General Comments

This study introduces the Kinetic Model of Oxidative Potential (KM-OP), a numerical framework designed to quantify the molecular drivers of oxidative potential (OP) in ambient particulate matter (PM). By integrating laboratory-derived rate coefficients with field data from multiple cities (Grenoble, Paris, and London Summer/Winter), the authors evaluate the relative contributions of transition metal ions (TMI), quinones, and secondary organic aerosols (SOA) to reactive oxygen species (ROS) production and antioxidant depletion. A primary finding of this work is the identification of SOA as a dominant driver of antioxidant-based OP across diverse urban sites, whereas Cu was found to specifically dominate the production of hydrogen peroxide (H2O2). Overall, the study provides significant insights into the chemical mechanisms of PM toxicity. I have a few specific comments and technical questions listed below for the authors' consideration.

We would like to thank the reviewer for taking the time to review our manuscript and for their feedback. We have corrected our manuscript according to the reviewer's comments and suggestions, and provide point-by-point answers below. The reviewer's comments are given in blue, our responses in black, and updates to the manuscript in *black italic*. When only a part of a sentence was changed, that part was underlined.

Specific Comments

Lines 102-109: The authors mention that the system is "under-determined" and use an ensemble of parameter sets. What is the degree of variance for the rate coefficients within this ensemble? Specifically, are there key reactions (e.g., Fenton-like reactions or quinone redox cycling) that show high sensitivity or wide uncertainty ranges?

Thank you for the comment. We have revised the manuscript to explicitly report the variability in the kinetic parameters obtained from the ensemble. Specifically, we now include a box-and-whisker plot summarizing the distributions of the optimized rate coefficients across all the parameter sets in the SI. As the reviewer correctly states, key reactions such as Fenton-like processes and quinone redox cycling exhibit comparatively large uncertainty ranges. This is due to both the limited experimental constraints and the large variability in the literature regarding their kinetics. To account for this, we allowed broader bounds during the global optimization for these reactions.

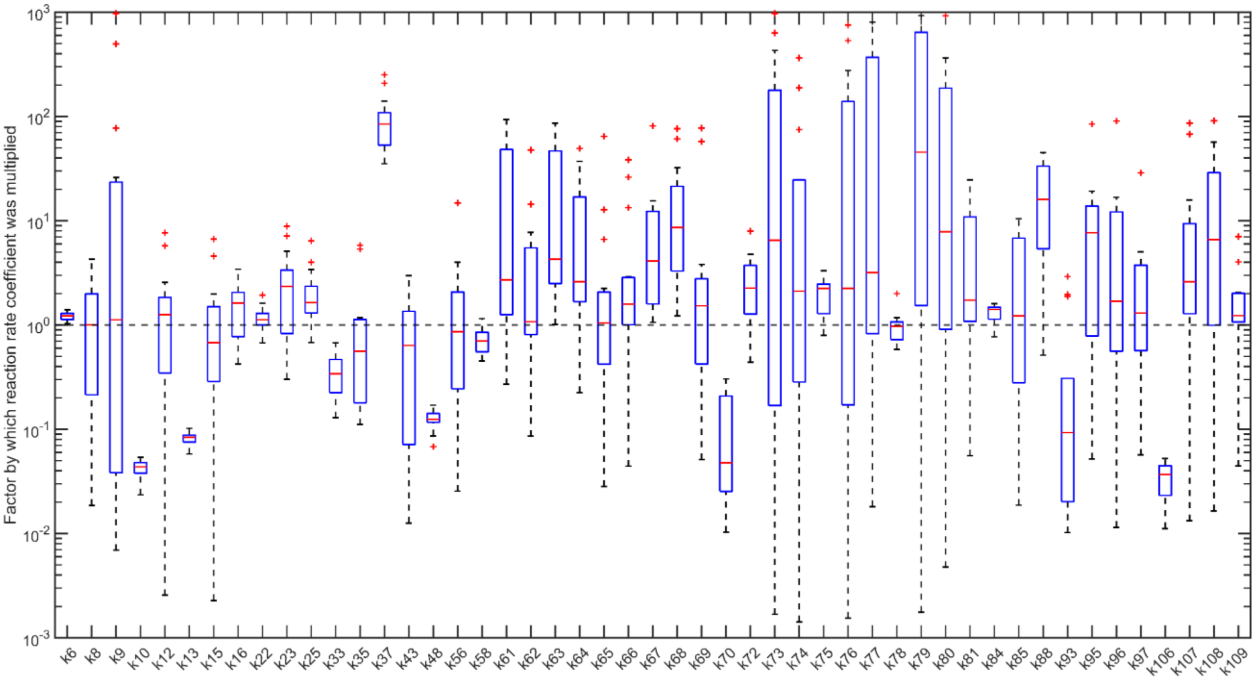


Fig R1: Ranges for kinetic parameters obtained with global optimization to experimental data. Multiple optimizations give rise to estimations of fit parameter uncertainty.

