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DEVELOPMENTS AND APPLICATIONS OF MULTI-SCALE INHALED AEROSOL DOSIMETRY MODELS IN COMPLETE HUMAN RESPIRATORY SYSTEMS

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MINI-SYMPOSIUM PROPOSAL

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Exposure to micro-/nano- airborne particulate matters has gained interests from researchers because of the toxic health risks and therapeutic benefits to humans induced by inhalation. For example, respiratory infectious disease transmission begins from the deposition of pathogens carried by airborne particulate matter into the respiratory tract. Since infection initiation is usually region specific, local dosages (e.g., lung deposited, tissue, and delivered doses) in pulmonary routes and systemic regions are essential for precise risk assessments. On the other hand, pulmonary targeted drug delivery becomes more favorable both for lung and systemic disease treatments, due to the strong capability of the lung to absorb pharmaceuticals. The local dosage information is also essential for the evaluation of targeted delivery efficacy. However, because of ethical reasons and lack of reliable measurements, experiments or clinical tests are not able to provide such high-resolution data on humans. Therefore, developing and applying the accurate and realistic computer simulation model will significantly contribute to answer the above public health questions, scientifically.

Accordingly, computational fluid-particle dynamics (CFPD) models were developed and applied for simulating the transport and deposition of different types of particulate matters in human upper airways, based on Euler-Lagrange and Euler-Euler methods. Specifically, advanced CFPD models were developed with more underlying physics and less simplifications for unconventional particulate matters, such as non-spherical fibers, hygroscopic droplets, etc. [2-5] However, only the local deposition information provided by CFPD models is not sufficient for risk assessments or effective pulmonary drug delivery designs. Indeed, it is necessary to link different numerical models to extend exposure and deposition modeling to health endpoints, i.e., tissue and delivered dose at targeted sites in lungs and systemic regions. Meanwhile, breakthroughs also need to be achieved for CFPD models to obtain local deposition information under realistic breathing cycles. These breakthroughs include: (1) running simulations in human respiratory systems with entire conducting and respiratory zones, and (2) encompassing more underlying physics such as moving airway boundary, mucus clearance, particle-particle interactions in small airways and alveoli, etc.

We would like to use this occasion for discussing the whole range of progresses and challenges related to the development of the framework of this multi-scale numerical model with applications on lung aerosol dynamics. The ultimate goal is to establish a roadmap to link different numerical models and build the framework of the new multi-scale numerical model, which will extend exposure and lung

deposition predictions to health endpoints, e.g., tissue and delivered doses by the absorption and translocation into alveolar regions and systemic regions. It will enable simulations of extremely complex airflow-particle-structure dynamics of the entire human respiratory system at detailed levels never undertaken before. There are following **topical areas** we suggest for the discussion at the mini-symposium:

- Whole-lung geometry construction with entire conducting zone,
- Cutting edge hybrid models (e.g., CFPD-PBPK models) with applications towards circulation predictions of toxic/therapeutic aerosols in human body,
- Advanced numerical modelling for particle transport and deposition in alveoli.

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