Response to reviewers for the paper:

A multi-instrumental approach for calibrating two real-time mass spectrometers using high performance liquid chromatography and positive matrix factorization

Schueneman et al., *Aerosol Research,* 2024

We thank the reviewers for their useful and constructive comments on our paper and for their time spent reviewing it. To guide the review process, we have copied the reviewer comments in black text. Our responses are in regular blue font. We have responded to all the editor and referee comments and made alterations to our paper (**in bold text**). Changes to text in figure captions are shown ***in bold italic text.*** All line numbers for the changes refer to the discussion manuscript version.

Anonymous Referee #1:

R1.0. Summary: This manuscript presents an extremely thorough study where the authors combine and compare several aerosol instruments together with an HPLC. While the technical aspects of the study, both instrumental and analytical (e.g. PMF analyses) show that the authors clearly know what they are doing, the paper at the same time becomes very technical, and as such, can be tough to follow at times. The target of the study relates to improving calibrations of complex organic aerosol mixtures using state-of-the-art mass spectrometers, which is a very important topic, in particular for the EESI system. However, while there is discussion on the needs for improved calibrations, I find the exact aim, and in particular the main conclusion, largely lacking. Overall, this manuscript presents detailed results from a good experimental study, and I find them suitable for publication in AR, but the manuscript still requires some amount of work to make it more readable and to make more clear what message the authors want to convey with this work. I list my main comments below.

After re-reading the manuscript and after reading the input from both reviewers, we agree that the conclusions were not clearly or succinctly stated. Our revised conclusion reads:

“In this study, we introduced a novel multi-instrumental calibration method for EESI and AMS that uses HPLC and PMF to separate complex standard mixtures and SOA into individual species or sub-groups of species present in the mixture. Our proof-of-concept test using individual pure standards demonstrated close agreement (±20%) between direct and multi-instrumental calibration factors, indicating this method’s quantitative ability. In a second proof-of-concept using a

mostly resolved standard mixture, EESI direct and multi-instrumental calibration factors agree within a factor of 2 for low volatility species. We note that this method is not suitable for semivolatile species whose C^* is similar or higher than the concentration of aerosol sampled inside the SMPS DMA column. These results suggest that this method can be used to reliably determine species sensitivities for completely and mostly resolved chromatograms.

When HPLC alone failed to fully resolve individual analytes, PMF on AMS data successfully resolved individual analytes time series in a simple standard mixture. However, in more complex standard and SOA mixtures, while PMF provided some additional chromatographic separation, the PMF solution showed signs of factor mixing. This was especially evident in the □-pinene+NO_3 SOA mixture, which contained many similar analytes, resulting in a less well resolved PMF solution. While approximate EESI and AMS calibration factors were obtained, these sensitivities are affected by the inherent error in the PMF solution. In practice, while some mixtures may be adequately resolved by HPLC alone, AMS PMF can improve the chemical resolution of complex systems.

Future studies should prioritize improving the chromatography for the system of interest, potentially through changing the column type and/or mobile phase gradients, or using systems with higher intrinsic resolution such as UPLC (Kenseth et al., 2023)**. During the experiments shown in this manuscript we were limited to a C_{18} column, which is primarily suited for separating less polar species. However, in the polar standard mixture shown here and in scenarios involving significant oxidation and smaller precursor gases, the resulting products are likely too polar to be adequately separated by a C_{18} column. In those experiments, a column with a polar stationary phase would allow for the separation of SOA components. Kenseth et al. (2023) showed substantially higher chromatographic resolution with their UPLC system, which would improve the performance of our method.**

In conclusion, our method offers a valuable tool for quantifying EESI and AMS sensitivities in mixtures, especially pertinent for laboratory-generated SOA lacking pure standards or characterized by unknown isomeric forms. This technique can also be applied to other real-time aerosol mass spectrometers. To our knowledge, this technique stands as one of very few available methods for rapid calibration of EESI and AMS for SOA species that are unavailable as pure standards, emphasizing its significance in atmospheric research."

In terms of the more general comment on the technical/hard to follow nature of this manuscript, we have revised the text at multiple locations to improve clarity and simplify

our discussion. They are best reviewed in the tracked changes document, and we do not attempt to reproduce them here.

R1.1. Purpose and main result. Both from the abstract, the introduction, and the conclusions, the sections largely state that existing calibration methods are imperfect, followed by what was (or will be) done in this study. Thus, a clear aim is not clearly outlined, and therefore the conclusions are missing the part where the authors state whether the study was successful or not. The conclusions now state things like "approximate calibration factors were obtained" and "we introduce a new technique for better quantifying instrument responses", but it still remains unclear how much this (quite complicated) approach improved the quantification of OA mixtures, if at all.

See R1.0 above, including a completely revised conclusion section.