In general, reaction rate coefficients that are well characterized in the literature were assigned narrower optimization bounds, whereas reactions that are less well characterized in the literature were allowed to vary over a wider range.

The reaction rate coefficients k6, k10, k13, k16, k22, k25, k33, k37, k48, k58, k75, k78, k84, and k106 are narrowly constrained. These reactions are either well established in the literature or directly involve the antioxidant probes for which laboratory data were available. For example, k6, k10, k13, k16 andk33 correspond to the initial reactions of quinones and transition metals with ascorbic acid. k22, k25, k37 and k48 are associated with OH production. k58 is the reaction of DTT with HO_2. k75 and k78 are the initial reactions of quinones with DTT. k84 is the reaction of DHA with H_2O. k106 is the complexation of Cu(II) with GSH. These reactions are therefore both mechanistically well understood and directly constrained by experimental observations in this study. Other reaction rate coefficients are not as tightly constrained. We find that this especially concerns reactions involving copper, where the reaction mechanism is rather complex and leaves room for ambiguity in the global optimization.

We added the following sentence to the revised manuscript:

L. 110-111: *The distributions of the optimized rate coefficients across all the parameter sets are shown in Fig. S1.*

Line 110: Since the “Org” component parameters were ported from literature rather than fitted during the MCGA process, did the authors investigate whether the transition metal ion and quinone parameters were forced to non-physical values to compensate for any inaccuracies in the fixed organic mechanism?

Our training dataset did not include systems containing both transition metals and organic species, or organics and quinones. Therefore, the parameters involving transition metal ions were never optimized in systems including organic compounds whose reactivity would be compensated for.

Lines 162-164: The 2-hour filter extraction period is not explicitly modeled. Considering that ROS can be lost through aqueous-phase chemistry during this time, could this omission result in a systematic underestimation of the initial OP of the PM samples?

The reviewer raises an important point. As described in the manuscript (L.200-203), we acknowledge that ROS may undergo aqueous-phase reactions during the 2-hour filter extraction period, which could in principle influence the measured OP using filter-based methods.

Line 200-203: “Note that in the filter-based assays used for this study, there is an extraction step during which the filter samples are shaken at physiological conditions (pH 7, 37.5°C) in a simulated lining fluid, in the absence of a probe reactant species. While a longer extraction time increases the amount of dissolved material and thus, e.g., DTT activity (Calas et al., 2017), it may also lead to loss of ROS as a result of aqueous-phase chemistry (Campbell et al., 2025).”

In principle, radical-radical recombination reactions may lead to the loss of ROS. At this point and without experimental data to compare to, however, we would rather not speculate about the effect of the extraction period in the paper.

Line 181-183: For the London sites (MY and HOP), median soluble metal fractions were used in the absence of direct measurements. Given the importance of Cu and Fe in your ROS findings, how sensitive is your conclusion that metals are "minor contributors" to variations in these assumed solubility fractions?

The reviewer brings up a valid issue . The solubility of metals is an important parameter. In the absence of site-specific measurements for the London sites (MY and HOP), we used median literature values (0.19 for Fe and 0.48 for Cu). To assess the sensitivity of our conclusions, we ran a simulation with twice as high (0.38 for Fe and 0.96 for Cu) and twice as low (0.095 for Fe and 0.24 for Cu) solubilities, which we have now added to the SI and show in Figs. R2-R5 below. Overall, results are not affected very strongly. OP^{DHA} is influenced by the transition metal solubility, since the contributions of metals to OP are high for OP^{DHA}, which we already show in the manuscript (Fig. S17, S18). For OP^{H2O2}, copper is a dominant contributor, as previously shown in the manuscript (Fig. 8d), hence increasing its soluble content increases the OP. For OP^{DTT} and OP^{OH}, organic species remain the dominant contributors across the full range of tested solubilities.

We also added the following sentences to the revised manuscript:

L. 463-465: Due to the absence of data on the water-soluble fractions of metals at the London sites, we performed a sensitivity analysis by varying Fe and Cu solubilities within a factor of two

(Fig. S29 and S30). The sensitivity analysis shows that, while OP^{DHA} and OP^{H2O2} are influenced by metal solubility, OP^{DTT} and OP^{OH} were less affected (Fig. S31 and S32).

