Fine and ultrafine particles from indoor sources -
Effects on healthy humans in a controlled exposure study and on lung epithelial cells *in vitro.*

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Study background

- Exposure to ambient particulate matter (PM) is a leading cause of global morbidity and mortality (Lim et al., 2012)
- Associations between air pollution and adverse health effects have been confirmed in many epidemiological studies (Brook et al., 2010; Cesaroni et al., 2014)
- The fraction of ultrafine particles (UFP) is considered to play a dominant role in the adverse health effects of ambient PM:
  - ✓ greater surface area per mass compared with larger-sized particles
  - ✓ Biological reactivity (e.g. generation of oxidants)
  - ✓ High predicted deposition efficiency, accessibility to alveolar space and translocation into pulmonary interstitium and blood (HEI Review Panel on Ultrafine Particles, 2013; Miller et al., 2017).

Study background – EPIA project

- Health effects of particles from indoor sources?
  - ✓ Substantial sources and exposure levels amounts of fine and ultrafine particles leading to high exposure levels

    (Sørensen et al., 2005; Ward and Noonan, 2008; Ghio et al., 2012).
  - ✓ Consideration of cumulative exposures due to the length of time spent indoors

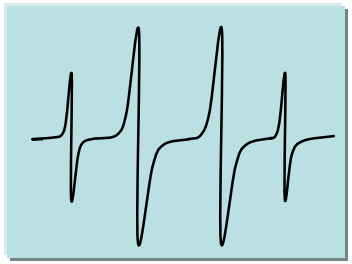
Aims:

To characterise the release of fine and ultrafine particles from relevant indoor sources in terms of their physicochemical properties (chemical composition, size distribution, surface area, reactive oxygen species generation) and to link these properties their ability to induce adverse health effects in humans.

EPIA - Effects of ultrafine Particles from Indoor Activities

EPIA project

Institute of Energy and Environmental Technology (IUTA) e.V.



Physicochemical characterisation & exposure

In vitro toxicology evaluation

Randomized cross-over controlled exposure study

IUF-Leibniz Research Institute for Environmental Medicine

Institute of Occupational, Social and Environmental Medicine, Heinrich-Heine-University

Indoor sources

Indoor Particle Sources

- **Burning candles**
- **Toasting**
- **Baking pizza**
- **Frying sausages**
- **Vacuum cleaning**
- **Stove**
- **Hot air radiator**
- **Alcohol burner**
- **Gas burner**
- **Grinding of nanoparticle-containing paint**

Characterisation

Selection of relevant sources to include in health effects study

Characterisation

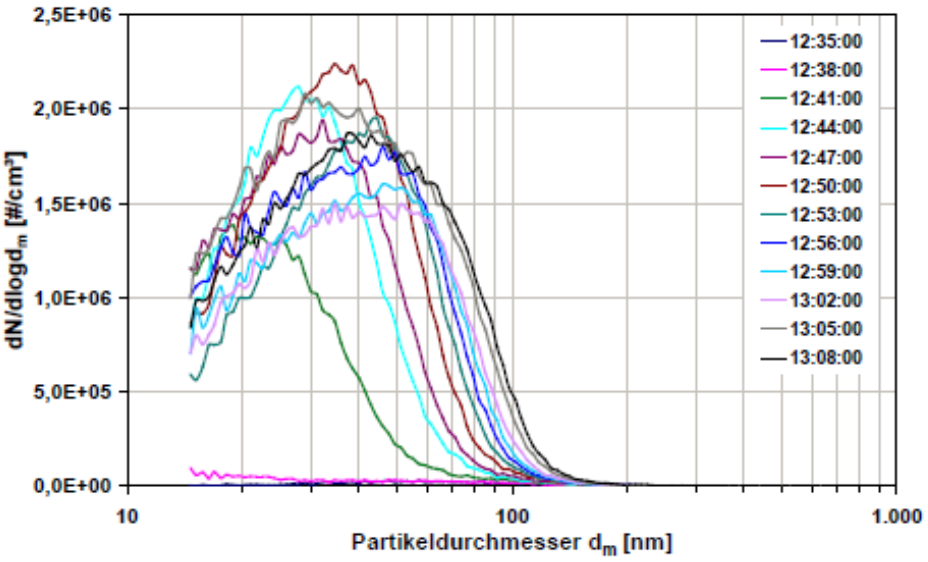
- ✓ Size specific mass concentatrations (PM2.5 and PM1), particle number concentration and size distribution (~6 nm – 20 µm) (APS, SMPS, FMPS)
- ✓ Lung deposited surface area concentration (LDSA) (NSAM)
- ✓ Intrinsic ROS formation (reactive oxygen species) (ESR)
- ✓ Particle bound organic compounds (AMS)
- ✓ Morphology (TEM)
- ✓ Gaseous organic compounds
- ✓ EC/OC (Analyser)
- ✓ Gases (CO, O_3)

