RESPONSE TO REVIEWERS' COMMENTS

The authors thank both reviewers for their feedback on the manuscript. We have responded to all the comments except one (which was unclear) by making changes to the manuscript to improve clarity, highlight the unique attributes of our experimental method, and address questions and errors pointed out by reviewers. The comments of each reviewer have been numbered for ease of reference.

Reviewer RC1

Comment 1. However, I miss the obvious: a comparison of mass spectra between the averaged spectrum of either chamber-generated or ambient OA using (1) offline HPLC-VIA-I-CIMS against (2) the corresponding online VIA-I-CIMS spectrum. Figure S4 and S6 are showing already the offline spectra – but how does this compare against online VIA-I-CIMS spectra? This is the central comparison that would enable the authors to make statements about the significance of filter sampling artefacts, and/or cluster artefacts in the online VIA-CIMS, to provide a more comprehensive organic aerosol characterization. I like to encourage the authors to add this comparison if the online data are available.

Author response. The text on lines 334–337 now reads: "Although outside the scope of the present study, this apparatus could also be used to systematically evaluate possible artifacts incurred by filter sampling and other sample handling procedures used in off-line analysis by comparing averaged mass spectra generated with HPLC-VIA-CIMS with those from online VIA-CIMS measurements."

Technical Points

Comment 2. Line 15: IMO a company name should not be stated in the abstract, only in the methods part.

Author response. The reference to Aerodyne was removed from the abstract.

Comment 3. Line 21: Is this the amount injected on column? I find injected mass on column more intuitive.

Author response. The text on lines 20–22 now reads:

"Instrument response was found to be linear (R^2>0.97) over an order of magnitude (0.2–3.0 nmol or 2–30 nmol on column) for each of the 12 standards."

Comment 4. Line 67: what is meant by "low transmission" specifically? From the GC column into the ion source? In modern GC-MS this is usually not an issue, and compounds which are passed over the column also make the way into the ion source in heated transfer lines.

Author response. The text on lines 66–71 now reads:

"A disadvantage of using GC to separate OA constituents is the low transmission of multifunctional compounds through the column due to irreversible adsorption and/or thermal decomposition, although this can be ameliorated to some degree by chemical derivatization of hydroxyl, carbonyl, carboxyl (Yu et al., 1998, 1999), and hydroperoxide (Docherty et al., 2004) groups to increase analyte stability and volatility; and by the use of specialized GCs that utilize reduced pressure (Vasquez et al., 2018) or cryo-trapping (Robinson et al., 2024)."

Comment 5. Line 136: while it is true that a low pH improves chromatographic peak shapes, it also suppresses ionization of organic acids in ESI. Would this setup here work with post-column addition of ammonia to increase pH and potentially increase ionization efficiency of negative ions as in ESI?

Author response. The text on lines 139–142 now reads:

"It is also worth noting that because compound evaporation and ionization are spatially separated in I-CIMS instruments (unlike in ESI), I-CIMS is not susceptible to ionization suppression caused by non-ideal electrospray conditions required to counteract the high conductivity and surface tension imparted to droplets by organic acids (Apffel et al. (1995)."

Comment 6. Line 154: I am very surprised that this large void volume of 300 mL does not cause a chromatographic peak broadening. Why was such a large volume chosen?

Author response. The text on lines 160–162 now reads:

"This bulb volume was chosen to maximize the distance between the nebulizer tip and the bottom of the bulb in order to reduce impaction of the nebulizer spray while not affecting peak broadening, as shown below."

Comment 7. Line 156: Is this large flow of dry N2 necessary to reduce the water dependency? Because it is diluting the eluting compounds from the LC.

Author response. The text on lines 163–166 now reads:

"The total flow through the nebulizer bulb was adjusted to 3.5 LPM by flowing dry N_2 through a port orthogonal to the nebulizer spray; the N_2 flow rate was chosen to be consistent with the manufacturer's recommendations for VIA performance and was also found to optimize analyte signal in preliminary testing (Fig. S2)."

Comment 8. Fig. 2: Can the increasing sensitivity with increasing retention time be caused by the higher organic content in the mobile phase?

