Summary

In this study, the authors introduce a chemical kinetic model of oxidative potential (KM-OP), developed using data from laboratory studies on the OP of individual/mixtures of chemical constituents for the production of reactive oxygen species (ROS) and consumption of antioxidants such as ascorbic acid AA and antioxidant proxies such as dithiothreitol DTT. The authors subsequently apply this model to field measurement data from France and UK to predict the OP using inputs such as concentration of transition metals, quinones, and secondary organic aerosols (SOA). A major strength is the integration of literature rate coefficients with a broad compilation of lab datasets, followed by inverse modeling using the Monte Carlo Genetic Algorithm (MCGA). Given the underdetermination and non-orthogonality of parameters, the ensemble-based fitting strategy is both reasonable and scientifically mature. The results from this study revealed SOA to be the main driver of DTT and AA consumption, with only minor contributions from Cu and Fe.

General Comments

The development of a kinetic model based on laboratory studies to quantify the OP of PM based on the chemical composition of PM is a topic of significant relevance and importance in enhancing our understanding of the health impacts of PM. The successful development of a robust and accurate kinetics-based model to predict the OP of PM will allow us to quantify OP without needing to measure it. I commend the authors on their attempts to address this ambitious challenge.

The main strengths of the manuscript are the robust incorporation of the wide array of chemical reactions into the model, and a decent agreement between the model and the laboratory-based kinetic OP experiments using 1 or 2 chemical reagents. In general, I think the manuscript is a bit lengthly, and could be shortened a bit.

We would like to thank the reviewer for taking the time to review our manuscript and for their detailed 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.

However, several critical flaws undermine the robustness of the results and the representativeness of the model, undermining its broader applicability, some of which are

- Inconsistency in the OP-assays and OP-measurement protocols between sites that were used to predict the OP based on chemical composition. Two sites used offline measurements of OP-DTT and OP-AA, while the third site measured OP-DHA using online measurements. The OP was not predicted for any sites that measured OP-OH or OP-H_2O_2. The comparison could either be limited to only the OP that overlaps between sites, or the number of predicted sites could be increased to encompass all five OP-endpoints predicted using the model.

The reviewer is correct that OP predictions were not performed for OP^{OH} or OP^{H2O2}. This limitation arises from the availability of input data. We had access to data from Grenoble and Paris, which include measurements of OP^{AA} and OP^{DTT}, and data from London, consisting of measurements of OP^{DHA} based on an online assay. We do not have access to field measurements that simultaneously provide detailed chemical composition (including transition metals and organics), which are required as inputs for the model, and OP^{OH} or OP^{H2O2}.

We agree that increasing the number of sites and harmonizing OP endpoints would be ideal. Restricting the analysis to Grenoble and Paris would allow direct comparison using the same OP assays (OP^{AA} and OP^{DTT}). However, we chose to also include the London dataset because it provides an additional test of the model under different conditions and highlights the inherent difficulty of harmonizing OP measurements due to the multitude of influencing factors (Dominutti et al. 2025). Specifically, the London winter data demonstrates that the model captures OP variability at a site outside France, based on measurements from a different research group and using a distinct (online) OP assay. We believe that this broader comparison strengthens the generality of the model despite the differences in OP protocols.

The shortcoming the reviewer outlined is now mentioned in the revised manuscript:

L. 486-488: Note that, while the model was trained on OH and H_2O_2 formation data from the laboratory, a validation of model-predicted OP^{OH} or OP^{H2O2} with field data was not conducted due to the lack of datasets combining detailed PM composition with OP measurements.

- Methodology has a lot of assumptions that are incorrect and could lead to severe oversimplification of the OP prediction and its underestimation.
- The modelled kinetics of DTT/AA consumption deviate a lot from experimentally quantified kinetics, with no reasons provided for this deviation.

We agree with the reviewer that the model does not perfectly reproduce all experimental datasets. This may in part be due to simplifying assumptions that are necessary in any modelling endeavor, but here mostly arise from combining data from different experiments, techniques and laboratories, which introduces the possibility of disagreement within the training data set (Dominutti et al., 2025). As we use a single, consistent set of kinetic parameters for all experiments, the fitted model strikes a balance between differing data sets. This approach ensures that the model maintains general applicability and performs robustly across different conditions. In addition, many rate coefficients are constrained to literature values rather than optimized for specific datasets. This is done to reduce the risk of overfitting. This achievement is already highlighted in the manuscript:

L. 493-495: For the first time, a model with a single kinetic parameter set leads to good agreement with such a large set of laboratory data. Previously, fits had only been obtained for single datasets (Campbell et al., 2023; Exposito et al., 2024).

We added the following text to the revised manuscript:

L. 495-498: The global optimization approach used in this study ensures the general applicability and robustness of the model. Remaining deviations between model and experiment may either be due to simplifying assumptions of the model or due to disagreement of data from different sources. We expect that, as more data sets will be added to the training data set, the model will lean towards a consensus of all data, and may be used to identify differing and potentially inaccurate data sets.

The predicted OP values seem to be a large underestimation from the measured OP values in at least two of the six comparisons, and give trends that are contradictory to the experimentally determined values.

- The field validation conclusions of this study are over definitive. It is implied satisfactory performance across all three sites in the abstract and conclusions section, but the London summer data comparison yields poor results (R^2 = -0.06), and the London winter data still exhibits underestimation. This is insufficient to constitute reliable multi-site validation.

