

1 **Supplementary information to**

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

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44 **S1. ELF antioxidant concentrations**

45 Four low molecular weight antioxidants are included in this study, ascorbate (AsCH), glutathione (GSH),
46 uric acid (UA) and α -tocopherol (α -Toc).¹ The concentrations of AsCH, GSH, and UA in the ELF are 40 μ M,
47 108 μ M, and 200 μ M, respectively.^{2,3} The total α -Toc concentration in the ELF is reported as 0.7 μ M,³
48 however, in the presented study α -Toc is assumed to reside in the surfactant layer of the ELF with a
49 concentration of 200 μ M. It is found that pollutant exposure can lead to a spike in C_{ZROS} at pollutant
50 concentrations above 100 μ g m⁻³ in the model (Fig. S3a) due to NO₂-driven depletion of ELF antioxidants
51 within the two hours simulation time (Fig. S3b). The reaction mechanism of ROS formation by NO₂ involves
52 formation of GS \cdot (R84-85, Tab. S1) and reaction to GSSG \cdot (R89), leading to O₂ \cdot^- production (R91).^{4,5} In the
53 presence of physiological concentrations of UA and AsCH, GS \cdot is efficiently recycled to GSH (R96, R100)
54 and GSSG \cdot formation a minor reaction pathway. However, at low levels of UA and AsCH, this O₂ \cdot^- formation
55 pathway becomes increasingly important.

56
57 Although earlier studies have shown that antioxidants can be consumed in bronchoalveolar lavage fluid
58 after pollutant exposure,⁶ a study using healthy volunteers suggested that the ELF antioxidants may not be
59 fully depleted,⁷ even after exposure to high pollutant concentrations. Kelly et al. found antioxidant
60 concentrations to be non-zero 1.5 hours after exposure to 2 ppm NO₂ stopped, and in some cases
61 exceeded the initial antioxidant concentration several hours after exposure due to antioxidant
62 replenishment.⁷ We are not aware of kinetic data that details the replenishment rates of antioxidants in ELF,
63 but we can assume that they are likely fast enough to prevent full depletion of antioxidants in our two-hour
64 simulations, preventing a spike in C_{ZROS} (Fig. S3a). Thus, for simplicity, antioxidant and surfactant
65 concentrations are assumed to stay constant in this study.

66
67 In Fig. S3b, antioxidant consumption rates are shown as a function of NO₂, PM2.5 and O₃ concentration.
68 The dashed line represents the antioxidant consumption rate above which the initial concentration of low
69 molecular mass antioxidants depletes within two hours of pollutant exposure. Note that, without
70 consideration of enzymatic reactions and antioxidant replenishment, it represents a lower limit for healthy
71 individuals.

72 73 **S2. ELF enzymatic reactions**

74 Reactions of the enzymes superoxide dismutase (SOD) and catalase are included in the chemical
75 mechanism (R124, R125, Tab. S1). In our previous work, the SOD-catalyzed reaction of two O₂ \cdot^- forming
76 H₂O₂ and O₂ was described as a second-order reaction with respect to O₂ \cdot^- and a rate coefficient of 2.70 \times
77 10⁻¹² cm⁻³ s⁻¹.^{1,8} Dismutation of O₂ \cdot^- by SOD is a multi-step process, in which one O₂ \cdot^- is oxidized to O₂,
78 another reduced to H₂O₂, and operates close to the diffusion limit.⁹ Because SOD activity is often reported
79 in terms of a single rate and turnover number, we combine both steps into one effective reaction of SOD

80 and O_2^- yielding 0.5 H_2O_2 and 0.5 O_2 (R124, Tab. S1). Note that this reaction is first order with respect to
81 both, O_2^- and enzyme.

82 Cantin et al. (1990) showed experimentally that catalase is the most important molecule in H_2O_2 defense
83 of the ELF, exceeding the glutathione peroxidase concentration by nearly two orders of magnitude.¹⁰ The
84 reaction between catalase and H_2O_2 is a two-step reaction in which a molecule of H_2O_2 reacts with catalase
85 to form an enzyme-substrate complex, which then further reacts with another molecule of H_2O_2 to release
86 H_2O and O_2 . Because catalase activity is often reported in terms of a single rate and turnover number, we
87 combine both steps into one effective reaction of catalase and H_2O_2 , yielding 0.5 H_2O and 0.5 O_2 (R125,
88 Tab. S1).¹¹

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

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

96

97 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
98 $36.8 \pm 2.0\ U\ mL^{-1}$,¹⁰ which translates to an enzyme concentration of SOD of 0.58 – 6.5 nM using Eq. S1.
99 Note that, the enzymatic reactions in this study do not occur in excess of substrate. Thus, a second-order
100 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
101 (k_{R124} , Tab. S1).^{15,16}

102 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 $3 \times$
103 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 –
104 24 pM. Second-order rate coefficients for catalase have been measured in the range of $1.6 \times 10^{-14} - 1.6 \times$
105 $10^{-13}\ cm^{-3}\ s^{-1}$. For this study, we use a rate coefficient of $3.2 \times 10^{-14}\ cm^{-3}\ s^{-1}$ (k_{R125} , Tab. S1).^{11,17}

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

110 Note that the presence of PM may decrease the activity of antioxidant enzymes, as shown for SOD
111 previously.¹⁸ At the high PM concentrations for which these effects were observed, however, antioxidant

112 enzymes contribute only marginally to overall ROS scavenging and interconversion in the model (Figs.
113 4b,d). Thus, enzyme inhibition by PM_{2.5} requires further investigation in future experimental and modelling
114 studies to clarify whether enzyme inhibition promotes the shift to the PM_{2.5}-dominated kinetic regime of
115 ROS conversion.

116

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

118 **ELF**

119 OH reacts with nearly all matter present in the ELF with a rate coefficient approaching diffusion limitation.¹⁹
120 Because of this unspecific reactivity, effective scavenging of OH radicals, e.g. through lung antioxidants, is
121 not possible.^{19,20} As an estimate, we assume that the amount of protein in the ELF corresponds to the total
122 amount of dissolved organic matter. The protein mass in the ELF amounts to approximately 10 mg per mL
123 lung fluid.³ Using an average molecular weight of ~125 g mole⁻¹ of a single amino acid, the total amino acid
124 concentration in the ELF can be estimated to ~80 mmol L⁻¹. A second-order reaction of amino acids with
125 OH is included, using a reaction rate coefficient on the order of 1.66 x 10⁻¹² cm³ s⁻¹ (R122, Tab. S1).²¹
126 Because proteins are folded, not all amino acids will be surface exposed, and thus accessible reaction
127 partners for OH. In general, spherical proteins have fewer surface exposed amino acids due to a smaller
128 surface-to-volume ratio, while elongated, cuboid or conical proteins have more surface exposed amino
129 acids. Furthermore, the surface exposure of amino acids depends on the physical properties, e.g. the
130 polarity of the respective amino acid.²² Therefore, as an order of magnitude estimation, we assume that
131 50% of all amino acids are surface exposed in the ELF, yielding an effective amino acid concentration of
132 ~40 mmol L⁻¹ and, in turn, a lifetime of OH with respect to reaction with dissolved organic matter of 2.5 x
133 10⁻⁸ s.

134

135 Pryor estimated the lifetime of OH in a cell to 10⁻⁹ s, assuming a rate coefficient of 1 x 10⁹ M⁻¹ s⁻¹ (equivalent
136 to 1.66 x 10⁻¹² cm³ s⁻¹) and an effective organic matter concentration of 1 mol L⁻¹.²¹ From comparing the
137 ELF protein mass of ~10 mg mL⁻¹ to the cellular protein mass of ~250 mg mL⁻¹, we infer that the ELF must
138 be about ~25 times more dilute compared to a cell with respect to dissolved organic matter.^{2,23,24} Multiplying
139 Pryor's OH lifetime in cells with this dilution factor yields an estimate for the OH lifetime in ELF of ~2.5 x
140 10⁻⁸ s, which is identical to the estimate above and consolidates our description of OH reactivity.