We have also revised the abstract to reflect all of the new changes included below:

"Abstract. Obtaining quantitative information for molecular species present in aerosols from real-time **mass spectrometers** such as an Extractive Electrospray time-of-flight Mass Spectrometer (EESI) and an Aerosol Mass Spectrometer (AMS) can be challenging. **Typically, molecular species are calibrated directly through the use of pure standards. However, in some cases (e.g. secondary organic aerosol [SOA] formed from volatile organic compounds [VOCs]) direct calibrations are impossible, as many SOA species can either not be purchased as pure standards or have ambiguous molecular identities. In some cases,** bulk OA sensitivities are used to estimate molecular sensitivities. **This approach is not sufficient for EESI, which measures molecular components of OA, because** different species can have sensitivities that vary by a factor of more than 30. **Here, we introduce a method to obtain EESI calibration factors when standards are not available, and we provide a thorough analysis of the feasibility, performance, and limitations of this new technique. In this method, complex aerosol mixtures were separated with** high performance liquid chromatography (HPLC) followed by aerosol formation via atomization. **The separated aerosols were then measured** by an EESI and **an** AMS, **which allowed us to obtain sensitivities for some species present in standard and SOA mixtures.** Pure compounds were used to test the method and characterize its uncertainties, **and obtained sensitivities were consistent within** ±20% **when comparing** direct **calibrations vs** HPLC **calibrations for a pure standard, and within a factor of 2 for a standard mixture. In some cases,** species were not **completely resolved** by chromatography, **and** Positive Matrix Factorization (PMF) **of** AMS **data** enabled **further separation. This method should be applicable to other real-time MS techniques. Improvements in chromatography are possible that would allow better separation in complex mixtures.** "

R1.1.1. Both abstract and conclusions highlight that the new method matches within 20% with single compound standards, if measured from a simple mixture, but what is the added value then compared to simply running those standards? This 20% is compared to uncertainties of orders of magnitude, but this seems to be comparing quite different things, and should not be taken as a measure of the improvement provided by this new method. The orders of magnitude difference in EESI sensitivity is inherent to that method, and cannot be decreased by any kind of calibration.

We discuss the need for this method in the revised abstract and conclusions sections (see responses to R1.0 and R.1.1 above) and in the newly added Sect. 3.4 (R1.1.2). In short, in many situations standards are not available, so direct calibration is not possible. It is in that situation that this new method can provide unique information.

R1.1.2. The word “real-time” is mentioned in the title and first sentence of the abstract, but this manuscript only shows offline analyses. It also remains unclear to me whether this offline analysis is meant to be a permanent installation to be used also during actual sampling with the EESI or AMS, or simply for calibration. And if only for calibration, would it still need to be included at e.g. a field site, with periodic switching to the HPLC? It seems that if the HPLC calibration is not done for every sample/mixture, the calibrations will have limited use, as the ions in the EESI spectra will represent different isomer distributions for every different mixture. Again, it remains unclear what the purpose and aimed use of this new method ultimately is. What do the authors recommend or expect for others to potentially use this approach in future?

The word “real-time” is needed, since the mass spectrometric detection needs to be much faster than the chromatographic time scale.

We have added the following (P4, intro, line 92-):

“Further, HPLC must be used here because the mass spectrometric detection needs to be much faster than the chromatographic time scale (on the order of seconds). Otherwise, this method is not applicable, and the different species separated by the chromatography would not be sufficiently resolved for speciated detection with the EESI and AMS.”

Although the method has been demonstrated with EESI and AMS here, we believe that it is applicable to any real time aerosol mass spectrometer (including both hard and soft ionization methods). We have added a mention of this fact to the revised conclusions section (see response to R1.0) and the abstract (R1.1). We have also

slightly changed the the title to clarify this point, which now is:

“A multi-instrumental approach for calibrating real-time mass spectrometers using high performance liquid chromatography and positive matrix factorization”

We have also added the following as a new results and discussion section (this will be Sect. 3.4)

“3.4 Discussion on the application of this method

In this paper, a novel technique was introduced that allows for the calibration of real-time mass spectrometers for individual species that cannot be obtained directly. This paper addresses the feasibility, performance, and limitations of this technique, all of which are necessary for any future use of this method.

The original purpose of this method was to calibrate species in SOA formed from laboratory chamber experiments. In many cases, the identity of the species was unknown, or the species could not be purchased as a pure standard. During those chamber experiments, SOA composition was measured in real-time with AMS, EESI, and SMPSs. SOA was also pulled through a Teflon filter, extracted in solvent, injected into the HPLC.

One application of this method would allow calculating yields for different SOA species produced from the oxidation of individual VOCs. This would allow for a better understanding of the chemical and partitioning mechanisms controlling the SOA composition and formation, along with providing information on which species are contributing the most to environmental and human health issues caused by SOA (e.g. higher light absorption or increased toxicity).

