the adaptive peak fitting algorithm - red triangles (A = 238) and green stars (A = 235). Note the hydride-related peaks on the trailing tail for each peak.



Figure S 6: CRM 129-A, corrected TOF spectrum (CRW) showing the isotopic variants of the UO_3^{1+} ion species (black dots = empirical data). (a) Blue hollow circles indicate the total result of the adaptive peak fitting algorithm. (b) The individual peaks determined by the adaptive peak fitting algorithm - red triangles (A = 238) and green stars (A = 235). Note the hydride-related peaks on the trailing tail for each peak.



Figure S 7: Boron, corrected TOF spectrum (CRW) showing the isotopic variants of the B^{1+} ion species (black dots = empirical data). (a) Blue hollow circles indicate the total result of the adaptive peak fitting algorithm. (b) The individual peaks determined by the adaptive peak fitting algorithm - green stars (A = 11) and red triangles (A = 10).



Figure S 8: CBN, corrected TOF spectrum (CRW) showing the isotopic variants of the B^{1+} ion species (black dots = empirical data). (a) Blue hollow circles indicate the total result of the adaptive peak fitting algorithm. (b) The individual peaks determined by the adaptive peak fitting algorithm - green stars (A = 11) and red triangles (A = 10).