Supplementary information to

Hydroxyl radical production by air pollutants in epithelial lining fluid governed by interconversion and scavenging of reactive oxygen species

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S1. ELF antioxidant concentrations

Four low molecular weight antioxidants are included in this study, ascorbate (AscH), glutathione (GSH), uric acid (UA) and α-tocopherol (α-Toc). The concentrations of AscH, GSH, and UA in the ELF are 40 µM, 108 µM, and 200 µM, respectively. The total α-Toc concentration in the ELF is reported as 0.7 µM. However, in the presented study α-Toc is assumed to reside in the surfactant layer of the ELF with a concentration of 200 µM. It is found that pollutant exposure can lead to a spike in C_{EROS} at pollutant concentrations above 100 µg m\(^{-3}\) in the model (Fig. S3a) due to NO\(_2\)-driven depletion of ELF antioxidants within the two hours simulation time (Fig. S3b). The reaction mechanism of ROS formation by NO\(_2\) involves formation of GS\(^-\) (R84-85, Tab. S1) and reaction to GSSG\(^-\) (R89), leading to O\({}_2^-\) production (R91). In the presence of physiological concentrations of UA and AscH, GS is efficiently recycled to GSH (R96, R100) and GSSG\(^-\) formation a minor reaction pathway. However, at low levels of UA and AscH, this O\({}_2^-\) formation pathway becomes increasingly important.

Although earlier studies have shown that antioxidants can be consumed in bronchoalveolar lavage fluid after pollutant exposure, a study using healthy volunteers suggested that the ELF antioxidants may not be fully depleted, even after exposure to high pollutant concentrations. Kelly et al. found antioxidant concentrations to be non-zero 1.5 hours after exposure to 2 ppm NO\(_2\) stopped, and in some cases exceeded the initial antioxidant concentration several hours after exposure due to antioxidant replenishment. We are not aware of kinetic data that details the replenishment rates of antioxidants in ELF, but we can assume that they are likely fast enough to prevent full depletion of antioxidants in our two-hour simulations, preventing a spike in C_{EROS} (Fig. S3a). Thus, for simplicity, antioxidant and surfactant concentrations are assumed to stay constant in this study.

In Fig. S3b, antioxidant consumption rates are shown as a function of NO\(_2\), PM2.5 and O\(_3\) concentration. The dashed line represents the antioxidant consumption rate above which the initial concentration of low molecular mass antioxidants depletes within two hours of pollutant exposure. Note that, without consideration of enzymatic reactions and antioxidant replenishment, it represents a lower limit for healthy individuals.

S2. ELF enzymatic reactions

Reactions of the enzymes superoxide dismutase (SOD) and catalase are included in the chemical mechanism (R124, R125, Tab. S1). In our previous work, the SOD-catalyzed reaction of two O\({}_2^-\) forming H\(_2\)O\(_2\) and O\(_2\) was described as a second-order reaction with respect to O\({}_2^-\) and a rate coefficient of 2.70 \times 10\(^{-12}\) cm\(^{-3}\) s\(^{-1}\). Dismutation of O\({}_2^-\) by SOD is a multi-step process, in which one O\({}_2^-\) is oxidized to O\(_2\), another reduced to H\(_2\)O\(_2\), and operates close to the diffusion limit. Because SOD activity is often reported in terms of a single rate and turnover number, we combine both steps into one effective reaction of SOD...
and O$_2^-$ yielding 0.5 H$_2$O$_2$ and 0.5 O$_2$ (R124, Tab. S1). Note that this reaction is first order with respect to both, O$_2^-$ and enzyme.

Cantin et al. (1990) showed experimentally that catalase is the most important molecule in H$_2$O$_2$ defense of the ELF, exceeding the glutathione peroxidase concentration by nearly two orders of magnitude.$^{10}$ The reaction between catalase and H$_2$O$_2$ is a two-step reaction in which a molecule of H$_2$O$_2$ reacts with catalase to form an enzyme-substrate complex, which then further reacts with another molecule of H$_2$O$_2$ to release H$_2$O and O$_2$. Because catalase activity is often reported in terms of a single rate and turnover number, we combine both steps into one effective reaction of catalase and H$_2$O$_2$, yielding 0.5 H$_2$O and 0.5 O$_2$ (R125, Tab. S1).$^{11}$

The catalytic activity of a particular enzyme in biological samples is often reported using the enzyme unit (U) per sample volume or mass. One U is defined as the amount of enzyme needed to catalyze one micromole of substrate per minute. The catalytic activity of a biological sample is generally determined by monitoring substrate decomposition in excess of substrate. Under these conditions, catalytic activity is maximal and a first order dependence exists between the velocity of the enzymatic reaction ($v_{max}$, in U mL$^{-1}$) and the enzyme concentration (Eq. S1).$^{12}$ The proportionality factor is the turnover number $k_{cat}$, sometimes referred to as catalytic constant, and can be used to infer enzyme concentrations.$^{13}$

$$[\text{Enzyme}] = \frac{v_{max}}{k_{cat}}$$ (Eq. S1)

For SOD, $k_{cat}$ is reported to range between $10^5 – 10^6$ s$^{-1}.$$^{9,14}$ The activity of SOD in ELF was measured as $36.8 \pm 2.0$ U mL$^{-1},$ which translates to an enzyme concentration of SOD of 0.58 – 6.5 nM using Eq. S1. Note that, the enzymatic reactions in this study do not occur in excess of substrate. Thus, a second-order rate coefficient for the reaction of SOD with O$_2^-$ of $2.65 \times 10^{-12}$ cm$^3$ s$^{-1}$ is used in the chemical mechanism ($K_{R124}$, Tab. S1).$^{15,16}$

Catalase activity in ELF has been estimated to be $3.7 \pm 0.6$ U mL$^{-1}$ and for $k_{cat}$, values in the range of $3 \times 10^6$ and $4 \times 10^7$ s$^{-1}$ can be found.$^{10,13}$ From these numbers, we derive a concentration of catalase of $1.3 – 24$ pM. Second-order rate coefficients for catalase have been measured in the range of $1.6 \times 10^{-14} – 1.6 \times 10^{-13}$ cm$^3$ s$^{-1}$. For this study, we use a rate coefficient of $3.2 \times 10^{-14}$ cm$^3$ s$^{-1}$ ($k_{R125}$, Tab. S1).$^{11,17}$

Given the broad reported ranges of $v_{max}$ and $k_{cat}$, and the difficulty of sampling ELF, we acknowledge that there is large uncertainty associated with the concentrations of SOD and catalase in the ELF. Therefore, we restrict the determination of enzyme concentration to order of magnitude estimations and use 1 nM for SOD and 5 pM for catalase in this study.

Note that the presence of PM may decrease the activity of antioxidant enzymes, as shown for SOD previously.$^{18}$ At the high PM concentrations for which these effects were observed, however, antioxidant
enzymes contribute only marginally to overall ROS scavenging and interconversion in the model (Figs. 112 4b,d). Thus, enzyme inhibition by PM2.5 requires further investigation in future experimental and modelling studies to clarify whether enzyme inhibition promotes the shift to the PM2.5-dominated kinetic regime of ROS conversion.