Another application is inferring calibration factors for important species in field datasets. This could be done by collecting filters to use with this method, including using UPLC for higher resolution. Alternatively, if specific primary sources or SOA precursors are known to be important for a dataset, those can be sampled in the lab to determine key species and their calibration factors.

One example of a field application is the FIREX-AQ field campaign, where the Jimenez lab at the Univ. of Colorado Boulder operated an EESI (Pagonis et al., 2021). During that campaign, direct calibrations were performed daily

using either 4-nitrocatechol or levoglucosan. In the laboratory, these calibrations were also carried out daily, before chamber experiments and before running the HPLC calibration method. If species-specific sensitivities are obtained in the lab, then they can be ratioed to either 4-nitrocatechol or levoglucosan, providing the relative sensitivity of individual analytes. The relative sensitivity can be referenced to the sensitivities obtained in the field, allowing for the budgeting of ambient SOA for multiple species."

Bringing an HPLC to the field is also possible in principle, but it would require further work to streamline the technique as well as sufficient field personnel.

Regarding the isomers, this is a limitation that we already acknowledged in the submitted version (P3, line 38), as reproduced below:

"EESI can detect individual molecular ions (referred to henceforth as either molecular ions or individual species, even if they may comprise several isomers) from the particle-phase with 1 s time resolution (Lopez-Hilfiker et al., 2019; Pagonis et al., 2021)**."**

R1.2. EESI quantification. Perhaps this relates to the fact that this manuscript is very technical overall, but I was not able to follow how the EESI calibration factors (e.g. Table 2) were determined. For a well-separate ions, the SMPS signal can be compared to the EESI ion, as they both contain the total measured signal. But in the SOA mixture, only some 7 ions were selected for the comparison, but I would assume that the EESI sees hundreds of ions with many of them overlapping in this same range, and these 7 only contribute a fraction of the total signal. Still, they are compared to the PMF factors that together sum up to the entire signal from the SOA. This should be clarified better. I also urge the authors to consider which technical details are important to present in the main text, and what could potentially be moved to the SI, to make the overall story easier to follow.

We have added the following text on P12, line 330, to clarify this point:

"**In step 9, the SMPS was used as the EESI reference for calculating CF_x^E when the analytes were resolved from chromatography alone. As discussed for the mixtures shown in Sect. 3.1, 3.2, and 3.3, we never obtained complete chromatographic separation. In cases of overlapping analytes, the SMPS used here did not have the time-resolution to be used as the EESI reference. Instead, we referenced the EESI to the AMS by first calibrating the total AMS signal to the total SMPS signal for mixed peaks. We then used PMF results for the corrected AMS data and compared individual AMS PMF factors time series to EESI time series to calculate CF_x^E."**

While the EESI does allow us to obtain signals across a wide *m/z* range, it is known from Claflin and Ziemann (Claflin and Ziemann, 2018) that 95% of the SOA made during the reaction of □-pinene+NO_3 is composed of only 8 different species, which are shown in Table 1 in that paper.

We amended the relevant text (P21, line 485) to read:

"This SOA system has been studied in depth previously and **95% of the SOA mass is composed of 8 unique products, shown in Table 1 in Claflin and Ziemann (2018) and Table S6 here** (Claflin and Ziemann, 2018). **Of the 8 known products, we identified molecular ions that are attributed to a monomer (*m/z* 268.1, assumed to be $[C_{10}H_{15}NO_6\text{-}Na]^+$) and 5 dimers. Some of the dimers elute as different isomers, but the EESI HR ions observed corresponded to *m/z* 451.2 ($[C_{20}H_{32}N_2O_8\text{-}Na]^+$), *m/z* 467.2 ($[C_{20}H_{32}N_2O_9\text{-}Na]^+$), *m/z* 483.2 ($[C_{20}H_{32}N_2O_{10}\text{-}Na]^+$), and *m/z* 499.2 ($[C_{21}H_{36}N_2O_{10}\text{-}Na]^+$), all of which were identified in Claflin and Ziemann (2018). We also observed two additional ions, *m/z* 388.2 and *m/z* 465.2, whose structures remain unknown. To better compare the differences in the chromatogram obtained here vs that shown in Claflin and Ziemann (2018), we compare the UV-Vis time series in Fig. S9. The chromatograms are similar, although their chromatogram had slightly better resolution. Differences in observed species could potentially arise due to the age of the SOA extract used here (~1 year) vs. the fresh SOA extract used in that study, fragmentation of species in the EESI (e.g. *m/z* 388.2), or other experimental factors."**

Fig. S9 can be found in the SI. We have simplified Sect. 3.3 (and many of the other sections) to allow for better flow and clarity. We either reworded the text with no loss of content or moved some of the text to the SI, e.g. P19 of the SI now reads:

"Not every peak observed in Claflin and Ziemann (2018) was identified here, which is likely due to lack of EESI sensitivity to some species and potential decomposition of SOA products (specifically for the trimer identified in Claflin and Ziemann (2018)). In contrast, some EESI HR ions that do not correspond to peaks identified in Claflin and Ziemann (2018) were detected here, but structures for those species are unknown. All identified individual peaks are shown in Fig. S13"

Other changes made in response to this comment are shown in the tracked changes version of the revised manuscript and SI.