We agree with the reviewer that the model does not perform equally well across all sites and that the agreement is weaker for the London datasets, particularly during summer. We will revise the abstract and conclusions to better reflect these limitations and avoid overstating the level of agreement.

It is important to note, however, that this work represents, to our knowledge, the first attempts to mechanistically model OP across multiple sites using a unified framework. As such, the chemical mechanism is simplified, and some discrepancies with field observations are expected. Despite these limitations, the model captures the correct order of magnitude and key trends for several datasets, which we consider a meaningful first step toward a more comprehensive predictive framework.

We also note that differences in instrumentation and assay protocols across sites introduce additional uncertainty that may contribute to the observed discrepancies. Improved harmonization of OP measurement techniques and more comprehensive datasets would likely enhance model performance in future applications.

We made the following modification to the abstract:

We apply the model to field measurement data of PM composition and OP <u>from three European cities (Grenoble, Paris, London), obtaining good correlations (R^2 > 0.75) and low model bias (< 15 %) for 4 out of 6 data sets.</u>

We also modified the conclusion:

L.499-501: We find a good agreement between the model and field data at the *two French measurement sites. Moreover, the model captures the overall magnitude of OP at the London sites.*

We also modified the results section when describing the scatter plots involving the London datasets:

L.375-378: For the London sites (roadside location MY in the summer, Fig. 7C and urban background location HOP in winter, Fig. 7F), the modelled OP values generally fall within the same order of magnitude as the field data. For the HOP site, the correlation between model and field data is high (R^2 = 0.76), but the model generally underestimates OP^{DHA} (MSLE = 0.11, bias: -34.7%). In contrast, the model shows less bias (14.2%), but no correlation with the field data at the MY site (R^2 = -0.06, MSLE = 0.15).

- SI is not well organized and does not follow the flow of the manuscript. **Figures is SI seem to be like placeholders with no description accompanying them.**

We now added the following descriptions for the figures.

Figures S2-S10 show the main sources and sinks for different model species with respect to the chemical reactions that they undergo in the model.

Figures S2 and S3 show the main chemical reactions that contribute to H_2O_2 production as a function of quinones and copper, respectively.

Across all quinones, we find that the main source of H_2O_2 is the reaction of ascorbic acid (AA) with HO_2, leading to the formation of ascorbyl radical (AA•) and H_2O_2 (R49, Tab. S1, Fig. S1). For NQN12, at high concentration, the share of H_2O_2 from R49 reduces and the reaction of ascorbyl radical with O_2^- (R81, Tab. S1) increases resulting in an equal share for both (Fig. S2a).

For copper, we find that at low concentrations, the main source of H_2O_2 stems from the reaction of ascorbic acid (AA) with HO_2, leading to the formation of ascorbyl radical (AA•) and H_2O_2 (R49, Tab. S1, Fig S1), at higher Cu concentrations, we find that Cu(I) + O_2^- (R35, Tab. S1) also starts to contribute to H_2O_2 production.

Figure S4 shows the main chemical reactions that contribute to OH production as a function of copper. At low Cu concentrations, OH production occurs mostly through the reaction of AA with H_2O_2 (R48, Tab. S1), while at higher concentrations of Cu, the pseudo-Fenton reaction of Cu(I) with H_2O_2 (R56, Tab. S1) is the most important.

Figure S5 shows the concentration of ROS and TMs (Cu (A), Fe (B)) over time in the presence of ascorbic acid.

Figure S6 shows the main chemical reactions that contribute to DHA production as a function of Cu concentrations. The largest source of DHA is the disproportionation reaction

of the ascorbyl radical (AA•, R44, Tab. S1), which can be produced by the redox reaction between AA and TMIs such as Fe and Cu ions.

Figure S7A shows the main reactions of DTT in the presence of manganese. The largest sink for DTT at low Mn(II) concentrations is HO_2 (R58, Tab. S1), while at higher concentrations, it is Mn(II) and Mn(III).

Figure S7B shows the concentration of DTT at the end of the simulation as a function of Mn(II) concentrations.

Figure S7C shows the main reaction channels that HO_2 undergoes in the simulation as a function of Mn. At higher Mn(II) concentrations, HO_2 reacts with Mn(II) to form MnO_2.

Figure S7D shows the MnO_2 concentration as a function of time. The higher the initial Mn concentration, the more MnO_2 accumulates in the kinetic model.

Figure S8A shows the concentration of DTT at the end of the simulation as a function of Cu(II) concentrations. Fig S8B shows the main reactions of DTT in the presence of Cu. The largest sink of DTT is the formation of $[Cu^{2+}(DTT^{2-})_2]^{2-}$ complex.

Figure S9 shows the main reactions that DTT undergoes in the simulation. The main reactions that DTT undergoes are DTT + HO_2 and DTT + quinones.

Figure S10 shows the concentration of DTT at the end of the simulation as a function of quinone concentrations.

Despite this, study is interesting and potentially valuable, and appropriate for the journal's readership. However, the methodological and interpretive issues may limit the strength of the manuscript in its current form. These critical flaws impact the results and their interpretability. This also limits the wider-applicability and robustness of the model. In my opinion, after careful revision that addresses or clearly highlights these limitations (for future work to identify and address them), this manuscript could be a useful contribution to the literature.

