

Reactive Oxygen Species (ROS) – a potential new health relevant metric

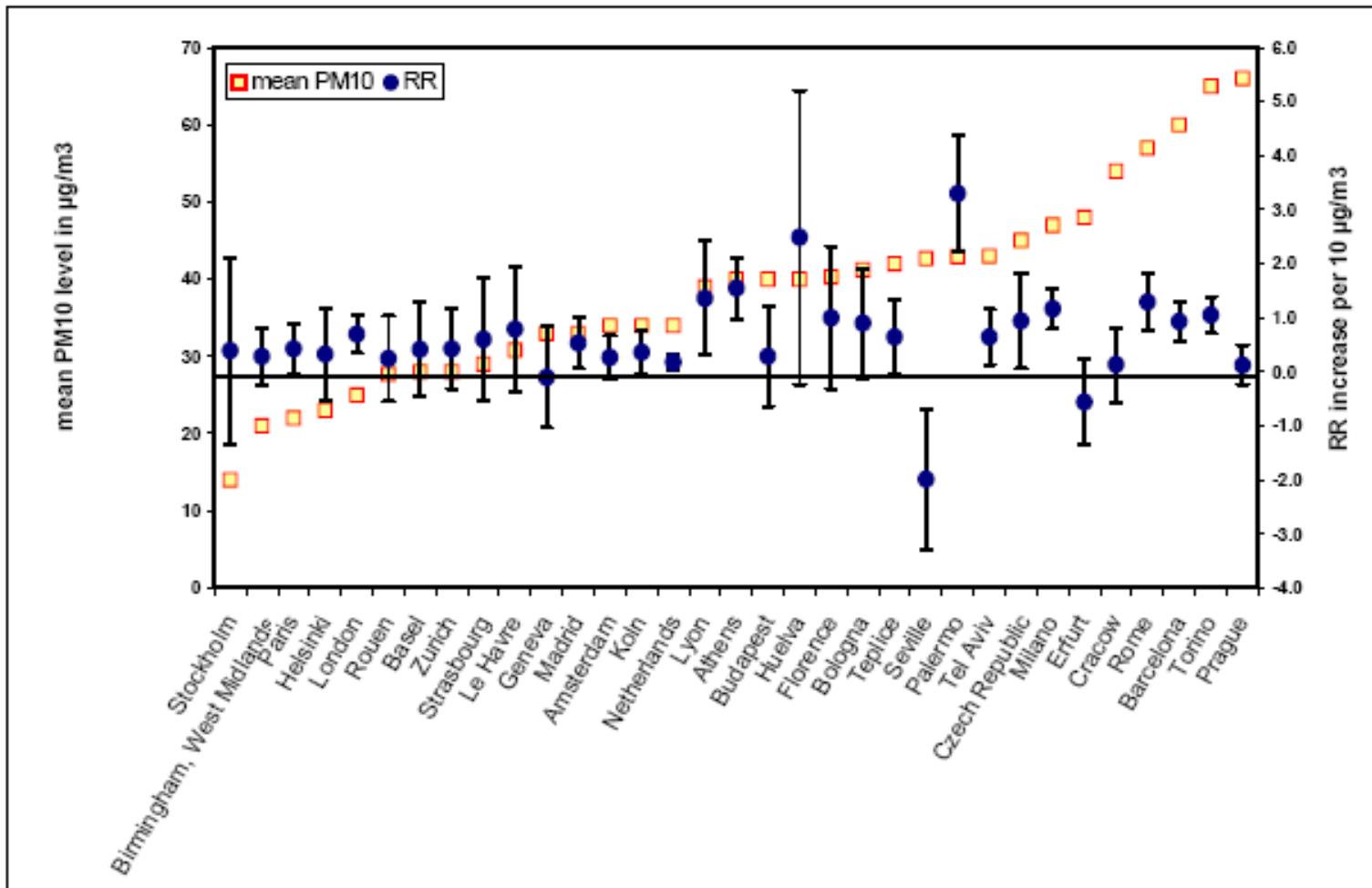
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MRC-HPA Centre for Environment & Health



Exposure to particulate air pollution is associated with an average loss of life expectancy of six-eight months in Europe due to adverse cardio-respiratory health effects



Ranking of estimates for all-cause mortality by annual average levels of PM₁₀



Ambient particles carry 'oxidants' or components which generate 'oxidants'