Sources selected for exposure studies

Candle burning

Toasting bread

Frying sausages



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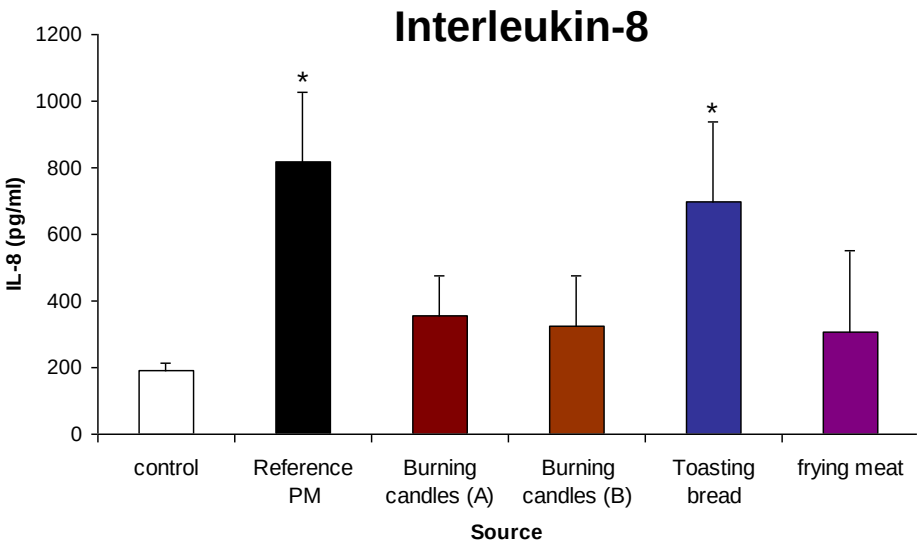
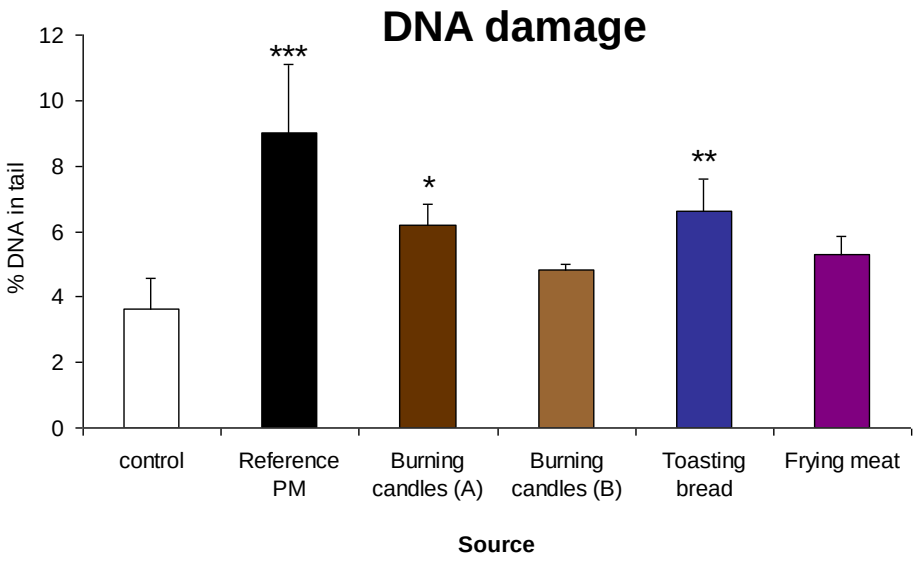
Effects of indoor particles in A549 cells

(50 µg/cm^2, $PM_{2.5}$)





Reference PM → *Wessels et al (2010) Environ Sci Technol*

Design volunteer study

- Randomized cross-over contolled exposure study
  (55 healthy volunteers)

- Temperature-controlled exposure chamber

- Two hours exposure, three sources, each at two exposure levels:

  - ✓ Candle burning (CB)
  - ✓ Toasting bread (TB)
  - ✓ Frying sausages (FS)
  - ✓ **Sham exposure: „Air refresher“**

- Exposure: same day and time of the week, at least 2 weeks apart

Study population (n=55)

Characteristic	Measure
Age, years (mean±SD)	33.0 (16.6)
Born in Germany, n (%)	35 (64.8)
Male, n (%)	28 (50.9)
Weight, kg (mean±SD)	72.6 (14.0)
Height, cm (mean±SD)	174.3 (9.2)
Economic activity, n (%)	
High School Graduation	42 (79.3)
Employed	25 (47.2)
Smoking status, n (%)	
Ex-smoker	3 (5.6)
Never-smoker	51 (94.4)
History of allergy, n (%)	
Allergy	17 (32.7)
Transport mode, n (%)	
Car	106 (40.3)
Public transportation	145 (55.1)
On foot	2 (0.8)

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Article

Respiratory Effects of Fine and Ultrafine Particles from Indoor Sources—A Randomized Sham-Controlled Exposure Study of Healthy Volunteers

Vanessa J. Soppa [1,*], Roel P. F. Schins [1], Frauke Hennig [1], Bryan Hellack [2], Ulrich Quass [2], Heinz Kaminski [2], Thomas A. J. Kuhlbusch [2,3], Barbara Hoffmann [1,4] and Gudrun Weinmayr [1]

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Arterial blood pressure responses to short-term exposure to fine and ultrafine particles from indoor sources – A randomized sham-controlled exposure study of healthy volunteers

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Effect parameters

- *Local* oxidative stress and inflammation → Markers of inflammation in nasal lavage fluid & exhaled nitric oxide (FeNO test)
- *Systemic* oxidative stress, inflammation →Inflammation markers in blood
- Respiratory system (spirometry)
- Cardiovascular system: Blood pressure, **pulse wave analysis (PWA)**, pulse wave velocity (PWV), Heart rate variability (HRV)
- Visuomanual coordination (Pegboard)

