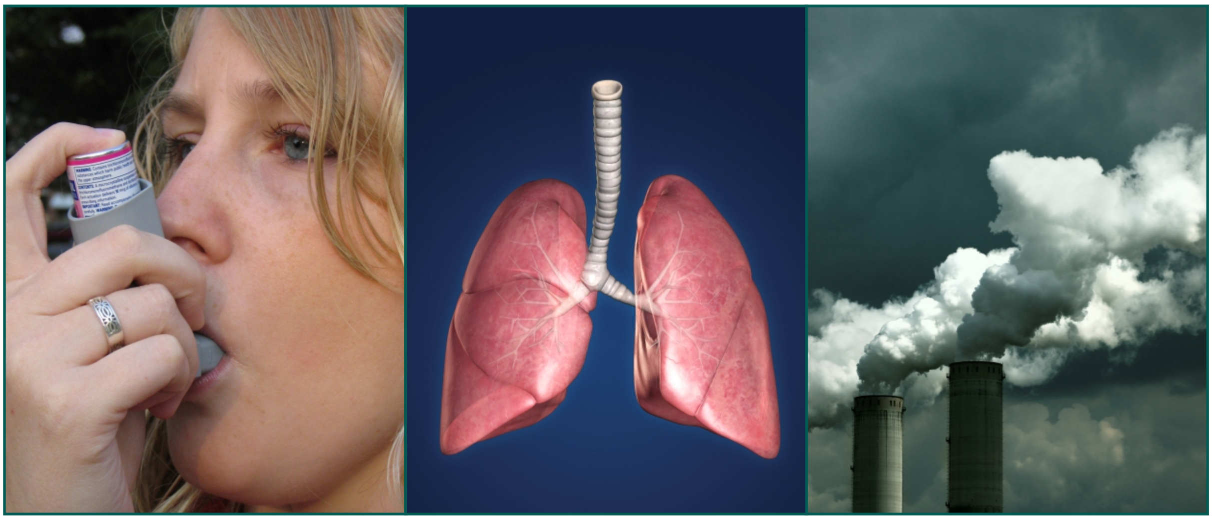
Aerosol Optical Tweezers in Drug Delivery to the Lung and Lung Toxicology Research

Professor Don Clark



Drug Delivery to the Lung

Drug delivery to the lung has for many years been an important field of development with respect to treating asthma and chronic obstructive pulmonary disease (COPD). In addition recent research has focussed on other diseases where delivery of drugs to the lung is advantageous either for speed of response (delivery of insulin for diabetes) or to target other lung diseases (lung cancers and cystic fibrosis). The delivery of bronchodilators in asthma and COPD can be achieved using relatively simple technology as the target area is broad and the consequences of variations in the dose is generally quite benign. For other clinical objectives much tighter control of dose (insulin) or targeting of a particular area of the lung (cancer) are vital to successful treatment. This requires close control of the characteristics of the aerosol from the point of generation to the target deposition area.

Deposition of aerosol particles from the buccal cavity to the alveoli is primarily a function of the particle size and velocity. Although particle size can be controlled at the generator, as soon as it is inhaled it is likely to change due to hygroscopic growth in the 100% humidity of the lung. The extent and rate of that change will be a function of the hygroscopicity of the material. Investigation techniques typically rely on a series of individual measurements under fixed conditions that are brought together to infer the behaviour of the dynamic processes. Clearly such techniques lack precision and cannot provide any time resolved information.

Lung Toxicology

As with drug delivery to the lung, the effects of the inhalation of toxic particulate material may depend on where in the lung it is deposited. The dose will also be dependent on what proportion is deposited rather than exhaled. The lung may be damaged either by material that is deliberately inhaled (tobacco smoke) or by exposure to industrial or environmental pollutants. To accurately assess the effects of inhalation it is important to fully understand both the physical and chemical changes that may occur during the passage through the respiratory tract. Again single condition snap shot measurements, often of residual particle size, cannot provide information relating to the evolution of the aerosol with time in a changing environment.

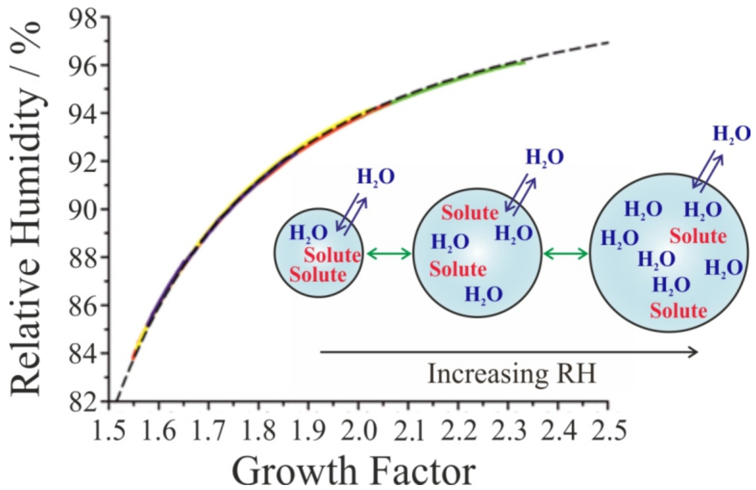
Aerosol Optical Tweezers (Biral AOT 100)

Aerosol Optical Tweezers (AOT) is a technique that, for the first time, offers the means to observe the evolution of physical and chemical changes taking place in droplets in airborne suspension. The AOT can capture and hold microscopic droplets in the focus of a laser beam for periods ranging from seconds to days, if necessary. During this time the characteristics and composition of the particle can be monitored microscopically and by Raman spectroscopy while the humidity or composition of the surrounding gas is changed in ways that mimic the conditions that the aerosol would encounter in practice.

Cavity enhanced Ramen spectroscopy of trapped droplets provides a technique for the measurement and monitoring of changes in particle size. This delivers exceptional sensitivity (<1nm) and time resolution (<1s) that is not achievable by any other technique. The same technique also enables the refractive index of particles to be measured and monitored with an accuracy of 0.05%. This latter measurement, together with observation of changes to the Raman spectra, enables changes to the chemistry of the particle to be monitored.

Partial or complete deliquescence of the inhaled particle may occur in the humid conditions of the lung and the resultant physical parameters of the droplet, such as viscosity and surface tension, may affect its fate following deposition. These parameters can be measured by trapping droplets in two different laser foci and then bringing them into contact in a controlled manner. Observing the dynamics of the resultant fusion of the two droplets enables both parameters to be accurately measured.

The Aerosol Optical Tweezers offers, for the first time, a technique that enables the direct and detailed observation of the complex, discrete phase processes that take place in the environment of the lung. It offers a research tool that can deliver a step-change in capability to those involved in both drug delivery and lung toxicology research.



About the Author

Don joined Biral in 2005 following his retirement from Dstl, Porton Down where he had been the leader of aerosol science and biological detection research groups. His initial work for Biral involved the development of instruments for biodetection, a field in which Biral was a world leader. Don is now active in the development of the AOT 100, the world's first aerosol optical tweezers instrument and is looking at applications for the AOT 100, as well as researching new opportunities in aerosol characterisation and climate research.