S3. Unspecific reaction of OH radicals with organic matter and estimated OH lifetime in the ELF

OH reacts with nearly all matter present in the ELF with a rate coefficient approaching diffusion limitation.\(^{19}\) Because of this unspecific reactivity, effective scavenging of OH radicals, e.g. through lung antioxidants, is not possible.\(^{19,20}\) As an estimate, we assume that the amount of protein in the ELF corresponds to the total amount of dissolved organic matter. The protein mass in the ELF amounts to approximately 10 mg per mL lung fluid.\(^3\) Using an average molecular weight of ~125 g mole\(^{-1}\) of a single amino acid, the total amino acid concentration in the ELF can be estimated to ~80 mmol L\(^{-1}\). A second-order reaction of amino acids with OH is included, using a reaction rate coefficient on the order of 1.66 \(\times 10^{-12}\) cm\(^3\) s\(^{-1}\) (R122, Tab. S1).\(^{21}\)

Because proteins are folded, not all amino acids will be surface exposed, and thus accessible reaction partners for OH. In general, spherical proteins have fewer surface exposed amino acids due to a smaller surface-to-volume ratio, while elongated, cuboid or conical proteins have more surface exposed amino acids. Furthermore, the surface exposure of amino acids depends on the physical properties, e.g. the polarity of the respective amino acid.\(^{22}\) Therefore, as an order of magnitude estimation, we assume that 50% of all amino acids are surface exposed in the ELF, yielding an effective amino acid concentration of ~40 mmol L\(^{-1}\) and, in turn, a lifetime of OH with respect to reaction with dissolved organic matter of \(2.5 \times 10^8\) s.

Pryor estimated the lifetime of OH in a cell to \(10^9\) s, assuming a rate coefficient of \(1 \times 10^9\) M\(^{-1}\) s\(^{-1}\) (equivalent to \(1.66 \times 10^{-12}\) cm\(^3\) s\(^{-1}\)) and an effective organic matter concentration of 1 mol L\(^{-1}\).\(^{21}\) From comparing the ELF protein mass of ~10 mg mL\(^{-1}\) to the cellular protein mass of ~250 mg mL\(^{-1}\), we infer that the ELF must be about ~25 times more dilute compared to a cell with respect to dissolved organic matter.\(^{2,23,24}\) Multiplying Pryor’s OH lifetime in cells with this dilution factor yields an estimate for the OH lifetime in ELF of \(~2.5 \times 10^8\) s, which is identical to the estimate above and consolidates our description of OH reactivity.

We find that inclusion of this second-order loss reaction of OH results in a decrease of momentary OH concentrations by one order of magnitude compared to our earlier calculations (Fig. 2a).\(^1\) This finding suggests that OH will react unspecifically with organic matter and only secondarily with antioxidants (7%) in the ELF. Due to the fast reaction of OH, spatial gradients of reactants could play a role in OH fate, e.g. through local depletion of antioxidants around a dissolving particle or inhomogeneous distribution of organic matter and PM2.5 constituents in the ELF. However, for the calculations in this study, starting concentrations of antioxidants and organic matter were homogeneous across the bulk ELF.
S4. Particulate pollutant concentrations in the ELF

The ELF concentrations of redox-active PM2.5 constituents, \( C_{\text{ELF,Y}} \), with Y standing for copper, iron, SOA, or quinones, are calculated using Eq. S2.¹

\[
C_Y = \frac{C_{\text{gas,PM2.5}} \times VR \times t_{\text{acc}} \times d_{\text{PM2.5}} \times MF_Y \times SF_Y}{M_Y \times V_{\text{ELF}}} \quad \text{(Eq. S2)}
\]

Inhaled particles can reside in the ELF for several hours.²⁵ For this study, we assume a residence time of PM2.5 of 2 hours and use this as accumulation time of inhaled particles (\( t_{\text{acc}} \)) and simulation time (\( t_{\text{sim}} \)) to mimic a pseudo steady-state of ROS concentrations that would be achieved through continuous inhalation, in line with our previous studies.¹ It should be noted that there is some uncertainty regarding the residence time of PM2.5 in the ELF, with estimates on PM2.5 clearance also exceeding 2 hours.²⁶ As lung ventilation rate, \( VR \), 1.5 m³ h⁻¹ is used, and the PM2.5 deposition fraction in the ELF, \( d_{\text{PM2.5}} \), is assumed to be 0.45.¹,²⁷ The total ELF volume, \( V_{\text{ELF}} \), is set to 20 mL.¹,²⁸ This study only includes copper and iron as transition metals, because these are the only two that have been shown to significantly produce ROS in surrogate ELF (sELF).²⁹,³⁰ The fractional solubilities, \( SF_Y \), of copper and iron ions were discussed and tested extensively in our previous study, including the effects of varying trace metal solubilities.¹ In line with the main results of our previous study, the fractional solubilities of copper and iron ions are set to 0.4, 0.1, respectively.¹ Due to the relatively small concentration of iron ions and the large concentration of potential organic ligands, iron ions are expected not to precipitate in the ELF.³¹ For the organic fraction in PM2.5, full solubility is assumed. Mass fractions (\( MF \)) of redox-active PM2.5 constituents are derived from field observations and tabulated in Tables S4-S6. Not all references in Tables S4 and S6 include PM2.5 concentrations. In such cases, PM2.5 concentrations are estimated based on similar geographical locations and indicated with an asterisk. Additionally, secondary organic aerosol (SOA) forms ROS and is included in the model.³²-³⁴ However, because the exact mechanism of ROS formation by SOA in the ELF, first order formation rates of \( \text{H}_2\text{O}_2 \) and OH by SOA were parameterized based on experimental observations.¹,³²,³³ Quinones in PM2.5 are included in this study as previously described.¹ Three quinones are included that were shown to form ROS in sELF, phenanthrenequinone (PQN), 1,2-naphthoquinone (1,2-NQN), and 1,4-naphthoquinone (1,4-NQN) in a molar ratio of 2:1:1.²⁹

S5. Gas-phase pollutant concentrations in the ELF

Exposure to gas-phase oxidants, \( \text{O}_3 \) and NO₂ is quantified in the model using a simplified breathing mechanism. In our previous study, it was assumed that the concentrations of these gas-phase oxidants in the lung were equal to their respective ambient concentrations. However, because of the reactivity of these oxidants, we find that lung gas-phase concentrations of these oxidants are depressed and limited by supply from inhalation of ambient air. In order to get accurate estimates for the amount of gas-phase oxidants
transferred to the surfactant layer and ELF, an average lung volume of four L, an average breath volume of 1.5 L and an average duration of a breath of 3.6 s are used to compute mass fluxes into and out of the lung (Table S2). Application of this simplified breathing mechanism results in a significant decrease in the amount of gaseous oxidants in the surfactant layer and ELF. Therefore, neither O₃, nor NO₂ are saturated in ELF with respect to their ambient concentrations in this study (Fig. S5).

S6. Acid dissociation
In this study, corresponding acid/base-pairs are treated as a single species in the numerical computation of ordinary differential equations (ODE). This effectively reduces the stiffness of the ODE system and applies to glutathione (GSH/GS), superoxide radicals (HO₂/O₂⁻) and peroxynitrous acid (ONOOH/ONOO⁻). Instead of treating each species explicitly with separate differential equations and explicit protonation and deprotonation reactions, the pKa of these species was used to calculate the acid/base-ratio at the pH of the ELF (Table S2). Then, if a reaction requires only one of the two species to react, the rate of that reaction was multiplied with the inferred fraction of the reacting species.

