Multilinear Calibration of Lattice Boltzmann pMDI Spray Simulation

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INTRODUCTION

Treatment efficacy of medication delivered by pressurized metered dose inhalers (pMDI) depends on particle sizes produced by the propellant release, and subsequent entrainment in airway flows, a complicated physico-chemical process involving droplet formation, evaporation, and interaction with inspiration airflow.
This study introduces a hybrid approach for computational modeling of pMDI spray based upon:

1. A computationally efficient graphics processing unit (GPU) implementation of a lattice Boltzmann method (LBM) for multiphase transport processes;
2. A multilinear multifactor statistical analysis of experimental device performance in terms of fundamental physical quantities characterizing the formulation.

The approach can be interpreted as a statistical calibration of parameters within an LBM simulation, incorporating fundamental physical principles through the model formulation, but accounting for missing information by processing of experimental results. Initial testing of approach correctness has been carried out using data from a single spray measurement, with full validation awaiting completion of an on going experimental program.

METHODS – Lattice Boltzmann Method

The Boltzmann equation for time evolution of the PDF $f^{(s)}(t,\mathbf{x},\mathbf{v})$ with $f^{(s)}(t,\mathbf{x},\mathbf{v})\mathbf{dxdv}$ signifying the probability of finding a molecule of some chemical species s at time t in phase-space volume $\mathbf{dxdv}$ is given by:

$$\frac{\partial f^{(s)}}{\partial t}+\mathbf{v}\cdot\nabla_{\mathbf{x}}f^{(s)}+\mathbf{g}\cdot\nabla_{\mathbf{v}}f^{(s)}=\Omega^{(s)}(f,f)$$

and is discretized on a regular three-dimensional (3D) spatial lattice [9], with velocities constrained to belong to a finite set oriented along lattice directions (D3Q19).
A single-species multirelaxation time model is used to approximate the collision integral:

$$\Omega_{\alpha}^{(s)}(f,f)\equiv\tilde{\Omega}_{\alpha}^{(s)}(f^{(s)},f^{(s)})=-\sum_{\beta}\Lambda_{\alpha\beta}^{(s)}(f^{(s)}{}_{\beta}-f_{\beta}^{(s,eq)})$$

Time advancement is carried out through the "stream and collide" algorithm:

$$f_{\alpha}^{(s)}(t+\delta_t,\mathbf{x}+\mathbf{c}_{\alpha}\delta_t)-f_{\alpha}^{(s)}(t,\mathbf{x})=\tilde{\Omega}_{\alpha}^{(s)}(t,\mathbf{x})+\frac{1}{2}\left[S^{(s)}{}_{\alpha}(t,\mathbf{x})+S^{(s)}{}_{\alpha}(t+\delta_t,\mathbf{x}+\mathbf{c}_{\alpha}\delta_t)\right]$$

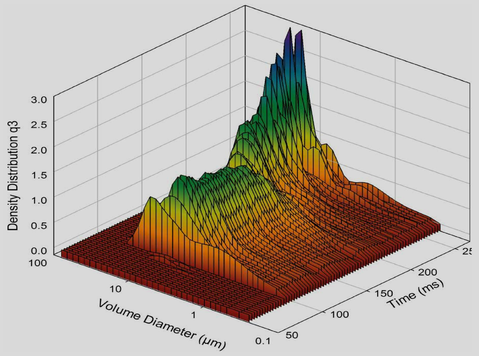
DATA ANALYSIS – Multifactor statistics

LBM model contains parameters characterizing microscopic interactions:

1. Relaxation modes $\Lambda^{(s)}_{\alpha\beta}$
2. Surface tension coefficients $\kappa^{(s)}$

Denote model parameters as $U=\{\Lambda^{(s)}_{\alpha\beta},\kappa^{(s)},\ldots\}$ .The model parameters are extracted from experimental (laser diffraction, Fig. 1) measurements of spray formation.

FIGURE 1



Particle size distribution in pMDI spray as determined by laser diffraction analysis

Multifactor analysis extends standard SVD decomposition of 2-factor correlation $D=U_1\Sigma U_2^T$

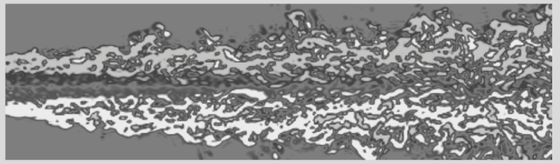
to N-rank tensor $D=\mathrm{Z}\times U_1\times\ldots\times U_N$

with each 2-factor correlation $U_1,\ldots,U_N$ corresponding to a standard SVD.

RESULTS & DISCUSSION

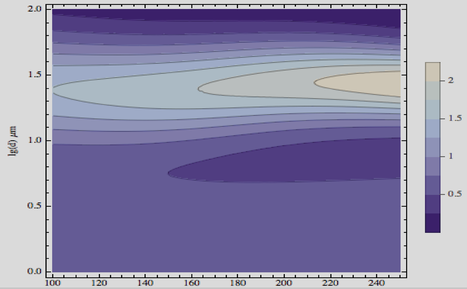
Calibration of particle size data from one experiment (Fig. 1) was carried out and identified parameters introduced in LBM calculation. Spray density contours shown in Fig. 2, Particle size distributions are shown in Fig. 3, Computation of flow in realistic airway model shown in Fig. 4.

FIGURE 2



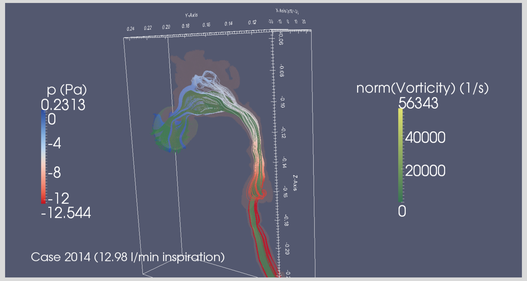
Density contours at exit from pMDI nozzle as computed by LBM.

FIGURE 3



Particle size distribution of computed spray. Late-time bimodal distribution of experimental data (Fig. 1) is reproduced.

FIGURE 4



Multiphasic air-spray flow in upper airway geometry extracted from patient MRI scan.

The multilinear formalism allows disentangling the effect of individual parameters upon the data of interest. Here, the formalism was used for calibration of the LBM model, bypassing the need for detailed, molecular dynamics computation of surface tension, phase separation effects.
Ongoing work will extract the influence of spray formulation parameters upon particle size distributions.
Efficient graphics processing unit (GPU) implementation allows computation in complicated geometry and prediction of airway deposition patterns.

CONCLUSIONS

A simulation method based upon fundamental physical principles with parameters calibrated from multilinear, multifactor analysis of experimental spray particle size distributions has been introduced. The mathematical model allows identification of the effect of molecular-level quantities (e.g. surface tension, intermolecular forces) upon pMDI performance. The mathematical formalism has undergone successful preliminary testing against synthetic data extracted from a single laser diffraction experiment. Qualitative comparison of particle sizes shows good agreement, but full validation requires multilinear statistical parameter calibration of the LBM model against multiple experimental particle distribution measurements. Work is currently in progress on processing of experimental data to allow systematic evaluation of how pMDI formulation parameters affect device performance. This study was supported by U.S. FDA through grant 1U01FD004943-01.