

STUDY OF DYNAMICS OF AIRFLOW AND AEROSOL TRANSPORT AND
DEPOSITION IN HUMAN UPPER AIRWAYS USING LARGE-EDDY
SIMULATIONS

By

Jacob Cole Pratt

Reetesh Ranjan
Associate Professor
(Advisor)

Kidambi Sreenivas
Professor
(Committee Member)

Charles Margraves
UC Foundation Professor
(Committee Member)

STUDY OF DYNAMICS OF AIRFLOW AND AEROSOL TRANSPORT AND
DEPOSITION IN HUMAN UPPER AIRWAYS USING LARGE-EDDY
SIMULATIONS

By

Jacob Cole Pratt

A Thesis Submitted to the Faculty of the University of
Tennessee at Chattanooga in Partial
Fulfillment of the Requirements of the Degree
of Master of Science: Engineering

The University of Tennessee at Chattanooga
Chattanooga, Tennessee

May 2026

ABSTRACT

This study employs a large-eddy simulation (LES) strategy to investigate airflow and aerosol dynamics in the human upper airways using a truncated SimInhale configuration. Inflow conditions include three steady inhalation flow rates (14.2, 53.2, and 71 L/min), representing quasi-laminar, moderate, and high turbulence conditions, and a realistic cyclic breathing scenario. Under steady flow, monodisperse (1–10 μm) and polydisperse aerosols are analyzed. The study shows that complex airflow dynamics directly influence aerosol transport and deposition, causing global deposition to increase nonlinearly with particle size and Reynolds number, with the larynx being a primary deposition location in turbulent cases. For the polydisperse analysis using uniform, Gaussian, and Rosin-Rammler distributions, the Rosin-Rammler yielded the lowest deposition, while the uniform had the highest. Simulation of the realistic breathing cycle with monodisperse particles shows that deposition occurs almost entirely during the inspiratory phase, with the expiratory phase acting as a clearance mechanism.

ACKNOWLEDGEMENTS

I would like to acknowledge my advisor, Dr. Reetesh Ranjan, for his instrumental mentorship, guidance, and support throughout this research. I would also like to thank Dr. Charles Margraves and Dr. Kidambi Sreenivas for serving on my thesis committee and for their valuable time and feedback. I am also grateful to the Fluid and Combustion Modeling Group for their support and collaboration. I also acknowledge the National Science Foundation (Grant #2324691) and the Department of Mechanical Engineering at the University of Tennessee Chattanooga (UTC) for supporting this research. Lastly, I thank the UTC Research Institute for providing all the high-performance computing resources to carry out the simulations in this work.

TABLE OF CONTENTS

ABSTRACT	iii
ACKNOWLEDGEMENTS	iv
LIST OF FIGURES	vii
LIST OF TABLES	x
LIST OF ABBREVIATIONS	xi
LIST OF SYMBOLS	xiii
CHAPTER	
1. INTRODUCTION	1
1.1 Background and Motivation	1
1.2 Key Technical Objectives	7
1.3 Thesis Layout	9
2. LITERATURE REVIEW	10
2.1 Monodisperse Injection	11
2.2 Polydisperse Particle Distribution	13
2.3 Cyclic Breathing	16
2.4 Summary	18
3. MATHEMATICAL FORMULATION AND COMPUTATIONAL STRATEGY . .	20
3.1 Governing Equations	20
3.2 Subgrid Modeling	23
3.3 Numerical Methodology	25
4. SETUP AND SIMULATION STRATEGY	27
4.1 Problem Description	27
4.2 Flow Parameters	29

4.2.1	Monodisperse Injection during Steady Inflow Conditions	30
4.2.2	Polydisperse Injection during Steady Inflow Conditions	31
4.2.3	Monodisperse Injection during Cyclic Inflow Conditions	34
4.3	Computational Mesh	36
4.4	Simulation Strategy	37
5.	DYNAMICS DURING MONODISPERSE INJECTION	40
5.1	Instantaneous Flow Features	40
5.2	Time-Averaged Airflow	46
5.3	Aerosol Deposition Characteristics	57
5.4	Aerosol Transport Statistics	65
5.5	Summary	71
6.	AEROSOL DEPOSITION DURING POLYDISPERSE CONDITIONS	73
6.1	Global Deposition	74
6.2	Local Deposition	83
6.3	Summary	89
7.	AEROSOL DEPOSITION DURING REALISTIC BREATHING CYCLE	91
7.1	Description of Airflow	91
7.1.1	Cyclic Breathing	91
7.1.2	Steady Inhalation and Exhalation	96
7.2	Aerosol Deposition Characteristics	99
7.2.1	Global Deposition	100
7.2.2	Local Deposition	102
7.3	Summary	106
8.	CONCLUSIONS	108
8.1	Key Accomplishments	109
8.2	Future Outlook	114
	REFERENCES	116
	VITA	122

LIST OF FIGURES

4.1	Schematic of the complete SimInhale geometry (left) and the truncated geometry used in this study (right)	28
4.2	Probability density function for uniform, Rosin-Rammler, and Gaussian distributions used in the simulations for polydisperse injection of aerosol particles . .	33
4.3	Time varying velocity at the inlet	35
4.4	Computational mesh at the inlet boundary with a zoomed-in view showing the hybrid unstructured mesh with near-wall prism layers (a) and a side view of the mesh in the inlet, nasal cavity, and trachea regions of the geometry (b, c). The near-wall prism layers are used throughout the geometry to accurately capture the near-wall dynamics	36
5.1	Coherent vortical structures from Case A (a), Case B (b), and Case (c) identified using iso-surface of Q-criterion ($Qd_{in}^2/U_b^2 = 5$) and colored by the normalized velocity magnitude	42
5.2	Spatial distribution of aerosol particles at $2T_f$ after the injection in three cases with $d_p = 1 \mu\text{m}$ (a-c), and $d_p = 10 \mu\text{m}$ (d-f). Blue and red colored particles correspond to deposited and active particles within the computational domain, respectively	44
5.3	Contours of time-averaged normalized velocity magnitude (a, d), resolved turbulent kinetic energy (b, e), and eddy viscosity (c, f) in the central sagittal plane from cases A and C. Sections A1-A2 through F1-F2 in these figures refer to the locations where transverse profiles are extracted	48
5.4	Time-averaged normalized velocity magnitude at six cross-sections comparing the three cases. The reference results correspond to a past LES study using the SimInhale benchmark geometry [1]	51
5.5	Time-averaged resolved turbulent kinetic energy at six cross-sections comparing the three cases. The reference results correspond to a past LES study using the SimInhale benchmark geometry [1]	54

5.6	Global deposition fraction as a function of the particle diameter (a) and the non-dimensional deposition parameter (χ) [2] (b) for the three cases. The reference LES results and <i>in vitro</i> data [1] in subfigure (a) correspond to Case B ($Re = 3745$) conditions with the complete SimInhale geometry	58
5.7	Schematic of airway showing seven sections, where local deposition fraction and average velocity magnitude and slip velocity are obtained (a) and local deposition fraction in three cases obtained from all seven particle streams (b) . .	61
5.8	Variation of local deposition fraction in seven sections for six particle streams with different values of d_p	63
5.9	Normalized average velocity magnitude (u^*) of six particle streams and airflow for cases A (a), B (c), and C (e) and normalized slip velocity for cases A (b), B (d), and C (f) through various corresponding sections of airway at $2T_f$ after particle injection	67
5.10	Normalized velocity fluctuations (u') of six particle streams and airflow for cases A (a), B (b), and C (c) through various sections of airway at $2T_f$ after particle injection	70
6.1	Schematic of the airway showing the seven sections where local deposition is measured	74
6.2	Variation of global deposition fraction (GDF_1) with respect to bins of particle diameter for Gaussian (a), Rosin-Rammler (b), and the Uniform distributions (c). Here, the reference curve corresponds to the monodisperse results at $Re = 3745$	77
6.3	Global deposition fraction (GDF_2) as a function of the particle diameter normalized for Gaussian (a), Rosin-Rammler (b), and Uniform distributions (c) . .	78
6.4	Global deposition fraction (GDF_2) as a function of the particle diameter bin for $Re = 1000$ (a), 3745 (b), and 5000 (c)	81
6.5	Variation of local deposition fraction in seven sections for Gaussian (a), Rosin-Rammler (b), and Uniform distributions (c). Here, the reference corresponds to local deposition at $Re = 3745$ with monodisperse distribution	85
6.6	Variation of local deposition fraction in seven sections for $Re = 1000$ (a), 3745 (b), and 5000 (c). Here, the reference corresponds to local deposition at $Re = 3745$ with monodisperse distribution	87

7.1	Velocity magnitude at six cross-sections (A–F) comparing different times to the reference case. Here, the reference results corresponds to steady inhalation at $Re = 3745$	93
7.2	Time-averaged and normalized velocity magnitude at six cross-sections (A–F) comparing inhalation and exhalation compared to the reference case. Here, the reference results corresponds to steady inhalation at $Re = 3745$	97
7.3	Global deposition fraction as a function of particle diameter for the steady inhalation, steady exhalation, and cyclic cases compared with the reference case. Here, the reference results corresponds to steady inhalation at $Re = 3745$. .	101
7.4	Local deposition fraction in three cases obtained from all seven particle streams, excluding the exhalation case, as all the particles were deposited in section one for the exhalation case	103
7.5	Local deposition fraction as a function of the particle diameter for the cyclic (a), steady inhalation (b), and stead exhalation (c) cases	105

LIST OF TABLES

4.1	Simulation parameters for the three cases considered in this study. Each case is simulated with seven streams of non-interacting monodisperse particles . . .	31
4.2	Simulation parameters for the nine cases considered in this study. Each case represents a unique combination of flow conditions and particle size distribution types	32
4.3	Simulation parameters for the three cases considered in this study. Each case is simulated with seven streams of non-interacting monodisperse particles . . .	34
4.4	Details of parameters of the hybrid unstructured mesh used in the present study. Here, $\Delta r_{\min}$ denotes the minimum height of the computational cell adjacent to the wall, λ is the average expansion ratio of the prism layers, ΔV is the volume of the computational cell, and y^+ is the near-wall resolution in inner wall units	37
6.1	Particle deposition results for nine simulation cases, categorized by Reynolds number and particle size distribution type	82

LIST OF ABBREVIATIONS

DNS, Direct Numerical Simulation

E-E, Eulerian–Eulerian Framework

E-L, Eulerian–Lagrangian Framework

PIV, Particle Image Velocimetry

RANS, Reynolds-Averaged Navier–Stokes

SGS, Subgrid-Scale

WALE, Wall-Adapting Local Eddy-Viscosity Model

UTC, University of Tennessee at Chattanooga

PSD, Particle Size Distribution

MDI, Metered-Dose Inhaler

COPD, Chronic Obstructive Pulmonary Disease

LES, Large-Eddy Simulation

MRI, Magnetic Resonance Imaging

PET, Positron Emission Tomography

QCT, Quantitative Computed Tomography

HRCT, High-Resolution Computed Tomography

CRW, Stochastic Continuous Random Walk

CT, Computed Tomography

LDA, Laser Doppler Anemometry

CFD, Computational Fluid Dynamics

DPI, Dry-Powder Inhaler

MMAD, Mass Median Aerodynamic Diameter

GSD, Geometric Standard Deviation

PISO, Pressure Implicit with Splitting of Operator

SIMPLE, Semi-Implicit Method for Pressure-Linked Equations

LRRI, Lovelace Respiratory Research Institute

PDF, Probability Density Function

CPU, Central Processing Unit

AMD, Advanced Micro Devices

TKE, Turbulent Kinetic Energy

r.m.s., Root-Mean-Square

LDF, Local Deposition Fraction

GDF, Global Deposition Fraction

LIST OF SYMBOLS

Re , Reynolds number

Q_v , Volumetric flow rate

d_p , Particle diameter

St , Stokes number

μ , Dynamic viscosity

τ_{SGS} , Subgrid-scale stress tensor

k , Turbulent kinetic energy

σ , Geometric standard deviation

G , Filter kernel

$\overline{\Delta}$, Filter width

u_i , i^{th} Cartesian component of the velocity vector

p , Pressure

ρ , Density

ν , Kinematic viscosity

ρ_p , Particle density

m_p , Particle mass

x_{pi} , Particle position

v_{pi} , Particle velocity

u_i^+ , Instantaneous carrier phase velocity at particle location

τ_p , Particle time constant

ϕ , Empirical correlation for Stokes drag

Re_p , Particle Reynolds number

g , Gravitational acceleration

m_f , Mass of the fluid

δ_{ij} , Kronecker delta

ν_t , Eddy viscosity

$\overline{S}_{ij}$, Resolved strain-rate tensor

C_w , Model constant

g_{ij} , Velocity gradient tensor

Sd_{ij} , Traceless symmetric part of the square of the velocity gradient tensor

$\mathcal{I}$, Interpolation operator

u_i^{sgs} , Subgrid dispersion velocity

Δt_f , Flow time step size

$\dot{m}_p$, Mass flow rate of particles injection

U_b , Bulk velocity at the inlet

d_{in} , Inlet diameter

τ_f , Characteristic time scale of the flow

$\mathcal{O}$, Order of magnitude

$\Delta r_{\min}$, Minimum height of computational cell adjacent to the wall

λ , Average expansion ratio of the prism layers

ΔV , Volume of the computational cell

y^+ , Near-wall resolution in inner wall units

L_{pipe} , Axial extent of the pipe

T_f , Flow-through time

L_c , Representative length of the computational domain

$\langle \phi \rangle$, Running-time average of a flow variable

t_0 , Starting time of averaging

T , Duration of averaging

Q , Q-criterion

χ , Non-dimensional deposition parameter

u^* , Sectional normalized average velocity magnitude

$|\mathbf{u}|_{\text{avg,f/p}}$, Sectional volumetric average of velocity magnitude of airflow or particles

u_s^* , Local slip velocity

u' , Local normalized velocity fluctuation

$|\mathbf{u}|_{\text{r.m.s,f/p}}$, Root-mean-square of velocity fluctuations

GDF_1 , Normalized global deposition fraction

GDF_2 , Contribution of each size bin to total deposition

GDF_3 , Total global deposition fraction

$|U|$, Instantaneous velocity magnitude

$\langle \bar{U} \rangle$, Time-averaged velocity magnitude

CHAPTER 1

INTRODUCTION

In this chapter, the background and motivation of this study are discussed. Following this, the technical objectives are described. Finally, an outline of this thesis is presented.

1.1 Background and Motivation

Pulmonary diseases such as asthma, cystic fibrosis, chronic obstructive pulmonary disease (COPD), pulmonary infection, and lung tumors occur due to the combined effects of anatomical modifications of the airways, bronchial hyper-responsiveness, inflammation, and basilar airflow reduction [3–5]. Such diseases can lead to significant mortality. For example, it is estimated that nearly 65 million people suffer from COPD, leading to about 3 million deaths worldwide [6]. Therefore, timely diagnosis and effective treatment of such diseases are vital to reducing mortality. Several pulmonary diseases can be treated by employing aerosolized drug delivery [7–10], where an improved regional deposition of the inhaled drug is key to maximizing the efficiency and minimizing the side-effects of the inhaled drugs. Although recent advancements in the radiological imaging techniques such as magnetic resonance imaging (MRI), positron emission tomography (PET), quantitative computed tomography (QCT), high-resolution computed tomography (HRCT), etc., have enabled an objective assessment of the phenotype of airways and other anatomical features through *in*

vivo and *in vitro* measurements, the required information for an effective treatment still tends to be limited. To this end, computational tools can be immensely useful to predict airflow and localized deposition in the respiratory airways as well as in the peripheral regions to optimize the effectiveness of the inhaler therapies. The focus of this study is to examine the effects of inflow conditions on the airflow and aerosol dynamics within the upper airways of a realistic human airway.

Aerosol deposition within pulmonary flows corresponds to the broader category of dispersed multiphase flows, which comprise a carrier phase and a disperse phase [11–13]. Such flows can be classified as a dilute suspension, a dense suspension, or a granular flow depending upon the mass and the volume loading of the dispersed phase. We consider a dilute suspension approximation with a one-way coupling, which is usually considered adequate for such flows within the respiratory airways [1, 14, 15]. In such cases, only the carrier phase affects the evolution of the aerosol particles. Numerical prediction of such flows is still extremely challenging due to the added complexity of the aerosol dynamics to the evolution of the carrier phase flow. In particular, the flow field within pulmonary regions exhibits the presence of features such as laminar to turbulent transition, separation, recirculation, shear layers, etc., which are difficult to predict by computational models. Such flow features, in turn, directly affect the aerosol dynamics, thus increasing the difficulties to realize a predictive computational strategy.

For the computational modeling of pulmonary flows with aerosol particles, two primary computational frameworks are commonly employed, namely, Eulerian–Lagrangian (E-

L) and Eulerian–Eulerian (E-E) approaches [7, 16]. In both these frameworks, the carrier phase is modeled using an Eulerian approach; however, the treatment of the dispersed phase differs. In the E-E framework, the dispersed phase is treated as a continuum, with its transport equations solved in an Eulerian manner. In contrast, the E-L approach tracks the evolution of individual particles (or parcels) in a Lagrangian manner. In this study, we adopt the E-L formulation to capture particle dynamics, which facilitates robust modeling of turbulence-induced dispersion, polydispersity, and particle collisions [1, 17, 18].

Within the E-L framework, typically, a point-particle strategy is utilized to track the evolution of particles. Additionally, a variety of computational approaches have been used to simulate the carrier phase flow, which differ in fidelity and computational cost. These include direct numerical simulation (DNS), large-eddy simulation (LES), and Reynolds-averaged Navier-Stokes (RANS) techniques. DNS resolves all pertinent spatial and temporal scales and is therefore ideal for fundamental studies at low to moderate Reynolds numbers [19–22] or simplified geometries [23]. LES, by contrast, explicitly computes the large-scale structures while modeling the subgrid-scale (SGS) effects, and RANS approximates all turbulent fluctuations. Although RANS-based approaches, such as the low Reynolds number two-equation models combined with appropriate near-wall corrections [24] and the use of stochastic continuous random walk (CRW) model based on the normalized Langevin equation for particle dispersion [25] can yield results comparable to LES, previous studies have demonstrated that LES generally outperforms RANS in predicting aerosol deposition [1, 18, 26, 27]. Therefore, we employ the point-particle LES strategy in the present study for simulating the airflow.

Past LES-based studies [1, 28–32] have explored different aspects of airflow and aerosol deposition in airways. Matida et al. [28] studied an idealized mouth–throat model and showed that LES captured the transient vortical flow emerging after the oral airway constriction, leading to improved deposition results compared to RANS [17] that agreed with *in vitro* measurements. Jin et al. [33] studied the human upper respiratory tract and observed that the increase of particle diameter, particle density, and breathing intensity improved deposition efficiency in the upper region, in agreement with the experimental results. Jayaraju et al. [29] also demonstrated the advantages of LES compared to RANS in simulating aerosol transport through the extrathoracic airways by performing a detailed comparison of turbulence modeling strategies in a realistic mouth-throat geometry. In particular, it was observed that LES agreed better with the particular image velocimetry (PIV) results in capturing the flow field in the pharynx region, thus leading to improved particle deposition predictions, especially for smaller inhaled droplets below 5 μm . Lambert et al. [30] studies a patient-specific CT-based model of the human respiratory tract, encompassing the mouth, larynx, and a seven-generation bronchial tree, and observed a good agreement of the aerosol deposition with prior experimental data in a multi-generation cast (e.g., [34]). An asymmetry was observed in deposition within lungs, which was attributed to the laryngeal jet flow and anatomical asymmetry in the bronchial tree. These results underscore the importance of considering patient-specific airways, which can reveal subtle deposition patterns during aerosolized drug delivery due to the interaction of flow with the variations in the anatomy. Ghahramani et al. [31] studied a realistic model of human upper airways using

LES and RANS and observed that secondary flows affect particle deposition, especially in the oropharynx and larynx regions, and prediction by LES compared better with experiment due to its ability to accurately capture secondary flow regions. Koullapis et al. [1] carried out a collaborative benchmarking study by considering the SimInhale geometry and comparing different LES and RANS strategies. The study showed that for steady inhalation of micron-scale particles, certain RANS turbulence models tend to capture the overall trend and hot spots of deposition. However, they tend to over-predict total deposition relative to LES when compared to experimental results.

Apart from steady inhalation conditions, LES has also been employed to examine aerosol delivery under special breathing conditions and airway configurations. For example, Farnoud et al. [32] simulated pulsating inhalation through a patient-specific nasal airway and examined two nasal inhaler designs to identify optimal design and breathing protocols. These results highlight the efficacy of LES for such optimization studies, as it can accurately capture unsteady flow dynamics (e.g., oscillatory jets, vortex shedding) that influence the transport and deposition of aerosolized medication deposits in the airways. Jin et al. [33] used LES to compare steady and unsteady inflow conditions in a realistic upper respiratory tract and reported that the deposition efficiency was better in the unsteady configuration.

Past LES-based studies have shown that in the extrathoracic airways, deposition primarily occurs due to particle impaction on the airway walls—an effect driven by high velocities and rapid changes in flow direction. Generally, larger particles deposit more readily by impaction than smaller ones, while turbulent dispersion plays a crucial role in influencing

the trajectories of smaller particles [35]. These studies have illustrated the need to employ patient-specific, realistic human airways to accurately predict transport and deposition of aerosol particles. However, to perform parametric computational studies of various aspects of local/global deposition of aerosol particles, such as the effects of steady and unsteady inhalation, size of particles, inhaler designs, polydispersity, etc., in the human upper airways, the computational expense still tends to be high due to the complexities of the geometry. Therefore, the first objective of this study is to establish a three-dimensional (3D) configuration for human upper airways that can be utilized for efficient LES-based parametric studies. Specifically, we consider a truncated geometry corresponding to the SimInhale configuration, which comprises the inlet, nasal cavity, pharynx, larynx, trachea, and carina regions. Such an approach allows us to examine the airflow and deposition characteristics efficiently without the computational expense of simulating all generations of the airway tree. It has also been employed in previous studies [36–38] where a hybrid 3D/1D modeling technique was used to efficiently simulate the flow in the upper airways while using a network model for the distal bronchi. We employ a point-particle wall-resolved LES strategy with the E-L framework in the present study, where a mapped strategy is used to specify the inflow boundary condition, and SGS effects for the carrier phase are accounted for by using the wall-adapting local eddy viscosity (WALE) model [39]. The verification and validation study is performed by comparing the results with a past study that simulated the complete SimInhale geometry [1].

The other objective of this study is to use the established LES strategy to examine the effects of inflow conditions and particle size distributions (PSD) on the dynamics and statistics of airflow, and transport and deposition of aerosol particles of different sizes within the upper airways. Specifically, we first analyze three steady inhalation conditions with flow rate, $Q_v = 14.2, 53.2,$ and 71 L/min, which leads to inflow Reynolds numbers, $Re = 1000, 3745,$ and 5000 , respectively. The steady inflow conditions correspond to quasi-laminar, moderate turbulence, and high turbulence conditions at the inlet. With these steady inhalation conditions, we examine the deposition for both monodisperse ($1 - 10 \mu\text{m}$) and polydisperse particle injections. Secondly, we implement a realistic breathing cycle at the inlet of the airway to analyze how deceleration and flow reversal affect the airflow and particle deposition within the airway. For all the cases considered in this study, we analyze first- and second-order turbulence statistics of airflow, and global and local deposition of aerosol particles.

1.2 Key Technical Objectives

This thesis’s goal is to investigate airflow and aerosol dynamics in the human upper airway using LES and an EL framework, as well as different inflow conditions and particle injection strategies. The key technical objectives are:

- **Validate the LES Strategy:** The focus of this objective is to validate the LES-based modeling strategy within the EL framework for a realistic human upper airway based on the SimInhale benchmark configuration [1]. To validate the results, airflow at a Reynolds number of 3745 is compared to results from literature, where first-order and second-order statistics are used for comparison. Along with airflow, particle deposition

characteristics such as local and global deposition are also validated at this Reynolds number.

- **Analyze the Effects of Inflow Rates on Airflow and Deposition:** In this objective, the effects of three inflow rates ($Q_v = 14.2, 53.2,$ and 71 L/min) corresponding to quasi-laminar, moderate turbulence, and high turbulence conditions at the inlet on airflow and particle behavior are analyzed. The goal of this analysis is to examine how turbulence affects the airflow in terms of velocity and turbulent kinetic energy, as well as the global and local deposition and secondary statistics for monodisperse aerosol particles ($1\text{--}10\text{ }\mu\text{m}$). This will establish the coupled effects between Reynolds and Stokes numbers on aerosol transport and deposition characteristics.
- **Examine the Effects of Polydisperse Distributions on Deposition:** Building on the monodisperse results, this objective aims to examine how polydisperse particle distributions, which are more representative of realistic aerosol injection, such as metered-dose inhalers, affect the particle deposition. This analysis is conducted across all three flow regimes ($Re=1000, 3745,$ and 5000) and uses Gaussian, Rosin-Rammler, and uniform particle size distributions (PSD) for mean particle size of $5\text{ }\mu\text{m}$. To accomplish this objective, local and global depositions for both monodisperse and polydisperse injection are compared.
- **Analyze Airflow Dynamics and Aerosol Transport During Realistic Breathing Cycles:** The final objective of this thesis is to expand on the steady inflow conditions and implement a physiologically realistic breathing cycle. This breathing cycle

includes both inhalation and exhalation, which will aid in examining how deceleration and flow reversal affect both airflow and local and global depositions in human airways.

1.3 Thesis Layout

The layout of this thesis, with a total of eight chapters, is as follows. A literature review is presented in Chapter 2. In Chapter 3, the mathematical formulation and numerical methodology employed in this study are discussed. Chapter 4 discusses the computational setup of the flows and particle injection being simulated. Chapter 5 validates monodisperse aerosols and airflow with steady inflow conditions using established studies and examines aerosol transport and deposition comprehensively. In Chapter 6, polydisperse PSDs are analyzed, with a comparison of their local and global deposition to the corresponding monodisperse cases. Chapter 7 analyzes the effects of realistic breathing conditions for both airflow and particle deposition. Lastly, the results of this study and possibilities for future research are discussed in Chapter 8.

CHAPTER 2

LITERATURE REVIEW

The accurate modeling of aerosol deposition and airflow in human respiratory systems has been achieved through the use of experimental, analytical, and computational methods. Experimental methods such as in *vitro* studies using particle image velocimetry (PIV), laser Doppler anemometry (LDA), and aerosol photometry can provide visualization and quantification of airflow and deposition patterns. However, they are constrained by the geometric complexity and limited spatial resolution [7, 15, 34]. Analytical approaches have also been used, which, when based on simplified geometries, can yield insight into transport mechanisms, but can rarely be applied to realistic airway topologies.

Due to these limitations, computational fluid dynamics (CFD) has emerged as one of the main frameworks for simulating pulmonary airflow and particle transport. Using CFD, airflow is usually modeled using one of three approaches, which include Direct Numerical Simulation (DNS), Large-Eddy Simulation (LES), and Reynolds-Averaged Navier–Stokes (RANS). DNS provides the highest fidelity by resolving all turbulence scales; however, it is only computationally efficient for simple geometries and lower Reynolds numbers [19–21]. In comparison, LES resolves the large turbulent eddies directly while modeling the subgrid-scale (SGS) effects, and capturing the unsteady vortical structures, which strongly influence the trajectories of aerosol particles [1, 18, 26, 27]. Lastly, there is RANS, which

is computationally inexpensive, but relies on turbulence closures that time-average the flow field and often underpredict the transient separation and secondary flows that are necessary for accurate prediction of aerosol transport and deposition [18, 26, 27].

Other than airflow, there is also the particle phase to track, where two frameworks are commonly used. These include the Eulerian-Eulerian (E-E) and the Eulerian-Lagrangian (E-L) approaches. In the E-E formulation, the dispersed phase is represented as a continuum, where the transport equations are solved in an Eulerian frame of reference. In the E-L formulation, particles are tracked through the resolved airflow field, and are commonly used for aerosol transport in human airways [1, 14, 15]. The E-L framework, when combined with LES, enables simulations of dispersion, impaction, as well as particle-wall interactions under physiologic flow conditions. Due to this, many recent studies, including the present work, employ a point-particle, wall-resolved LES strategy to accomplish both physical accuracy as well as physical realism.