141

142 We find that inclusion of this second-order loss reaction of OH results in a decrease of momentary OH
143 concentrations by one order of magnitude compared to our earlier calculations (Fig. 2a).¹ This finding
144 suggests that OH will react unspecifically with organic matter and only secondarily with antioxidants (7%)
145 in the ELF. Due to the fast reaction of OH, spatial gradients of reactants could play a role in OH fate, e.g.
146 through local depletion of antioxidants around a dissolving particle or inhomogeneous distribution of organic
147 matter and PM_{2.5} constituents in the ELF. However, for the calculations in this study, starting
148 concentrations of antioxidants and organic matter were homogeneous across the bulk ELF.

149

150 **S4. Particulate pollutant concentrations in the ELF**

151 The ELF concentrations of redox-active PM_{2.5} constituents, $C_{ELF,Y}$, with Y standing for copper, iron, SOA,
152 or quinones, are calculated using Eq. S2.¹

153

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

154

155 Inhaled particles can reside in the ELF for several hours.²⁵ For this study, we assume a residence time of
156 PM_{2.5} of 2 hours and use this as accumulation time of inhaled particles (t_{acc}) and simulation time (t_{sim}) to
157 mimic a pseudo steady-state of ROS concentrations that would be achieved through continuous inhalation,
158 in line with our previous studies.¹ It should be noted that there is some uncertainty regarding the residence
159 time of PM_{2.5} in the ELF, with estimates on PM_{2.5} clearance also exceeding 2 hours.²⁶ As lung ventilation
160 rate, VR , 1.5 m³ h⁻¹ is used, and the PM_{2.5} deposition fraction in the ELF, $d_{PM2.5}$, is assumed to be 0.45.^{1,27}
161 The total ELF volume, V_{ELF} , is set to 20 mL.^{1,28} This study only includes copper and iron as transition metals,
162 because these are the only two that have been shown to significantly produce ROS in surrogate ELF
163 (sELF).^{29,30} The fractional solubilities, SF_Y , of copper and iron ions were discussed and tested extensively
164 in our previous study, including the effects of varying trace metal solubilities.¹ In line with the main results
165 of our previous study, the fractional solubilities of copper and iron ions are set to 0.4, 0.1, respectively.¹
166 Due to the relatively small concentration of iron ions and the large concentration of potential organic ligands,
167 iron ions are expected not to precipitate in the ELF.³¹ For the organic fraction in PM_{2.5}, full solubility is
168 assumed. Mass fractions (MF) of redox-active PM_{2.5} constituents are derived from field observations and
169 tabulated in Tables S4-S6. Not all references in Tables S4 and S6 include PM_{2.5} concentrations. In such
170 cases, PM_{2.5} concentrations are estimated based on similar geographical locations and indicated with an
171 asterisk. Additionally, secondary organic aerosol (SOA) forms ROS and is included in the model.³²⁻³⁴
172 However, because the exact mechanism of ROS formation by SOA in the ELF, first order formation rates
173 of H₂O₂ and OH by SOA were parameterized based on experimental observations.^{1,32,33} Quinones in PM_{2.5}
174 are included in this study as previously described.¹ Three quinones are included that were shown to form
175 ROS in sELF, phenanthrenequinone (PQN), 1,2-naphthoquinone (1,2-NQN), and 1,4-naphthoquinone (1,4-
176 NQN) in a molar ratio of 2:1:1.²⁹

177

178 **S5. Gas-phase pollutant concentrations in the ELF**

179 Exposure to gas-phase oxidants, O₃ and NO₂ is quantified in the model using a simplified breathing
180 mechanism. In our previous study, it was assumed that the concentrations of these gas-phase oxidants in
181 the lung were equal to their respective ambient concentrations. However, because of the reactivity of these
182 oxidants, we find that lung gas-phase concentrations of these oxidants are depressed and limited by supply
183 from inhalation of ambient air. In order to get accurate estimates for the amount of gas-phase oxidants

184 transferred to the surfactant layer and ELF, an average lung volume of four L, an average breath volume
185 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
186 lung (Table S2). Application of this simplified breathing mechanism results in a significant decrease in the
187 amount of gaseous oxidants in the surfactant layer and ELF. Therefore, neither O_3 , nor NO_2 are saturated
188 in ELF with respect to their ambient concentrations in this study (Fig. S5).

189

190 **S6. Acid dissociation**

191 In this study, corresponding acid/base-pairs are treated as a single species in the numerical computation
192 of ordinary differential equations (ODE). This effectively reduces the stiffness of the ODE system and
193 applies to glutathione (GSH/GS^-), superoxide radicals (HO_2/O_2^-) and peroxyxynitrous acid ($ONOOH/ONOO^-$).
194 Instead of treating each species explicitly with separate differential equations and explicit protonation and
195 deprotonation reactions, the pKa of these species was used to calculate the acid/base-ratio at the pH of
196 the ELF (Table S2). Then, if a reaction requires only one of the two species to react, the rate of that reaction
197 was multiplied with the inferred fraction of the reacting species.

198

199 **S7. pH of the ELF**

200 Following estimations by Holma (1985, 1989), the pH of the ELF was assumed to stay constant upon air
201 pollutant exposure.^{35,36} In diseased individuals such as asthmatics³⁷, chronic obstructive pulmonary
202 disease,³⁸ or cystic fibrosis patients³⁹ the pH of the ELF may be decreased. Figure S6 shows the ROS
203 concentration, production, interconversion and transition metal valence state at pH 7 and pH 4 as a function
204 of PM2.5 concentration. Panel a shows that $C_{\Sigma ROS}$ displays a very similar behavior at pH 4 and pH 7. C_{O_2}
205 and C_{HO_2} are slightly increased at low PM2.5 concentrations, but depressed at elevated PM2.5
206 concentrations (panel b). This reduction is due to a higher rate of Fe^{2+} -mediated interconversion of HO_2
207 and O_2^- to H_2O_2 (Table S1, R38 and R39), which in turn is due to a higher Fe^{2+}/Fe^{3+} ratio (panel c). The
208 Cu^+/Cu^{2+} ratio shows the opposite trend at reduced pH (panel j).

209 Panel e shows that at pH 4, $N_{\Sigma ROS}$ is marginally reduced compared to pH 7. In panel f, $N_{\Sigma ROS}$ is broken
210 down to its components. $P_{O_2^-}$ is slightly reduced due to decreased Cu^+ -dependent O_2^- formation (Table S1,
211 R54). P_{OH} is slightly increased due to the higher Fe^{2+}/Fe^{3+} ratio and the according increase in the Fenton
212 reaction (Table S1, R40).

213 Panel g shows that $CF_{O_2 \rightarrow H_2O_2}$ is slightly decreased at low PM2.5 concentration and slightly increased at
214 higher PM2.5 concentrations compared to pH 7. Panel h shows that $CF_{H_2O_2 \rightarrow OH}$ is mostly unaffected by a
215 change in pH. The reduction in $N_{\Sigma ROS}$ (panel e) paired with the increase in P_{OH} (panel f) at higher PM2.5
216 concentrations results in a larger OH fraction (panel i) and a larger increase in OH dose (panel j) at pH 4.

217 Reduced pH in the ELF may additionally lead to a reduction in antioxidant enzyme activity,¹⁷ increased
218 transition metal solubility,⁴⁰ and increased OH yield from the Fenton reaction.^{41,42} These effects are not
219 included in the presented study, and are expected to all reduce ROS buffering and promote the PM2.5-

220 controlled OH radical production regime, which may exacerbate oxidative stress. Furthermore, in the
221 presented study SOA produces H₂O₂ and OH,^{32,33} which at lower pH may increasingly shift towards only
222 H₂O₂ production, without OH getting formed.^{43,44} However, a thorough investigation of pH effects is beyond
223 the scope of the presented study and warrants future investigations.