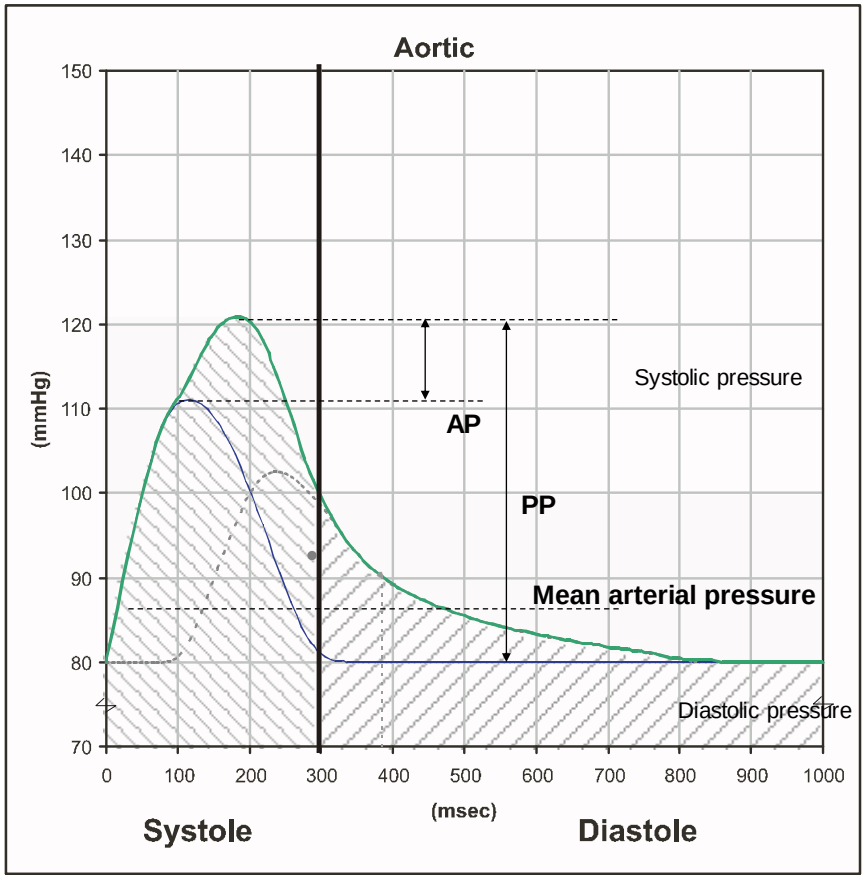
	Pre-exposure (baseline)	During exposure	Directly after exposure	2 h after exposure	4 h after exposure	24 h after exposure
Diary	x	x	x	x	x	x
Nasal lavage	x			x		x
FeNO-Test	x			x		x
Blood collection	x			x		x
PWA	**x**		**x**	**x**	**x**	**x**
PWV and HRV	x		x			x
Blood pressure	x	x	x	x	x	x
Lung function	x				x	x
PEG-Board-Test	x				x	x

Pulse wave analysis → Arterial stiffness (AS)

- Air pollution has been linked to AS (Mehta et al., 2014)
- Risk factor for cardiovascular disease, independent of other risk factors (Veerasamy et al., 2014)
- Stiffness of elastic arteries (e.g. aorta) is linked to increased (cardiovascular) mortality in:
  - Uncomplicated hypertension (Laurent et al., 2001)
  - Diabetes mellitus type 2 (Cruickshank et al., 2002)
  - End-stage renal disease (Shoji et al., 2001)
  - Older individuals (Steppan et al., 2011)
  - General population (Willum-Hansen et al., 2006).
- **Increased AS has been observed with exposure to diesel exhaust and wood smoke, which are both rich in UFP**
- **(Lundback et al., 2009; Unosson et al., 2013)**

Arterial stiffness (AS): Pulse wave analysis

•SphygmoCor® System (CPV; AtCor Medical, Sydney, Australia).



Augmentation Pressure (AP)

Augmentation Index
= AP/PP in %
⇒ Indicator for arterial stiffness

Mean arterial pressure
⇒ Systemic resistance

Exposure characteristics

	PMC [µg/m³]			PSC
	PM_1	**$PM_{2.5}$**	**PM_{10}**	[µm²/cm³]
Room air	3.2 ± 0.5	4.7 ± 1.0	6.2 ± 2.0	22.8 ± 2.1
Candles				
Level 1	47.9 ± 9.2	52.6 ± 12.0	55.9 ± 13.7	2,200.5 ± 137.8
Level 2	79.3 ± 11.9	80.9 ± 13.8	83.7 ± 16.7	3,839.6 ± 248.6
Toasting				
Level 1	37.7 ± 7.0	62.6 ± 27.7	125.6 ± 87.1	1,769.1 ± 318.0
Level 2	79.9 ± 16.1	81.6 ± 16.6	84.6 ± 18.6	3,779.4 ± 577.0
Frying				
Level 1	71.3 ± 28.2	84.4 ± 37.3	100.0 ± 51.9	1,325.0 ± 432.6
Level 2	207.8 ± 62.4	235.2 ± 81.4	296.9 ± 133.9	3,455.7 ± 660.0

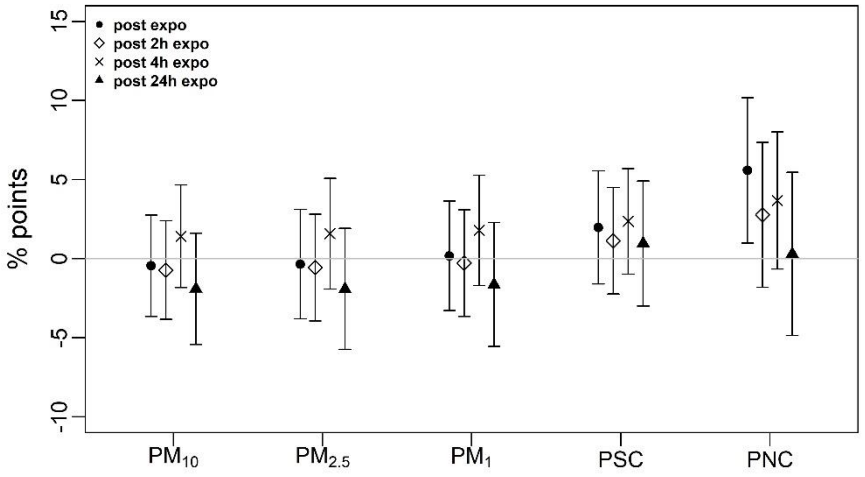
	PNC [#/cm³]			
	< 100 nm	**0,5-1 µm**	**0,5-2.5 µm**	**0,5-10 µm**
Room air	0.3 ± 0.1 (*10^4)	2.3 ± 0.4	3.3 ± 0.8	3.4 ± 0.8
Candles				
Level 1	190.8 ± 16.3(*10^4)	6.2 ± 3.8	9.7 ± 5.7	9.9 ± 5.7
Level 2	267.0 ± 20.6(*10^4)	1.8 ± 2.3	2.7 ± 3.3	2.8 ± 3.5
Toasing				
Level 1	90.4 ± 14.1(*10^4)	8.4 ± 3.8	19.0 ± 11.9	21.3 ± 13.9
Level 2	155.8 ± 17.6(*10^4)	3.1 ± 0.5	4.3 ± 0.8	4.4 ± 0.8
Frying				
Level 1	31.1 ± 9.4(*10^4)	17.1 ± 10.2	24.3 ± 14.6	24.9 ± 15.2
Level 2	60.7 ± 11.8(*10^4)	49.5 ± 30.1	65.6 ± 41.1	67.8 ± 42.8