2.1 Monodisperse Injection

In aerosol particle transport and deposition research, monodisperse aerosol deposition is widely studied, as it provides controlled conditions that help isolate the effects of particle diameter and airflow intensity on the mechanisms of deposition. When using monodisperse injection, all the particle sizes in the stream are the same size, which enables direct comparison of inertial impaction, gravitational settling, and turbulent dispersion within different regions of the airway.

In the early computational studies of monodisperse aerosol deposition, RANS and steady laminar simulations were used to investigate the impacts of particle size on the deposition efficiency within airways [17, 26]. However, approaches such as these were unable to resolve the instantaneous flow structures causing the localized impaction. Following studies using LES methods, which captured the transient airflow, including the vortices and secondary flows, it was observed that such flow features have a major impact on deposition in areas such as the larynx and pharynx [28–30]. One of these studies, performed by Matida et al. [28], used LES for monodisperse aerosol deposition in an idealized mouth-throat model and showed improved agreement with experimental data. The results in this study, when compared to RANS, were better due to the resolution of vortical jets past the glottal constriction. In this study, the authors also found that when using LES, total deposition within the airway increased with particle size, as particles with a diameter of $5\text{ }\mu\text{m}$ had a 50.7% higher deposition when compared to $2.5\text{ }\mu\text{m}$ particles. In addition to this, Jayaraju et al. [29] validated LES airflow in human airways results using PIV, and found that the prediction of flow separation and particle deposition in realistic geometries using LES was much better when compared to RANS. Due to this, monodisperse aerosol particles with a diameter smaller than $5\text{ }\mu\text{m}$ had a higher accuracy of prediction with LES, as RANS overestimated deposition in the larynx and trachea. However, as particle size increased above $5\text{ }\mu\text{m}$ both LES and RANS had comparable results.

Lambert et al. [30] expanded on these efforts using a patient-specific airway, which included bronchial generations and showed that the laryngeal jet and airway curvature govern

deposition patterns as well as deposition efficiency, having a dependence on Stokes number. Additionally, it was also found that large monodisperse particles ($30\text{ }\mu\text{m}$) were predominantly deposited in the oral region, while 95% of smaller particles ($2.5 - 5\text{ }\mu\text{m}$) passed through the oral cavity and into the trachea for transport into the lung. Later, Ghahramani et al. [31] used LES and RANS for a realistic upper-airway geometry and found that secondary flows affect particle deposition, especially in the oropharynx and larynx regions. They also found that increasing flow rate from 30 to 60 L/min resulted in a 45% increase in deposition within the upper airway for particles with a $5\text{ }\mu\text{m}$ diameter.

Across these studies, it was found that in monodisperse injection, there is a nonlinear increase in particle deposition with particle diameter, especially in shear regions such as the oropharynx and larynx. Additionally, the flow rate and choice of turbulent model can have a great impact on deposition and airflow results. With these studies and results, they established monodisperse particle injection as a step toward validating particle interaction models and being able to more accurately model more realistic particle injections, such as polydisperse aerosol distributions.

2.2 Polydisperse Particle Distribution

Particle deposition of injected aerosols within human airways is strongly dependent on the particle size as discussed in section 2.1. Due to this, the deposition is strongly influenced by the particle size distribution (PSD) used for the injected particles. In realistic cases where aerosol particles are generated by medical devices such as metered-dose inhalers and dry-powder inhalers (DPIs), the particles are polydisperse instead of monodisperse [7]. As

deposition of aerosol particles is nonlinear with an increase of size, polydisperse distributions can have complex deposition behavior where particles smaller than $5\text{ }\mu\text{m}$ follow streamlines and larger ones do not because of inertia [40]. Therefore, accurate PSD is needed to predict the local and global deposition for realistic particles.

Many computational studies have used Gaussian (or lognormal), Rosin-Rammler, and uniform distributions to accurately examine polydisperse aerosol transport and deposition. Lognormal distribution, which is equivalent to Gaussian in log diameter space, is commonly used to model the experimental aerosols and is usually specified by using the mass median aerodynamic diameter (MMAD) and the geometric standard deviation (GSD) [7]. Gemci et al. [41] used a lognormal distribution ($\text{MMAD} = 2.6\text{ }\mu\text{m}$, $\sigma = 1.9\text{ }\mu\text{m}$, $0.5 \leq D \leq 5.5\text{ }\mu\text{m}$) for a 17-tract human airway simulation, which was based on cascade-impactor measurements. In this study, they found that the deposition fraction increased from 73.5% when using monodisperse particles with a diameter of $2.6\text{ }\mu\text{m}$ to 74.7% for the lognormal polydisperse distribution. Similarly, Legh-Land et al. [42] used a lognormal distribution ($\text{MMAD} = 10.5\text{ }\mu\text{m}$, $\sigma = 1.8\text{ }\mu\text{m}$) for representation of an aerosol plume. In this study, they found that total deposition of the droplets increased as particle size went up to around $10\text{ }\mu\text{m}$ where deposition began to decrease with larger particle sizes. Additionally, the relative humidity had no impact on particle deposition under $10\text{ }\mu\text{m}$, and for particles larger than this, as humidity increased, deposition went down due to increased impaction in the extrathoracic region. Together, these studies show that lognormal distributions can be a physically realistic method for representing polydispersity.

As mentioned previously, the Rosin-Rammler distribution has also been employed in human airway deposition studies. Islam et al. [43] applied the Rosin-Rammler distribution for polydisperse particles between 1 and 10 μm in a CT-based airway model and found that the highly asymmetric airflow within the airway resulted in a higher flow rate in the right lung and a deposition hotspot along the tracheal wall. This study also found that the turbulence has a greater impact on particles larger than 5 μm while smaller particles (1 - 3 μm) were not as affected, especially at higher flow rates. In a related study, Islam et al. [44] also used the Rosin-Rammler distribution to analyze airflow and particle deposition in different-aged lungs. Similarly, it was found that as the flow rate increased, there was an increase in total deposition within the airway, while at low flow rates, particles followed the streamlines and penetrated farther into the airways. Additionally, as the airway size decreased (increase in age), there was an increase in deposition, with most particles depositing in the mouth-throat region.

Along with Gaussian (lognormal) and Rosin-Rammler distributions, the uniform distribution can be used as a form of polydispersity, as it is in this study. Although it is rarely used in any research as it lacks the realistic features of real aerosol particle distributions, it can serve as a simplified baseline to isolate the influence of distribution shape. By having a mean diameter and spread constant across PSDs, there can be a direct assessment of how statistical form affects deposition trends. Using these three distributions, polydispersity can be specified in a simulation to allow for a more realistic study of deposition when compared to monodisperse particle injection.

2.3 Cyclic Breathing

In all the computational studies mentioned so far, steady or quasi-steady inhalation conditions have been imposed at the inlet of the airway, which typically correspond to constant volumetric flow rates. This allows for simplification and valuable insights into particle deposition and airflow, but it neglects the unsteady dynamics of a full breathing cycle where there is acceleration, deceleration, and flow reversal. In a realistic breathing cycle, these dynamics can cause vortices and shear structures that can change the local and global deposition. Therefore, to be as accurate as possible, these cyclic dynamics need to be considered.

In steady inhalation studies, complex flow features can still be examined in human airways, especially at higher flow rates. For example, Rahimi-Gorji et al. [45] studied particle transport in a realistic airway geometry with flow rates of 10–60 L/min, where secondary motions and vortices, as well as flow features such as the formation of the turbulent laryngeal jet formed. It was also examined that these vortices and secondary flows at higher flow rates increased deposition. However, as mentioned previously, this neglects the flow reversal that occurs during the transition to exhalation. In a study by Piemjaiswang et al. [46], a complete inhalation-exhalation cycle was considered, and different breathing frequencies were examined. It was shown that decelerating the flow and having a full flow reversal can impact the airflow and deposition. During inhalation, wall shear stress was very high along the anterior of the trachea wall, and after flow reversal, the wall shear stress was high on the right side. In the study, it was also found that at lower breathing frequencies, there was a

flushing effect where particles that were not deposited during inhalation got exhaled during exhalation.

Similar time-varying inlet studies by Kuga et al. [47] and Atzeni et al. [48] have also been done to examine realistic breathing conditions. Kuga et al. [47] found that within the nasal cavity and trachea, there were differences between the steady and transient flow rates, and that under steady inflow conditions, particle deposition and transport cannot be accurately predicted. Additionally, micro particles between 5 and 10 μm showed higher deposition for a steady flow rate than that of transient. In contrast to this, Atzeni et al. [48] examined a higher total deposition with a transient flow rate compared to the steady with a 4% increase in deposition. This contradiction shows that different types of transient flow rates, geometry, and particle size can have an impact on the total deposition.

Building on these efforts, Qi et al. [49] studied a transient simulation of airflow in a CT-derived airway tree with 122 terminal bronchi. The inflow condition used (also used in this current study) includes a 5.1 s respiratory cycle with tidal volume of 500 mL and an inhalation-to-exhalation ratio of 1:2. Airflow analysis revealed that pressure decreased from the trachea towards the outlets during inspiration and increased during exhalation with a velocity of 6.64 m/s and 4.71 m/s during inhalation and exhalation, respectively. It was also found that there were differences in streamline patterns between inhalation and exhalation at the bifurcations. During inhalation, airflow moves faster along the inside of the bifurcation due to flow division, while during exhalation, this reverses, and there is a higher velocity along the outer side, leading to more mixing.

Overall, transient cyclic inflow conditions at the inlet, which model realistic breathing conditions, introduce complex flow features such as acceleration, deceleration, and reversal that can have an impact on airflow and aerosol transport when compared to steady inhalations. Despite the more accurate conditions when using this inflow, there can still be different results due to variations in cycle profiles, breathing frequencies, and numerical implementations, as seen in the mentioned studies.

2.4 Summary

The accurate modeling of aerosol deposition and airflow in human respiratory systems has been achieved through the use of experimental, analytical, and computational methods. Among these, CFD has become the main tool for modeling both airflow and particle transport within human airways. Within CFD, DNS is used for its ability to resolve all turbulent scales, RANS is used for its inexpensive computation, and LES is used for its capability of resolving large-scale turbulent eddies. LES has become a preferred choice due to its high accuracy and lower computational cost compared to DNS. The LES airflow model is typically paired with an E-L framework to track particle parcels through the air, enabling the realistic prediction of both impaction and dispersion.

Research in the aerosol transport and deposition field has used these CFD approaches to model simple monodisperse particle injections with steady flow to more complex and realistic cases. Many studies found that using LES resulted in better airflow and deposition results than RANS when validating with experimental data, as it was able to accurately resolve key flow features such as the laryngeal jet. In this research, it was also shown

that the deposition of aerosol particles is highly dependent on particle size and flow rate due to impaction, with larger particles being much more likely to deposit, especially with higher flow rates. With this dependence on particle size, it is also critical to accurately model the particle sizes based on realistic inhalers using PSDs such as lognormal and Rosin-Rammler distributions. Using such distributions, it was discovered that even at the same mean diameter, monodisperse and polydisperse deposition can vary because of the inertial effects and the presence of differently sized particles during polydisperse injection.

Even with these more accurate results of particle deposition when switching from monodisperse to polydisperse, airway simulations can be further improved by using realistic cyclic inflow breathing conditions. In a realistic breathing cycle, there is acceleration, deceleration, and flow reversal during the transition from inhalation and exhalation, which steady inflow studies omit. In these realistic breathing cases, it has been observed that this deceleration and flow reversal impact airflow and, as a result, can significantly affect local and global deposition, particularly in realistic human airways.

CHAPTER 3

MATHEMATICAL FORMULATION AND COMPUTATIONAL STRATEGY

We employ the well-established Eulerian-Lagrangian (E-L) computational framework to perform point-particle large-eddy simulation (LES) in the present study. In this chapter, we first describe the governing equations employed in this framework. Afterward, we present the details of the subgrid models. Finally, we discuss the numerical methodology used to solve the governing equations.

3.1 Governing Equations

As the particle-laden turbulent flow considered here corresponds to the dilute suspension regime, we consider a one-way coupled scenario, where the carrier phase (airflow) affects the dynamics of the dispersed phase (aerosol particles), whereas the dispersed phase does not affect the carrier phase.

We consider the airflow dynamics within the airways to be governed by the incompressible Navier-Stokes equations. The corresponding LES equations in the Eulerian framework are obtained by performing spatial filtering of the governing equations. Here, the spatial filtering of a field variable $\phi(\mathbf{x}, t)$ is performed, leading to the filtered (resolved) field

variable $\bar{\phi}(\mathbf{x}, t)$ through

$$\bar{\phi}(\mathbf{x}, t) = \int_{\Omega} \phi(\mathbf{x}', t) G(\mathbf{x}, \mathbf{x}'; \bar{\Delta}) d\mathbf{x}', \quad (3.1.1)$$

where $\bar{\Delta}$ is the filter width and $G(\mathbf{x}, \mathbf{x}'; \bar{\Delta})$ is the filter kernel. In this study, the kernel is chosen to be a box filter expressed as

$$G(\mathbf{x}, \mathbf{x}'; \bar{\Delta}) = \begin{cases} 1 & \text{if } |\mathbf{x} - \mathbf{x}'| \leq \frac{\bar{\Delta}}{2}, \\ 0 & \text{otherwise,} \end{cases} \quad (3.1.2)$$

which essentially is a local volume averaging of a field variable. Furthermore, we employ the widely used implicit LES strategy, where the computational grid acts as the spatial filter [50].

The spatially-filtered incompressible Navier-Stokes equations are given by

$$\frac{\partial \bar{u}_i}{\partial x_i} = 0, \quad (3.1.3)$$

$$\frac{\partial \bar{u}_i}{\partial t} + \frac{\partial \bar{u}_i \bar{u}_j}{\partial x_j} = -\frac{1}{\rho} \frac{\partial \bar{p}}{\partial x_i} + \nu \frac{\partial^2 \bar{u}_i}{\partial x_j \partial x_j} - \frac{\partial \tau_{ij}^{\text{sgs}}}{\partial x_j}. \quad (3.1.4)$$

Here, u_i denotes the i^{th} Cartesian component of the velocity vector with $i = 1, 2, 3$, p is the pressure, and ρ and ν denote the density and kinematic viscosity of the fluid. In addition, $\tau_{ij}^{\text{sgs}} = (\overline{u_i u_j} - \bar{u}_i \bar{u}_j)$ denotes the SGS stress tensor, which requires an additional closure model. The governing equations given by Eq. (3.1.3) and Eq. (3.1.4) correspond to mass

and momentum balance equations, respectively, and are complete after specifying problem-specific initial and boundary conditions.

The dispersed phase is tracked in a Lagrangian manner with a point-particle approximation [51]. It comprises spherical particles with constant diameter, d_p , density, ρ_p , and mass, m_p . The governing equations for the time evolution of the particle position, x_{pi} , and particle velocity, v_{pi} , are given by

$$\frac{dx_{pi}}{dt} = v_{pi}, \quad (3.1.5)$$

$$m_p \frac{dv_{pi}}{dt} = m_p \frac{\phi(Re_p)}{\tau_p} (u_i^+ - v_{pi}) - g(m_p - m_f)\delta_{i3}, \quad (3.1.6)$$

where u_i^+ is the instantaneous velocity of the carrier phase at the particle's location, $\tau_p = \frac{d_p^2}{18\nu} \frac{\rho_p}{\rho}$ is the particle time constant, and $\phi(Re_p)$ is an empirical correlation for particle Reynolds number-dependent Stokes drag $\left(Re_p = \frac{\rho_p d_p |u_i^+ - v_{pi}|}{\rho\nu}\right)$. Here, δ_{ij} denotes the Kronecker delta. Following past studies [52], the empirical correlation $\phi(Re_p)$ is specified as

$$\phi(Re_p) = \begin{cases} 24(1 + \frac{1}{6}Re_p^{2/3}), & Re_p \leq 1000, \\ 0.424Re_p^{0.24}, & Re_p \geq 1000. \end{cases} \quad (3.1.7)$$

Note that in the present study, the particle-to-fluid density ratio, $(\rho_p/\rho = 761.67 \gg 1)$, tends to be large. Therefore, the effects of unsteady drag, added mass, Basset history forces, and particle-to-particle collisions are neglected following past studies [13, 53].

3.2 Subgrid Modeling

Both Eulerian and Lagrangian equations presented in Sec. 3.1 require closure models for the subgrid terms. These terms include the SGS stress tensor, τ_{ij}^{sgs} , and the instantaneous velocity of the carrier phase at the particle's location, u_i^+ . Here, we briefly describe the approaches to model these terms.

The SGS stress, τ_{ij}^{sgs} , is closed using the gradient diffusion hypothesis through:

$$\tau_{ij} - \frac{1}{3}\tau_{kk}\delta_{ij} = 2\nu_t\bar{S}_{ij}, \quad (3.2.1)$$

where ν_t denotes the eddy viscosity and $\bar{S}_{ij} = \frac{1}{2}\left(\frac{\partial\bar{u}_i}{\partial x_j} + \frac{\partial\bar{u}_j}{\partial x_i}\right)$ is the resolved strain-rate tensor. The eddy viscosity ν_t is obtained using the widely-used wall-adapting local eddy viscosity (WALE) model [39]. In this model, ν_t is given by

$$\nu_t = (C_w\Delta)^2 \frac{(Sd_{ij}Sd_{ij})^{3/2}}{(S_{ij}S_{ij})^{5/2} + (Sd_{ij}Sd_{ij})^{5/4}}, \quad (3.2.2)$$

where C_w is a model constant and Sd_{ij} is the traceless symmetric part of the square of the velocity gradient tensor $\left(g_{ij} = \frac{\partial\bar{u}_i}{\partial x_j}\right)$. In the present study, $C_w = 0.325$ is specified. The expression for Sd_{ij} is given by

$$Sd_{ij} = \frac{1}{2}(g_{ij}^2 + g_{ji}^2) - \frac{1}{3}\delta_{ij}g_{kk}^2, \quad (3.2.3)$$

where $g_{ij}^2 = g_{ik}g_{kj}$.

The WALE model addresses key limitations of other algebraic models, such as the Smagorinsky model [54] and the dynamic eddy viscosity model [55], by correctly scaling the eddy viscosity in the near-wall region and incorporating rotational effects into turbulence modeling. In addition, unlike the dynamic eddy viscosity model [55], it does not require homogeneous directions for averaging to determine the dynamic model coefficients.

The coupling between the carrier and dispersed phases occurs through the instantaneous velocity of the carrier phase u_i^+ at the particle's location, as described in Sec. 3.1. While performing a DNS, this velocity is obtained by interpolating u_i from the computational grid to the particle's position. However, in LES, only the spatially filtered velocity field $\bar{u}_i$ is solved, and therefore, u_i^+ must be approximated using a subgrid dispersion model. This is usually accomplished through

$$u_i^+ = \mathcal{I}(\bar{u}_i) + u_i^{\text{sgs}}, \quad (3.2.4)$$

where $\mathcal{I}$ is the interpolation operator and u_i^{sgs} represents the effects of subgrid dispersion. Following past studies focused on deposition within airways [1, 30, 56, 57], a no-model strategy is adopted here, implying that the effects of subgrid dispersion are neglected, i.e., $u_i^{\text{sgs}} = 0$. Although this simplification may lead to inaccuracies in predicting particle dynamics, particularly when the SGS kinetic energy is substantial, or the particle time constant is small, it provides a simplified approach [58].

3.3 Numerical Methodology

The point-particle LES is performed using an extended version [40, 59] of the well-established OpenFOAM software [60]. The E-L framework is built upon the *pimpleFoam* solver, which enables simulation of turbulent flows w/o inertial particles. It is a three-dimensional (3D), parallel, finite-volume solver. The extended version of the solver employs different types of spatial discretization schemes and subgrid models.

The solver for the carrier phase employs unstructured spatial discretization with a collocated cell-centered variable arrangement. The use of finite-volume discretization allows for an easier formulation using an unstructured computational mesh, which is useful for the simulation of complex configurations. Additionally, it can discretely ensure all the conservation laws. A formally second-order-accurate method is used for the spatial discretization, while the time integration of the semi-discrete equations is performed using a second-order-accurate backward difference scheme. To ensure pressure-velocity coupling for incompressible flows, the PIMPLE algorithm is employed, which is a combination of the PISO [61] (Pressure Implicit with Splitting of Operator) and the SIMPLE [62] (Semi-Implicit Method for Pressure-Linked Equations) algorithms.

The time evolution of the governing equations for the dispersed phase (see Eq. (3.1.5) and Eq. (3.1.6)) is performed using a first-order-accurate explicit scheme with a sub-cycling strategy. In the sub-cycling approach, a sequence of particle-tracking steps is performed, with the maximum time step for particle tracking specified to be the same as the flow time step size, Δt_f . The evolution of particle trajectories is computed using an efficient

algorithm where, instead of tracking the position of particles in the Cartesian coordinates, their position is tracked in barycentric coordinates. Such an approach enables the use of arbitrary cell shapes and efficient interpolation and other geometrical operations [63]. The algorithm tracks particles as they move from one computational cell to another, and face crossings are used to identify when a particle exits a computational cell [64].

CHAPTER 4

SETUP AND SIMULATION STRATEGY

In this chapter, we describe the details of the computational setup and cases that are considered to examine the dynamics of airflow and aerosol deposition under different scenarios. We consider three types of scenarios: monodisperse injection of aerosol particles at three inlet flow rates, polydisperse injection using three different injection distributions at three inlet flow rates, and monodisperse injection during a cyclic breathing cycle. Apart from the details of these cases, we also describe the details of the computational mesh and the simulation strategy employed in this study.

4.1 Problem Description

We consider a truncated portion of the SimInhale benchmark geometry [1] in this study, which is shown in Fig. 4.1. The complete SimInhale geometry includes the oral cavity, larynx, and tracheobronchial airways down to the 12th generation of the branching. It was originally developed by obtaining HRCT scans of a rubber cast model based on an adult male’s inflated lung, combined with data from the Lovelace Respiratory Research Institute (LRRI) for the upper airways, and a dental impression for the oral cavity. This configuration has been used for verification and validation against experimental results, such as those obtained using CT and PET, which provide detailed deposition data for comparison [1]. In

this study, we consider a truncated portion of the geometry to facilitate computationally efficient parametric studies for the assessment of strategies for aerosol-based drug injection, which still retain the regions of primary interest where significant variations in airflow and aerosol dynamics tend to occur.

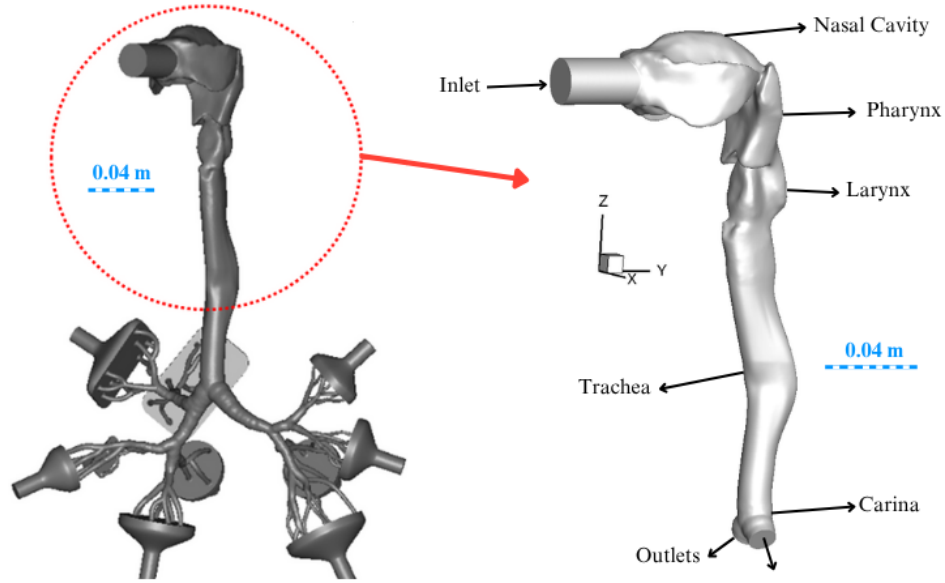


Figure 4.1 Schematic of the complete SimInhale geometry (left) and the truncated geometry used in this study (right)

The truncated geometry includes the extrathoracic and parts of the intrathoracic airways, specifically up to the carina and the main bronchi. This region encompasses significant flow variations and complex features like flow separation, laminar-to-turbulent transitions, turbulence production, and shear layers, which are critical for understanding the transport and deposition of aerosol particles [30, 64]. Note that the extrathoracic airways and the initial segments of the intrathoracic airways exhibit the occurrence of most deposition, especially for larger particles. The truncated geometry allows us to examine the airflow and

deposition characteristics efficiently without the computational expense of simulating all 12 generations of the airway tree. Such an approach has also been employed in previous studies [36–38] where a hybrid 3D/1D modeling technique was used to efficiently simulate the flow in the upper airways while using a network model for the distal bronchi. Using a simplified yet realistic airway model, as considered in this study, strikes a balance between computational efficiency and accuracy in replicating physiological conditions, making it an optimal choice for assessing the effects of inflow conditions and particle size distributions (PSD) on aerosol transport and deposition, which is a key focus of this study.

The airflow in the truncated airway geometry is driven by specifying quasi-laminar or turbulent conditions at the inlet corresponding to steady inhalation conditions and a time-varying, realistic breathing cycle. At the two outlets, the outflow boundary condition is specified, which accounts for backflow/recirculating flow at the boundary. All walls of the geometry are considered to be rigid, where a no-slip boundary condition is specified. Further details of simulation parameters and cases considered in this study are discussed in Sec. 4.2.

4.2 Flow Parameters

In this section, we describe the simulation parameters and flow conditions employed in the present study. Three categories of simulations are considered to capture a broad range of respiratory airflow and particle transport scenarios. These include steady inflow with monodisperse injection of aerosol particles; steady inflow with polydisperse injection of aerosol particles; and cyclic breathing scenario with monodisperse injection of aerosol

particles. These cases are considered to examine the effects of inlet flow rate, particle inertia, polydisperse injection, and realistic breathing patterns.

4.2.1 *Monodisperse Injection during Steady Inflow Conditions*

We consider three cases, labeled as cases A, B, and C, to comprehensively assess the impact of varying steady inhalation flow rate (Q_v) and monodisperse particle size (d_p) on the airflow dynamics and particle deposition behavior within the upper airway. Table 4.1 summarizes the simulation parameters for the three cases in terms of inlet flow rate (Q_v), diameter of particle (d_p), mass flow rate of particles injection ($\dot{m}_p$), and non-dimensional numbers, Re and St . Here, $Re = U_b d_{in} / \nu$ and $St = \tau_p / \tau_f$, where U_b represents the bulk velocity at the inlet boundary, d_{in} denotes the inlet diameter, ν is the kinematic viscosity of the fluid, τ_p is the particle time constant, and $\tau_f = d_{in} / U_b$ is the characteristic time scale of the flow. The three values of Q_v or Re are chosen to analyze the behavior of airflow under different flow regimes (quasi-laminar, moderate turbulence, and high turbulence conditions at the inlet) and their consequent impact on particle deposition patterns. The seven distinct values of d_p ranging from 1 μm to 10 μm are considered to represent a range of behaviors, from small, potentially respirable particles to larger ones that might have different deposition tendencies within the simulated environment. Note that Case B also has reference data available from past study with full SimInhale configuration [1], which facilitates verification and validation of the computational strategy considered in this study.

Table 4.1 Simulation parameters for the three cases considered in this study. Each case is simulated with seven streams of non-interacting monodisperse particles

Case	Q_v [L/min]	d_p [μm]	$\dot{m}_p$ [$\times 10^6$ kg/s]	Re	St
A	14.2	1-10	0.0019 - 1.9	1000	0.0001 - 0.01
B	53.2	1-10	0.0019 - 1.9	3745	0.0004 - 0.04
C	71	1-10	0.0019 - 1.9	5000	0.0005 - 0.05

In all the cases considered here, at the inflow boundary, a fully turbulent inflow boundary condition is specified by employing a mapped strategy (discussed in Sec. 4.4). At the outlet boundary, an outflow boundary condition is specified, which accounts for backflow/recirculating flow at the boundary. A no-slip boundary condition is imposed on all the rigid airway walls. In each case, the evolution of the seven mono-disperse and non-interacting particle streams is considered with d_p of 1, 2, 2.5, 4.3, 6, 8, and 10 μm , which leads to a variation of St from $\mathcal{O}(10^{-4}) - \mathcal{O}(10^{-2})$. After the airflow is established in the computational domain, streams of particles are injected at a rate of 4×10^6 particles per second over a duration of 0.025 s, leading to a total of 100,000 injected particles for each value of d_p in the three cases.

