ABSTRACT

GURUMURTHY, ADITHYA. Lung-Aerosol Dynamics Simulations with Novel Applications to Vaping Devices. (Under the direction of Dr. Clement Kleinstreuer).

Reliable analyses of the fate of inhaled toxic or therapeutic aerosols from various devices, such as electronic-cigarettes or medical inhalers are of great importance for the health-care industry. The transport/deposition of inhaled particles is largely determined by the inlet conditions and lung-airway geometries. Detailed physical insight can be obtained via predictive computer simulations of airflow and particle dynamics. Induced modifications of the inlet conditions and hence the resulting fluid-particle flow fields would in-turn affect the transport/deposition of inhaled aerosols and vapors. This is the fundamental idea behind vaping outcome or customized drug delivery, ie, modification of the inlet flow field conditions (via a new mouthpiece or inhaler modification) for direct aerosol delivery to targeted sites. The novel idea of implementing helical airflow and particle-trajectory patterns at the mouth inlet for vaping devices is explored in this thesis.

Specifically, swirling flow at different Stokes numbers is simulated and analyzed in realistic human upper airways for micron-size particles. As expected, swirling flows reduce the axial momentum of the air-particle stream entering the airways; thus, affecting the particle deposition in the oral cavity and beyond. Special attention is given to electronic-cigarettes, which require a certain percentage, say 30%, of inhaled (flavor) chemicals to deposit in the oral cavity to account for taste; then, the rest of the dosage flows to the deeper lung region for the drug effect. The required deposition fraction of aerosols in the oral cavity, specifically to the back of the tongue, is achieved by varying the amount of swirl in the fluid-particle flow stream. A new non-dimensional number is proposed which is helpful in assessing the deposition fraction of particles/vapors in the human oral cavity. A novel mouthpiece design that would facilitate the delivery of helical flow is
proposed and tested for its applicability to electronic cigarettes with slight modifications to medical inhalers.

The final part of the thesis involves modelling and simulation of the three-dimensional, dual-path whole lung airway model (WLAM), presently just including the conducting airways (Generation 15). WLAM is a representative human lung model featuring patient-specific upper airways from mouth to generation 3, followed by triple bifurcating units (TBUs) that extend in series and parallel to generation 23, where the conducting airways end at generation 15. The main objective of this study is to lay a foundation to predict accurately and realistically inhaled aerosol/vapor deposition in human lung airway models.

After model development and programming in C++, computer experiments for all cases were carried out with the open-source computational fluid dynamics (CFD) tool box OpenFOAM <https://www.openfoam.com/>.
Lung-Aerosol Dynamics Simulations with Novel Applications to Vaping Devices

by
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DEDICATION

To my parents, sister and grandparents, for their unconditional love and support

In the loving memory of both of my beloved grandfathers

And

In memory of Ayush Agrawal
BIOGRAPHY

Adithya Gurumurthy was born on June 16th, 1994 to Mr. R. Gurumurthy and Mrs. Srividhya Gurumurthy in Tiruchirappali, Tamil Nadu, India. After completing his high school education, Adithya pursued a Bachelor’s degree in Mechanical Engineering at SSN College of Engineering, Chennai, India and graduated in 2015 with distinction and state rank. After completing his Bachelor’s degree, he worked as a research assistant to his professor in his undergraduate school for a year and moved to Raleigh in 2016 to pursue his Master’s at North Carolina State University. He will be receiving his Master’s degree in the 2018 Fall term and intends to pursue a Ph.D. degree under the guidance of Dr. C. Kleinstreuer in the Computational Multi-Physics Lab at NC State.
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CHAPTER 1

Introduction and Overview

1.1. Introduction

The assessment of the fate of inhaled particles is of primary concern in toxicological and therapeutic studies. Estimating the risk/dosage of pollutants/drugs requires as a first step, the analysis of depositional patterns of inhaled aerosols in human airways; this is followed by pharmacokinetic studies to determine the migration of the pollutants/drugs to systemic regions. Aerosols refer to the suspension of fine particles, ie, solids and liquids, in the micron or nanometer range dispersed in air and/or the mucus layers. Inhaled substances may include vapors, droplets and a large variety of particulate matter that may be soluble or insoluble. The \textit{in vivo} assessment of particle deposition in lungs is usually achieved by positron emission tomography (PET), or single photon emission computer tomography (SPECT) and with high resolution computed-tomography (CT) or gamma scintigraphy. These techniques involve inhalation of radio-labelled particles (radioactive isotopes) that are then tracked by detecting the gamma rays emitted by them. The trajectory and dispersion of these particles can then be monitored\textsuperscript{1}.

Conducting such experimental \textit{in vivo} studies, apart from being limited, may cause a lot of human strain (eg, radiation sickness). Another critical question is the assessment of toxicity by subjecting laboratory animals (rodents in general) to chemicals and their scaled-up implications to human health. Although \textit{in vitro} studies tend to eliminate health concerns, they suffer from the fact that they are far from being patient specific. Thus, a Computational Fluid-Particle Dynamics (CF-PD) or \textit{in silico} approach for determining the fate of inhaled particles can be a very reliable alternative. This is pillared by the advancements in this field in terms of raw computing power, math modelling and image visualization, which together can result in fast, realistic and accurate predictions without
The CF-PD approach for studying the deposition patterns of particles numerically by solving appropriate fluid-particle dynamics equations, is studied in this thesis. Of interest are improvements in regional transport and deposition patterns, facilitating custom aerosol delivery by modifying the inlet conditions for basic inhalation devices, with a primary focus on a new mouthpiece for vaping devices.

1.2. Toxicology and therapeutic aspects of particle deposition

The deposition of particles is affected by many factors\(^2\), a thorough understanding of which, will be very useful in assessing the deposition of particles in human airways. These include, characteristics of the particles (eg, distribution, size, shape, density, hygroscopicity, and surface charge); the breathing pattern and inhalation conditions; and the anatomy of the respiratory tract. Amongst the three, the particle size is a key parameter as it distinguishes micron particles from nanoparticles based on their respective effective diameter, which directly affects the nature and type of trajectory and deposition site\(^3\).

Deposition of ultrafine particles that are within 100 nm in diameter are major components of air pollution and of potential health risk due to lung tumors and/or inflammation\(^4\). Concerning cancer in the respiratory system, it accounts for more deaths than any other cancer in both men and women\(^5\) (American Cancer Society, 2012). Another major health concern is the inhalation of cigarette smoke, which causes permanent damage to the lungs due to the presence of combustible products (US Department of Health and Human Services 2014\(^6\)) and exacerbates the risk of cardiovascular diseases\(^7\). Electronic nicotine delivery systems (ENDs), popularly known as electronic-cigarettes (e-cigarettes) have been commercialized, correctly claiming to be less harmful than conventional tobacco cigarettes. E-cigarettes are aimed at helping frequent smokers to quit by providing a safer-alternative\(^8,9\). They are devices that contain an electric atomizer powered by a battery with a replaceable cartridge
containing a water-based liquid (known by e-liquid) that is composed of propylene glycol, glycerin, water, flavors and variable amounts of nicotine. An e-cigarette avoids the combustible products produced from a conventional cigarette, by generating a flavored droplet-vapor mixture by heating the e-liquid in the atomizer. An alternative e-cigarette is of the “heat-not-burn” variety, where a tobacco strip is just heated to a critical temperature and the resulting vapors are inhaled.

Aside from particle size, the shape of the particles also affects their penetration into the deep lung. This touches upon another major aspect of particle deposition assessment, which is therapeutics. For example, it was reported that ellipsoidal/elongated particle shape in contrast to spherical could potentially facilitate penetration and deposition in deeper airway regions\(^1\). Thus, formulation of drugs in such shapes are beneficial for drug delivery. The delivery of therapeutic aerosols through inhalation has been in the use for centuries now, where the first known relevance sources back to ~1554 BC in an ancient Egyptian papyrus scroll\(^{10}\). Advancements right from its early times till today, confirm the efficacy of such methods and its importance. Pulmonary drug delivery is a popular non-invasive medication technique where drugs are administered orally to treat both lung and systemic diseases. It is also becoming the preferred route for insulin delivery, pain management, cancer therapy, and nano-therapeutics. Lung diseases include asthma, cystic fibrosis (CF), chronic obstructive pulmonary disorders (COPDs), acute respiratory distress syndrome (ARDS) and pulmonary fibrosis. These diseases cause serious distress in an individual and can also be fatal at times. Pulmonary drug delivery to deep lung regions facilitates an elegant way of non-invasive drug delivery to systemic internal organs as well.

Popular methods of pulmonary drug delivery involve using devices such as pressurized Metered Dose Inhalers (pMDIs), Dry Powder Inhalers (DPIs) and Nebulizers, each being characteristically different and adopted for different scenarios\(^{10,11}\). There are many debates as to what corresponds
to the “ideal inhaler” but they all roughly direct to one common direction. O’Connor\textsuperscript{12} reported that an ideal inhaler is the one that has the following characteristics: “Accurate and consistent in effective drug delivery; easy and convenient to use; easy to teach, learn and remember how to use correctly; capable of delivering a range of drugs; accurate dose counter; patient feedback of dose taken; convenient to carry; robust; visually appealing to the patient; easily identifiable in terms of the drug/strength contained in the inhaler; and propellant-free”. Nevertheless, for any inhaler’s successful operation, targeting of drugs to the desired locations in the lung is of primary importance. Targeting is the term that is used throughout this thesis, which corresponds to a method/goal to bring the drug aerosols from their release points to the desired locations in the airways for optimal effectiveness. This may be achieved by a combination of factors that include optimal particle characteristics, inlet fluid-particle waveforms, particle release position and drug-aerosol dosage. Particle deposition distribution by modifying the inlet conditions is of key interest in this thesis.

1.3. Drug targeting and swirling flows

Key advancements in drug formulations have not only widened the scope of pulmonary drug delivery but have also increased its cost. Hence, there is a need to ensure that expensive drugs are deposited in the desired airway location for their effect. This is achieved by optimizing the inhaler design that alters the flow characteristics. Thus, both drug formulation and device design have widened the scope of pulmonary drug delivery medication\textsuperscript{13}. Drug deposition in the upper oral cavity due to inertial impaction and thus its limited concentrations in the deeper lung airways is a common problem in DPIs and pMDI\textsuperscript{14}. Several techniques like employment of spacers\textsuperscript{11,15} and positioning of the inhaler\textsuperscript{16} are hence of active research interest. Kleinstreuer et al.\textsuperscript{16,17} have come up with a methodology for targeting of particles by assessing the likelihood of their deposition at
different airway sites, with respect to their inlet position. This is achieved by backtracking the particles from the deposited zones to the inlet position and generating a particle release map (PRM). It has also been found that the angular positioning of the inhaler would also reduce oropharyngeal deposition\textsuperscript{16}. However, considering electronic cigarette application, it is desirable to have certain amount of vapor deposition near the back of the tongue region to account for taste, in addition to deep lung deposition for drug effect.

The possibility of applying a new mouthpiece generating swirling flow for custom-based direct drug delivery is explored in this thesis. Swirl flows are of much significance in heat transfer and mass transfer enhancement due to the stirring effect it causes\textsuperscript{18}. They are characterized by their tangential velocities, which majorly contribute to the main stream resultant velocity. They can be well suited for inhalers and e-cigarettes. Swirling flows can help reduce drug deposition in the throat and improve dosage to deep lung sites. This is due to their significant tangential velocity component, which reduce the axial inertia of drugs from DPI or pMDIs that otherwise deposit in the oral cavity by inertial impaction. Swirling flows are also characterized by large shear gradient forces near the walls, which will cause a lift force that triggers resuspension of particles from the wall into the flow\textsuperscript{19}. This prevents the immediate deposition of vapors near the lip region, which in-turn allows deposition in the deeper tongue zones to account for taste, while considering e-cigarettes.

Swirling flows can be generated by ‘swirl generators’ that encompasses any method/fixture to generate a tangential component of velocity. It may include using twisted tubes, axial blades, helical inserts, tangential injectors or using guided vane swirl generators in a flow stream. It is difficult to continually maintain large values of tangential velocity components without any external perturbation and hence swirl flows usually decay over time. Decaying swirl is a
characteristic of any swirling flow that is allowed to enter any domain with a certain momentum and allowed to traverse freely. Thus, varying amounts of swirl that decays at different times is of key importance to direct drug delivery as it allows one to control the deposition in the oral cavity. However, a continuous swirling flow may be created by using twisted tubes, inserts or using helical vanes that are present all along the conduit. This aspect of twisted tubing is used for designing a novel inhaler/e-cigarette mouthpiece to continuously maintain the required swirl before entering the oral cavity.

1.4. Human lung airway models

Conducting realistic CF-PD analysis heavily depends on the geometry of the human lung that is being used for solving fluid flow and particle transport equations. The anatomy of human lung can be associated closely to a tree in the sense that both have their characteristic bifurcating pattern. Analogous to the tree trunk that bifurcates to branches, which in-turn bifurcate to smaller branches and finally leaves, human airways consist of oral cavity, trachea (or windpipe) that bifurcate into bronchi, which further bifurcate into bronchioles and finally to the alveoli (or air sacs). Similar to the tree the wall thickness reduce after every bifurcation, for example the airway walls are thick and they keep reducing upon bifurcation into thin alveoli walls. The tube that bifurcates into two daughters is called the parent. The daughter tubes are referred to as ‘generations’ in the lung airways. The trachea bifurcates into generation 1, which bifurcate into generation 2 and so on. Thus, the n\textsuperscript{th} generation is composed of 2\textsuperscript{n} airways. The human lung comprises of 23 generations with alveoli starting from generation 16, where gas exchange occurs. Thus generations 0 – 15 are conducting airways that facilitate the incoming fluid (air) into the lung and generations 16-23 are respiratory zones where gas exchange occurs (see Figure 1.1). Modelling and simulation of such
complex and intricate geometries are of challenge till date. Approximating lung geometries that are commercially feasible and computationally reliable is another area of active research focus.