S7. pH of the ELF
Following estimations by Holma (1985, 1989), the pH of the ELF was assumed to stay constant upon air pollutant exposure. In diseased individuals such as asthmatics, chronic obstructive pulmonary disease, or cystic fibrosis patients the pH of the ELF may be decreased. Figure S6 shows the ROS concentration, production, interconversion and transition metal valence state at pH 7 and pH 4 as a function of PM2.5 concentration. Panel a shows that C_ΣROS displays a very similar behavior at pH 4 and pH 7. C_O₂⁻ and C_HO₂ are slightly increased at low PM2.5 concentrations, but depressed at elevated PM2.5 concentrations (panel b). This reduction is due to a higher rate of Fe²⁺-mediated interconversion of HO₂ and O₂⁻ to H₂O₂ (Table S1, R38 and R39), which in turn is due to a higher Fe²⁺/Fe³⁺ ratio (panel c). The Cu⁺/Cu²⁺ ratio shows the opposite trend at reduced pH (panel j).

Panel e shows that at pH 4, N_ΣROS is marginally reduced compared to pH 7. In panel f, N_ΣROS is broken down to its components. P_O₂⁻ is slightly reduced due to decreased Cu⁺-dependent O₂⁻ formation (Table S1, R54). P_OH is slightly increased due to the higher Fe²⁺/Fe³⁺ ratio and the according increase in the Fenton reaction (Table S1, R40).

Panel g shows that CF_O₂⁻→H₂O₂ is slightly decreased at low PM2.5 concentration and slightly increased at higher PM2.5 concentrations compared to pH 7. Panel h shows that CF_H₂O₂→OH is mostly unaffected by a change in pH. The reduction in N_ΣROS (panel e) paired with the increase in P_OH (panel f) at higher PM2.5 concentrations results in a larger OH fraction (panel i) and a larger increase in OH dose (panel j) at pH 4.

Reduced pH in the ELF may additionally lead to a reduction in antioxidant enzyme activity, increased transition metal solubility, and increased OH yield from the Fenton reaction. These effects are not included in the presented study, and are expected to all reduce ROS buffering and promote the PM2.5-
controlled OH radical production regime, which may exacerbate oxidative stress. Furthermore, in the presented study SOA produces H₂O₂ and OH,\(^{32,33}\) which at lower pH may increasingly shift towards only H₂O₂ production, without OH getting formed.\(^{43,44}\) However, a thorough investigation of pH effects is beyond the scope of the presented study and warrants future investigations.
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### Table S1. Chemical reactions, rate constants as used in the KM-SUB-ELF, with reference

| #  | Reaction                                                                 | Rate constant (cm$^3$ s$^{-1}$ or s$^{-1}$) | Reference |
|----|--------------------------------------------------------------------------|---------------------------------------------|-----------|
| 1  | NO$^*$ + O$_3$ → NO$_2^*$ + O$_2$                                         | 2.05 × 10$^{-14}$                           | 45,46     |
| 2  | NO$_2^*$ + O$_3$ → NO$_3^*$ + O$_2$                                       | 4.85 × 10$^{-17}$                           | 45,46     |
| 3  | NO$^*$ + NO$^*$ + O$_2$ → NO$_2^*$ + NO$_2^*$                             | 8.93 × 10$^{-20}$                           | 45,46     |
| 4  | NO$^*$ + NO$_3^*$ → NO$_2^*$ + NO$_2^*$                                   | 2.57 × 10$^{-11}$                           | 45,46     |
| 5  | NO$_2^*$ + NO$_3^*$ → NO$^*$ + NO$_2^*$ + O$_2$                           | 7.73 × 10$^{-16}$                           | 45,46     |
| 6  | NO$_2^*$ + NO$_3^*$ → N$_2$O$_5$                                         | 1.21 × 10$^{-12}$                           | 45,46     |
| 7  | *OH + O$_3$ → HO$_2^*$ + O$_2$                                           | 8.20 × 10$^{-14}$                           | 45,46     |
| 8  | *OH + H$_2$O$_2$ → HO$_2^*$ + H$_2$O                                     | 1.73 × 10$^{-12}$                           | 45,46     |
| 9  | HO$_2^*$ + O$_3$ → *OH + O$_2$ + O$_2$                                    | 8.24 × 10$^{-16}$                           | 45,46     |
| 10 | *OH + HO$_2^*$ → H$_2$O + O$_2$                                         | 1.08 × 10$^{-10}$                           | 45,46     |
| 11 | HO$_2^*$ + HO$_2^*$ → H$_2$O$_2$ + O$_2$                                  | 5.09 × 10$^{-12}$                           | 45,46     |
| 12 | HO$_2^*$ + HO$_2^*$ → H$_2$O$_2$                                         | 3.50 × 10$^{-12}$                           | 45,46     |
| 13 | *OH + NO$^*$ → HONO                                                      | 8.91 × 10$^{-12}$                           | 45,46     |
| 14 | *OH + NO$_2^*$ → HNO$_3$                                                  | 8.91 × 10$^{-12}$                           | 45,46     |
| 15 | *OH + NO$_3^*$ → HO$_2^*$ + NO$_2^*$                                     | 2.00 × 10$^{-11}$                           | 45,46     |
| 16 | HO$_2^*$ + NO$^*$ → *OH + NO$_2^*$                                       | 8.24 × 10$^{-12}$                           | 45,46     |
| 17 | HO$_2^*$ + NO$_2^*$ → HO$_2$NO$_2$                                       | 6.87 × 10$^{-13}$                           | 45,46     |
| 18 | HO$_2$NO$_2$ → HO$_2^*$ + NO$_2^*$                                       | 2.49 × 10$^{-1}$                            | 45,46     |
| 19 | *OH + HO$_2$NO$_2$ → NO$^*$ + H$_2$O + O$_2$                             | 2.96 × 10$^{-12}$                           | 45,46     |
| 20 | HO$_2^*$ + NO$_3^*$ → *OH + NO$_2^*$                                     | 4.00 × 10$^{-12}$                           | 45,46     |
| 21 | *OH + HONO → NO$_2^*$ + H$_2$O                                          | 5.78 × 10$^{-12}$                           | 45,46     |
| 22 | *OH + HNO$_3$ → NO$^*$ + H$_2$O                                         | 1.37 × 10$^{-13}$                           | 45,46     |
| 23 | N$_2$O$_5$ → NO$_2^*$ + NO$_3^*$                                         | 1.83 × 10$^{-1}$                            | 45,46     |

**Gas-phase reactions**

**Surfactant reactions**

| #  | Reaction                                                                 | Rate constant (cm$^3$ s$^{-1}$ or s$^{-1}$) | Reference |
|----|--------------------------------------------------------------------------|---------------------------------------------|-----------|
| 24 | SPB + *OH → SPB-ox                                                      | 1.70 × 10$^{-11}$                           | 47–49     |
| 25 | POG + *OH → POG-ox                                                      | 1.70 × 10$^{-11}$                           | 1         |
| 26 | SPB + O$_3$ → SPB-ox                                                   | 1.00 × 10$^{-14}$                           | 50,51     |
| 27 | POG + O$_3$ → POG-ox + 0.17 H$_2$O                                      | 1.66 × 10$^{-16}$                           | 52–55     |
| 28 | aToc + OH → aToc-ox                                                    | 4.50 × 10$^{-13}$                           | 56        |
| 29 | aToc + O$_3$ → aToc-ox                                                 | 1.20 × 10$^{-18}$                           | 57        |