4.2.2 Polydisperse Injection during Steady Inflow Conditions

To study the impact of inhalation flow rates and PSDs on airflow dynamics and aerosol deposition, nine cases are considered and are labeled A1-A3 ($Re = 1000$), B1-B3 ($Re = 3745$), and C1-C3 ($Re = 5000$). This results in a total of nine cases with three different flow rates and distributions. Table 4.2 summarizes the simulation parameters for these nine cases in terms of inlet flow rate (Q_v), particle diameter range (d_p), and the

non-dimensional Reynolds (Re) and Stokes (St) numbers. The three values of Q_v (and corresponding Re) are chosen to analyze airflow behavior under different regimes: quasi-laminar (14.2 L/min), moderate turbulence (53.2 L/min), and high turbulence (71.0 L/min). These inflow conditions remain unchanged from the monodisperse cases to allow for comparison between the monodisperse and polydisperse particle injections.

Table 4.2 Simulation parameters for the nine cases considered in this study. Each case represents a unique combination of flow conditions and particle size distribution types

Case	Distribution Type	Q_v [L/min]	d_p [μm]	Re	St
A1	Uniform	14.2	0.1 - 9.9	1000	$1.05 \times 10^{-6} - 1.03 \times 10^{-2}$
A2	Gaussian	14.2	0.1 - 9.9	1000	$1.05 \times 10^{-6} - 1.03 \times 10^{-2}$
A3	Rosin-Rammler	14.2	0.1 - 9.9	1000	$1.05 \times 10^{-6} - 1.03 \times 10^{-2}$
B1	Uniform	53.2	0.1 - 9.9	3745	$3.94 \times 10^{-6} - 3.86 \times 10^{-2}$
B2	Gaussian	53.2	0.1 - 9.9	3745	$3.94 \times 10^{-6} - 3.86 \times 10^{-2}$
B3	Rosin-Rammler	53.2	0.1 - 9.9	3745	$3.94 \times 10^{-6} - 3.86 \times 10^{-2}$
C1	Uniform	71.0	0.1 - 9.9	5000	$5.27 \times 10^{-6} - 5.16 \times 10^{-2}$
C2	Gaussian	71.0	0.1 - 9.9	5000	$5.27 \times 10^{-6} - 5.16 \times 10^{-2}$
C3	Rosin-Rammler	71.0	0.1 - 9.9	5000	$5.27 \times 10^{-6} - 5.16 \times 10^{-2}$

As mentioned previously, each flow condition has three different size distributions in which the particles are injected. The three distributions selected for this study include uniform, Gaussian, and Rosin-Rammler as seen in Table 4.2. Figure 4.2 shows the probability density function for each distribution, which was post-processed after the simulations were finished. All distributions in the cases have a minimum and maximum diameter of 0.1 μm and 9.9 μm , respectively, and a mean of 5 μm . The Gaussian distribution is specified with

a standard deviation of $2.839 \mu\text{m}$, and the Rosin-Rammler distribution is defined with a spread parameter of 1.83.

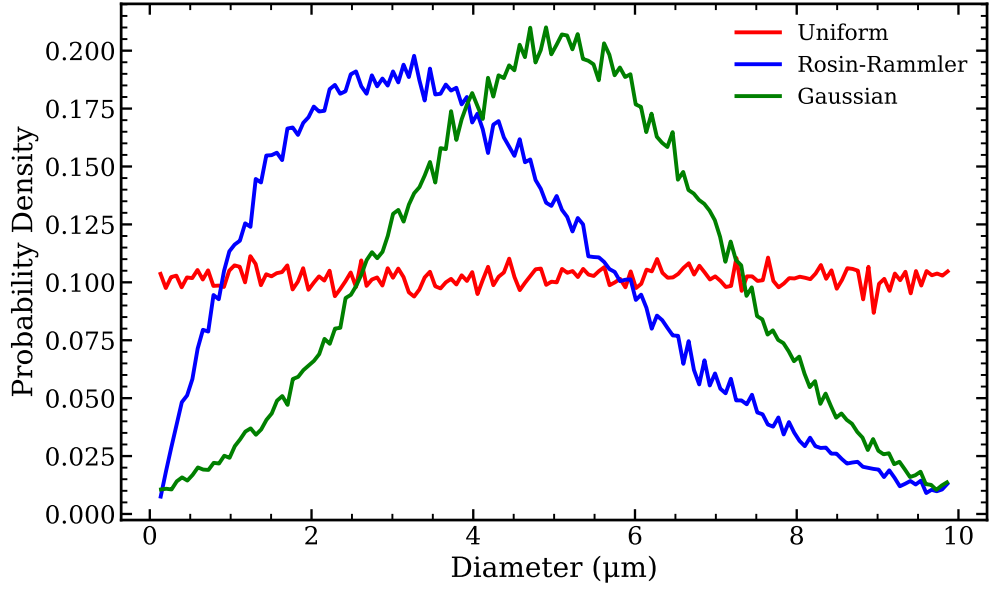


Figure 4.2 Probability density function for uniform, Rosin-Rammler, and Gaussian distributions used in the simulations for polydisperse injection of aerosol particles

In all nine cases, the boundary conditions stay the same as in the monodisperse cases. A fully turbulent inflow boundary condition is specified by employing a mapped strategy (discussed in Sec. 4.4). At the outlet boundary, an outflow boundary condition is specified, which accounts for backflow/recirculating flow at the boundary. A no-slip boundary condition is imposed on all the rigid airway walls. After the airflow is established in the computational domain, a stream of non-interacting polydisperse particles is injected at a rate of 4×10^6 particles per second over a duration of 0.025 s. This results in a total of 100,000 injected

particles for each case, with the diameter of each particle sampled from the corresponding size distribution.

4.2.3 Monodisperse Injection during Cyclic Inflow Conditions

To study the effects of inhalation and exhalation in a realistic breathing cycle, three cases are considered, which are summarized in Table 4.3. The three cases considered are a realistic cyclic breathing condition, steady inhalation, and steady exhalation, which allow for a comparison of airflow and particle deposition for transient and time-averaged steady-state inflow conditions.

Table 4.3 Simulation parameters for the three cases considered in this study. Each case is simulated with seven streams of non-interacting monodisperse particles

Case	Q_v [L/min]	d_p [μm]	$\dot{m}_p$ [$\times 10^6$ kg/s]	Re	St
Cyclic	Varying	1-10	0.0019 - 1.9	Varying	Varying
Inhalation	16.8	1-10	0.0019 - 1.9	1170	1.25e-04 - 1.25e-02
Exhalation	8.66	1-10	0.0019 - 1.9	605	6.43e-05 - 6.43e-03

The cyclic case simulates a realistic calm breathing pattern based on a tidal volume of 500 mL and a rate of 12 breaths per minute, which results in a 5 s respiratory cycle with an inspiration-to-expiration time ratio of 1:2 [49]. The time-varying sinusoidal velocity profile specified at the inlet is shown in Fig. 4.3. The steady inhalation and exhalation cases are steady-state inflow simulations where the inlet flow rates (Q_v) are based on the time-averaged values from the inhalation and exhalation phases of the cyclic case, respectively.

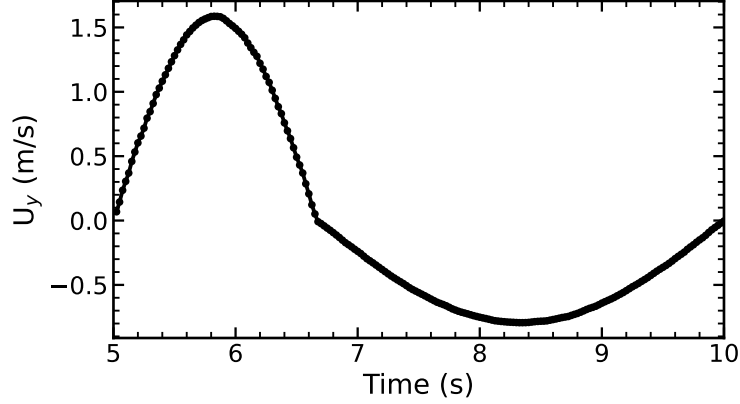


Figure 4.3 Time varying velocity at the inlet

For boundary conditions in these cases, the time-varying velocity profile shown in Fig. 4.3 is imposed at the inlet boundary for the cyclic case, while the steady inhalation and exhalation cases use a Dirichlet inlet boundary condition. For all three cases, an outflow boundary condition that accounts for potential backflow is used, and a no-slip boundary condition is imposed on all rigid airway walls. In each of the three cases, the evolution of seven monodisperse and non-interacting particle streams is considered with d_p of 1, 2, 2.5, 4.3, 6, 8, and 10 μm , and are injected into the airway after 1 cycle for the cyclic case and after 2 flows through time for the steady cases. The particle sizes considered correspond to a Stokes number (St) variation from approximately $\mathcal{O}(10^{-5})$ to $\mathcal{O}(10^{-2})$. After the airflow is established, streams of particles are injected at a rate of 4×10^6 particles per second over a duration of 0.025 s, leading to a total of 100,000 injected particles for each value of d_p in all three cases.

4.3 Computational Mesh

A body-fitted unstructured mesh is used in this study to perform wall-resolved LES. The mesh is designed to capture the complex flow features in the upper airways. Figure 4.4 shows the mesh at the inlet boundary and a zoomed-in side view of the mesh in the inlet, nasal cavity, and trachea regions. The mesh comprises tetrahedral elements in the interior of the domain and prism layers adjacent to the walls. The use of prism layers in the near-wall region allows for better control over the near-wall grid resolution, ensuring that the near-wall dynamics are accurately captured. This is crucial for simulating complex flow features, such as laminar-to-turbulent transition, boundary layer development, and flow separation/reattachment, which significantly influence the transport and deposition of aerosol particles.

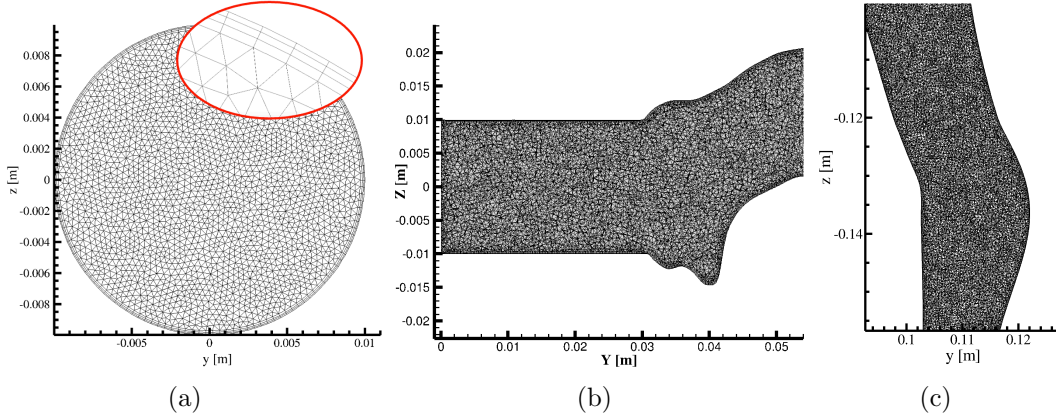


Figure 4.4 Computational mesh at the inlet boundary with a zoomed-in view showing the hybrid unstructured mesh with near-wall prism layers (a) and a side view of the mesh in the inlet, nasal cavity, and trachea regions of the geometry (b, c). The near-wall prism layers are used throughout the geometry to accurately capture the near-wall dynamics

Table 4.4 Details of parameters of the hybrid unstructured mesh used in the present study. Here, $\Delta r_{\min}$ denotes the minimum height of the computational cell adjacent to the wall, λ is the average expansion ratio of the prism layers, ΔV is the volume of the computational cell, and y^+ is the near-wall resolution in inner wall units

Parameter	Value
$\Delta r_{\min}$ [mm]	0.0523
Number of prism layers	3
λ	1.2
$(\Delta V_{\min}, \Delta V_{\text{avg}}, \Delta V_{\max})$ [mm ³]	(0.000529, 0.0167, 0.125)
Average y^+	0.664
Number of cells	6.09×10^6

In this study, a single computational mesh was employed in all cases. Table 4.4 summarizes the key parameters of the computational mesh, including the volume of the computational cells (ΔV_c), the height of the cells adjacent to the wall ($\Delta r_{\min}$), the average expansion ratio of the prism layers (λ), and the near-wall resolution in terms of y^+ . The mesh used in this study consists of approximately 6.09 million cells, with the smallest cell volume in the near-wall region being 0.000529 mm³. While designing the mesh, the near-wall resolution in this study was targeted to achieve an average y^+ value close to 1 in the highest Re case to ensure that no further wall modeling is needed by LES. Past studies [40, 65] have performed grid sensitivity analysis with this geometry, where the computational mesh employed in the present study has been found to be adequate.

4.4 Simulation Strategy

As stated in Sec. 4.2, a mapped boundary condition is used to specify the inflow boundary conditions for the monodisperse and polydisperse cases. In this approach, an auxiliary precursor simulation is performed by simulating the fully developed flow within

a pipe for each case. The axial extent of the pipe is $L_{\text{pipe}} = 15d_{\text{in}}$, where the diameter, d_{in} , is specified to be the same as the inlet diameter of the airway geometry. Additionally, the computational mesh on an axial plane of the pipe matches the mesh on the inlet of the airway geometry to ensure an accurate mapping of the spatio-temporal data. Overall, an unstructured mesh comprising 8×10^5 finite volume cells is used for simulating the pipe flow. The flow within the pipe is driven by ensuring a constant bulk velocity corresponding to each case, as a periodic boundary condition is used along the axial (streamwise) direction. Similar to the airway geometry, a no-slip boundary condition is specified on the walls of the geometry. The pipe flow simulations are performed for the entire duration of the airway simulations to ensure accurate spatio-temporal data at the inlet of the airway is specified. During this duration, planes of data located at $L_{\text{pipe}}/2$ having all the field variables are extracted and saved at each time step, which is subsequently used for the airway simulations.

The flow field within the airway geometry is first simulated for about 5 flow-through times (T_f) in the monodisperse and polydisperse cases, where $T_f = L_c/U_b$. Here, L_c is a representative length of the computational domain along the direction of the mean flow. After gathering the airflow statistics over $2T_f$ in each monodisperse case, seven streams of particles in each case are injected at a rate of 4×10^6 particles per second over a duration of 0.025 seconds, which results in a total of 100,000 particles injected for each value of d_p within the computational domain. For the polydisperse cases, particles are injected at a rate of 4×10^6 particles per second over a duration of 0.025 seconds, which results in a total of

100,000 particles injected for each polydisperse distribution. The flow field with particles is simulated for a further of $2T_f$, after which aerosol deposition is examined.

The three cases considered for cyclic analysis follow the same monodisperse injection strategy, with seven streams of particles in each case being injected at a rate of 4×10^6 particles per second over a duration of 0.025 seconds, which results in a total of 100,000 particles injected for each value of d_p . For the cyclic time-varying case, these particles are injected at the beginning of the second cycle, whereas in the steady inhalation and exhalation, injection begins after 2 flows through time. In the steady inhalation and exhalation cases, the flow field is time-averaged from 2 to 4 flows through time, while no time-averaging is applied for the cyclic case.

The airflow statistics are obtained by performing a running-time average of a flow variable, $\phi(\mathbf{x}, t)$, through

$$\langle \phi \rangle(\mathbf{x}) = \frac{1}{T} \int_{t_0}^{t_0+T} \phi(\mathbf{x}, t) dt, \quad (4.4.1)$$

where t_0 and T denote the starting time of averaging and duration of averaging, respectively.

All the simulations in this study have been performed in parallel using 112 CPU cores on an in-house cluster utilizing the AMD EPYC 7662 64-core processor. The computational cost for simulating one T_f is about 3000 CPU hours.

CHAPTER 5

DYNAMICS DURING MONODISPERSE INJECTION

In this chapter, we first describe the key instantaneous features of the airflow and transport and deposition of the aerosol particles. Afterward, we present results from time-averaged statistics of airflow. This is followed by a discussion of the effects of Q_v and d_p or Re and St on the global and local aerosol deposition characteristics. Finally, we analyze the first- and second-order statistics of aerosol transport through airways in comparison to the airflow to examine the role of the inertia of particles.

5.1 Instantaneous Flow Features

Coherent vortical structures within human airways play a critical role in the transport and deposition of aerosol particles in airways [66]. Figure 5.1 shows the instantaneous structures for the three cases, which are identified using the iso-surface of the normalized Q-criterion [67], i.e., $Qd_{in}^2/U_b^2 = 5$. We observe elongated vortical structures within the nasal cavity region in all cases, which can be attributed to the flow expansion/separation that leads to complex 3D flow patterns and an increased level of mixing in this region. This is also associated with enhanced levels of turbulence apparent from the occurrence of small-scale structures, particularly in cases B ($Re = 3745$) and C ($Re = 5000$). The flow direction changes towards the end of the nasal cavity region, leading the flow into the pharynx and

larynx regions, where we can observe much longer coherent structures along the flow direction. These structures are sustained through the trachea region. However, within the trachea region, we also observe the appearance of small-scale structures, which can be attributed to the presence of a shear layer and complex geometric modulations of the structures. This is particularly evident in cases B and C, whereas in Case A, where Re corresponds to a quasi-laminar flow ($Re = 1000$), only long coherent structures aligned along the flow direction are observed. These structures tend to have much higher velocity magnitude ($\sim 2U_b$) in the post-larynx region in all cases. This is due to a combination of anatomical and fluid dynamic factors. In particular, the constriction of the airway in the larynx region leads to an increased velocity magnitude to ensure mass conservation. Additionally, as the air exits the narrow glottal region of the larynx into the wider post-laryngeal (tracheal) space, it behaves like a free jet, which creates a high-speed core of airflow that persists downstream into the trachea. The sudden expansion of flow from the glottis into the wider airway leads to the formation of shear layers and coherent vortical structures. Qualitatively, the coherent structures in cases B and C tend to be similar and differ from the structures in Case A, which highlights the effect of Re . With an increase in Re , more small-scale structures tend to appear, which is a well-known behavior of wall-bounded turbulent flows.

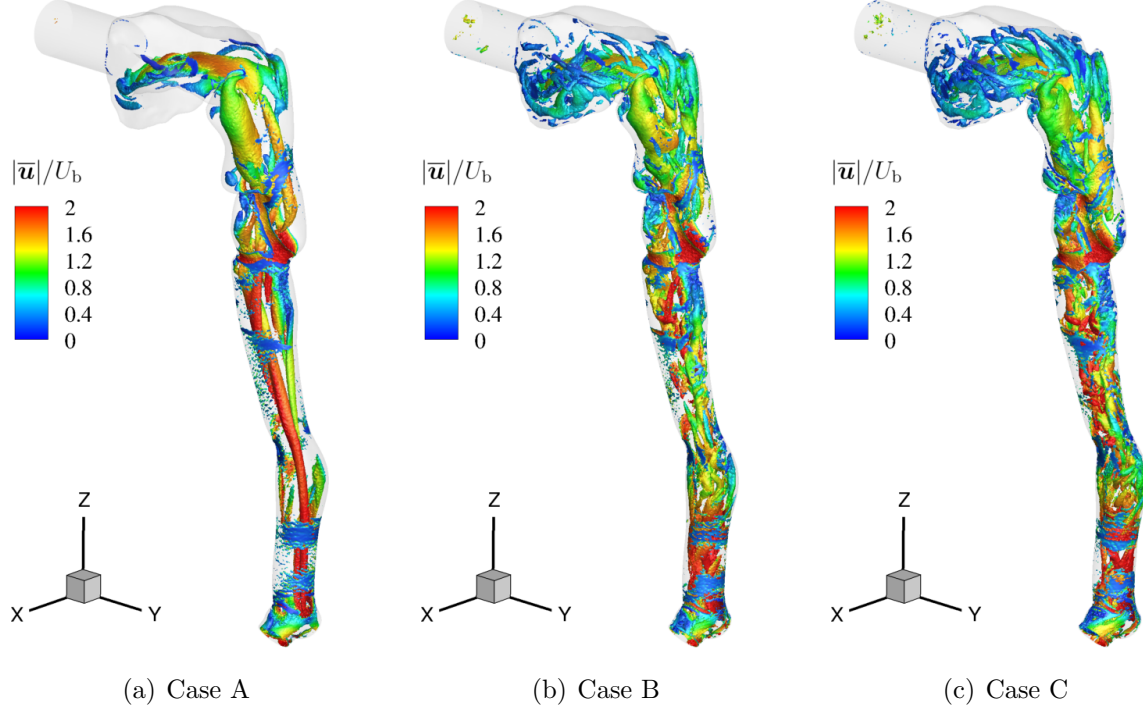


Figure 5.1 Coherent vortical structures from Case A (a), Case B (b), and Case (c) identified using iso-surface of Q -criterion ($Qd_{in}^2/U_b^2 = 5$) and colored by the normalized velocity magnitude

The instantaneous spatial distribution of the inertial aerosol particles is dependent upon both the airflow and the size of the particles. Figure 5.2 shows the distribution of particles with sizes $1 \mu\text{m}$ and $10 \mu\text{m}$ in all three cases, where particles are segregated into two types, namely deposited (blue color) and active or transported (red color). The effect of an increase in Re is apparent from the distribution of particles of both sizes, particularly between low and high Re cases. Specifically, for $d_p = 1 \mu\text{m}$, the active particles are observed in the nasal cavity region in all cases; however, the longer coherent structures in Case A (see Fig. 5.1) tend to affect the distribution of the particles in the post cavity region. In cases B and C, these particles are more uniformly distributed in the post-cavity region compared

to Case A, where the imprint of underlying coherent structures is evident from preferential accumulation of particles. The deposition of these particles also exhibits the effects of Re . In the low Re case, particles are mainly deposited near the inlet section, within the pharynx and larynx regions, and the bifurcation near the carina. However, in the high Re cases, we also observe deposition of these particles occurring in the nasal cavity region, which can be attributed to the complex 3D flow and enhanced mixing in this region, as discussed before. As $d_p = 1 \mu\text{m}$ particles have $St \ll 1$, they tend to follow the flow, which facilitates movement of these particles closer to the wall, leading to their deposition in the cavity region. However, in the trachea region, these particles tend to remain within the core region (away from the walls) in all three cases, leading to their deeper penetration till the start of the bifurcation region.

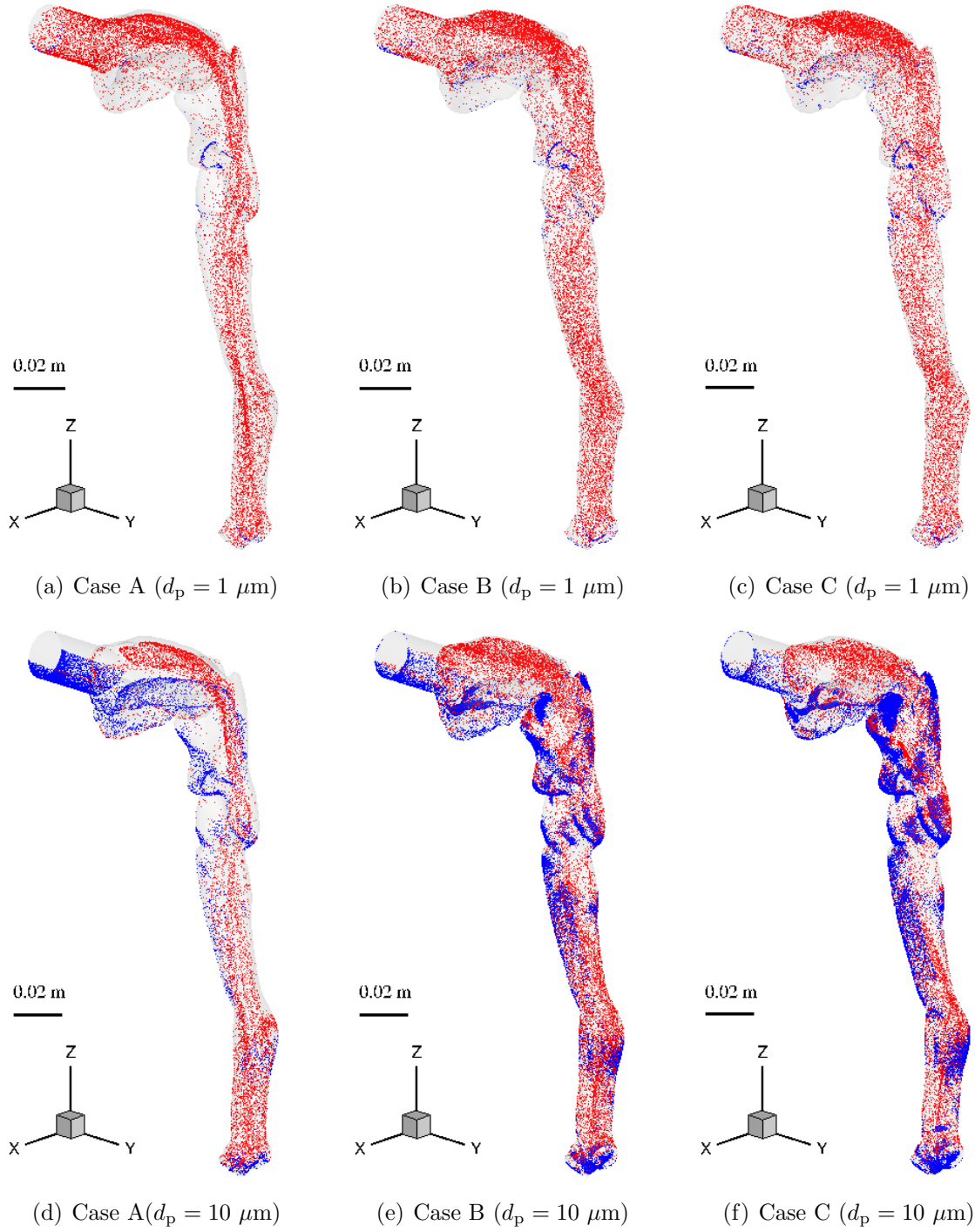


Figure 5.2 Spatial distribution of aerosol particles at $2T_f$ after the injection in three cases with $d_p = 1 \mu\text{m}$ (a-c), and $d_p = 10 \mu\text{m}$ (d-f). Blue and red colored particles correspond to deposited and active particles within the computational domain, respectively

The effect of an increase in d_p , which implies an increase in St ($\mathcal{O}(10^{-2})$) is evident in all three cases. These particles show much higher levels of deposition and preferential concentration throughout the airway region, particularly in high Re cases. The observed differences in distribution between particles of size $1\ \mu\text{m}$ and $10\ \mu\text{m}$ occur primarily due to differences in their aerodynamic behavior, governed by particle size, mass, and inertia. For example, $10\ \mu\text{m}$ particles have greater inertia, and therefore, such particles do not follow curved airflow streamlines, especially in regions with abrupt bends (like the nasal cavity or pharyngeal wall) where they tend to exhibit preferential concentration in low-speed regions. Therefore, such particles tend to impact and deposit on the airway walls, as we can observe here. The inertial effects on the local deposition of $d_p = 10\ \mu\text{m}$ are pronounced with an increase in Re . For example, Case C with the highest Re exhibits high deposition throughout the airway region, whereas Case A with the lowest Re shows lower levels of deposition throughout the airway, which implies that even inertial particles can penetrate deeper regions of airflow in low Re flows. The effects of an increase in Re and St on deposition are consistent with past studies [2, 30].

The results for the instantaneous airflow features and particle distribution discussed here show that the transport and deposition of particles can be significantly affected by both airflow dynamics (Re) and the inertia of the injected particles (St). This is further affected by the anatomy of the airway, which changes abruptly within the upper airway, comprising expansion, changes in curvature, constriction, and complex modulation of airway

walls. These aspects of the transport and deposition of aerosol particles will be discussed further in Sec. 5.3.