Amongst different morphometric human lung models available, Weibel’s lung model is the most widely used. Many other models are also available but are fundamentally based on the dimensions reported by Weibel from generations 0 to 23. For this study, two different models for the human upper airways have been employed. The first model is called Model I, featuring an idealized geometry, based on the approximated design parameters reported by Cheng et al., 1999. It consists of oral cavity, pharynx, larynx, trachea bronchi and bifurcations up to generation 3. This model is used for conducting preliminary computational tests and model validations due to its relative simplicity. A patient-specific, representative upper airway model, called Model II, is used.
for analyzing realistic scenarios and reporting accurate deposition patterns. Model II was developed from a magnetic resonance imaging (MRI) scan of a healthy male. Model II represents human airways up to generation 3. Assessing particle transport in the deeper lung regions is achieved by attaching triple bifurcating units (TBUs) that are modelled based on the dimensions provided by Weibel²⁰,²². A representative dual path whole lung airway model (WLAM) is created starting with the Model II upper airways and attaching two sets of TBUs after each generation, one representing right lung and the other for the left lung, all the way down to generation 23 (Kleinstreuer and Kolanjiyil²³,²⁴). The alveoli that start to occur from generation 16 onwards, are modelled by approximating them to be spherical structures with cylindrical projections that are used to attach them to the airway walls. Generations 22 and 23 are represented by double bifurcating units (DBUs). In this thesis, air flow and particle transport simulations are carried out for the conducting airways, which comprises of upper airways up till generation 15. A simple one-dimensional sketch as well as the 3D-dual-path Model II are shown in Figures 1.2a, b.

1.5. Research summary

The goal of this thesis is to establish suitable inlet conditions for fluid flow and particle streams that would benefit custom-based direct drug delivery with applications mainly to electronic cigarettes and with modifications to medical inhalers. This is achieved by conducting CF-PD analyses with human lung airway models. The use of the open-source CFD tool box OpenFOAM® (Open Field Operation and Manipulation) for conducting computational tests is first validated for its efficacy in Chapter 3 based on the supporting theory and necessary assumptions discussed in Chapter 2. The implication of applying swirling air-particle flow streams at the airway inlet on particle deposition is thoroughly explored in Chapter 4. Proof-of-concept studies are conducted in the idealized upper airways (Model I) and then later on extended to the realistic Model II. A new
non-dimensional number is proposed that is helpful in assessing the particle deposition patterns in the oral cavity for any required application (ie, e-cigarettes or medical inhalers). This is followed by modelling a novel mouthpiece that would facilitate the delivery of swirling flow air-particle streams at the oral inlet. The final part of the thesis elucidates the methodology of simulating aerosol flow streams through human lung airways using the 3D-dual-path human whole-lung airway model (WLAM).

Figure 1. 2 (a). Triple bifurcating units.
Figure 1.2 (b). The dual-path human whole-lung airway model (WLAM).
CHAPTER 2

Theory

2.1. Introduction

This chapter highlights the key aspects of mathematical model development and conducting Computational Fluid - Particle Dynamics (CF-PD) simulations. Performing a computational study that is accurate enough to match with a real-life scenario and efficient in providing reliable results is always a challenge. Hence certain assumptions need to be made (see Section 2.2). The governing equations that are being solved describe the conservation laws and account for all the necessary source and sink terms that are relevant to the scenario. Section 2.3 describes the governing equations for fluid flow and particle transport along with the necessary boundary conditions. A brief introduction to helical flows is given in Section 2.4, where a non-dimensional number, called the swirl number, is introduced, which in conjunction with the Stokes number are critical for characterizing helical fluid-particle streams. A note on particle deposition mechanisms and their influence in human lung airways is presented in Section 2.5. The use of OpenFOAM for conducting numerical simulations is described in Section 2.6.

2.2. Assumptions

- The conducting fluid medium, ie, air, is assumed to be incompressible, as there are very little temperature changes as well as low pressure and velocity fields within the human airways.

- Rigid airway walls. The fluid flow and particle deposition are studied up to generation 3 for the realistic upper airway model (Model II) and generation 15 for the dual path Whole Lung Airway Model (WLAM), where the change in lung volume is assumed constant and the expansion of the lung is neglected. Deforming walls might affect the fluid flow and
vice versa, especially in the alveolar region where the fluid-structure interaction problem would have to be addressed.

- **Dilute suspension.** In a CF-PD analysis, being a multiphase scenario, there is a minimum of two phases (carrier fluid and particles), each phase occupying a volume fraction. Treating this multiphase problem as a dilute suspension means that the particles do not crowd the entire flow domain and are present in volume fractions in the range of $10^{-3}$. Typically droplets in gas flow, solid particles in a liquid/gas flow or bubbly flows are examples of dilute particle suspensions. The particle-particle interaction (collisions, particle agglomeration, etc.) is neglected when a dilute particle suspension assumption is made.

- **One-way coupling of particles.** Dilute particle suspensions can be treated as either one-way coupled or two-way coupled. One-way coupling, assumed here, means that the particle transport is affected by the fluid flow and not vice versa.

- **Particle shape and size.** The droplets (or solid particles) are spherical in shape. This assumption allows us to accurately evaluate the drag force in the laminar/transitional/turbulent regime as per Schiller and Nauman (1933) (see Equation (2.14)). Both micron- as well as nano-particles ($d_p > 100\text{nm}$) are considered.

- **Mucus layer is ignored.** The presence of the micron-size mucus layer will demand a special boundary condition at the upper airway walls, as the mucus layer is not stationary. This may affect particle transport and deposition. This will be taken into account in the future.

- **Evaporation and condensation** of the droplets are not considered, as the focus is primarily on the impact of novel inlet conditions on the aerosol transport pattern.
2.3. Fluid flow and particle transport equations

2.3.1. Fluid flow equations

For simulating the puffing inhalation used for the e-cigarette study, the flow is in the laminar regime. The governing equations for this case are given by Equation (2.1) and (2.2) to (2.4). For validating the particle deposition (Section 3.3) and the WLAM simulation (Chapter 5), light, medium and heavy breathing profiles were considered. In such cases, the air flow is transitional-to-turbulent from the larynx to generation 3. Turbulence is accounted for by incorporating the Reynolds-averaged Navier-Stokes equations (RANS) and modelling the Reynolds stresses by using the Boussinesq hypothesis (1877) and adopting modelling techniques for the eddy viscosity. The transitional-to-turbulent regimes are best captured by the Shear Stress Transport K-Omega (SST k-ω) turbulence model for representing the eddy viscosity. Thus, the SST k-ω turbulent model equations were solved along with the fluid transport equations. They are described by Equations (2.5) to (2.8).

The Navier-Stokes equations

\[ \nabla \cdot \mathbf{u} = 0 \]  \hspace{1cm} (2.1)

\[ \frac{\partial u_x}{\partial t} + (\mathbf{u} \cdot \nabla)u_x = -\frac{1}{\rho} \frac{\partial p}{\partial x} + \nu \nabla^2 u_x \]  \hspace{1cm} (2.2)

\[ \frac{\partial u_y}{\partial t} + (\mathbf{u} \cdot \nabla)u_y = -\frac{1}{\rho} \frac{\partial p}{\partial y} + \nu \nabla^2 u_y \]  \hspace{1cm} (2.3)

\[ \frac{\partial u_z}{\partial t} + (\mathbf{u} \cdot \nabla)u_z = -\frac{1}{\rho} \frac{\partial p}{\partial z} + \nu \nabla^2 u_z + f_b \]  \hspace{1cm} (2.4)
Where, $\mathbf{u}$ denotes the velocity vector with $u_x$, $u_y$, and $u_z$ as components of velocity along the $x$, $y$, and $z$ directions. The partial derivative with respect to time is zero for all steady simulations. The density and kinematic viscosity of the carrier fluid are given by $\rho$ and $\nu$, respectively. The pressure is denoted by $p$. The body force (gravitational force) is denoted by $f_b$.

Turbulence induces a fluctuating velocity component in the velocity vector and pressure fields. Resolving turbulence and Reynolds-averaging the Navier-Stokes equations yield an additional term called the Reynolds stress tensor. The RANS equations are given below in tensor form.

$$\frac{\partial \mathbf{u}_i}{\partial x_i} = 0$$  \hspace{1cm} (2.5)

$$\frac{\partial \mathbf{u}_i}{\partial t} + \mathbf{u}_j \frac{\partial \mathbf{u}_i}{\partial x_j} = - \frac{1}{\rho} \frac{\partial p}{\partial x_i} + \frac{\partial}{\partial x_j} \left[ \nu \left( \frac{\partial \mathbf{u}_i}{\partial x_i} + \frac{\partial \mathbf{u}_i}{\partial x_j} \right) - \mathbf{u}'_j \mathbf{u}'_i \right]$$  \hspace{1cm} (2.6)

The velocity vector is represented by $\mathbf{u}_i$, where ‘$i$’ denotes the index. The $\mathbf{u}'_i$ denotes the fluctuating component of velocity, which results from the Reynolds splitting of velocity vector $\mathbf{u}_i$ into $\mathbf{u}'_i$ and $\mathbf{u}_i$, where $\mathbf{u}_i$ denotes the averaged component of velocity. The Reynolds stress term appears in the equation taking the form $-\mathbf{u}'_j \mathbf{u}'_i$. Turbulence modelling deals with modelling the Reynolds stress as described by Equation 2.7. This is based on the Boussinesq hypothesis (1877).

$$-\mathbf{u}'_j \mathbf{u}'_i = \nu_T \left( \frac{\partial \mathbf{u}_j}{\partial x_i} + \frac{\partial \mathbf{u}_i}{\partial x_j} \right) - \frac{2}{3} k \delta_{ij}$$  \hspace{1cm} (2.7)

The term $\nu_T$ is called the turbulent viscosity or eddy viscosity, $k$ is the turbulent kinetic energy and $\delta_{ij}$ is the Kronecker delta. Turbulence modelling deals with ways of approximating the turbulent viscosity with other turbulent parameters. The SST-$k-\omega$ turbulence model approximates
the turbulent viscosity as a function of the ratio of turbulent kinetic energy \( (k) \) and specific dissipation rate \( \omega \). The basic proportionality is given by ‘\( \sim \)’ symbol in Equation 2.8. The details of the SST k-\( \omega \) turbulence model is given in the Appendix (Equations (A.1) - (A.8)).

\[
\nu_T \sim \left( \frac{k}{\omega} \right) \tag{2.8}
\]

2.3.2. Particle transport equations

Euler-Lagrange model is adopted for particle tracking. ‘Euler’ applies to the carrier fluid being in a Eulerian reference frame and ‘Lagrange’ applying to the particles being in a Lagrangian reference frame. It treats the fluid to be in a continuous phase and particles to be in a discrete phase. The Euler-Lagrange modelling approach is generally applicable when the diameter of particles is greater than 100 nm and when the suspension is dilute. For relatively small spherical particles with low particle Reynolds number, given by \( Re_p = \frac{d_p |v - v_p|}{\nu} \ll 1 \), the particle transport equation takes the form of Newton’s second law of motion\(^{28,29}\) that is given by Equation (2.10).

The Euler-Lagrange model requests that the flow field has to be evolved prior to particle tracking. Because, the fluid-particle suspension is one-way coupled, where the particle trajectories are affected by the forces induced on them by the fluid. As the particles are in the Eulerian reference frame, one can obtain the trajectory of any individual particle, thereby tracking its path from its initial to its final stage. This makes Euler-Lagrange modelling a popular approach adopted for targeted drug delivery applications. The particle tracking is achieved by solving (time-marching) a system of Ordinary Differential Equations (ODEs) represented by Equations (2.9) and (2.10).

\[
\frac{dx_p}{dt} = v_p \tag{2.9}
\]
\[ m_p \frac{d\mathbf{v}_p}{dt} = \sum F_p \]  

(2.10)

where, \( \mathbf{x}_p \) denotes the position vector of a particle, \( m_p \) denotes the mass of the particle, \( \mathbf{v}_p \) denotes the velocity of the particle and source term represented by \( \sum F_p \) that denotes the summation of various forces acting on the particle. The force acting on the particle may include drag force, pressure gradient force, Brownian force, lift force, Basset force, gravity force, virtual mass force, etc. Most of the forces can be neglected based on the scenario, without much loss in the solution accuracy. For example, for micron sized particles with \( d_p > 1 \mu m \), effect of Brownian motion can be neglected. The particles are assumed to be water droplets and hence their density is far greater than that of the carrier fluid (air); hence, various forces, such as the Basset force, virtual mass force and pressure gradient force, can be neglected. The Magnus force can also be neglected as the particle does not have any spin. This results in the equation only having drag and gravitational forces. This is given by Equation (2.11).

\[ m_p \frac{d\mathbf{v}_p}{dt} = F_{\text{drag}} + F_{\text{gravity}} + F_{\text{Brownian}} \]  

(2.11)

The drag force and gravitational forces are expressed as \( F_{\text{drag}} \) and \( F_{\text{gravity}} \), respectively. The Brownian force is represented by \( F_{\text{Brownian}} \). It is circled because it is only applied for nanoparticles. The expansion of the forces is given below. All the forces act on every individual particle and are point forces.
**Drag Force**

The drag force is defined as the force experienced by the particle opposite to its relative motion with respect to the fluid flow. It is given by Equation (2.12).

\[
F_D = \frac{1}{2} \rho (v_{rel})^2 C_D A_P
\]  

(2.12)

Where, \(\rho\) is the density of the carrier fluid, \(v_{rel}\) is the relative velocity of the particle that is given by \(v - v_p\) with the subscript \(p\) denoting the velocity of the particle, \(C_D\) is the drag coefficient and \(A_P\) is the projected area of the particle. The drag coefficient for spherical particles in laminar regime, characterized by the particle Reynolds number, \(Re_p\) (Equation (2.15)) < 0.5, is given by Stokes (1851) as per Equation (2.13). The drag coefficient formulations for transitional and turbulent regimes are given in Equation (2.14) based on correlations by Schiller and Nauman (1933).

\[
C_D = \frac{24}{Re_p}
\]  

(2.13)

\[
C_D = \begin{cases} 
\frac{24}{Re_p} \left(1 + 0.15Re_p^2\right) & 0.5 \leq Re_p \leq 1000 \\
0.424 & Re_p > 1000 
\end{cases}
\]  

(2.14)

\[
Re_p = \frac{\rho_p v_{rel} d_p}{\mu}
\]  

(2.15)

Where \(d_p\) denotes the diameter of the particle and \(\mu\) denotes the dynamic viscosity of the carrier fluid. The projected area \(A_P\) is given by \(A_P = \frac{\pi}{4} d_p^2\).
**Gravitational force**

Particles experience acceleration due to gravity due to the earth’s gravitational force. Gravity plays a vital role in accounting for particle deposition due to sedimentation. The formulation of gravitational force in OpenFOAM also includes buoyancy force. Buoyancy is the upward force experienced by a body submerged in a fluid media. Buoyancy is implemented along with gravitational force by replacing particle density with the apparent density \((\rho_p - \rho_f)\). The gravitational force experienced by the particle is given by Equation (2.16). The subscripts \(P\) and \(f\) correspond to the particle and carrier fluid respectively. The mass of the particle is given by \(m_p\).

\[
F_g = m_p g \left(1 - \frac{\rho_f}{\rho_p}\right)
\]  

(2.16)

**Brownian force**

For particles of nano-scale diameters, which correspond to ultra-fine suspensions, the instantaneous momentum imparted to the particle by the fluid varies at random. This causes the particles to move in a random path, which is called Brownian motion. The transport of nanoparticles is mainly governed by Brownian motion, which increases as the nanoparticle size reduces from 100 to 1 nm\(^3\). The Brownian motion force \((F_B)\) is added in the Euler-Lagrange equation only when considering nanoparticles, it is described by Equations (2.17) – (2.19).

\[
F_B = \zeta \sqrt{\frac{\pi S_0}{\Delta t}} 
\]  

(2.17)

where \(\zeta\) denotes a zero-mean, unit-variance independent Gaussian random number, \(\Delta t\) is the time-step of particle integration and \(S_0\) is the spectral intensity function defined as:
\[ S_0 = \frac{216 \mu k_b T}{\pi^2 d_p^5 \rho_p^2 C_c} \]  

(2.18)

Here, \( \mu \) denotes the dynamic viscosity of the carrier fluid, \( k_b \) is the Boltzmann constant, \( T \) is the temperature of the carrier fluid, \( d_p \) and \( \rho_p \) are the diameter and density of the particle and \( C_c \) is the Cunningham correction factor given by,

\[ C_c = 1 + \frac{2\lambda}{d_p} \left( 1.17 + 0.525 e^{-\frac{0.78 d_p}{2\lambda}} \right) \]  

(2.19)

Where, \( \lambda \) denotes the mean free path of the carrier fluid (air) and is set to 65 nm.