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658 **Table S1.** Chemical reactions, rate constants as used in the KM-SUB-ELF, with reference

#	Reaction	Rate constant ($\text{cm}^{-3} \text{s}^{-1}$ or s^{-1})	Reference
<i>Gas-phase reactions</i>			
1	$\text{NO}^\bullet + \text{O}_3 \rightarrow \text{NO}_2^\bullet + \text{O}_2$	2.05×10^{-14}	45,46
2	$\text{NO}_2^\bullet + \text{O}_3 \rightarrow \text{NO}_3^\bullet + \text{O}_2$	4.85×10^{-17}	45,46
3	$\text{NO}^\bullet + \text{NO}^\bullet + \text{O}_2 \rightarrow \text{NO}_2^\bullet + \text{NO}_2^\bullet$	8.93×10^{-20}	45,46
4	$\text{NO}^\bullet + \text{NO}_3^\bullet \rightarrow \text{NO}_2^\bullet + \text{NO}_2^\bullet$	2.57×10^{-11}	45,46
5	$\text{NO}_2^\bullet + \text{NO}_3^\bullet \rightarrow \text{NO}^\bullet + \text{NO}_2^\bullet + \text{O}_2$	7.73×10^{-16}	45,46
6	$\text{NO}_2^\bullet + \text{NO}_3^\bullet \rightarrow \text{N}_2\text{O}_5$	1.21×10^{-12}	45,46
7	$\bullet\text{OH} + \text{O}_3 \rightarrow \text{HO}_2^\bullet + \text{O}_2$	8.20×10^{-14}	45,46
8	$\bullet\text{OH} + \text{H}_2\text{O}_2 \rightarrow \text{HO}_2^\bullet + \text{H}_2\text{O}$	1.73×10^{-12}	45,46
9	$\text{HO}_2^\bullet + \text{O}_3 \rightarrow \bullet\text{OH} + \text{O}_2 + \text{O}_2$	8.24×10^{-16}	45,46
10	$\bullet\text{OH} + \text{HO}_2^\bullet \rightarrow \text{H}_2\text{O} + \text{O}_2$	1.08×10^{-10}	45,46
11	$\text{HO}_2^\bullet + \text{HO}_2^\bullet \rightarrow \text{H}_2\text{O}_2 + \text{O}_2$	5.09×10^{-12}	45,46
12	$\text{HO}_2^\bullet + \text{HO}_2^\bullet \rightarrow \text{H}_2\text{O}_2$	3.50×10^{-12}	45,46
13	$\bullet\text{OH} + \text{NO}^\bullet \rightarrow \text{HONO}$	8.91×10^{-12}	45,46
14	$\bullet\text{OH} + \text{NO}_2^\bullet \rightarrow \text{HNO}_3$	8.91×10^{-12}	45,46
15	$\bullet\text{OH} + \text{NO}_3^\bullet \rightarrow \text{HO}_2^\bullet + \text{NO}_2^\bullet$	2.00×10^{-11}	45,46
16	$\text{HO}_2^\bullet + \text{NO}^\bullet \rightarrow \bullet\text{OH} + \text{NO}_2^\bullet$	8.24×10^{-12}	45,46
17	$\text{HO}_2^\bullet + \text{NO}_2^\bullet \rightarrow \text{HO}_2\text{NO}_2$	6.87×10^{-13}	45,46
18	$\text{HO}_2\text{NO}_2 \rightarrow \text{HO}_2^\bullet + \text{NO}_2^\bullet$	2.49×10^{-1}	45,46
19	$\bullet\text{OH} + \text{HO}_2\text{NO}_2 \rightarrow \text{NO}_2^\bullet + \text{H}_2\text{O} + \text{O}_2$	2.96×10^{-12}	45,46
20	$\text{HO}_2^\bullet + \text{NO}_3^\bullet \rightarrow \bullet\text{OH} + \text{NO}_2^\bullet$	4.00×10^{-12}	45,46
21	$\bullet\text{OH} + \text{HONO} \rightarrow \text{NO}_2^\bullet + \text{H}_2\text{O}$	5.78×10^{-12}	45,46
22	$\bullet\text{OH} + \text{HNO}_3 \rightarrow \text{NO}_3^\bullet + \text{H}_2\text{O}$	1.37×10^{-13}	45,46
23	$\text{N}_2\text{O}_5 \rightarrow \text{NO}_2^\bullet + \text{NO}_3^\bullet$	1.83×10^{-1}	45,46
<i>Surfactant reactions</i>			
24	$\text{SPB} + \bullet\text{OH} \rightarrow \text{SPB-ox}$	1.70×10^{-11}	47–49
25	$\text{POG} + \bullet\text{OH} \rightarrow \text{POG-ox}$	1.70×10^{-11}	1
26	$\text{SPB} + \text{O}_3 \rightarrow \text{SPB-ox}$	1.00×10^{-14}	50,51
27	$\text{POG} + \text{O}_3 \rightarrow \text{POG-ox} + 0.17 \text{H}_2\text{O}_2$	1.66×10^{-16}	52–55
28	$\text{aToc} + \text{OH} \rightarrow \text{aToc-ox}$	4.50×10^{-13}	56
29	$\text{aToc} + \text{O}_3 \rightarrow \text{aToc-ox}$	1.20×10^{-18}	57
<i>ELF reactions</i>			
30	$\text{O}_2^\bullet + \text{HO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{O}_2 + \text{OH}^\bullet + \text{O}_2$	1.70×10^{-13}	1,58
31	$\text{HO}_2 + \text{HO}_2 \rightarrow \text{H}_2\text{O}_2 + \text{O}_2$	1.40×10^{-15}	58