5.2 Time-Averaged Airflow

Now, we examine the effects of Re on the features of the time-averaged airflow. Fig. 5.3 (a) and (d) show the contours of the normalized time-averaged velocity magnitude ($|\langle \bar{\mathbf{u}} \rangle|/U_b$) in the central sagittal plane. Qualitatively, the results for cases B and C are similar and tend to differ from Case A; therefore, results are only shown for cases A and C for the sake of brevity. As expected, the boundary layer is thicker in Case A compared to Case B in the inlet section. The lack of transverse mixing in Case A in the nasal cavity region can be inferred from a thinner region of nearly uniform flow with a central core of higher velocity magnitude (see near section B1-B2 in Fig. 5.3(a)). Additionally, we observe a complex 3D separated flow region in all cases in the nasal cavity. The flow field tends to be nearly uniform away from the walls in the later parts of the pharynx and early parts of the larynx regions. This is particularly evident in Case C, which can be attributed to the effects of higher levels of transverse mixing in this case. Towards the end of the larynx region, due to the geometric constriction of the flow, a narrow, higher-speed jet is formed, leading to shear layers in the trachea region. The strength of the shear layers tends to be higher in Case A compared to Case C, and we can observe asymmetry of the flow on the anterior and posterior walls. Such a behavior is due to a difference in Re where the jet breakdown and vortex interactions dominate at higher Re , which is also evident from the instantaneous flow structures shown in Fig. 5.1. We observe asymmetry in the transverse variation of the

velocity magnitude in both cases in the upper parts of the trachea, which is due to the changes in the anatomy. Further downstream, the core jet remains nearly symmetric and uniform in Case A, whereas Case C exhibits asymmetry. Overall, the contours of $|\langle \bar{\mathbf{u}} \rangle|/U_b$ in Case C show similar behavior throughout the upper airway region as reported in a past study [1], thus demonstrating the adequacy of the truncated geometry considered in this study.

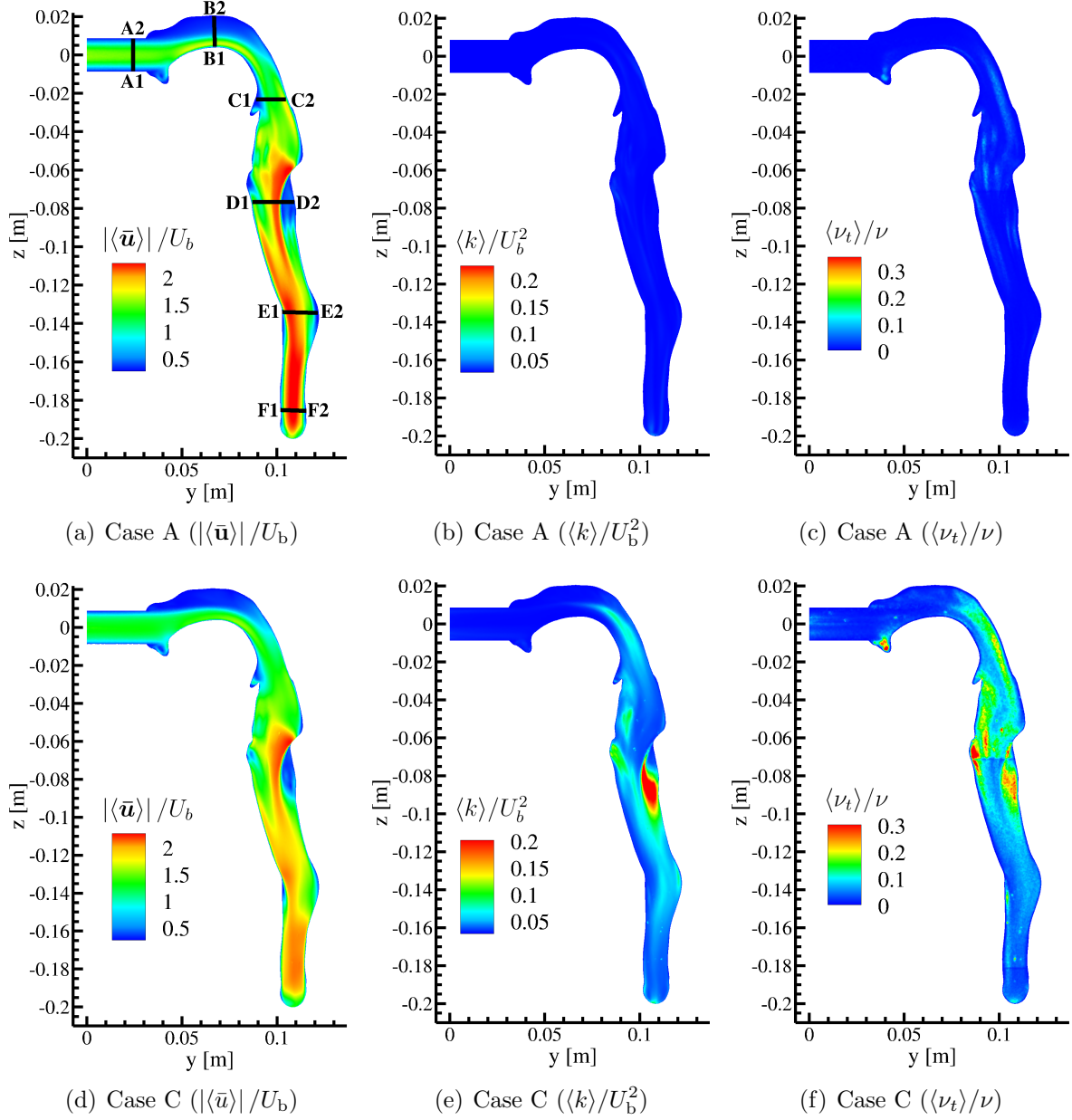


Figure 5.3 Contours of time-averaged normalized velocity magnitude (a, d), resolved turbulent kinetic energy (b, e), and eddy viscosity (c, f) in the central sagittal plane from cases A and C. Sections A1-A2 through F1-F2 in these figures refer to the locations where transverse profiles are extracted

The effects of Re can also be inferred from the contours of the normalized resolved turbulent kinetic energy ($|\langle k \rangle|/U_b^2$) and eddy viscosity ($|\langle \nu_t \rangle|/\nu$). Case A remains nearly

laminar throughout the airway region as evident from negligible values of $|\langle k \rangle|/U_b^2$ and $|\langle \nu_t \rangle|/\nu$. However, significant spatial variations of these quantities are observed in Case C and similarly in Case B (not shown here). We observe higher values of these quantities in the post-cavity region, particularly downstream of the glottis in the laryngeal region and trachea. The elevated turbulent kinetic energy (TKE) and eddy viscosity zones suggest that shear-layer instabilities enhance turbulence downstream of constrictions, consistent with past studies [28, 33]. Similar to the asymmetric variation of the core jet region, we also observe asymmetry in the spatial distribution of $|\langle k \rangle|/U_b^2$ and $|\langle \nu_t \rangle|/\nu$, which is due to the complex anatomy of the airway. The variation of $|\langle \nu_t \rangle|/\nu$ is also consistent with the regions of under-resolved turbulence, particularly in the pharynx, larynx, and upper trachea regions. The normalized eddy viscosity in these regions varies from 15-30%, thus indicating the need for a subgrid model in Case C and similarly Case B (not shown here). As the flow in Case A is laminar, the eddy viscosity adjusts itself, leading to negligible values. This further demonstrates the advantages of the WALE model [39], which tends to yield negligible values of ν_t in laminar flow regions without the need for a dynamic procedure as employed in the dynamic eddy viscosity model [55].

Figure 5.4 shows the transverse profiles of the normalized velocity magnitude ($|\langle \bar{\mathbf{u}} \rangle|/U_b$) at six cross sections A1-A2 through F1-F2 (see Fig. 5.3) to perform a quantitative comparison. We have also included results from a past fine-grid LES study with the full SimInhale geometry corresponding to Case B conditions [1] in Fig. 5.4 to assess the overall accuracy of the results from the present study. It is expected that a quantitative difference may occur

between Case B and the reference study, as even though these results correspond to the same value of Re , the exact locations of the six cross sections are not provided in the cited reference. The locations of extracted profiles are chosen to visually match the reference study.

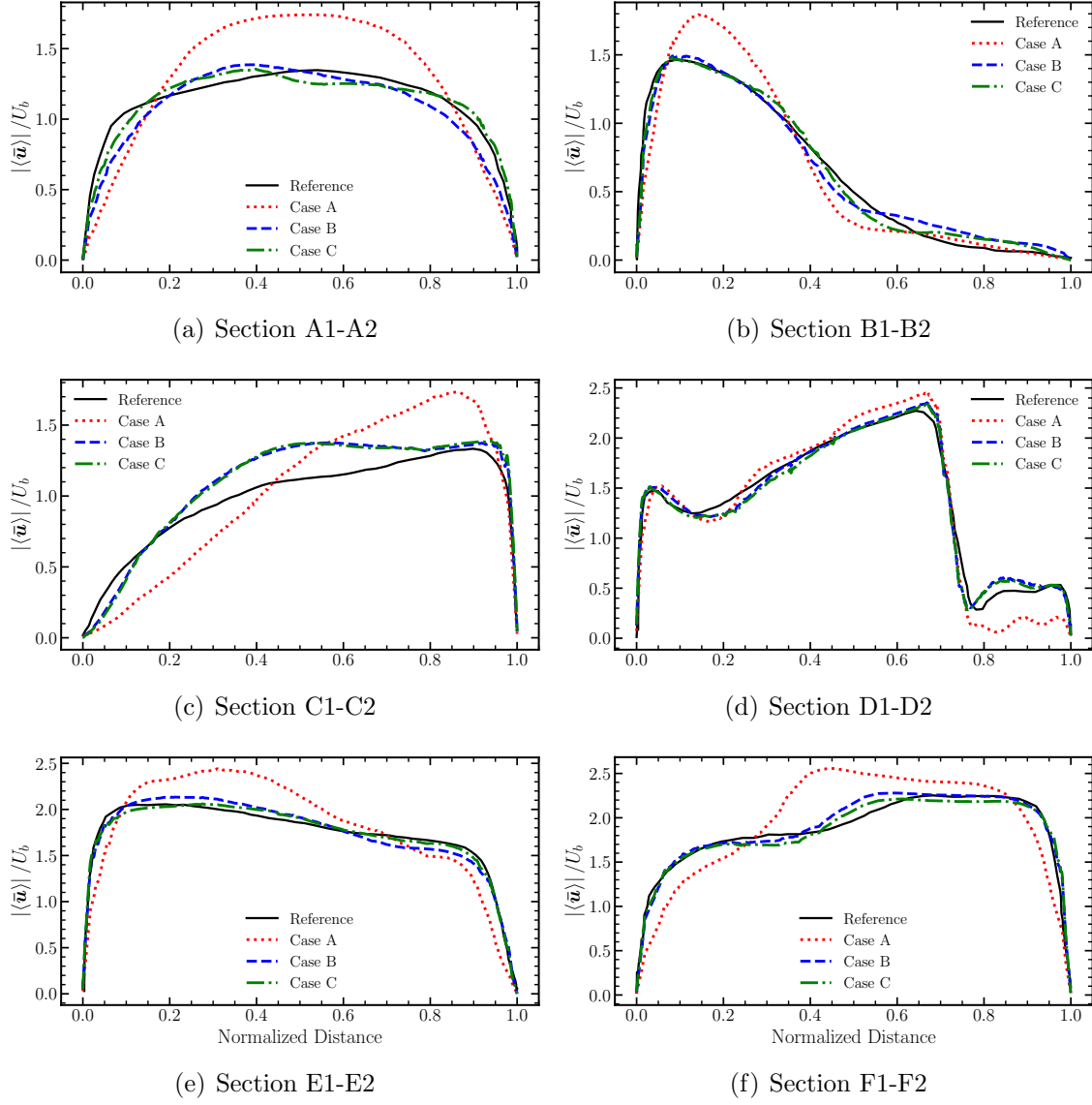


Figure 5.4 Time-averaged normalized velocity magnitude at six cross-sections comparing the three cases. The reference results correspond to a past LES study using the SimInhale benchmark geometry [1]

As discussed before, the profile at section A1-A2 in Case A, due to a lower value of Re , exhibits a quasi-laminar behavior. As this section is near the end of the inlet pipe along the axial direction, a nearly symmetric variation of profile is observed in all cases. With an

increase in Re , the profile tends to be flatter in the core region with an increased wall-normal gradient of the velocity magnitude. This is a well-known feature of wall-bounded flows. As expected, cases B and C, which are fully turbulent flows, the normalized profiles show a good agreement with the reference study.

At section B1-B2, we observe a significant change in the profile of $|\langle \bar{\mathbf{u}} \rangle|/U_b$, where asymmetric transverse variation occurs in all cases. This is due to the presence of flow expansion and recirculation near the posterior wall region. The effect of Re is particularly observed between cases A and B in terms of a flatter core region and a higher near-wall gradient near the anterior wall in Case B. A further increase in Re in Case C does not affect the profile significantly. This change in flow behavior from section A1-A2 to B1-B2 is consistent with the reference results [1].

At section C1-C2, which corresponds to the pharynx region, again a significant change in the profile of $|\langle \bar{\mathbf{u}} \rangle|/U_b$ occurs in all three cases due to a change in the curvature. This leads to a lower velocity magnitude near the anterior side compared to the posterior side. The profile from the low Re case exhibits further lower/higher values of $|\langle \bar{\mathbf{u}} \rangle|/U_b$ on the anterior/posterior sides compared to the other two high Re cases. Both high Re cases exhibit an overall good agreement with the reference results, which also exhibit the change in profile from the nasal cavity to the pharynx region. Further downstream at section D1-D2, a non-monotonic variation of $|\langle \bar{\mathbf{u}} \rangle|/U_b$ is observed, which is due to the the presence of shear layers at this location (see Fig. 5.3(a) and (d)). This behavior is observed in all cases, in good agreement with the reference results. The effect of Re is primarily evident in the vicinity of

the posterior wall, where lower values of $|\langle \bar{\mathbf{u}} \rangle|/U_b$ are observed in Case A compared to cases B and C. This implies a stronger shear layer on the posterior side, as discussed before (see Fig. 5.3(a) and (d)).

The effect of changes in the anatomy of the airway is evident from the profile of $|\langle \bar{\mathbf{u}} \rangle|/U_b$ at sections E1-E2 and F1-F2. In particular, at E1-E2, higher values are observed on the anterior side compared to the profile at section D1-D2 and at section F1-F2, where again, lower values are observed near the anterior wall. Overall, such a variation of the profile at these two sections is also in good agreement with the reference results. Similar to the other sections, the effects of Re are primarily evident from the differences in profiles of the low Re case and the other two high Re cases.

Note that the effects of Re in cases B and C are primarily observed in the inlet region and near the walls, because of the differences in the inlet velocity profile specified at the boundaries. However, beyond the larynx region, the effect of the inlet boundary condition on the normalized profiles is not observed, which has also been reported in the reference study [1]. However, low and high Re cases, i.e., Case A and Case B/C, show differences due to the quasi-laminar and fully turbulent conditions in these cases. Furthermore, high Re cases show good agreement with the reference study in capturing all the variations of the profiles throughout the truncated airway region.

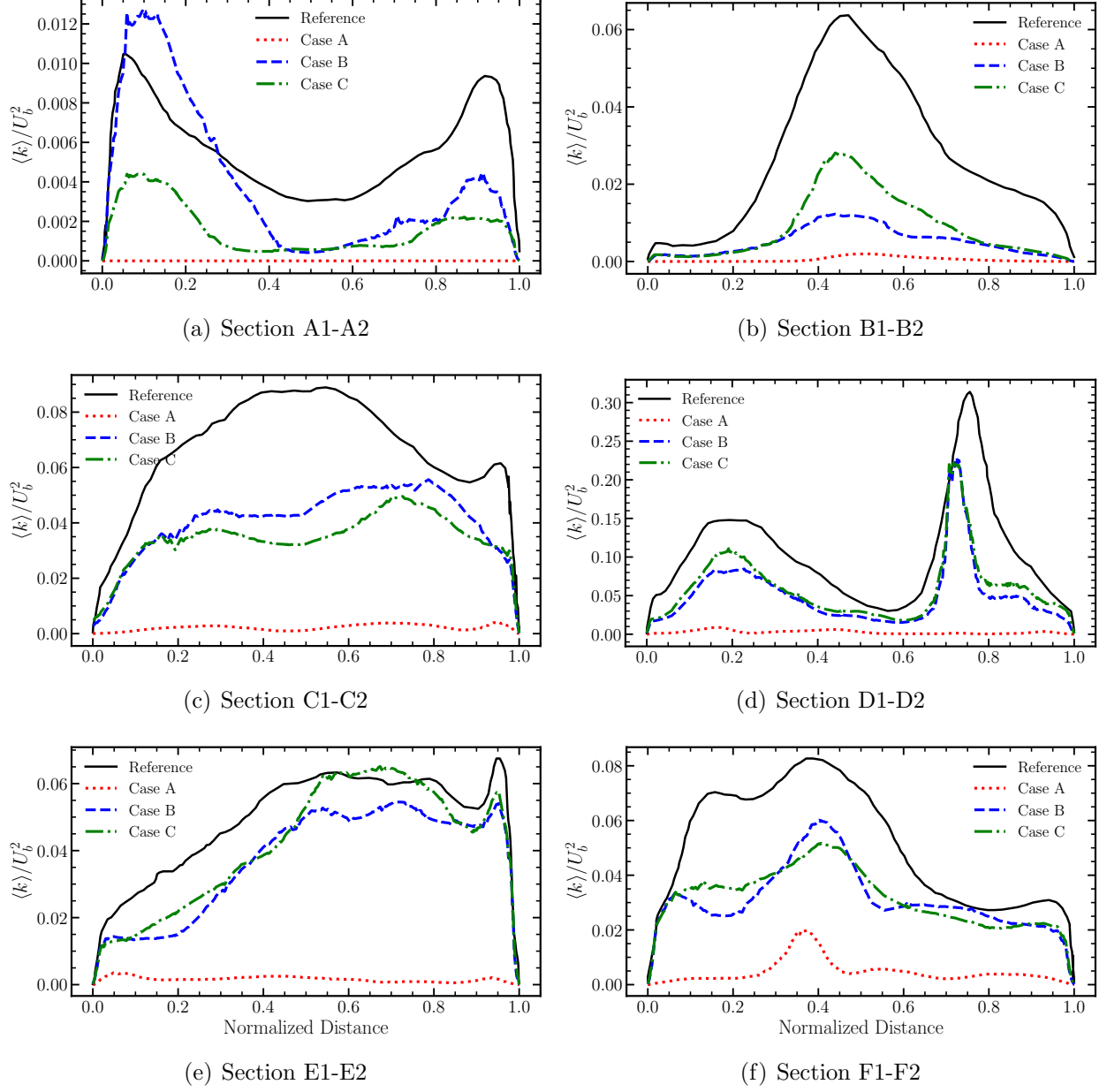


Figure 5.5 Time-averaged resolved turbulent kinetic energy at six cross-sections comparing the three cases. The reference results correspond to a past LES study using the SimInhale benchmark geometry [1]

A further assessment of the effects of Re is carried out in terms of the profiles of $\langle k \rangle / U_b^2$ at the six cross-sections, which are shown in Fig. 5.5. As the flow is quasi-laminar in

Case A, therefore, $\langle k \rangle / U_b^2$ is nearly negligible compared to the other two cases at all locations except at section F1-F2, which is close to the carina, where higher values of $\langle k \rangle / U_b^2$ occurs in the core region. On the other hand, the effect of Re in high Re cases, i.e., cases B and C, is observed in several sections throughout the airway region, with major differences occurring near the inlet and nasal cavity regions. Near the inlet region, asymmetry in the profile is observed in both cases, with peaks observed in the near-wall region. The peak value near the anterior wall is higher compared to the posterior wall, which is also observed in the reference study. The observed differences can be attributed to a much finer grid employed in the reference study compared to that used in the present study, which implies higher levels of TKE getting resolved in the reference study. For similar reasons, the near-wall peak values in Case C are lower compared to Case B, as the same computational grid is employed in these cases, thus leading to a higher resolved TKE in Case B compared to Case C.

At section B1-B2, the profile changes significantly compared to section A1-A2, leading to a peak of resolved TKE in the core region, in agreement with the reference case. However, at this location the peak value in Case C tends to be much higher compared to Case B, which can be attributed to higher level of production of TKE in this region in Case C. Note that this peak location corresponds to a shear layer at the outer edge of the recirculating region within the nasal cavity (see Fig. 5.3 (d) and (e)). At section C1-C2, a further increase in $\langle k \rangle / U_b^2$ occurs compared to the previous location due to flow constriction and curvature effects, which manifest into higher production of TKE. Further downstream, at section D1-D2, near the start of the trachea region, two peaks of TKE occur away from the anterior

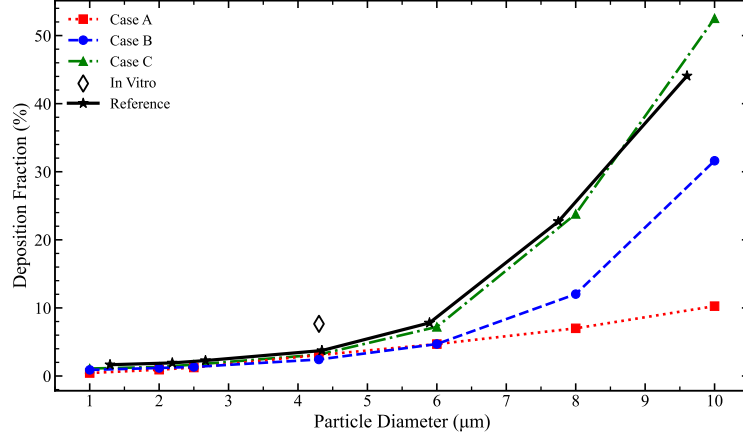
and posterior walls. This is due to the presence of a core jet region (see Fig. 5.3(d) and (e)), which is associated with two asymmetrical shear layers leading to production of TKE. The peak value of $\langle k \rangle / U_b^2$ is higher in all cases compared to the peak near the anterior wall, which is due to a stronger shear layer on the posterior side (see Figs. 5.3 and 5.4). The effect of Re in cases B and C tends to be minor at this location. Beyond this location, the shear layer expands, leading to a reduction in the production of TKE, which is evident in all cases. Additionally, a near-wall peak is observed in cases B and C, akin to the reference study on the posterior side. At section F1-F2 located closer to the carina, a peak of $\langle k \rangle / U_b^2$ occurs near the core in all cases, including Case A. This can be attributed to the flow acceleration and geometry bifurcation in this region, which manifests in the production of TKE.

The profiles of resolved TKE in cases B and C follow the trends observed in the reference study, where the TKE is affected by rapid variation in the flow field due to changes in the anatomy, effects of curvature, flow constrictions, etc. The normalized profiles from cases B and C tend to show similar quantitative variations at several locations. The observed differences can be attributed to the use of the same grid in both cases, as total TKE will be higher in Case C compared to Case B due to higher Re .

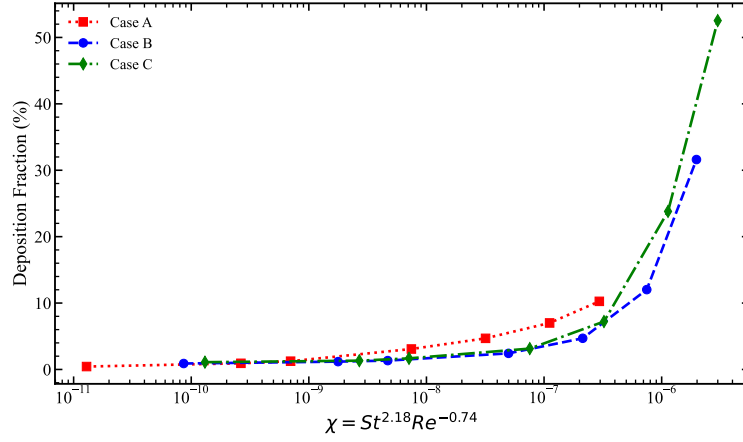
The results for mean velocity magnitude and resolved TKE discussed in this section illustrate the adequacy of the employed computational setup in accurately capturing the first- and second-order turbulence statistics. Next, we examine the characteristics of aerosol deposition with a particular focus on the effects of Q_v (Re) and d_p (St).

5.3 Aerosol Deposition Characteristics

We examine both global and local deposition of each particle stream. The deposition fraction is computed after $2T_f$ from the particle's injection time. The global deposition fraction is computed as a ratio of the total number of deposited particles in the computational domain and the total number of injected particles. The local deposition fraction is computed for seven segments of the computational domain formed by sections A1-A2 through F1-F2 (see Fig. 5.7(a)). It is defined as the ratio of the total number of deposited particles within a particular section and the total number of injected particles, and is obtained in a combined manner for all particle streams as well as the individual particle streams.



(a)



(b)

Figure 5.6 Global deposition fraction as a function of the particle diameter (a) and the non-dimensional deposition parameter (χ) [2] (b) for the three cases. The reference LES results and *in vitro* data [1] in subfigure (a) correspond to Case B ($Re = 3745$) conditions with the complete SimInhale geometry

Figure 5.6 (a) shows the total deposition fraction of the inhaled aerosol particles obtained for the three cases compared with the reference *in vitro* measurements and LES results [1]. The reference results correspond to the deposition fraction with the complete SimInhale geometry compared to the present study, where only a truncated geometry is modeled. Therefore, it is expected that the global deposition fraction obtained in the present

study from Case B will be lower than the reference results. In all cases, the deposition fraction increases monotonically and nonlinearly with d_p and Q_v (Re). The small-sized particles ($1\ \mu\text{m}$) exhibit low deposition in all cases, while large-sized particles ($10\ \mu\text{m}$) show high deposition fractions, particularly at higher Re . These trends are consistent with past studies, including the SimInhale benchmark, and confirm the size-dependent nature of the inertial impaction [1, 29, 33, 35, 68].

The global deposition results reveal the strong influence of the flow regime on the aerosol transport within the airway. In Case A, the deposition fraction increases gradually from 0% to 10% across the particle size range considered in this study. This modest rise reflects weak inertial forces under low Re conditions, allowing particles to follow airflow streamlines more closely within the core region of the airway (see Fig. 5.2), thus facilitating a deeper penetration of such particles in airways. The results for Case B tend to differ from Case A for $d_p > 5\ \mu\text{m}$, and show a sharper increase in deposition that approaches 30% with $d_p = 10\ \mu\text{m}$. In Case C, where the flow field has higher levels of turbulence intensity throughout the airway geometry, the influence of inertia is most pronounced. For particles with $d_p > 5\ \mu\text{m}$, the deposition fraction increases sharply and reaches about 55% at $10\ \mu\text{m}$. This exponential-like behavior of deposition with d_p reflects more intense inertial impaction, driven by higher flow accelerations and turbulence intensity in this case, particularly around anatomical constrictions like the glottis [29, 33]. These results underscore the importance of flow regime on the transport and deposition of aerosol particles in the upper airways.

In all three cases, the deposition fraction for small particles remains low and nearly indistinguishable, highlighting the dominance of diffusive transport in this size range. Larger particles, however, show a sharp transition toward inertia-driven behavior, a trend well documented in both *in silico* and *in vitro* studies [68]. The results in this study accurately capture this transitional behavior. The dependence of deposition fraction on Re highlights the importance of increasing inspiratory flow rates, disproportionately impacting the larger particles. In particular, a higher flow rate leads to increased Re and St , thereby increasing particle-wall collisions. Such a behavior is consistent with the findings of Golshahi et al. [2]. This is evident from Fig. 5.6(b) where we show the deposition fraction with respect to a non-dimensional deposition parameter ($\chi = St^{2.18} Re^{-0.74}$) proposed by Golshahi et al. [2]. We can observe that the three cases show a good collapse of the deposition fraction with this scaling.