**ELF reactions**

| #  | Reaction                                                                 | Rate constant (cm$^3$ s$^{-1}$ or s$^{-1}$) | Reference |
|----|--------------------------------------------------------------------------|---------------------------------------------|-----------|
| 30 | O$_2^*$ + HO$_2$ + H$_2$O → H$_2$O$_2$ + OH$^*$ + O$_2$                 | 1.70 × 10$^{-13}$                           | 1,58      |
| 31 | HO$_2$ + HO$_2$ → H$_2$O$_2$ + O$_2$                                    | 1.40 × 10$^{-15}$                           | 58        |
32. \( O_2^- + O_2^- + 2H^+ \rightarrow H_2O_2 + O_2 \)
33. \( H_2O_2 + \cdot OH \rightarrow HO_2 + H_2O \)
34. \( \cdot OH + \cdot OH \rightarrow H_2O \)
35. \( \cdot OH + O_2^- \rightarrow O_2 + OH^- \)
36. \( \cdot OH + HO_2 \rightarrow H_2O + O_2 \)
37. \( H_2O_2 + HO_2 \rightarrow \cdot OH + O_2 + H_2O \)
38. \( Fe^{2+} + O_2^- + 2H^+ \rightarrow Fe^{3+} + H_2O_2 \)
39. \( Fe^{2+} + HO_2 + H^+ \rightarrow Fe^{3+} + H_2O_2 \)
40. \( Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + \cdot OH + OH^- \)
41. \( Fe^{2+} + \cdot OH \rightarrow Fe^{3+} + OH^- \)
42. \( Fe^{2+} + H_2O_2 \rightarrow Fe^{4+} + H_2O \)
43. \( Fe^{3+} + H_2O_2 \rightarrow Fe^{2+} + HO_2 + H^+ \)
44. \( Fe^{3+} + HO_2 \rightarrow Fe^{2+} + O_2 + H^+ \)
45. \( Fe^{4+} + Fe^{2+} \rightarrow Fe^{3+} + Fe^{3+} \)
46. \( Fe^{3+} + Asch \rightarrow Fe^{2+} + Asc^- \)
47. \( Fe^{4+} + Asch \rightarrow Fe^{3+} + Asc^- \)
48. \( Fe^{2+} + O_2 \rightarrow O_2^- + Fe^{3+} \)
49. \( Cu^+ + HO_2 + H^+ \rightarrow Cu^{2+} + H_2O_2 \)
50. \( Cu^+ + O_2^- + H_2O \rightarrow Cu^{2+} + H_2O_2 + OH^- \)
51. \( Cu^{2+} + HO_2 \rightarrow Cu^+ + O_2 + H^+ \)
52. \( Cu^{2+} + O_2^- \rightarrow Cu^+ + O_2 \)
53. \( Cu^{2+} + Asch \rightarrow Cu^+ + Asc^- \)
54. \( Cu^+ + O_2 \rightarrow Cu^{2+} + O_2^- \)
55. \( Cu^+ + H_2O_2 \rightarrow Cu^{2+} + \cdot OH + OH^- \)
56. \( Cu^+ + H_2O_2 \rightarrow Cu^{3+} + OH^- + OH^- \)
57. \( Cu^+ + Cu^{3+} \rightarrow Cu^{2+} + Cu^{2+} \)
58. \( Cu^{2+} + H_2O_2 \rightarrow Cu^+ + O_2^- + H^+ \)
59. \( PQN + Asch \rightarrow PQN^+ + Asc^- \)
60. \( PQN^+ + O_2 \rightarrow PQN + O_2^- \)
61. \( PQN^+ + O_2^- + 2H^+ \rightarrow PQN + H_2O_2 \)
62. \( NQN12 + Asch \rightarrow NQN12^+ + Asc^- \)
63. \( NQN12^+ + O_2 \rightarrow NQN12 + O_2^- \)
64. \( NQN12^+ + O_2^- + 2H^+ \rightarrow NQN12 + H_2O_2 \)
65. \( NQN14 + Asch \rightarrow NQN14^+ + Asc^- \)
66. \( NQN14^+ + O_2 \rightarrow NQN14 + O_2^- \)
67. \( NQN14^+ + O_2^- + 2H^+ \rightarrow NQN14 + H_2O_2 \)
68. \( UA + O_3 \rightarrow Products \)
| Reaction                                                                 | Rate Constant   |
|-------------------------------------------------------------------------|-----------------|
| UA + OH → Products + OH⁻                                                | $1.20 \times 10^{-11}$ |
| GSH + OH → Products + OH⁻                                               | $1.50 \times 10^{-11}$ |
| GSSG + OH → Products + OH⁻                                              | $1.50 \times 10^{-11}$ |
| Asc* + Asc* + H⁺ → Asc + DHA                                            | $5.00 \times 10^{-16}$ |
| AscH + O₂⁺ + H⁺ → Asc⁺ + H₂O₂                                          | $5.10 \times 10^{-17}$ |
| AsCH + HO₂ → AsC⁺ + H₂O₂                                               | $2.65 \times 10^{-17}$ |
| AsCH + OH → Products + OH⁻                                              | $1.80 \times 10^{-11}$ |
| AsCH + O₃ → Products                                                   | $9.10 \times 10^{-17}$ |
| 1.25 GS⁻ + 0.5 O₃ → Products                                           | $9.60 \times 10^{-20}$ |
| 1.25 GSH + 0.5 O₃ → Products                                           | $9.60 \times 10^{-20}$ |
| GSOO + GSOO → 0.56 O₂⁺ + Products                                      | $6.79 \times 10^{-13}$ |
| O₂⁺ + GSH → GSO⁺ + OH⁻                                                | $3.32 \times 10^{-19}$ |
| NO₂⁺ + GS⁻ → GSNO₂                                                    | $4.98 \times 10^{-12}$ |
| GSOO⁺ + NO₂⁺ → GSOONO₂                                                | $2.49 \times 10^{-12}$ |
| GSOO₂⁻ → GSOO⁺ + NO₂⁻                                                | $7.5 \times 10^{-1}$ |
| NO₂⁺ + GS⁻ → NO₂⁻ + GS⁺                                               | $4.00 \times 10^{-13}$ |
| NO₂⁺ + GSH → NO₂⁻ + GS⁺ + H⁺                                           | $1.66 \times 10^{-14}$ |
| GSOO⁺ + GSH → GSO⁺ + GSOH                                              | $3.32 \times 10^{-15}$ |
| GSO + NO₂ → GSOONO                                                    | $7.47 \times 10^{-12}$ |
| GSOONO → Products                                                     | $7.00 \times 10^{2}$ |
| GS⁻ + GS⁻ → GS⁻ + GS⁻                                                 | $1.59 \times 10^{-14}$ |
| GSSG⁻ → GS⁻ + GS⁻                                                     | $1.60 \times 10^{5}$ |
| GSSG⁻ + O₂ → GSSG + O₂⁻                                               | $8.30 \times 10^{-12}$ |
| GS⁻ + GS⁻ → GSS                                                       | $8.30 \times 10^{-12}$ |
| GSO⁻ + GSO⁻ → Products                                                | $9.96 \times 10^{-14}$ |
| GS⁻ + H₂O₂ → GSOH + OH⁻                                               | $1.60 \times 10^{-21}$ |
| GS⁻ + AsCH → GSH + Asc⁺                                               | $1.00 \times 10^{-12}$ |
| UA + NO₂⁺ → UA⁺ + NO₂⁻                                                | $3.00 \times 10^{-14}$ |
| AsCH + NO₂⁺ → Asc⁺ + NO₂⁻                                             | $5.80 \times 10^{-14}$ |
| UA⁺ + AsCH → UA + Asc⁺                                                | $1.70 \times 10^{-15}$ |
| GS⁻ + UA → GSH + UA⁻                                                  | $5.00 \times 10^{-14}$ |
| O₂⁺ + NO₂⁺ → O₂NOO⁻                                                   | $7.50 \times 10^{-12}$ |
| O₂NOO⁻ → NO₂⁻ + O₂                                                    | $7.00 \times 10^{-1}$ |
| O₂NOO⁻ → O₂⁺ + NO₂⁻                                                  | $1.10 \times 10^{0}$ |
| NO₂⁺ + NO₂⁺ → N₂O₄                                                   | $7.50 \times 10^{-13}$ |
| Equation | Reactions | Rate Constant | References |
|----------|-----------|---------------|------------|
| 105 | $\text{N}_2\text{O}_4 \rightarrow \text{NO}_2^* + \text{NO}_2^*$ | $6.90 \times 10^5$ | 81 |
| 106 | $\text{N}_2\text{O}_4 + \text{H}_2\text{O} \rightarrow \text{NO}_2^- + \text{NO}_3^- + 2\text{H}^+$ | $1.00 \times 10^3$ | 4 |
| 107 | $\text{O}_2^- + \text{O}_3 + \text{H}_2\text{O} \rightarrow \text{OH} + 2\text{O}_2 + \text{OH}^-$ | $2.50 \times 10^{-12}$ | 82 |
| 108 | $\text{HO}_2 + \text{O}_3 \rightarrow \text{OH} + 2\text{O}_2$ | $1.66 \times 10^{-17}$ | 82 |
| 109 | $\text{NO}_2^- + \cdot\text{OH} \rightarrow \text{NO}_2^* + \text{OH}^-$ | $8.80 \times 10^{-12}$ | 80 |
| 110 | $\cdot\text{OH} + \text{NO}_2^* \rightarrow \text{ONO}_2^-$ | $7.50 \times 10^{-12}$ | 4 |
| 111 | $\cdot\text{OH} + \text{NO}_2^- \rightarrow \text{ONO}_2$ | $7.50 \times 10^{-12}$ | 4 |
| 112 | $\text{ONO}_2 \rightarrow \text{NO}_2^- + \cdot\text{OH}$ | $3.00 \times 10^{-1}$ | 4 |
| 113 | $\text{ONO}_2 \rightarrow \text{NO}_3^- + \text{H}^+$ | $7.00 \times 10^{-1}$ | 4 |
| 114 | $\text{ONO}_2^- + \text{GSH} \rightarrow \text{NO}_2^- + \text{GSO}_2$ | $1.10 \times 10^{-18}$ | 83 |
| 115 | $\text{GSO}_2^- + \text{NO}_2^* \rightarrow \text{GSOO}_2$ | $7.50 \times 10^{-12}$ | 4 |
| 116 | $\text{GSOO}_2 + \text{H}_2\text{O} \rightarrow \text{Products}$ | $7.00 \times 10^2$ | 4 |
| 117 | $\text{ONO}_2 + \text{AscH} \rightarrow \text{Im}_1$ | $1.66 \times 10^{-15}$ | 84 |
| 118 | $\text{Im}_1 \rightarrow \text{ONO}_2 + \text{AscH}$ | $5.00 \times 10^{-2}$ | 84 |
| 119 | $\text{Im}_1 \rightarrow \text{Im}_2$ | $4.00 \times 10^1$ | 84 |
| 120 | $\text{Im}_2 \rightarrow \text{Im}_1$ | $5.00 \times 10^0$ | 84 |
| 121 | $\text{Im}_2 + \text{AscH} \rightarrow \text{Asc} + \text{DHA} + \text{NO}_2^- + \text{H}_2\text{O}$ | $1.66 \times 10^{-19}$ | 84 |
| 122 | $\text{Im}_2 \rightarrow \text{Asc} + \text{NO}_3^- + \text{H}^+$ | $8.50 \times 10^{-1}$ | 84 |
| 123 | $\text{ONO}_2 + \text{UA} \rightarrow \text{UA}^{\text{rad}} + \text{NO}_2 + \text{Products}$ | $2.60 \times 10^{-19}$ | 85 |
| 124 | $\text{O}_2^- + \text{SOD} + \text{H}^+ \rightarrow 0.5 \text{H}_2\text{O}_2 + \text{SOD}$ | $2.65 \times 10^{-12}$ | See text S2. |
| 125 | $\text{H}_2\text{O}_2 + \text{catalase} \rightarrow \text{H}_2\text{O} + 0.5 \text{O}_2 + \text{catalase}$ | $3.20 \times 10^{-14}$ | See text S2. |
| 126 | $\cdot\text{OH} + \text{organic matter} \rightarrow \text{oxidized organic matter}$ | $1.66 \times 10^{-12}$ | 21.65 |
Table S2. Input parameters to the KM-SUB-ELF model