Statistical analysis

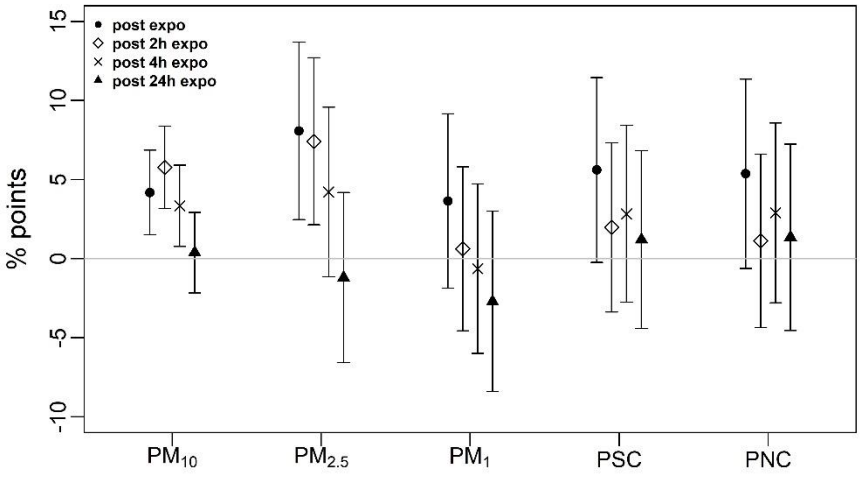
- Linear mixed regression analysis with random participant intercept
- Separate analysis for each exposure (CB, TB and FS)
- Independent variables: personal cumulative exposure to the particle metrics size-specific particle mass, particle number and surface area during the exposure sessions
- Dependent variable: intra-individual difference to t_0
- Interaction term: exposure*time point
- Covariates: age, height, weight, sex, temperature and humidity in the exposure chamber, travel time to the study location before exposure, mode of transportation and ambient $PM_{2.5}$ concentration (averaged over the last five days before study day)