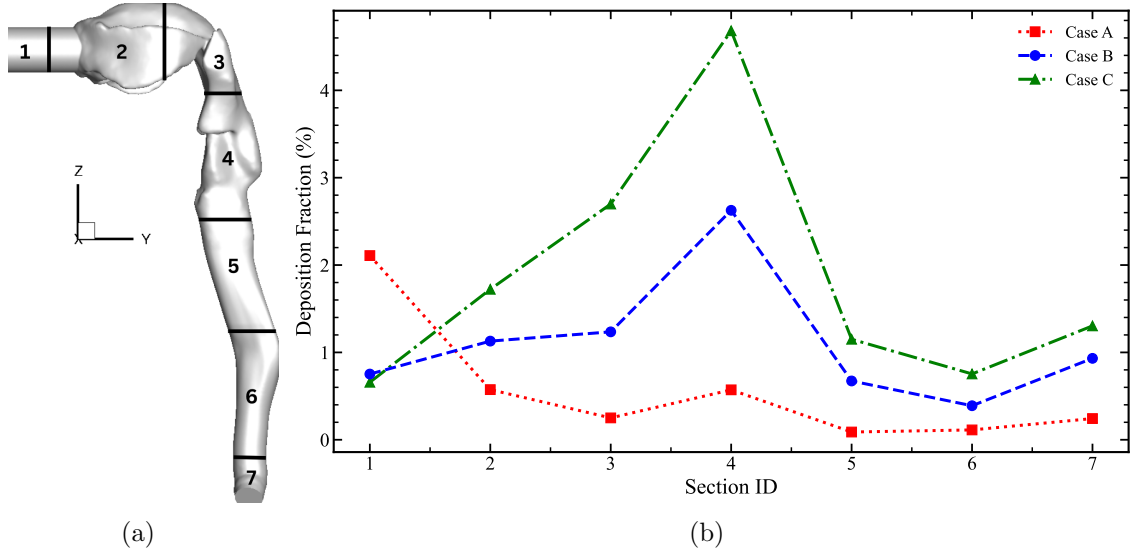


Figure 5.7 Schematic of airway showing seven sections, where local deposition fraction and average velocity magnitude and slip velocity are obtained (a) and local deposition fraction in three cases obtained from all seven particle streams (b)

The local deposition fraction quantifies the percentage of aerosol particles that adhere to specific regions of the airway geometry. This metric is essential for evaluating the efficiency and efficacy of aerosol-based drug delivery in different parts of the airways. We consider seven sections of the airways, which are shown in Fig. 5.7(a), to examine the local deposition. These sections correspond to critical anatomical regions, including the inlet, nasal cavity, pharynx, larynx, trachea, and carina.

As shown in Fig.5.7(b), the regional deposition varies strongly with an increase in Re . Here, the local deposition fraction is calculated for all particle streams together. In Case A with the lowest Re , the local deposition is generally lower than in cases B and C across most airway sections, consistent with the expectation that reduced inertia allows particles to follow core airflow streamlines more closely and penetrate deeper within airways (see Fig. 5.2

(a) and (d)). However, an exception is observed in Section 1, where Case A exhibits the highest local deposition. This may reflect weak initial momentum, causing early particle settling near the inlet. Beyond Section 1, the aforementioned variation continues in the laminar regime, with the inertial impaction being minimal, and more particles reach as far as the trachea and carina. Prior LES studies have similarly shown that laminar inhalation promotes more uniform particle distribution and allows penetration up to 5th generation bronchi, whereas high-flow, turbulent conditions tend to concentrate deposition in the upper airway, preventing deeper transport [30].

With an increase in Re from laminar to turbulent cases, however, the local deposition pattern changes significantly. In Case B, enhanced inertia causes more particles to impact the airway walls in the bends and narrow sections (nasal cavity, pharynx, larynx), reducing the portion of aerosol reaching the distal regions. In Case C, a large majority of the injected particles are trapped in the head and throat regions via impaction, with the laryngeal area in particular acting as a deposition hotspot. Consequently, far fewer particles survive to deposit at the trachea or carina at the highest flow rate. Such a variation of upstream-biased deposition with increasing Re or flow rate is a direct result of the stronger inertial forces and turbulence at higher Re and St , which drive particles into contact with the airway walls rather than allowing them to follow the core airflow streamlines around the airway bends. These results for the local deposition are consistent with past studies, which showed that higher inspiratory flow rates produce greater inertial impaction in curved and constricted sections of the airway, leading to elevated deposition in those regions [28, 30, 69].

In particular, the larynx emerges as a dominant deposition spot at high Re , as the fluid jet through the glottal constriction tends to collide with the downstream walls, causing a concentration of particle deposits in the laryngeal region. This is consistent with a higher deposition of particles in higher Re and St cases shown in Fig. 5.2.

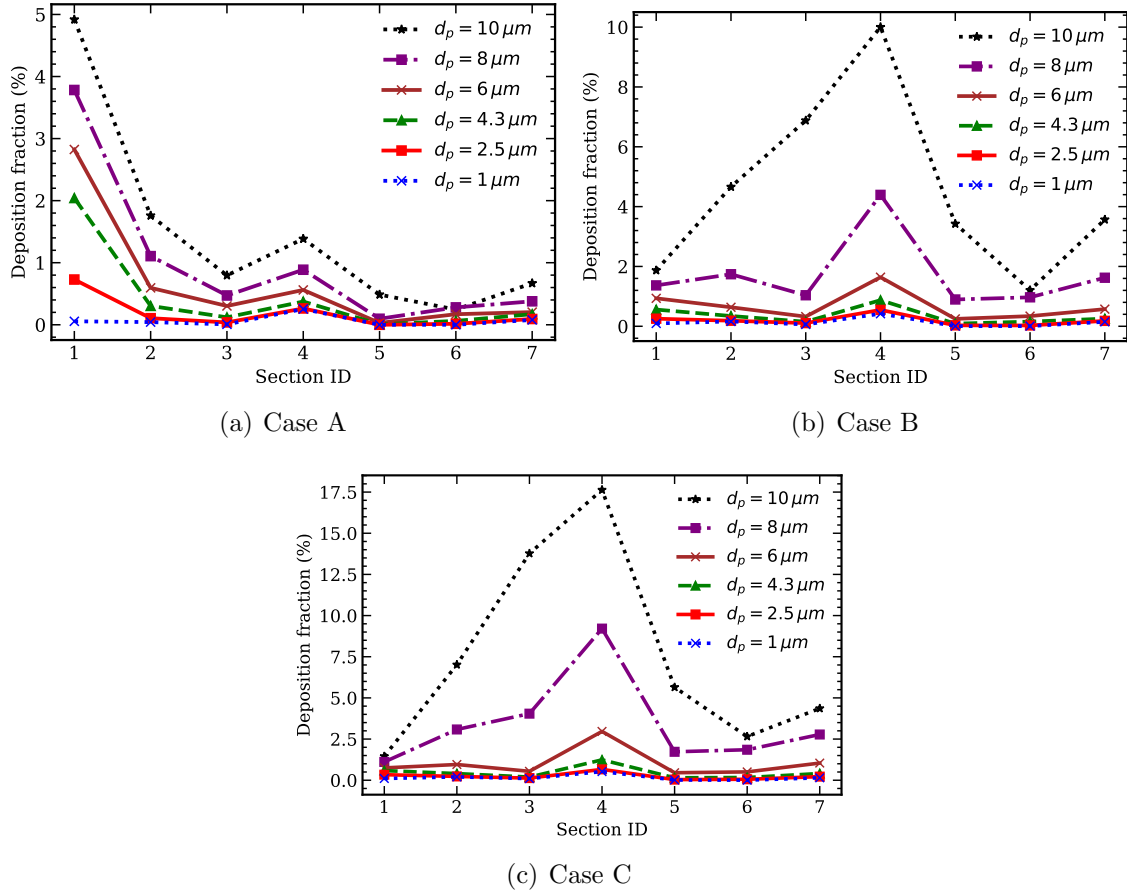


Figure 5.8 Variation of local deposition fraction in seven sections for six particle streams with different values of d_p

Now, we examine the effects of d_p or St on the local deposition within the airway in the three cases, which are shown in Fig. 5.8. For the sake of clarity, we show results for

six values of d_p , namely 1, 2.5, 4.3, 6, 8, and 10 μm . The overall variation observed for the combined local deposition fraction, as discussed before (see Fig. 5.7), remains consistent in each case with particle streams of different sizes.

In Case A, which has the lowest Re , maximum local deposition occurs in the first section, followed by a decrease till section 3. An abrupt increase occurs in the larynx region (section 4), which is followed by a gradual decrease and saturation in downstream sections. However, the effects of d_p are noticeable where the local deposition fraction tends to increase with d_p . For example, the 10 μm particle stream shows nearly a 5 times local deposition compared to the 2.5 μm particle stream through the airway sections.

Similar to the combined local deposition in cases B and C discussed before, qualitatively, each particle stream exhibits similar trends of the local deposition fraction through the seven sections of the airway. However, the local deposition increases nonlinearly within each section with respect to d_p , implying the effects of St . For example, the ratio of local deposition of 10 μm to 2.5 μm particle streams is about 25 in the laryngeal region (section 4), where maximum deposition occurs in Case B. This ratio increases to about 30 in Case C, thus indicating a nonlinear dependence of the local deposition on Re . In these cases, we observe an abrupt increase in local deposition in section 7, which is more pronounced for particle streams with higher d_p . Such a behavior occurs due to the bifurcation of the geometry, which introduces complex flow leading to the movement of particles closer to the wall, thus facilitating their deposition. It is also evident that the trend of highest deposition occurring in sections 2, 3, and 4 holds primarily for particles larger than 5 μm . For smaller

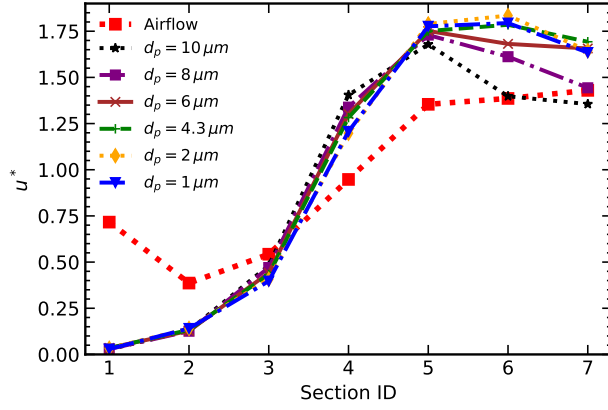
particles, this pattern is less consistent, and the deposition remains low and relatively uniform across the sections. These results emphasize that while Re and St affect the locally dominant deposition mechanisms within the airway, the complexity of the flow also affects the deposition of particles.

5.4 Aerosol Transport Statistics

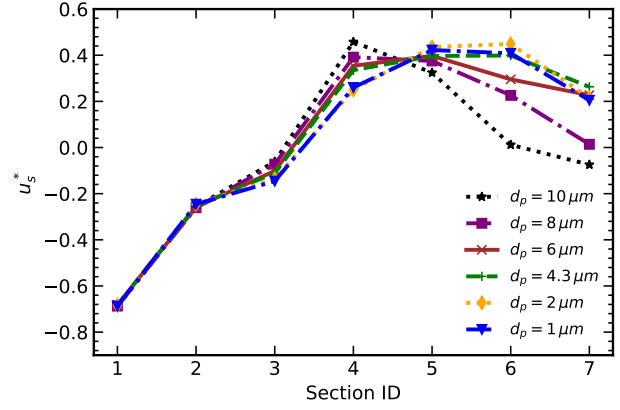
The local transport and deposition of aerosol particles depend upon the complexity of the flow field due to anatomical variations, inertia of the particles, gravity, and diffusion. As the present study focuses on the variation of Q_v and d_p , which implies a variation of Re and St , we examine the characteristics of inertial effects in terms of the statistics of the aerosol transport across different sections of the airway. Specifically, we obtain the sectional normalized average velocity magnitude (u^*) and normalized velocity fluctuation (u') of airflow and each particle stream. Here, $u^* = |\mathbf{u}|_{\text{avg,f/p}}/U_b$, where $|\mathbf{u}|_{\text{avg,f/p}}$ denote the sectional volumetric average of velocity magnitude of airflow or particles stream and $u_s^* = (|\mathbf{u}_{\text{avg,f}}| - |\mathbf{u}_{\text{avg,p}}|)/U_b$ denote the local slip velocity. In addition, the local normalized velocity fluctuation is expressed as, $u' = |\mathbf{u}|_{\text{r.m.s,f/p}}$, where the subscript ‘r.m.s.’ denotes the root-mean-square of the fluctuations.

Fig. 5.9 shows the first-order statistics of the aerosol transport and airflow in terms of u^* and u_s^* . In all three cases, u^* for the airflow decreases from section 1 to 2 and then increases gradually till section 5, and saturates afterwards. As discussed before, the decrease till section 2 occurs due to the expansion of the flow in the nasal cavity region from the inlet. Afterward, a gradual increase in u^* occurs due to the flow constriction. The saturation in

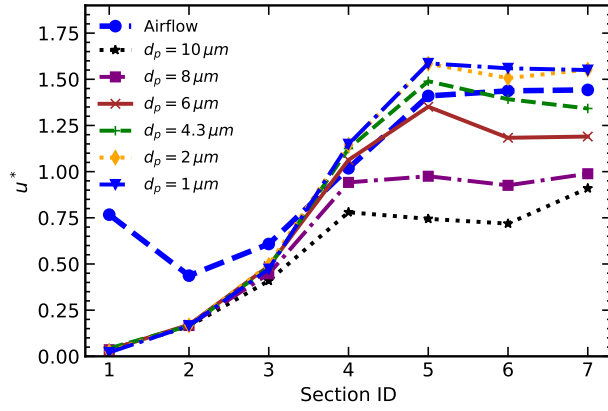
the final sections of the airway geometry is due to a nearly constant cross-section of the trachea region (see Fig. 5.3).



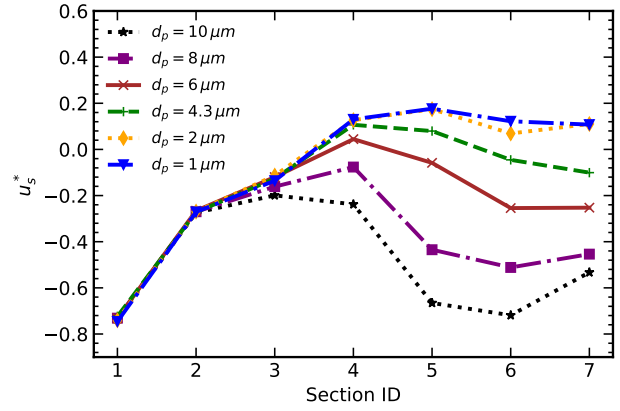
(a) Case A



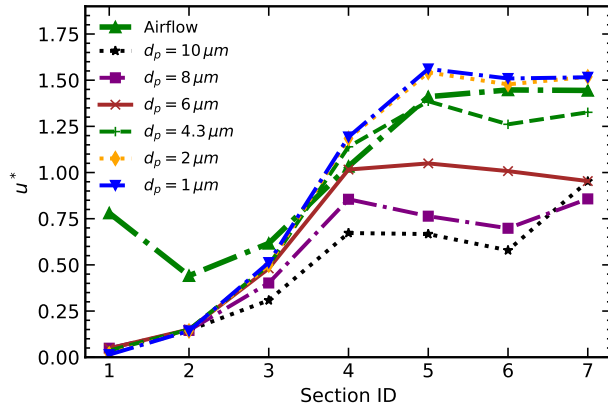
(b) Case A



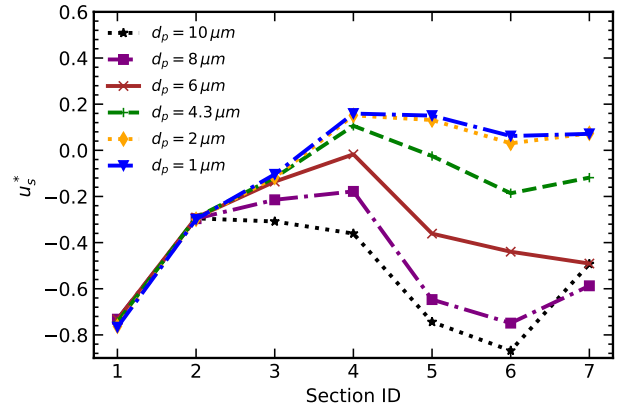
(c) Case B



(d) Case B



(e) Case C



(f) Case C

Figure 5.9 Normalized average velocity magnitude (u^*) of six particle streams and airflow for cases A (a), B (c), and C (e) and normalized slip velocity for cases A (b), B (d), and C (f) through various corresponding sections of airway at $2T_f$ after particle injection

The effects of particle inertia are apparent in all cases. For each particle stream, up to the pharynx region, u^* tends to collapse with lower values compared to the airflow leading to a negative slip velocity, u_s^* . Note that at this time, i.e., $2T_f$, section 1 has only those particles that are deposited, therefore, we observe negligible values of u^* in this section, which increases gradually in later sections, where the effects of d_p are also observed, particularly in the high Re cases. As discussed before, particles with $d_p \ll 5 \mu\text{m}$ tend to follow the average velocity of the airflow in the high Re cases, which, as discussed before, allows such particles to penetrate deeper within the airway. This is apparent from the variation of u_s^* for these particles in cases B and C, where u_s^* tends to be small in later sections of airway. On the other hand, particles with $d_p > 5 \mu\text{m}$ have lower u^* compared to the airflow and show dependence on d_p . This implies that such particles tend to lag the airflow, i.e., such particles are located much closer to the low-speed regions of the flow, leading to inertial impaction as the dominant mechanism of deposition. The effects of d_p can also be interpreted in terms of St , where for a particular case, an increase in d_p is associated with an increase in St . Therefore, we observe that the particle stream with the largest St leads to much smaller slip velocity, implying that such particles are located in the near-wall region with a higher probability of deposition (see Fig. 5.8).

Unlike the high Re cases, a different variation of u^* is observed in the quasi-laminar Case A, where all particles show a deviation away from the airflow velocity magnitude. Essentially, u^* of particles is consistently higher than that of the airflow beyond section 3, which relaxes towards the airflow in the trachea. However, this approach of u^* of particles

to that of airflow is dependent on d_p , with larger particles tending to approach u^* at a faster rate. This leads to a finite slip velocity even for the smaller-sized particles. Such a behavior can be attributed to the effects of wall-normal variation of airflow in the quasi-laminar case compared to the turbulent cases. The velocity profile in this case attains a shape with peak magnitude near the core of the airway and a thicker boundary layer (see Fig. 5.4), whereas turbulent cases tend to have a thinner boundary layer with a flatter core region (see Fig. 5.3). A higher slip velocity of smaller size particles imply such particles tend to remain within core regions of the airway, thus facilitating deeper penetration in airways. However, large-sized particles tend to have a smaller slip velocity, implying such particles tend to remain closer to the walls, thus having a higher probability of their deposition.

Figure 5.10 shows the variation of u' within the airway region of the airflow and the six particle streams. As expected, in Case A, which has quasi-laminar inlet conditions, the airflow fluctuations tend to be small and increase gradually towards the last section. This is consistent with the contours and profiles of the resolved TKE shown in Figs. 5.3 and 5.5 for this case. On the other hand, in the turbulent cases, we observe a gradual increase in u' of the airflow reaching a peak in the post-larynx region due to flow constriction. In later sections of the airway, the fluctuations tend to saturate due to expansion of the shear layer.

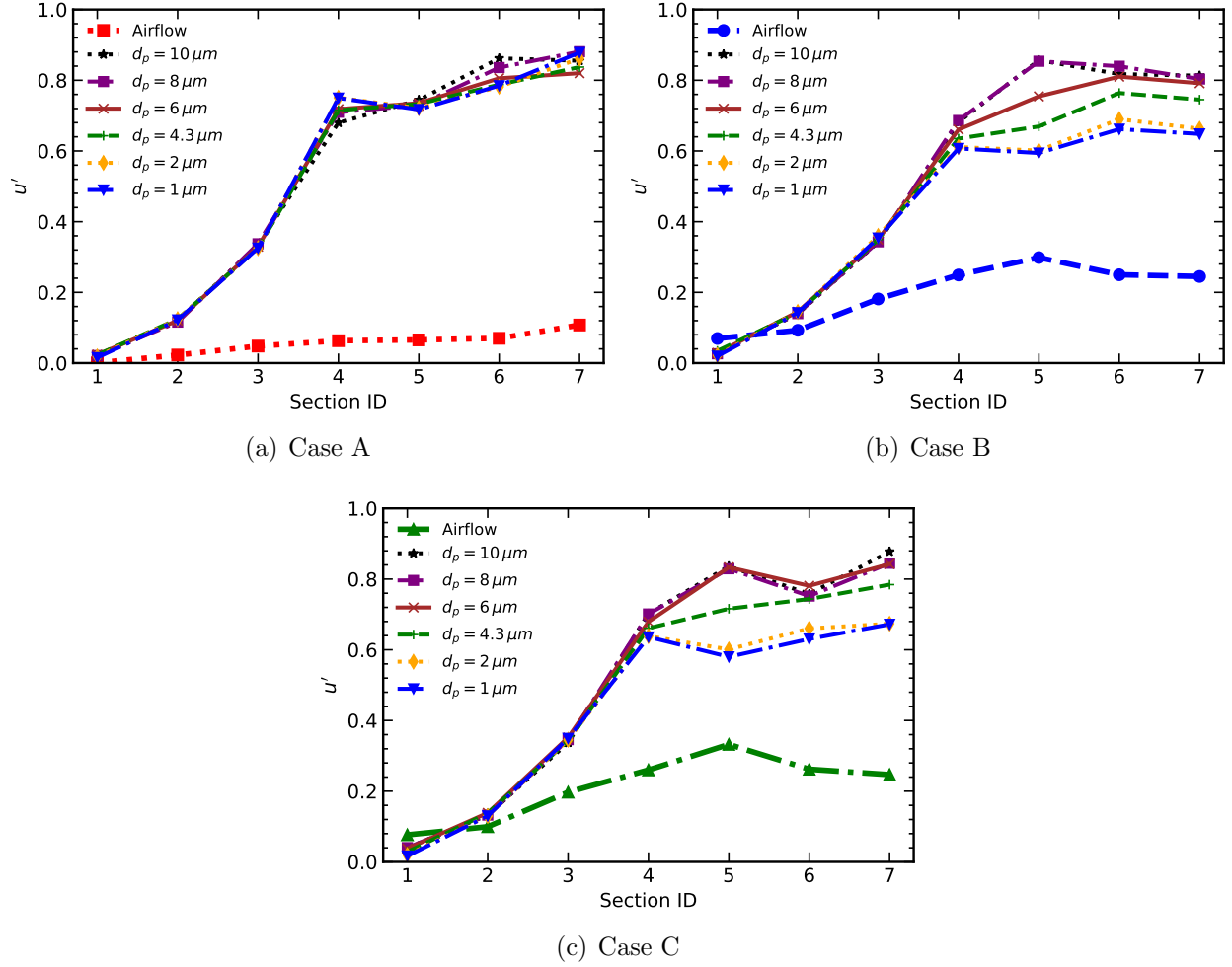


Figure 5.10 Normalized velocity fluctuations (u') of six particle streams and airflow for cases A (a), B (b), and C (c) through various sections of airway at $2T_f$ after particle injection

The velocity fluctuation of the particle streams shows a much different behavior in quasi-laminar and turbulent cases. In Case A, even though the airflow has smaller fluctuations throughout the airway, the particle streams exhibit a rapid increase in the fluctuations up to the larynx, after which a gradual increase occurs in the later parts of the airway. The value of $u' \sim 0.9$ indicates a significant fluctuation of the particle velocity, which can be

attributed to the effects of complex geometry, which lead to the presence of flow features such as flow acceleration, shear layers, recirculation, etc. These effects tend to be more pronounced compared to the effects of St , as in this case, we do not observe much variation due to the changes in d_p throughout the airway. However, turbulent cases, i.e., cases B and C, exhibit a different variation of u' , where we observe the effects of St in the later parts of the airway (after the larynx region). In particular, higher d_p particles exhibit higher fluctuations, which can be attributed to the effects of the inertia of particles. In all three cases, we observe higher values of u' of particles compared to the airflow. These results indicate that the geometrical complexity induces significant variations in the flow field, which manifests in the fluctuations of the particle velocity, an effect independent of St . However, with an increase in Re , the effects of particle inertia affect the variation of u' , indicating a St effect.

The first-and second-order statistics of particle velocity in comparison to the airflow statistics show that the aerosol transport discussed in this section is affected by the global non-dimensional parameters Re and St as well as the anatomy of the airway and wall-normal flow variation. These effects add to the complexity of deposition, which in turn can significantly affect the efficiency and efficacy of aerosolized drug delivery.

5.5 Summary

In this chapter, airflow and aerosol deposition and transport were examined in the human upper airways for monodisperse particle injections and different flow regimes. Cases with higher flow rates produced complex flow features such as vortical structures, shear layers, and more turbulence, which resulted in a strong influence on particle motion and de-

position. Examining particle size revealed that small particles ($St \ll 1$) followed streamlines, allowing for deeper penetration into the airway, while larger particles ($St = \mathcal{O}(10^{-2})$) experienced inertial impaction, which resulted in higher deposition. The time-averaged airflow results for velocity magnitude and TKE agreed well with the SimInhale benchmark case. Deposition analysis revealed that global deposition increased nonlinearly with both particle size and Re , and local deposition shifted to the nasal cavity and larynx at higher flow rates.

CHAPTER 6

AEROSOL DEPOSITION DURING POLYDISPERSE CONDITIONS

In this chapter, we examine the global and local aerosol deposition characteristics during polydisperse injection. Under such conditions, an injected particle stream comprises particles of varying sizes. We consider a mean particle diameter of $5\text{ }\mu\text{m}$ with a range of $0.1 - 9.9\text{ }\mu\text{m}$ and examine the effects of three types of injection distributions, namely, uniform distribution, normal distribution, and Rosin Rammler distribution. Furthermore, we examine the aerosol deposition at three values of the inflow Reynolds number (Re), leading to a total of nine cases. A detailed description of the injection parameters is provided in Sec. 4.2.2. In all cases, the aerosol injection is performed in the established airflow and, similar to the monodisperse cases, the deposition fraction is computed after two flow-through times, i.e., $2T_f$ from the particle's injection time.

The local deposition fraction (LDF) is calculated for seven distinct segments of the airway geometry, as illustrated in Fig. 6.1. It is defined as the ratio of the number of particles deposited within a specific section to the total number of particles injected into the domain. For the global deposition, we define three distinct metrics to fully characterize the deposition behavior across the range of particle sizes. First, the normalized global deposition fraction, denoted as GDF_1 , quantifies the deposition efficiency for specific particle size ranges. It is calculated as the ratio of the number of particles deposited for a given diameter range

(bin) and the total number of particles initially injected within that same bin. Second, the contribution of each size bin to the total deposition is quantified by GDF_2 . This metric is defined as the ratio of the number of particles deposited from a specific diameter bin and the total number of particles injected across all bins. Finally, the total global deposition fraction, GDF_3 , represents the overall deposition for each simulation case. It is computed as the ratio of the total number of deposited particles of all sizes and the total number of injected particles.

