Dose Determination of Airborne Particles for in vitro Exposure at the Air / Liquid Interface

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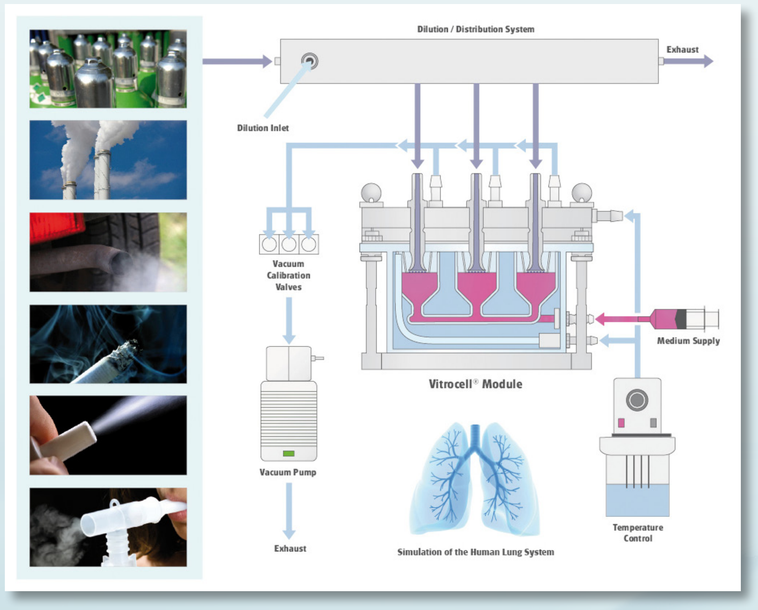
Background

The assessment of toxicological effects of airborne nanoparticles to the human organism is of major importance in disease research. The presence of nano and ultrafine particles can be found both in indoor and outdoor atmospheres which include workplaces and living areas.

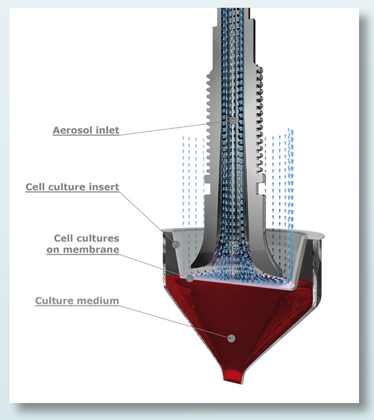
The degree of contribution to diseases of such particles is still a widely unknown factor as testing methods are only in the early phase of development. Over the last years, the use of in vitro methods received an increasing importance as the related equipment for aerosol generation and exposure to airborne particles were developed more and more to proven levels. The exposure of lung cells to particles at the air/liquid interface is the prime choice over existing submerse conditions, because interaction of particles with cell culture media is avoided.

Furthermore, the exact dose determination under submerse conditions, thus which amount has reached the cells, is extremely difficult. With the use of the VITROCELL® Crystal Quartz Microbalance and its direct integration into the VITROCELL® Exposure Modules, the dose is monitored online as ng/cm² and is therefore a powerful research tool.

A typical system flow chart

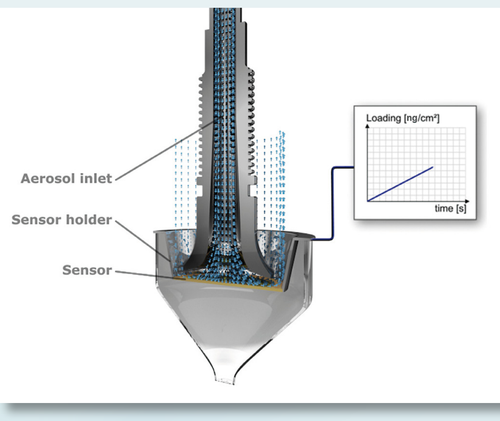


Air / Liquid Interface Exposure



Primary cultures and cell lines from the respiratory tract are exposed in modules which are specially designed for direct contact between the cells and the test atmosphere (air/liquid interface).

Dose Control

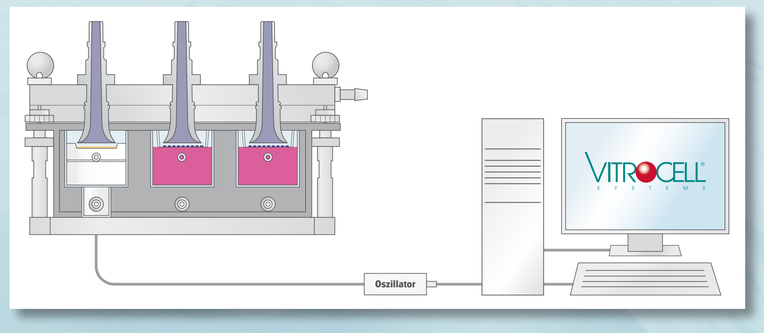


The microbalance sensor can be fitted in the VITROCELL® 6 CF Stainless Steel, VITROCELL® 12 CF Stainless Steel and VITROCELL® 12 HT-CF modules. It is capable of measuring the deposition in the module at a resolution of 10 nanogram/cm² and second.