| Parameter   | Description                                                                 | Value         |
|-------------|------------------------------------------------------------------------------|---------------|
| $K_{H_{\text{O}_3}}$ | Henrys law equilibrium constant for O$_3$ [aq]/[gas]                       | $1.7 \times 10^{-1}$ |
| $K_{H_{\text{NO}_2}}$ | Henrys law equilibrium constant for NO$_2$ [aq]/[gas]                        | $2.2 \times 10^{-1}$ |
| $K_{H_{\text{NO}}}$   | Henrys law equilibrium constant for NO [aq]/[gas]                            | $3.9 \times 10^{-2}$ |
| $K_{H_{\text{OH}}}$   | Henrys law equilibrium constant for OH [aq]/[gas]                            | $4.3 \times 10^{2}$  |
| $K_{H_{\text{H}_2\text{O}_2}}$ | Henrys law equilibrium constant for H$_2$O$_2$ [aq]/[gas]              | $1.7 \times 10^{3}$  |
| $\omega_{\text{O}_3}$  | Mean thermal velocity of O$_3$                                          | $3.7 \times 10^{4}$  cm s$^{-1}$ |
| $\omega_{\text{NO}_2}$ | Mean thermal velocity of NO$_2$                                          | $3.8 \times 10^{4}$  cm s$^{-1}$ |
| $\omega_{\text{NO}}$   | Mean thermal velocity of NO                                              | $4.7 \times 10^{4}$  cm s$^{-1}$ |
| $\omega_{\text{OH}}$   | Mean thermal velocity of OH                                              | $6.2 \times 10^{4}$  cm s$^{-1}$ |
| $\omega_{\text{HO}_2}$ | Mean thermal velocity of HO$_2$                                        | $4.5 \times 10^{4}$  cm s$^{-1}$ |
| $\omega_{\text{H}_2\text{O}_2}$ | Mean thermal velocity of H$_2$O$_2$                                        | $4.4 \times 10^{4}$  cm s$^{-1}$ |
| $MW_{\text{aa}}$      | Average molecular weight of amino acids                                    | $125$ g mole$^{-1}$ |
| $MW_{\text{Cu}}$      | Molecular weight copper                                                   | $63.6$ g mole$^{-1}$ |
| $MW_{\text{Fe}}$      | Molecular weight iron                                                     | $55.6$ g mole$^{-1}$ |
| $MW_{\text{SOA}}$     | Average molecular weight SOA                                              | $250$ g mole$^{-1}$ |
| $MW_{\text{PQN}}$     | Molecular weight phenanthrenequinone (PQN)                                | $208.2$ g mole$^{-1}$ |
| $MW_{\text{NQN}}$     | Molecular weight naphthoquinone (NQN)                                     | $158.2$ g mole$^{-1}$ |
| $pK_{a_{\text{GSH}}}$ | Acid dissociation constant of GSH                                         | $8.8$            |
| $pK_{a_{\text{HO}_2}}$ | Acid dissociation constant of HO$_2$                                      | $4.8$            |
| $pK_{a_{\text{ONOOH}}}$ | Acid dissociation constant of ONOOH                                        | $6.5$            |
| $VR$                | Lung ventilation rate                                                     | $1.5$ m$^3$h$^{-1}$ |
| $BR$                | Breathing rate                                                            | $16$ min$^{-1}$  |
| $FCR$               | Functional residual capacity of the lung                                  | $2750$ cm$^3$   |
| $TV$                | Tidal Volume – Breath volume                                              | $1500$ cm$^3$   |
| $SA_{\text{ELF}}$   | Total ELF surface area                                                    | $890000$ cm$^2$ |
| $T_{\text{RT}}$      | Respiratory tract temperature                                              | $37^\circ$C      |
| $pH_{\text{ELF}}$    | pH of the ELF                                                             | $7$             |
### Table S3. List of symbols and definitions