2.3.3. Boundary conditions

The boundary conditions for the velocity is discussed first. For all the flow simulations, the no-slip boundary condition is given at the wall patches, as the walls are assumed to be rigid and stationary. Dirichlet boundary condition is specified at the inlet, either set to normal velocity inlet, parabolic velocity inlet or swirling flow at the inlet, depending upon the case being studied. Neumann boundary condition or zero gradient boundary condition is specified at the outlet boundaries. This ensures that there is no obstruction at the outlet and the fluid freely flows out of the domain.

The Neumann boundary condition for pressure is enforced at the wall boundaries. This ensures that there is no external suction/blowing happening through the walls. As the inlet boundary is specified by a Dirichlet condition for velocity, Neumann boundary condition for pressure is
applied here. The outlets are set to a Dirichlet boundary condition where the gauge pressure is set to zero. This ensures that the flow is driven by velocity alone.

Particles are injected at the inlet boundary, along with the carrier fluid. A ‘stick’ boundary condition is given at the walls, which ensures that the particle attains zero velocity when it approaches a distance equivalent to its radius from the wall. The particles are set to freely flow or ‘escape’ out of the outlet patches where they exit the domain. The implementation of the boundary conditions is discussed in Section 2.6.4.

2.4. Helical flows

Swirling or helical flows are types of flows where the tangential and axial components of velocity are somewhat of the same order of magnitude. They occur in many engineering scenarios, such as combustion chambers, turbomachinery, cyclone separators, etc. They also occur in blood flow, where complex helical flows are a characteristic of pulsatile large-artery hemodynamics. Tornados are other examples of such naturally occurring flows. Helical, i.e., swirling, flow streamlines appear cork-screw-like.

Swirl flow dynamics in human airways is studied by using a characteristic non-dimensional number called the swirl number. The swirl number, S, is defined as the ratio of angular and linear momentum. The swirl number (S) is mathematically defined by Equation (2.20), based on Figure 2.1.
As described in Figure 2. U, V and W are components of velocity along axial, radial and tangential directions, R is the radius of the pipe/upper bound.

2.5. Particle deposition

2.5.1. Deposition mechanism and impact on human airways

As the particles are assumed to be non-deforming, they deposit in the airway wall when they near a distance equal to their radius from the wall. The presence of mucus layer in the walls of the airways (till the trachea) ensure that the particles do not entrain into the airflow stream after its deposition. The fundamental means of particle deposition are inertial impaction, sedimentation and diffusion. Inertial impaction, as its name describes, is the deposition of particle owing to its inertia. The particle strikes a surface and deposits there due to its speed. Sedimentation is governed by gravity. When the particle loses its momentum and its residence time increases, it ultimately settles down due to the action of gravitational forces, and deposits in that area. Diffusion is the
movement of particles towards a certain direction due to a concentration gradient of particles that is present along that direction. Apart from the fundamental mechanisms of particle deposition, the characteristics of the particle, like shape (spherical, elliptical, etc.), size (micrometer, nanometer) and property (density, young’s modulus, Poisson’s ratio) also affects its deposition. Deposition of particles are also affected by the geometry of the environment where they are being transported. Geometrical bifurcations (carinal ridges), 90° turns, constrictions etc., are local ‘hot-spots’ for particle deposition, as the possibility of the particle to near the wall is higher.

Another very important parameter that governs particle deposition is the inlet condition of the carrier fluid. The inlet condition of the carrier fluid governs the velocity distributions in the domain. Since the drag force, which depends on the carrier fluid velocity, is one of the major contributors to particle inertia (Equation (2.11)), it affects the particle deposition. Breathing patterns (light, medium and heavy) here, play a vital role in particle deposition distribution in the human airways. It was shown that the particle deposition of larger diameter particles increased along the tracheobronchial airways till generation 12 as the breathing rate decreased\textsuperscript{36}. Determining where the particles are injected into the domain also, affects its deposition.

Deposition of particles may occur by means of one or more modes of deposition. Particles entering the mouth have more inertia and come across the 180° bend across the oropharynx region on towards the larynx. The deposition in the oral cavity is hence governed mainly by inertial impaction. Owing to their larger size, microspheres are more affected by deposition due to inertial impaction compared to nanospheres. Inertial impaction coupled with sedimentation plays a vital role for deposition of particles around the glottis region after the larynx. The deposition of particles in the trachea is governed by sedimentation and impaction due to turbulent dispersion, where the flow is turbulent downstream from the glottis. The flow is in the transitional regime up till
generation 3 and then becomes re-laminarized\textsuperscript{26}. The particle inertia carries over to facilitate deposition by inertial impaction in the first few bifurcations. As the particle inertia reduces, the efficacy of particle deposition due to sedimentation is predominant compared to inertial impaction in the deeper lung generations. It was shown by Kleinstreuer et al., 2007\textsuperscript{37} that sedimentation plays a major role, in addition to inertial impaction, for micron particles (diameters $1 - 7 \text{ μm}$) in generations 6 to 9. The deposition of particles in the deeper lung regions, from generations 15-23, is dominated by diffusion. Sub-micron and nanoparticle depositions along the alveolar regions is dominated by diffusion mechanism, however, sedimentation also plays a huge role in the deposition of micron sized particles.

2.5.2. Quantifying particle deposition

The deposition of particles depends on the type of study particle tracking/multiphase approach being followed. For an Euler-Lagrange modelling approach, as every individual particle is being tracked, its position where it deposits at a boundary, is known. Thus, the percentage of deposition of particles at the boundary is a parameter known as Deposition Fraction (DF) given by Equation (2.21).

$$\text{DF}_{\text{particle}} = \frac{\text{number of deposited particles in a specific region}}{\text{number of particles entering the mouth/inlet}}$$ \hspace{1cm} (2.21)

The deposition fraction can also be expressed in the form of percentage values. Another important parameter that is popularly used is the Deposition Efficiency, given by Equation (2.22).

$$\text{DE}_{\text{particle}} = \frac{\text{number of deposited particles in a specific region}}{\text{number of particles entering this region}}$$ \hspace{1cm} (2.22)
Usually, since Euler-Lagrange modelling approach is limited to microspheres with diameter $d_p$ in the range of $d_p > 100 \, nm$, Euler-Euler modelling approach is used for nano-spheres in the range $1 < d_p < 100 \, nm^{38}$. The Euler-Euler approach treats particles to be in a continuous phase and evolves the particle concentration using a convection-diffusion equation. The effects of isolatable individual forces acting on the particle are usually absorbed/modelled in a diffusive source term in the convection-diffusion equation. The Euler-Euler approach for particle tracking is described by Equation (2.23).

$$\frac{\partial Y}{\partial t} + \frac{\partial}{\partial x_j}(u_j Y) = \frac{\partial}{\partial x_j}\left(D_p \frac{\partial Y}{\partial x_j}\right)$$  \hspace{1cm} (2.23)

Where, $Y$ denotes the mass fraction, $t$ denoting time, $x_j$ and $u_j$ denoting space variable and velocity vector with $j$ being the index ($j=1, 2, 3$) and $D_p$ is the Stokes-Einstein diffusion coefficient. The regional deposition fraction and deposition efficiency are given by Equations (2.24) and (2.25)$^{39}$.

$$DF_{region} = \frac{\sum_{i=1}^{n} (A_i j_{wall,i})}{(Q_{mouthin} Y_{mouthin})}$$  \hspace{1cm} (2.24)

$$DE_{local} = \frac{\sum_{i=1}^{n} (A_i j_{wall,i})}{(Q_{localin} Y_{localin})}$$  \hspace{1cm} (2.25)

Where, $A_i$ is the area of the boundary cell (index $i$) and $j_{wall,i}$ is the particle flux across the local boundary cell. It is given by Equation (2.26).

$$j_{wall,i} = -D_p \frac{\partial Y}{\partial \eta_{wall,i}}$$  \hspace{1cm} (2.26)
Where, $\frac{\partial}{\partial \eta}$ denotes normal wall gradient. $Q$ in equation 2.24 and 2.25 denotes the flow rate with suffixes “localin” and “mouthin” denoting the inlet at any specific region and the mouth inlet respectively.

Euler-Lagrange modelling approach is performed in this thesis and hence Equations (2.21) and (2.22) are used for quantifying particle deposition. The diameter of the particle is expressed in the form of a non-dimensional group that is relevant to particle dynamics, called the Stokes number. It characterises the behaviour of particles suspended in fluid flow. The Stokes number is given by Equation (2.27).

$$St = \frac{\rho_p d_p^2 U}{9 \mu D}$$

Where, $\rho_p$ and $d_p$ denote the particle density and diameter respectively, $U$ denotes the characteristic velocity of the carrier fluid, $\mu$ denotes the dynamic viscosity of the carrier fluid and $D$ denotes the characteristic length of the conduit (usually diameter for pipe flows).

2.6. Computational Fluid-Particle Dynamics (CF-PD)

2.6.1. Introduction to OpenFOAM

Computer experiments were performed using a cost-free, open-source Computational Fluid Dynamics tool box, OpenFOAM® (Open Field Operation and Manipulation). OpenFOAM has a wide user-base ranging from commercial and academic organizations across most areas of engineering and science. It is built to facilitate the user to conduct any form of computational study by providing features right from meshing (blockMesh and snappyHexMesh) to solving (using OpenFOAM applications) complex fluid flows involving chemical reaction, multiphase flow,
turbulence and heat transfer, solid dynamics, electromagnetics etc. Also, post-processing and analyzing the results can be done, using the third-party open source application ParaView.

The codes for OpenFOAM are written in C++ which, being an Object-Oriented Programming paradigm, brings in various handy features/concepts like classes and objects, encapsulation, hereditary and polymorphism. This helps the user to understand the code structure quickly and, being open source, facilitates the user to have complete freedom to customize and extend its functionality. The user can fully utilize the computing power by running simulations in parallel. The method of parallel computing used by OpenFOAM is called domain decomposition, where the geometry and associated fields are broken into pieces and allocated to separate processors for solving the governing equations. Running simulations in parallel involve an additional three-step procedure: decomposition of the mesh and fields, running the application in parallel and post-processing the decomposed case. OpenMPI (Message Passing Interface) implementation is followed for running in parallel, although OpenFOAM allows for other libraries to be used.

To use OpenFOAM, before executing the solver, a case must be set-up. Section 2.6.2 deals with the basics of OpenFOAM case structure.

2.6.2. OpenFOAM case structure

The simulations to be performed by OpenFOAM are in directories that follow a specific structure as given in the figure below. The hierarchy of an OpenFOAM case that contains the minimum set of files needed to run a simulation is shown in Figure 2.2.
The `<case>` directory is the location of your simulation. It branches into three main directories, the system, constant and time directories. There is only one constant and system directory, but there can be many time directories.

The time directories hold the solution for your variables (like p, u, T etc.) at different points of time in your simulation. They are labelled starting from ‘0’, which is called as the zero folder, to the final simulation end time. The initial and boundary conditions are specified in the zero folder before the start of the simulation. OpenFOAM allows the user to give different kinds of boundary conditions for velocity, pressure etc. right from the most commonly used ones like noSlip, which

Figure 2. 2. OpenFOAM case structure.
denotes the no-slip boundary condition for velocity, to complex time varying boundary conditions using OpenFOAM add-on swak4Foam (Swiss Army Knife for FOAM). Being open source, it also allows the user to develop a custom boundary condition that can be implemented in the zero folder.

The constant directory houses the polyMesh directory and other relevant dictionaries that hold information pertaining to the simulation, denoted by xProperties in Figure 2.2. The xProperties, for example may be, transportProperties – that carries information regarding the carrier fluid (Newtonian/non-Newtonian, viscosity, density, thermal diffusivity etc.), turbulenceProperties – that carries information relating to the way in which turbulence is treated (RANS, LES, DNS), kinematicCloudProperties – that carries information relating to Lagrangian particle tracking for particle dynamics. The polyMesh folder contains information relating to the mesh that is readable by the OpenFOAM. It houses dictionaries like boundary, cellZones, faces, points, neighbor etc.