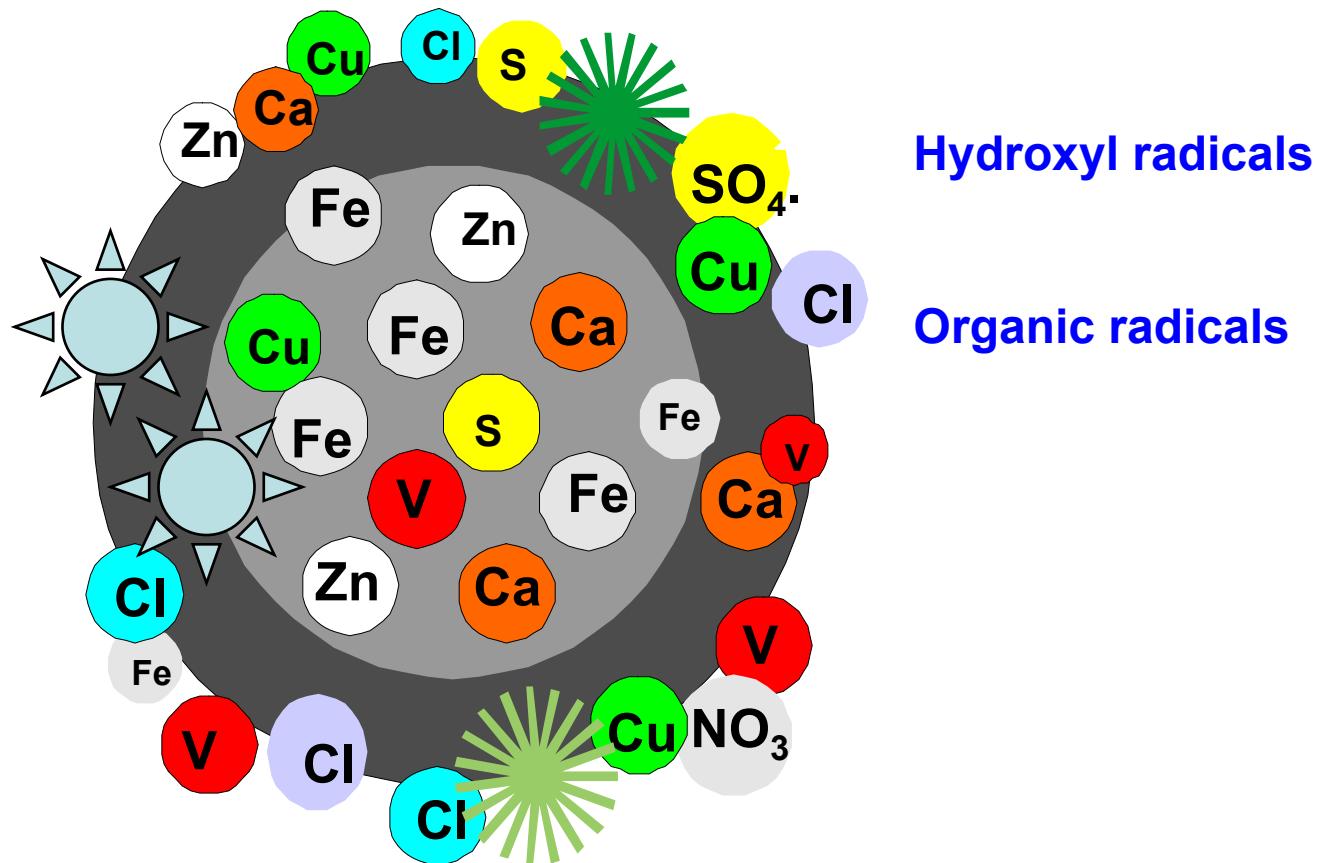
Transition metals

Quinones, PAHs

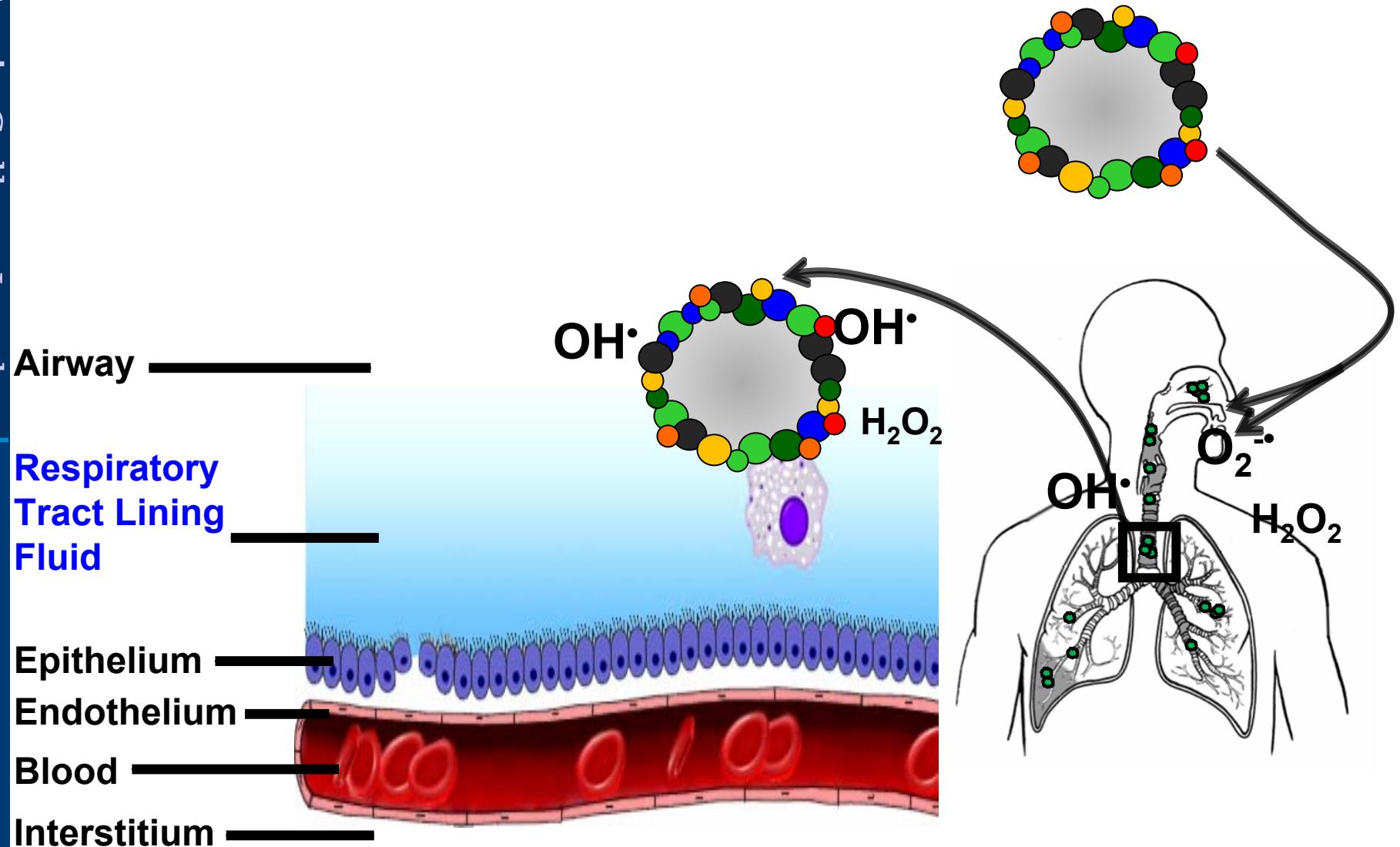
Biological material