Specific Comments

Abstract:

Comment #1 (Minor Comment):

1. Although Dithiothreitol is a reducing agent with antioxidant properties that replicates biological mechanisms, it should not be considered a conventional antioxidant. It is not naturally present in the human body, nor is it synthesized biologically, nor is it present in foods that we intake. Therefore, it should not be called an antioxidant. A more appropriate term for DTT in place of "antioxidant" would be a "surrogate for biological reductants".

   Thank you very much, we have now changed the wording accordingly.

Here we introduce a chemical kinetic model of oxidative potential (KM-OP) to elucidate and quantify the effects of PM on the production of ROS and the consumption of ascorbic acid (AA) and dithiothreitol (DTT).

2. Please use the correct chemical notation for hydroxyl radical (·OH or $OH^{\cdot}$) in place of OH.

   Thank you, we now add the radical dot to OH throughout the manuscript.

3. It would be better to introduce the name of the chemical Hydrogen Peroxide (H_2O_2) when introducing its chemical formula.

   We have added the spelled-out name when it first appears in the text (line 15).

Introduction

Comment #2 (Minor Comment): *Lines 30-35 – Page 2*; Keep consistent terminology for the OP measured using the hydrogen peroxide method (i.e.,). Presently its being presented as both and in this section.

Thank you for this comment, we now refer to the total peroxide assay as OP^{DCFH}.

Methods

Comment #3 (Minor Comment): *Lines 90 – 95 – Page 4;* Provide a few references of other studies that have used the stiff differential equation solver ode23tb in Matlab.

We now added some previous studies that have used the stiff differential equation solver ode23tb in Matlab.

L93-96: *KM-OP is an autogenerated model script based on a user-supplied chemical mechanism and consists of a system of differential equations, which are solved iteratively using the stiff differential equation solver ode23tb in Matlab, which has performed well in the past in complex kinetic models (Muller et al. 2022, Rapp et al. 2025, Mishra et al. 2025).*

Comment #4: *Lines 95 – 100 and the SI in general*: In its current form, the SI is not organized as per the order of its first mention in the main manuscript. For example, it is mentioned in lines 95 – 100 of the manuscript; however, this section is only on page 39 of SI and not the start.

This makes it difficult and distracting to the reader as the SI flow does not follow the manuscript flow, and readers would need to keep going back and forth within the SI to follow the order of the manuscript.

Please change the SI ordering to match the referencing in the manuscript so that the readers can easily move from one section of the SI to the next one as they are reading the manuscript.

The SI is organized by content type (figures, tables, text). Within each category, the order follows the referencing in the main manuscript. Therefore, although Table S1 is referenced early in the manuscript, it appears later in the SI. We would like to keep this commonly used structure.

Comment #4: *Lines 115 – 185, Page 5-7 and corresponding SI*:

- To my understanding, the HULIS data, the ion chromatography data, etc., from the Grenoble sites are not used as input parameters in the model. If so, these details are not pertinent to the topic of discussion in the manuscript and can be removed.

  We agree with the reviewer and have now removed this from the manuscript.

- Table S3 is misaligned in the SI when moving from page S27 to S28 and S29. Please align this to improve the readability of the table, as the table headings are only given on the first page. This comment applies to the tables for the other three sites, too.

  We now include the table headings in all tables.

- The authors mention in lines 160 -165, that the PM samples were extracted using a Gamble + DPCC solution and vortexed for 2h for the OP analyses. It is also mentioned that the soluble concentrations of Cu, Fe, and Mn were used as inputs in the model based on the table captions in S3 and S4. By soluble fraction of metals, are the authors referring to the water-soluble metal concentrations or Gamble + DPCC-metal concentrations?

  We used water-soluble metal concentrations as inputs in the model, which is now specified in the text.

  L. 128-129: In addition, for this work, the *water*-soluble fraction of the key metals involved in ROS generation (Cu, Mn and Fe) was determined by ICP-MS/MS analyses on the remaining filter samples.

  L. 189-191: No fitting of model parameters was performed to match the field data (forward modeling), i.e., the model developed using the laboratory data was simply applied on the chemical composition data measured in the field, including the *water*-soluble fractions of TMIs, organics, and if available, quinones.

- Were the extraction procedures same for the ICP-MS analyses of the soluble-metals as they were for OP? As the metals have soluble metal concentrations as inputs for the model, were the extraction procedure for the OP and soluble-metal analyses using the same solvent and vortex duration. This is critical information that needs to be provided to ensure that the model input is the same as the metal concentration in the OP extract.

  The extraction conditions for determining OP and soluble metal concentrations were not the same. It was technically not possible for us to use DPPC+Gamble solution for the determination of metal solubility, as this would have contaminated the ICP-MS spectrometer with salts, so the filters were extracted using ultra-pure water. Therefore, there will be some uncertainty between water soluble and Gamble + DPPC- soluble metal

concentrations. Nonetheless, Calas et al., 2017 have shown that the difference in OP in these two mediums are at most 15%.

- The OP measured in London summer site is using an online instrument that incorporates a PILS, as the authors mention in lines 175 – 180. To my understanding, if the OP of the liquid suspension in PILS is analysed, it would also account for the OP of the water-insoluble metal components as well. Please provide information as to whether these measurements were water-soluble or total OP, as solubility factors were incorporated to get the metal inputs for the model? Moreover, it would be optimal to use metal solubility factors from literature that are from the same sampling site. Was this the case for the literature presented in Table S6, as the metal solubility factor data show very large variations for the same metals Fe (0.08 – 0.42), Cu (0.29 – 0.94), and Mn (0.16 – 0.45).