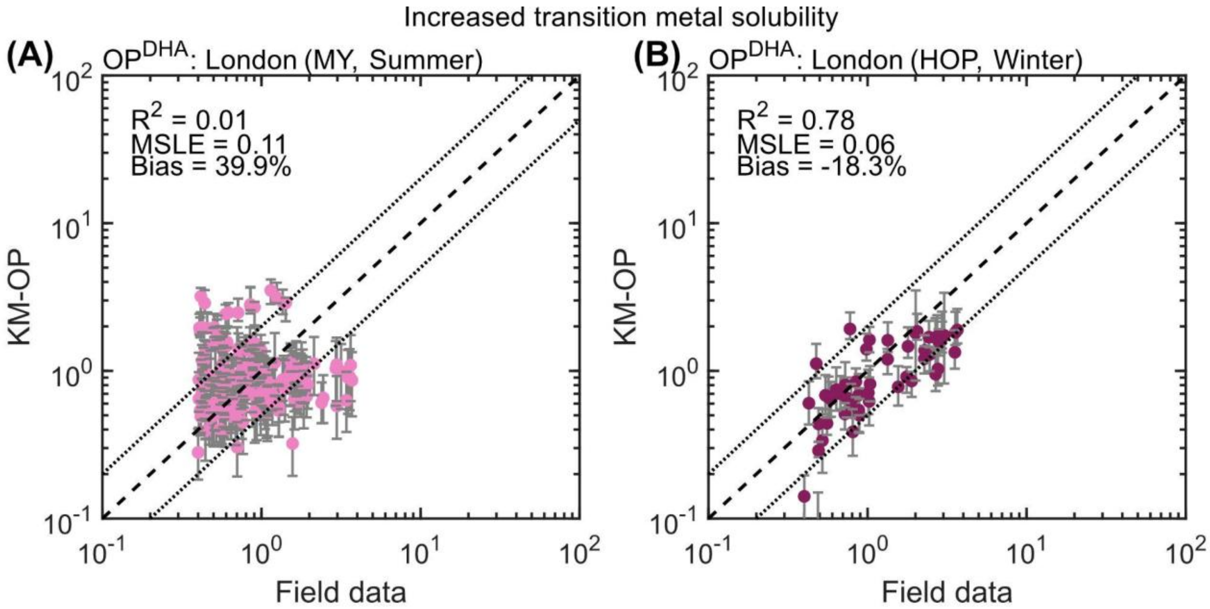


Fig R2: Sensitivity study of using increased soluble fractions of transition metal ions for the simulation of OP^{DHA} for particulate matter samples collected in London during (A) summer and (B) winter.