Hydroxyl radicals

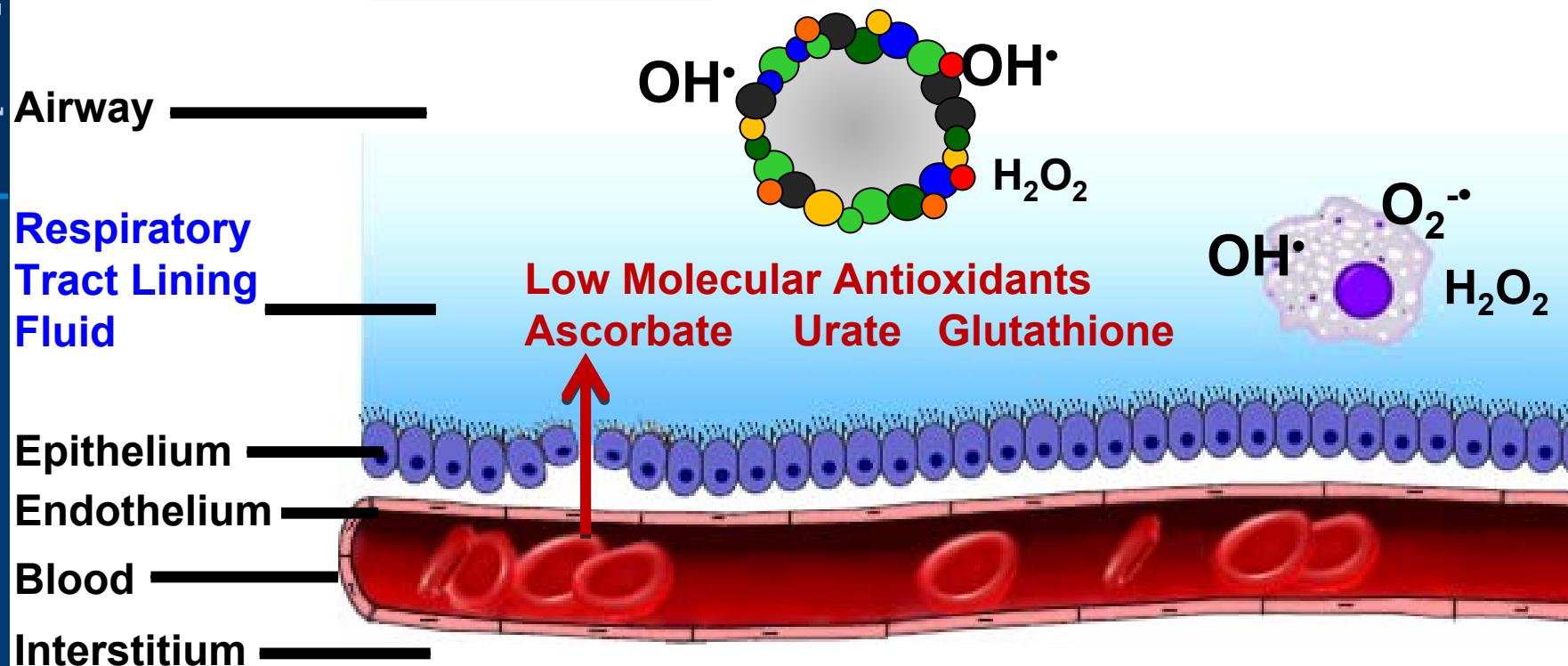
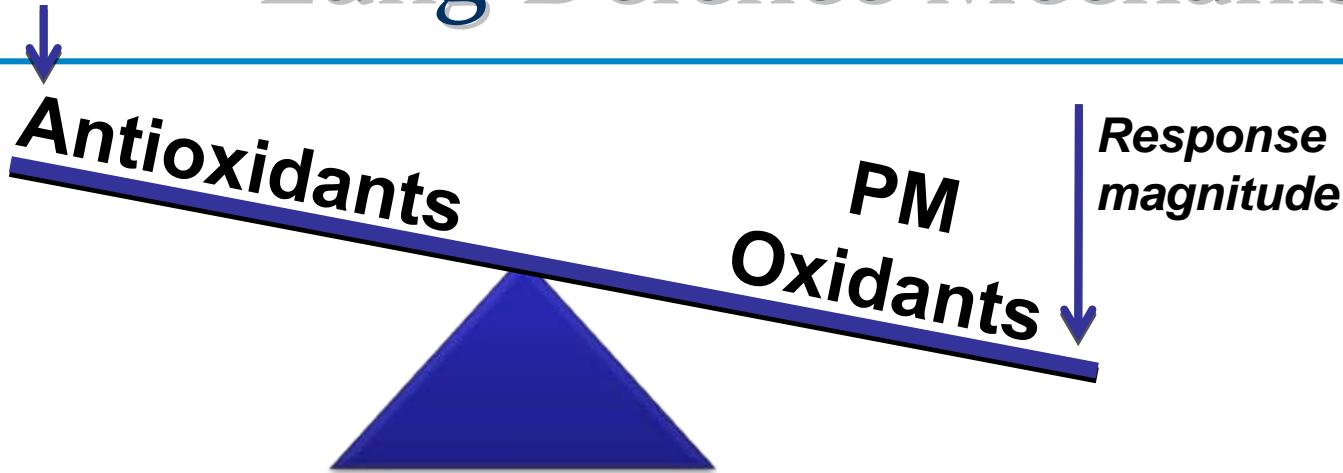
Organic radicals