Specific comments:

R1.3. All the signals in the AMS are very high. How much SOA was collected on the filter in the first place to produce such high concentrations after HPLC separation and atomization?

We are adding the answer to this question in the main text and SI

We have added the following text on P5, line 108-:

"During these experiments, ~372-1378 μg m^{-3} SOA was made within the large reaction chamber. This material was collected on a filter for ~120 minutes at a flow rate of 14 L min^{-1}. Following dissolution in solvent, ~16-56 μg of SOA was injected into the HPLC. Further discussion is included in Sect. S4."

We have also added text to the SI, P16:

"The AMS signal during the □-pinene+NO_3 HPLC experiment was high, ranging from ~ 100-4000 μg m^{-3}. For low volatility species, these high concentrations are not necessary. However, in many systems, the volatility of the produced products will range many orders of magnitude in C^*. To best calibrate for low-volatility and semi-volatile products, higher concentrations of SOA should be injected into the column. For the □-pinene+NO_3 SOA that was shown here, the chamber experiment (as discussed in Claflin and Ziemann, 2018), started with the addition of ~ 200 μg m^{-3} ammonium sulfate seed, 1 ppm of □-pinene, and 0.3 ppm N_2O_5 (in a 8.0 m^3 Teflon FEP chamber). All of the N_2O_5 was reacted, meaning ~0.3 ppm of □-pinene was reacted. The amount of SOA formed can be calculated using the known SOA yields, concentrations, and flow rates.

First, 0.3 ppm □-pinene is converted into a mass concentration. Following this step, the mass concentration is multiplied by the known SOA yield (Eq. S1)

$$SOA\ yield = \frac{\Delta SOA}{\Delta VOC} \qquad \textbf{Eq. S1}$$

The SOA yield for this system ranges from ~ 27- ~ 105% (Boyd et al., 2015)**. If 30% of the □-pinene reacted, then the amount of SOA was formed ranged from 372 μg m^{-3} to 1378 μg m^{-3}. This concentration of aerosol was then collected on a filter at a flow rate of 14 L min^{-1} for 120 minutes. This would imply that 625 μg - 2315 μg of SOA was collected on the filter. Assuming a 100% extraction efficiency of SOA, the amount of material injected into the column can be quantified as such (Eq. S2)**

$$Injected\ mass = \frac{mass\ SOA}{volume\ ACN} \times injected\ volume\ solution \qquad \textbf{Eq. S2}$$

A typical volume of acetonitrile (ACN) used would be ~ 2 mL, therefore the concentration of SOA in ACN would range from 313 μg mL^{-1} - 1158 μg mL^{-1}. The maximum injected volume is 50 μL, therefore the total injected mass ranges from 16 μg - 58 μg.

To confirm these results, we use the largest peak in the chromatogram (*m/z* 451.2, retention time ~ 55 minutes) in an example. According to Claflin and Ziemann (2018),

this peak is responsible for ~ 55% of the total SOA in this system. Therefore, anywhere from 8.8 µg - 32 µg of the injected mass comes from that peak. However, only 0.55% of that mass makes it to the instruments, so the instruments should observe 0.048-0.18 µg.

The observed AMS mass concentration was roughly 2000 µg m^{-3} using the corrected CF_x^A. If we assume the peak is a triangle, we can estimate the area by multiplying the observed peak mass concentration by the total peak elution time (~ 2 minutes on average) and dividing by 2. This value is 2000 µg m^{-3} × min. The AMS flow was ~0.1 L min^{-1} or 1×10^{-4} m^3 min, so the AMS sampled ~0.2 µg, which is very close to the 0.18 µg estimated above.

These injected solution concentrations were able to produce the AMS concentrations observed in Fig. 7, Fig. S8, Fig. S10, and Fig. S12. For species with a volatility (C*) > 100 µg m^{-3}, there would be substantial evaporation, > 50% at equilibrium. While some evaporation would occur for species with a volatility < 100 µg m^{-3}, like 4-nitrocatechol in Fig. 4, the SMPS, AMS, and EESI seem to mostly agree.

It should be noted that, in our setup, < 1% of the injected mass made it to the mass spectrometers. The use of the collected sample could be optimized further, allowing the analysis of smaller amounts of mass by this method."

R1.4. Line 238: "atomic ratio of oxygen plus nitrogen to carbon (O+N:C)". Should this be (O+N):C? If not, then I would not call it a ratio.