Author response. The text on lines 185–191 now reads:

"The increase in dicarboxylic acid signal with increasing carbon number up to sebacic acid in Fig. 2 is the opposite of the trend observed by Lee et al. (2014) for direct evaporation of succinic,

glutaric, adipic, and azelaic acid into a I-CIMS. This suggests that the signals observed here may have been influenced by the HPLC and/or VIA, perhaps due to differences in the composition of solvent drops exiting the HPLC or other factors that might affect evaporation, decomposition, and wall loss in the VIA. This could be investigated in the future by, for example, using isocratic HPLC, varying the vaporizer temperature, and measuring the aerosol size distribution."

Comment 9. It would be interesting to see whether the formed aerosol size distribution after the nebulizer is different with different mobile phase composition.

Author response. See response to RC1 Comment 8.

Comment 10. Did you try an isocratic HPLC run? This could show the effect of the different mobile phase composition on ionization efficiency.

Author response. See response to RC1 Comment 8.

Comment 11. Line 212: hydrogen should be written instead of H

Author response. The text on lines 228–230 now reads:

"SOA formed by ozonolysis of α-pinene was chosen for method evaluation with a complex OA as it has been well characterized and is known to contain carboxylic acid monomer and dimer products that are detected by I-CIMS with high sensitivity (Lopez-Hilfiker et al., 2014) and are often isobaric or differ by only two hydrogen atoms (Ma et al., 2007a; Zhao et al., 2024)."

Comment 12. Fig. 3: is the DAD signal blank corrected? Hence is the increased baseline from the sample?

Author response. The text on lines 147–148 now reads:

"The HPLC-DAD chromatograms were baseline corrected using injections of solvent blanks."

Comment 13. Line 265: I cannot imagine that cannabis cultivation is dominant over emissions from forests?

Author response. The text on lines 283–285 now reads:

"The detection of these compounds is unsurprising given the prevalence of monoterpenes in the Denver area from biogenic emissions, personal care products, and cannabis cultivation (La Casa | ASCENT, 2024; Gkatzelis et al., 2021; Wang et al., 2020)."

Comment 14. Line 273 and Line 285 / Figure 4, Figure S6: I am surprised about all the organic nitrates detected on a filter considering their short lifetimes of a few hours (Lee et al., PNAS,

2016). Are you sure that all these CHNO compounds are organic nitrates? Are organic nitrates more stable than Lee et al. has published?

Author response. The text on lines 316–323 now reads:

"The detection of $C_{10}H_yNO_x$ species in the OA samples is also consistent with measurements by Lee et al. (2016), who described a diurnal pattern of monoterpene-derived multifunctional alkyl nitrates, with concentrations peaking in the early morning hours, in the southeast United States. Although their real-time measurements combined with modelling indicated lifetimes of 2–4 h, previous studies by DeVault and Ziemann (2021) and DeVault et al. (2022a, 2022b) showed that organic nitrates formed from monoterpene oxidation reactions were stable for at least several days after filter sampling and extraction processes similar to those used here. While it is possible that some of the CHNO species are not organic nitrates, our results shown in Figures 4 and S6 are consistent with the C_{10} organic nitrate distributions observed by Lee et al. (2016) during the early morning hours of their study period."

Comment 15. Line 279: "either ocimene or limonene" - this can be any other monoterpene

Author response. The text on lines 298–300 now reads:

"Three dimer species, $C_{20}H_{32}N_2O_{11}$, $C_{20}H_{32}N_2O_{12}$, and $C_{20}H_{32}N_3O_{12}$, were attributed to particle-phase accretion reactions of monomers formed through the reaction of monoterpenes with nitrate radicals (DeVault et al., 2022b; Faxon et al., 2018; Takeuchi et al., 2022)."

Comment 16. Line 304: Investigation on which compounds contribute to BrC with LC-DAD/PDA-HRMS is not new – has been done by several groups (e.g. Laskin, Nizkorodov, Moschos/Surratt, Huang, …). Mostly on nitroaromatics and BBOA.

Author response. The text on lines 330–332 now reads:

"In future work, the DAD could also be used to provide semi-quantitative analysis of light-absorbing compounds for which standards are not available."

Reviewer RC2

Comment 1. I believe that the advantage of HPLC-VIA-MS over traditional HPLC-MS should be elaborated further, as this point is not clearly to me. Line 80-81, the author compared the typical HPLC-MS with the HPLC-VIA-MS method. However, it looks to me that typical HPLC-MS can detect more compounds that HPLC-VIA-MS method, so it did not specify why HPLC-VIA-MS is going to be valuable in examining the chemical composition of organic aerosols.