PM carries oxidants into the lung

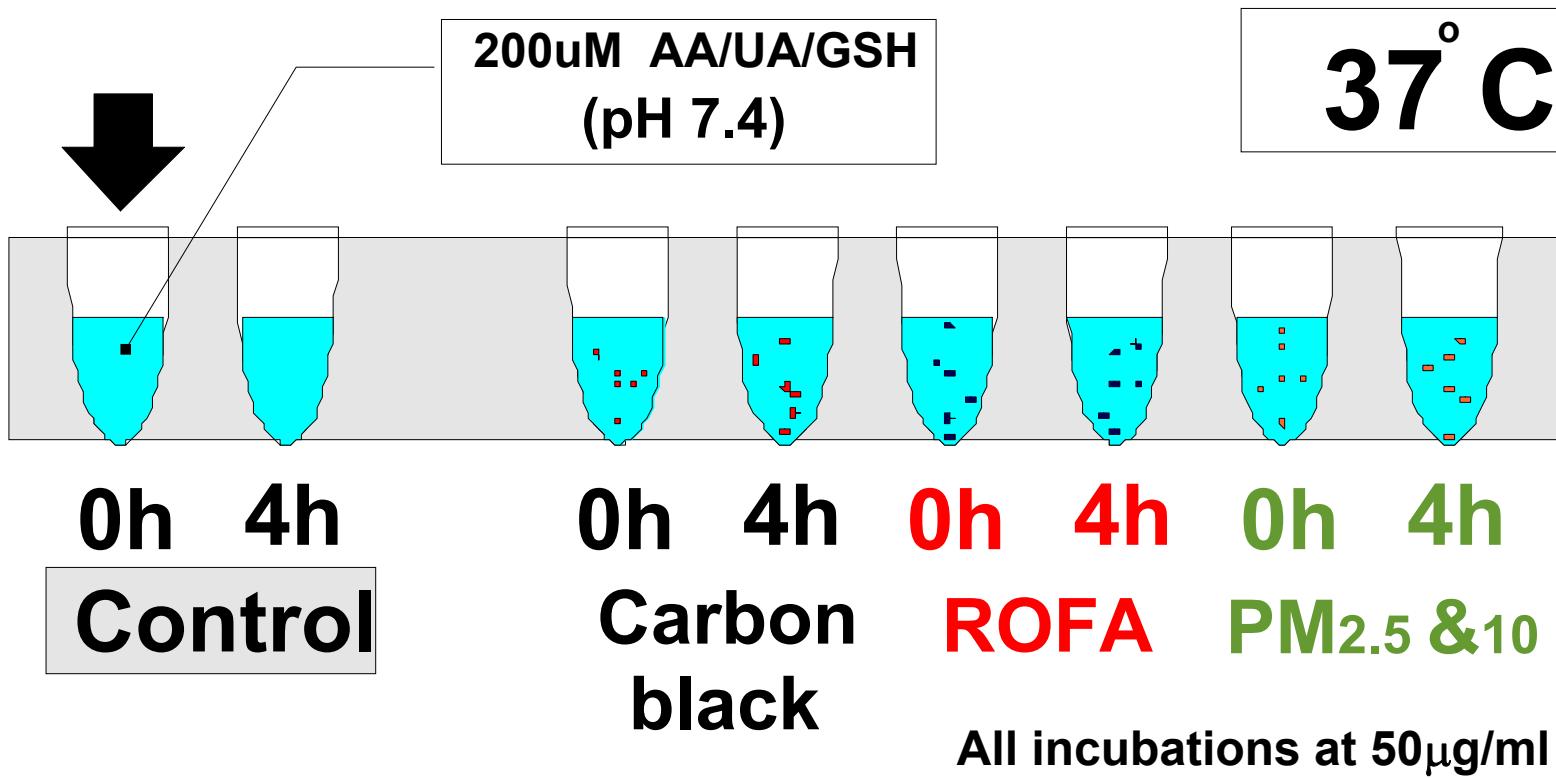


Lung Defence Mechanism



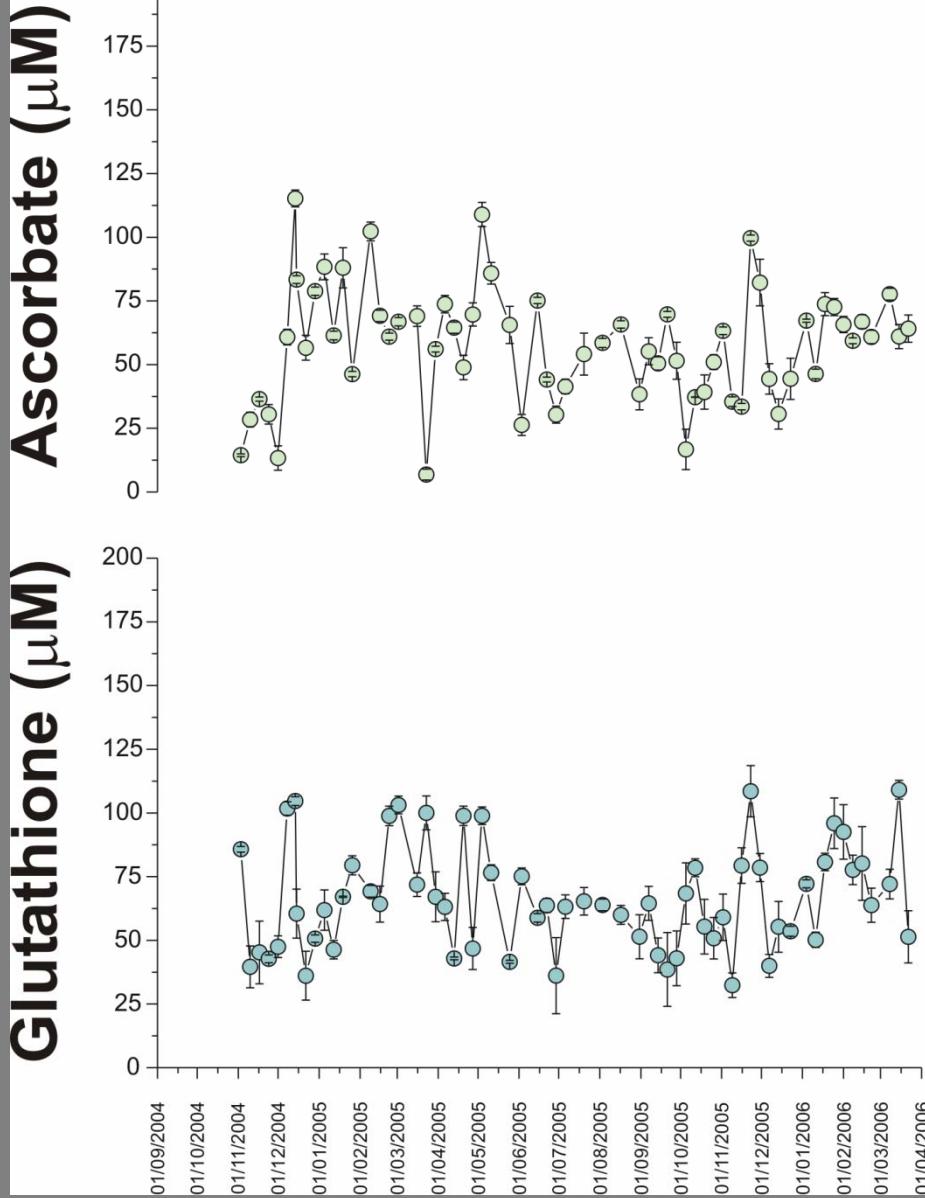
Particle Exposure Model

Artificial lung fluid



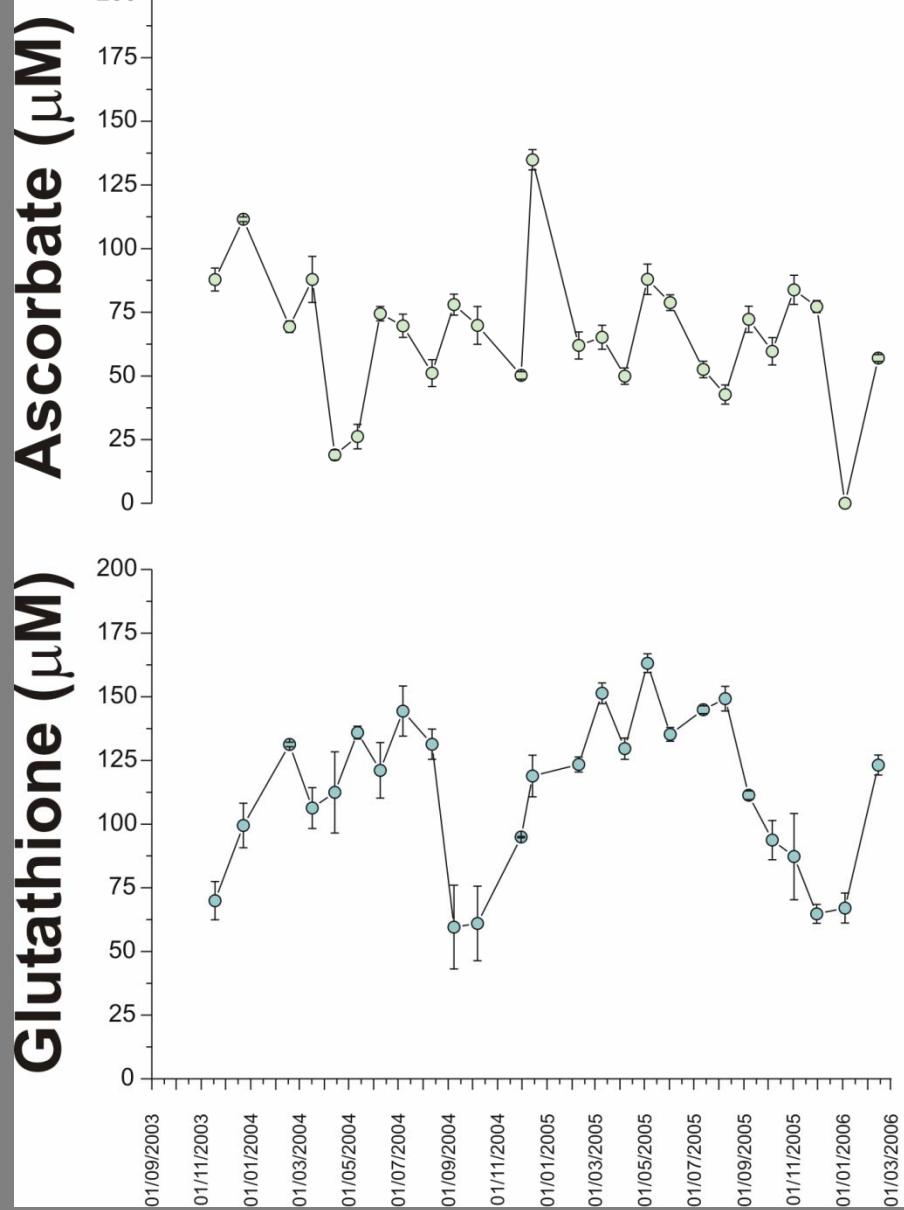