We have corrected the text (P9, line 238) as:

"**([O+N]:C)**"

R1.5. Figure 6 K&L: There seems to be a distinct signal at m/z 60 in both these factors. Does that not suggest that part of the levoglucosan signal has been split into these factors?

In Fig. S7, we show the pure calibration AMS mass spectra for malic acid and the PMF factor mass spectra shown in Fig. 6K/L. While we do see some signal at *m/z* 60 in the pure calibration, when compared to the PMF mass spectra, it suggests that there is some *m/z* 60 coming from an additional source (likely levoglucosan).

We do mention that levoglucosan was not fully resolved with PMF (P21, line 468).

We have added this text to the following paragraph (P 21, line 471):

"L-malic acid and citric acid also co-elute with levoglucosan. For citric acid, L-malic acid, and

levoglucosan the mass spectra shown in Fig. 6j-6l are somewhat similar. **For L-malic acid and levogluocsan, m/z 60 makes up some of the observed signal. While m/z 60 is a known levoglucosan AMS ion, the direct calibration mass spectra for malic acid also shows some signal at m/z 60. The PMF mass spectra for L-malic acid has a slightly higher ratio of m/z 60 relative to the other ions, which could suggest that there is some mixing between the L-malic acid and levoglucosan factors."**

R1.6. Line 507: The elemental formulas would be interesting to see also in the main text.

They have been added, see response to R1.2 above.

R1.7. Lines 545-555: Is all this really shown in Table S6? I don't see anything about the sensitivities there.

Table S6 only shows the structures. We have reworded the manuscript to be clearer about this detail (P24, line 542-):

"Further, some EESI HR ions eluted multiple times (e.g. m/z 451.2). Claflin and Ziemann (2018) identified the structure of this ion for the third peak (shown in Table S6). However, this ion is measured twice more, from 38-43 minutes**, which suggests the presence of isomers. Isomers can have different structures (shown in Table S6) and different** CF_x^E**. One example is m/z 483.2, where one isomer has a** CF_x^E **= 327.2 and a second isomer has a** CF_x^E **= 54.2 counts** s^{-1} μg^{-1} m^3**."**

Anonymous Referee #2:

R2.0. Summary: The article of Schueneman et al. introduces a new approach for calibrating two real-time mass spectrometers, EESI and AMS by using the liquid chromatograph and positive matrix factorization.

This method is innovative and provides a novel approach for the calibration of mass spectrometers for individual organic species that are difficult to calibrate by using a traditional atomizer, DMA and CPC setup. It seems that this method is more beneficial for the EESI but can also improve the data analysis of the AMS for the unknown organic species. This manuscript is well-written and fluent but it is rather demanding to read as it has so many technical details and the terminology is difficult to follow at times. This article is suitable for publication in Aerosol Research after minor revision.

General comments:

R2.1. I suggest making the article more concise ja check that the terminology is unambiguous. I also recommend summarizing in Conclusion section the benefits and the limitations of the method (for example this method may not be suitable for volatile species). As already mentioned, this method seems to be more advantageous for the EESI but what are the benefits for the HR-AMS. Does it enable the detection of species at a molecular level in real atmospheric/emission samples?

Per this suggestion, and similar input from reviewer 1, we have changed many parts of the manuscript to more clearly state the important conclusions. Please see the entirety of these responses, as well as the manuscript with tracked changes for the specific edits.

We have summarized our major findings in the conclusion section, which is reproduced in response to comment R1.0. We have also reworked the abstract, see R1.1.

We have added the following text to the conclusions section to clarify the point about semivolatile species:

"We note that this method is not suitable for semivolatile species whose C^* is similar or higher than the concentration of aerosol sampled inside the SMPS DMA column."

This method can be useful for EESI, AMS, and/or other real-time aerosol mass spectrometers. See response to R1.0 for further details and added text on this point.

Specific comments:

R2.2. Page 1 (abstract), line 17; "enable their direct calibration", this direct calibration does not refer to same direct calibration as that used earlier in the abstract and later in the

manuscript (monodisperse aerosol with an atomizer)?

This sentence is no longer in the abstract (R1.1).

R2.3. page 5, line 117; “the SOA is unlikely to have changed over this period (one year)”, this is somewhat contradictory as it is said in Page 22 that the differences in the UV-Vis chromatograms could potentially rise due to the age of the SOA extract used here (~1 year)

We have changed the following text to read (P5, line 117):

“That study showed that the SOA is composed entirely of acetal dimers, which are exceptionally stable, so the SOA is unlikely to have changed **significantly** over this period.”

As a result of improving the flow of the manuscript (see response to R1.0), we removed the sentence about the age of the SOA on P22.

R2.4. page 8, lines 207-208; I suggest to change “calibration factor CFxE“ to “EESI calibration factor CFxE”. There is also one parenthesis missing.