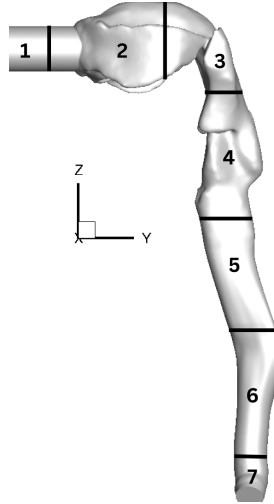


Figure 6.1 Schematic of the airway showing the seven sections where local deposition is measured

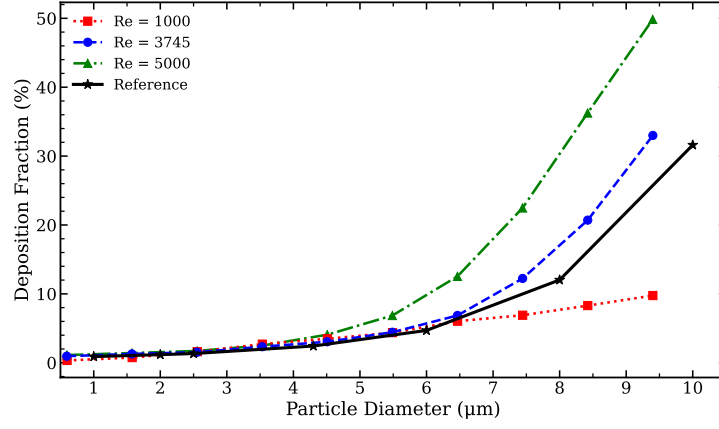
6.1 Global Deposition

Figure 6.2 shows the global deposition fraction (GDF_1) as a function of bins of particle diameter for the three particle size distributions. A strong, consistent dependence on both particle diameter (d_p) and Reynolds number (Re) is evident across all nine cases. For each

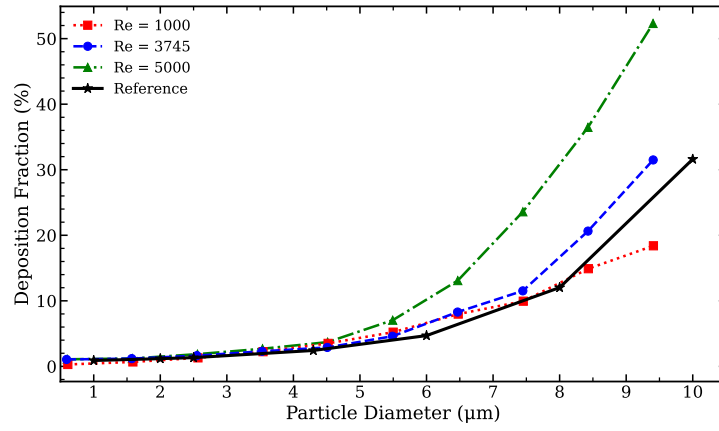
distribution type, the deposition fraction increases monotonically and nonlinearly with d_p . Small particles ($d_p < 5 \mu\text{m}$) exhibit low deposition fractions, while larger particles show a significantly higher propensity for deposition, especially at elevated flow rates. These trends are consistent with the monodisperse results and further demonstrate the role of inertial impaction as the dominant deposition mechanism.

The results also reveal the significant influence of the flow regime on deposition efficiency, irrespective of the initial particle size distribution. In the low Re cases ($Re = 1000$), the deposition fraction for all distributions increases gradually, reaching approximately 10% for the largest particles. This modest rise reflects weaker inertial forces, allowing most particles to follow the airflow streamlines. For the moderate Re case ($Re = 3745$), there is a sharper increase in deposition for particles with $d_p > 9 \mu\text{m}$, approaching 35%. Notably, the results for this case align closely with the reference monodisperse data, suggesting that the deposition efficiency of a given particle size is not significantly altered by the presence of other sizes in a polydisperse distribution under these flow conditions and that the solver is accurate for polydisperse distributions. In the highest Re case ($Re = 5000$), where the flow is more turbulent, the influence of inertia is the most pronounced. The deposition fraction increases sharply for larger particles, reaching approximately 50% at $9.5 \mu\text{m}$. This demonstrates the intensified inertial impaction driven by higher flow accelerations in the upper airway. Critically, the near-identical nature of the curves across the Gaussian, Rosin-Rammler, and Uniform distribution plots indicates that GDF_1 is largely independent of the

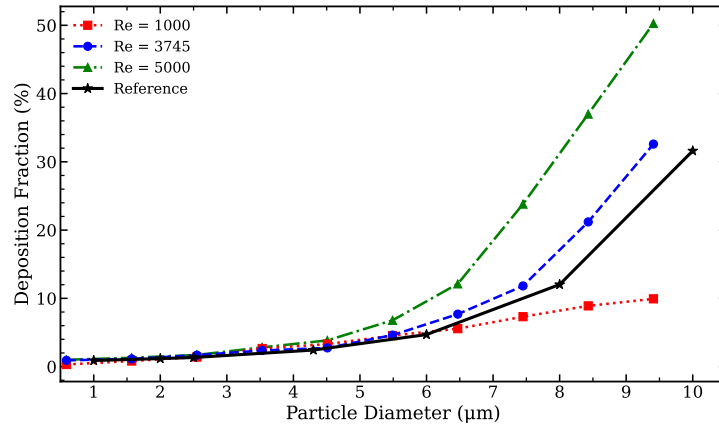
shape of the size distribution, being primarily governed by the particle's individual inertia and the flow characteristics.



(a) Gaussian

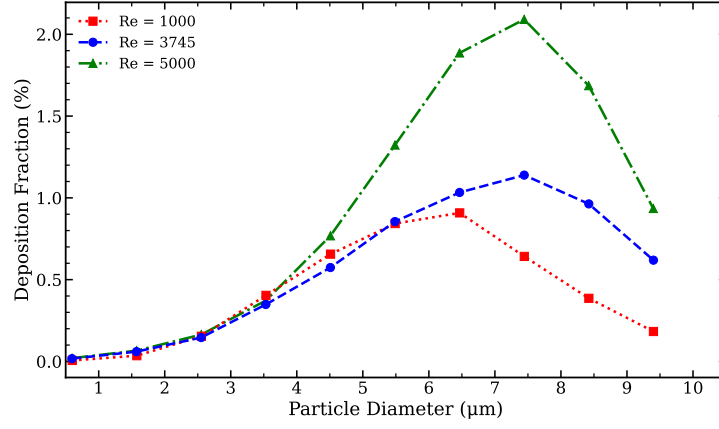


(b) Rosin-Rammler

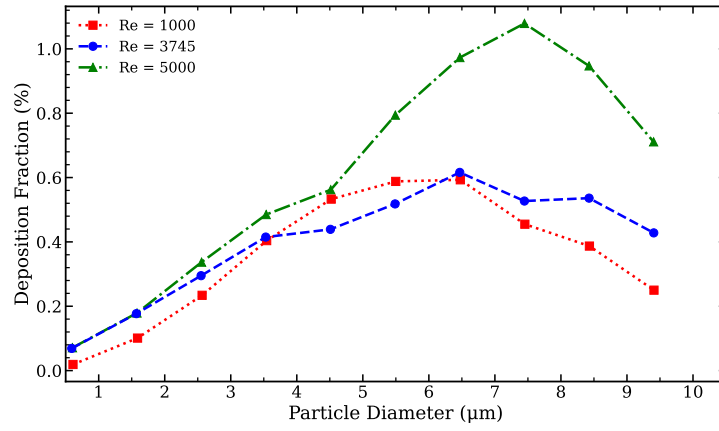


(c) Uniform

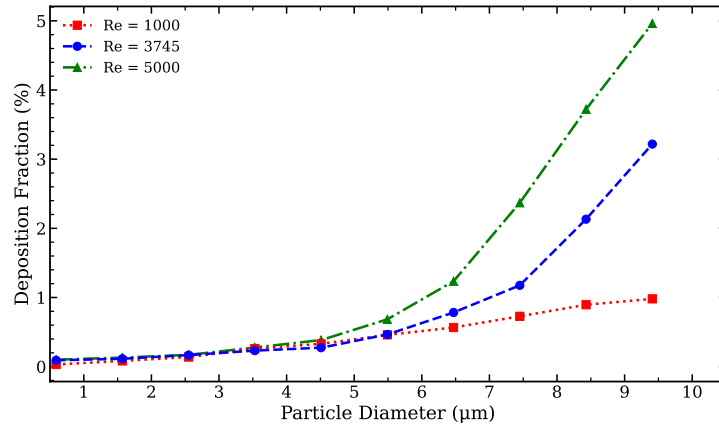
Figure 6.2 Variation of global deposition fraction (GDF_1) with respect to bins of particle diameter for Gaussian (a), Rosin-Rammler (b), and the Uniform distributions (c). Here, the reference curve corresponds to the monodisperse results at $Re = 3745$



(a) Gaussian



(b) Rosin-Rammler



(c) Uniform

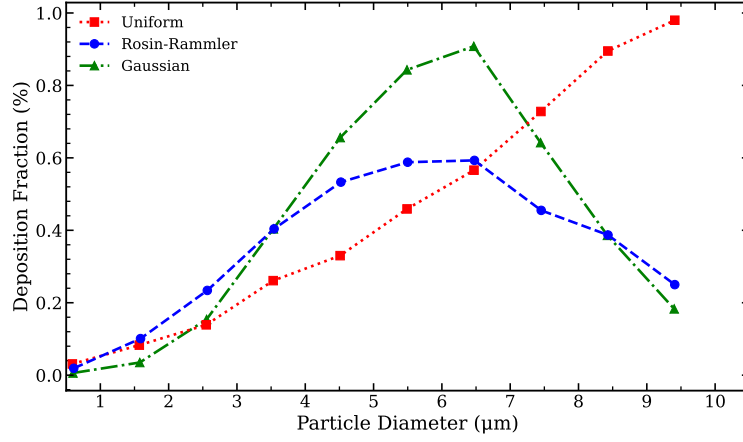
Figure 6.3 Global deposition fraction (GDF_2) as a function of the particle diameter normalized for Gaussian (a), Rosin-Rammler (b), and Uniform distributions (c)

In contrast, the contribution of each particle size bin to the total deposition, quantified by GDF_2 and shown in Fig. 6.3, is strongly dependent on the initial size distribution. For the Gaussian and Rosin-Rammler distributions, which are more representative of realistic aerosols, the deposition fraction does not increase monotonically. Instead, it rises to a peak before declining for the largest particle sizes. This behavior reflects the interplay between the increasing deposition efficiency of larger particles (as shown by GDF_1) and the decreasing number of particles present in those larger size bins. The peak in the GDF_2 curve represents the particle diameter range that contributes most significantly to the total deposited mass. For the Gaussian distribution at $Re = 5000$, this peak occurs around $d_p = 7.5 \mu m$. For the Uniform distribution, where the number of particles is constant across all bins, the GDF_2 curve follows the same monotonically increasing trend as the GDF_1 curve, as there is no decrease in particle count in each bin to counteract the rising deposition efficiency. This highlights that while the deposition probability of an individual particle is independent of the distribution, the overall deposition profile is a direct consequence of the aerosol's size characteristics.

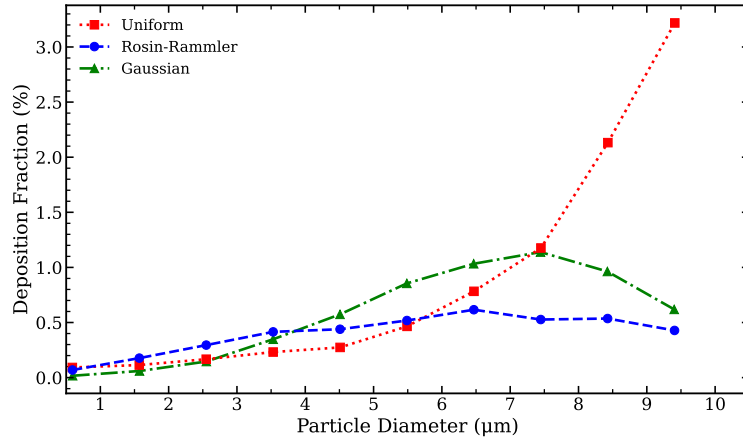
Furthermore, the effect of the Reynolds number on these deposition profiles is significant. For both the Gaussian and Rosin-Rammler distributions, an increase in Re not only elevates the magnitude of the peak GDF_2 value but also shifts the peak toward a larger particle diameter. For instance, in the Gaussian case, the peak contribution shifts from approximately $6.5 \mu m$ at $Re = 1000$ to $7.5 \mu m$ at $Re = 5000$. This is due to the higher inspiratory flow rates at higher Re , which disproportionately enhance the deposition of larger

particles, causing them to become the dominant contributors to the total deposited mass. For the uniform distribution, increasing Re simply amplifies the monotonically increasing trend, further steepening the curve and underscoring the heightened impaction efficiency for larger particles under more turbulent flow conditions.

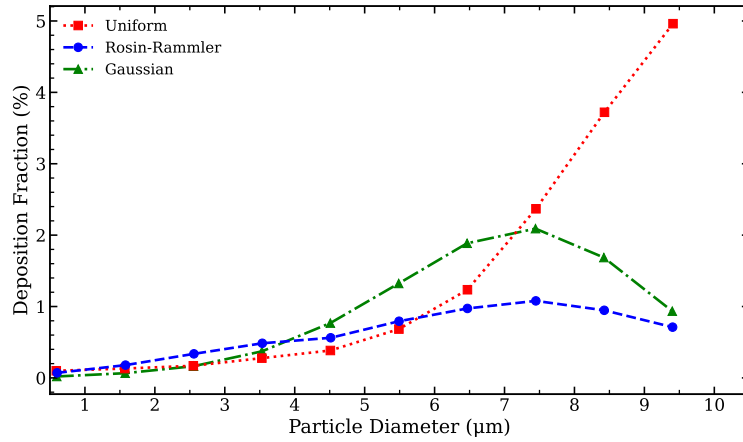
A complementary perspective is provided in Fig. 6.4, which facilitates a direct comparison of the GDF_2 profiles for the three distributions at each value of Reynolds number. In the lower flow rate case ($Re = 1000$), the Gaussian and Rosin-Rammler distributions exhibit qualitatively similar profiles, peaking near $d_p = 6.5 \mu m$, though the Gaussian distribution consistently shows a higher peak contribution across all Reynolds numbers. In contrast, the uniform distribution's profile shows a monotonically increasing behavior with particle diameter. As Re increases, the differences between the distributions are amplified. For the Gaussian and Rosin-Rammler cases, the post-peak drop-off in deposition becomes less severe at higher Re , suggesting that the enhanced deposition efficiency for the largest particles begins to partially counteract their lower population. The most significant effect is seen with the uniform distribution. Because it injects a high number of large particles, the steep increase in deposition efficiency at high Re leads to an exponential-like growth in its GDF_2 profile. Consequently, the gap between the deposition from large particles in the uniform case and the peak deposition from the more realistic distributions widens substantially at $Re = 3745$ and $Re = 5000$, demonstrating that the interplay between flow rate and the specific shape of the particle size distribution is critical in defining the overall deposition characteristics.



(a) Case A



(b) Case B



(c) Case C

Figure 6.4 Global deposition fraction (GDF_2) as a function of the particle diameter bin for $Re = 1000$ (a), 3745 (b), and 5000 (c)

Table 6.1 Particle deposition results for nine simulation cases, categorized by Reynolds number and particle size distribution type

Case	Distribution Type	Re	Particles Deposited	GDF ₃ (%)
A1	Gaussian	1000	4217	4.2
A2	Rosin-Rammler	1000	3564	3.6
A3	Uniform	1000	4471	4.5
B1	Gaussian	3745	5750	5.8
B2	Rosin-Rammler	3745	4019	4.0
B3	Uniform	3745	8648	8.6
C1	Gaussian	5000	9305	9.3
C2	Rosin-Rammler	5000	6134	6.1
C3	Uniform	5000	14030	14.0

Finally, the total global deposition fraction (GDF₃), summarized in Table 6.1, integrates these complex behaviors into a single metric of overall efficiency. A detailed analysis of these values reveals the distinct roles of both the particle size distribution and the flow regime. Across all three Reynolds numbers, a consistent trend is observed in deposition efficiency among the distributions. Rosin-Rammler yields the lowest GDF₃, followed by the Gaussian, with the Uniform distribution consistently producing the highest total deposition. This hierarchy is a direct reflection of the population of larger particles in each distribution. The Rosin-Rammler is skewed towards finer particles, while the uniform distribution contains a higher number of large particles, which have a higher probability of deposition via inertial impaction. However, the magnitude of the difference between these distributions is strongly modulated by the flow regime. In the low flow rate case (Re = 1000), the overall inertial forces are weak, and the differences in total deposition are minimal across different distributions, with all three cases falling within a narrow range (3.6% to 4.5%). In this regime, the higher population of large particles in the uniform leads to only a slight increase

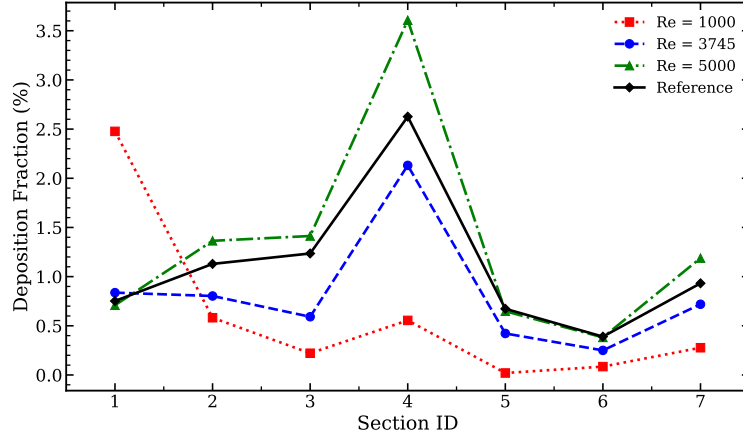
of GDF_3 . As the flow rate increases, this behavior changes. At $Re = 5000$, the differences are magnified among distributions; GDF_3 for the uniform distribution (14.0%) is now over 1.5 times that of the Gaussian (9.3%) and more than double that of the Rosin-Rammler (6.1%). This demonstrates that the increased flow turbulence and higher particle inertia disproportionately amplify the impact of the larger particles present in the uniform distribution. Therefore, while the deposition of any single particle is governed by its inertia, the total deposition of a polydisperse aerosol is critically dependent on the number of large particles within the initial distribution, an effect that becomes overwhelmingly dominant under turbulent inspiratory conditions.

6.2 Local Deposition

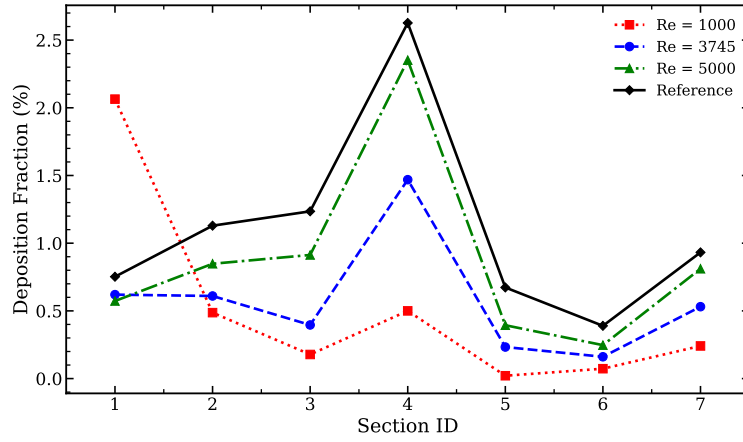
The local deposition fraction quantifies the percentage of aerosol particles that adhere to specific regions of the airway geometry. This metric is essential for evaluating the efficiency and efficacy of aerosol-based drug delivery in different parts of the airways. We consider seven sections of the airways, as shown in Fig. 6.1, to examine the local deposition. These sections correspond to critical anatomical regions, including the inlet, nasal cavity, pharynx, larynx, trachea, and carina.

The regional deposition patterns for each of the three distributions are presented in Fig. 6.5, illustrating a strong dependence on the Reynolds number. At the lowest flow rate ($Re = 1000$), deposition is highest in the first section (inlet) for all distribution types, followed by a significant decrease in subsequent sections. This indicates that under low-inertia conditions, weak initial momentum leads to early particle settling near the inlet,

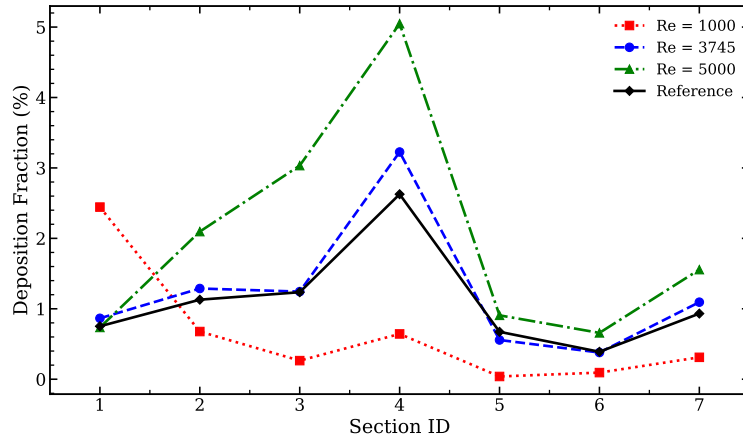
while the remaining particles are able to follow the core airflow streamlines and penetrate deeper into the airways with minimal further deposition. This behavior is consistent with the monodisperse aerosol injection findings and promotes a more uniform particle distribution in the distal regions.



(a) Gaussian



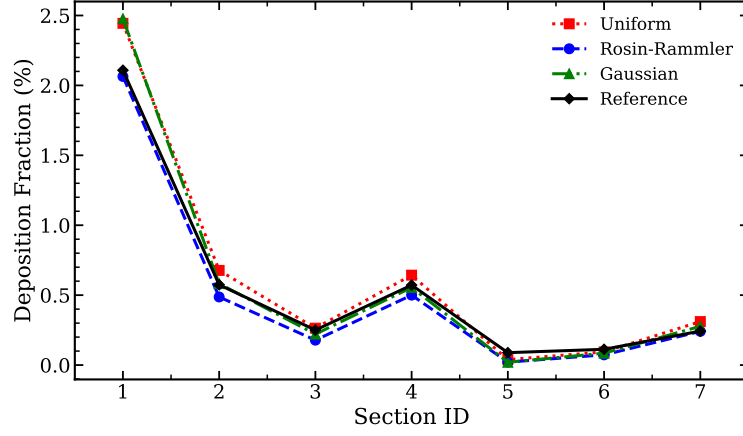
(b) Rosin-Rammler



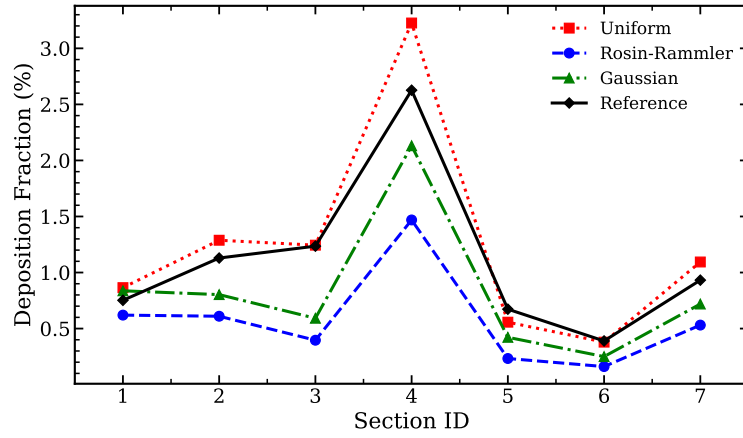
(c) Uniform

Figure 6.5 Variation of local deposition fraction in seven sections for Gaussian (a), Rosin-Rammler (b), and Uniform distributions (c). Here, the reference corresponds to local deposition at $Re = 3745$ with monodisperse distribution

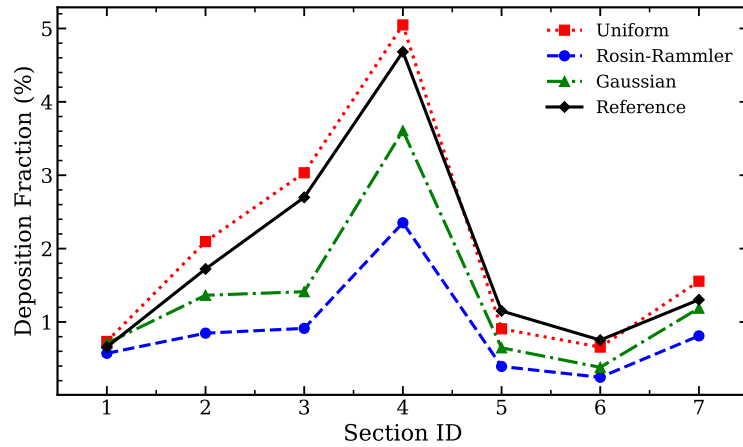
With an increase in flow rate leading to $Re = 3745$ and $Re = 5000$, the deposition pattern changes fundamentally. For all three distributions, the laryngeal region (Section 4) emerges as a pronounced deposition hotspot. The magnitude of deposition in this section increases substantially with Re , driven by intense inertial impaction as the airflow accelerates through the glottal constriction. For the uniform distribution at $Re = 5000$, this effect is particularly pronounced, with over 5% of all injected particles depositing in this single section. This upstream-biased deposition at higher flow rates significantly reduces the number of particles available to penetrate to the trachea and carina regions (Sections 5-7). These results confirm that for polydisperse aerosols, as with monodisperse, higher inspiratory flow rates concentrate deposition in the upper airway, with the larynx acting as the primary filter. The local deposition profiles for the polydisperse cases at $Re = 3745$ also show a strong qualitative agreement with the reference monodisperse data, reinforcing the validity of these trends.



(a) $Re = 1000$



(b) $Re = 3745$



(c) $Re = 5000$

Figure 6.6 Variation of local deposition fraction in seven sections for $Re = 1000$ (a), 3745 (b), and 5000 (c). Here, the reference corresponds to local deposition at $Re = 3745$ with monodisperse distribution

A more direct comparison of the effect of the particle size distribution on local deposition is presented in Fig. 6.6. At the low flow rate ($Re = 1000$), the local deposition profiles for all three polydisperse distributions and the monodisperse reference case are nearly indistinguishable. The convergence of these profiles demonstrates that when inertial forces are weak, the specific shape of the particle size distribution has a negligible impact on regional deposition patterns. In this laminar regime, deposition is primarily governed by the flow itself, and the subtle differences in particle inertia across the distributions are insufficient to cause divergent trajectories, implying that for low-flow inhalation, the choice of distribution model may not be critical for predicting regional deposition.

As the flow becomes moderately turbulent at $Re = 3745$, clear distinctions emerge between the distributions, particularly in the anatomically complex regions from Section 2 to Section 5. A consistent hierarchy is established; the Rosin-Rammler distribution yields the lowest local deposition, followed by the Gaussian, and then the uniform distribution, which shows the highest deposition. This trend is a direct consequence of the varying populations of large, high-inertia particles in the injected distribution of particles. Furthermore, the upstream deposition trends diverge. For the Rosin-Rammler and Gaussian distributions, which have fewer large particles, deposition decreases from Section 1 to 3 as their smaller, less-inertial dominant particles are better able to follow the flow streamlines and penetrate deeper within the upper airway. In contrast, the uniform and monodisperse cases, both characterized by an abundance of large particles, show an increase in deposition through these

same sections, culminating in a pronounced laryngeal peak (Section 4) that is significantly higher than that of the other two distributions.

In the highest flow rate case ($Re = 5000$), these differences are magnified further. The deposition hierarchy (Rosin–Rammmler < Gaussian < Uniform) becomes even more pronounced, especially in the laryngeal hotspot, where the uniform distribution’s peak is now substantially higher than all other cases. A significant shift occurs in the upstream behavior of the Rosin-Rammmler and Gaussian distributions; instead of decreasing, deposition now shows a slight increase from Section 1 to 3. This reversal suggests that even the mid-diameter range particles, not just the largest ones, begin to experience significant inertial impaction under these highly turbulent conditions. Meanwhile, the deposition profiles for the uniform and monodisperse cases remain qualitatively similar, showing a quasi-linear increase from the inlet to the laryngeal peak, as their behavior is overwhelmingly dominated by high-inertia particles. The key finding from this is that the initial particle size distribution is a critical parameter for predicting local deposition, but its influence is strongly coupled with the flow regime. In laminar flow, its effect is minimal, but in the moderate and high turbulent conditions, it dictates the magnitude and location of regional deposition hotspots.

6.3 Summary

In this chapter, global and local deposition were examined for three different PSDs at three different inlet flow rates. The results show that for a given particle bin size, the global deposition efficiency (GDF_1) is governed directly by the particle inertia and Re , independent of the PSD used. For total deposition across all particle sizes (GDF_3) and local

deposition, the uniform distribution produced the highest amount of deposition, the Rosin-Rammler distribution had the lowest deposition, and the Gaussian had a total deposition in between. This trend was observed since total deposition by particle size (GDF_2) peaks at approximately $7\text{ }\mu\text{m}$ and then declines for Rosin-Rammler and Gaussian, and increases monotonically for the uniform case, even for larger particles. For local deposition, similar trends were observed for higher flow rates, especially in the larynx region, where a clear hierarchy emerged for deposition magnitude: Rosin-Rammler < Gaussian < Uniform. However, at lower flow rates, deposition is minimal across all three distributions, with the PSD having no impact on the deposition trends.