Marylebone Road - MY1

November 2004 - March 2006



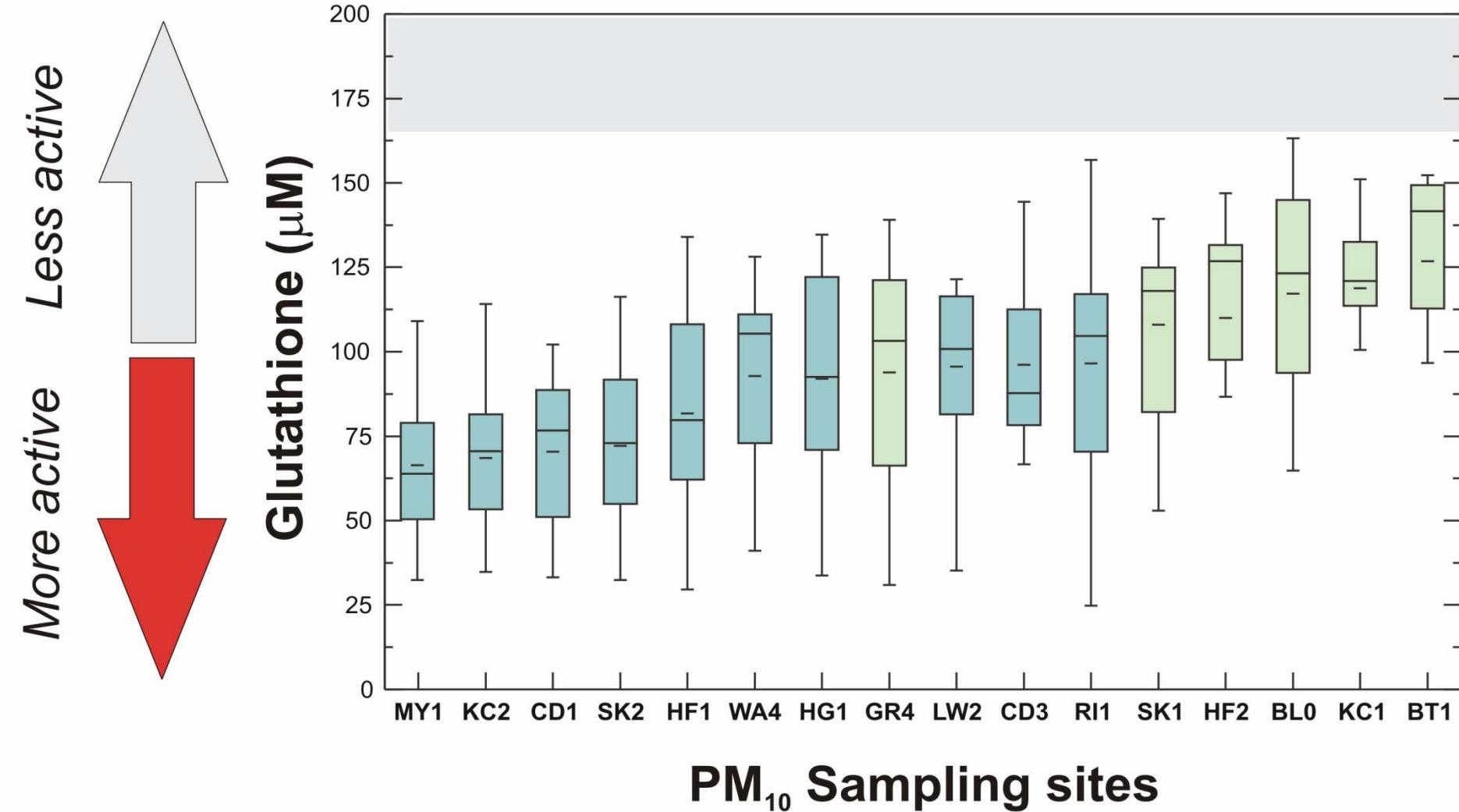
Bloomsbury Square - BL0

November 2004 - March 2006



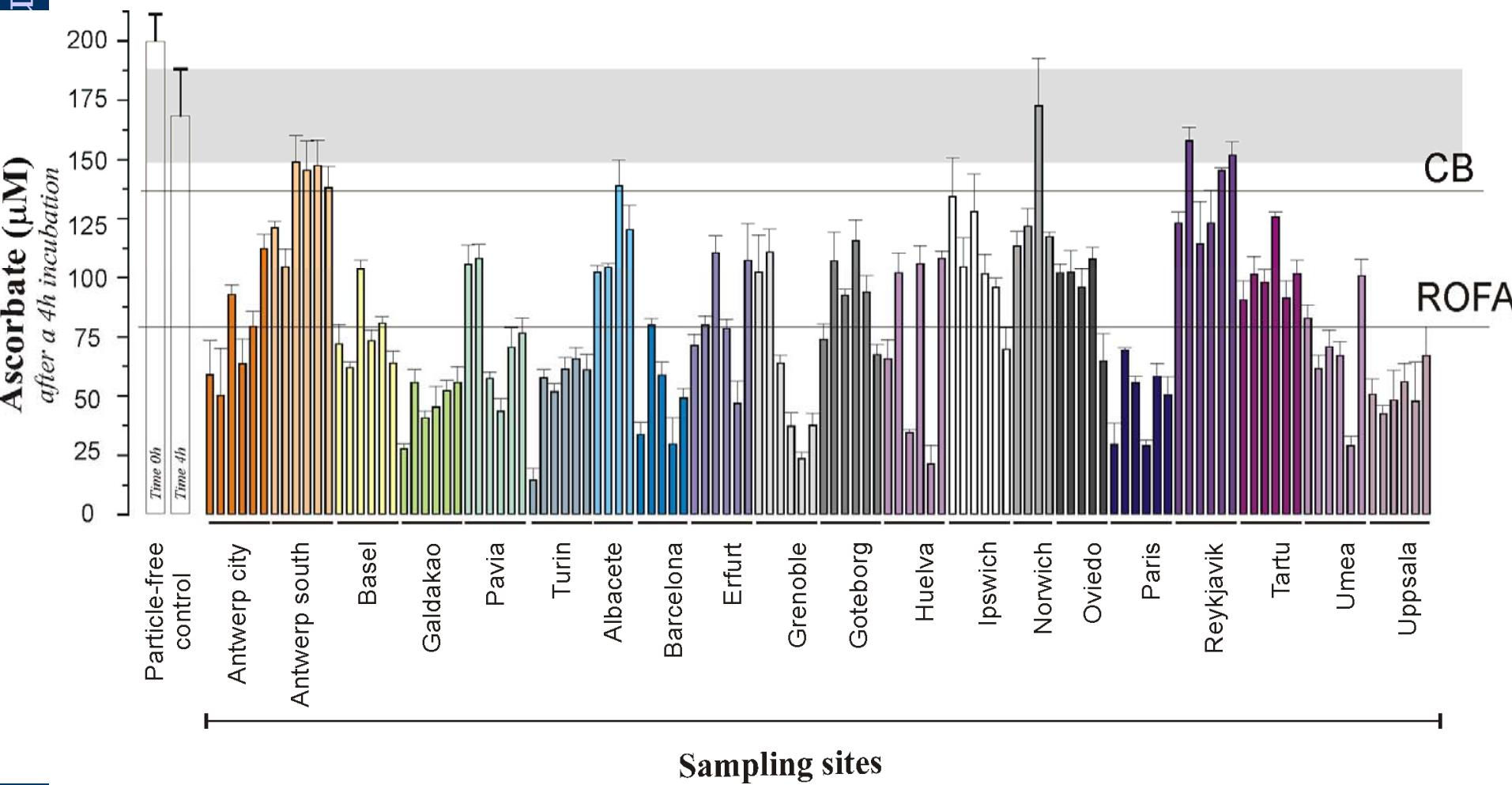
PM oxidative potential at various sites across London