  The online oxidative potential ascorbic acid instrument (OOPAAI), which provides the online OP data, contains an in-line filter which removes insoluble components from the system before the 37 ^{o}C reaction bath. Therefore, OOPAAI only measures the soluble fraction of PM that drives OP^{DHA}.

  The following has been added to clarify:

  L. 178-180: The PM2.5 sample was washed off the impactor continuously at an AA flow rate of 60 µl/min, *passing through an in-line filter to remove insoluble components*. The resulting AA-soluble PM2.5 mixture is then allowed to react for 20 minutes at 37 ^{o}C.

  Moreover, in the current model framework, only the water-soluble fraction of metals is considered. This is based on the assumption that water-insoluble metal components primarily participate via surface-mediated processes, which are not explicitly represented in the kinetic scheme. We will clarify this assumption in the revised manuscript.

  L.191-192: *While water-insoluble PM may increase total OP via surface reactions (Gao et al., 2020), these processes are not represented in KM-OP.*

  We agree that using site-specific metal solubility factors would be preferable. However, such measurements are limited and not available for all sites considered in this study. Consequently, we used literature values compiled from multiple locations (Table S6) when solubility measurements were not available. The wide range in reported solubility factors (e.g., Fe, Cu, Mn) reflects variability across environments. We acknowledge that this introduces uncertainty into the model and will emphasize this limitation more clearly in the revised manuscript.

  L. 391-393: *Note that, no site-specific solubility measurements were available and we used solubility factors from the literature, which introduces additional uncertainty when modelling the London datasets.*

- No data is provided for the London Winter as the authors mention that the data will be presented in a future publication. However, if that data is used as input to the model and

presented as outputs in this publication, I think it should at least be provided as a separate review-only SI. Were the metals for this site also solubility adjusted?

We will provide this data as separate review-only SI. Yes, the metal concentrations for this site were also adjusted for solubility.

- The OP measurements in the sites employing offline (France) and online (UK) protocols are using different solvents to measure the OP of PM. This will severely impact the final OP measured using the two methods. Therefore, I am not sure how representative it would be to model both of them kinetically, without accounting for the differences in the solvents used for the OP measurement.

  We agree with the reviewer that differences in solvent composition between offline (France) and online (UK) OP measurement protocols may influence the reported OP values. These methodological differences are not explicitly represented in the current kinetic framework and may contribute to discrepancies between modeled and measured OP.

  We have added a statement in the manuscript acknowledging this limitation. We note that while OP values can depend on the solvent medium, previous work (Calas et al., 2017) suggests that at low concentrations of PM components, OP values remain comparable across different solvents.

  L. 205-207: *OP values may depend on the solvent medium used in the assay; however, previous studies suggested that at low PM concentrations, differences between solvents are reduced (Calas et al., 2017). This effect is not explicitly accounted for in the current model and may contribute to inter-site variability.*

Comment # 5: Lines 190 – 210: Several assumptions made in the section about the application to field data are unreasonable due to being incorrect and severely undermine the representativeness of the model.

1. It is mentioned that Organics and Quinones were assumed to be fully soluble. This is incorrect and severely undermines the representativeness of the model and its generalizability, especially for the offline samples (and the online samples if the OP measured there are water-soluble OP and not total OP).

Water-soluble organic carbon (WSOC) is usually much smaller than Organic Carbon (OC), and studies have reported that WSOC only constitutes around 20 – 65% of the total OC.[1,2] These solubilities are comparable to or smaller than those of Cu and Mn in tables S3-S6. Moreover, quinones are well known to be insoluble or have very low solubility in water, too.

I acknowledge that the offline OP analyses were in a different medium other than water (Gamble + DPCC), and that organics and quinones may have different solubility in this medium as

compared to water. Is this a polar solvent, and have studies explored the solubility of quinones and organics in this medium? This assumption of organics and quinones being soluble is only valid if there is sufficient evidence that quinones and organics are highly soluble in this medium.