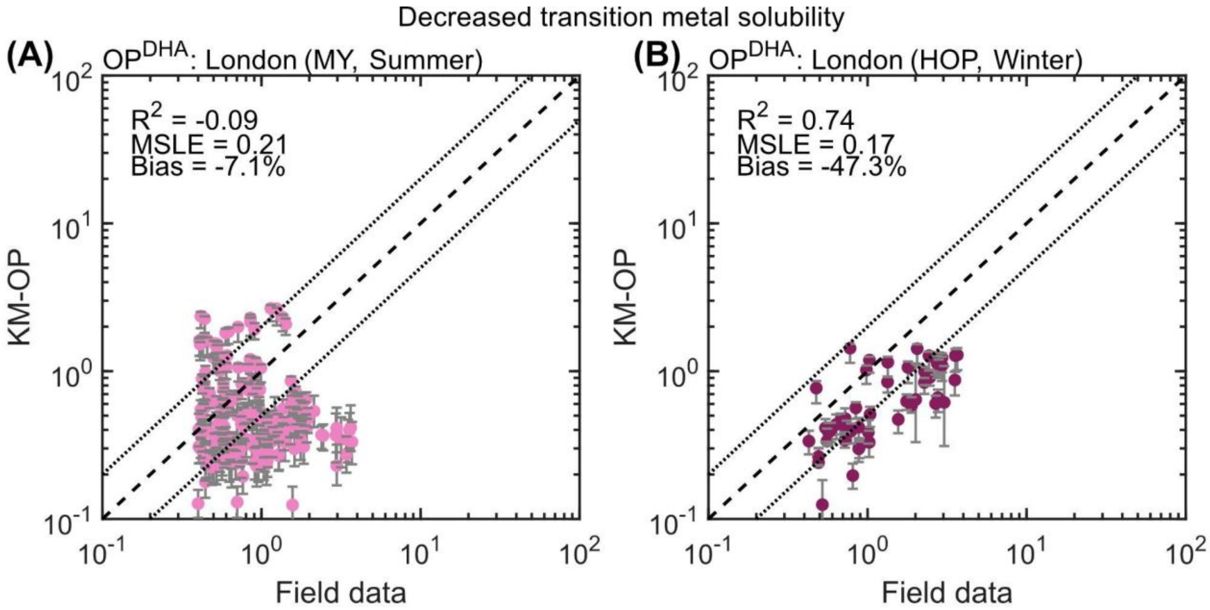
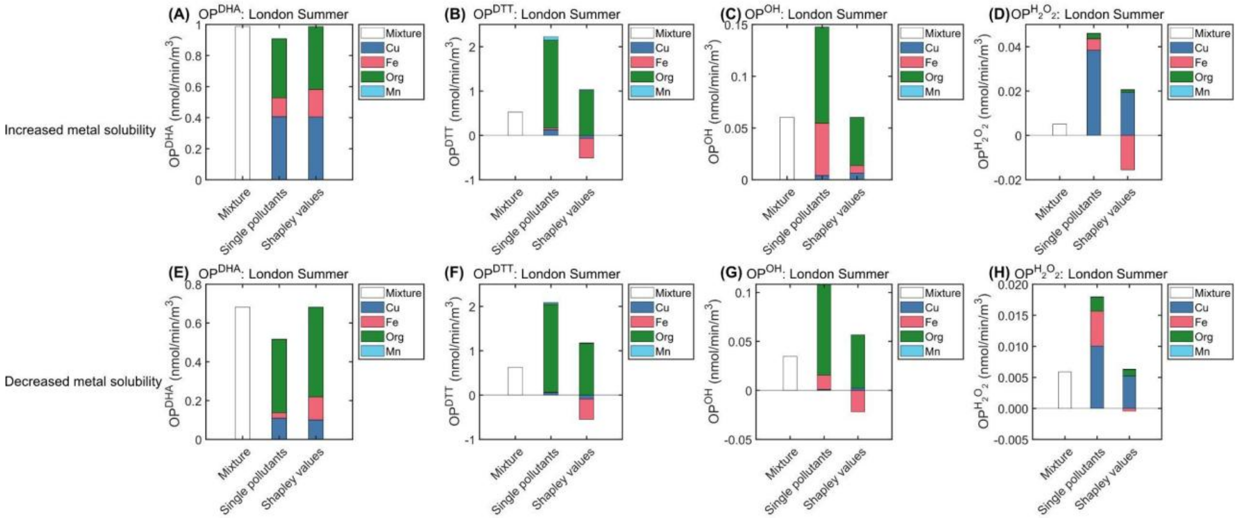
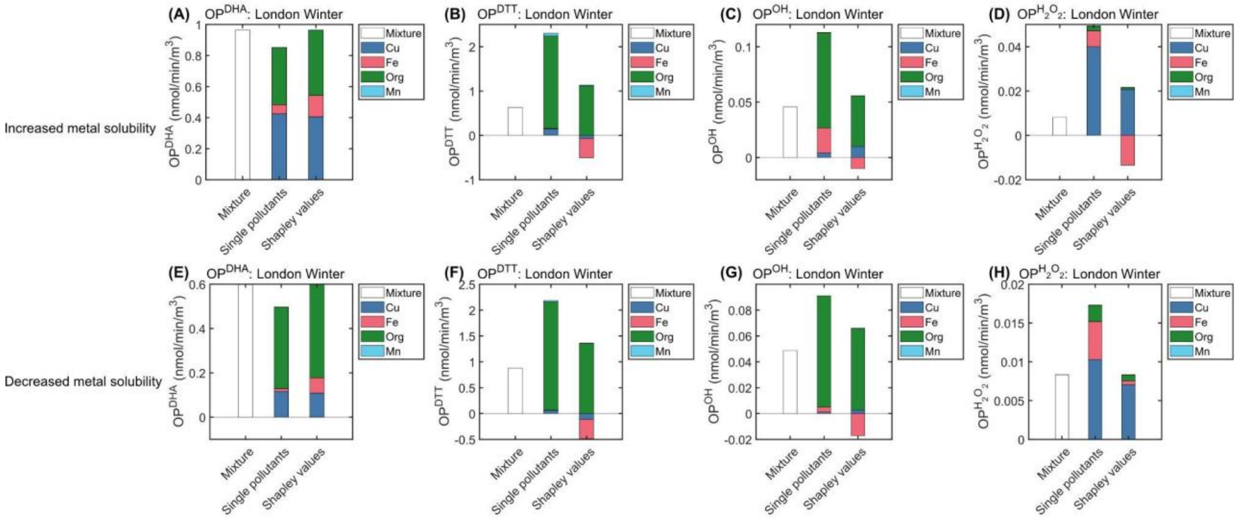


Fig R3: Sensitivity study of using lowered soluble fractions of transition metal ions for the simulation of OP^{DHA} for particulate matter samples collected in London during (A) summer and (B) winter.



