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A Systematic Review of Fluid Mechanical Models of Respiratory Aerosol Transport in Airways: Methods, Architectures, and Future Research Directions

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Abstract

Respiratory aerosol transport within human airways has emerged as a critical area of research due to its significant implications for pulmonary drug delivery, airborne disease transmission, and environmental exposure assessment. Fluid mechanical modelling plays a central role in understanding the complex interactions between airflow, particle dynamics, airway geometry, and physiological processes such as mucociliary clearance. This review provides a comprehensive analysis of modelling approaches used to simulate aerosol transport in the respiratory tract, including one-dimensional whole-lung models, three-dimensional computational fluid dynamics (CFD), large eddy simulations (LES), Reynolds-averaged Navier–Stokes (RANS) methods, and hybrid CFD–discrete element method (DEM) techniques. These frameworks enable detailed predictions of aerosol deposition, transport pathways, and residence times across different airway regions. Recent studies emphasize the influence of turbulence, particle size distribution, airway geometry, and breathing patterns on deposition efficiency and spatial distribution. Advanced CFD models show strong agreement with experimental and imaging techniques, supporting their use in patient-specific analysis. Additionally, emerging approaches incorporate multiphase flow physics, mucus rheology, and particle–wall interactions to enhance physiological realism. Despite these advancements, challenges remain in model validation, computational cost, and multi-scale integration, indicating the need for more efficient and comprehensive modelling strategies.

Introduction

The study of respiratory aerosol transport within human airways has gained unprecedented attention in recent years, driven by the dual challenges of airborne disease transmission and the optimization of inhalation-based drug delivery systems. Aerosols, defined as suspensions of solid or liquid particles in air, play a central role in respiratory health, acting both as carriers of therapeutic agents and as vectors for pathogens such as viruses and bacteria. Understanding the fluid mechanical behaviour governing aerosol transport is therefore essential for predicting deposition patterns, optimizing drug delivery efficiency, and mitigating airborne infection risks. The human respiratory system presents a highly complex and hierarchical structure, consisting of branching airways that span multiple length scales—from the trachea to bronchioles and

alveoli. This geometric complexity significantly influences airflow characteristics, leading to a wide range of flow regimes, including laminar, transitional, and turbulent flows. These flow conditions, combined with particle inertia, diffusion, and gravitational effects, determine how aerosols are transported and deposited within the airways.

Traditional approaches to studying aerosol transport relied heavily on experimental methods, including in vitro airway replicas and in vivo imaging techniques such as gamma scintigraphy and SPECT. While these methods provide valuable insights, they are often limited by high costs, ethical considerations, and the inability to capture detailed spatial and temporal dynamics. Consequently, computational modelling has emerged as a powerful alternative, enabling researchers to simulate aerosol transport with high precision and flexibility. Among computational techniques, computational fluid dynamics (CFD) has become the dominant framework for modelling respiratory airflow and particle transport. CFD models solve the governing Navier–Stokes equations to simulate airflow, coupled with particle tracking models such as the Lagrangian discrete phase model (DPM) or Eulerian approaches. These models can capture key phenomena such as turbulent dispersion, particle impaction, sedimentation, and diffusion. Notably, CFD simulations have demonstrated strong agreement with experimental data when realistic boundary conditions and airway geometries are used, highlighting their reliability in predicting aerosol deposition patterns.

Over time, fluid mechanical models have evolved from simplified one-dimensional (1D) whole-lung models to sophisticated three-dimensional (3D) simulations that incorporate patient-specific airway geometries derived from medical imaging. Early models focused on average deposition fractions across the respiratory tract, whereas modern approaches aim to resolve localized deposition patterns at the level of individual airway branches. This shift has been enabled by advances in computational power and numerical methods, allowing for the simulation of complex multiphase flows involving air, particles, and biological fluids. Recent studies have further expanded the scope of aerosol modelling by incorporating additional physical processes, such as mucus interaction, particle hygroscopic growth, and chemical reactions within the airway environment. For example, CFD-based models have been developed to simulate aerosol transport through the mucus layer, accounting for its non-Newtonian properties and its role in particle clearance. These models provide deeper insights into the effectiveness of inhaled therapies and the mechanisms governing pathogen transport in the respiratory system.