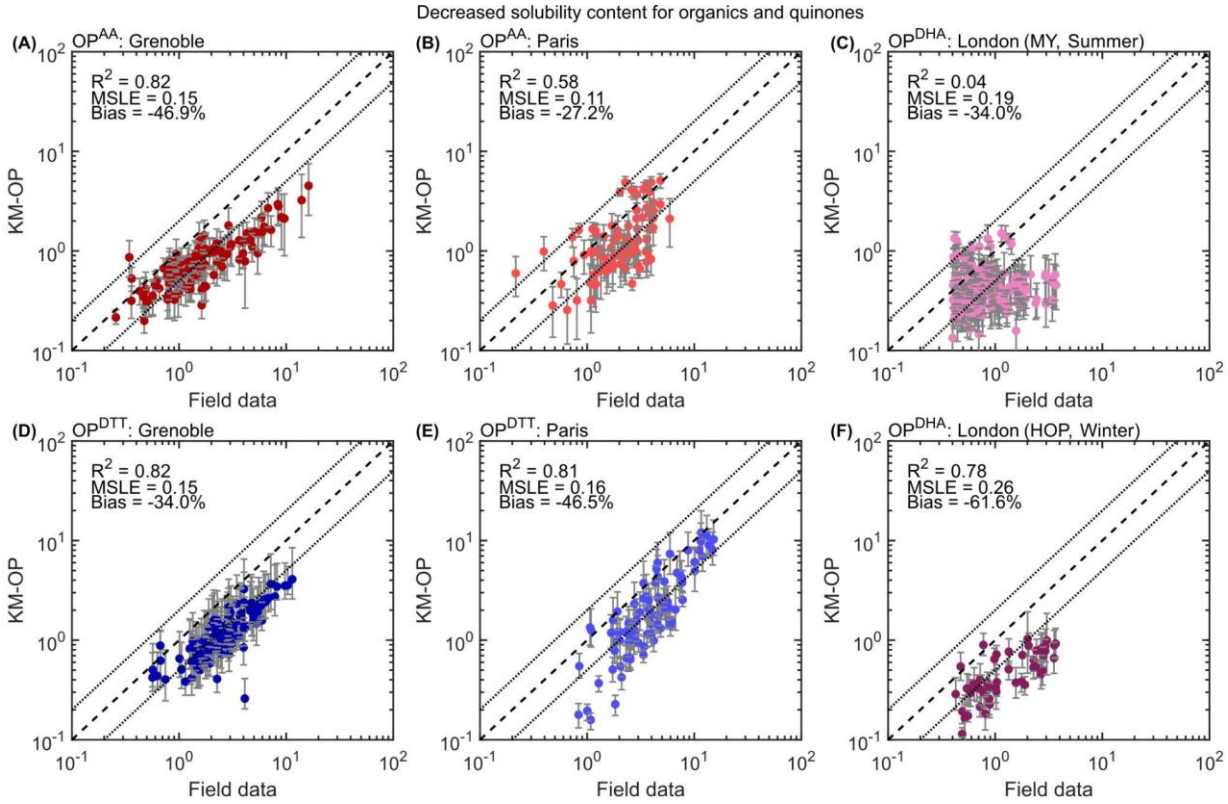
I recommend incorporating the appropriate solubility factors for organics and quinones and using that as the model input to obtain a more representative model.

We thank the reviewer for highlighting the point regarding the solubility of organics and quinones. To address this, we have now performed a sensitivity analysis in which we apply a soluble fractions of 40% for organic carbon and 10% for quinones based on literature-reported ranges for water-soluble organic carbon (WSOC; 20–65% of total OC; Ram et al., 2012, Lammel et al., 2020, Yu et al., 2024). The results are shown below (Fig. R9) and are included in the SI (Fig. S14). The analysis shows that while the absolute OP values are somewhat reduced when using this solubility fraction, the overall trends and site-to-site comparisons remain consistent.

We note that organic hydroperoxides are water-soluble while other organic species such as PAHs and cooking aerosols are not. However, these species are also not known to be redox-active and thus do not play a role in the model. As the ROOH fraction is responsible for the OP of the organic species in the model, reducing this fraction to 40% solubility means that the model underestimates the data.

We note that for the offline assays (Gamble + DPCC solution), data on the solubility of organics and quinones are scarce. Future work could incorporate site- and solvent-specific solubility factors as more data become available.

L.393-394: *A sensitivity analysis accounting for water-insoluble organic and quinone species (Ram et al., 2012; Lammel et al., 2020; Yu et al., 2024) showed reduced absolute OP values, but consistent overall trends and site-to-site comparisons (Fig. S14).*



R9: Sensitivity study on the correlation of model-predicted and measured OP using a solubility factor of 40% for organics and quinones.

1. The authors assume the organic peroxide content in organic aerosol to be 50%. This number is very high. Are the authors referring only to secondary organic aerosols? If so, this needs to be specified.

We assume a hydroperoxide content of 50% in total organic aerosol. We adjusted the text in the abstract from SOA to OA to avoid confusion. We are aware that the peroxide content is likely higher in fresh secondary organic aerosol (Docherty et al., 2005, Krapf et al., 2016, Wang et al., 2023, Li et al., 2024, Li et al., 2025) and lower in certain types of primary organic aerosol, but use this compromise in the absence of measurement data.

Please also refer to our response to reviewer #1 and the new sensitivity study on the organic hydroperoxide content shown in Figs. S12 and S13. In our conclusions, we acknowledge that uncertainties remain in the treatment of organic aerosol that should be addressed in future studies:

L.533-544: Here, using total OA obtained in field measurements, with a focus on organic hydroperoxides as reactive species, and ascribing a single peroxide content for all types of OA resulted in a better agreement between field data and model results. The model could be improved by differentiating between types of OA, such as SOA, biomass burning aerosol,

bioaerosol, etc and by adding other reactive organic compounds. For this, comprehensive kinetic experiments with different types of OA are needed. In particular, OP response may be affected by both SOA precursor identity (e.g., biogenic vs. anthropogenic) or the degree of SOA aging (Tuet et al., 2017; Antiñolo et al., 2015; Chowdhury et al., 2018), which is currently not represented in the model. The degree of oxygenation of organic compounds may not only affect their ability to produce ROS in aqueous solution directly, but may also influence the solubility of metals in the complex internal mixtures of PM in the atmosphere. Future studies should investigate how to infer and integrate such properties of OA from filter analysis. Furthermore, primary particles resulting from traffic or biomass burning will need to be deconvoluted from organics in the model through identification of components driving their redox chemistry.