We have made the suggested change and added the parenthesis (P8, lines 207-208):

“Here, we define a new variable, **EESI** calibration factor (CF_x^E, in μg m^{-3} $counts^{-1}$ s), such that…”

R2.5. page 9, lines 119-220; “background remained < 2 μg/m3”. That sounds quite large to me. How much was it relative to the peak concentrations? What are the detection limits of this method for the species? What was the source of the background signal, only solvent?

The background was < 2 μg m^{-3} in between peaks as they eluted from the column. The background when the HPLC was not running was < 0.1 μg m^{-3}. This suggests that the AMS and SMPS backgrounds during the HPLC run were caused by impurities in the HPLC solvents or a small amount of contamination from prior HPLC runs.

We have modified the relevant text to provide additional clarity (P9, lines 219-221):

“AMS backgrounds were measured for 6 seconds every 52 seconds. **Outside of HPLC runs, the AMS background was < 0.1 μg m^{-3}. Between eluting peaks** additional backgrounds **were taken** to test for solvent **residue and/or residual influence from previous HPLC runs. These backgrounds were generally < 2 μg m^{-3} for both the AMS and the SMPSs. The detection limit (DL) and limit of quantification between eluting peaks was 0.7 μg m^{-3} and 2.2 μg m^{-3}, respectively, suggesting that background-subtracted concentrations above 2.2 μg m^{-3} can be accurately measured.**”

We note that Figures 4 and 7 show that the lowest measured mass was ~ 30 μg m^{-3} (Fig. 7).

R2.6. page 9, line 228-229; I suggest changing “response factor” to “AMS response factor”

We have made the requested addition (P9, lines 228-230):

“Here, the quantification of different particle-phase species that have been separated by HPLC (and thus are mostly in single component particles) is assessed for the AMS. This is a function of RIE_X*CE_X (a.k.a. “**AMS** response factor”, or) for a species X”

R2.7. page 9, line 230-231; “An RIE of 1.4 is typically applied to ambient aerosol.” I don’t see any reason to use a single RIE value for total ambient aerosol. Should this be “to ambient OA”?

This was a mistake, we have corrected it to say (P9, lines 231-232):

“An RIE of 1.4 is typically applied to ambient **organic** aerosols (Canagaratna et al., 2007)”

R2.8. page 11, lines 315-316; I suggest adding the instruments used to calculate composition-dependent density (SMPS, AMS) as they are mentioned in all the other cases.

We have made the following change (P11, lines 316-317):

“Calculation of composition-dependent density using the measured elemental composition or d_{va}/d_m measured densities **from AMS and SMPS data**.”

R2.9. Page 13, Section 3.1. Mass Balance of the Analyte in the Experimental System; this section could be moved to Supplemental material

This section is simple and relatively short. It needs to be kept in the main paper as any other users of this method in the future may want to replicate this mass balance for their system. It also points out that much more efficient use of the sample material than in this study is possible.

R2.10. Page 13-14; lines 358-363; The description of the direct calibration method should be in the methods section.

We removed the text on P13-14 and added it to P10. The paper now reads as (P10, lines 276-282):

“**2.5.4 Direct Calibration Procedure**

Direct calibration refers to the standard method of generating monodisperse aerosol from a calibrant solution with a Collison atomizer (TSI model 3076) drying with a

Nafion dryer, size selecting at 275 nm with a TSI 3080 electrostatic classifier / 3081 DMA, removing double-charged particles with an impactor, measuring the particle concentration with a 3775 CPC, and measuring with the EESI and/or AMS. The EESI and AMS sensitivities were obtained by comparing their signals to the particle mass calculated from the known particle volume, estimated density, and CPC particle concentration."

We also edited the text on P13-14 as:

"These species were first calibrated directly in order to obtain CF_x^E and CF_x^A**, as described in Sect. 2.5.4.**"

R2.11. Page 14, Figure 3 caption; What is the difference between uncalibrated and raw data? "Monodisperse calibration factor" needs to be explained.

This caption has been revised to read (P14, Fig. 3 caption):

"Figure 3. Single standard calibrations for (A) uncalibrated HPLC data for phthalic acid, (B) uncalibrated HPLC data for 4-nitrocatechol, (C) HPLC phthalic acid data calibrated using the sensitivity derived from the direct calibration, (D) HPLC 4-nitrocatechol data calibrated using the sensitivity derived from the direct calibration, (E) integrated Gaussian peaks from (C), and (F) integrated Gaussian peaks from (D)."

R2.12. Page 18, Figure 5; If this is a 6-factor solution, what is the 6th factor? Figure shows the time series and mass spectra only for 5 factors. Same comment for Figure 6, what are the other factors?