Another important advancement in fluid mechanical modelling is the integration of turbulence modelling techniques, such as large eddy simulation (LES) and Reynolds-averaged Navier–Stokes (RANS) models. Turbulence plays a critical role in aerosol dispersion, particularly in the upper airways and during high flow rates associated with activities such as coughing or speaking. Diffusion-based models have also been introduced to capture the spread of aerosols in confined environments and their interaction with ventilation systems, demonstrating the importance of airflow conditions in determining aerosol concentration and exposure levels. Despite these advancements, several challenges remain in the field of respiratory aerosol modelling. One of the primary challenges is the accurate representation of airway geometry and boundary conditions, which can vary significantly between individuals. Patient-specific modelling requires high-resolution imaging data and sophisticated mesh generation techniques, which can be computationally intensive. Additionally, the validation of computational models against experimental or clinical data remains a critical issue, as discrepancies can arise due to simplifications in model assumptions or uncertainties in input parameters.

Another challenge lies in bridging the gap between different spatial and temporal scales. Aerosol transport involves processes occurring at the microscopic level, such as particle–wall interactions and Brownian motion, as well as macroscopic phenomena such as airflow distribution across the lung. Developing multi-scale models that can accurately capture these interactions remains an active area of research. In conclusion, fluid mechanical modelling of respiratory aerosol transport has evolved into a highly interdisciplinary field, combining principles from fluid dynamics, aerosol science, biology, and computational modelling. The advancements achieved between 2018 and 2023 have significantly enhanced our ability to simulate and predict aerosol behaviour in the respiratory system. However, further research is needed to address existing challenges and to develop more accurate, efficient, and clinically relevant models.

Literature Review

Koullapis et al. (2018) conducted one of the most comprehensive studies on respiratory aerosol transport using high-resolution computational

fluid dynamics (CFD) simulations combined with realistic airway geometries derived from imaging data. The study focused on simulating airflow and particle deposition in the upper and central airways under varying breathing conditions. The authors utilized a Lagrangian particle tracking approach to model aerosol dynamics, capturing mechanisms such as inertial impaction, gravitational sedimentation, and Brownian diffusion. Their results demonstrated that particle size and inhalation flow rate significantly influence deposition patterns, with larger particles predominantly depositing in the upper airways due to inertial effects. The study also emphasized the importance of anatomical variability, showing that subject-specific airway geometries can lead to substantial differences in deposition efficiency. This work contributed significantly to validating CFD-based respiratory models against experimental datasets and established a benchmark for future patient-specific modeling approaches.

Poorbahrami et al. (2019) explored aerosol transport in human airways using Reynolds-Averaged Navier–Stokes (RANS) turbulence models, focusing on the effects of turbulent airflow on particle dispersion. The study investigated multiple turbulence closure models, including k–ε and k–ω formulations, to evaluate their effectiveness in predicting aerosol behaviour. The results indicated that turbulence significantly enhances particle mixing and dispersion, especially for particles in the micron range. The authors found that while RANS models provide computational efficiency, they may underpredict localized turbulent structures compared to higher-fidelity models such as LES. Nevertheless, the study demonstrated that RANS-based approaches remain useful for large-scale simulations where computational resources are limited. Importantly, the research highlighted the need for improved turbulence modelling to accurately capture aerosol transport in transitional flow regimes within the respiratory tract.

Elghobashi (2019) presented a theoretical and computational framework for modelling multiphase turbulent flows, which has direct implications for respiratory aerosol transport. The study introduced a classification of particle–fluid interactions based on particle concentration and coupling strength, distinguishing between one-way, two-way, and four-way coupling regimes. In the context of respiratory aerosols, the study emphasized that most inhaled particles fall within the one-way coupling regime, where particles are influenced by airflow but do not significantly affect it. The framework provided a foundation for selecting appropriate modelling strategies in CFD simulations. Additionally, the study discussed the importance of resolving turbulence scales to accurately predict particle dispersion, particularly for fine aerosols. This work has been widely cited in respiratory modelling studies and has guided the development of hybrid CFD–DEM and LES-based approaches.

Kolanjiyil and Kleinstreuer (2019) investigated the role of particle shape, size distribution, and hygroscopic growth in respiratory aerosol transport using advanced CFD simulations. Unlike traditional models that assume spherical particles, this study incorporated non-spherical particle dynamics and hygroscopic effects, which are particularly relevant for pharmaceutical aerosols and environmental pollutants. The authors demonstrated that particle growth due to humidity significantly alters deposition patterns, increasing deposition in deeper lung regions. Their simulations also showed that elongated or irregularly shaped particles exhibit different aerodynamic behaviours compared to spherical particles, affecting their transport and deposition efficiency. This study highlighted the importance of incorporating realistic particle properties into fluid mechanical models to improve prediction accuracy in both medical and environmental applications.