1. The authors assume the insoluble particles are not redox-active. This is incorrect, as Gao et al.[3] reported that water-insoluble PM species contribute to 20% of the total OP. Similarly, studies quantified the methanol-soluble OP (as this increases the solubility of organics and quinones) have also consistently reported the methanol-soluble OP to be over 50% higher than the water-soluble OP, indicating water-insoluble substances contribute to the OP of PM.[4,5] Water-insoluble species such as quinones are also well known to contribute to OP-DTT.[6]

We thank the reviewer for this important point. We agree that water-insoluble PM components can contribute to the overall OP. However, the mechanisms by which these species contribute to OP are not always clearly attributable to homogeneous redox chemistry and may involve surface-mediated processes that are not explicitly represented in the current kinetic framework.

In this study, we therefore focus on the water-soluble fraction of transition metals, which can be more directly incorporated into the aqueous-phase chemical mechanism. For simplicity, we do not explicitly account for surface reactions of insoluble particles. We note, however, that organic species, including quinones, are treated as effectively soluble in the model, and their contribution to OP is therefore included.

We added the following to the manuscript:

L. 191-192: "While water-insoluble PM may increase total OP via surface reactions (Gao et al., 2020), these processes are not represented in KM-OP."

L. 545-546: We changed “and by describing the surface chemistry of insoluble particles from these sources” to: *Additionally, incorporating heterogeneous surface chemistry of insoluble particles represents an important direction for future model development.*

Results

Comment #6: Figure 3 and associated text:

The results obtained from the KM-OP model here corresponds and compares well with what has been reported in Charrier et al. 2014, 2015.[7,8] In figure 3c, the datapoints presented do not match with those reported in Charrier et al. 2015[7], which only show concentrations till 1000 nM, and also

report a linear increase in ·OH generation with increasing Fe concentrations unlike the KM-OP model simulations in Figure 3C. Are there any reasons behind this mismatch between the experimentally determined results and the model simulations?

While the published figures in Charrier et al., 2015 display Fe concentrations only up to 1000 nM, the underlying dataset obtained directly from J. Charrier, which we used for our analysis, includes Fe concentrations exceeding 1000 nM. Note that the SI of Charrier et al., 2015 shows Fe concentrations that go beyond 1000 nM. We state in our Acknowledgements section that we received data through personal communication with J. Charrier.

The main takeaway in my understanding from this section is in figures S1-S3, where the dominant reactions that lead to H_2O_2 and ·OH generations in different concentration regimes of quinones and Cu are presented. However, the figures are shown only in the SI with very limited textual explanation, making it very difficult to fully interpret these results. What is the definition of normalized sources of H_2O_2 in those figures? Please provide a detailed explanation of those figures in the SI.

We now added additional text for the figures in the SI. Please see our response above.

Comment #7: Figure 4 and associated text:

- In Figure 4a, it looks like the fit ensemble of the model consistently overestimates the AA consumption rates compared to all three experimental conditions. The AA concentration in the experimental data is almost on the cusp of the model uncertainty and is sometimes higher than the model range.
- In the case of Cu, the model data shows an exponential reduction in the AA concentration, which is unlike experimental data that shows a linear reduction in AA. What is causing this large deviation in the kinetics of AA consumption due to the presence of Cu?

  We agree with the reviewer that the model shows a larger uncertainty for AA consumption by Cu and does not capture the linear behavior of the data published by Exposito and colleagues. This is because the model is calibrated against all available experimental datasets simultaneously. Consequently, it is not always possible to perfectly reproduce the kinetics of individual experiments, especially when fitting multiple datasets with differing conditions, and the model reacts with a spreading out of the fit ensemble, reflecting this uncertainty. Please see our detailed response above.

- In table S1, what are the values given in the range? Is it the kinetic rate coefficients? If so, what are the units? Please provide these details.

  Yes, these are reaction rate coefficients. As units differ based on the reaction order, they are provided in the table header.

- Why is the range of values for a lot of reactions that are not from literature very high, spanning 4-6 orders of magnitude?

For reactions that are not well characterized in the literature, we set broad optimization boundaries to allow the fitting procedure sufficient flexibility to identify rate coefficients that are consistent across multiple experimental datasets. This approach reflects the inherent uncertainty in these poorly constrained reactions that cannot be further constrained by the set of experimental training data. We typically observe such wide ranges for reactions that are relatively non-influential in the overall fitting process or form non-orthogonal pairs with other reactions (Berkemeier et al., 2013; Berkemeier et al., 2017).

We now include a box–whisker analysis (see Fig. S1), which highlights which reactions are well constrained by the optimization and which exhibit high variability, as outlined in our response to reviewer 1.

Moreover, we now also provide the best-fit values alongside the parameters' ranges within the fit ensemble.

Comment #8: Figure 5 and associated text:

- There is clear differences between the model simulations of Cu in Charrier et al. 2012, [6] and Exposito et al. 2024, reflecting the differences in the experimental data due to the differences in their respective DTT concentrations, 100 and 50 µM, respectively. Which of these two simulations was incorporated to predict the OP-DTT of the field data from Grenoble and Paris? What were the DTT concentrations for OP measurements for those samples from Grenoble and Paris?