November 2004 - March 2006

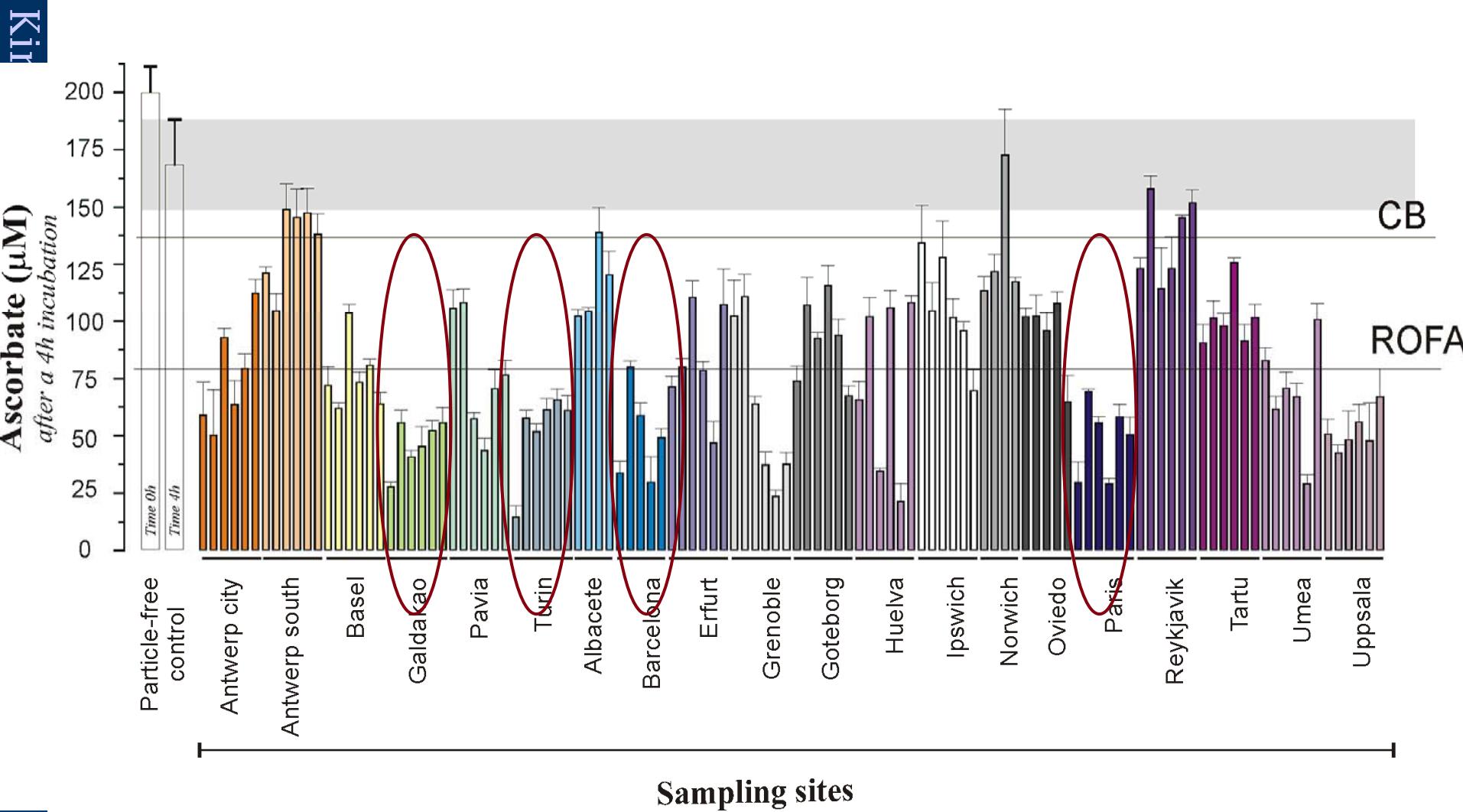


Regional and Temporal Variation in PM_{2.5} oxidative activity across Europe

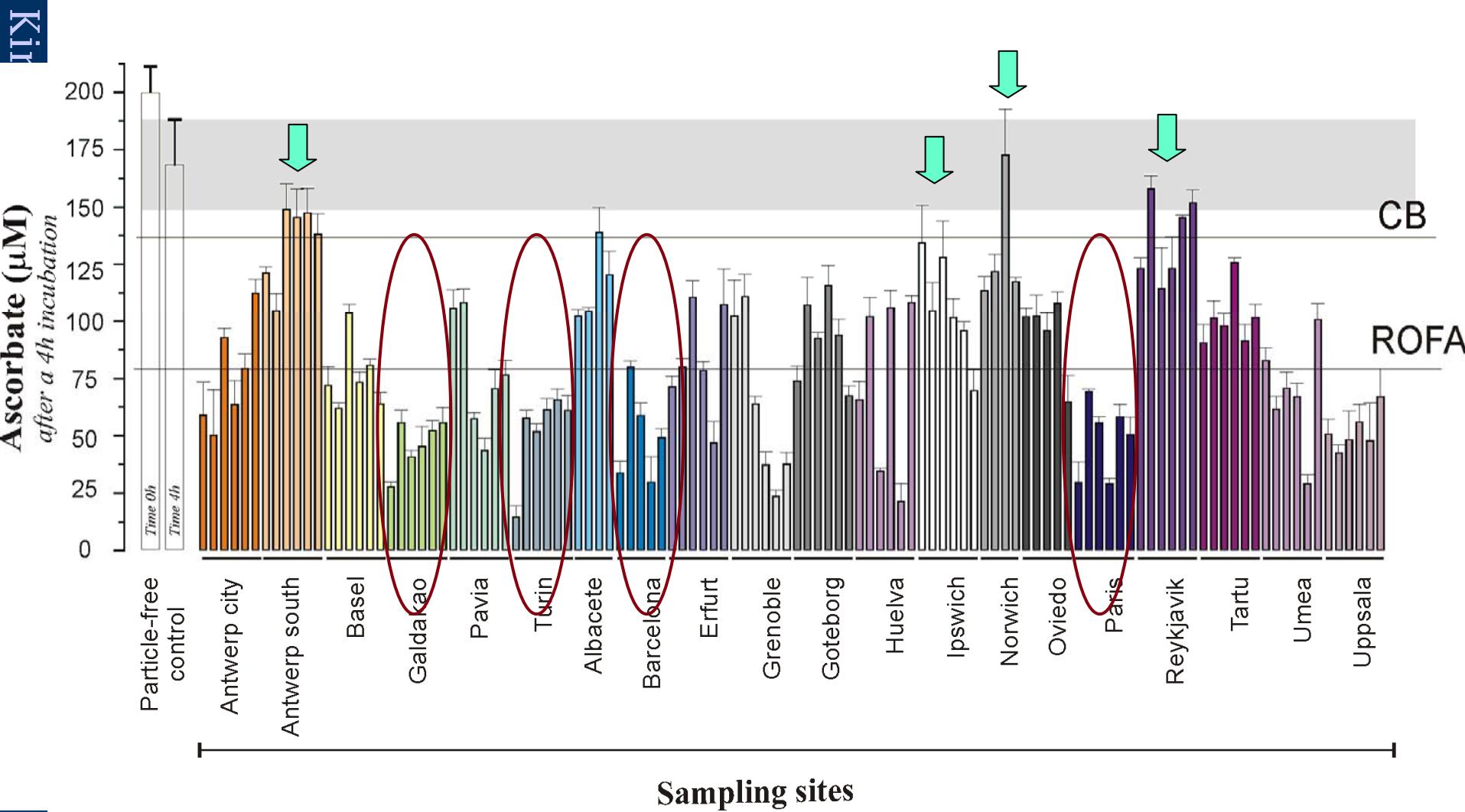
Kill



High Activity Sites



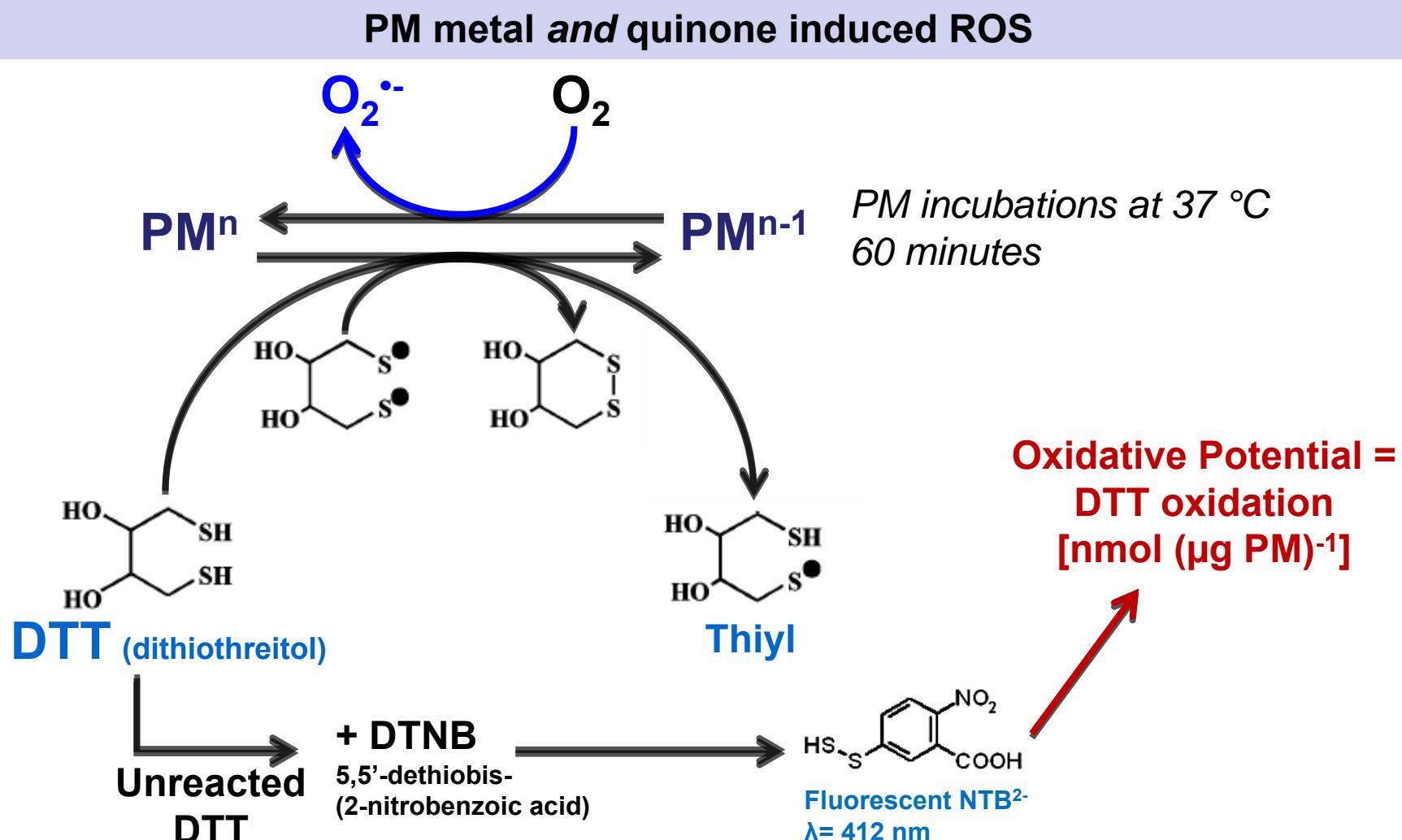
Low Activity Sites



Popular Acellular Models for Measuring OP

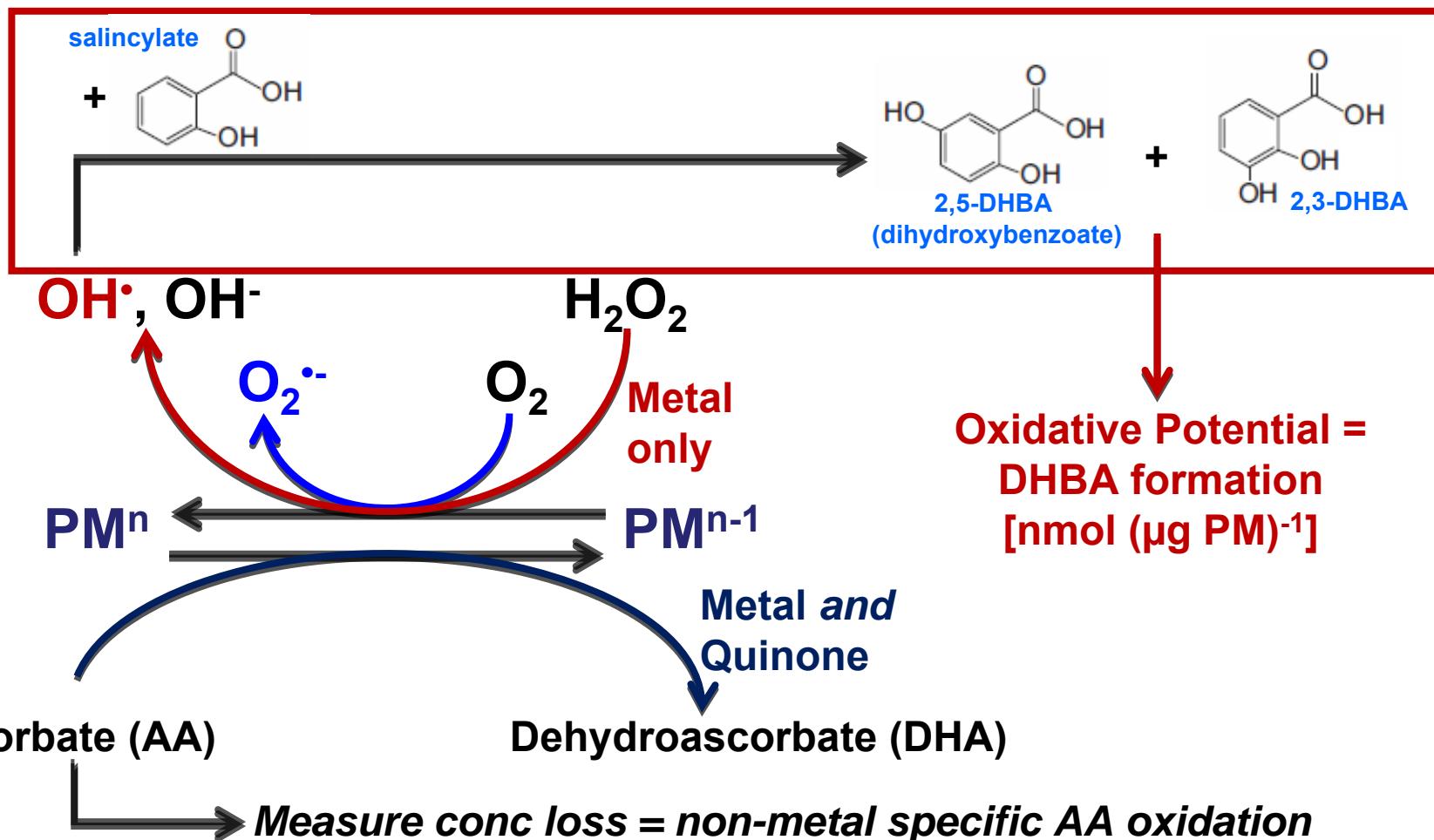
1. Lung lining fluid model – measures both GSH and ascorbate oxidation
2. Thiol Oxidation