Particle metrics and augmentation index

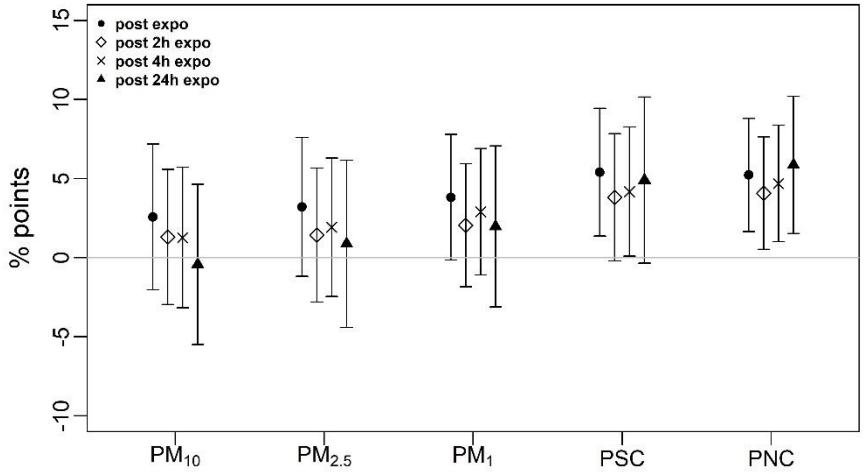
Candle burning



Toasting bread



Frying sausages



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