  We thank the reviewer for pointing this out. All of the available laboratory datasets (Fig. 3-6) were used to calibrate the reaction rate coefficients in the KM-OP model, and thus all of these simulations were incorporated to predict the OP-DTT of the field data. When predicting the field data, we used the DTT concentrations that were actually applied in the corresponding field measurements. The specific experimental conditions for the Grenoble and Paris datasets are provided in section 2.4.1 of the manuscript. As we state in the manuscript, the DTT concentration in the assay was 42 µM. As stated above, we think that the differences between the Exposito et al. 2024 and the Charrier et al. 2012 data are not only concentration effects, but likely also experimental discrepancies.

  The DTT loss-rates become non-linear at higher quinone concentrations using the KM-OP model for 1,2 NQN and PQN in figure 5d. What is the reason or mechanistic explanation behind this, as this does not match with the previously reported literature using laboratory experimental data?

  As stated in the manuscript (L. 315–318), the non-linearity arises because, at higher concentrations of 1,2-NQN and PQN, the DTT concentration decreases by more than 50% over the course of the simulation (Fig. S10). This depletion leads to an apparent slow down of the kinetics.

- In 5d, yet again, we observe that the model simulates an exponential reduction in the DTT concentrations due to reactions with PQN and 1-2 NQN. This does not align with what

was reported experimentally in Xiong et al. 2017.[9] Moreover, we see that the experimental results are on the upper bound of the error of the model simulations, with the model ensemble mean overestimating the DTT loss rates. Please comment on what may be causing this mismatch between the model simulations and experimental measurements?

As stated above, the model strikes a balance between different data sets (here, among others, especially Xiong et al. 2017 and Charrier et al., 2012) and reacts by increasing the uncertainty when mismatches arise. This uncertainty is propagated all the way through to the comparison of model and field data via the ensemble solutions (error bars in Figs. 7 and 9).

- Please provide detailed explanations for the figures S6 – S9 in the SI.

As stated above, we now added additional text for figures in the SI.

Comment #9: Figure 7 and associated text:

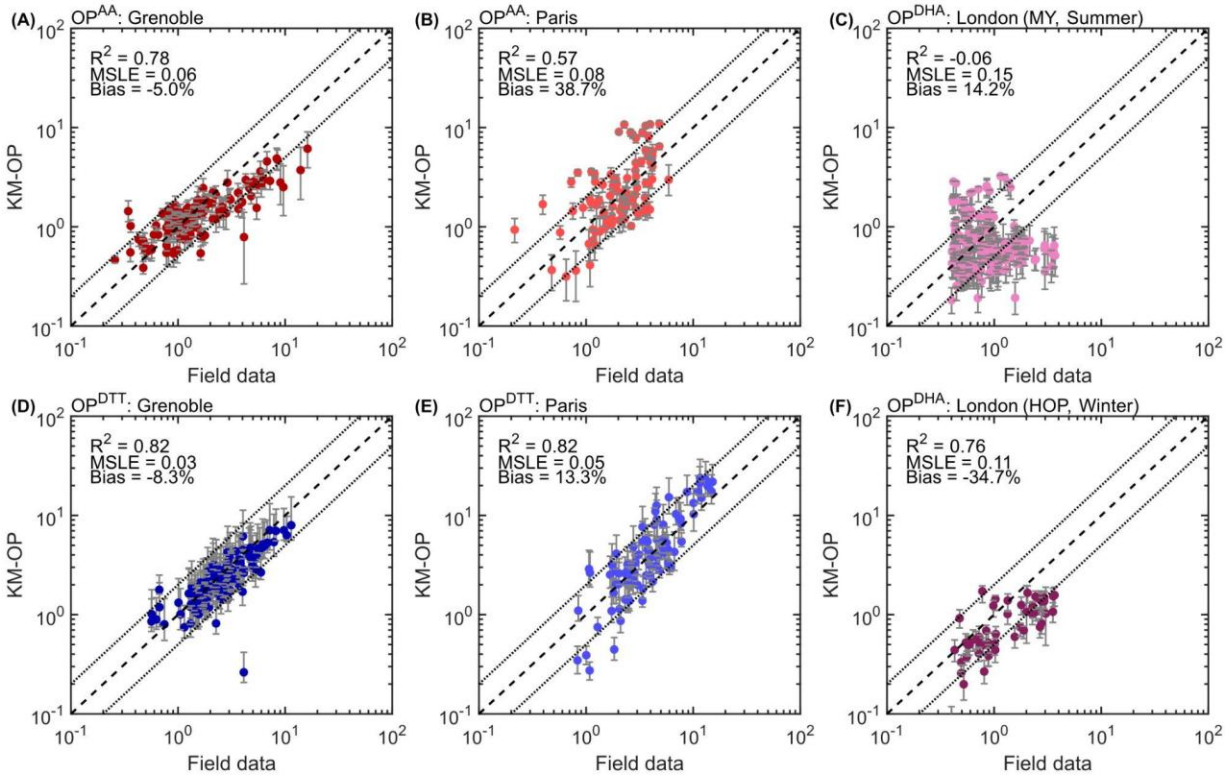
1. As the reaction rates of organics, which are not really shown in prior sections or SI, how did the model use the organic model input data to predict the OP presented in Figure 8?

The KM-OP model incorporates organic species through the reactions listed in Table S1 and are shown in Fig.1. The rate coefficients for these reactions were taken from the literature and evaluated against available experimental data from Tong et al., 2018 and Tuet et al., 2017 as shown in Fig. 6. These reactions allow the model to predict the contribution of organics to OP, which is reflected in the results presented in Figure 8.