3. Ascorbate Oxidation
4. Electron Paramagnetic Resonance
5. Fluorescent Probes – DCFH Oxidation / Profluorescent nitroxides

II. Thiol Oxidation



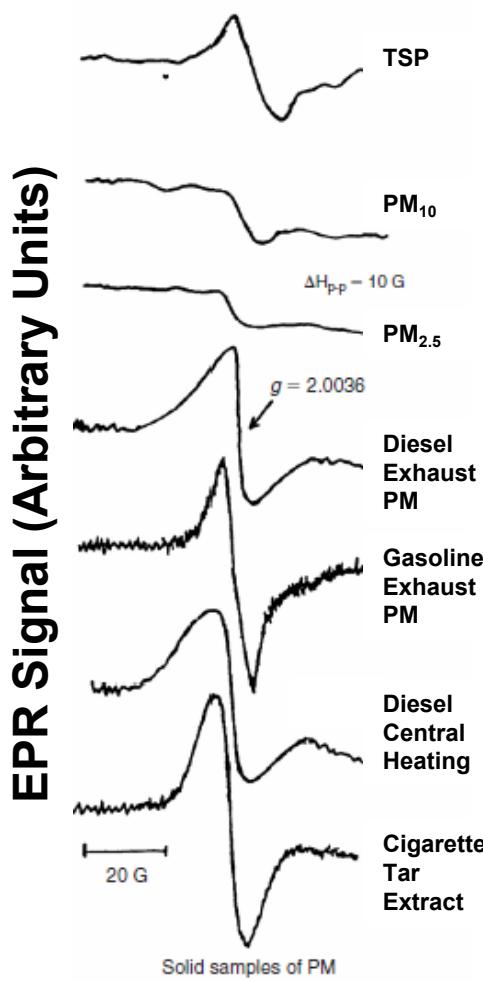
III. Ascorbate Oxidation

PM induced ROS: metals ONLY



IV. Electron Paramagnetic Resonance (EPR)

PM bound and metal/quinone induced ROS



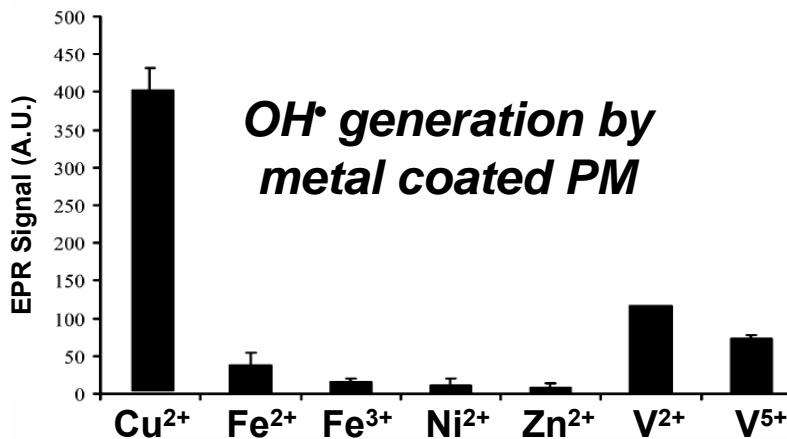
OH[·] generation by PM spin trapped using DMPO (5,5-dimethyl-1-pyrroline-N-oxide);