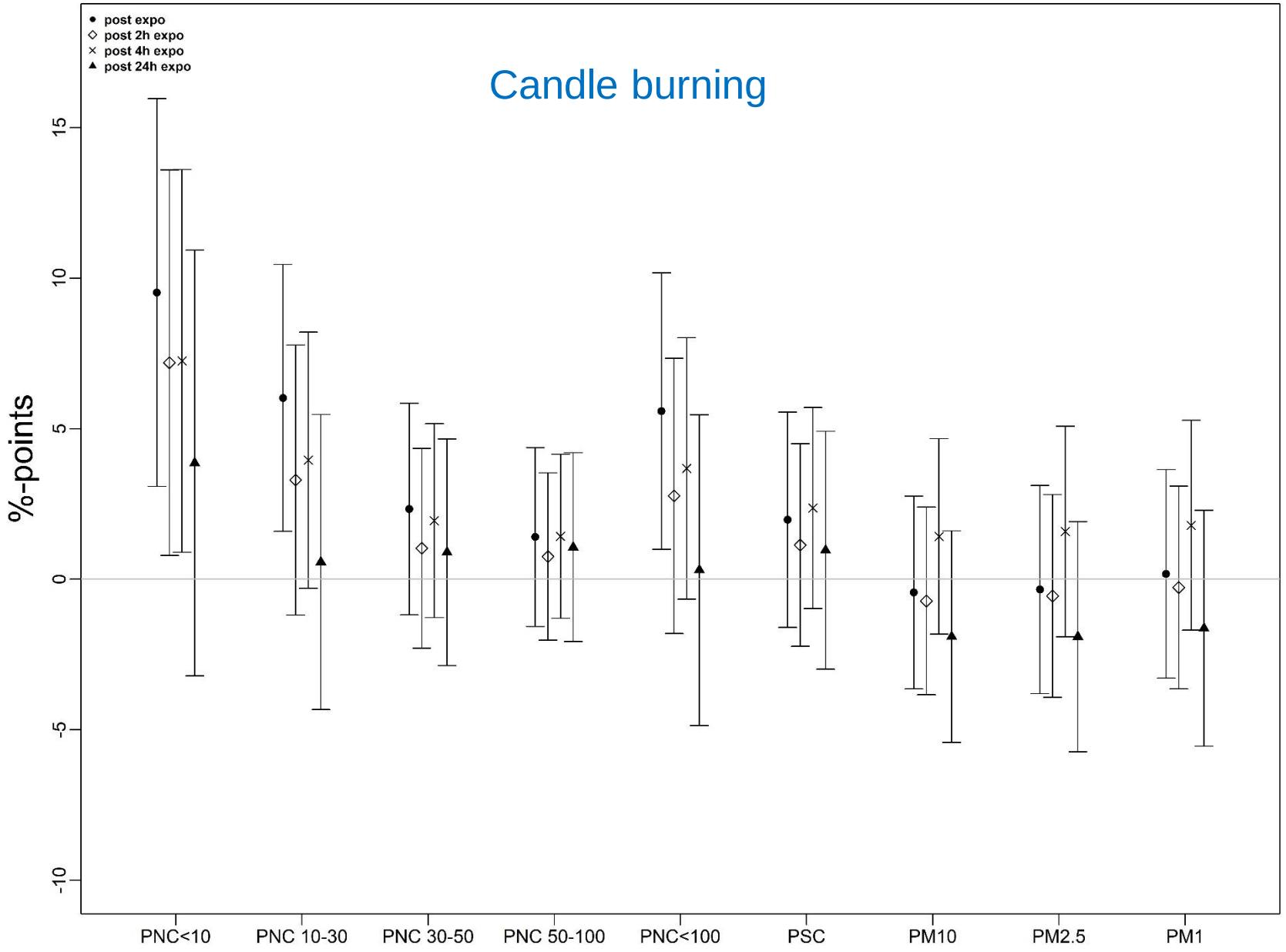
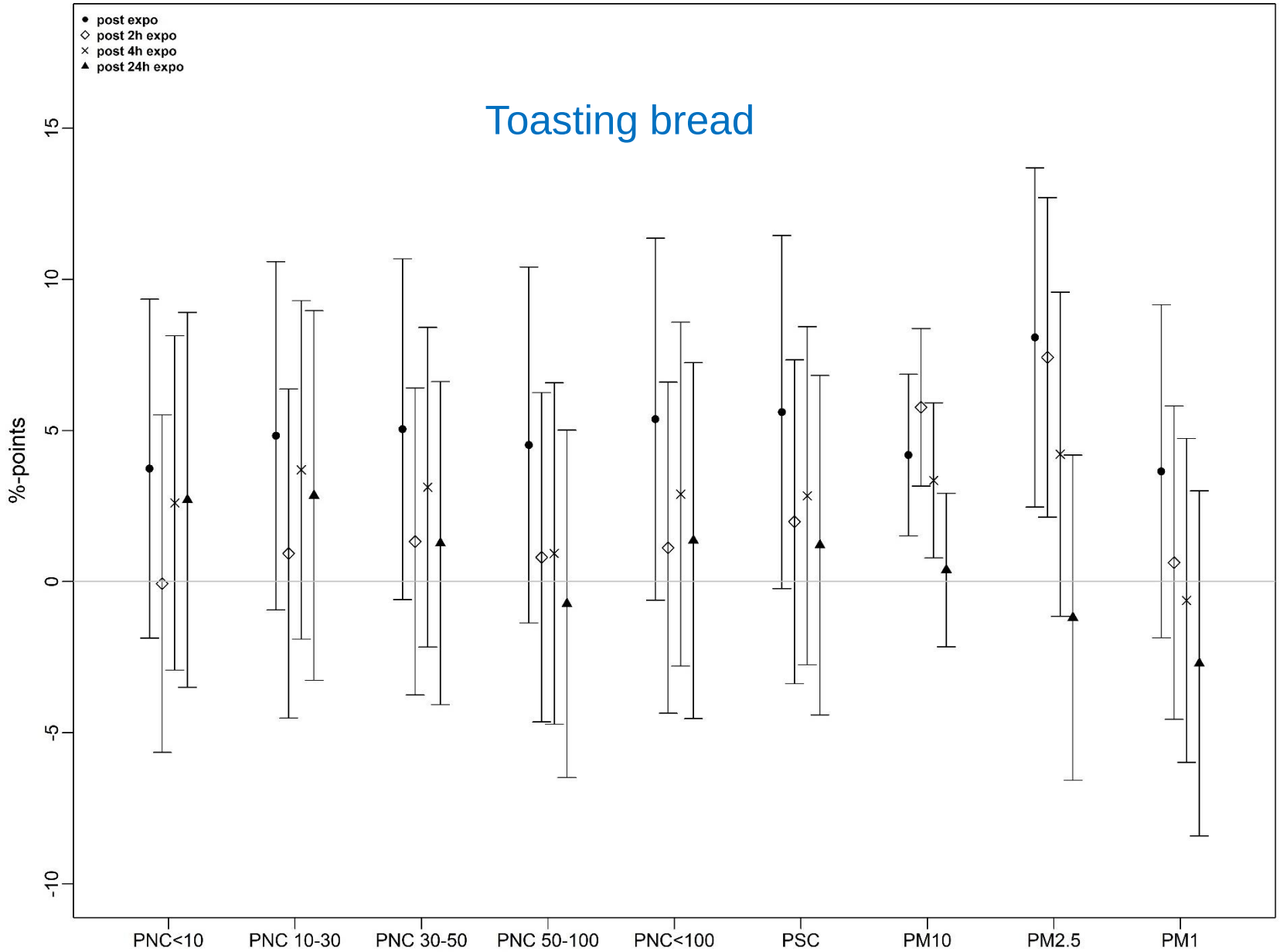
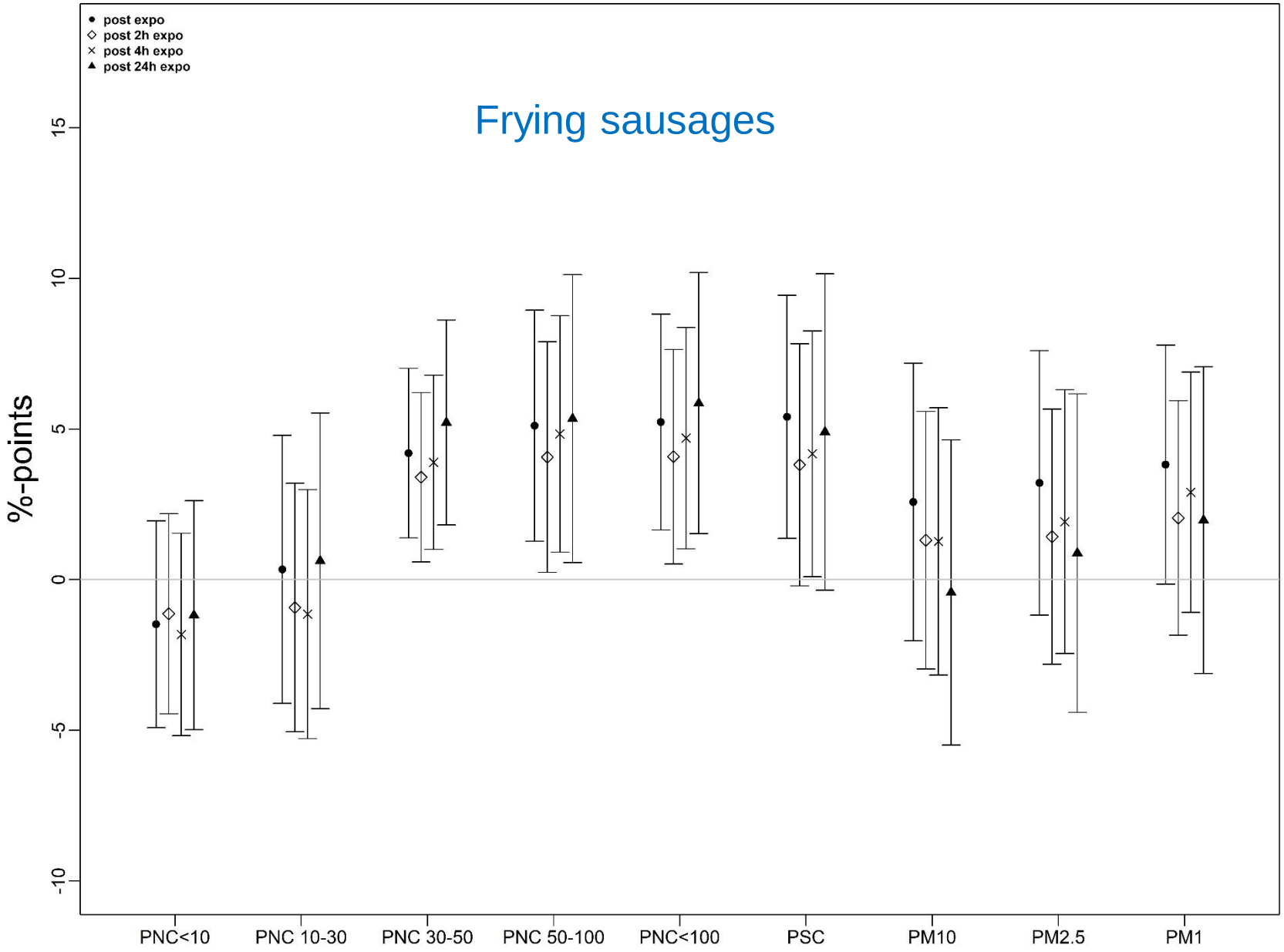
Candle burning