CHAPTER 7

AEROSOL DEPOSITION DURING REALISTIC BREATHING CYCLE

In this chapter, we investigate airflow and particle deposition under realistic, time-varying breathing conditions. Unlike the steady inflow cases examined previously, the cyclic breathing model captures the full inhalation–exhalation cycle, allowing assessment of the transient flow features and their impact on aerosol transport. Three cases are analyzed: steady-state inhalation, steady-state exhalation, and a complete cyclic breathing condition. The airflow dynamics are first examined to examine the unsteady velocity profiles and flow asymmetries that arise throughout the cycle. Subsequently, both global and local aerosol deposition characteristics are evaluated for monodisperse injection of seven streams of particles as discussed in Chapter 5 to quantify how the temporal variations in the inlet flow rate and direction influence overall deposition efficiency and spatial distribution within the airways.

7.1 Description of Airflow

7.1.1 *Cyclic Breathing*

To understand the effects of the unsteady breathing pattern on the airflow, we first examine the instantaneous flow features at different phases of the cycle. Figure 7.1 shows the transverse profiles of the instantaneous velocity magnitude ($|U|$) at six cross-sections

(A-F). The analysis is performed at three distinct time instances, $t=6$ s, corresponding to the approximate peak of the inhalation phase, $t=8$ s, corresponding to the approximate peak of the exhalation phase, and $t=10$ s, representing the end of the exhalation cycle, where the inlet flow rate is nearly zero. These profiles are compared with time-averaged results from a steady-state inhalation case at $Re = 3745$, which serves as a reference to highlight the key differences between transient and steady-state airflow dynamics.

The profile at section A, located near the end of the inlet along the axial direction, exhibits a nearly symmetric variation in all cases. The profile at $t = 6$ s, which corresponds to the peak inhalation with an average Re of 1170, exhibits a turbulent flow-like profile with a relatively flat core region and high near-wall gradients. This behavior is qualitatively similar to the fully turbulent steady-state reference case ($Re = 3745$), although the peak velocity magnitude is significantly lower, consistent with the reduced instantaneous flow rate. In contrast, the profiles during the exhalation phase are different. At $t = 8$ s, during peak exhalation (average $Re = 605$), the value of the axial velocity is much lower and the profile is more parabolic in shape with asymmetric behavior. By the end of the cycle at $t = 10$ s, the flow has nearly ceased, with the velocity magnitude being close to zero across the entire cross-section. These results demonstrate the effects of cyclic breathing conditions imposed at the inflow boundary. Furthermore, the variations in the profile over time indicate the changing nature of the flow, which shows a turbulent-like profile during inhalation to a quasi-laminar profile during exhalation.

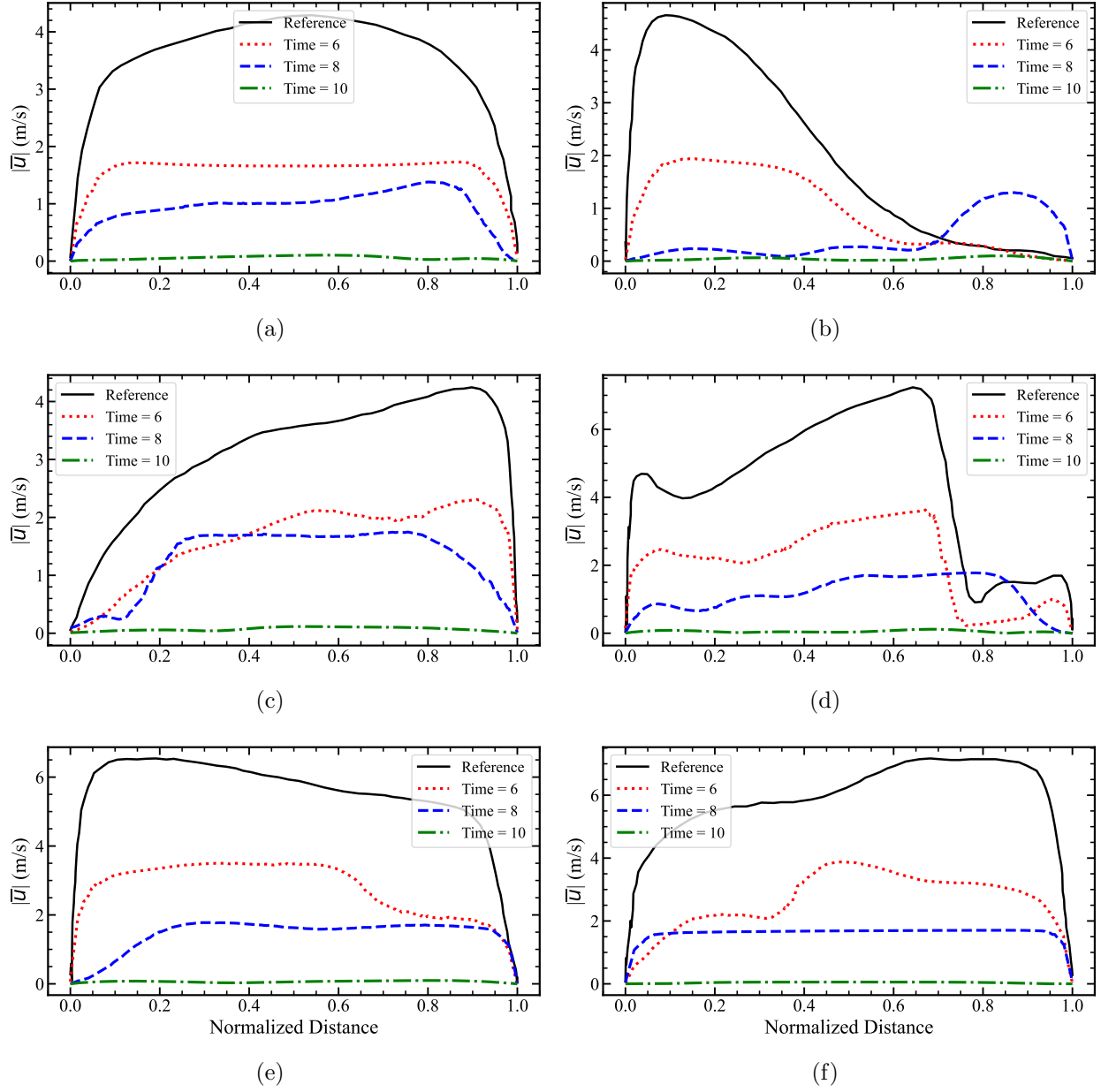


Figure 7.1 Velocity magnitude at six cross-sections (A–F) comparing different times to the reference case. Here, the reference results corresponds to steady inhalation at $Re = 3745$

In section B, a significant change in the profile of the velocity magnitude is observed due to the flow expansion in the nasal cavity. The profile at $t = 6$ s (inhalation) be-

comes highly asymmetric, mirroring the behavior of the steady-state reference case with a high-velocity region concentrated near the anterior wall. This indicates the formation of a prominent separation and recirculation zone near the posterior wall. In contrast, the profile at $t = 8$ s (exhalation) also exhibits an asymmetric profile, but with the velocity peak skewed toward the posterior wall, opposite to the inhalation case. This flow reversal is a direct consequence of the reversed flow direction. During exhalation, the flow converges from the wider pharynx region towards the inlet, causing the main flow path to attach to the posterior side of the nasal cavity. However, the overall velocity magnitude and the degree of asymmetry are smaller than during the inhalation phase, indicating that the prominent separation zone seen during inspiration does not fully form during expiration.

Further downstream at section C, which corresponds to the pharynx region, the effect of the airway curvature is evident. The profile during the inhalation cycle at $t = 6$ s is asymmetric, with higher velocity magnitude toward the posterior side, a trend that is consistent with the steady-state reference case. This demonstrates that even under unsteady conditions, the geometry dictates the primary flow path and momentum distribution during inhalation. The exhalation profile at $t = 8$ s, while significantly more uniform than the inhalation profile, shows a subtle asymmetry with a slightly higher velocity gradient near the posterior wall compared to the anterior side. This indicates that even at the lower exhalation flow rate, the airway curvature still exerts a minor influence on the velocity distribution.

In section D, located near the laryngeal constriction, the flow accelerates to form a glottal jet. The steady-state reference profile shows a distinct non-monotonic shape with two

peaks, which are signatures of the shear layers bordering the jet core. The profile at $t = 6$ s also exhibits this double-peaked structure, confirming the presence of a strong, jet-like flow during the peak inhalation phase. Conversely, during peak exhalation ($t = 8$ s), no such jet structure is apparent. The velocity profile exhibits lower values and exhibits a simple, broader peak, indicating that the flow does not form the strong shear layers evident during inhalation.

The effect of changes in the anatomy of the airway is evident from the profiles at sections E and F, which show the evolution of the flow in the trachea. The inhalation profile at $t = 6$ s continues to show complex, asymmetric features that qualitatively follow the high-Re steady-state results. This indicates that the flow structures generated upstream, particularly the glottal jet, persist and evolve throughout the upper trachea. In contrast, the exhalation profiles at $t = 8$ s and $t = 10$ s exhibit a lower magnitude of velocity, thus reinforcing that the flow field during exhalation is dynamically much simpler than during inhalation.

Overall, these results demonstrate a contrast between the airflow dynamics of the inhalation and exhalation phases within a single breathing cycle. The inspiratory phase, even at a lower instantaneous Re than the steady-state case, reproduces all the key complex flow features, including separation, skewed profiles due to curvature, and a strong glottal jet. The expiratory phase, however, is characterized by a much weaker and less complex, quasi-laminar flow field that lacks these prominent features. This temporal asymmetry in

flow behavior is critical for affecting the transport and deposition of particles under realistic breathing conditions.

7.1.2 *Steady Inhalation and Exhalation*

Next, we examine the time-averaged features of the steady-state inhalation and exhalation cases to understand how the mean flow fields differ from the fully turbulent reference case. Figure 7.2 shows the transverse profiles of the time-averaged velocity magnitude, normalized by the bulk inlet velocity ($\langle \bar{U} \rangle / U_b$), at six cross-sections (A–F). This normalization enables a direct comparison of the profile shapes, independent of the flow rate differences between the cases.

At section A, which is near the inlet, the inhalation case ($Re = 1170$) exhibits a nearly symmetric profile with a mildly flattened core, characteristic of a quasi-turbulent inflow. In contrast, the exhalation case ($Re = 605$) shows a distinct asymmetry, with the velocity peak shifted toward one side of the inlet. The fully turbulent reference case ($Re = 3745$) displays a flatter core, indicative of a developed turbulent flow. These results confirm that while the values of Re are lower during inhalation and exhalation, the anatomical changes immediately downstream of section A affect the flow field at this section, leading to a velocity profile much different compared to a laminar flow. This is more noticeable for the exhalation case, which is expected as the flow field is reversed, thus leading to the observed asymmetry in the velocity profile.

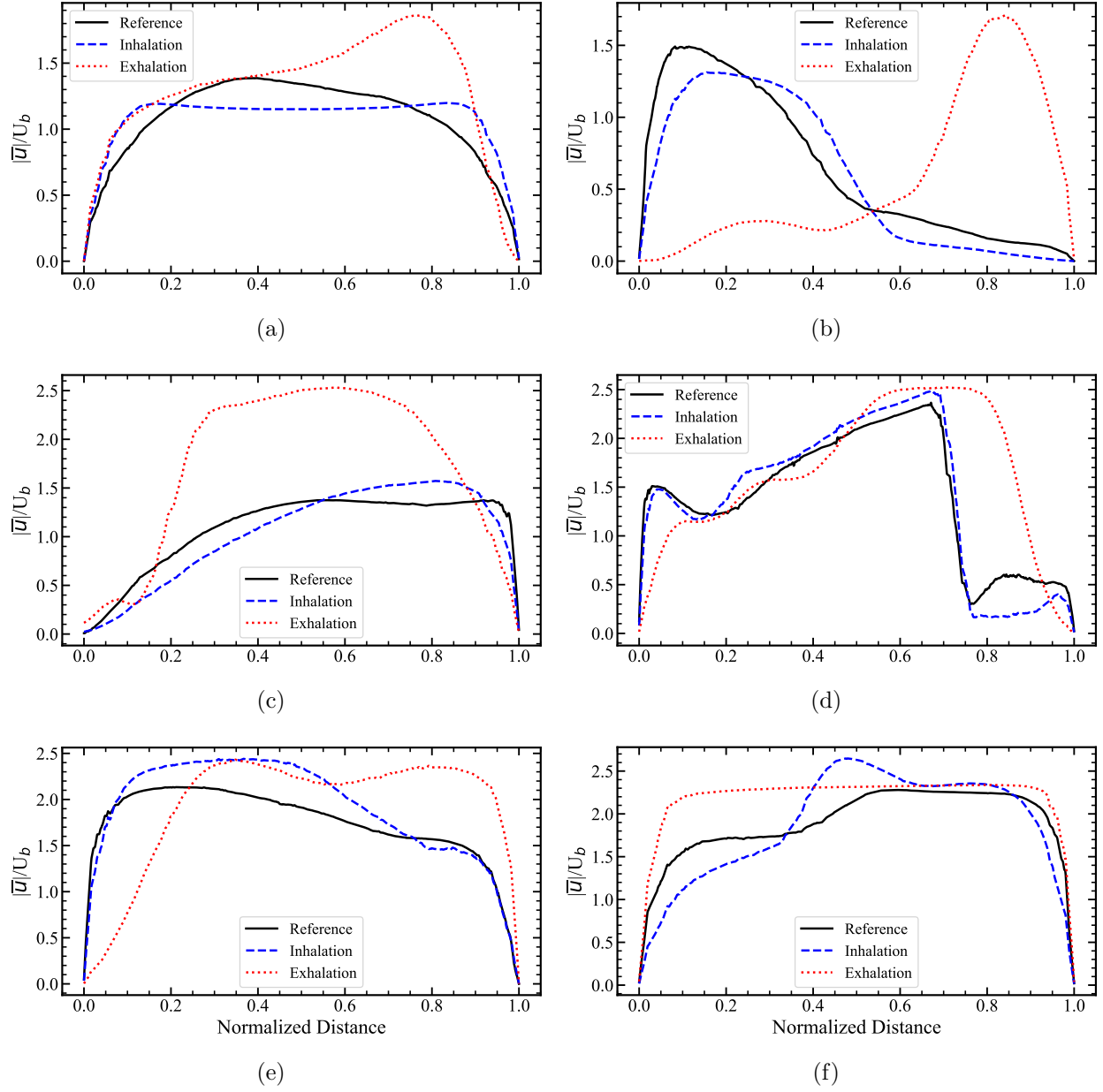


Figure 7.2 Time-averaged and normalized velocity magnitude at six cross-sections (A–F) comparing inhalation and exhalation compared to the reference case. Here, the reference results corresponds to steady inhalation at $Re = 3745$

In section B, located in the nasal cavity, the flow becomes highly asymmetric. The inhalation case shows a distinct velocity peak near the anterior wall, consistent with the

development of a recirculation region along the posterior wall and qualitatively similar to the reference case. The exhalation case, on the other hand, exhibits an opposite skewness with the peak shifted toward the posterior wall. Notably, when normalized by its lower bulk velocity, the exhalation profile shows a sharp and narrow peak, revealing that although the absolute magnitude is smaller, the local flow is concentrated within a confined passage near the posterior wall.

At section C, corresponding to the pharyngeal region, the inhalation profile remains skewed toward the posterior side due to the airway curvature, maintaining good qualitative agreement with the reference case. The exhalation profile is flatter overall but retains a mild posterior skewness, suggesting that geometric effects continue to shape the flow path even under lower-speed exhalation conditions.

In section D, near the laryngeal constriction, the inhalation case develops a distinct double-peaked shape, a clear signature of the glottal jet. The normalized peak is comparable to or slightly higher than that of the high- Re reference case, and the shear-layer structure of the jet is well captured. Conversely, the exhalation profile lacks this double-peak feature of the velocity profile, showing a single, broad maximum that indicates the absence of a strong jet during reverse flow through the glottis.

Sections E and F, corresponding to the upper and lower trachea, show the downstream evolution of these flow structures. The inhalation profiles remain asymmetric with elevated peaks near one wall, qualitatively following the reference trend, indicating that the upstream jet and curvature effects persist. The exhalation profiles, in contrast, are flat-

ter and nearly uniform, confirming that the flow field is dynamically simpler and lacks the high-shear structures observed during inhalation. This is because the flow field is reversed, leading to a much different development within this region.

Overall, the time-averaged results from the steady inhalation case, despite its lower Reynolds number, reproduce the essential flow characteristics of the high- Re reference case, including flow separation, curvature-induced asymmetry, and glottal jetting. The steady exhalation case, in contrast, exhibits a smoother, quasi-laminar flow that lacks these features but presents a distinctive, sharply peaked normalized velocity distribution in the nasal cavity due to the reversed flow direction.

7.2 Aerosol Deposition Characteristics

Now, we examine the deposition characteristics of the aerosol particles by analyzing both global and local deposition. For the steady-state inhalation and exhalation cases, the deposition fraction is computed after two flow-through times ($2T_f$) from the particle injection time. For the cyclic case, particles were injected at the start of the second cycle ($t = 5$ s), and the deposition was analyzed at the end of that cycle ($t = 10$ s). Here, one cycle corresponds to 5 s. The global deposition fraction is computed as the ratio of the total number of deposited particles in the computational domain to the total number of injected particles. The local deposition fraction, which will be discussed subsequently, is computed for seven segments of the airway (see Fig. 6.1).

7.2.1 Global Deposition

Figure 7.3 shows the global deposition fraction of the aerosol particles obtained for the three cases, compared with the steady-state, high- Re reference case. A general observation for the inspiratory-driven cases (inhalation, cyclic, and reference) is that the deposition fraction increases monotonically and nonlinearly with particle diameter (d_p). This trend is consistent with the past studies and confirms the size-dependent nature of inertial impaction as the primary deposition mechanism in forward airflow [1, 33]. As particle size and inertia increase, their trajectories deviate more significantly from the flow streamlines, leading to higher rates of impaction at airway bends and constrictions. The exhalation case, however, presents a different behavior that shows the critical influence of the bulk flow direction.

The global deposition results for the exhalation case are uniquely high, with a deposition fraction of approximately 37% for 1 μm particles, which is substantially greater than the deposition of even 10 μm particles in the other two cases. This counterintuitive result is a direct consequence of injecting particles into a reversed, expiratory flow field. The opposing airflow acts as a barrier to the particles' initial momentum, causing them to decelerate rapidly and significantly increasing their residence time within the complex geometry of the upper airways. This prolonged residence time, combined with the flow directing particles back towards the inlet region, results in a very high probability of impaction on the airway walls, irrespective of particle size. The slight dip in deposition for 2 μm particles in this case may suggest a complex interplay where particles of this specific size have just enough inertia

to penetrate slightly further before being swept back, but not enough to impact as readily as the larger particles.

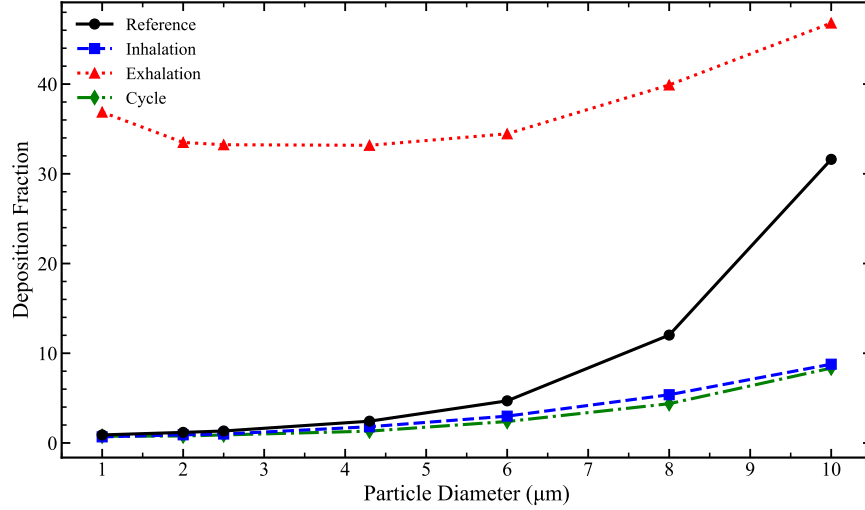


Figure 7.3 Global deposition fraction as a function of particle diameter for the steady inhalation, steady exhalation, and cyclic cases compared with the reference case. Here, the reference results corresponds to steady inhalation at $Re = 3745$

A key finding from this analysis is the close agreement between the deposition curves for the steady inhalation case ($Re = 1170$) and the full cyclic case. Both cases exhibit a gradual increase in deposition, starting from near-zero for $1 \mu\text{m}$ particles and rising to a deposition fraction of approximately 9-10% for $10 \mu\text{m}$ particles. The fact that these two distinct cases yield very similar deposition outcomes provides strong evidence that nearly all particle deposition in a realistic breathing cycle occurs during the inspiratory phase. The subsequent expiratory phase, characterized by lower velocities and a less complex flow field, appears to have a negligible direct effect on causing further deposition of particles already within the airway. The observed deposition fractions in both cases are significantly lower than

the high- Re reference case, which is expected given the lower flow rates and consequently weaker inertial forces.

Furthermore, a subtle but consistent difference is observed where the deposition fraction for the steady inhalation case is always slightly higher than that of the cyclic case across all particle sizes. This minor difference suggests an important secondary role for the exhalation phase of the breathing cycle, that of a clearance mechanism. While expiration does not significantly contribute to deposition, it effectively removes a small fraction of particles that remain airborne after the inhalation phase has concluded. These particles are successfully carried out of the airway, resulting in a slightly lower net deposition fraction for the full cycle compared to a scenario with continuous, steady inhalation. This highlights an aspect of realistic breathing, where the expiratory flow, while not a primary deposition driver, can influence the final deposited dose by clearing the airway of suspended aerosol particles.

7.2.2 *Local Deposition*

The local deposition fraction quantifies the percentage of aerosol particles that adhere to specific regions of the airway geometry, which is essential for targeting drug delivery. We consider seven sections of the airways, as shown in Fig. 6.1, to examine the local deposition patterns.

First, we analyze the local deposition fraction calculated for all particle streams combined, as shown in Fig. 7.4. The regional deposition patterns reveal subtle but important differences between the inspiratory flow conditions. The high- Re reference case is characterized by a single, dominant deposition peak in the larynx (Section 4), with deposition

steadily increasing through the upstream sections (1-3). In contrast, the steady inhalation case exhibits a bimodal distribution with two distinct peaks of similar magnitude, one in the nasal cavity (Section 2) and another in the larynx (Section 4). The cyclic case presents yet another pattern, with deposition showing a roughly linear decrease from the inlet (Section 1) to the pharynx (Section 3) before rising again at the larynx (Section 4). While the overall magnitudes of the steady inhalation and cyclic cases are comparable, these differences in peak locations highlight that steady versus unsteady inhalation produces different regional hotspots of aerosol particles. In the downstream sections (5-7), all three inspiratory flows show a similar qualitative shape, differing primarily in magnitude. This suggests that once the flow passes the laryngeal jet, its subsequent evolution in the trachea is less sensitive to the inflow condition.

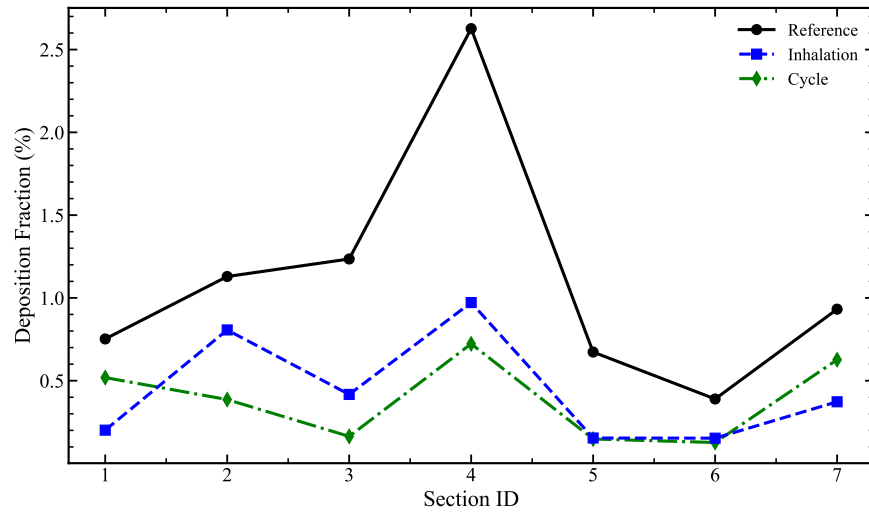
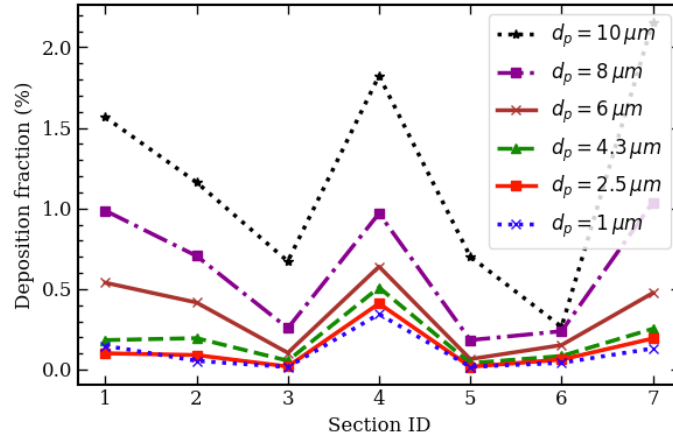
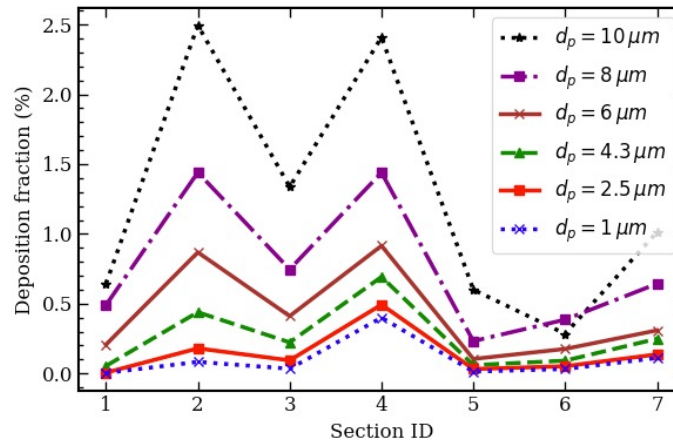


Figure 7.4 Local deposition fraction in three cases obtained from all seven particle streams, excluding the exhalation case, as all the particles were deposited in section one for the exhalation case

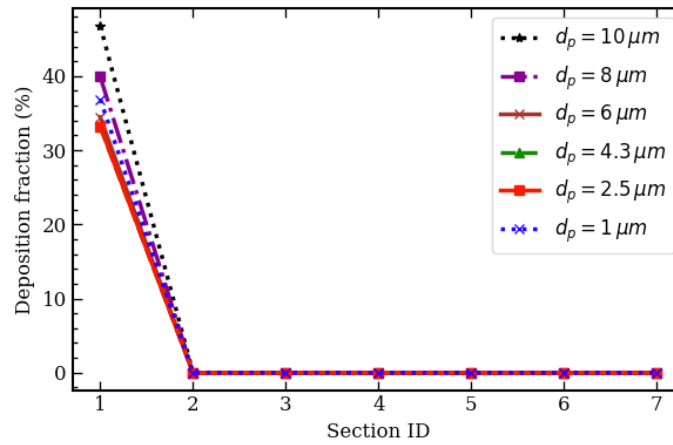
Now, we examine the effects of particle diameter (d_p) on the local deposition within each of the three primary cases, as shown in Fig. 7.5. This detailed breakdown reveals the strong interplay between particle inertia, flow condition, and airway anatomy. In both the cyclic case (Fig. 7.5(a)) and the steady inhalation case (Fig. 7.5(b)), the local deposition fraction increases substantially with d_p in every section, a clear marker of inertia-driven deposition. The qualitative shape of the deposition profile for any individual particle size generally follows the pattern observed in the combined analysis for that case. For instance, the bimodal peaks in sections 2 and 4 for the inhalation case and the decreasing-then-increasing trend for the cyclic case are present across the particle size range. However, the prominence of these features is highly dependent on the particle size. For smaller particles ($1\text{ }\mu\text{m}$ to $4.3\text{ }\mu\text{m}$), the deposition magnitude is low and the profiles are relatively flat, showing only modest variations between sections. As particle size increases to larger values ($6\text{ }\mu\text{m}$ to $10\text{ }\mu\text{m}$), the deposition magnitude increases significantly, and the characteristic peaks and valleys of each profile become much more significant. While these larger particles follow the same general deposition shape, the visual differences in magnitude between them are substantial, highlighting a nonlinear relationship between particle inertia and regional impaction efficiency.