Methods

The VITROCELL® Exposure System consists of an aerosol generator selected for the optimal aerosolization of substances. It includes the possibility to vary doses by dilution. Then an aerosol sample stream is guided to the exposure module which consists of an exposure top with specially designed inlets and a heated base module to receive the cell culture media and cells which are cultivated on cell culture inserts. According to the capacity needs there is a choice of using inserts in the 6, 12 or 24 well format. Exposure can take place from 3 up to 24 inserts at stable and individually controlled conditions.

The novel microbalance system can be integrated in the module for use before the experiment for validation purposes of the aerosol delivery or during the experiment as process control.
The direct reading gives an exact online picture of the exposure situation and delivery of the test substance.

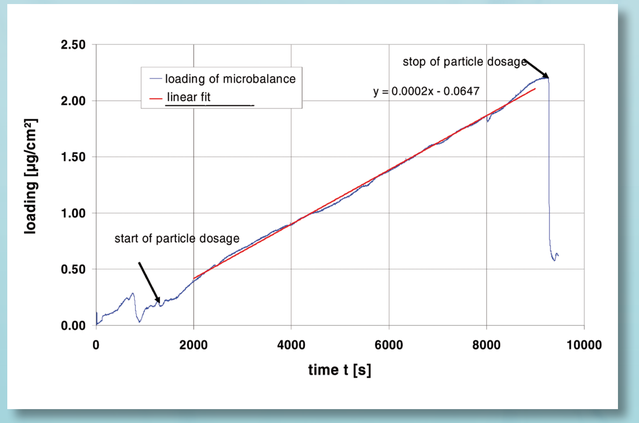


Module Operation with Cell Cultures and Online Control

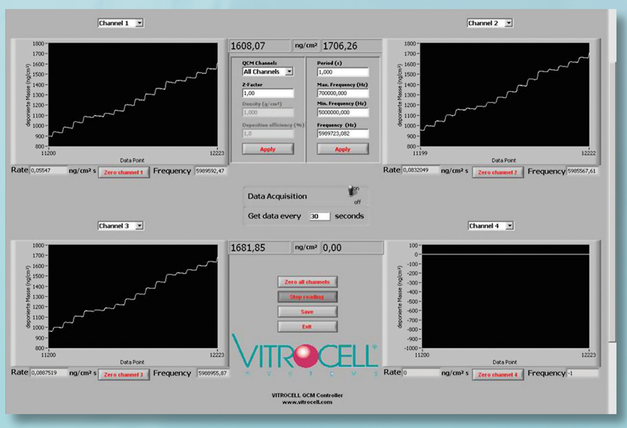
Results

Recent publications (Mülhopt S. et al. 2009) demonstrated the usability as well as the reliability of the Crystal Quartz Microbalance.

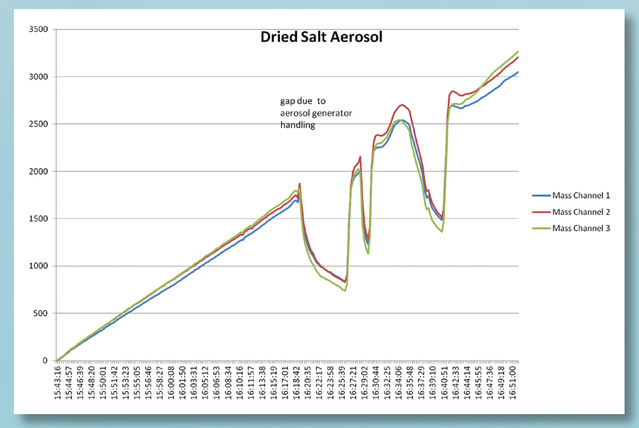
Other expamples using tobacco smoke and salt solution show the potential of the system for dose determination and online monitoring.



Loading of the quartz crystal microbalance in ng/(cm²*s) over time
Data source: Karlsruhe Institute of Technology



Exposure of tobacco smoke with 3 sensors in 1 module
Data source: VITROCELL Systems GmbH



Exposure of dried salt aerosol with 3 sensors in 1 module
Data source: VITROCELL Systems GmbH / TNO

References

S. Mülhopt, A. Comouth, A. Grotz, T. Krebs, H.-R. Paur, The QCM - Online Dose Measurement with high relative Humidity, European Aerosol Conference 2009, Karlsruhe, Abstract T103A01

Sonja Mülhopt, S. Diabaté, T. Krebs, C. Weiss and H.-R. Paur, (2009) Journal of Physics: Conference Series 170 (2009) 012008; doi:10.1088/1742-6596/170/1/012008

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