post expo
post 2h expo
post 4h expo
post 24h expo
Toasting bread
%-points
15
10
5
0
-5
-10
PNC<10
PNC 10-30
PNC 30-50
PNC 50-100
PNC<100
PSC
PM10
PM2.5
PM1

Frying sausages



Summary and conclusions

- Two-hour exposures to high concentrations of fine and ultrafine particles from common indoor sources in healthy adults are variably associated with:
  - ✓ decreases in lung function, increases in arterial blood pressure
  - ✓ increases in augmentation index and augmentation pressure (markers for arterial stiffness)

- Effects of the examined sources varied (also *in vitro*), likely due to the differences in physical and chemical composition of the emitted particles

- The effects can be considered of relevance since activation of similar biological mechanisms have been shown for short-term exposures to outdoor particles

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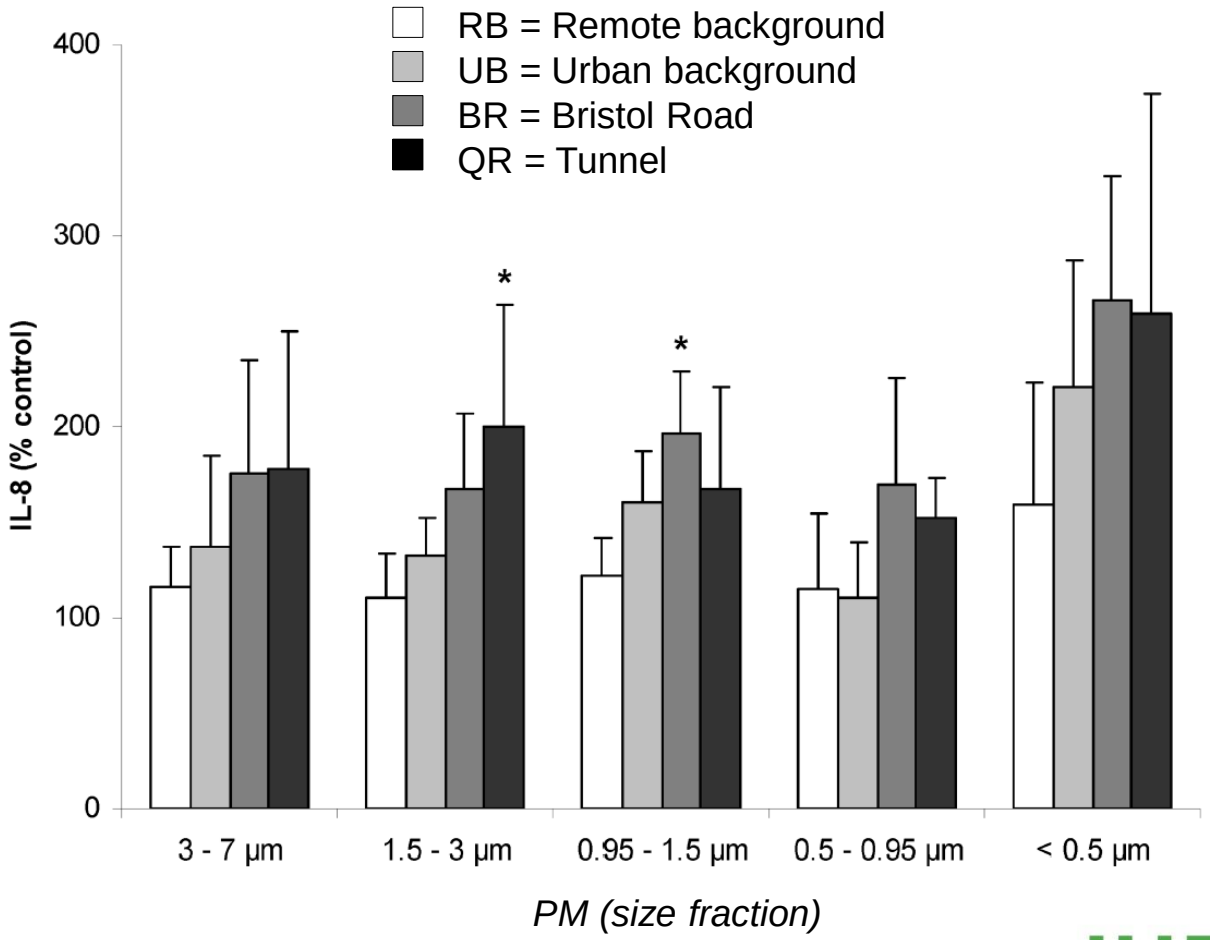
Oxidant generation and toxicity of size-fractionated PM in A549 human lung epithelial cells

Mace Head Research station, Connemara, Ireland (west coast)

Queensway underpass (A38), Birmingham, UK



Wessels et al (2010) Environ Sci Technol

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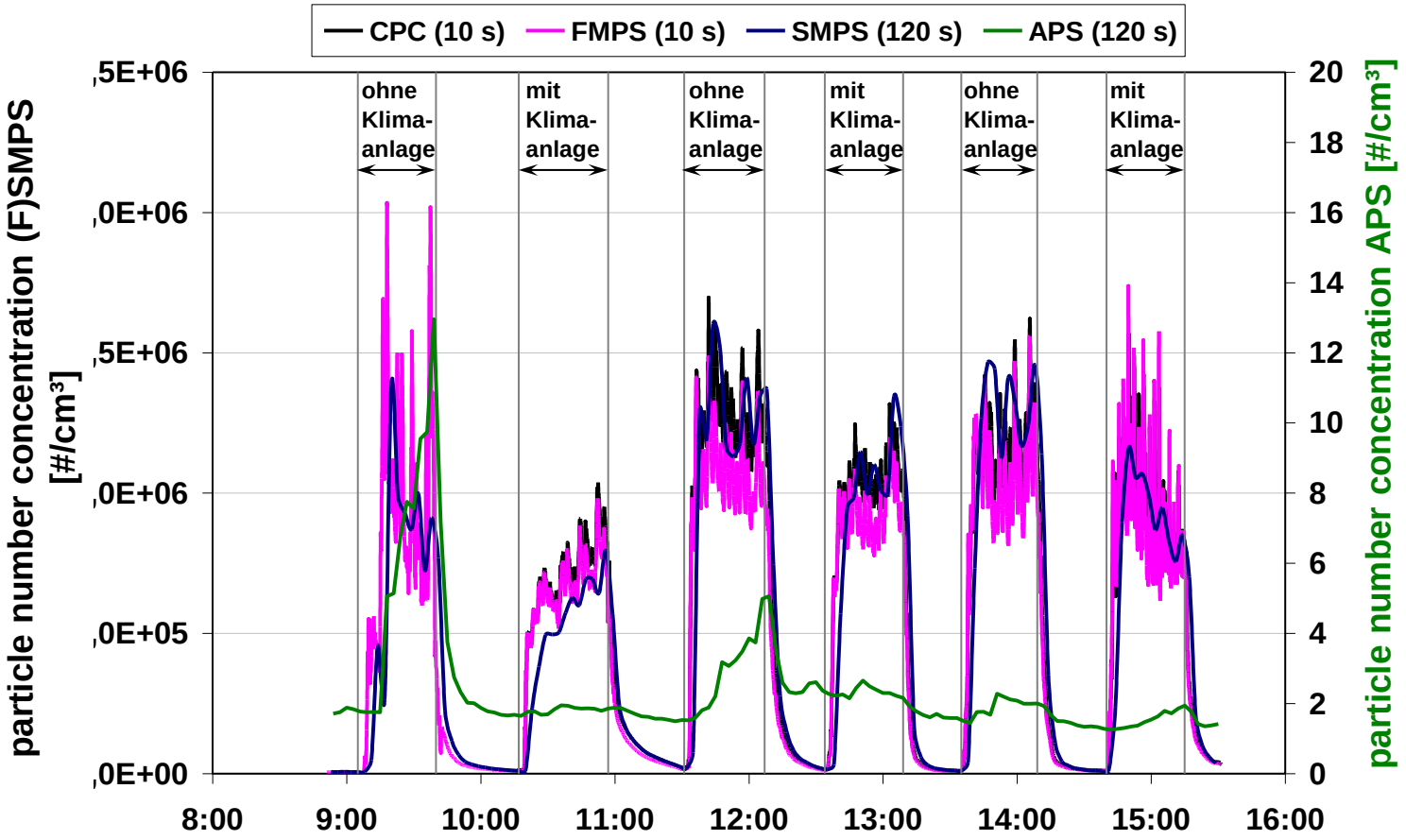
- Size-specific number concentration of particles (Fast Mobility Particle Sizer (FMPS, Model 3091, TSI), (5.6 nm to 560 nm) and Aerodynamic Particle Sizer (APS, Model 3321, TSI) (0.6 µm to 20 µm)
- Alveolar deposited surface area particle concentration by Nanoparticle Surface Area Monitor (NSAM, Model 3550, TSI).
- Size-specific mass concentrations of PM_1, $PM_{2.5}$ and PM_{10} calculated from particle size and number concentrations assuming spherical particles and a particle density of 1 g/cm^3.
- High-Resolution Time-of-Flight Aerosol Mass Spectrometry enabled a continuous (1/s) acquisition of complete mass spectra of individual particles with aerodynamic diameter of 60 - 600 nm, and enabled the resolution of distinct chemical species based on mass defect.
- For the ultrafine particles a Nanometer Aerosol Sampler (NAS) was used to create samples of the aerosols charging them onto a substrate. This substrate was removed and examined using a Total Reflection X-ray Fluorescence (TXRF) to characterize the elemental composition of the ultrafine fraction.
- Organic carbon and elemental carbon (OC-EC) aerosol analysis was conducted with the Sunset OC-EC Analyzer from samples sampled on quartz fiber filters.