| Symbol  | Meaning                                                                 | SI unit    |
|---------|-------------------------------------------------------------------------|------------|
| CY      | ELF concentration of PM2.5 constituent Y                                 | µmol L⁻¹   |
| Cgas,PM2.5 | Ambient gas phase concentration of PM2.5                              | µg m⁻³     |
| CEROS   | ROS concentration in the ELF during or after model simulation           | nmol L⁻¹   |
| dm,PM2.5 | Fraction of PM2.5 that deposits in the ELF                              | µg         |
| DPM2.5  | Dose of PM2.5 deposited in the ELF                                       | nmol L⁻¹   |
| Ii→j    | Gross chemical interconversion between individual ROS in the ELF        | nmol L⁻¹   |
| IΣROS   | Gross chemical interconversion between all ROS in the ELF               | nmol L⁻¹   |
| MF_Y    | PM2.5 mass fraction of constituent Y                                    | g mol⁻¹    |
| M_Y     | Molar mass of PM2.5 constituent Y                                       | g mol⁻¹    |
| NΣROS   | Cumulative production of ROS in the ELF                                 | nmol L⁻¹   |
| N'ΣROS  | Cumulative production rate of ROS in the ELF                            | nmol L⁻¹ s⁻¹ |
| PΣROS   | Gross chemical production of ROS in the ELF                             | nmol L⁻¹   |
| P'ΣROS  | Gross chemical production rate of ROS in the ELF                        | nmol L⁻¹ s⁻¹ |
| P_Y     | Gross chemical production of an individual ROS in the ELF              | nmol L⁻¹   |
| SF_Y    | Soluble fraction of PM2.5 constituent Y in ELF                          | h          |
| tacc    | Accumulation time of PM2.5 in the ELF                                   | h          |
| t_sim   | Model simulation time                                                   | h          |
| VELF    | Volume of the ELF                                                      | mL         |
| VR      | Lung ventilation rate                                                  | m³ h⁻¹     |
| YOH     | OH yield in the ELF                                                     | pmol       |

### Table S4. Mathematical formulas used to calculate ELF ROS metrics

- \( k_{ROS} = \sum_{i>j} k_{i\rightarrow j} \)
- \( N_{ROS} = P_{ROS} - k_{ROS} \)
- \( N'_{ROS} = (P_{ROS} - k_{ROS}) / t_{sim} \)
- \( P'_{ROS} = P_{ROS} / t_{sim} \)
**Table S5.** PM2.5 and transition metal concentrations with mass fractions as quantified in PM2.5 collected at different sampling sites throughout the world.