Lambert et al. (2020) developed a patient-specific airway modelling framework integrating medical imaging, CFD, and experimental validation techniques. The study utilized CT scan data to reconstruct detailed airway geometries and performed simulations of aerosol transport under various breathing conditions. A key contribution of this work was the validation of simulation results using in vivo imaging techniques, demonstrating strong agreement between predicted and observed deposition patterns. The authors also explored the impact of pathological conditions, such as airway constriction, on aerosol transport, showing that disease-induced changes can significantly alter airflow distribution and particle deposition. This study marked an important step toward personalized medicine, حـ بث CFD models can be used to tailor inhalation therapies based on individual patient anatomy and physiology.

Zhang et al. (2020) investigated respiratory aerosol transport using Large Eddy Simulation (LES) to capture transient turbulent structures in the upper and central airways. Unlike RANS models, LES resolves large-scale turbulent eddies while modelling smaller scales, providing higher fidelity in predicting airflow fluctuations. The study demonstrated that turbulence plays a dominant role in aerosol dispersion during high inhalation rates, such as during exercise or

coughing. The authors observed that LES-based models significantly improved the prediction of localized deposition hotspots compared to RANS approaches. Additionally, the study highlighted that fine particles (<2.5 μm) are strongly influenced by turbulent diffusion, leading to deeper penetration into the lungs. This work emphasized the importance of high-resolution turbulence modelling for accurately simulating aerosol transport under dynamic breathing conditions.

Feng et al. (2020) focused on aerosol transport under transient breathing conditions, incorporating cyclic inhalation–exhalation patterns into CFD simulations. The study revealed that unsteady airflow significantly affects particle trajectories and residence time within the airways. The authors showed that during inhalation, particles tend to follow streamlined paths, whereas exhalation introduces recirculation zones that can trap particles and increase deposition probability. The model also accounted for particle size distribution, demonstrating that smaller particles remain suspended longer and are more likely to reach alveolar regions. This study contributed to understanding real-world respiratory conditions, moving beyond steady-state assumptions commonly used in earlier models.

Longest and Holbrook (2020) provided an in-depth analysis of aerosol drug delivery mechanisms, focusing on optimizing inhalation therapies using CFD-based modelling. The study introduced advanced hybrid modelling approaches, combining Eulerian airflow simulation with Lagrangian particle tracking to evaluate deposition efficiency across different inhaler designs. The authors demonstrated that device geometry, particle release velocity, and inhalation profile significantly influence drug delivery efficiency. Their findings suggested that optimized inhaler designs could improve targeted drug delivery to specific lung regions, reducing drug wastage and side effects. This study has been instrumental in bridging the gap between fluid mechanics and pharmaceutical applications.

Islam et al. (2021) explored the impact of airway geometrical variations and disease conditions on aerosol transport using patient-specific CFD models. The study compared healthy and diseased airway structures, such as those affected by asthma and chronic obstructive pulmonary disease (COPD). Results showed that airway narrowing and irregularities significantly alter airflow patterns, leading to increased turbulence and uneven aerosol deposition. In diseased lungs, particles were more likely to deposit in constricted regions, reducing drug delivery efficiency to deeper lung areas. The study highlighted the necessity of incorporating pathological variations into fluid mechanical models for accurate clinical predictions and personalized treatment planning.

Choi et al. (2021) investigated multiphase airflow and aerosol interactions using coupled CFD–DEM (Discrete Element Method) simulations. This approach allowed for detailed modelling of particle–particle and particle–wall interactions, which are often neglected in simpler models. The study demonstrated that particle agglomeration and collision significantly influence transport behaviour, especially at higher particle concentrations. The authors also examined the effects of humidity and temperature on aerosol dynamics, showing that environmental conditions can alter particle size and deposition characteristics. This research advanced the understanding of complex multiphase interactions in respiratory flows and highlighted the limitations of single-phase modelling approaches.

Koullapis et al. (2021) extended their earlier work by developing a multi-scale whole-lung modelling framework that integrates 3D CFD simulations of upper airways with 1D models of peripheral lung regions. This hybrid approach significantly reduced computational cost while maintaining high accuracy in predicting aerosol deposition across the entire respiratory tract. The study demonstrated that coupling different spatial scales enables efficient simulation of particle transport from the trachea down to alveolar regions. The authors also highlighted that fine particles (<1 μm) predominantly reach deeper lung zones due to diffusion-dominated transport, whereas larger particles deposit earlier due to inertial effects. This work represents a major advancement in bridging micro- and macro-scale modelling in respiratory fluid mechanics.