R4: Sensitivity study on the contributions of different PM constituents to OP^{DHA}, OP^{DTT}, OP^{OH}, OP^{H2O2} in London during summer with (A-D) 2 times higher and (E-H) 2 times lower metal solubility.



R5: Sensitivity study on the contributions of different PM constituents to OP^{DHA}, OP^{DTT}, OP^{OH}, OP^{H2O2} in London during winter with (A-D) 2 times higher and (E-H) 2 times lower metal solubility.

Line 194: The model assumes a fixed 50% organic hydroperoxide (ROOH) content for the organic fraction. Since SOA is identified as the primary driver of OP, how would the model's performance and the "good agreement" with field data change if this fraction were varied (e.g., to 20% or 80%)?

Thank you for the comment. The reviewer is correct that the organic hydroperoxide content in OA can vary and the value will have an impact on the model results. To assess the sensitivity of the model, we performed additional simulations with ROOH fractions of 20% and 80%, as suggested by the reviewer. The results are shown in Figs. R6-7 below and added to the SI of the revised manuscript. Overall, the results show that the model maintains high correlation with the field data across this range, albeit it slightly overestimates OP at 80% peroxide content and underestimates the data at 20% peroxide content. These findings indicate that while the absolute magnitude of OP is sensitive to the ROOH fraction, the overall trends and correlations with field measurements remain robust.

It is important to note here that the organic composition data used for model development are derived from filter-based measurements, which may not capture short-lived organic species. In contrast, online OP measurements may be more sensitive to these short-lived species. As a result, the model may underestimate OP at sites where such species contribute significantly to oxidative activity. In fact, the simulations with 80 % ROOH fraction resolve the underestimation of the London winter data, which uses online-OP instrumentation, by improving the bias from -34.7% to -8.3%.

We added the following sentences in the revised manuscript:

L. 384-391: Peroxides constitute a significant fraction of atmospheric OA, but their abundance varies widely depending on precursors and oxidative processing (Docherty et al., 2005, Krapf et al., 2016, Wang et al., 2023, Li et al., 2024, Li et al., 2025). A sensitivity analysis over a ROOH fraction range of 20–80% of total OA indicates that the model underestimates OP at an ROOH fraction of 20 % and overestimates OP at an ROOH fraction of 80 % (Figs. S12 and S13). The overall trends and correlations with field measurements, however, remain robust. We note that the simulations with 80% ROOH fraction resolve the underestimation of the London winter data, which uses online-OP instrumentation, by improving the bias from -34.7% to -8.3%, suggesting the presence of short-lived organic species that are only captured using the online instrument (Krapf et al., 2016, Utinger et al. 2023, Campbell et al. 2025).