The other factor was the background factor in all cases. The PMF background factor was < 2 μg m^{-3}. We changed the caption for Figure 5 (P18):

"Figure 5. Time series for the ***AMS*** *PMF solution, (A) stacked plot of each factor and AMS NO_3, (B)-(F) PMF factor with CF_x^A applied to individual species, along with EESI concentrations. (G) $Q/Q_{expected}$ vs. number of PMF factors, chosen solution circled in yellow. (H)-(L) mass spectra (colored by associated AMS HR family) for each AMS PMF factor.* ***A 6 factor solution was chosen, with only 5 factors plotted here. The remaining factor was attributed to the background signal, and was < 2 μg m^{-3} at all times."***

We also changed the caption for Figure 6:

"Figure 6. (A) time series of AMS total OA (assumed =1.4), EESI HR ion, and absorbance (max=4×10^6, milli-absorbance units). (B)-(G) AMS PMF factor (assumed =1.4) and EESI

HR ion for 6 calibrants. (H) Stacked PMF factor solution time-series, (G) $Q/Q_{expected}$ for AMS PMF solution, a 9-factor solution was chosen (yellow circle) with FPEAK=0.2, and (J)-(O) AMS family-colored mass spectra for 6 PMF factors. ***For levoglucosan and succinic acid, 2 factors were combined. The remaining factor was attributed to the background signal (< 2 µg m^{-3} at all times).”***

We updated the Figure 7 caption:

“Figure 7. Results of an HPLC run for SOA from β-pinene + NO_3 (A) AMS, SMPS, and UV-Vis chromatograms (milli-absorbance units), with inset showing peak from 50-60 minutes. (B) Time series and Gaussian fits for the peak between 16 and 20 minutes (without using PMF), (C) EESI HR ions time series (D) time integrated mass concentrations (ion signal) for AMS OA and NO_3, SMPS total mass, and EESI+ HR ion (m/z=268.1). (E)-(J) show ***some*** *AMS PMF factors against measured EESI+ HR ions. (G), (I), and (J) represent split AMS PMF factors for the measured EESI+ HR ions. The AMS PMF factors have a ranging from 1.46-1.97 as shown in Fig. S3 and Table 2. Densities are applied to the SMPS data, shown in Fig. S8.”*

We also updated the text on P23:

“In Fig. 7e-7j, AMS PMF time series **that increased during** the middle third of the run are shown alongside EESI HR ions.”

R2.13. Page 22, Table 2; Column title “AMS PMF factor(s)” is a bit unclear, is it the number of PMF factors or Associated PMF factor(s)?

It’s the PMF factors associated with that AMS EESI HR ion. For clarity, we have decided to move that column to the SI.

Here is how the main table reads:

“Table 2. EESI HR ion, CF_x^E (counts s^{-1} µg^{-1} m^3), CF_x^E/CF_{levo}^E, and CF_x^A. CF_{levo}^E = 441.6 counts s^{-1} µg^{-1} m^3. CF_x^E was calculated using the AMS PMF [Org]×1.05 (the average [NO_3] contribution was ~5%, Fig. S3).”

EESI ion	CF_x^E (counts s^{-1} µg^{-1} m^3)	CF_x^E/CF_{levo}^E (unitless)	CF_x^A (unitless)
268.1	270	0.61	1.46
388.2	10.9	0.023	1.97

451.2 (1)	407	0.92	1.97
451.2 (2)	423	0.96	1.73
451.2 (3)	83.2	0.19	1.97*
465.2 (1)	670	1.5	1.97
465.2 (2)	170	0.38	1.97
467.2	139	0.31	1.73
483.2	435	0.99	1.97
499.2	54.2	0.12	1.97

* Incomplete SMPS data, assuming =1.97."

And the SI:

As described in Sect. 3.3, EESI HR ions were matched to AMS PMF factors using the shape of the time series' as well as the retention times. The EESI HR ions and associated AMS PMF factors are shown in Table S7.

"**Table S7. EESI HR ion and corresponding AMS PMF factor(s)"**

EESI HR ion	**Associated AMS PMF factor(s)**
268.1	**-**
388.2	**9, 13**
451.2 (1)	**13**
451.2 (2)	**13**
451.2 (3)	**-**
465.2 (1)	**2**
465.2 (2)	**10**
467.2	**5,8**

483.2	**14**

R2.14. Page 24, line 548; Fig. S3, is this the correct figure number?