| Sampling location                          | PM2.5 (µg m\(^{-3}\)) | Fe (ng m\(^{-3}\)) | Cu (ng m\(^{-3}\)) | Fe mass fraction | Cu mass fraction | Reference |
|-------------------------------------------|-------------------------|---------------------|---------------------|------------------|------------------|-----------|
| Amazon (wet season)                       | 1.65                    | 33                  | 0.07                | 2.00 × 10\(^{-2}\) | 4.24 × 10\(^{-5}\) | 86        |
| Mace Head (Ireland)                       | 4.2                     | 5.68                | 0.71                | 1.35 × 10\(^{-3}\) | 1.69 × 10\(^{-4}\) | 87        |
| Amazon (dry season)                       | 4.87                    | 19                  | 0.8                 | 3.90 × 10\(^{-3}\) | 1.64 × 10\(^{-4}\) | 86        |
| Edinburgh (Scotland)                      | 7.1                     | 27.6                | 1.39                | 3.89 × 10\(^{-3}\) | 1.96 × 10\(^{-4}\) | 88        |
| West Midlands (UK, rural)                 | 7.6                     | 51.3                | 13.5                | 6.75 × 10\(^{-3}\) | 1.78 × 10\(^{-4}\) | 89        |
| West Midlands (UK, urban)                 | 9                       | 80.2                | 13.9                | 8.91 × 10\(^{-3}\) | 1.54 × 10\(^{-3}\) | 89        |
| Skukuza (South Africa)                    | 9.4                     | 51                  | 0.41                | 5.43 × 10\(^{-3}\) | 4.36 × 10\(^{-5}\) | 90        |
| Amazon (Serro do Navio)                   | 9.87                    | 120                 | 1.65                | 1.22 × 10\(^{-2}\) | 1.67 × 10\(^{-4}\) | 91        |
| Amazon (Cuiabá)                           | 10.5                    | 175                 | 1.55                | 1.67 × 10\(^{-2}\) | 1.48 × 10\(^{-4}\) | 91        |
| West Midlands (UK, rural, average)        | 10.5                    | 87.1                | 20                  | 8.30 × 10\(^{-3}\) | 1.91 × 10\(^{-3}\) | 89        |
| West Midlands (UK, urban, average)        | 11.6                    | 102                 | 21.9                | 8.79 × 10\(^{-3}\) | 1.89 × 10\(^{-3}\) | 89        |
| Helsinki (Finland)                        | 11.8                    | 96                  | 3.1                 | 8.14 × 10\(^{-3}\) | 2.63 × 10\(^{-4}\) | 92        |
| Tampa (Florida)                           | 12.7                    | 79                  | 2.4                 | 6.22 × 10\(^{-3}\) | 1.89 × 10\(^{-4}\) | 93        |
| Toronto (Canada)                          | 12.7                    | 55                  | 2.5                 | 4.33 × 10\(^{-3}\) | 1.97 × 10\(^{-4}\) | 94        |
| South Phoenix (Texas)                     | 12.95                   | 147                 | 7.6                 | 1.14 × 10\(^{-2}\) | 5.87 × 10\(^{-4}\) | 95        |
| Tehran (inside a school dormitory)        | 14                      | 102.13              | 22.17               | 7.30 × 10\(^{-3}\) | 1.58 × 10\(^{-3}\) | 96        |
| Tehran (inside a retirement home)         | 15                      | 130.78              | 25.1                | 8.72 × 10\(^{-3}\) | 1.67 × 10\(^{-3}\) | 96        |
| South-Eastern Italy (background sites)    | 16.4                    | 86.8                | 3.1                 | 5.29 × 10\(^{-3}\) | 1.89 × 10\(^{-4}\) | 97        |
| Patras (Greece)                           | 17.4                    | 124                 | 7.28                | 7.13 × 10\(^{-3}\) | 4.18 × 10\(^{-4}\) | 98        |
| Yeongwol (South Korea)                    | 19.7                    | 31.2                | 9.8                 | 1.58 × 10\(^{-3}\) | 4.98 × 10\(^{-4}\) | 99        |
| Budapest (Hungary)                        | 20                      | 430                 | 18.3                | 2.15 × 10\(^{-2}\) | 9.15 × 10\(^{-4}\) | 100       |
| South-Eastern Italy (industrial sites)    | 21.7                    | 85                  | 5.1                 | 3.92 × 10\(^{-3}\) | 2.35 × 10\(^{-4}\) | 97        |
| Location                                      | Value1 | Value2 | Value3          | Value4          | Value5          |
|-----------------------------------------------|--------|--------|-----------------|-----------------|-----------------|
| Zabrze (upper Silesia, Poland)                | 22     | 160.8  | 6.5             | $7.31 \times 10^{-3}$ | $2.96 \times 10^{-4}$ |
| Chuncheon (South Korea)                       | 23     | 29.6   | 9.9             | $1.29 \times 10^{-3}$ | $4.30 \times 10^{-4}$ |
| Detroit (Michigan)                            | 23     | 234    | 6               | $1.02 \times 10^{-2}$ | $2.61 \times 10^{-4}$ |
| Megalopolis (Greece)                          | 23     | 87     | 4.02            | $3.78 \times 10^{-3}$ | $1.75 \times 10^{-4}$ |
| Tehran (outside a retirement home)            | 24     | 238.81 | 25.99           | $9.95 \times 10^{-3}$ | $1.08 \times 10^{-3}$ |
| South-Eastern Italy (urban sites)             | 24.1   | 78.8   | 5.7             | $3.27 \times 10^{-3}$ | $2.37 \times 10^{-4}$ |
| Tehran (outside a school dormitory)           | 26     | 280    | 32.42           | $1.08 \times 10^{-2}$ | $1.25 \times 10^{-3}$ |
| Anaheim (California)                          | 26.8   | 29.6   | 39.6            | $1.11 \times 10^{-3}$ | $1.48 \times 10^{-3}$ |
| Milan (Summer, Italy)                         | 27.2   | 186    | 10              | $6.84 \times 10^{-3}$ | $3.68 \times 10^{-4}$ |
| Jeddah City (Saudi Arabia)                    | 28.4   | 590    | 5.6             | $2.08 \times 10^{-2}$ | $1.97 \times 10^{-4}$ |
| Hong Kong                                     | 29     | 140    | 5.7             | $4.83 \times 10^{-3}$ | $1.97 \times 10^{-4}$ |
| Rio de Janeiro (Brazil)                       | 29.2   | 307    | 35              | $1.05 \times 10^{-2}$ | $1.20 \times 10^{-3}$ |
| Katowice (upper Silesia, Poland)              | 31     | 157    | 8.2             | $5.07 \times 10^{-3}$ | $2.65 \times 10^{-4}$ |
| Porto Marghera (Italy)                        | 31     | 200    | 9.3             | $6.45 \times 10^{-3}$ | $3.00 \times 10^{-4}$ |
| Erzgebirge (Germany)                          | 32.5   | 188    | 3               | $5.79 \times 10^{-3}$ | $9.23 \times 10^{-5}$ |
| Barcelona (Spain)                             | 35     | 260    | 52              | $7.43 \times 10^{-3}$ | $1.49 \times 10^{-3}$ |
| Santa Catarina (Mexico)                       | 36.15  | 466    | 16              | $1.29 \times 10^{-2}$ | $4.42 \times 10^{-4}$ |
| Escobedo (Mexico)                             | 37.78  | 493    | 13              | $1.31 \times 10^{-2}$ | $3.44 \times 10^{-4}$ |
| Arnhem (the Netherlands)                      | 38.95  | 241    | 13.5            | $6.19 \times 10^{-3}$ | $3.47 \times 10^{-4}$ |
| Mira Loma (Southern California, average)      | 41.8   | 581    | 75              | $1.39 \times 10^{-2}$ | $1.79 \times 10^{-3}$ |
| Taif (residential area, Saudi Arabia)         | 46     | 2000   | 5.3             | $4.35 \times 10^{-2}$ | $1.15 \times 10^{-4}$ |
| Taif (industrial site, Saudi Arabia)          | 47     | 2300   | 13              | $4.89 \times 10^{-2}$ | $2.77 \times 10^{-4}$ |
| Azusa (California)                            | 47.1   | 281.9  | 13.4            | $5.99 \times 10^{-3}$ | $2.85 \times 10^{-4}$ |
| Edison (New Jersey)                           | 49.6   | 1953   | 10              | $3.94 \times 10^{-2}$ | $2.02 \times 10^{-4}$ |
| Bursa (Turkey)                                | 53     | 875    | 15              | $1.65 \times 10^{-2}$ | $2.83 \times 10^{-4}$ |
| Karachi (summer, Pakistan)                    | 55.89  | 3360   | 56              | $6.01 \times 10^{-2}$ | $1.00 \times 10^{-3}$ |
| New Delhi (summer, high traffic, India)       | 58.2   | 710    | 20              | $1.22 \times 10^{-2}$ | $3.44 \times 10^{-4}$ |
| Sampling location                        | PM2.5 ($\mu$g m$^{-3}$) | SOA ($\mu$g m$^{-3}$) | SOA mass fraction | Reference |
|-----------------------------------------|--------------------------|------------------------|-------------------|-----------|
| Amazon (Brazil)                         | 1.8                      | 0.34                   | 0.189             | 130       |
| Hyttijärvi (Finland)                    | 2                        | 1.2                    | 0.60              | 131       |
| Storm Peak (Colorado)                   | 2.1                      | 0.7                    | 0.333             | 131       |
| Iron and copper medians                 | –                        | –                      | 8.14 x 10^{-3}    | This study |