Oxidative Potential
= EPR spectra measured of DMPO-OH adducts [Arbitrary Units]

- **PM bound ROS**



- **PM metal induced ROS production**

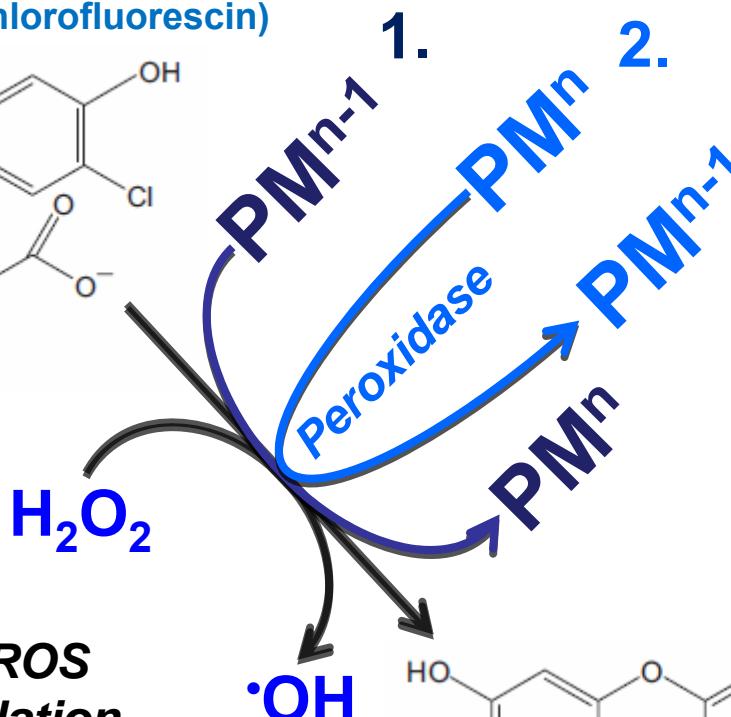
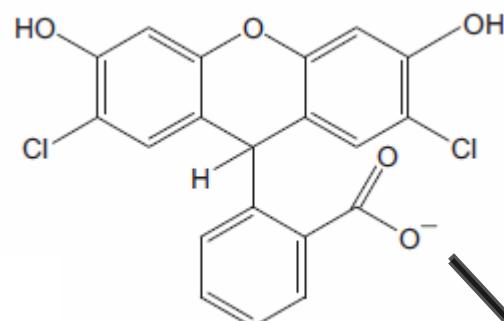


OH[·] generation by metal coated PM

Va. Fluorescent Probes

PM bound and metal induced ROS

DCFH (2'-7'-dichlorofluorescin)

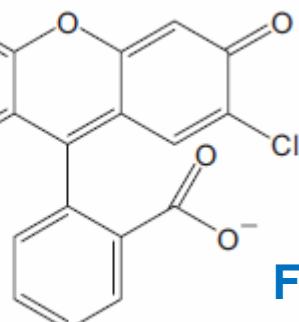


Non-specific ROS mediated oxidation of DCFH

OP by DCFH oxidation can be used to indicate:

1. *PM bound ROS*
Organic free radicals
2. *PM metal induced ROS*
(+ peroxidase)

Oxidative Potential =
 H_2O_2 concentration equivalent [nM (μg PM) $^{-1}$]



Fluorescent DCF
 $\lambda = 525$ nm

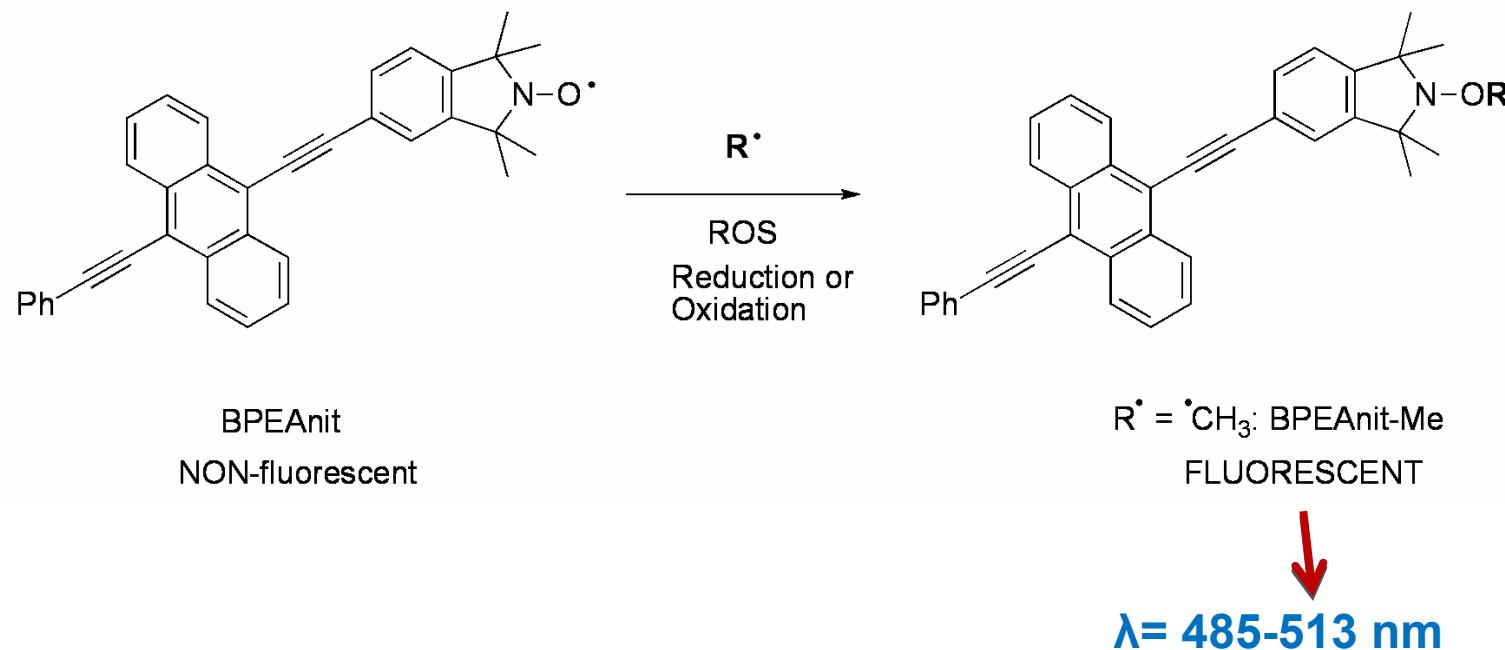
Vb. Fluorescent Probes

PM bound and metal induced ROS

BPEAnit

(9,10-bis(phenylethynyl)anthracene + nitroxide ring)

OP by BPEAnit oxidation can be used to indicate:
PM bound ROS
Organic free radicals



$$\lambda = 485-513 \text{ nm}$$

Measurement of PM Oxidative Potential (OP) with Acellular Models

- *Rapid screening technique which serves as a biologically pertinent index of PM toxicity integrating heterogeneities in PM size, surface area and composition into a single metric.*
- *Acellular OP models quantify the ability of PM to drive damaging biological oxidation mediated by inherently redox active PM chemical constituents.*
 - *PM bound reactive oxygen species*
 - *Organic free radicals*
 - *PM induced production of reactive oxygen species*
 - *Transition Metals*
 - *Quinones + other organics*

Acknowledgements

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THANK YOU FOR YOUR ATTENTION!