The system directory has minimum of 3 important dictionaries, namely, controlDict, fvSchemes and fvSolution. The controlDict dictionary contains information relating to the solver(application) being called, the time-step to be used, solution save files, start time/end time, external libraries that are to be included and other simple post-processing options. The fvSchemes denotes the discretization schemes being used to solve, for example gradient, divergence or Laplacian operations. The fvSolution holds information relating to the equation solvers (e.g. Gauss elimination), tolerances and other algorithm control settings. The system directory can also have additional dictionaries like blockMeshDict, (for OpenFOAM meshig), decomposeParDict (for parallel computing) etc. depending upon the simulation.
2.6.3. Case set-up

This section briefly describes the case set up to conduct fluid-particle dynamics simulations using OpenFOAM. As discussed in Section 2.3.2, one-way coupled fluid-particle simulations are carried out by evolving the flow first, followed by executing the particle simulation after flow convergence. For all the steady simulations performed in this thesis, OpenFOAM’s incompressible, steady state, turbulent solver simpleFoam is used. Lagrangian particle tracking is achieved using OpenFOAM’s solver icoUncoupledKinematicParcelFoam with modifications. Transient simulations are conducted by coupling OpenFOAM’s incompressible, turbulent, transient solver pimpleFoam and the Lagrangian particle tracking solver icoUncoupledKinematicParcelFoam with modifications.

The zero folder was set with initial values for pressure, velocity and SST k-ω turbulence parameters along with the necessary boundary conditions. A custom boundary condition for swirling flows based on Section 2.4 was formulated in OpenFOAM.

2.6.4. Boundary conditions in OpenFOAM

Boundary conditions limit the values of the flow variables that are being solved in the domain. In a computational domain, they are enforced by setting values in the imaginary ‘ghost’ cells that are set(s) of layer(s) of cells mirroring the boundary cells outside the domain. The boundary conditions in OpenFOAM are specified in the zero folder. In this directory, there are different sub-directories for each variable (pressure, velocity, temperature, etc.) being solved. The initial and boundary conditions pertaining to them individually, can be set here. Different boundary conditions for different kinds of patches are given in Table 2.1 and Table 2.2.
Case (A): Laminar flow field.

Table 2.1. Boundary conditions for pressure and velocity.

<table>
<thead>
<tr>
<th>Boundary patch type</th>
<th>Velocity Type</th>
<th>Velocity Syntax</th>
<th>Pressure Type</th>
<th>Pressure Syntax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inlet</td>
<td>Dirichlet</td>
<td>fixedValue</td>
<td>Neumann</td>
<td>zeroGradient</td>
</tr>
<tr>
<td>Outlet</td>
<td>Neumann</td>
<td>zeroGradient</td>
<td>Dirichlet</td>
<td>fixedValue set to uniform 0</td>
</tr>
<tr>
<td>Walls</td>
<td>No slip</td>
<td>noSlip/fixedValue</td>
<td>Neumann</td>
<td>zeroGradient</td>
</tr>
</tbody>
</table>

Case (B): Turbulent flow field.

Table 2.2. Boundary conditions for turbulence parameters.

<table>
<thead>
<tr>
<th>Boundary patch type</th>
<th>Turbulent kinetic energy Type</th>
<th>Turbulent kinetic energy Syntax</th>
<th>Specific dissipation frequency Type</th>
<th>Specific dissipation frequency Syntax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inlet</td>
<td>Dirichlet</td>
<td>fixedValue</td>
<td>Dirichlet</td>
<td>fixedValue</td>
</tr>
<tr>
<td>Outlet</td>
<td>Neumann</td>
<td>zeroGradient</td>
<td>Neumann</td>
<td>zeroGradient</td>
</tr>
<tr>
<td>Walls</td>
<td>Dirichlet</td>
<td>kqRWallFunction</td>
<td>Dirichlet</td>
<td>omegaWallFunction</td>
</tr>
</tbody>
</table>

For any laminar flow simulation, boundary conditions from case (A), Table 2.1, are set for pressure and velocity. Additional boundary conditions for turbulence parameters, turbulent kinetic energy and specific dissipation rate are set, following case (B), Table 2.2, while accounting for turbulence. Boundary conditions for only turbulent kinetic energy and specific dissipation frequency are specified in Table 2.2 as SST-$k\omega$ turbulence model is used to model the turbulent/eddy viscosity to accurately capture the transitional-to-turbulent regime. Brief descriptions of the boundary conditions being used are given below.
**fixedValue**

This boundary condition enforces the solver to always maintain the value given by the fixedValue boundary condition at the boundary patch where it is specified. The syntax is given below.

\[
\text{<patchName>}
\{
    \text{type} \quad \text{fixedValue};
    \text{value} \quad \text{uniform} \quad \langle \text{value} \rangle;
\}
\]

The `<patchName>` is the name of the patch at which it is being specified, `type` corresponds to the name of the boundary condition that is being used/recognized by the solver and the value enforced at that patch is given by `value`. The value can correspond to a scalar (pressure, turbulent kinetic energy, temperature, etc.) or a vector (e.g. velocity). The values for a vector are specified in parenthesis.

**noSlip**

It is a special kind of fixedValue boundary condition, where the value is always set to zero.

**zeroGradient**

This boundary condition indicates that the gradient of the variable normal to the boundary surface is zero. It follows Equation (2.28).

\[
\frac{\partial \phi}{\partial \eta} = 0
\]  

(2.28)

Where, \( \phi \) corresponds to any flow variable and \( \eta \) is the normal vector to the boundary patch. This is achieved by setting the ‘ghost’ cells to have the same value of \( \phi \) as the internal cells adjacent to the boundary patch.
Wall functions

Turbulence induces a fluctuating component in the flow variables and the Reynolds stress term (described in Section 2.3.1) that alter the velocity profile and the near-wall physics. The wall is divided into three different regions, starting from nearest to farthest from the wall, viscous sublayer, buffer layer and log-law region. The layers are categorized according to the value of the non-dimensional wall distance function $y^+$ that is given by Equation (2.29).

$$y^+ = \frac{u_\tau y}{\nu}$$

(2.29)

Where, $u_\tau$ is the friction/shear velocity that is the square-root of the ratio between wall shear stress and density of the fluid, $y$ is the distance to the wall and $\nu$ is the kinematic viscosity of the fluid.

The viscous sublayer is the region in the domain where the $y^+ < 5$, the log-law layer corresponds to $30 < y^+ < 200$ and the region in between is the buffer layer. Viscous stresses dominate over turbulent stresses in the viscous sublayer and the log-law layer is the region where the vice-versa is true (called the turbulent core). The transitional layer between the two layers is the buffer layer, where both viscous stresses and turbulence stresses are of equal magnitudes and order. The values of the turbulent parameters can be clearly specified at the viscous sublayer and the log-law layer, but not so clearly in the buffer layer. Wall functions are hence used to resolve this issue. They are empirical relations that are used to satisfy the physics of the flow from near wall to the turbulent core.

kqRWallFunction

This is a special kind of boundary condition for the turbulent kinetic energy ($k$) in OpenFOAM that is given at the boundary patches. It is a type of a zeroGradient Neumann boundary condition near the wall and assumes a value specified by ‘value’ in the core, for the first iteration. Its syntax is given below.
omegaWallFunction

These are special boundary conditions for specific turbulent dissipation rate (ω) in OpenFOAM. It is a special wall function which can switch between viscous and log-law region according to $y^+$ values, using a blending function. In the intersection of the viscous sublayer and log-law region value is calculated through blending the viscous and log-law sublayer value. The syntax is given below,

<code>
<wall boundary patch>
{
    type omegaWallFunction;
    value $internalField;
}
</code>

2.6.5. Numerical schemes

The Navier-Stokes equations for fluid flow and the Lagrangian equation for particle tracking appear in partial differential equation form and they need to be converted into discretized form for conducting CF-PD analysis. This is achieved by discretization schemes that need to be carefully chosen for balancing between accuracy of the solution and efficiency of its computation. This section describes the various numerical schemes used for temporal and spatial discretization.
**Temporal discretization schemes**

The time discretization schemes can be selected by simply typing the desired scheme under `ddtSchemes` section, in the `fvSchemes` dictionary in system directory. Partial differential with respect to time may not be discretized for the steady state simulations and hence they are set to `steadyState` that signals the solver to set any time derivative to zero. For the transient simulations, first order implicit Euler scheme is used by setting `euler` under `ddtSchemes`.

**Gradient schemes**

Similar to the time discretization scheme, the gradient scheme is also set in `fvSchemes` dictionary under `gradSchemes`. Gradient schemes for individual variables can be set, for all simulations performed in this thesis, Gauss linear scheme was used. The Gauss linear scheme requires interpolation of the field variables at the cell boundaries. Hence, an interpolation scheme, namely linear interpolation was specified under the `interpolationSchemes` sub-dictionary.

**Divergence schemes**

The divergence schemes for individual variables can be specified under `divSchemes` in `fvSchemes` file. Gauss linear scheme is used for calculating the divergence operation for all variables except specific turbulence dissipation frequency (ω) and turbulent kinetic energy (k), where bounded gauss limited linear was used.

**Laplacian scheme**

The Laplacian operation occurs in the viscous terms of the incompressible Navier-Stokes equations. They computed by using Gaussian integration of the gradients over the cell. Thus, it requires the gradients of the variable at the cell boundaries to be calculated prior to its computation. To interpolate the gradients at the boundaries, linear interpolation is used. The Laplacian scheme
is specified under laplacianSchemes and the interpolation is specified under interpolationScheme sub-dictionary in the fvSchemes dictionary.

**2.6.6. Solution algorithm and control**

The equation solvers with their necessary parameters needed for carrying out the solution of variables, tolerances and relaxation factors are all specified in the fvSolution dictionary. Specific solvers/algorithms for each of the flow variable being solved (p, U, T, etc.) can be specified in this dictionary. Geometric Algebraic Multi Grid (GAMG) solver was used for solving pressure and velocity, smooth solver was used for solving turbulent kinetic energy and specific turbulence dissipation frequency. The GAMG solver produces a quick solution on a mesh with smaller number of cells and then maps this solution to the finer (or original) mesh. Incorporating a GAMG solver reduced computation time without compensating on the solution accuracy. Smooth solver was used for solving model equations for specific turbulence dissipation frequency and turbulent kinetic energy. Gauss-Seidel was used as a smoother, which is required by the smooth solver.

**2.6.7. Modeling, meshing and post-processing**

All fundamental airway geometries, ie, Model I, Model II, and the TBUs are in-house models. The novel mouthpiece and its function were positively reviewed by NCSU’s OTCNV (Review #18153) on 03/18/2018. Its geometry was imaged by using the computer-aided design software SolidWorks® 2018. Meshing of all geometries was carried out using mesh generation software ANSYS ICEM CFD® 16. Post-processing was achieved with the help of Tecplot® 360 Ex 2015 R2 and open-source data analysis and visualization software Paraview 5.5.1.
CHAPTER 3
Model Validations

3.1. Introduction

As described in Section 2.6, the computer experiments were performed using a cost-free, open source Computational Fluid Dynamics tool box OpenFOAM®. This chapter confirms the validity of using the proposed OpenFOAM solvers and methodology to conduct CF-PD simulations and analyses. It is divided into two sections, i.e., Section 3.2 where the reliability of Euler-Lagrange particle tracking in OpenFOAM is compared with experimental results from Bushi et al., 2005\textsuperscript{41}. Section 3.3 validates the use of OpenFOAM for evaluating particle transport and deposition for turbulent flow\textsuperscript{42,43} in human lung airways by matching results with experimental observations from Cheng et al., 1999\textsuperscript{21}.

3.2. Lagrangian particle tracking in OpenFOAM

The Euler-Lagrange modelling technique solves the fluid flow and particle transport equations in different reference planes. The fluid flow is treated as a continuous phase and the governing equations for it based on Eulerian reference plane, are solved iteratively using the Semi-Implicit Method for Pressure Linked Equations (SIMPLE) algorithm. The Lagrangian particle tracking method, being in the Lagrangian frame of reference, requires the particle positions to be evolved by time marching technique using Equation (2.11). As this procedure requires the fluid velocities at each point, the steady state Euler-Lagrange CF-PD simulations are conducted by solving the flow till convergence (based on tolerance limits set in fvSolutions) followed by using these solutions to evolve the particle cloud\textsuperscript{44}. However, transient simulations for the WLAM are conducted (see Chapter 5) by solving for the particle transport equations after the flow solution is converged for that time-step.
As described in Section 2.6.3, steady fluid simulations are conducted using OpenFOAM’s steady state, turbulent solver **simpleFOAM**. After a converged solution for the flow is obtained, particles are injected into the domain through the inlet patch, same as where the fluid enters. The Euler-Lagrange model used for particle tracking is incorporated in OpenFOAM using the solver **icoUncoupledKinematicParcelFoam**. The fate of each particle can be determined by knowing its final position. Computational results for particle tracking from OpenFOAM are compared with experimental results by Bushi et al., 2005\(^{41}\), where *in vitro* experiments were conducted for tracking spherical particles through a Y-shaped bifurcation.

### 3.2.1. Geometry and mesh

The geometry of the Y-bifurcation is shown in *Figure 3. 1*. It consists of a parent tube with diameter 6 mm bifurcating to two daughter tubes with diameters 6 mm and 4 mm respectively. Uniformly sized spherical particles were used for the particle simulations. The diameter of the parent tube is depicted as \(D_0\) and the diameter of the two daughters are depicted as \(D_1 (=D_0)\) and \(D_2 (=2\frac{D_0}{3})\) in *Figure 3. 1*. 
The geometry is decomposed into approximately 0.4 million elements. The fluid and particles stream enter through the parent tube and exit through the daughter tubes.

3.2.2. **Results and discussions**

The experimental analysis aimed at studying the hemodynamic factors determining the trajectory of emboli across a ‘Y’ channel. Spherical particles of different diameters were used under steady flow conditions, representing the emboli in a bifurcating artery. The selective entry of particles to the daughter tubes was studied for four different out-flow ratios. This was studied by determining the number of particles that entered the daughter tubes for different controlled flow rates (Q1 and Q2) across each outlet (D1 and D2). The results were reported based on the ratio of particles...
entering/exiting the two daughter tubes (N1/N2) for different volumetric flow rates across them (Q1/Q2). The fluid was considered Newtonian.

For simulating such arterial flows, a fully-developed parabolic flow profile corresponding to a Reynolds number (Re) of 500 was given at the inlet patch. The outlet patches were given with appropriate boundary conditions as described in section 2.6.4. Two different particle sizes, 0.6 mm and 1.6 mm are used for comparison with the experimental results. The particles are considered to be neutrally buoyant, meaning the particle density is equal to that of the carrier fluid. The effect of other body forces, like gravitational forces, are neglected. The number of particles exiting D1 is N1 and the number of particles exiting through D2 is N2. Particle independent study was conducted to ensure that the results are not affected by the number of particles injected. To achieve this 10k, 30k and 90k particles were used. The results for N1/N2 varied within 0.5 % difference between the 30k and 90k cases and hence 30k particles were injected.
Figure 3. 2. Ratio of 0.6 mm particles through the outlets.

