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Particle mass monitoring by Quartz Crystal Microbalance using electrostatic deposition enhancement

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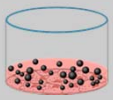
Background and goal

To investigate biological effects of nanoparticles, which are inhaled by humans, in vitro tests under submerged conditions are often used as the method of choice. However, this technique does not represent the inhalation process in the human lung. Therefore, the Karlsruhe Institute of Technology (KIT) and VITROCELL Systems developed a fully automated Exposure Station to simulate the processes in the lung and investigate the biological effects of nanomaterials at the **Air-Liquid Interface** measuring the dose-response relationship.

The goal of this study is to provide a QCM with electrostatic deposition enhancement as a highly sensitive on-line tool for determination of the surface dose.

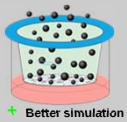
Submerged exposure

Collected particles are suspended in medium and applied on the cell cultures



- \+ Simple
- \- Collection of particles necessary
- \- Changes of particle properties by suspending them in medium
- \- No defined dose because of the colloidal behavior

Air liquid interface (ALI) exposure

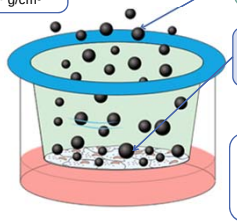


Airborne particles are contacted as aerosol to the cell culture surface

- \+ Better simulation of inhalation
- \+ Unchanged aerosol
- \+ Precise dose determination
- \- Complex system

Dosimetry

Fluid: gas (air)
Viscosity ~ 1 µPa*s
Density ~ 10^{-3} g/cm³



Airborne particles:
Number concentration c_N [1/cm³]
Mass concentration c_M [µg/cm³]

Particles on cell surface
Number concentration c_N [1/cm²]
Mass concentration c_M [µg/cm²]

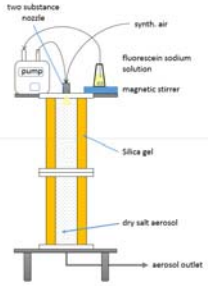
Deposition efficiency

$$f = \frac{deposited\ particle\ mass/number}{exposed\ particle\ mass/number}\ [\%]$$

- Fluorescein sodium dosimetry (FNA)
  - Spectroscopic measurement of deposited mass
  - c_M [µg/cm²]
- Quartz crystal microbalance
  - Online measurement of mass dose per area
  - c_M [µg/cm²]
  - f(t)

Fluorescein sodium dosimetry (FNA)

- Fluorescein sodium in water c_m = 1 g/l
- Continuous stirring
- Flow at two phase nozzle $\dot{V}_{liquid} = 20\ ^{ml}/_{h}$
- Drying zone: silica gel, $l_{drying\ zone}$ = 1 m



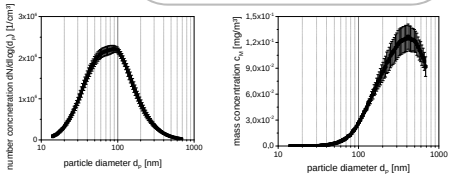
Standard aerosol generation according the VDI guideline 3491

$$f = \frac{deposited\ mass\ determined\ by\ fluorescence\ spectroscopy}{exposed\ mass\ calculated\ from\ the\ size\ distribution}$$

$$f = \frac{c_m\ /_t}{\sum_i (N_i \cdot \frac{d^3 \cdot \pi}{6} \cdot \rho_P) \cdot \dot{V}} \cdot \frac{\mu g\ /_h}{\frac{g}{cm^3} \cdot \frac{cm^3}{h}}$$

Increase factor by electrostatic deposition enhancement:

$$m = \frac{electrostatically\ deposited\ mass\ dose}{diffusional\ deposited\ mass\ dose}$$



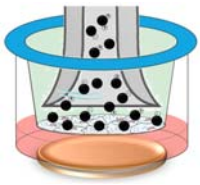
Number size distribution (left) and mass size distribution (right) of fluorescein sodium aerosol measured with a SMPS (DMA 3071, CPC 3775, TSI Inc., St Paul MN, USA) inside the drying reactor.

Air-Liquid-Interface (ALI) Exposure in the VITROCELL® Automated Exposure Station

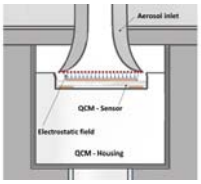
Specification	
Cell exposure	Up to 24 cell cultures: 4 VITROCELL® 6/6 CF stainless steel modules of 6 well format
Aerosol	• Direct aerosol sampling via size selective inlet: $PM_{2.5}$ inlet with 1 m³/h • Aerosol conditioning to 37°C and 85 % relative humidity.
Negative control	Humidified synthetic air
Dose enhancement	**Electrostatic deposition by applying a potential of up to 1500 Volts is optional for each cell culture separately**
Dose monitoring	• **Online surface dose monitoring by a Quartz Crystal Microbalance (QCM) in µg/cm².** • Integrated sampling probes in the reactor for aerosol measurements a for example SMPS, FTIR, filter …
Automatization / Quality insurance	Integrated standard routines for leak tests, exposure experiments and more with comprehensive data acquisition
Dimensions	2187 x 1124 x 623 mm (H x B x T)

Online dose monitoring by QCM with electrostatic deposition enhancement

(Mülhopt et al., 2016b)

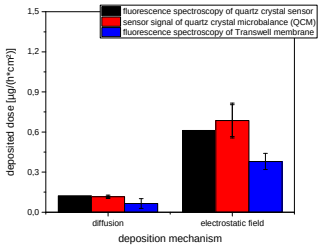


- An electrical field is formed between aerosol inlet and sensor surface.
- Sensor surfaces:
  - Cell culture layer (left)
  - QCM crystal (right)
- Charged particles flow above the sensor surface.

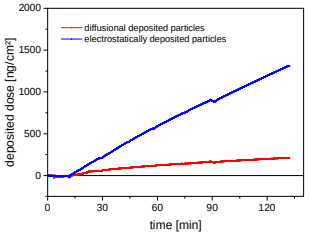


- Charged particles deposit on the sensor surface.
- Electrical field shows no biological effects in AlamarBlue and LDH assays (Mülhopt et al., 2016a)
- Dose per time is increased on the cells.
- The QCM monitors the dose in ng/cm² according to Sauerbrey (1959).

Results



Mass doses on Transwell membrane inserts and on quartz crystal sensor determined by fluorescence spectroscopy and by QCM measurement.



Mass loading signal on quartz crystal sensor of a QCM online measurement for diffusional and electrostatically deposited particles.

- The exposed particle dose per exposure time and area was determined from SMPS data to 10 µg/h.
- The diffusional deposition efficiency of fluorescein sodium are determined to f = 1.5 ± 0.1 %.
- The increase factor by applying an electrical field could be determined to m = 6
- The comparison of fluorescence spectroscopy data with QCM signal shows good agreements for both diffusional and electrostatic deposition.

Conclusions and Outlook

- QCM using electrostatic deposition successfully tested.
- The comparison to spectroscopic methods show a good agreement.
- The QCM technology provides a useful tool to determine doses online of diffusional as well as in electrostatic precipitated aerosols.
- The charge distribution will be measured to verify the increase factor m.
- The deposition efficiencies will be compared to data from numerical simulation.

References

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