Particle deposition model for the Balb/c mouse respiratory tract

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The mouse lung has become increasingly important as a surrogate of the human lung to investigate the health effects of inhaled toxicological and pharmaceutical aerosols. The main structural difference between the mouse and the human lung is the branching structure of the airway system, i.e. the distinctly asymmetric or monopodial branching in the mouse lung as compared to the relatively symmetric branching of the human lung.

The asymmetric tracheobronchial airway geometry of the Balb/c mouse is based on a rigorous statistical analysis of several lung casts (Madl *et al*, 2010). In the absence of pertinent morphometric data for the acinar airways of the mouse lung, a scaled-down version of the asymmetric model of the rat acinar region (Koblinger *et al*, 1995) was used, assuming structural, though not dimensional, similarity. For the calculation of inhaled particle deposition in the mouse lung, bronchial and acinar airway diameters and lengths were scaled down to a functional residual capacity (FRC) of 0.5 cm^3. Due to the monopodial airway structure, the number of bronchial airway generations ranges from 5 to 34, with a mean of 13.8, and that of acinar airway generations from 2 to 22, with a mean of 6.1.

For the calculation of inhalability and nasal deposition, the semi-empirical equations proposed by Asgharian *et al*. (2014) were applied. Deposition in bronchial and acinar airways was computed with the stochastic IDEAL deposition model specifically developed for the rat lung (Koblinger and Hofmann, 1995). Default breathing parameters were: tidal volume V_T = 0.2 cm^3, and breathing frequency f = 300 min^{-1}.

Regional, i.e. extrathoracic (ET), tracheo-bronchial (TB) and acinar (A), deposition fractions of inhaled unit density particles with diameters ranging from 10 nm to 10 µm are plotted in Figure 1. While total deposition of submicron particles exhibits the well-known U-shape, the effect of inhalability, which is also shown in this figure, significantly reduces deposition of micrometer-sized particles. Because of nasal pre-filtration, particles with diameters greater than about 3 µm can hardly reach the deep lung. Thus the use of the mouse model for health effects studies with these larger particles is only possible with endotracheal aerosol delivery.

The distribution of deposition fractions among lung airway generations of 0.01, 0.1 and 1 µm diameter particles, i.e. particles which can reach the lungs, are shown in Figure 2. Deposition fractions exhibit significant peaks in central bronchial and bronchiolar airway generations, with almost no deposition in the most distant acinar airways. This apparent decrease of deposition fractions in the peripheral airways is caused by the decreasing fraction of airways in the distal airway generations of the asymmetric lung model, and not by decreasing deposition efficiencies.

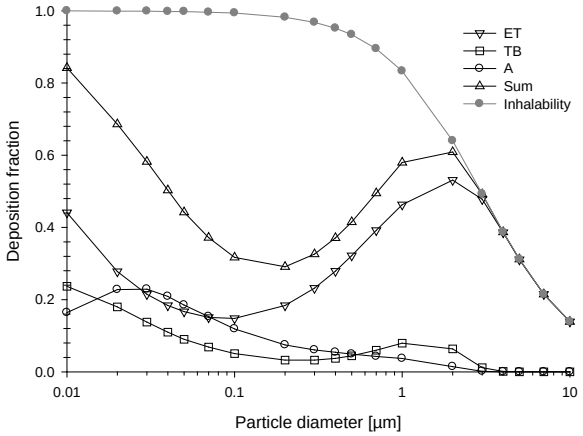

Figure 1. Regional deposition fractions of unit density particles in the Balb/c mouse respiratory tract.

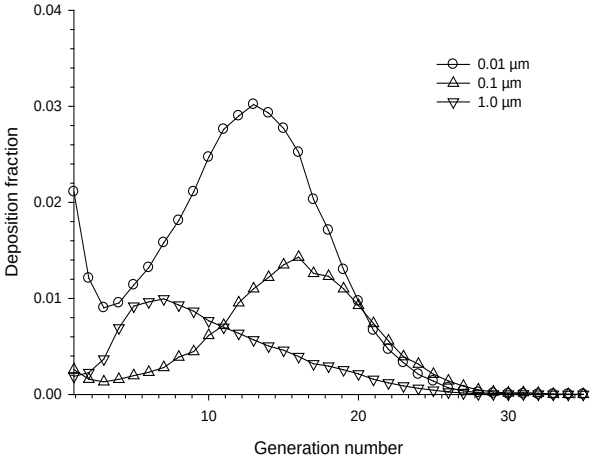

Figure 2. Deposition fractions of 0.01, 0.1 and 1 µm unit density particles as a function of airway generation number.

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