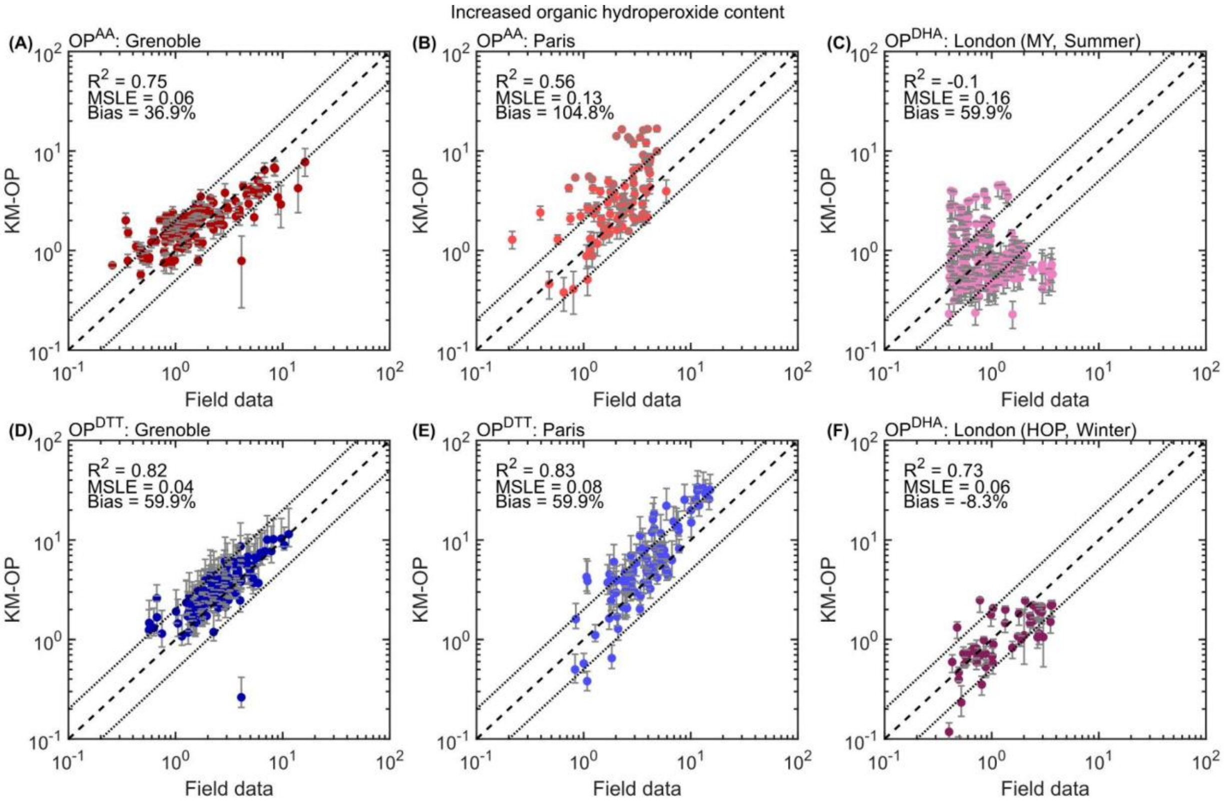


Fig R6: Sensitivity study on the correlation of model-predicted and measured OP using an increased organic hydroperoxide (ROOH) content of 80% of total OA.