Table S6. PM2.5 and SOA concentrations with mass fractions as quantified in PM2.5 collected at different sampling sites throughout the world.
| Location                                      | Temperature | Humidity | Precipitation | Notes     |
|-----------------------------------------------|-------------|----------|----------------|-----------|
| Jungfraujoch (Switzerland)                    | 2.2         | 1.2      | 0.545          |           |
| Duke Forest (North Carolina)                  | 2.8         | 1.3      | 0.464          |           |
| Chebogue Pt. (Canada)                         | 2.9         | 1.5      | 0.517          |           |
| Edinburgh (Scotland)                          | 3           | 1.2      | 0.400          |           |
| Mainz (Germany)                               | 4.3         | 1.1      | 0.256          |           |
| Boulder (Colorado)                            | 4.4         | 2.5      | 0.568          |           |
| Manchester (winter, UK)                       | 5.2         | 0.6      | 0.115          |           |
| Chelmsford (UK)                               | 5.3         | 1.8      | 0.340          |           |
| Vancouver (Canada)                            | 7           | 2.5      | 0.357          |           |
| Okinawa (Japan)                               | 7.9         | 1.7      | 0.215          |           |
| Off New England Coast                         | 8.5         | 4.9      | 0.576          |           |
| Thompson Farm (New Hampshire)                 | 9.5         | 4.2      | 0.442          |           |
| Zurich (winter, Switzerland)                  | 9.6         | 4.3      | 0.448          |           |
| Cheju (South Korea)                           | 10.7        | 4        | 0.374          |           |
| Fukue (Japan)                                 | 11          | 3.6      | 0.327          |           |
| New York City (winter, New York)              | 11.6        | 2.6      | 0.224          |           |
| New York City (summer, New York)              | 12.2        | 4.8      | 0.393          |           |
| Pinnacle Park (New York)                      | 12.3        | 5.4      | 0.439          |           |
| Houston (Texas)                               | 12.8        | 2.7      | 0.211          |           |
| Tokyo (summer, Japan)                         | 13.2        | 4.7      | 0.356          |           |
| Manchester (summer, UK)                       | 14.3        | 3        | 0.210          |           |
| Pittsburgh (Pensylvania)                      | 14.7        | 3.1      | 0.211          |           |
| Tokyo (winter, Japan)                         | 16.2        | 2.3      | 0.142          |           |
| Taunus (Germany)                              | 16.3        | 7.9      | 0.485          |           |
| Riverside (California)                        | 19.1        | 7        | 0.366          |           |
| Zurich (summer, Switzerland)                  | 25.5        | 5.1      | 0.200          |           |
| Mexico City (Mexico)                          | 26.8        | 8.1      | 0.302          |           |
**Table S7.** PM2.5, Phenanthrenequinone (PQN), 1,4-naphthoquinone (1,4-NQN) and 1,2-naphthoquinone (1,2-NQN) concentrations with mass fractions as quantified in PM2.5 collected at different sampling sites throughout the world. *see SI section on particulate pollutant concentrations in the ELF.*

| Sampling location                  | PM2.5 (µg m\(^{-3}\)) | PQN (ng m\(^{-3}\)) | 1,2-NQN (ng m\(^{-3}\)) | 1,4-NQN (ng m\(^{-3}\)) | PQN mass fraction | 1,2-NQN mass fraction | 1,4-NQN mass fraction | Reference |
|-----------------------------------|------------------------|----------------------|--------------------------|--------------------------|------------------|-----------------------|-----------------------|-----------|
| Umea (Sweden)                     | 7.8                    | Unknown              | Unknown                  | 0.03                     | 2.6 × 10\(^{-6}\) | 1.3 × 10\(^{-6}\)     | 1.3 × 10\(^{-6}\)     | 133       |
| Athens (Greece)                   | 35.6                   | 0.071                | 0.157                    | 0.26                     | 2.69 × 10\(^{-6}\) | 5.95 × 10\(^{-6}\)    | 9.86 × 10\(^{-6}\)    | 134       |
| Mazar-e Sharif (Afghanistan)     | 69                     | Unknown              | Unknown                  | 0.027                    | 1.06 × 10\(^{-6}\) | 5.28 × 10\(^{-7}\)    | 5.28 × 10\(^{-7}\)    | 133       |
| Kabul (Afghanistan)               | 86                     | Unknown              | Unknown                  | 0.2                      | 6.28 × 10\(^{-6}\) | 3.14 × 10\(^{-6}\)    | 3.14 × 10\(^{-6}\)    | 133       |
| Atascadero (California)           | 5*                     | 0.023                | 0.0127                   | 0.0246                   | 6.21 × 10\(^{-6}\) | 3.43 × 10\(^{-6}\)    | 6.64 × 10\(^{-6}\)    | 120       |
| Birmingham (UK)                  | 15*                    | 4.6                  | 3.2                      | 1.7                      | 4.14 × 10\(^{-4}\) | 2.88 × 10\(^{-4}\)    | 1.53 × 10\(^{-4}\)    | 136       |
| Lake Elsinore (California)       | 20*                    | 0.311                | 0.246                    | 0.14                     | 2.1 × 10\(^{-5}\) | 1.66 × 10\(^{-5}\)    | 9.45 × 10\(^{-6}\)    | 135       |
| Norfolk (UK)                     | 5*                     | 0.058                | 0.024                    | 0.012                    | 1.57 × 10\(^{-5}\) | 6.48 × 10\(^{-6}\)    | 3.24 × 10\(^{-6}\)    | 137       |
| Riverside (California)           | 25*                    | 0.57                 | 0.06                     | 0.23                     | 3.08 × 10\(^{-5}\) | 3.24 × 10\(^{-6}\)    | 1.24 × 10\(^{-5}\)    | 138       |
| *Quinones median*                | –                      | –                    | –                        | –                        | 6.28 × 10\(^{-6}\) | 3.43 × 10\(^{-6}\)    | 6.64 × 10\(^{-6}\)    | *This study* |
Figure S1. Mass fractions of all redox-active PM2.5 constituents quantified in field data (Tabs. S5-7). The median mass fraction of each redox-active PM2.5 constituent is indicated by the red horizontal line.
Figure S2. (a) ROS concentration, $C_{\text{ROS, end}}$, after pollutant exposure, and (b) the average ROS concentration, $C_{\text{ROS, avg}}$, during pollutant exposure as a function of PM2.5 concentration. The solid lines represent a standard composition of PM2.5 using median mass fractions of the redox-active constituents. Black markers represent calculations using explicit PM2.5 composition field data (Tab. S5-7)
Figure S3. (a) ROS concentrations, $C_{\text{ROS}}$, as a function of pollutant concentration with and without consideration of antioxidant depletion in the model. One µg of the co-pollutant NO$_2$ is added per µg PM2.5. For O$_3$, a constant concentration of 30 µg m$^{-3}$ was used, independent of PM2.5 concentration. (b) Antioxidant consumption rate of NO$_2$, PM2.5 and O$_3$ as a function of pollutant concentration. The dashed line indicates the antioxidant consumption rate at which the ELF antioxidants would deplete in healthy humans within two hours of pollutant exposure without the consideration of enzymes or antioxidant replenishment.
Figure S4. Gross chemical production of individual ROS in the ELF solely associated with and as a function of the concentration of three pollutants: (a) PM2.5, (b) O₃, and (c) NO₂. Simulations were carried out using only the single pollutant. In panel a, the solid lines represent standard PM2.5 composition, and the markers represent explicit PM2.5 composition data for redox-active constituents (Tabs. S5-7). O₃ does not contribute to production of O₂⁻ or OH in the model.

Figure S5. Aqueous-phase (a) NO₂ concentration and (b) O₃ concentration in the ELF as a function of pollutant concentration and comparison to hypothetical saturation with respect to ambient air. Dashed lines indicate saturation concentrations assuming Henry’s law equilibrium, which are calculated using the ambient gas phase pollutant concentration and the dimensionless water–air partitioning coefficients for O₃ and NO₂, respectively (Table S2).
Figure S6. Effect of using different pH on the main results (panels a,b, e-j) and transition metal valence state (panels c,d) using the median mass fractions of all redox-active PM2.5 constituents, co-varied NO$_2$ (PM2.5:NO$_2$ = 1:1) and an O$_3$ concentration of 30 µg m$^{-3}$. 