Dong et al. (2021) investigated the influence of breathing patterns and inhalation profiles on aerosol transport using CFD simulations with dynamic boundary conditions. The study compared slow, normal, and rapid inhalation scenarios and found significant variations in airflow velocity distribution and particle deposition efficiency. Rapid inhalation produced stronger turbulence and enhanced deposition in the upper airways, while slow inhalation facilitated deeper lung penetration of fine particles. The authors emphasized that inhalation technique plays a critical role in optimizing aerosol drug delivery and should be carefully considered in clinical practice. This study contributed to the growing body of work

focusing on patient behaviour as a key parameter in respiratory modelling.

Li et al. (2022) explored aerosol transport in alveolar regions using high-resolution CFD models that incorporate detailed alveolar geometries and wall motion. Unlike previous studies focusing primarily on upper airways, this research addressed the complexities of airflow and particle dynamics in the deep lung. The authors demonstrated that alveolar expansion and contraction during breathing significantly influence particle deposition patterns. Their results showed that Brownian diffusion dominates transport for ultrafine particles (<0.5 μm), leading to high deposition efficiency in alveolar sacs. The study provided valuable insights into gas exchange regions and highlighted the importance of modelling alveolar mechanics for accurate prediction of aerosol behaviour.

Wang et al. (2022) focused on aerosol transport in realistic airway geometries reconstructed from medical imaging, incorporating machine learning techniques to enhance simulation efficiency. The study combined CFD with data-driven surrogate models, reducing computational time while maintaining acceptable accuracy. The authors demonstrated that machine learning models can predict deposition patterns based on key input parameters such as particle size, flow rate, and airway geometry. This hybrid approach represents a significant step toward real-time simulation and clinical application of respiratory aerosol models. Additionally, the study highlighted the potential of AI in optimizing inhalation therapies and predicting disease progression.

Talaat and Xi (2022) investigated the effects of thermal gradients and humidity on respiratory aerosol transport using coupled heat and mass transfer models. The study showed that temperature differences between inhaled air and airway surfaces lead to condensation and evaporation processes, altering particle size during transport. Hygroscopic growth was found to significantly increase deposition in deeper lung regions, particularly for pharmaceutical aerosols. The authors also demonstrated that thermal effects can influence airflow patterns and particle trajectories, emphasizing the need to incorporate thermodynamic processes into fluid mechanical models. This work advanced the understanding of environmental and physiological influences on aerosol dynamics.

Xi et al. (2022) investigated regional aerosol deposition in subject-specific airway models using advanced CFD simulations with detailed anatomical reconstruction. The study emphasized inter-subject variability by comparing multiple airway geometries obtained from CT imaging. Results showed that even minor anatomical differences can lead to significant variations in airflow distribution and particle deposition patterns. The authors also analysed the influence of particle size spectrum (0.1–10 μm) and found that deposition mechanisms transition from diffusion-dominated to inertia-dominated as particle size increases. This study reinforced the necessity of personalized modelling for accurate prediction of respiratory aerosol behaviour and highlighted the limitations of generic airway models.

Koullapis et al. (2022) further advanced whole-lung aerosol transport modelling by incorporating stochastic representations of airway branching and variability. The study introduced probabilistic modelling techniques to account for uncertainties in airway geometry and breathing conditions. By integrating stochastic methods with CFD, the authors were able to generate statistically robust predictions of aerosol deposition across populations. The results demonstrated that variability in airway structure and breathing patterns significantly affects deposition efficiency, particularly in peripheral lung regions. This work contributed to population-scale modelling and risk assessment, especially relevant for airborne disease transmission studies.

Kleinstreuer et al. (2023) presented a comprehensive study on CFD-based aerosol transport with emphasis on pharmaceutical applications, particularly inhaler optimization. The research integrated fluid–particle interaction models with device-specific boundary conditions, enabling accurate simulation of aerosol release and transport from inhalers into the respiratory tract. The study demonstrated that optimizing particle size distribution and inhalation flow rate can significantly improve drug delivery efficiency to targeted lung regions. Additionally, the authors highlighted the role of turbulence modulation and particle–wall interactions in determining deposition outcomes. This work has direct implications for the design of next-generation inhalation therapies.

Wei et al. (2023) explored aerosol transport under realistic environmental and physiological conditions, including variations in humidity, temperature, and breathing intensity. Using Multiphysics CFD simulations, the study showed that environmental factors significantly influence aerosol dynamics, particularly through hygroscopic growth and evaporation. The authors also examined aerosol dispersion during activities such as speaking and coughing,

demonstrating that transient airflow conditions can lead to complex transport patterns and increased spread of fine particles. This research is particularly relevant for understanding airborne disease transmission and highlights the importance of integrating environmental variables into respiratory models.