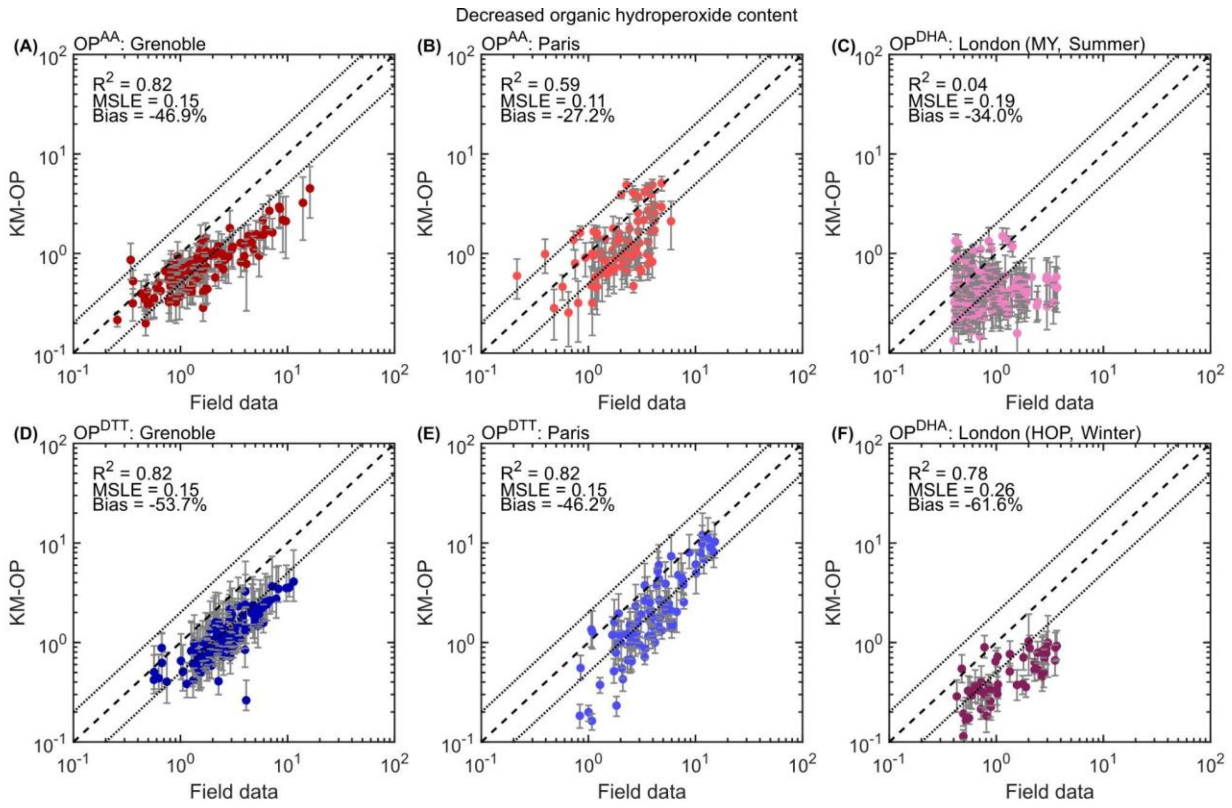


Fig R7: Sensitivity study on the correlation of model-predicted and measured OP using a decreased organic hydroperoxide (ROOH) content of 20% of total OA.

Line 375: The correlation for the London Summer site is reported with a negative coefficient (R^2 = -0.06). Could the authors clarify the statistical basis for a negative R^2 in this context? Furthermore, to what specific factors is this lack of correlation attributed? While the discussion mentions the presence of labile organic compounds, it would be helpful to understand if the discrepancy might also stem from temperature-dependent kinetic effects that are not currently parameterized in the KM-OP mechanism, particularly given the high-temperature conditions noted during that sampling period.

Thank you for raising this point. The negative R^2 observed for the London summer dataset indicates a lack of correlation rather than a meaningful inverse relationship.

Following the suggestion of the reviewer, we compared the model results to meteorological parameters. The results are shown in Fig. R8 below and are added to the SI of the revised manuscript. The yellow scatter points represent higher values of a given meteorological condition. Overall, we find no obvious trend with various meteorological conditions. We find that the model tends to underestimate OP at lower wind speeds, but do not find an influence of wind direction. Moreover, with regards to temperature and humidity, the model has a slight tendency to overestimate OP for samples that were collected on days with higher air temperature and lower relative humidity, and a slight tendency to underestimate OP for samples that were collected on days with lower air temperature and higher relative humidity.

L. 398-403: *Additional analysis with meteorological parameters for the summer data shows some variability in model performance (Fig. S15). Model disagreement occurs at two distinct time periods. The analysis shows a slight tendency of the model to underestimate OP at lower wind speeds and exhibits a slight positive bias with increasing temperature. However, these effects are not consistent across the dataset, and no clear or systematic trends emerge. While such nuances suggest potential influences of meteorological conditions on OP, it remains unclear how these effects could be incorporated into an improved model parameterization.*