32	$O_2^{\bullet-} + O_2^{\bullet-} + 2H^+ \rightarrow H_2O_2 + O_2$	3.82×10^{-16}	58
33	$H_2O_2 + \bullet OH \rightarrow HO_2 + H_2O$	5.50×10^{-14}	59
34	$\bullet OH + \bullet OH \rightarrow H_2O_2$	8.60×10^{-12}	60
35	$\bullet OH + O_2^{\bullet-} \rightarrow O_2 + OH^-$	1.30×10^{-11}	47
36	$\bullet OH + HO_2 \rightarrow H_2O + O_2$	1.20×10^{-11}	60
37	$H_2O_2 + HO_2 \rightarrow \bullet OH + O_2 + H_2O$	4.98×10^{-21}	61
38	$Fe^{2+} + O_2^{\bullet-} + 2H^+ \rightarrow Fe^{3+} + H_2O_2$	3.10×10^{-14}	1,58
39	$Fe^{2+} + HO_2 + H^+ \rightarrow Fe^{3+} + H_2O_2$	1.99×10^{-15}	62
40	$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + \bullet OH + OH^-$	4.30×10^{-18}	63
41	$Fe^{2+} + \bullet OH \rightarrow Fe^{3+} + OH^-$	5.30×10^{-13}	64
42	$Fe^{2+} + H_2O_2 \rightarrow Fe^{4+} + H_2O$	9.50×10^{-18}	1
43	$Fe^{3+} + H_2O_2 \rightarrow Fe^{2+} + HO_2 + H^+$	3.32×10^{-24}	63
44	$Fe^{3+} + HO_2 \rightarrow Fe^{2+} + O_2 + H^+$	3.30×10^{-18}	58
45	$Fe^{4+} + Fe^{2+} \rightarrow Fe^{3+} + Fe^{3+}$	6.60×10^{-18}	41
46	$Fe^{3+} + AscH \rightarrow Fe^{2+} + Asc^{\bullet}$	1.10×10^{-19}	1
47	$Fe^{4+} + AscH \rightarrow Fe^{3+} + Asc^{\bullet}$	7.60×10^{-19}	1
48	$Fe^{2+} + O_2 \rightarrow O_2^{\bullet-} + Fe^{3+}$	5.20×10^{-21}	1
49	$Cu^+ + HO_2 + H^+ \rightarrow Cu^{2+} + H_2O_2$	2.30×10^{-12}	1
50	$Cu^+ + O_2^{\bullet-} + H_2O \rightarrow Cu^{2+} + H_2O_2 + OH^-$	5.80×10^{-15}	1
51	$Cu^{2+} + HO_2 \rightarrow Cu^+ + O_2 + H^+$	1.60×10^{-11}	1
52	$Cu^{2+} + O_2^{\bullet-} \rightarrow Cu^+ + O_2$	8.30×10^{-12}	1
53	$Cu^{2+} + AscH \rightarrow Cu^+ + Asc^{\bullet}$	1.40×10^{-18}	1
54	$Cu^+ + O_2 \rightarrow Cu^{2+} + O_2^{\bullet-}$	6.90×10^{-20}	1
55	$Cu^+ + H_2O_2 \rightarrow Cu^{2+} + \bullet OH + OH^-$	2.40×10^{-20}	1
56	$Cu^+ + H_2O_2 \rightarrow Cu^{3+} + OH^- + OH^-$	5.00×10^{-19}	1
57	$Cu^+ + Cu^{3+} \rightarrow Cu^{2+} + Cu^{2+}$	5.80×10^{-12}	1
58	$Cu^{2+} + H_2O_2 \rightarrow Cu^+ + O_2^{\bullet-} + H^+$	3.80×10^{-24}	1
59	$PQN + AscH \rightarrow PQN^{\bullet} + Asc^{\bullet}$	1.20×10^{-20}	29
60	$PQN^{\bullet} + O_2 \rightarrow PQN + O_2^{\bullet-}$	4.60×10^{-13}	1
61	$PQN^{\bullet} + O_2^{\bullet-} + 2H^+ \rightarrow PQN + H_2O_2$	3.30×10^{-12}	1
62	$NQN12 + AscH \rightarrow NQN12^{\bullet} + Asc^{\bullet}$	1.50×10^{-19}	29
63	$NQN12^{\bullet} + O_2 \rightarrow NQN12 + O_2^{\bullet-}$	4.60×10^{-13}	1
64	$NQN12^{\bullet} + O_2^{\bullet-} + 2H^+ \rightarrow NQN12 + H_2O_2$	3.30×10^{-12}	1
65	$NQN14 + AscH \rightarrow NQN14^{\bullet} + Asc^{\bullet}$	6.30×10^{-21}	29
66	$NQN14^{\bullet} + O_2 \rightarrow NQN14 + O_2^{\bullet-}$	4.60×10^{-13}	1
67	$NQN14^{\bullet} + O_2^{\bullet-} + 2H^+ \rightarrow NQN14 + H_2O_2$	3.30×10^{-12}	1
68	$UA + O_3 \rightarrow \text{Products}$	9.60×10^{-17}	57

69	$UA + \cdot OH \rightarrow \text{Products} + OH^-$	1.20×10^{-11}	65
70	$GSH + \cdot OH \rightarrow \text{Products} + OH^-$	1.50×10^{-11}	66
71	$GSSG + \cdot OH \rightarrow \text{Products} + OH^-$	1.50×10^{-11}	Assumed to be the same as R67
72	$Asc\cdot + Asc\cdot + H^+ \rightarrow AscH + DHA$	5.00×10^{-16}	67
73	$AscH + O_2^{\cdot-} + H^+ \rightarrow Asc\cdot + H_2O_2$	5.10×10^{-17}	1
74	$AscH + HO_2 \rightarrow Asc\cdot + H_2O_2$	2.65×10^{-17}	68
75	$AscH + \cdot OH \rightarrow \text{Products} + OH^-$	1.80×10^{-11}	69
76	$AscH + \cdot O_3 \rightarrow \text{Products}$	9.10×10^{-17}	57
77	$1.25 GS^- + 0.5 O_3 \rightarrow \text{Products}$	9.60×10^{-20}	57
78	$1.25 GSH + 0.5 O_3 \rightarrow \text{Products}$	9.60×10^{-20}	57
79	$GSOO + GSOO \rightarrow 0.56 O_2^{\cdot-} + \text{Products}$	6.79×10^{-13}	70
80	$O_2^{\cdot-} + GSH \rightarrow GSO\cdot + OH^-$	3.32×10^{-19}	71-73
81	$NO_2^{\cdot} + GS\cdot \rightarrow GSNO_2$	4.98×10^{-12}	4
82	$GSOO\cdot + NO_2^{\cdot} \rightarrow GSOONO_2$	2.49×10^{-12}	70
83	$GSOONO_2 \rightarrow GSOO\cdot + NO_2^{\cdot}$	7.5×10^{-1}	70
84	$NO_2^{\cdot} + GS^- \rightarrow NO_2^- + GS\cdot$	4.00×10^{-13}	4
85	$NO_2^{\cdot} + GSH \rightarrow NO_2^- + GS\cdot + H^+$	1.66×10^{-14}	74
86	$GSOO\cdot + GSH \rightarrow GSO\cdot + GSOH$	3.32×10^{-15}	4
87	$GSO + NO_2 \rightarrow GSOONO$	7.47×10^{-12}	4
88	$GSOONO \rightarrow \text{Products}$	7.00×10^2	4
89	$GS\cdot + GS^- \rightarrow GSSG\cdot$	1.59×10^{-14}	4,5
90	$GSSG\cdot \rightarrow GS\cdot + GS^-$	1.60×10^5	4,5
91	$GSSG\cdot + O_2 \rightarrow GSSG + O_2^{\cdot-}$	8.30×10^{-12}	4,5
92	$GS\cdot + GS\cdot \rightarrow GSSG$	8.30×10^{-12}	5
93	$GSOH + GSH \rightarrow GSSG + H_2O$	1.20×10^{-18}	75
94	$GSO\cdot + GSO\cdot \rightarrow \text{Products}$	9.96×10^{-14}	4
95	$GS^- + H_2O_2 \rightarrow GSOH + OH^-$	1.60×10^{-21}	75
96	$GS\cdot + AscH \rightarrow GSH + Asc\cdot$	1.00×10^{-12}	76,77
97	$UA + NO_2^{\cdot} \rightarrow UA\cdot + NO_2^-$	3.00×10^{-14}	78,79
98	$AscH + NO_2^{\cdot} \rightarrow Asc\cdot + NO_2^-$	5.80×10^{-14}	78,79
99	$UA\cdot + AscH \rightarrow UA + Asc\cdot$	1.70×10^{-15}	77
100	$GS\cdot + UA \rightarrow GSH + UA\cdot$	5.00×10^{-14}	74
101	$O_2^{\cdot-} + NO_2^{\cdot} \rightarrow O_2NOO\cdot$	7.50×10^{-12}	4,80
102	$O_2NOO\cdot \rightarrow NO_2^- + O_2$	7.00×10^{-1}	4
103	$O_2NOO\cdot \rightarrow O_2^{\cdot-} + NO_2^{\cdot}$	1.10×10^0	4
104	$NO_2^{\cdot} + NO_2^{\cdot} \rightarrow N_2O_4$	7.50×10^{-13}	81