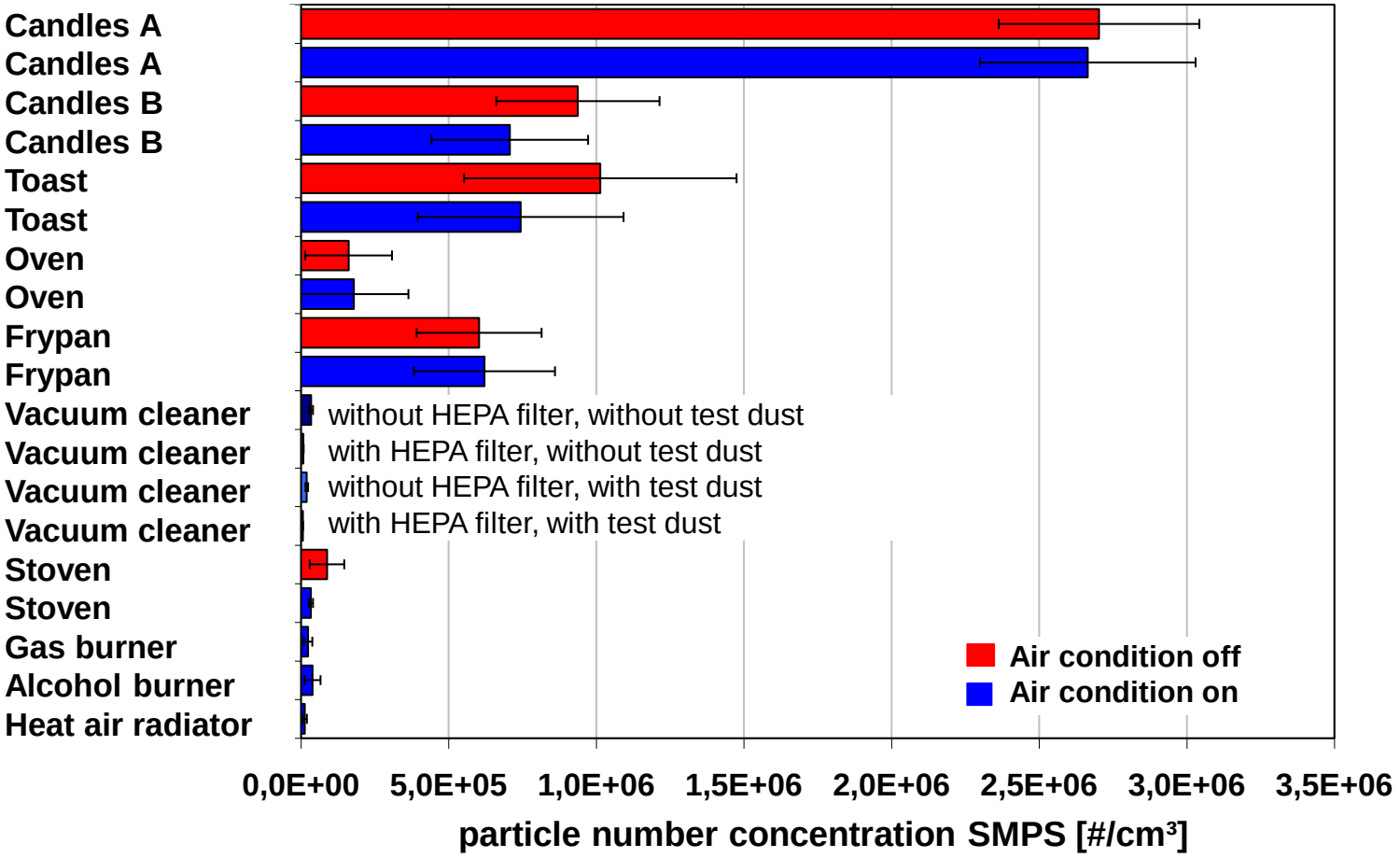
EPIA - Characterisation

Example: Toasting (mean particle number concentration six runs)



Characterisation

Particle number concentrations (30 min.)



Characterisation

PM mass concentrations (calculated from SMPS data)

★= PM1 mass by filter weighting, n = 6