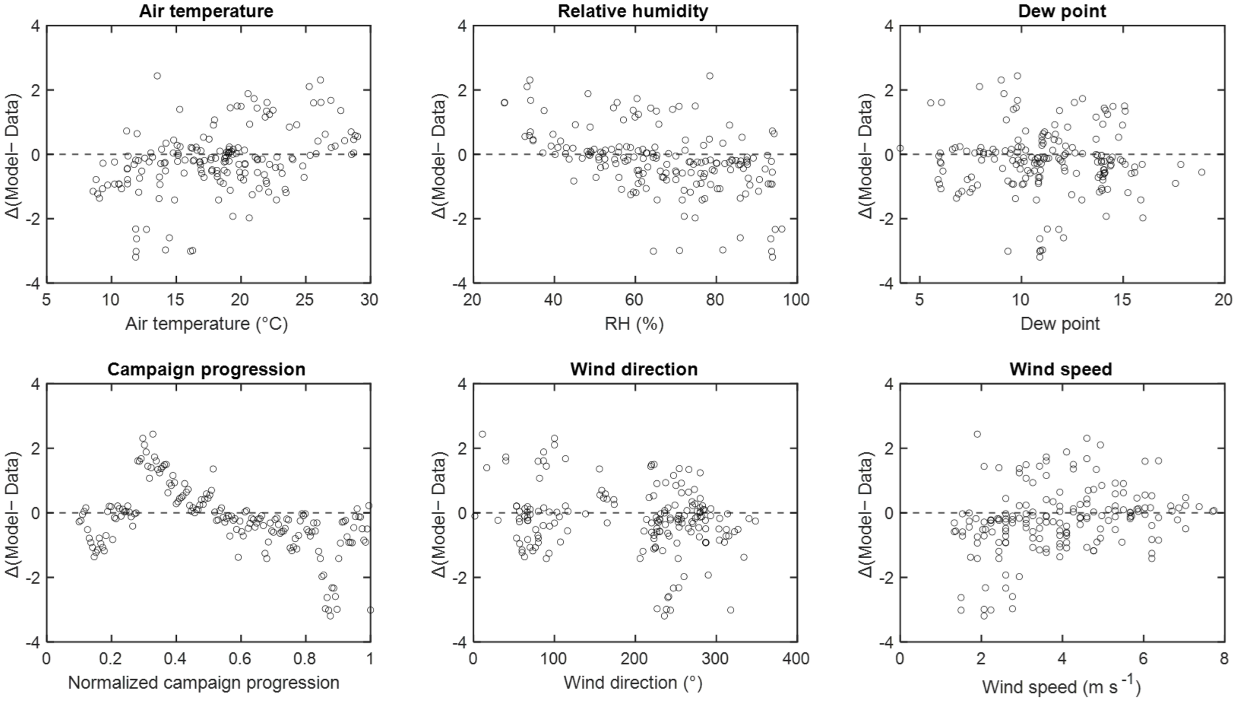


Fig. R8: Difference between model predicted and measured OP particulate matter samples collected in London during summer as a function of meteorological conditions.

Lines 385-386: Regarding the role of highly oxygenated organics, the authors suggest these species may act as ligands and enhance metal solubility. However, could these organics also sequester transition metal ions? It would be beneficial to discuss whether such metal-ligand complexation might actually reduce the concentration of free metal ions available for catalytic ROS production, and therefore act as an inhibitory factor rather than a promoter of oxidative potential.

We agree that highly oxygenated organic species may not only enhance metal solubility through complexation but can also sequester transition metal ions (TMIs).

The effect of such metal–ligand interactions is unclear. Previous studies (Rush and Koppenol, 1990; Gonzalez et al., 2021) have shown that certain ligands, such as EDTA, can enhance

Fenton-like reactivity. In contrast, other studies (Charrier et al. 2012) have demonstrated that ligand complexation can reduce OP in DTT assays. Thus, this is a rather complex issue and warrants further experimental investigation before incorporation into kinetic models.

We added the following to the manuscript:

L. 403-408: Highly oxygenated organics may produce more ROS directly, and may also act as ligands (e.g., oxalate Shahpoury et al., 2024a), enhancing metal solubility. Previous studies have shown that certain ligands, such as EDTA, can enhance Fenton-like reactivity (Rush and Koppenol*, 1990; Gonzalez et al., 2021), but other studies have demonstrated that ligand complexation can reduce OP in DTT assays (Charrier et al. 2012). Thus, the influence of metal–ligand interactions on OP warrants further experimental investigation before incorporation into kinetic models.*

Lines 415-437: The results indicate that Cu dominates H2O2 production, yet SOA is the strongest contributor to antioxidant depletion OP^AA and OP^DTT. Why does the high flux of H2O2 from Cu not lead to a more substantial depletion of AA and DTT in the model simulations?

The reviewer highlights an important message of our work. While Cu is a dominant contributor to H_2O_2 production, this does not directly translate into strong depletion of AA and DTT because H_2O_2 is relatively unreactive toward these antioxidants. The direct reaction of H_2O_2 with DTT is comparatively slow and therefore contributes only weakly to overall DTT consumption. In contrast, SOA contributes significantly to the production of more reactive radical species, such as OH, which reacts much more rapidly with AA and DTT.

L. 457-459: *Although Cu strongly enhances H_2O_2 production, its contribution to OP^{AA} and OP^{DTT} is small because the reaction of H_2O_2 with AA and DTT is relatively slow. In contrast, SOA contributes significantly to the production of •OH, which reacts rapidly with AA and DTT.*

Lines 483-485: The correlation between modeled OP^OH and OP^DTT (R^2 = 0.7) is lower than OP^OH and OP^AA or OP^OH and OP^DHA. Is there a distinct, non-radical-mediated oxidation or non-redox removal pathway (e.g., DTT-electrophile adduct formation via Michael addition) that remains significant? It would be helpful to discuss whether the presence of such non-redox removal pathways contributes to the observed discrepancy in the DTT results compared to the other antioxidant metrics.

Thank you for this excellent question. In our kinetic model, we incorporate the mechanism proposed by Kachur et al., 1997 in which DTT can be lost in direct reaction and complexation with copper. According to our model, Cu(II)DTT + DTT reaction is the largest sink reaction for DTT in laboratory experiments (Fig. S8).

L. 476-479: *Nonetheless, the correlation of OP^{OH}* with *OP^{DTT} is slightly lower than that of OP^{OH}* with *OP^{AA}, or OP^{OH} with OP^{DHA}. The weaker correlation of OP^{OH} with OP^{DTT} reflects the additional DTT loss pathways not directly linked to ROS production, such as the formation of Cu(II)–DTT complexes, which constitute a sink for DTT in the model.*

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