Author response. The text on lines 79–86 now reads:

"However, while these approaches are capable of separating complex mixtures and generating high-resolution mass spectra, the devices used to nebulize, vaporize, and ionize OA components following HPLC fractionation can suffer from matrix effects in ESI and EESI, and they are generally integrated in such a way as to allow limited opportunity for independently and easily varying the ionization method. This is a considerable drawback, considering the wide variety of CIMS reagent ions now available for selectively ionizing different compound classes and achieving exceptionally high detection sensitivity, the recently developed capability for rapidly switching among multiple reagent ions (Alton et al., 2024) for more comprehensive CIMS analysis, and the advantage of being able to analyze gas- and particle-phase compounds with the same CIMS methods."

Comment 2. Line 108: please include the weight of the filter before and after the collection in the SI.

Author response. The filter masses have been added to Table S1 in Section S1 of the Supplemental.

Table S1. Masses of PTFE filters pre- and post-sampling from chamber. All mass acquired was assumed to be SOA formed through the reaction of α-pinene and O_3.

Filter No.	Pre-Sampling Mass (mg)	Post-Sampling Mass (mg)	SOA Mass (mg)
1	89.388	90.075	0.687
2	90.021	90.715	0.694

Comment 3. Line 149: how was the flow rate of 3.5 lpm determined to be most efficient in limiting wall loss and thermal decomposition?

Author response. The text on lines 163–166 now reads:

The total flow through the nebulizer bulb was adjusted to 3.5 LPM by flowing dry N_2 through a port orthogonal to the nebulizer spray; the N_2 flow rate was chosen to be consistent with the manufacturer's recommendations for VIA performance and was also found to optimize analyte signal in preliminary testing (Fig. S2)."

Comment 4. What is the residence time of aerosols in the nebulizer/flask interface before entering the VIA-CIMS? Did the author consider this residence time when comparing the timing of the DAD signal and the CIMS signal?

Author response. The text on lines 268–273 now reads:

"After retention time alignment with the I-CIMS time series, the DAD signal reveals the preservation of peak shape during nebulization and evaporation in the VIA, which is most clearly observed for the peaks at 8 min ($C_{10}H_{16}O_4$), 10.5 min ($C_9H_{14}O_4$), and 12.5 min ($C_{10}H_{16}O_5$, $C_{10}H_{16}O_6$) (Fig 3, top). This is reasonable, since for a N_2 flow rate of 3.5 LPM and a bulb volume of 300 mL the residence time in the bulb is ~5 s compared to a delay time between the DAD and CIMS signals of ~2 s, indicating that most of the aerosols are rapidly transmitted through the bulb to the VIA as well-defined packets with little mixing between them due to dispersion."

Comment 5. The time for the aerosols in the nebulizer/flask system should have a distribution as not all aerosols would exit the flask at the same time. Will this cause broadening of the peaks or overlapping of the adjacent peaks of different compounds in VIA-CIMS?

Author response. See response to RC2 Comment 4.

Comment 6. Sections 3.2 and 3.3 only showed a handful of compounds. How many compounds can the VIA-CIMS system see for the mass of the SOA collected in this study?

Author response. The text on lines 233–239 now reads:

"Analysis of a 30 μg injection of the SOA by HPLC-VIA-CIMS identified numerous reaction products, but for clarity a subset of these was selected here (and in the section below) based on relative contributions to the total I-CIMS signal (Figs. S3 and S4) and prevalence in the literature to illustrate the performance of the HPLC-VIA-CIMS system. Although a comprehensive analyte list was not compiled, the diversity of compounds detected by this system can be seen in the averaged mass spectra shown in Figures S4 and S6. These spectra provide a qualitative view of the numerous other analytes detected in the mass range that was measured. It should be noted that the number of detectable compounds is more likely to be limited by injection mass rather than total collected aerosol mass."

Comment 7. Is it enough to perform non-target analysis, or the number of the detectable compounds are heavily limited by the mass of the SOA collected?

Author response. The authors are not sure what is meant by "non-target analysis" in this case, as the detection and tentative identification of monoterpene oxidation products in chamber-generated and field-collected OA constitute non-targeted analysis under what we believe to be the conventional definition of the term. While the use of I-CIMS will limit the detectable

analytes to oxygenated organics, a pre-determined list of target compounds was not used outside of Section 3.1.