Figure 3. 3. Ratio of 1.6 mm particles through the outlets.
By analyzing Figure 3.2 and Figure 3.3, it can be observed that CF-PD results with OpenFOAM are in good agreement with the experimental results reported by Bushi et al., 2005\textsuperscript{41}. All of the results are well within 4\% error except in the case of 1.6 mm particles were the flow ratios of 2.5 and 4 have errors of approximately 12\%. This error arises as some particles are trapped in the recirculating zones for this case, and never exit through the outlet. The results hence validate the reliability of OpenFOAM’s one-way coupled particle tracking solver.

### 3.3. Particle deposition

The deposition of particles is of primary interest in this thesis. The mechanisms governing particle deposition is discussed in section 2.5. The deposition of particles in an Euler-Lagrange model can be monitored by evaluating the deposition fraction or the deposition efficiency, as described in section 2.5.2. This section validates the use of OpenFOAM for studying particle deposition in human lung airways. Steady state air-particle flow simulations are conducted in an idealized human upper airway model (Model I) and compared with the results obtained by Cheng et al., 1999\textsuperscript{21}.

#### 3.3.1. Geometry and mesh

The idealized lung model (Model I) is composed of an oral cavity based on a dental impression of a human volunteer, pharynx, larynx, trachea and bifurcations up till generation 3 based on dimensions measured from a cadaver. The computer aided design (CAD) model was based on the specifications used by the experimental study. The geometry is shown in Figure 3.4.

The Model I comprise of the oral inlet (20 mm in diameter), followed by the oropharynx, glottis, larynx, trachea, bronchi and bifurcations up to generation 3. It was discretized into 2.7 million elements out of which about 1.5 million were tetrahedral and the rest being prism elements. The
upper airways are labelled in Figure 3.4. The glottis is a small constriction (see Figure 3.4) after the pharynx.

![Figure 3.4. Idealized lung airway model - Model I.](image)

3.3.2. Turbulence modeling

In human airways, the presence of the narrow glottis followed by a sudden expansion into the trachea induces turbulence in the air flow downstream for even moderate breathing conditions (i.e., $Q > 12$ LPM), the regime here is transitional-to-turbulence\textsuperscript{45}. In this thesis, the SST k-ω RANS framework is used for capturing this flow regime. This approach models the turbulent stresses and
solves for the averaged equations for fluid flow. Hence the fluctuating velocity components \(u'\) are not explicitly available by the solver.

This directly affects the particle trajectories in the Euler-Lagrange model. In general, when RANS model is used for solving fluid flows, they are coupled with eddy interaction model (EIM or discrete random walk (DRW) models), while solving for particle transport that accounts for the interaction of the particles with the turbulent eddies\(^{42}\). This involves modelling the fluid’s fluctuating components of velocity following a stochastic approach. The EIM however is inaccurate when the particle size is comparable to the eddy’s length scale, two-way coupling scenarios and particle-particle interaction cases\(^{42}\). Thus, it is applicable for the current scenario.

The fluctuating components of velocity is modelled following Equation (3.1)\(^{46,47}\)

\[
\mathbf{u}' = \xi \sqrt{\frac{2}{3} k}
\]  
(3.1)

Where, \(\mathbf{u}'\) is a vector (with components say, \((u'_x, u'_y, u'_z)\)) that refers to the fluctuating velocity components, \(k\) is the turbulent kinetic energy that is solved in the RANS equations and \(\xi\) represents random numbers with zero mean and unit variance of Gaussian distribution. However, the drawback of this model is the assumption of turbulent isotropy, meaning the components of velocity fluctuations are equal \((u'_x = u'_y = u'_z)\). In Mayank et al., 2016\(^{48}\) a formulation is discussed to correct this discrepancy by including wall damping functions for the fluctuating component of the velocity normal to the wall (represented by \(u'_n\)) in regions where \(y^+ < 10\). This formulation is semi-empirical and specific for Model I. It is described in Equations (3.2) and (3.3).

\[
u_n' = f_v \xi \sqrt{\frac{2}{3} k}
\]  
(3.2)
where, $f_v$ denotes the damping function given by:

$$f_v = a \cdot St \cdot (\exp(b \cdot qr)) \cdot (1 - e^{c \cdot y^+}) \quad (3.3)$$

Where $St$ is the Stokes number (Equation (2.27)) and $y^+$ is the non-dimensional wall distance function (Equation (2.29)), $qr$ is the ratio of maximum inhalation flow rate (corresponds to $Q = 60$ LPM) to the simulated flow rate, $a, b$ and $c$ are model coefficients set to 1, 0 and -0.02 respectively for Model I. This formulation is applied in OpenFOAM by modifying the existing stochastic particle dispersion model `stochasticDispersionRAS`.

### 3.3.3. Results and discussions

Cheng et al.\textsuperscript{21} reported that wax models were used to make the cast for Model I, which is made using silicone rubber material and polystyrene latex fluorescent particles were used. Three different breathing profiles were considered that denote light, medium and heavy breathing, corresponding to the volumetric flow rates ($Q$) of 15, 30 and 60 LPM. The deposition fraction (DF) of particles (of varying Stokes numbers) in the oral cavity and pharynx were reported as well.

It was observed that the deposition in the oral cavity increases adversely based on the size of the particles, which is due to inertial impaction of particle deposition. A curve fitting was done which represent deposition pattern that resembles an ‘S’ curve. The deposition fraction results are used as a reference for comparing with OpenFOAM. The boundary conditions and case set up are based on parameters described in Sections 2.6.3 and 2.6.4.

Constant velocities that correspond to light, medium and heavy breathing profiles were given at the inlet with other appropriate boundary conditions to pressure and turbulence parameters (see Section 2.6.4). Sphere-drag and gravitational forces were considered for the particle simulations. The results from OpenFOAM are reported in Figure (a) - (c). It can be observed that the
OpenFOAM simulation results are in good agreement with the results reported by Cheng et al.\textsuperscript{21}; thereby validating OpenFOAM use for particle tracking. Particle independent study was done for 50k, 100k and 120k particles and 100k particles were injected at the inlet.

However, some discrepancies can be observed for $\text{St} > 0.1$, where the OpenFOAM results slightly over-predict in the oral cavity the particle deposition by around 10 -15%. This is because with larger particle diameters inertia of the particles increases, contributing greatly towards deposition. The drag force plays a crucial role in determining the particle’s momentum and it is formulated under the assumption that particles are perfectly spherical. However, Cheng et al.\textsuperscript{21}, reported the particle characteristic size but not its shape. There is a possibility that some of the particles used may not have been perfect spheres; hence, changing the drag forces acting on them. Sample simulation results (for $\text{St} = 0.04$ and $Q = 15$ LPM) depicting the particle deposition (in red) and velocity profile contour at the mid-section of the geometry are given in Figure 3.6.
Figure 3.5 (a). Deposition fraction in the oral cavity and pharynx for light breathing rate.
Figure 3.5. Deposition fraction in the oral cavity and pharynx for (b) moderate and (c) heavy breathing rates.
Figure 3.6. CF-PD simulation corresponding to a flow rate of 15 LPM and Stokes number of 0.04.
CHAPTER 4

Swirling Fluid-Particle Flow Dynamics

4.1. Inhalation conditions for vaping devices

Inhalation of aerosols/drugs from various vaping devices, including e-cigarettes and inhalers, are subject to fluid-particle interaction and related physics. The fundamental idea of modifying the inlet conditions of the air-particle flow streams to achieve predetermined segmental deposition for aerosol/drug targeting (Section 1.3) is explored in this chapter.

Specifically, achieving custom segmental deposition of inhaled droplets by utilizing helical or swirling flow streams and its control is simulated and analysed. As discussed in Sections 1.3 and 2.4, helical, i.e., swirling flows are generated when a tangential velocity component develops in an axial flow, say, through a pipe and their flow streamlines appear cork-screw-like. Naturally, they reduce the momentum of the fluid in axial direction. Hence, they enhance the deposition through sedimentation (applicable to e-cigarettes) or reduce deposition through inertial impaction (applicable to medical inhalers). Their applicability to e-cigarettes is focussed on in this thesis.

There is a need to control the amount of nicotine and flavours delivered by vaping devices to the deep lung (to break-even between drug effect and health concerns) and to the back of the mouth (for the taste/flavour). The inhalation profile for an experienced e-cigarette user is given in Figure 4.1 (a). A typical e-cigarette user takes longer puffs at lower air volume rates\textsuperscript{49,50}. A curve fitting for this inhalation profile following Equation (4.1) is given by Vansickel et al., 2014\textsuperscript{49}.

\[ Q_{in} = -0.0118 \ t^9 + 0.1529 \ t^8 - 0.2119 \ t^7 - 6.4209 \ t^6 + 47.4445 \ t^5 - 151.5906 \ t^4 + 255.3924 \ t^3 - 224.9871 \ t^2 + 91.5612 \ t + 1.3663 \]  \hspace{1cm} (4.1)
Figure 4.1 (a). Realistic EC puff profiles (Vansickle et al., 2014) of a regular EC user.

Figure 4.1 (b). Quasi-transient inhalation flow profile for e-cigarette puffing.
Observing Figure 4.1 (a), the flow rate is for the most part steady and peaks at about 20 ml/s, which does not facilitate for deposition in the oral cavity due to fluid-particle inertia. Thus, the deposition is less there, causing large uncontrolled amounts of drug dosage to the deep lung. The e-cigarette being a “healthier” option compared to smoking conventional cigarettes becomes a question. The deposition of drug in the oral cavity is improved by enhancing deposition due to sedimentation with the use of swirling flows. This allows controlled dosage to the lung and also accounts for taste.

As the puffing profile (Figure 4.1 (a)) resembles a steady state, a representative quasi-transient flow rate corresponding to an average inhalation profile of approximately 1 LPM is considered for e-cigarette puffing/inhalation. This is shown in Figure 4.1 (b). For this representative inhalation profile, the effect of swirling flow on particle deposition is first analyzed with Model I with truncated upper oral airways, followed by Model II, which is based on human upper airways that spans from mouth to generation 3.

4.2. Simulation Results with Model I

As described earlier in Section 2.4, swirl flow dynamics in human airways is studied using a characteristic non-dimensional number called the swirl number (S) (see Equation (2.20)). Another critical non-dimensional number that is used alongside the swirl number for characterizing direct drug delivery (through inertial impaction) is the Stokes number (St). Their product (S*St) represents a new non-dimensional group, useful for mouthpiece design optimization that can facilitate custom based drug delivery. The deposition of particles is monitored by the deposition fraction (DF) (Equation (2.21)).
Results from tests performed with the geometry obtained by truncating the idealized lung geometry (Model I), which is the in-house upper airway geometry based on specifications by Cheng et al., 1999 are shown in this following section. The truncated upper airway geometry is shown in Figure 4.2.

Figure 4.2. Truncated upper airway model – Model I.

The region marked in blue is the inlet for the helical air-particle stream. The diameter of the inlet tube is 6 mm. This denotes the mouthpiece representing that of an e-cigarette or medical inhaler. The region that appears red is part of the lips/mouth. The surface in silver depicts the walls of the oral cavity, pharynx, glottis, and larynx. The truncated portion in the bottom (outlet) leads to the trachea and bronchi, i.e., the remaining air-particle stream enters the trachea.

The geometry is discretized into 1.6 million elements composing of 0.5 million prism cells along the walls and 1.1 million tetrahedral cells covering the interior. 100k particles are injected at the inlet for all cases.
4.2.1. Effect of implementing swirling flow

To compare the effect of swirling flow injection with other methods, a deposition study for particles of 5µm (St = 0.0075) was carried out. The smallest particle size that is considered for the study is 5µm. The following cases are analysed:

- Normal, i.e., horizontal, air-particle flow into the inlet tube.
- Angular air-particle flow injection: 10-degree positive angle vs. 10-degree negative angle with respect to the horizontal axis.
- Swirling air-particle flows with swirl numbers 0.6, 1, 1.3, 2, 4 and 6.

<table>
<thead>
<tr>
<th>Case</th>
<th>Axial Component of Velocity (m/s)</th>
<th>Tangential Component of Velocity (m/s)</th>
<th>U magnitude (m/s)</th>
<th>Swirl Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.4243</td>
<td>0.4243</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>2</td>
<td>0.33</td>
<td>0.5</td>
<td>0.6</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>0.27</td>
<td>0.54</td>
<td>0.6</td>
<td>1.3</td>
</tr>
<tr>
<td>4</td>
<td>0.19</td>
<td>0.57</td>
<td>0.6</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>0.1</td>
<td>0.59</td>
<td>0.6</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>0.066</td>
<td>0.596</td>
<td>0.6</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 4.1. Cylindrical components of Velocity for different Swirl numbers.
The flow contours (along the mid plane) are shown in Figures 4.3 (b)-(e). The cylindrical components of velocity pertaining to the different swirl numbers used is shown in Table 4.1. The streamlines are shown in the swirling flow to visualize the cork-screw-like flow pattern at the inlet (see Figure 4.3 (d)-(e)). The contours of other swirl numbers are not shown due to space constraints. The deposition of particles in the oral cavity is given in Table 4.2.
Figure 4.3 (b)-(e). Comparison of Injection Modes.

(b) Normal Injection.
(c) Angular Injection of 10 degrees.
(d) Swirling Flow of $S = 0.6$.
(e) Swirling Flow of $S = 6$. 
The oral deposition is improved from 6% (Normal injection) to 37% (Swirling flow of S=6). Thus, the effect of helical flow greatly improves the local deposition of inhaled aerosols in the human oral cavity. This can be attributed to the strong swirling zones created in the mouth near the inlet region. These zones reduce axial inertia, increase the particle residence time, and thereby contribute to enhanced particle deposition through sedimentation in selected regions. The comparison (velocity contours) between swirling flow of $S = 0.6$ and $S = 6$ is shown in Figure 4.4. The strong swirling zones that reduce inertial forces much early-on can be observed for the higher swirl number case.

### 4.2.2. Droplet depositions for new non-dimensional number

The type of vaping/medical device being used will dictate the Stokes number relating to the particle dynamics. So, deposition of particles based on a new non-dimensional number, i.e., the product of swirl number and Stokes number ($S \times St$) is studied. The Stokes number has been increased by
increasing the particle size diameter and keeping the characteristic velocity constant (U = 0.6 m/s). The data for Stokes number calculation is given in Table 4.3. The results are shown in Figure 4.5.