(a) Cyclic



(b) Steady inhalation



(c) Steady exhalation

Figure 7.5 Local deposition fraction as a function of the particle diameter for the cyclic (a), steady inhalation (b), and steady exhalation (c) cases

The steady exhalation case (Fig. 7.5(c)) presents a fundamentally different and highly localized deposition pattern. An overwhelming majority of the deposition, between 30-45% of all injected particles, occurs in section 1, near the inlet region, with deposition in all subsequent sections (2 through 7) being nearly zero. This extreme localization not only highlights a unique deposition mechanism but also serves as a verification of the model's physical realism, correctly predicting that particles fail to penetrate the airway against the opposing expiratory flow. While this mechanism is so dominant that it traps particles of all sizes, inertial effects are still a clear factor. The deposition fraction within Section 1 is not uniform; it increases with particle size, with 10 μm particles showing the highest deposition, followed by 8 μm , and so on. This demonstrates that even when the bulk flow forces immediate deposition, larger particles with greater inertia impact the walls more readily upon entering the reversed flow field. This result carries a significant practical implication for aerosol therapy. If a drug is administered while a patient is exhaling, the dose will be entirely deposited in the upper-most region, failing to reach the target airways and necessitating re-injection for the treatment to be effective.

7.3 Summary

This chapter examined both airflow and particle deposition within the human upper airways using a realistic time-varying breathing condition and steady inflows. The cyclic case, when compared to steady inhalation and exhalation, showed unsteady flow features that strongly influenced local deposition. The inhalation phase produced complex and turbulent-like flow features such as recirculation and a strong glottal jet. In contrast, the exhalation

phase remained smoother and quasi-laminar, with fewer flow features. Examining the deposition revealed that most particles were deposited during the inhalation phase, while the exhalation phase had a small impact on the total deposition, acting as a clearance mechanism. It was also shown that, like the monodisperse cases, deposition increased monotonically with particle size due to inertial impaction. Local deposition analysis revealed that most particles were deposited in the nasal cavity and larynx during inhalation, while all particles were deposited in the inlet during exhalation due to the flow reversal.

CHAPTER 8

CONCLUSIONS

Numerical investigation of aerosolized drug delivery, which is typically used to treat pulmonary diseases, can provide detailed information, which, along with advanced imaging techniques, can enable an effective patient-specific treatment procedure. In this study, we employed a point-particle LES strategy to investigate the effects of steady and cyclic inhalation conditions on the airflow and aerosol dynamics within human upper airways. To facilitate efficient parametric studies, we considered a truncated portion of the well-established SimInhale benchmark configuration, which comprised the extrathoracic and parts of the intrathoracic airways. We simulated three inhalation conditions with flow rates of $Q_v = 14.2$, 53.2, and 71 L/min, leading to $Re = 1000$, 3745, and 5000 representing quasi-laminar, moderate turbulence, and high turbulence conditions for monodisperse and polydisperse particle injections. To simulate realistic breathing conditions, we used a time-varying sinusoidal velocity profile representing a calm breathing pattern, and time-averaged steady inflows and outflows for inhalation and exhalation. For cases with monodisperse particle injection, seven monodisperse particle streams with particle diameters ranging from $1 \mu m - 10 \mu m$ were tracked. For polydisperse particle injection, the three particle size distributions (PSDs) were considered, which included Gaussian, Rosin-Rammler, and uniform distributions with particle diameter ranging from $0.1 \mu m - 9.9 \mu m$ having a mean of $5 \mu m$. A comprehensive

analysis of results from these cases was performed in terms of instantaneous features of air-flow and aerosol dynamics, turbulence statistics of airflow, local and global deposition of aerosol particles, and statistics of aerosol transport.

8.1 Key Accomplishments

The key accomplishments of this study are summarized as follows:

- **Instantaneous Flow and Monodisperse Aerosol Dynamics During Steady**

Inhalation: The analysis of instantaneous flow field during the steady inhalation conditions showed elongated coherent structures forming in the nasal cavity region, which persisted through the airway in all cases. As expected, the two higher Re cases showed more small-scale structures, whereas the quasi-laminar case showed much longer bulk flow-oriented coherent structures. The instantaneous distribution of aerosol particles showed dependence on both Q_v and d_p , with higher Q_v cases exhibiting more uniform dispersion of $d_p = 1\ \mu\text{m}$ particles and enhanced deposition in the nasal cavity due to increased mixing. Particles of size $d_p = 10\ \mu\text{m}$ exhibited stronger inertia-driven effects, leading to greater deposition and preferential concentration throughout the airway, particularly in high Re cases.

- **Flow Statistics During Steady Inhalation:** The time-averaged airflow for the monodisperse cases showed a distinct behavior of the quasi-laminar case compared to the turbulent cases. Specifically, in the nasal cavity region, the low Re case showed limited transverse mixing and a thicker boundary layer compared to the higher Re cases. In addition, the transverse profiles of normalized velocity magnitude at six

locations across the airway region showed flatter core regions and steeper wall gradients, typical of turbulent flows in high Re cases compared to the low Re case. Profiles across all sections captured key anatomical influences, such as asymmetry due to flow expansion, curvature, and asymmetric shear layers, with high Re cases aligning closely with results from the reference study. We observed higher values of the resolved TKE and eddy viscosity in the post-cavity, laryngeal, and tracheal regions in the high Re cases, indicating stronger turbulence generation due to shear-layer instabilities and complex anatomical effects.

- **Monodisperse Aerosol Deposition During Steady Inhalation:** The global deposition for the monodisperse cases showed a nonlinear dependence on Q_v or Re and d_p or St , with small particles ($d_p < 5 \mu\text{m}$) showing minimal deposition and larger particles ($d_p > 5 \mu\text{m}$) exhibiting sharp increases in deposition with d_p , particularly in high Re cases. The deposition in high Re cases was driven by stronger turbulence and flow accelerations, especially near anatomical constrictions. Quantitatively, in the $Re = 5000$ case, deposition was about 55%, whereas it was 10% in the $Re = 1000$ case for the largest stream of particles ($d_p = 10 \mu\text{m}$). The global deposition fraction from the three cases also showed a good collapse with the non-dimensional deposition parameter ($\chi = St^{2.18} Re^{-0.74}$) reported in a past study. The local deposition also varied strongly with Re and St , reflecting the interplay of inertia and turbulence on particle transport. In the low- Re case, particles followed core streamlines, resulting in deeper penetration in the airways, except for slightly elevated deposition near the

inlet due to weak initial momentum. In contrast, high- Re cases showed pronounced deposition in the nasal cavity, pharynx, and especially the larynx, where jet impaction intensified particle trapping and limited penetration to distal regions. Quantitatively, the deposition of $10\ \mu\text{m}$ particles was 30 times higher than $2.5\ \mu\text{m}$ particles in the larynx region in the highest Re case.

- **Monodisperse Aerosol Transport Statistics During Steady Inhalation:** The analysis of velocity and its fluctuations and the slip velocity of aerosol particles within the monodisperse cases during steady inhalation showed that apart from the global parameters such as Re and St , the local anatomy of airways and associated flow complexities jointly control aerosol transport and deposition in the upper airways. In high- Re cases, small particles ($d_p < 5\ \mu\text{m}$) followed the airflow closely, enabling their deeper penetration, while larger particles ($d_p > 5\ \mu\text{m}$) lagged the flow, due to their movement toward near-wall low-speed regions, which led to their deposition through the inertial impaction mechanism. In the quasi-laminar case, even smaller particles ($d_p < 5\ \mu\text{m}$) exhibited higher slip velocities compared to larger particles, which is due to the transverse flow variations in such flows leading to movement of such particles in the core region and thus facilitating their deeper penetration. In all cases, the velocity fluctuation of aerosol particles was significantly higher than that of the airflow, which again showed the effects of flow complexities induced by geometric variations of the airway. The effect of St on the velocity fluctuations of particles was only observed in

turbulent cases, thus indicating the role of particle inertia getting pronounced with an increase in the turbulence intensity of the airflow.

- **Polydisperse Aerosol Deposition During Steady Inhalation:** In chapter 6, global and local deposition were examined using Gaussian, Rosin-Rammler, and uniform PSDs at three different steady inflow conditions representing quasi-laminar, moderately turbulent, and high turbulent flow scenarios. The analysis used normalized global deposition (GDF_1), total global deposition by particle bin sizes (GDF_2), total global deposition (GDF_3), and local deposition fraction (LDF) across the 7 sections in the airway. Results show that for a given particle size (GDF_1), the deposition efficiency is governed directly by the particle inertia and Re regardless of the PSD used. For total deposition across all particle sizes (GDF_3) and local deposition, the uniform distribution, which has many large particles, produced the highest amount of deposition, the Rosin-Rammler distribution with particles skewed to the left had the lowest deposition, and the Gaussian was in between. This is due to the fact that total deposition by particle size (GDF_2) peaks at approximately $7\text{ }\mu\text{m}$ and then declines for Rosin-Rammler and Gaussian, and increases monotonically for the uniform case, for larger particles. For local deposition, similar trends were examined for higher flow rates, especially in the larynx, where a clear hierarchy emerged for deposition magnitude: Rosin-Rammler $<$ Gaussian $<$ uniform. However, at lower flow rates, deposition is minimal across all three PSDs, with the PSD having negligible impact on the deposition trends.

- **Airflow During Realistic Breathing Cycle:** To evaluate the effects of a physiologically realistic breathing cycle on key flow features and aerosol transport, a time-varying cyclic breathing, steady-state inhalation, and steady-state exhalation case were simulated. Results showed that even at lower instantaneous flow rates compared to the turbulent inflow reference case, the inhalation phase exhibited complex and turbulent-like flow features, including flow separation, skewness from the curved airway geometry, and a strong glottal jet. During the exhalation phase, the resulting flow was weaker and more quasi-laminar-like, lacking some of the complex features when compared with the inhalation phase. However, it was observed that when reversing the flow during the exhalation phase, the flow shifts from the anterior to the posterior side of the nasal cavity, showing the influence of deceleration and reversed flow.
- **Monodisperse Aerosol Deposition During Realistic Breathing Cycle:** The analysis of monodisperse aerosol deposition for the cyclic breathing cases showed a strong dependence on particle size and flow direction. For cases with inspiration (steady inhalation and cyclic breathing), the global deposition increased monotonically with particle diameter due to inertial impaction. In comparison, the exhalation case had a very high deposition even for particles smaller than $5\ \mu\text{m}$, as particles were injected into reversed flow, which increased deposition near the inlet. Comparison between the steady inhalation and cyclic cases revealed very similar global deposition trends, indicating that most of the deposition within the upper airway occurs during inhalation, with the exhalation phase acting as a clearance mechanism, causing slightly lower

deposition. Local deposition analysis showed differing trends among the three cases, with steady inhalation causing bimodal peaks in the nasal cavity and larynx, cyclic producing a linear decrease up to the larynx, and all particles depositing in the inlet for the steady exhalation case.

8.2 Future Outlook

To improve the research, future studies can consider the following:

- **Examine the Role of SGS Dispersion Model:** In this study, a no-model strategy for the subgrid-scale dispersion is used, where the subgrid dispersion effects are neglected. This is a simplified approach, but it leads to inaccuracies when predicting the dynamics of smaller-sized particles ($\mathcal{O}(1)\mu\text{m}$). To more accurately predict particle dynamics, a structural stochastic model that reconstructs the entire subfilter velocity field or a stochastic model that retrieves some statistical features of the subfilter velocity field could be utilized to examine the effects of such models on aerosol transport and deposition.
- **Examine Mucus Interaction and Dynamics:** The simulations in this study assumed that particles deposit on the walls when contacted and that the walls are rigid. To make this more realistic, a surface film of mucus could be implemented on the walls, with the dynamics of the mucus and mucus-particle interaction modeled. This implementation would allow for the effects of rebound and particle capture by the mucus, as well as airflow on the mucus, to be examined.

- **Extend the Mesh to the Full Geometry:** The mesh used for the simulations in this study is a truncated version of the SimInhale benchmark case up to the carina. Although this makes the simulations much more computationally efficient, future work could extend the airway model to all 12 airway generations. This extension would allow for a more complete analysis, especially for lower flow rates and smaller particles.

REFERENCES

- [1] P. Koullapis, S. C. Kassinos, J. Muela, C. Perez-Segarra, J. Rigola, O. Lehmkuhl, Y. Cui, M. Sommerfeld, J. Elcner, M. Jicha, I. Saveljic, N. Filipovic, F. Lizal, L. Nicolaou, Regional aerosol deposition in the human airways: The siminhale benchmark case and a critical assessment of in silico methods, *European Journal of Pharmaceutical Sciences* 113 (2018) 77–94.
- [2] L. Golshahi, R. Vehring, M. L. Noga, W. H. Finlay, In vitro deposition of micrometer-sized particles in the extrathoracic airways of children during tidal oral breathing, *Journal of Aerosol Science* 57 (2013) 14–21.
- [3] W. W. Busse, R. F. J. Lemanske, Asthma, *New England Journal of Medicine* 344 (2001) 350–362.
- [4] J. F. Devine, Chronic obstructive pulmonary disease: an overview, *American Health & Drug Benefits* 1 (2008) 34.
- [5] K. Matsunaga, T. Hirano, A. Oka, A. Tanaka, K. Kanai, T. Kikuchi, A. Hayata, H. Akamatsu, K. Akamatsu, Y. Koh, et al., Progression of irreversible airflow limitation in asthma: correlation with severe exacerbations, *The Journal of Allergy and Clinical Immunology: In Practice* 3 (2015) 759–764.
- [6] World Health Organization, Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach, World Health Organization, 2007.
- [7] W. H. Finlay, The mechanics of inhaled pharmaceutical aerosols: An introduction, Elsevier/Academic Press, Amsterdam, 2001.
- [8] N. R. Labiris, M. B. Dolovich, Pulmonary drug delivery. Part I: physiological factors affecting therapeutic effectiveness of aerosolized medications, *British Journal of Clinical Pharmacology* 56 (2003) 588–599.
- [9] Q. T. Zhou, S. S. Y. Leung, P. Tang, T. Parumasivam, Z. H. Loh, H.-K. Chan, Inhaled formulations and pulmonary drug delivery systems for respiratory infections, *Advanced Drug Delivery Reviews* 85 (2015) 83–99.
- [10] M. Cazzola, F. Cavalli, O. S. Usmani, P. Rogliani, Advances in pulmonary drug delivery devices for the treatment of chronic obstructive pulmonary disease, *Expert Opinion on Drug Delivery* 17 (2020) 635–646.

- [11] S. Elghobashi, On predicting particle-laden turbulent flows, *Applied Scientific Research* 52 (1994) 309–329.
- [12] C. T. Crowe, T. R. Troutt, J. N. Chung, Numerical models for two-phase turbulent flows, *Annual Review of Fluid Mechanics* 28 (1996) 11–43.
- [13] S. Balachandar, J. K. Eaton, Turbulent dispersed multiphase flow, *Annual Review of Fluid Mechanics* 42 (2010) 111–133.
- [14] C. Kleinstreuer, Z. Zhang, Laminar-to-turbulent fluid-particle flows in a human airway model, *International Journal of Multiphase Flow* 29 (2003) 271–289.
- [15] P. W. Longest, L. T. Holbrook, In silico models of aerosol delivery to the respiratory tract—development and applications, *Advanced Drug Delivery Reviews* 64 (2012) 296–311.
- [16] W. Hofmann, Modelling inhaled particle deposition in the human lung—A review, *Journal of Aerosol Science* 42 (2011) 693–724.
- [17] E. A. Matida, W. H. Finlay, C. F. Lange, B. Grgic, Improved numerical simulation of aerosol deposition in an idealized mouth–throat, *Journal of Aerosol Science* 35 (2004) 1–19.
- [18] S. T. Jayaraju, M. Brouns, S. Verbanck, C. Lacor, Fluid flow and particle deposition analysis in a realistic extrathoracic airway model using unstructured grids, *Journal of Aerosol Science* 38 (2007) 494–508.
- [19] C.-L. Lin, M. H. Tawhai, G. McLennan, E. A. Hoffman, Characteristics of the turbulent laryngeal jet and its effect on airflow in the human intra-thoracic airways, *Respiratory Physiology & Neurobiology* 157 (2007) 295–309.
- [20] S. S. Varghese, S. H. Frankel, P. F. Fischer, Direct numerical simulation of stenotic flows. part 1. steady flow, *Journal of Fluid Mechanics* 582 (2007) 253–280.
- [21] Y. Wang, S. Elghobashi, On locating the obstruction in the upper airway via numerical simulation, *Respiratory Physiology & Neurobiology* 193 (2014) 1–10.
- [22] L. Nicolaou, T. Zaki, Direct numerical simulations of flow in realistic mouth–throat geometries, *Journal of Aerosol Science* 57 (2013) 71–87.
- [23] C. Li, J. Jiang, H. Dong, K. Zhao, Computational modeling and validation of human nasal airflow under various breathing conditions, *Journal of Biomechanics* 64 (2017) 59–68.
- [24] K. Bass, P. W. Longest, Recommendations for simulating microparticle deposition at conditions similar to the upper airways with two-equation turbulence models, *Journal of Aerosol Science* 119 (2018) 31–50.

- [25] A. Dehbi, Prediction of extrathoracic aerosol deposition using rans-random walk and les approaches, *Aerosol Science and Technology* 45 (2011) 555–569.
- [26] K.-W. Stapleton, E. Guentsch, M. K. Hoskinson, W. H. Finlay, On the suitability of $k-\epsilon$ turbulence modeling for aerosol deposition in the mouth and throat: a comparison with experiment, *Journal of Aerosol Science* 31 (2000) 739–749.
- [27] Y. Liu, E. A. Matida, J. Gu, M. R. Johnson, Numerical simulation of aerosol deposition in a 3-D human nasal cavity using RANS, RANS/EIM, and LES, *Journal of Aerosol Science* 38 (2007) 683–700.
- [28] E. A. Matida, W. H. Finlay, M. Breuer, C. F. Lange, Improving prediction of aerosol deposition in an idealized mouth using large-eddy simulation, *Journal of Aerosol Medicine* 19 (2006) 290–300.
- [29] S. T. Jayaraju, M. Brouns, C. Lacor, B. Belkassem, S. Verbanck, Large eddy and detached eddy simulations of fluid flow and particle deposition in a human mouth–throat, *Journal of Aerosol Science* 39 (2008) 862–875.
- [30] A. R. Lambert, P. O’Shaughnessy, M. H. Tawhai, E. A. Hoffman, C.-L. Lin, Regional deposition of particles in an image-based airway model: large-eddy simulation and left-right lung ventilation asymmetry, *Aerosol Science and Technology* 45 (2011) 11–25.
- [31] E. Ghahramani, O. Abouali, H. Emdad, G. Ahmadi, Numerical investigation of turbulent airflow and microparticle deposition in a realistic model of human upper airway using les, *Computers & Fluids* 157 (2017) 43–54.
- [32] A. Farnoud, I. Baumann, M. M. Rashidi, O. Schmid, E. Gutheil, Simulation of patient-specific bi-directional pulsating nasal aerosol dispersion and deposition with clockwise 45° and 90° nosepieces, *Computers in Biology and Medicine* 123 (2020) 103816.
- [33] H. H. Jin, J. R. Fan, M. J. Zeng, K. F. Cen, Large eddy simulation of inhaled particle deposition within the human upper respiratory tract, *Journal of Aerosol Science* 38 (2007) 257–268.
- [34] Y. Zhou, Y.-S. Cheng, Particle deposition in a cast of human tracheobronchial airways, *Aerosol Science and Technology* 39 (2005) 492–500.
- [35] C. Darquenne, Aerosol deposition in health and disease, *Journal of Aerosol Medicine and Pulmonary Drug Delivery* 25 (2012) 140–147.
- [36] M. Monjezi, R. Dastanpour, M. Saidi, A. Pishevar, Prediction of particle deposition in the respiratory track using 3d–1d modeling, *Scientia Iranica* 19 (2012) 1479–1486.
- [37] A. V. Kolanjiyil, C. Kleinstreuer, Computationally efficient analysis of particle transport and deposition in a human whole-lung-airway model. part i: Theory and model validation, *Computers in Biology and Medicine* 79 (2016) 193–204.

- [38] A. Kuprat, M. Jalali, T. Jan, R. Corley, B. Asgharian, O. Price, R. Singh, S. Colby, C. Darquenne, Efficient bi-directional coupling of 3d computational fluid-particle dynamics and 1d multiple path particle dosimetry lung models for multiscale modeling of aerosol dosimetry, *Journal of Aerosol Science* 151 (2021) 105647.
- [39] F. Nicoud, F. Ducros, Subgrid-scale stress modelling based on the square of the velocity gradient tensor, *Flow, Turbulence and Combustion* 62 (1999) 183–200.
- [40] D. Mahida, E. Durant, P. Kumar, R. Ranjan, Study of airflow and aerosol deposition characteristics within human airways using large-eddy simulations, in: *APS Division of Fluid Dynamics Meeting Abstracts*, pp. H01–007.
- [41] T. Gemci, V. Ponyavin, R. Collins, T. E. Corcoran, S. C. Saha, M. S. Islam, Cfd study of dry pulmonary surfactant aerosols deposition in upper 17 generations of human respiratory tract, *Atmosphere* 13 (2022) 726.
- [42] V. Legh-Land, A. E. Haddrell, D. Lewis, D. Murnane, J. P. Reid, Water uptake by evaporating pmdi aerosol prior to inhalation affects both regional and total deposition in the respiratory system, *Pharmaceutics* 13 (2021) 941.
- [43] M. S. Islam, S. C. Saha, T. Gemci, I. A. Yang, E. Sauret, Z. Ristovski, Y. T. Gu, Euler–lagrange prediction of diesel-exhaust polydisperse particle transport and deposition in lung: Anatomy and turbulence effects, *Scientific Reports* 9 (2019) 12423.
- [44] M. S. Islam, P. Larpruenrudee, S. I. Hossain, M. Rahimi-Gorji, Y. Gu, S. C. Saha, G. Paul, Polydisperse aerosol transport and deposition in upper airways of age-specific lung models, *International Journal of Environmental Research and Public health* 18 (2021) 6239.
- [45] M. Rahimi-Gorji, T. B. Gorji, M. Gorji-Bandpy, Details of regional particle deposition and airflow structures in a realistic model of human tracheobronchial airways: two-phase flow simulation, *Computers in Biology and Medicine* 74 (2016) 1–17.
- [46] R. Piemjaiswang, S. Shiratori, T. Chaiwatanarat, P. Piumsomboon, B. Chalermssin-suwan, Computational fluid dynamics simulation of full breathing cycle for aerosol deposition in trachea: Effect of breathing frequency, *Journal of the Taiwan Institute of Chemical Engineers* 97 (2019) 66–79.
- [47] K. Kuga, R. Kizuka, N. D. Khoa, K. Ito, Effect of transient breathing cycle on the deposition of micro and nanoparticles on respiratory walls, *Computer Methods and Programs in Biomedicine* 236 (2023) 107501.
- [48] C. Atzeni, G. Lesma, G. Dubini, M. Masi, F. Rossi, E. Bianchi, Computational fluid dynamic models as tools to predict aerosol distribution in tracheobronchial airways, *Scientific Reports* 11 (2021).

- [49] S. Qi, B. Zhang, Y. Teng, J. Li, Y. Yue, Y. Kang, W. Qian, Transient dynamics simulation of airflow in a ct-scanned human airway tree: More or fewer terminal bronchi?, *Computational and Mathematical Methods in Medicine* 2017 (2017) 1969023.
- [50] P. Sagaut, *Large eddy simulation for incompressible flows: an introduction*, Springer, 2006.
- [51] J. Kuerten, Point-particle DNS and LES of particle-laden turbulent flow-a state-of-the-art review, *Flow, Turbulence and Combustion* 97 (2016) 689–713.
- [52] A. Putnam, Integratable form of droplet drag coefficient, *ARS Journal* (1961) 1467–1468.
- [53] R. C. Hogan, J. N. Cuzzi, Stokes and reynolds number dependence of preferential particle concentration in simulated three-dimensional turbulence, *Physics of Fluids* 13 (2001) 2938–2945.
- [54] J. Smagorinsky, General circulation experiments with the primitive equations: I. the basic experiment, *Monthly Weather Review* 91 (1963) 99–164.
- [55] M. Germano, U. Piomelli, P. Moin, W. H. Cabot, A dynamic subgrid-scale eddy viscosity model, *Physics of Fluids* 3 (1991) 1760–1765.
- [56] X. Luo, J. Hinton, T. Liew, K. Tan, Les modelling of flow in a simple airway model, *Medical Engineering & Physics* 26 (2004) 403–413.
- [57] X. G. Cui, E. Gutheil, Les study on the poly-disperse particle deposition in the human upper airway, in: *Proceedings of the 12th Triennial International Conference on Liquid Atomization and Spray Systems (ICLASS)*.
- [58] V. Armenio, U. Piomelli, V. Fiorotto, Effect of the subgrid scales on particle motion, *Physics of Fluids* 11 (1999) 3030–3042.
- [59] T. Johnston, E. Durant, R. Ranjan, On the effects of subgrid dispersion in large-eddy simulation of particle-laden turbulent channel flow bounded by rough walls, in: *APS Division of Fluid Dynamics Meeting Abstracts*, pp. H22–003.
- [60] H. G. Weller, G. Tabor, H. Jasak, C. Fureby, A tensorial approach to computational continuum mechanics using object-oriented techniques, *Computers in Physics* 12 (1998) 620–631.
- [61] R. I. Issa, Solution of the implicitly discretised fluid flow equations by operator-splitting, *Journal of Computational Physics* 62 (1986) 40–65.
- [62] S. V. Patankar, D. B. Spalding, A calculation procedure for heat, mass and momentum transfer in three-dimensional parabolic flows, in: *Numerical prediction of flow, heat transfer, turbulence and combustion*, Elsevier, 1983, pp. 54–73.

- [63] T. Zirwes, F. Zhang, J. A. Denev, P. Habisreuther, H. Bockhorn, D. Trimis, Implementation of lagrangian surface tracking for high performance computing, in: High Performance Computing in Science and Engineering'20: Transactions of the High Performance Computing Center, Stuttgart (HLRS) 2020, Springer, 2022, pp. 223–236.
- [64] G. B. Macpherson, N. Nordin, H. G. Weller, Particle tracking in unstructured, arbitrary polyhedral meshes for use in cfd and molecular dynamics, *Communications in Numerical Methods in Engineering* 25 (2009) 263–273.
- [65] D. Mahida, Numerical investigation of airflow and aerosol deposition characteristics within human airways, Master's thesis, 2021.
- [66] J. Comer, C. Kleinstreuer, C. Kim, Flow structures and particle deposition patterns in double-bifurcation airway models. part 2. aerosol transport and deposition, *Journal of Fluid Mechanics* 435 (2001) 55–80.
- [67] J. Jeong, F. Hussain, On the identification of a vortex, *Journal of Fluid Mechanics* 285 (1995) 69–94.
- [68] P. Koullapis, S. C. Kassinos, M. P. Bivolarova, A. K. Melikov, Particle deposition in a realistic geometry of the human conducting airways: Effects of inlet velocity profile, inhalation flowrate and electrostatic charge, *Journal of Biomechanics* 49 (2016) 2201–2212.
- [69] R. Dey, H. K. Patni, S. Anand, Improved aerosol deposition predictions in human upper respiratory tract using coupled mesh phantom-based computational model, *Scientific Reports* 15 (2025) 14260.

VITA

Jacob Pratt was born in Bryan, Texas, to parents Tracie and Preston Pratt. In the spring of 2019, he began his undergraduate degree at the University of Tennessee at Chattanooga, where he earned his Bachelor of Science in Mechanical Engineering. After graduating, he continued his education at the University of Tennessee at Chattanooga, pursuing a Master of Science in Mechanical Engineering with advisor Dr. Reetesh Ranjan.