105	$\text{N}_2\text{O}_4 \rightarrow \text{NO}_2^\bullet + \text{NO}_2^\bullet$	6.90×10^3	81
106	$\text{N}_2\text{O}_4 + \text{H}_2\text{O} \rightarrow \text{NO}_2^- + \text{NO}_3^- + 2\text{H}^+$	1.00×10^3	4
107	$\text{O}_2^- + \text{O}_3 + \text{H}_2\text{O} \rightarrow \bullet\text{OH} + 2\text{O}_2 + \text{OH}^-$	2.50×10^{-12}	82
108	$\text{HO}_2 + \text{O}_3 \rightarrow \bullet\text{OH} + 2\text{O}_2$	1.66×10^{-17}	82
109	$\text{NO}_2^- + \bullet\text{OH} \rightarrow \text{NO}_2^\bullet + \text{OH}^-$	8.80×10^{-12}	80
110	$\bullet\text{OH} + \text{NO}_2^\bullet \rightarrow \text{NO}_3^- + \text{H}^+$	7.50×10^{-12}	4
111	$\bullet\text{OH} + \text{NO}_2^\bullet \rightarrow \text{ONOOH}$	7.50×10^{-12}	4
112	$\text{ONOOH} \rightarrow \text{NO}_2^\bullet + \bullet\text{OH}$	3.00×10^{-1}	4
113	$\text{ONOOH} \rightarrow \text{NO}_3^- + \text{H}^+$	7.00×10^{-1}	4
114	$\text{ONOO}^- + \text{GSH} \rightarrow \text{NO}_2^- + \text{GSOH}$	1.10×10^{-18}	83
115	$\text{GSO}^\bullet + \text{NO}_2^\bullet \rightarrow \text{GSOONO}$	7.50×10^{-12}	4
116	$\text{GSOONO} + \text{H}_2\text{O} \rightarrow \text{Products}$	7.00×10^2	4
117	$\text{ONOOH} + \text{AscH} \rightarrow \text{Im}_1$	1.66×10^{-15}	84
118	$\text{Im}_1 \rightarrow \text{ONOOH} + \text{AscH}$	5.00×10^2	84
119	$\text{Im}_1 \rightarrow \text{Im}_2$	4.00×10^1	84
120	$\text{Im}_2 \rightarrow \text{Im}_1$	5.00×10^0	84
121	$\text{Im}_2 + \text{AscH} \rightarrow \text{Asc} + \text{DHA} + \text{NO}_2^- + \text{H}_2\text{O}$	1.66×10^{-19}	84
122	$\text{Im}_2 \rightarrow \text{Asc} + \text{NO}_3^- + \text{H}^+$	8.50×10^{-1}	84
123	$\text{ONOOH} + \text{UA} \rightarrow \text{UA}^{\text{rad}} + \text{NO}_2 + \text{Products}$	2.60×10^{-19}	85
124	$\text{O}_2^\bullet + \text{SOD} + \text{H}^+ \rightarrow 0.5 \text{H}_2\text{O}_2 + \text{SOD}$	2.65×10^{-12}	See text S2.
125	$\text{H}_2\text{O}_2 + \text{catalase} \rightarrow \text{H}_2\text{O} + 0.5 \text{O}_2 + \text{catalase}$	3.20×10^{-14}	See text S2.
126	$\bullet\text{OH} + \text{organic matter} \rightarrow \text{oxidized organic matter}$	1.66×10^{-12}	21,65

660 **Table S2.** Input parameters to the KM-SUB-ELF model

Parameter	Description	Value
KH_{ccO_3}	Henry's law equilibrium constant for O_3 [aq]/[gas]	1.7×10^{-1}
KH_{ccNO_2}	Henry's law equilibrium constant for NO_2 [aq]/[gas]	2.2×10^{-1}
KH_{ccNO}	Henry's law equilibrium constant for NO [aq]/[gas]	3.9×10^{-2}
KH_{ccOH}	Henry's law equilibrium constant for OH [aq]/[gas]	4.3×10^2
KH_{ccHO_2}	Henry's law equilibrium constant for HO_2 [aq]/[gas]	1.7×10^3
$KH_{ccH_2O_2}$	Henry's law equilibrium constant for H_2O_2 [aq]/[gas]	9.9×10^4
ω_{O_3}	Mean thermal velocity of O_3	$3.7 \times 10^4 \text{ cm s}^{-1}$
ω_{NO_2}	Mean thermal velocity of NO_2	$3.8 \times 10^4 \text{ cm s}^{-1}$
ω_{NO}	Mean thermal velocity of NO	$4.7 \times 10^4 \text{ cm s}^{-1}$
ω_{OH}	Mean thermal velocity of OH	$6.2 \times 10^4 \text{ cm s}^{-1}$
ω_{HO_2}	Mean thermal velocity of HO_2	$4.5 \times 10^4 \text{ cm s}^{-1}$
$\omega_{H_2O_2}$	Mean thermal velocity of H_2O_2	$4.4 \times 10^4 \text{ cm s}^{-1}$
MW_{aa}	Average molecular weight of amino acids	125 g mole^{-1}
MW_{Cu}	Molecular weight copper	63.6 g mole^{-1}
MW_{Fe}	Molecular weight iron	55.6 g mole^{-1}
MW_{SOA}	Average molecular weight SOA	250 g mole^{-1}
MW_{PQN}	Molecular weight phenanthrenequinone (PQN)	$208.2 \text{ g mole}^{-1}$
MW_{NQN}	Molecular weight naphthoquinone (NQN)	$158.2 \text{ g mole}^{-1}$
pK_{aGSH}	Acid dissociation constant of GSH	8.8
pK_{aHO_2}	Acid dissociation constant of HO_2	4.8
pK_{aONOOH}	Acid dissociation constant of ONOOH	6.5
VR	Lung ventilation rate	$1.5 \text{ m}^3 \text{ h}^{-1}$
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_{ELF}	Total ELF surface area	890000 cm^2
T_{RT}	Respiratory tract temperature	37°C
pH_{ELF}	pH of the ELF	7

662 **Table S3.** List of symbols and definitions

Symbol	Meaning	SI unit
C_Y	ELF concentration of PM2.5 constituent Y	$\mu\text{mol L}^{-1}$
$C_{\text{gas,PM2.5}}$	Ambient gas phase concentration of PM2.5	$\mu\text{g m}^{-3}$
$C_{\Sigma\text{ROS}}$	ROS concentration in the ELF during or after model simulation	nmol L^{-1}
$d_{\text{PM2.5}}$	Fraction of PM2.5 that deposits in the ELF	
$D_{\text{PM2.5}}$	Dose of PM2.5 deposited in the ELF	μg
$I_{i \rightarrow j}$	Gross chemical interconversion between individual ROS in the ELF	nmol L^{-1}
$I_{\Sigma\text{ROS}}$	Gross chemical interconversion between all ROS in the ELF	nmol L^{-1}
MF_Y	PM2.5 mass fraction of constituent Y	
M_Y	Molar mass of PM2.5 constituent Y	g mol^{-1}
$N_{\Sigma\text{ROS}}$	Cumulative production of ROS in the ELF	nmol L^{-1}
$N'_{\Sigma\text{ROS}}$	Cumulative production rate of ROS in the ELF	$\text{nmol L}^{-1} \text{s}^{-1}$
$P_{\Sigma\text{ROS}}$	Gross chemical production of ROS in the ELF	nmol L^{-1}
$P'_{\Sigma\text{ROS}}$	Gross chemical production rate of ROS in the ELF	$\text{nmol L}^{-1} \text{s}^{-1}$
P	Gross chemical production of an individual ROS in the ELF	nmol L^{-1}
SF_Y	Soluble fraction of PM2.5 constituent Y in ELF	
t_{acc}	Accumulation time of PM2.5 in the ELF	h
t_{sim}	Model simulation time	h
V_{ELF}	Volume of the ELF	mL
VR	Lung ventilation rate	$\text{m}^3 \text{h}^{-1}$
Y_{OH}	OH yield in the ELF	μmol

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Table S4. Mathematical formulas used to calculate ELF ROS metrics

$$I_{\Sigma\text{ROS}} = \sum_{j,i>j} I_{i \rightarrow j}$$

$$N_{\Sigma\text{ROS}} = P_{\Sigma\text{ROS}} - I_{\Sigma\text{ROS}}$$

$$N'_{\Sigma\text{ROS}} = (P_{\Sigma\text{ROS}} - I_{\Sigma\text{ROS}}) / t_{\text{sim}}$$

$$P'_{\Sigma\text{ROS}} = P_{\Sigma\text{ROS}} / t_{\text{sim}}$$

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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 ($\mu\text{g m}^{-3}$)	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