This was a typo, the correct sentence reads (P24, line 548):

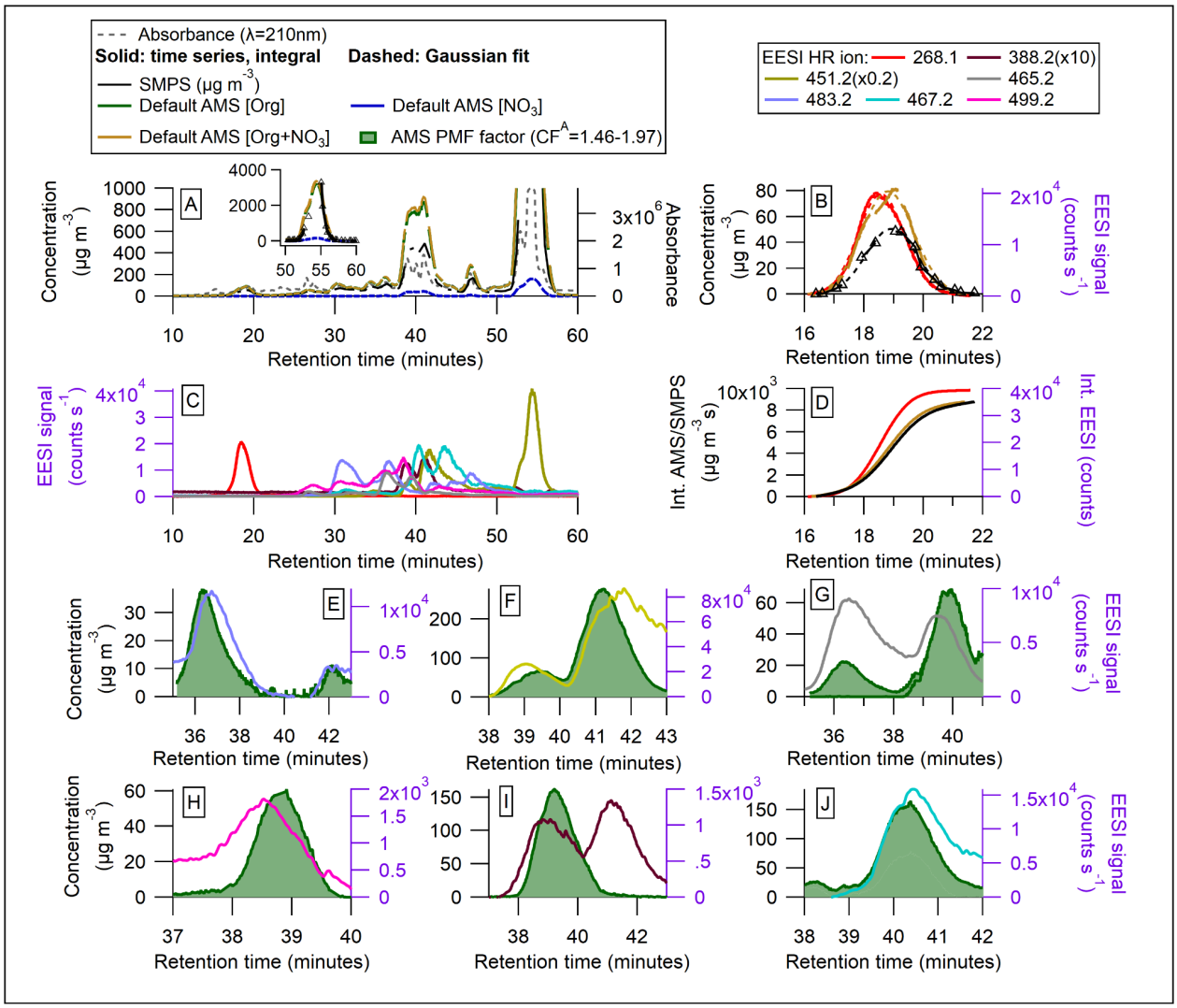
"For the mixed peaks CF_x^A was either **1.97 or 1.73, as discussed in Sect. S3 and shown in Fig. S3**."

The SI was also updated (P5).

"The nitrate contribution to the total mass for this peak was ~5.1%. Fitting the bulk peaks (which are composed of multiple eluents) may result in some error in the nitrate contribution approximation. CF_x^A **was calculated for the two peaks by referencing the AMS mass to the SMPS mass. For the first peak,** CF_x^A **= 1.97, for the second peak** CF_x^A **= 1.73**."

Figures corrections:

We noticed an error in panel D in figure 7. We are amending the correct figure here with the caption. This change does not affect any of the conclusions of the paper.



"*Figure 7. Results of an HPLC run for SOA from β-pinene + NO_3 (A) AMS, SMPS, and UV-Vis chromatograms (milli-absorbance units), with inset showing peak from 50-60 minutes. (B) Time series and Gaussian fits for the peak between 16 and 20 minutes (without using PMF), (C) EESI HR ions time series (D) time integrated mass concentrations (ion signal) for AMS OA and NO_3, SMPS total mass, and EESI+ HR ion (m/z=268.1). (E)-(J) show some AMS PMF factors against measured EESI+ HR ions. (G), (I), and (J) represent split AMS PMF factors for the measured EESI+ HR ions. The AMS PMF factors have a CF_x^A ranging from 1.46-1.97 as shown in Fig. S3 and Table 2. Densities are applied to the SMPS data, shown in Fig. S8.*"

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