![Figure 4.4. Velocity contours for Swirl number 0.6 (left) and Swirl number 6 (right).](image)

**Table 4.3. Stokes number calculation.**

<table>
<thead>
<tr>
<th>Case</th>
<th>Particle Diameter $d_p$ (m)</th>
<th>Stokes Number (St)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$5 \times 10^{-6}$</td>
<td>0.007</td>
</tr>
<tr>
<td>2</td>
<td>$6 \times 10^{-6}$</td>
<td>0.01</td>
</tr>
<tr>
<td>3</td>
<td>$13.4 \times 10^{-6}$</td>
<td>0.05</td>
</tr>
<tr>
<td>4</td>
<td>$16.9 \times 10^{-6}$</td>
<td>0.08</td>
</tr>
</tbody>
</table>
It can be observed that the oral deposition increases with larger $S^*St$ values. For a prescribed Stokes number, determined by the type of smoking/vaporizing device used, the desired local aerosol deposition can be achieved by selecting an appropriate swirl number. A desired range of deposition say from 20 to 40% in the oral cavity can be obtained for a combined swirl and Stokes number ranging from 0.02 to 0.035. One such configuration is of swirl number equal to 4 and Stokes number equal to 0.007 ($S^*St = 0.028$) that yields 23.7% deposition in the oral cavity, as shown in Figure 4.6. This figure gives a qualitative assessment of where the particles (red) are deposited in the oral cavity. It can be observed that most of the deposition occur in and near the tongue region and because of sedimentation.

Figure 4.5. Deposition Fractions for different combined Swirl and Stokes numbers.
4.2.3. Regional droplet deposition

A regional depositional study has been conducted for a quantitative assessment of particle deposition in the upper oral cavity, which will be vital for custom (taste) delivery. This is achieved by segmenting the geometry into different zones (Z-1 to Z-8) as shown in Figure 4.7. The depositional study is conducted for different swirl numbers (2, 4 and 6) and Stokes numbers (0.015, 0.0075 and 0.005), maintaining their product to be 0.03. The results are shown in Figure 4.8.
Figure 4.7. Zones Z-1 to Z-8 – Regional Deposition Study.
It can be observed that the particles are majorly deposited in the Z-2 zone, followed by Z-3 for all three swirl number cases. Zones Z-3 to Z-4 correspond to the back of the tongue and deposition in these regions majorly account for taste. The deposition in these zones for lower Stokes numbers (0.005) can hence be improved by increasing the swirl number (as per S*St value). The deposition fraction in zone Z-5 is highest for the swirl number of 6 since the Stokes number (and hence particle diameter) is very low in this case, thus enhancing deeper penetration.

The zones Z-6 to Z-8 are not shown in Figure 4.8, featuring almost zero-percent deposition fractions. The total deposition observed in the three cases were in the range of 23 – 24%. The rest of the particles escaped from the outlet, moving on to the tracheobronchial region.

Thus, custom segmental deposition in the oral cavity can be achieved by independently varying swirl and Stokes numbers, for a specific swirl*Stokes number (that dictates the overall deposition
in the oral cavity). The effectiveness of implementing a swirling flow in opposed to varying the Stokes number needs to be studied for targeting purposes. This is achieved by conducting a regional depositional study for three different swirl numbers (2, 4 and 6) keeping a fixed Stokes number (St = 0.0075). By increasing the swirl number, the deposition in the oral cavity increases (as per Figure 4.5, see Table 4.4). However, the deposition of particles in different regions (zones Z-1 to Z-8) of the oral cavity are different. Figure 4.9 describes the relative regional deposition fraction of particles (St = 0.0075) for different swirl numbers (2, 4 and 6). The relative regional deposition fraction (RDF) is given by Equation (4.2).

\[
\text{RDF}_{\text{particle}} = \frac{\text{Deposition Fraction in a certain zone}}{\text{Total Deposition Fraction in the oral cavity}} \tag{4.2}
\]

<table>
<thead>
<tr>
<th>Case</th>
<th>Inlet Condition / Swirl Number</th>
<th>S * St</th>
<th>Oral Deposition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal Injection (S = 0)</td>
<td>0</td>
<td>7.1</td>
</tr>
<tr>
<td>2</td>
<td>S = 2</td>
<td>0.015</td>
<td>9.15</td>
</tr>
<tr>
<td>3</td>
<td>S = 4</td>
<td>0.03</td>
<td>23</td>
</tr>
<tr>
<td>4</td>
<td>S = 6</td>
<td>0.045</td>
<td>38.7</td>
</tr>
</tbody>
</table>

Table 4.4. Deposition Fraction for St = 0.0075.
From Figure 4.9, it can be observed that the effect of swirling flow improves the particle deposition fraction in the deeper regions of the oral cavity (i.e., the Z-3, Z-4 and Z-5 zones) compared to the axial flow. The deposition of particles in these zones is crucial for enhancing the taste of the inhaled aerosol-vapor particles. A high RDF for a swirl number of 6 (compared to 2 and 4) is observed in zone Z-1 due to the strong swirling motion that enhance deposition by sedimentation here (Figure 4.3 (e)). Zones Z-6 to Z-8 are not shown in figure as they featured zero deposition for the swirling flows. In contrast, deposition fractions in zones Z-6 and Z-7 are 4% and 10% under normal flow conditions.

4.3. Simulations Results with Model II

The accuracy of the drug deposition predictions can be improved my incorporating a realistic upper airway model (Model II). The Model II is a patient-specific model, whose geometry was developed
from a magnetic resonance imaging (MRI) scan of a healthy male. The model has bifurcations up to generation 3 as shown in Figure 4.10.

The mesh used based on this geometry composed of 7.8 million elements of which 2 million elements were prism and the rest being tetrahedral cells. Particle independent study between 50k, 100k and 120k particles, is done to ensure that the deposition fraction is independent of the number of particles and 100k particles are injected at the mouth-piece inlet.
4.3.1. Droplet depositions for new non-dimensional number

As seen in the case for Model I Section 4.2.1, the impact of swirling flow increases the oral deposition fraction overall and enhances segmental deposition of particles in the deeper zones of the oral cavity. The effect of the new non-dimensional number is studied for the realistic upper airway model in this section. Different swirl numbers (S = 0.1, 0.2, 0.4, 0.5, 0.6, 1, 2 and 6) were used for the study. The Deposition Fraction in the upper airways encompassing mouth, oral cavity, pharynx and larynx, for different values of the non-dimensional number S*St is plotted in Figure 4.11 based on varying the swirl number for a fixed Stokes number.

![Deposition Fraction Graph](image)

**Figure 4.11. Deposition Fractions for different S*St values (based on fixed St).**

It can be observed that a similar trend for deposition fraction is obtained for Model II in comparison to the results obtained for Model I (*see Figure 4.5*), where the deposition fraction increases as the S*St value increases. However, the values of S*St are much lower for the same deposition fraction
in Model II. It can hence be inferred that the product of Swirl number (S) and Stokes number (St) is sensitive to the geometry being used. These Swirl numbers are much more realistic and achievable in comparison to the predictions by Model I. An optimal deposition of 20 – 40% in the upper oral airways is achieved for a S*St value of about 0.004. The deposition fraction in the upper airway (mouth, oral cavity, pharynx and larynx) for different Swirl numbers (for the same Stokes number of 0.0075) used is tabularized in Table 4.5.

Table 4.5. Deposition Fraction for different Swirl numbers.

<table>
<thead>
<tr>
<th>Case</th>
<th>Swirl number (S)</th>
<th>Deposition Fraction (Mouth, Oropharynx and Larynx)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.1</td>
<td>17.67</td>
</tr>
<tr>
<td>2</td>
<td>0.2</td>
<td>21.57</td>
</tr>
<tr>
<td>3</td>
<td>0.4</td>
<td>26.67</td>
</tr>
<tr>
<td>4</td>
<td>0.5</td>
<td>30.5</td>
</tr>
<tr>
<td>5</td>
<td>0.6</td>
<td>35.4</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>46</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>77</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>95</td>
</tr>
</tbody>
</table>

A parameter sensitivity study was conducted for a S*St value of 0.004 for three different swirl numbers 0.5, 0.6 and 1, with Stokes numbers 0.008, 0.0067 and 0.004 respectively. All three cases yielded 28 – 31% deposition in the oral cavity, thus confirming the applicability of S*St number.

4.3.2. Regional droplet depositions

A regional deposition study is carried for quantitative assessment of the fate of inhaled particles (St = 0.0075) depositing in different parts of the airways. To achieve this, the model is split into 6 zones (Z-1 to Z-6) from mouth to trachea to study the regional deposition fraction of particles.
Zones Z-1 to Z-6 encapsulate the oral cavity, pharynx and larynx. The zones were selected to span a distance, which is based on the order of magnitude of the inlet (28 mm). Figure 4.12 depicts zones Z-1 to Z-6 that was used for study. The deposition is evaluated up till generation 3. The patches depicting trachea to generation 3 are shown in Figure 4.13. The geometry has been rotated to show the patches clearly.

Figure 4.12. Zones Z-1 to Z-6 used for regional deposition study (Model II).
From Table 4.5, it can be observed that the realistic airway model (Model II) yields an optimal (20 to 40%) deposition in the oral cavity for a swirl number range of 0.5 to 1, when the Stokes number is 0.0075. Hence, regional deposition study is carried out for these swirling flows at the inlet to analyze the particle deposition fraction along the zones Z-1 to Z-5. This is shown in Figure 4.14. Zone Z-6 has not been shown as it gave negligible deposition fraction.
It can be observed that the deposition fraction of particles in the oral cavity and pharynx increase as the Swirl number increases. It is desirable to increase the deposition to an optimal value specifically in the zones Z-2, Z-3 and Z-4, to account for taste. Amongst the three Swirl numbers, the Swirl number $S = 0.6$ has relatively lower deposition fraction in Z-1 and more in Z-2 and the most in Z-3 totaling 30% in these zones. To study the fate of the remaining particles, the deposition fraction of particles in the trachea, generation 1, 2 and 3 are studied. They are plotted in Figure 4.15, for Swirl numbers 0.5, 0.6 and 1.
From Figure 4.15, it can be observed that the deposition fraction of particles in the trachea, generation 1, 2 and 3, between the three swirl numbers have minor differences. All three swirl numbers 0.5, 0.6 and 1 produce a total of 11.3%, 10.2% and 11.4% respectively in these regions, again swirl number of 0.6 being the least and thereby transferring more fraction of particles to the deep lung (for drug effect). The deposited particles (red) along with the resultant velocity profile for flow at the mid-plane is shown in Figure 4.16, for a swirl number of 0.6 and Stokes number of 0.0075.
It can be observed that most of the particles in the oral cavity deposit by sedimentation and not by inertial impaction. This is evident from the velocity contour, where the particle inertia reduces once it enters the domain. The velocity contours for other swirl numbers (S=0.1, 0.2, 0.4, 0.6, 1 and 2) are given in Appendix A.2.
4.4. Novel mouthpiece for helical-flow generation

The beneficial aspects of swirling flow have been studied and an optimal swirl number for any Stokes number can be determined by the new non-dimensional number. This section answers the question of how such flows can be implemented for drug delivery applications. Active generation of swirling flow, by means of a swirl generator\textsuperscript{51}, would be cumbersome to set up on a mouthpiece (inhaler or e-cigarette) as measures need to be taken for precise housing of the rotor and the presence of moving parts may be very sensitive and hence inhibit portability and ease of use. Passive generation of swirl, where swirl is purely generated by the duct alone\textsuperscript{52}, is a better option that can be suitable for inhaler/e-cigarette mouthpieces.

A novel design of a passive swirl generator is presented here, where curved/twisted microchannels that fill up the mouthpiece mimic the streamlines of a swirling flow (IP Review # 18153, 03/16/2018; OTCNV, NC State University). A desired swirl number can thus be achieved elegantly by just fabricating the curved microchannels to follow the streamlines of the flow.

4.4.1. Schematics of Mouthpiece for E-Cigarettes and Medical Inhalers

Cigarette-type devices are about 6 mm in diameter. The new mouthpiece can improve consumer satisfaction by achieving segmental compound deposition in both the mouth region (better taste) and the deeper lung region (drug delivery).

Helical air-particle streams (of desired swirl number) can be implemented by an assemblage of curved microchannel tubes that will produce the desired stream lines at the mouth inlet. The design specifications can hence be dictated by the streamlines observed. Figure 4.17 shows the streamlines for one such swirl number ($S = 0.6$ with $Q_{in} = 4.8$ LPM) through a mouthpiece of 6 mm diameter and 12 mm length. The inner streamlines are highlighted in red to distinguish from...
the outer ones. These micro-tubes may be fabricated with filter paper for disposable mouthpieces, or with metal/plastic.

Figure 4.18 and Figure 4.19 provide cut-away views of the curved micro-tubes for the small mouthpiece, applicable to, say, electronic cigarettes. Figure 4.20 and Figure 4.21 provide isometric and front views of the large mouthpiece for medical inhaler applications. A 3 mm rim between the casing and the channel assembly is retained to facilitate targeting of drugs to deeper lungs by angular injection\textsuperscript{23}. 

Figure 4.17. Particle-path (or streamline) traces for e-cig. mouthpiece.
Figure 4. 18. Mouth-Piece design for Electronic Cigarette application.

Figure 4. 19. Mid-plane view.
Figure 4. 20. Mouth-Piece design for Medical Inhaler application.

Figure 4. 21. Front view.
4.4.2. Pressure drop across custom mouthpiece

The presence of helical microchannels would increase the pressure drop and the possibility of micro/nanoparticle deposition across the mouthpiece. To address this, the pressure-drop across the inlet tube of diameter ‘D’ is compared with a mouthpiece where ‘n’ helical/parallel microchannels of diameter ‘d’ fill up the cross-sectional area. Assuming fully-developed Poiseuille-flow for base-case scenarios, the analytical solutions are compared to computationally generated results of helical flow in curved microtubes. The system sketch is shown in Figure 4.22.