Zabrze (upper Silesia, Poland)	22	160.8	6.5	7.31×10^{-3}	2.96×10^{-4}	101
Chuncheon (South Korea)	23	29.6	9.9	1.29×10^{-3}	4.30×10^{-4}	99
Detroit (Michigan)	23	234	6	1.02×10^{-2}	2.61×10^{-4}	102
Megalopolis (Greece)	23	87	4.02	3.78×10^{-3}	1.75×10^{-4}	98
Tehran (outside a retirement home)	24	238.81	25.99	9.95×10^{-3}	1.08×10^{-3}	96
South-Eastern Italy (urban sites)	24.1	78.8	5.7	3.27×10^{-3}	2.37×10^{-4}	97
Tehran (outside a school dormitory)	26	280	32.42	1.08×10^{-2}	1.25×10^{-3}	96
Anaheim (California)	26.8	29.6	39.6	1.11×10^{-3}	1.48×10^{-3}	103
Milan (Summer, Italy)	27.2	186	10	6.84×10^{-3}	3.68×10^{-4}	104
Jeddah City (Saudi Arabia)	28.4	590	5.6	2.08×10^{-2}	1.97×10^{-4}	105
Hong Kong	29	140	5.7	4.83×10^{-3}	1.97×10^{-4}	106
Rio de Janeiro (Brazil)	29.2	307	35	1.05×10^{-2}	1.20×10^{-3}	107
Katowice (upper Silesia, Poland)	31	157	8.2	5.07×10^{-3}	2.65×10^{-4}	101
Porto Marghera (Italy)	31	200	9.3	6.45×10^{-3}	3.00×10^{-4}	108
Erzgebirge (Germany)	32.5	188	3	5.79×10^{-3}	9.23×10^{-5}	109
Barcelona (Spain)	35	260	52	7.43×10^{-3}	1.49×10^{-3}	110
Santa Catarina (Mexico)	36.15	466	16	1.29×10^{-2}	4.42×10^{-4}	111
Escobedo (Mexico)	37.78	493	13	1.31×10^{-2}	3.44×10^{-4}	111
Arnhem (the Netherlands)	38.95	241	13.5	6.19×10^{-3}	3.47×10^{-4}	112
Mira Loma (Southern California, average)	41.8	581	75	1.39×10^{-2}	1.79×10^{-3}	113
Taif (residential area, Saudi Arabia)	46	2000	5.3	4.35×10^{-2}	1.15×10^{-4}	114
Taif (industrial site, Saudi Arabia)	47	2300	13	4.89×10^{-2}	2.77×10^{-4}	114
Azusa (California)	47.1	281.9	13.4	5.99×10^{-3}	2.85×10^{-4}	103
Edison (New Jersey)	49.6	1953	10	3.94×10^{-2}	2.02×10^{-4}	115
Bursa (Turkey)	53	875	15	1.65×10^{-2}	2.83×10^{-4}	116
Karachi (summer, Pakistan)	55.89	3360	56	6.01×10^{-2}	1.00×10^{-3}	117
New Delhi (summer, high traffic, India)	58.2	710	20	1.22×10^{-2}	3.44×10^{-4}	118

Milan (Winter, Italy)	58.6	309	18	5.27×10^{-3}	3.07×10^{-4}	104
Thessaloniki (cold period, Greece)	60.9	2890	93	4.75×10^{-2}	1.53×10^{-3}	119
Thessaloniki (warm period, Greece)	70.6	4094	66	5.60×10^{-2}	9.35×10^{-4}	119
Córdoba City (Argentina)	70.87	325	8	4.59×10^{-3}	1.13×10^{-4}	120
Shanghai (China)	71.61	424.93	9.47	5.93×10^{-3}	1.32×10^{-4}	121
Yong'an (Winter, China)	79.01	582.1	19.6	7.37×10^{-3}	2.48×10^{-4}	122
Yong'an (Spring, China)	83.26	736.1	16.5	8.84×10^{-3}	1.98×10^{-4}	122
Karachi (winter, Pakistan)	98.44	3706	39	3.77×10^{-2}	3.96×10^{-4}	117
Ji'nan (urban site, China)	101	1040	30	1.03×10^{-2}	2.97×10^{-4}	123
Guangzhou (China)	104.58	66	60	6.31×10^{-4}	5.74×10^{-4}	124
Argra (urban, India)	104.9	1900	200	1.81×10^{-2}	1.91×10^{-3}	125
Pune (India)	113.8	2090	339	1.84×10^{-2}	2.98×10^{-3}	126
Beijing (Summer, China)	125	1060	44.7	8.48×10^{-3}	3.58×10^{-4}	127
Ji'nan (industrial site, China)	130	2410	40	1.85×10^{-2}	3.08×10^{-4}	123
Beijing (Winter, China)	138	1330	53.2	9.64×10^{-3}	3.86×10^{-4}	127
Beijing (China)	182.2	1180	70	6.48×10^{-3}	3.84×10^{-4}	128
New Delhi (winter, high traffic, India)	276.9	1150	70	4.15×10^{-3}	2.53×10^{-4}	118
Peat fire episode (Indonesia)	640	4810	100	7.52×10^{-3}	1.56×10^{-4}	129
<i>Iron and copper medians</i>	–	–	–	8.14×10^{-3}	3.07×10^{-4}	<i>This study</i>

Table S6. PM2.5 and SOA concentrations with mass fractions as quantified in PM2.5 collected at different sampling sites throughout the world.

Sampling location	PM2.5 ($\mu\text{g m}^{-3}$)	SOA ($\mu\text{g m}^{-3}$)	SOA mass fraction	Reference
Amazon (Brazil)	1.8	0.34	0.189	130
Hyytiälä (Finland)	2	1.2	0.60	131
Storm Peak (Colorado)	2.1	0.7	0.333	131

Jungfrauoch (Switzerland)	2.2	1.2	0.545	131
Duke Forest (North Carolina)	2.8	1.3	0.464	131
Chebogue Pt. (Canada)	2.9	1.5	0.517	131
Edinburgh (Scotland)	3	1.2	0.400	131
Mainz (Germany)	4.3	1.1	0.256	131
Boulder (Colorado)	4.4	2.5	0.568	131
Manchester (winter, UK)	5.2	0.6	0.115	131
Chelmsford (UK)	5.3	1.8	0.340	131
Vancouver (Canada)	7	2.5	0.357	131
Okinawa (Japan)	7.9	1.7	0.215	131
Off New England Coast	8.5	4.9	0.576	131
Thompson Farm (New Hampshire)	9.5	4.2	0.442	131
Zurich (winter, Switzerland)	9.6	4.3	0.448	131
Cheju (South Korea)	10.7	4	0.374	131
Fukue (Japan)	11	3.6	0.327	131
New York City (winter, New York)	11.6	2.6	0.224	131
New York City (summer, New York)	12.2	4.8	0.393	131
Pinnacle Park (New York)	12.3	5.4	0.439	131
Houston (Texas)	12.8	2.7	0.211	131
Tokyo (summer, Japan)	13.2	4.7	0.356	131
Manchester (summer, UK)	14.3	3	0.210	131
Pittsburgh (Pensylvenia)	14.7	3.1	0.211	131
Tokyo (winter, Japan)	16.2	2.3	0.142	131
Taunus (Germany)	16.3	7.9	0.485	131
Riverside (California)	19.1	7	0.366	131
Zurich (summer, Switzerland)	25.5	5.1	0.200	131
Mexico City (Mexico)	26.8	8.1	0.302	131

Guangzhou (China)	69.1	12.5	0.181	132
Beijing (China)	79.9	16.6	0.208	132
Shanghai (China)	90.7	11.1	0.122	132
Beijing (China)	158.5	40.9	0.258	132
Xi'an (China)	345.1	53.5	0.155	132
SOA median	–	–	0.333	<i>This study</i>

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 ($\mu\text{g m}^{-3}$)	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
								120
Atascadero (California)	5*	0.023	0.0127	0.0246	6.21×10^{-6}	3.43×10^{-6}	6.64×10^{-6}	
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}	<i>This study</i>