2. The model correlation is good, and the MLSE is low. However, it is difficult to ascertain the degree of underestimation in the OP from the model output and compare it to the experimental data due to the use of a logarithmic scale. Please provide this value by either providing the average slope of the best-fit line in a linear graph or calculating the average of the ratios of the modelled/measured data for each site and OP endpoints, and mentioning this in the manuscript. This is critical information to evaluate the model performance.

Thank you for the suggestion. We now report the bias of the model as the average of (model - data)/data*100 for each site and OP endpoints, and use this in the discussions to evaluate model performance.

The equation is now listed in the SI, section S3.8.



R10: Correlation scatter plots of model-predicted and measured OP for particulate matter samples collected in three different sites across Europe.

3. Provide the average±SD values of the model output and compare them with the measurement data average±SD for each site and OP endpoint.

   Unfortunately, there are no replicates of the measurement data, so we cannot provide the standard deviation.

Comment #10: Figure 9 and associated text:

- The modelled OP in Figure 9 does not follow the trends of the measured OP and is contradictory to the measured data. For example, the OP-DHA values from the field data in London during both summer and winter are clearly much higher than the OP-AA values in both Grenoble and Paris. However, this seems to be contradictory to the model output in figure 9 where the values are higher in France.

  Thank you for the valuable comment. The apparent discrepancy arises from differences in units between the figures. In Fig. 7 the units of OP^{DHA} are nmol m^{-3} as this is the units of the output of the online instrument. In Fig. 9a, we showed OP^{DHA} in units of nmol/min/m^3 for ease of comparison with other OP assays.

  We decided to now show Fig. 7 also in the units of nmol/min/m^3 to avoid confusion.

This revision revealed an error in the original manuscript in Fig. 9B where OP^{DHA}, originally expressed in units of nmol m^{-3}, was being compared to OP metrics reported in nmol min^{-1} m^{-3}. Converting OP^{DHA} to the same units (nmol min^{-1} m^{-3}) improved its correlation with the other OP metrics from 0.18-0.80 to 0.65-0.87.

- The values of OP-OH and OP-H_2O_2 can be put on a different scale with pmol/(min.m^3) instead of being shown as a multiple of 10 or 30 to avoid confusion.

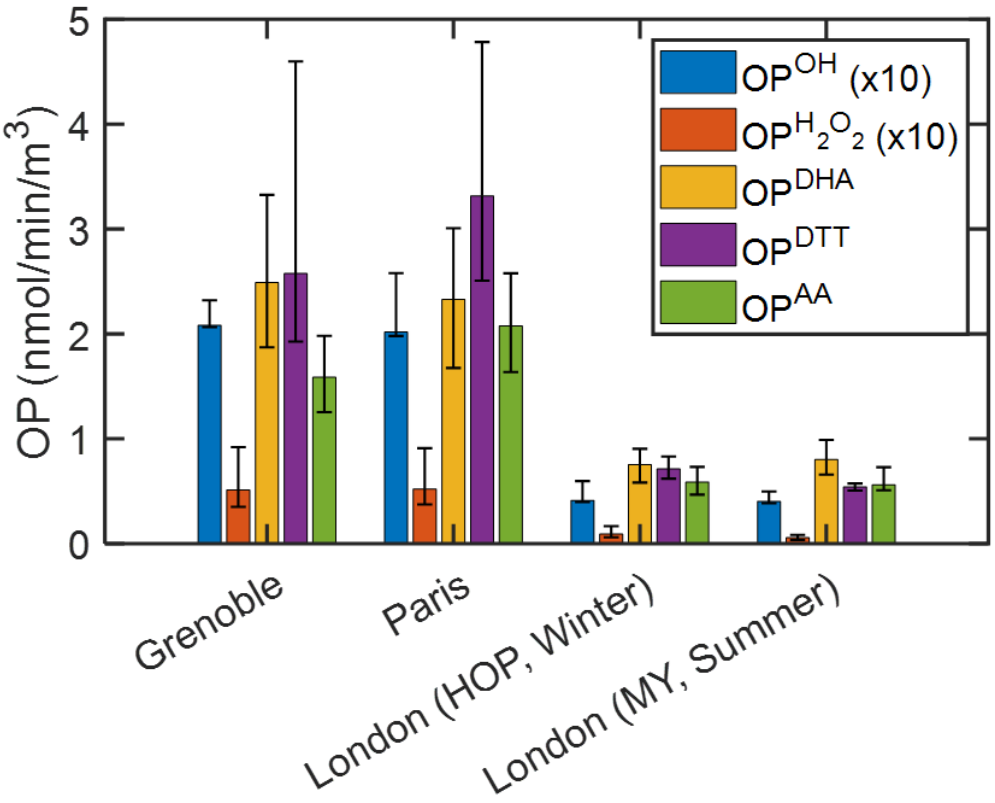
  Thank you for the suggestion. We think it is clearer to multiply both values by 10 instead of placing them on a different scale.

- The average OP-DHA values in the UK measured experimentally seem to be roughly around 10 nmol/(min·m^3), based on figure 7 (please provide the exact values). However, the model only predicts this to be around 1 nmol/(nmol·m^3). This is almost an order of magnitude lower. Similarly, I also think the model output for the French data is a significant underestimation of the measurements.

  As noted above, this discrepancy arose from differences in units between figures 7 and 9, which has now been resolved.

- Provide the error bars for the model output in figure 9.

  Thank you for the suggestion, we have now included error bars for the model output.



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