![Figure 4.22. 2-D sketch of mouthpiece with ‘n’ microchannels.](image)

For steady, laminar, incompressible fully-developed flow, the flow rate (Q) is given by Equation (4.5), where $\Delta p$ denotes the pressure drop across the mouthpiece, $\mu$ is the dynamic viscosity of the fluid (smoke), and $L$ is the length of the mouthpiece, both encapsulated in the constant $K$.

$$Q = \frac{\pi \Delta p D^4}{128 \mu L} ; \Delta p = \frac{K Q}{D^4} ; K = \frac{128 \mu L}{\pi} \quad (4.3)$$

Another important parameter to be accounted for is the packing fraction $\varepsilon$ (see Equation (6)).

$$\varepsilon = \frac{n \times A_{channel}}{A_{pipe}} \quad (4.4)$$
From Equation (4.4), the diameter of microchannel and the diameter of the mouthpiece are related as,

\[ d = D \sqrt{\frac{\varepsilon}{n}} \]  \hspace{1cm} (4.5)

As all twisted tubes are in parallel, the pressure drop in each will be the same. Starting with Poiseuille flow in straight pipe, from Equation (4.3) the pressure drop across one straight tube is given by,

\[ \Delta P_{system} = K \frac{Q_c}{d^4} \]  \hspace{1cm} (4.6)

For each microchannel, the flow rate \( Q_c \) through it would be related to the net flow rate \( Q \) by \( Q_c = Q/n \).

So, the pressure-drop equation now reads,

\[ \Delta P_{system} = K \frac{Q}{D^4} \left( \frac{n}{\varepsilon^2} \right) \]  \hspace{1cm} (4.7)

Comparing Equations (4.3) and (4.7) switching from a constant pipe to a ‘channel-filled’ mouthpiece set up the pressure drop across the system becomes \( \left( \frac{n}{\varepsilon^2} \right) \) times its original value. Hence it heavily depends on:

- The number of channels (n)
- The packing fraction (\( \varepsilon \))

Computer experiments are conducted to study the pressure drop for the following cases:

- Straight tube (of diameter D and d)
- Single curved tube
- Six curved tubes
- Twelve curved tubes
The contour plots for normalized pressure (P/ρ) (m²s⁻²), where ρ is the density of the fluid, are shown for all cases.

First, a simple mouthpiece of diameter, D = 6 mm, is set up and its pressure drop is studied for a flow rate of Q = 1.7 x 10⁻⁵ m³/s (corresponds to average puffing/inhalation at 1.02 LPM). The length of the pipe L = 0.05 m and the working fluid is air. The geometry of the system, along with the corresponding pressure contours are shown in Figure 4.23.

![Figure 4.23. Straight pipe with diameter D.](image)

The patch-averaged pressure-drop for the computational set up yielded 0.74 units. The normalized pressure contours for a straight pipe with diameter d = 1.4 mm is shown in Figure 4.24. This is a representative straight channel of a mouthpiece (D = 6 mm and L = 0.05 m) with a packing system that comprises of 9 channels.
It can be observed from Figure 4.24, that the pressure-drop across one single channel of diameter 1.4 mm for the same flow rate of average puffing/inhalation (Q = 1.02 LPM and $Q_c = Q/9$) is increased to 18.6 units (patch-averaged value). This is expected as the pressure-drop is inversely proportional to the fourth power of the diameter of the channel.

The pressure-drop across a single curved channel of diameter $d = 1.4$ mm, which represents a mouthpiece packing system that comprises of 9 curved channels is shown in Figure 4.25 in the form of normalized pressure contours.
The pressure-drop across the curved tube for an average puffing/inhalation flow rate ($Q=1.02$ LPM and $Q_c = Q/9$) is 21.6 units (patch-averaged value). In comparison to a straight tube of the same diameter, the pressure-drop increases by 16% (3 units). This may be tolerated for the swirling flow effect delivered by the custom mouthpiece.

The pressure drop is now studied for a mouthpiece ($D=6$ mm and $L=0.05$ m) with six and twelve curved tubes. The geometries are shown in Figure 4.26, they were both discretized into 5 million tetrahedral elements, to accurately capture the flow physics through the narrow ducts, for computational analysis. The tube diameter ($d$) in the six- and twelve-channel system are 1.8 and 1 mm, respectively. This leads to a packing efficiency (Equation (4.4)) of 0.54 and 0.33 respectively.
According to Equation (4.7), the pressure-drop would rise by a factor of \( \left( \frac{n}{\varepsilon^2} \right) \) times the original pressure-drop (0.74 units for the simple mouthpiece). The normalized pressure drop for six and twelve channel mouthpieces are represented in Figure 4.27 and Figure 4.28 respectively.
The pressure-drops for the six- and twelve-channel mouthpieces would yield 15.22 and 79.92 units, respectively. The computer-simulation results for surface averaged pressure-drops yielded 13.8 and 77.3 units, respectively; thus, showing good agreement with the theoretical predictions. Typically, the pressure-drop range for common conventional cigarettes, considering usual puffing inhalation, is about 30 to 80 mm of water\textsuperscript{53,54}. This corresponds to a range of 240 to 640 units of normalized pressure (m\textsuperscript{2}s\textsuperscript{-2}). Talbot and Williams (2011)\textsuperscript{54} studied the pressure-drop across various commercially available e-cigarettes in which the maximum pressure-drop for a particular brand was found to be 1200 units of normalized pressure. Hence, there is plenty of scope for increasing the number of channels to facilitate very fine tuning of swirl number while still residing in an acceptable pressure-drop range.
Pressure-drops are aspects of ‘internal resistance’ of a device. This is directly related to the Peak Inspiratory Flow Rate (PIFR) that is attainable by the device. Lower internal resistance implies that the device can attain higher PIFRs, also ensuring ease of use. In the case of Dry Powder Inhalers (DPIs) the PIFR is of interest as DPIs often demand high PIFRs for particle de-agglomeration, which is important in maintaining an acceptable fine particle fraction (FPF) that also depends on the mouthpiece design in addition to the powder formulation. Larger number of small sized (or finer) particles (high FPF) entering the airways, would imply lower deposition by means of inertial impaction in the oral cavity and hence, penetration of drugs to the deep lung for action.

Considering DPIs, swirling flows would facilitate reduced deposition fractions in the oral cavity as they have lower inertia along the axial direction compared to a normal flow for the same inspiratory flow rate. In addition to this, they can also be beneficial for delivering higher FPFs as they are characterized by dominant tangential velocities and shear stresses that are vital for particle de-agglomeration. A design optimization study for the new mouthpiece that is to be used for a DPI can be conducted that delivers higher attainable PIFRs and effective particle de-agglomeration.

4.4.3. Particle deposition

Another important consideration for designing the mouthpiece is the particle deposition that may occur across the curved microchannels. This is addressed in the following section, where the deposition of micron-size particles (3 μm) and nanoparticles (500 nm) is studied for the curved channels for the same flow rate \( Q = 1.02 \text{ LPM} \) that corresponds to the average puffing/inhalation profile.
The deposition of uniformly sized (3 μm) spherical particles is studied by determining the Deposition Fraction (DF) at the mouthpiece wall. The comparison is made between the 6-channel and 12-channel system as well as a straight tube. The worst-case condition for particle deposition was implemented, i.e., when an aerosol touches the wall it is deposited. The deposition fractions observed are shown in Figure 4.29.

It is evident from Figure 4.29 that the particle deposition in the walls increase as we switch to a ‘channel-filled’ set up. Also, as the number of channels increase (0, 6 and 12) the particle deposition fraction in the wall increases (0.54, 3.31, 10.6%). This may be the case as the same space is being filled with a greater number of smaller diameter channels, thus facilitating a greater number of particles to stick to the wall. The deposition in the walls of the channels will reduce when incorporating sub-micron/nanoparticles.
The deposition of uniformly sized nanoparticles (500 nm) in the curved microchannel mouthpiece is studied by determining the Deposition Fraction (DF). The effect of Brownian motion has been incorporated, as when the particle diameter approaches submicron/nanometer range, Brownian motion, drag and gravity are considered as dominant point forces away from the walls\textsuperscript{58} (Section 2.3.2, Equation (2.11)). The temperature of the droplets were set to 373K thereby mimicking a typical e-cigarette smoke. Because the particle size is now in the nano-meter range, it is reasonable to expect that particle-deposition is reduced, as nanoparticles tend to follow the flow field. The deposition results are shown in Figure 4.30.

![Deposition of nanoparticles in the mouthpiece](image.png)

Figure 4. 30. Deposition of nanoparticles in the mouthpiece.

It is evident from Figure 4.30 that the particle deposition increases with a higher number of curved microtubes. Also, the deposition of nanoparticles is much lower in all the cases when compared with micron-particles, i.e., 0.1, 2.5 and 6.8% in the straight pipe, six channel and twelve channel
mouthpieces. Thus, the deposition of nanoparticles is much lower (about 15-35%), which is advantageous as the inhaled smoke consists mainly out of nanodroplets and vapors.

In contrast to the deposition in the human airways, due to the absence of any mucus layer in the mouthpiece, there is a possibility that these particles may entrain in to the air flow stream for the next puffing/inhalation cycle.

4.5. Conclusions

- The deposition of inhaled aerosols in the human oral cavity can be improved by increasing the swirl number of the flow, where the product of Swirl number and Stokes number (S*St) is a promising new dimensionless group for optimal, custom-based drug-delivery applications. The proof-of-concept is described in Section 4.2.1 for an idealized upper oral airway geometry. This was followed by conducting tests with a realistic upper airway model, ie, with the Model II geometry (Section 4.3).

- The swirling fluid flow can be generated by injecting the fluid through curved meso/micro-channels that mimic the streamlines of any desired swirl number. The novel idea of implementing a mouthpiece for electronic cigarette and medical inhaler application is presented in Section 4.4.

- The pressure-drop across the new mouthpiece was explored in Section 4.4.2 and it was shown analytically and computationally that the pressure-drop depends on certain geometrical factors such as the packing efficiency, number of channels and the length of the mouthpiece. The pressure-drop across the mouthpiece was found to be well within a comfortable range for vaping applications.

- The particle deposition considering the worst-case scenario in the new mouthpiece with six and twelve helical channels was explored for both micron and nano-sized particles and was
found to increase with the number of channels filling the mouthpiece. Nanoparticle deposition was much lower (about 15 – 35% lower) when compared to micron-particle deposition.

4.6. Future work

- A typical, quasi-transient air flow field that approximated the puffing/inhalation profile of an e-cigarette smoker was considered for ease of conducting a thorough deposition study. However, transient air flow fields for realistic puffing/inhalation profiles with swirl needs to be explored.
- The deposition of micron-sized particles was studied for the swirling fluid-particle flow analysis to show the proof-of-concept. This needs to be followed by conducting a realistic e-cigarette study considering multi-component nano-droplets with phase change.
- The possibility of incorporating swirling flows for medical inhaler application can be explored with different inhalation flow profiles.
- The presence of the mucus layer was ignored, which would demand a special boundary condition at the wall as the mucus layer is not stationary and it would affect particle transport.
- The new e-cigarette mouthpiece needs to be optimized based on packing efficiency (ε), number of microchannels (n) and particle deposition, for accurately generating the desired swirl number. The possibility of extending its application to DPIs must also be explored with additional parameters for targeting purposes.
- The deposition was tracked only up till generation 3 for the realistic upper airway model. The lung has 23 generations and the particle needs to be tracked till they reach the alveoli that start from generation 16. The impact and versatility of the new non-dimensional group (S*St) can be further extended to the two-path/five-path Whole Lung Airway Model (WLAM).
CHAPTER 5

Whole Lung Airway Modeling

5.1. Introduction

Accurate and realistic computational prediction of inhaled aerosol deposition in human lung airways depends largely on the subject-specific geometry that is used to approximate the human respiratory system. The sheer complexity of the human airways that feature oral cavity, pharynx, larynx, trachea, bronchi and bifurcations down to generation 23, with alveoli appearing from generation 16, is a major challenge for predictive computer simulations. The details of the human lung and its modelling methods are discussed in Section 1.4. So far, simplified airway geometries were employed to simulate and analyze the fluid-particle dynamics, and hence the merits, of a new mouthpiece for vaping devices. For more extended applications, including direct drug-aerosol delivery to, say, lung tumors, more realistic airway models have to be considered.

This chapter describes the methodology of performing CF-PD simulations and analyses on the conducting airways of a 3D dual-path whole lung airway model (WLAM) in OpenFOAM, and its airflow and micron-particle deposition results which sets the stage for future applications. The CF-PD analysis is performed for the inhalation phase of light breathing with a tidal volume of 500 ml (Section 5.3). Tidal volume denotes the lung volume that represents the volume of air that is displaced between normal inhalation and exhalation. The procedural steps in conducting a CF-PD analysis using OpenFOAM is discussed in Section 5.4 and the results are presented in Section 5.5.

5.2. Geometry and mesh

The conducting airways of the WLAM comprise of the upper oral cavity, pharynx, larynx, trachea, bronchi and bifurcations up to generation 15. The dual-path WLAM consists of the patient-specific upper human airways from mouth to generation 3 (Model II), and triple bifurcating units (TBUs)
in series and parallel that extend till generation 15. A pair of TBUs are attached to two of the eight outlets from generation 3, one leading towards the left lung and the other to the right lung (see Figure 5.1).

Figure 5.1. Conducting airways of the dual-path WLAM.
The TBUs representing generations 4 – 15 are attached in series (for both left and right lung) by orienting them with respect to the gravitational vector ($\vec{g}$), which is assumed to act along the negative z direction. The initial TBUs are scaled based on morphometric measurements of human lung casts. The successive TBUs are scaled-down to match the outlet of the previous TBU generation before coupling them. This modelling approach follows the procedure by Kolanjiyil et al., 2017. The TBUs are designed in SolidWorks® and imported to ICEM® for its meshing. The upper airways (Model II) comprise of around 2 million prism elements and 5.8 tetrahedral elements totalling 7.8 million elements. Each TBU composed of roughly 600k ~ 700k elements. The dual path WLAM (conducting airways) totalled roughly 13 million elements.

5.3. Inhalation conditions for breathing

To study the effect of particle transport under light breathing inhalation conditions (volumetric flow rate of 15 LPM) a square wave is used. The inhalation phase lasts two seconds, which corresponds to a tidal volume of 500 ml. The square wave profile is shown in Figure 5.2.

![Figure 5.2 Light breathing - wave form (Kolanjiyil and Kleinstreuer)](image-url)
The particle transport of 3 μm spherical particles is studied by injecting 50k particles per second, thus 100k particles are injected over the span of two seconds. Both the fluid and particles enter the domain through the oral inlet. Since the flow rate is 15 LPM, the air flow in the human airways is in the transitional-to-turbulent regime therefore, SST k-ω turbulence modelling is used to capture this effect till generation 6, followed by which the flow is in the laminar regime.