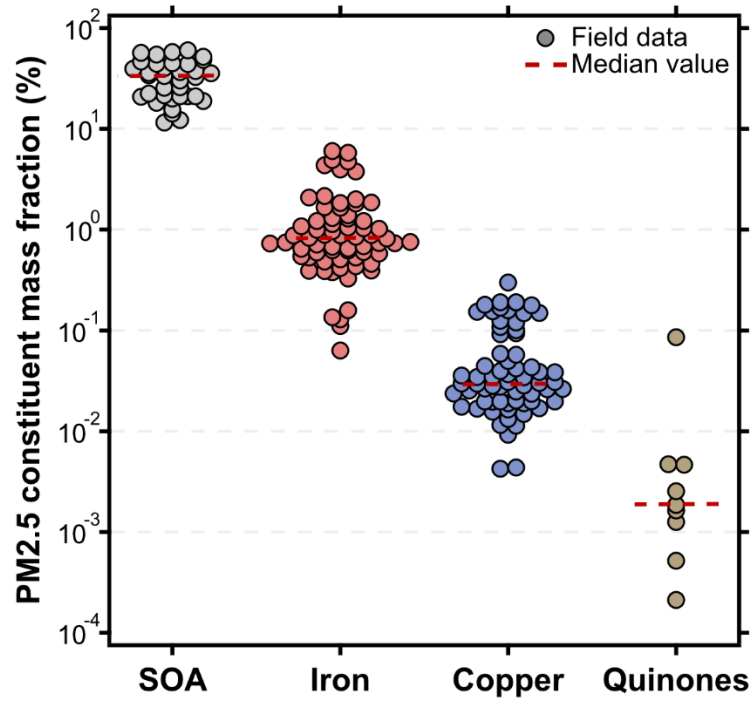


Figure S1. Mass fractions of all redox-active PM2.5 constituents quantified in field data (Tabs. S5-7). The median mass fraction of each redox-active PM2.5 constituent is indicated by the red horizontal line.

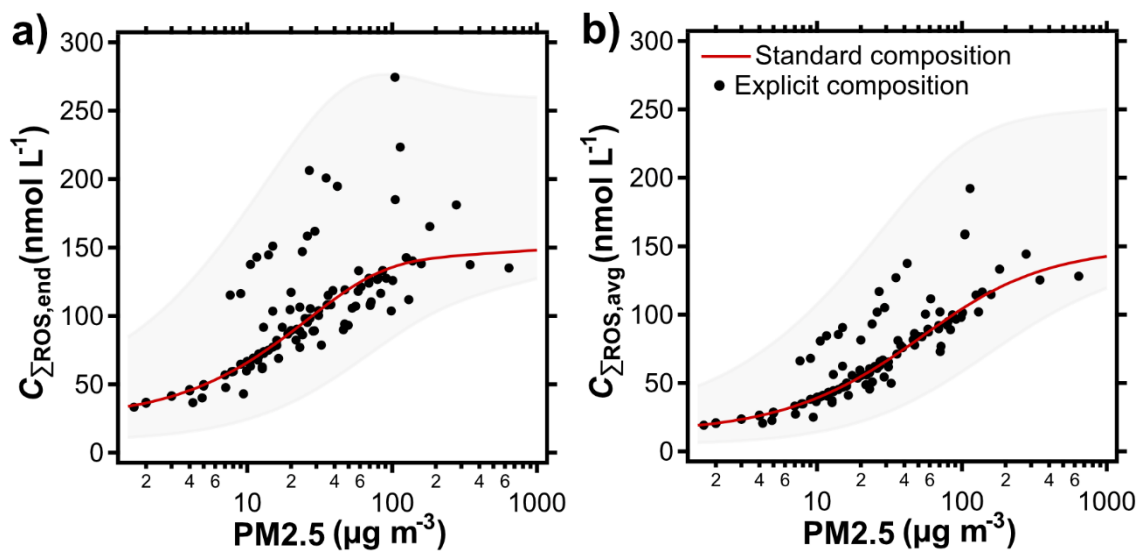


Figure S2. (a) ROS concentration, $C_{\Sigma ROS, end}$, after pollutant exposure, and (b) the average ROS concentration, $C_{\Sigma ROS, avg}$, during pollutant exposure as a function of PM2.5 concentration. The solid lines represent a standard composition of PM2.5 using median mass fractions of the redox-active constituents. Black markers represent calculations using explicit PM2.5 composition field data (Tab. S5-7)

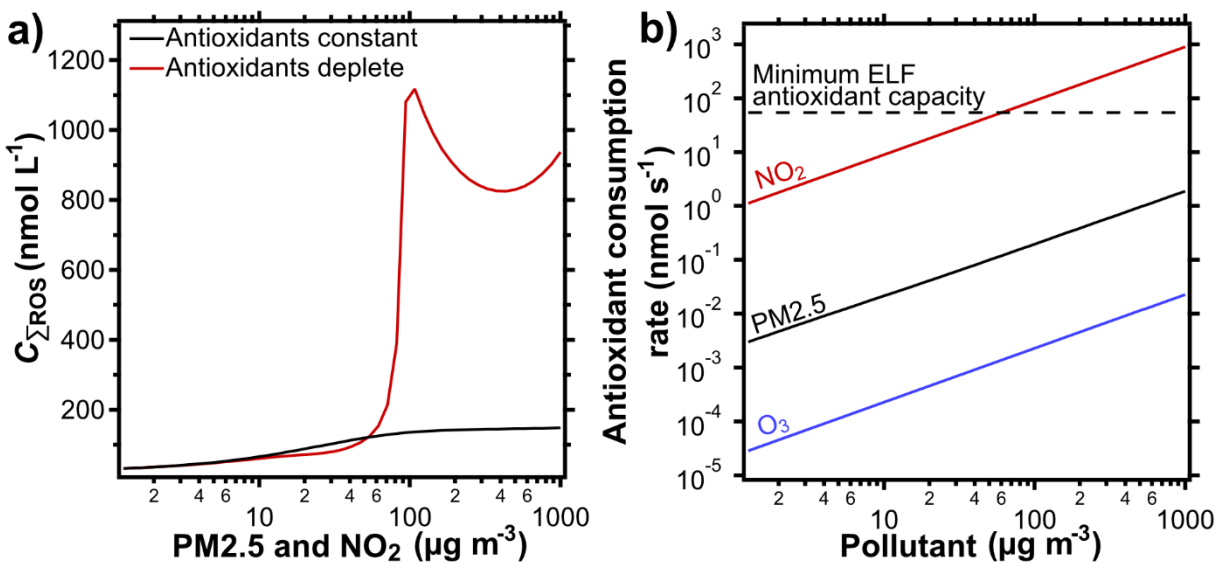


Figure S3. (a) ROS concentrations, $C_{\Sigma ROS}$, as a function of pollutant concentration with and without consideration of antioxidant depletion in the model. One μg of the co-pollutant NO₂ is added per μg PM2.5. For O₃, a constant concentration of 30 $\mu\text{g m}^{-3}$ was used, independent of PM2.5 concentration. (b) Antioxidant consumption rate of NO₂, PM2.5 and O₃ 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.

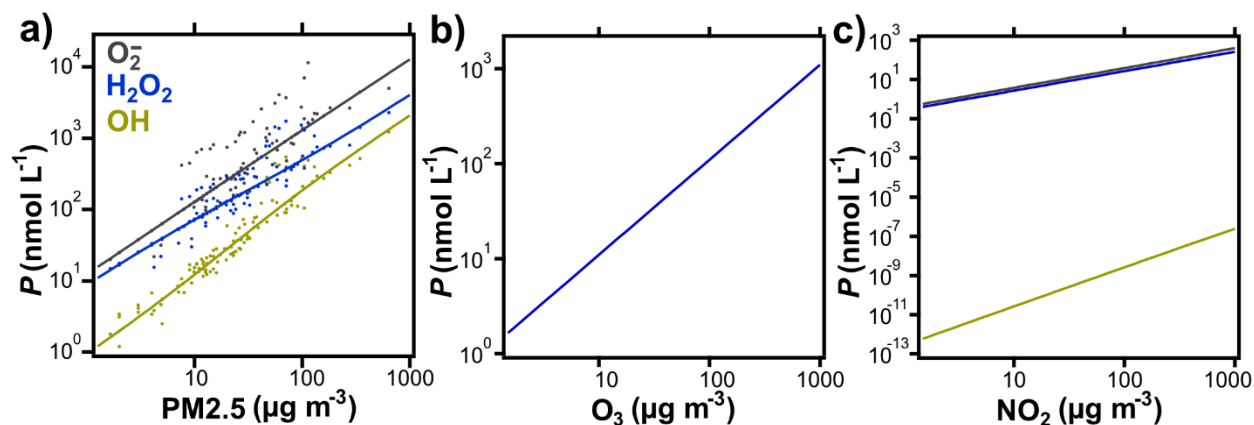


Figure S4. Gross chemical production of individual ROS in the ELF solely associated with and as a function of the concentration of three pollutants: (a) PM_{2.5}, (b) O₃, and (c) NO₂. Simulations were carried out using only the single pollutant. In panel a, the solid lines represent standard PM_{2.5} composition, and the markers represent explicit PM_{2.5} composition data for redox-active constituents (Tabs. S5-7). O₃ does not contribute to production of O₂⁻ or OH in the model.

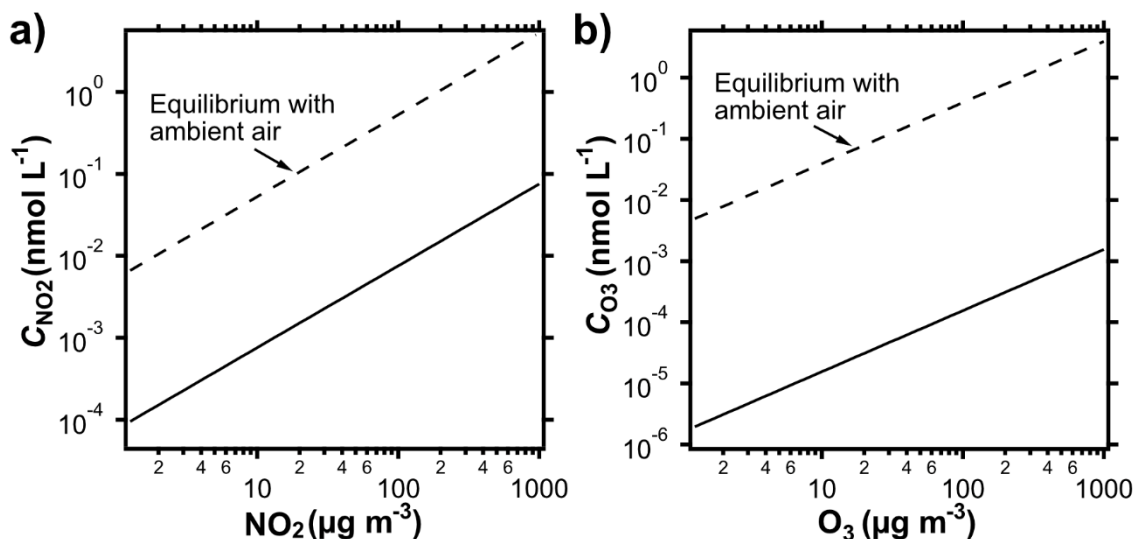


Figure S5. Aqueous-phase (a) NO₂ concentration and (b) O₃ concentration in the ELF as a function of pollutant concentration and comparison to hypothetical saturation with respect to ambient air. Dashed lines indicate saturation concentrations assuming Henry's law equilibrium, which are calculated using the ambient gas phase pollutant concentration and the dimensionless water–air partitioning coefficients for O₃ and NO₂, respectively (Table S2).

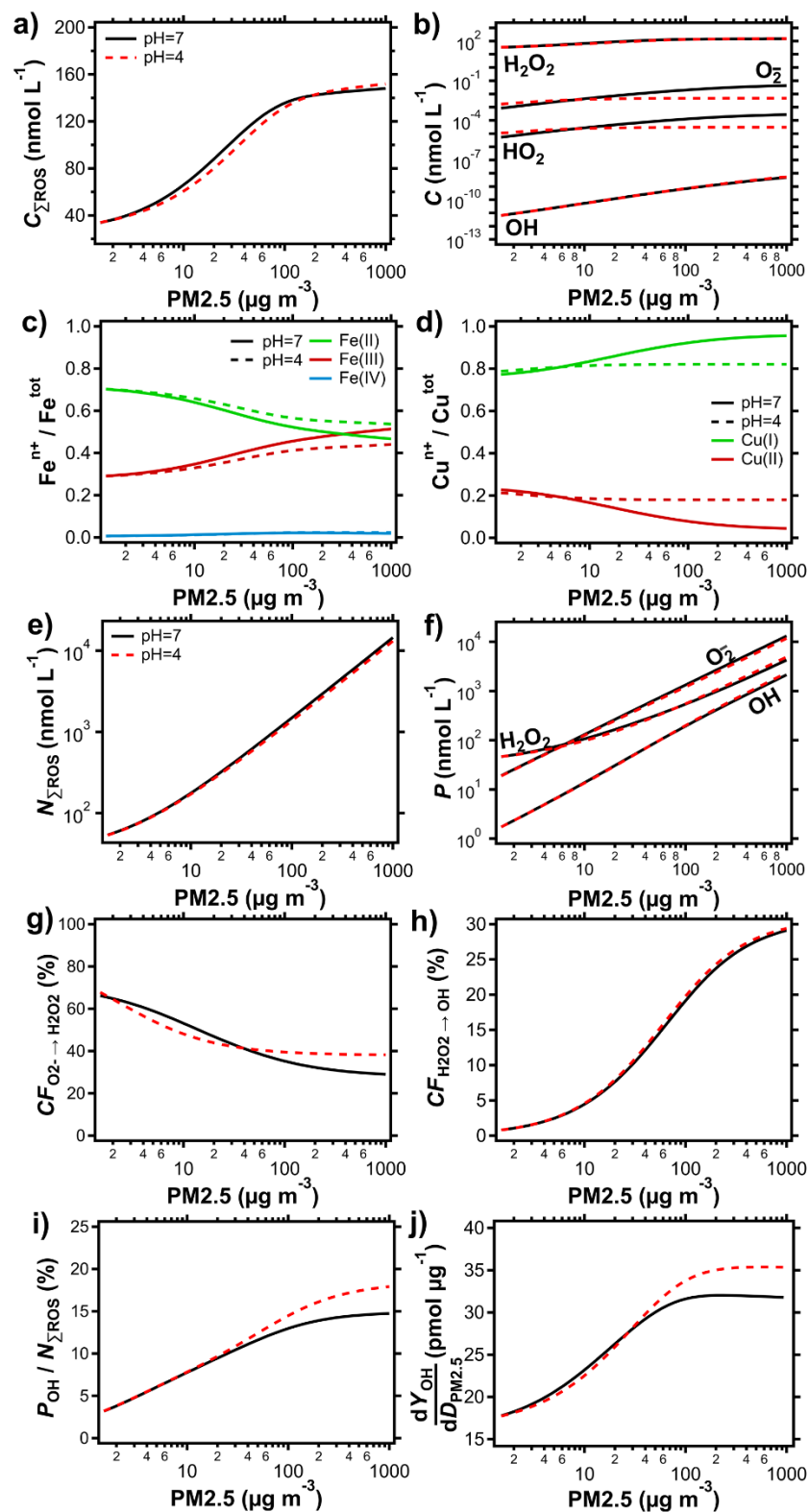


Figure S6. Effect of using different pH on the main results (panels a,b, e-j) and transition metal valence state (panels c,d) using the median mass fractions of all redox-active PM2.5 constituents, co-varied NO₂ (PM2.5:NO₂ = 1:1) and an O₃ concentration of 30 $\mu\text{g m}^{-3}$.