5.4. Computational methodology

The Euler-Lagrange modeling approach is followed assuming dilute particle suspension and one-way coupling (refer Section 2.3.2). A modified OpenFOAM solver is used to conduct transient fluid-particle simulations. To reduce the computational load for solving fluid and particles dynamics throughout the entire lung, the domain is broken into the Model II upper airways (mouth to generation 3), generation 4-6, generation 7-9, generation 10-12 and generation 13-15, for each lung (left and right). Simulations are conducted individually for each fragment and the solutions are stored at regular time-steps that is to be used for the successive generations. The following steps describe the complete procedure that is followed for executing CF-PD tests on the dual-path WLAM.

1. Transient CF-PD simulations corresponding to the inhalation profile were first conducted in the upper airways (Model II). During this process, the output from the OpenFOAM solver during run-time was saved in log files. These log files keep track of the time-step at which the particles ‘stick’ or ‘escape’ through boundary patches (see Section 2.3.3).

2. After completing the transient simulations for the upper airways, a particle injection file (for generations 4-6) is created by an in-house C++ code that reads the log file. The injection file contains information regarding the time at which a particle exits through an outlet patch for the previous simulation (ie, from G3). This file is used by the modified injection model, based
on OpenFOAM’s **patchInjection**, for simulating the successive generations, where the right number of particles are injected at the appropriate time.

3. Generation 3 has eight daughter airways featuring eight outlets, out of which two of the outlets are attached to the successive TBUs leading to the left and right lung. The average flow rate (flux) through these individual outlet patches is computed by employing the post-processing tool. This is used as an inlet condition for the fluid flow for generation 4-6.

4. CF-PD simulations for generations 4-6 was then carried out, separately for the left and right lungs, with the corresponding inlet flow rate. The injection file controls the time at which particles are to be injected into the domain. Another log file is generated for this simulation.

5. Steps 2-4 are followed for the successive generations until completion.

This procedure is illustrated in *Figure 5.3* in form of a flow-chart.

**5.5. Results and Discussion**

The results for the airflow fields are first presented, this is followed by the deposition results of microsphere particles.

**5.5.1. Airflow fields**

As the particle transport is one-way coupled, analyzing the fluid flow field may provide valuable insight to particle deposition. The airflow field corresponding to the upper airways is shown as velocity magnitude contours at the mid-plane cross-section in *Figure 5.4*. The flow accelerates to high velocities of about 2 m/s in the glottis region that serves as a constriction. The flow regime shifts from laminar to transitional-to-turbulent in this region with Reynolds number in the range of 2400. It re-laminarizes downstream due to the absence of any obstructions, sharp turn or bifurcation (carinal ridges) along the trachea.
Set initial conditions for Model II

Perform transient CF-PD analysis on Model II

Generate injection file and obtain outlet flow rates

Perform transient CF-PD analysis on successive generations

Have all conducting airways been simulated?

Post-processing of results

True

False

Figure 5. 3. Flow chart for conducting CF-PD simulations with WLAM.
Velocity contours and streamlines representing the flow field observed in generations 4-15 are shown for both the left and right lung in Figure 5.5. Most remarkable is the fact that there are quite higher velocities in the right lung (that peaks at 1.1 m/s) compared to the left one (peaks at 0.5 m/s) for the same outlet pressures. This can be attributed to the lung size, ie, the right lung is smaller than the left lung; thus, featuring increased air velocities for the same flowrates. A peak velocity of roughly 1 m/s and 0.7 m/s with skewed velocity profile is observed by Kolanjiyil et al.\textsuperscript{59} in generation 4-6 of the right and left lung respectively, thus making OpenFOAM results being in good agreement with previous studies. Another observation is that successive generations have discontinuous velocity profiles. This is because the flow simulations are not conducted continuously for the entire lung, but separately as described in Section 5.4.
Figure 5.5. Airflow fields for generations 4-15 left lung (top) and right lung (bottom).
In Figure 5.5b cross-sections from 1-1 to 6-6 are provided along generations 4 – 10 in the right lung. It can be observed that the velocity profiles are not parabolic in generations 4 – 6, ie, they are skewed towards the inner walls. This is due to two factors, sudden changes in cross-sectional area cause adverse local pressure gradients, which coupled with the fact that the pipe is curved, giving rise to secondary flow velocities that bring the fluid along the centerline towards the inner walls and thereby shifting the locations of peak velocities. This is evident while observing sections 1-1, 3-3 and 4-4. As the flow passes through more bifurcations and the airways straighten out, the effect of secondary velocities become weaker and the flow attains its original parabolic profile. This is observed in Sections 5-5 and 6-6. Both left lung and the right lung feature almost zero velocities along generations 10-15; thus, making particle diffusion and sedimentation the major contributors to particle deposition.

5.5.2. Particle deposition

The dual-path WLAM is a representative model for monitoring particle deposition. All the particles that escape through the outlets are added and injected to the representative TBU (either left or right lung) for the successive generations. As mentioned earlier (Section 5.3), the transport of 3μm particles was studied by injecting 50k particles per second over a duration of two seconds for the inhalation phase (500 ml tidal volume). The first particle exits the upper oral cavity at around 0.6 seconds to move on to generation 4 of the left lung and at 0.62 seconds to the right lung. A quantitative representation of the deposited particles (in red) during the inhalation phase after two seconds is shown in Figure 5. 6.

It can be observed that most of the particles deposit in the oral cavity and pharynx due to inertial impaction, while a certain number deposits in the glottis due to the confined space. Sparse amounts deposit in the trachea due to the turbulent flow downstream of the glottis. Bifurcations (carinal
ridges) serve as ‘hot spots’ for particle deposition, which is evident from the concentration of deposited particles observed in these zones throughout the conducting airways in Figure 5.6.

Figure 5.6 Particle deposition at the end of inhalation phase.
The deposition of particles in generations 4-6 is governed by both inertial impaction and sedimentation. However, the deposition in generations 7-15 is mainly because of sedimentation. This is evident from the locally deposited particles in these regions along the direction of gravitational vector (Figure 5.6). The regional deposition fraction of particles right from the oral cavity to generation 15 is shown with comparisons between right and left lung in Figure 5.7. The DF observed in the oral cavity is around 1%, which is more than what was observed by Kolanjiyil et al (predicted the deposition to be 0.65%). This may be due to the geometric-sensitivity of the eddy interaction model (EIM) that is used to account for turbulent interaction of the particles. The EIM needs to be corrected with new empirical constants (Equation (3.3)) for the Model II geometry. The particle deposition observed in the trachea to G3 is around 0.52%. It is evident that a greater number of particles are deposited in the right lung compared to the left. A similar trend is observed by Kolanjiyil et al., 2017. This is because a greater number of particles, around 32k,
transferred to the right lung compared to the left lung, where only 19k particles transferred at the end of two seconds. Another reason for this is because of the smaller size of the right lung compared to the left, thus increasing the probability of particle deposition. The number of particles escaping from each fragment (oral cavity to generation 15) towards the successive generations for each lung is given in Table 5. 1.

<table>
<thead>
<tr>
<th>Case</th>
<th>Towards left lung (number of particles)</th>
<th>Towards right lung (number of particles)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouth-G3</td>
<td>19219</td>
<td>32513</td>
</tr>
<tr>
<td>G4-G6</td>
<td>14903</td>
<td>29214</td>
</tr>
<tr>
<td>G7-G9</td>
<td>8819</td>
<td>24928</td>
</tr>
<tr>
<td>G10-G12</td>
<td>2539</td>
<td>19005</td>
</tr>
<tr>
<td>G13-G15</td>
<td>10</td>
<td>11447</td>
</tr>
</tbody>
</table>

Table 5. 1. Particle escaping at the end of the inhalation phase.

5.6. Conclusions

- A detailed computational fluid-particle analysis is conducted for the truncated dual-path WLAM. The validated results confirm the applicability of the cost-free open source CFD tool box, OpenFOAM <https://www.openfoam.com/>, for analyzing the fate of inhaled aerosols in human lung models.
- The methodology in conducting a CF-PD analysis using OpenFOAM is established and the results for a test case is validated by observing and comparing the airflow fields and particle deposition results.
This builds a foundation for extending particle tracking and targeting all the way down to generation 23.

5.7. Future work

- The eddy interaction model needs to be corrected with adjusted model coefficients (Equation (3.3)), for the patient-specific upper oral cavity (Model II). This would accurately predict the particle deposition in this region and in the trachea.

- Respiratory airways, ie, generations 16 – 23, can be oriented according to the gravitational vector and attached to the existing conducting airways. CF-PD simulations on the respiratory airways can then be conducted following the same methodological procedure explained in Section 5.4 with special boundary conditions to simulate the deforming alveoli.

- Exhalation phase can be simulated using the same procedure (Section 5.4) with appropriate boundary conditions to complete the simulations for one breathing cycle.

- The effect of swirling flows and modified inlet conditions can be studied with the WLAM for tracking and targeting particles in the deeper lung generations.

- Back-tracking of particles from the deep lung all the way to their initial positions in the oral inlet can be achieved to generate a particle release map (PRM)\textsuperscript{16,17} that will be very helpful for drug targeting in the deep lung.

- The dual-path WLAM can be extended to a five-path WLAM. This can be achieved by attaching five triple bifurcating units (TBUs) from generation 3 outlets that extend till generation 23 with three sets of TBU extensions representing the right lung and remaining for the left lung. This will improve the accuracy of the computational particle deposition prediction as it was shown that the dual-path WLAM proves to be more accurate than the single-path WLAM\textsuperscript{59}.
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Appendix A

A.1 SST K-Omega model formulation

The shear stress transport (SST) k-omega turbulence model was introduced by F.R. Menter in 1994. It was developed to accurately predict the turbulent flow regime in the turbulent boundary layer as well as in the turbulent core, using blending functions to switch between k-ω and k-ε turbulence models, near and away from the wall respectively. The blending functions require the computation of nearest wall distance, which adds a layer of complexity to this model compared to the standard k-ω and k-ε models. The SST k-ω turbulence model variant used in OpenFOAM is based on the 2003 model by F.R. Menter\textsuperscript{27}. The formulation of the two-equation model is given below.

\begin{equation}
\frac{\partial (\rho k)}{\partial t} + \frac{\partial (\rho U_i k)}{\partial x_i} = \tilde{P}_k - \beta^* \rho k \omega + \frac{\partial}{\partial x_i} \left[ (\mu + \sigma_k \mu_t) \frac{\partial k}{\partial x_i} \right] \tag{A.1}
\end{equation}

\begin{equation}
\frac{\partial (\rho \omega)}{\partial t} + \frac{\partial (\rho U_i \omega)}{\partial x_i} = \alpha \rho S - \beta \rho \omega^2 + \frac{\partial}{\partial x_i} \left[ (\mu + \sigma_k \mu_t) \frac{\partial \omega}{\partial x_i} \right] + 2(1 - F_1) \rho \sigma_{\omega^2} \frac{1}{\omega} \frac{\partial k}{\partial x_i} \frac{\partial \omega}{\partial x_i} \tag{A.2}
\end{equation}

Where \( k \) and \( \omega \) are the turbulent kinetic energy and specific turbulent dissipation rate and suffix \( t \) refers to turbulence, \( \tilde{P}_k \) is the production limiter, \( S_{ij} \) is the strain rate, \( F_1 \) is the blending function, \( S = \sqrt{2S_{ij}S_{ij}} \) (second invariant of strain rate tensor) and the rest are constants.

The blending function is given by

\begin{equation}
F_1 = \tanh \left\{ \min \left[ \max \left( \frac{\sqrt{k}}{\beta^* \omega y' \sqrt{\omega}}, \frac{500 \nu}{C_D k \omega y'^2} \right), \frac{4 \rho \sigma_{\omega^2} k}{C_D k \omega y'^2} \right] \right\} \tag{A.3}
\end{equation}

Where,

\begin{equation}
C_D k \omega = \max \left( 2 \rho \sigma_{\omega^2} \frac{1}{\omega} \frac{\partial k}{\partial x_i} \frac{\partial \omega}{\partial x_i}, 10^{-10} \right) \tag{A.4}
\end{equation}
$y$ is the distance from the nearest wall. $F_1$ switches between k-$\varepsilon$ and k-$\omega$ model, where it becomes zero away from the surface, thus switching to k-$\varepsilon$ model and becomes unity inside the boundary layer, thereby facilitating k-$\omega$ model here.

The turbulent viscosity $\nu_t$ is given by,

$$\nu_t = \frac{a_1 k}{\max(a_1 \omega, SF_2)}$$  \hfill (A.5)

Where $F_2$ is another blending function given by

$$F_2 = \tanh \left[ \max \left( \frac{2\sqrt{k}}{\beta^* \omega y}, \frac{500\omega}{y^2 \omega} \right) \right]^2$$  \hfill (A.6)

The production limiter $\tilde{P}_k$ is given by,

$$p_k = \mu_t \frac{\partial U_i}{\partial x_j} \left( \frac{\partial U_i}{\partial x_j} + \frac{\partial U_j}{\partial x_i} \right)$$  \hfill (A.7)

$$\tilde{P}_k = \min(p_k, 10 \cdot \beta^* \rho k \omega)$$  \hfill (A.8)

The constants are shown in Table A. 1.

<table>
<thead>
<tr>
<th>Constant</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$a_1$</td>
<td>0.3</td>
</tr>
<tr>
<td>$\alpha_1$</td>
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</tr>
<tr>
<td>$\alpha_2$</td>
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</tr>
<tr>
<td>$\alpha$</td>
<td>$\alpha_1 F + \alpha_2 (1 - F)$</td>
</tr>
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<td>$\beta^*$</td>
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</tr>
<tr>
<td>$\sigma_k$</td>
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</tr>
<tr>
<td>$\sigma_{\omega_1}$</td>
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</tr>
<tr>
<td>$\sigma_{\omega_2}$</td>
<td>0.856</td>
</tr>
</tbody>
</table>
A.2 Swirling air-flow fields with Model II

The following figures highlight the effect of reduction in axial inertia due to increase in swirl number. Resultant velocity contours are shown along the mid-plane section of Model II.

Figure A. 1. Comparison of swirl numbers. S=0.1 (left) vs S=0.2 (right).
Figure A. 2. Comparison of swirl numbers. S=0.4 (left) vs S=0.6(right).
A.3 Particle deposition in the WLAM

The deposition of particle in the 3D dual-path WLAM is shown at times $t = 1s$ and $t = 1.6s$ during the inhalation phase. These additional results augment Figure 5.6 that shows particle deposition at the end of inhalation phase ($t = 2s$).
Figure A. 4. Particle deposition results for WLAM at time = 1s.
Figure A. 5. Particle deposition results for WLAM at time = 1.6s.