Sznitman (2023) provided a critical review and modelling perspective on micro-scale aerosol transport in the alveolar region, focusing on acinar flow dynamics. The study emphasized the role of low Reynolds number flows, where viscous forces dominate and airflow exhibits recirculating patterns within alveolar sacs. Using both analytical and CFD-based approaches, the author demonstrated that particle deposition in the acinar region is governed primarily by diffusion and sedimentation, with minimal ազդեց of turbulence. The study also highlighted the importance of cyclic breathing and alveolar wall motion in enhancing particle mixing and deposition. This work offered valuable insights into deep lung transport mechanisms and emphasized the need for specialized modelling approaches for different airway regions.

Hofemeier et al. (2020) investigated particle deposition mechanisms in the acinar region using detailed CFD simulations combined with experimental validation. The study focused on ultra-fine particles (<1 μm) and demonstrated that Brownian diffusion is the dominant transport mechanism in deep lung regions. The authors incorporated realistic alveolar geometries and cyclic wall motion to simulate breathing conditions. Their findings revealed that alveolar expansion enhances mixing and increases deposition efficiency. Additionally, the study showed that particle residence time is a critical factor influencing deposition in the distal lung. This work contributed significantly to understanding micro-scale aerosol transport and highlighted the importance of including alveolar dynamics in fluid mechanical models.

Yin et al. (2021) explored aerosol transport in bifurcating airway structures using high-resolution CFD models. The study analysed airflow patterns at multiple airway generations and demonstrated that secondary flows and vortices formed at bifurcation points significantly influence particle trajectories. The authors found that particles with higher inertia tend to deviate from airflow streamlines and deposit at bifurcation walls, particularly at carinal ridges. The research emphasized that airway branching geometry plays a crucial role in determining regional deposition patterns. This study provided detailed insights into localized deposition mechanisms and improved the understanding of airflow–particle interactions in complex airway networks.

Darquenne (2020) presented a comprehensive review and modelling analysis of aerosol deposition in human lungs, integrating experimental observations with theoretical models. The study highlighted the interplay between different deposition mechanisms—impaction, sedimentation, and diffusion—and how their relative importance varies with particle size and breathing conditions. The author also emphasized the limitations of traditional models in capturing regional deposition variability and advocated for the use of advanced CFD techniques. The work provided a strong theoretical foundation for respiratory aerosol modelling and has been widely referenced in both clinical and engineering research.

Miyawaki et al. (2022) developed a numerical model for aerosol transport in diseased lungs, focusing on conditions such as asthma and airway obstruction. The study incorporated airway constrictions and mucus accumulation into CFD simulations to evaluate their impact on airflow and particle deposition. Results indicated that airway narrowing increases local airflow velocity, leading to enhanced inertial impaction and uneven deposition patterns. The authors also showed that mucus layers can trap particles, reducing their penetration into deeper lung regions. This research highlighted the importance of incorporating pathological features into fluid mechanical models for accurate clinical predictions.

Koullapis et al. (2023) introduced an advanced population-based respiratory aerosol modelling framework, integrating CFD with statistical and machine learning techniques. The study aimed to predict aerosol deposition across diverse populations by accounting for variability in airway geometry, breathing patterns, and particle properties. The authors demonstrated that combining CFD with data-driven approaches significantly improves prediction accuracy and reduces computational cost. The framework also enabled rapid assessment of aerosol exposure risks in different scenarios, including environmental pollution and infectious disease transmission. This work represents a major step toward scalable and clinically applicable respiratory modelling systems.

Tian et al. (2021) investigated aerosol transport under coughing and sneezing conditions using transient CFD simulations. The study focused on high-velocity expiratory events, which generate complex turbulent jets capable of transporting particles over long distances within the respiratory tract and beyond. The authors

demonstrated that turbulent eddies formed during coughing significantly enhance aerosol dispersion and promote deposition in upper airway regions. Additionally, the study showed that particle size plays a crucial role in determining whether aerosols are expelled or deposited within the airways. Fine particles were found to remain airborne longer, increasing the likelihood of deep lung penetration upon re-inhalation. This research is particularly relevant for understanding infectious disease transmission and highlights the importance of modelling transient, high-intensity respiratory events.

Liu et al. (2022) explored nanoparticle transport and deposition in the respiratory system using multiscale CFD models. The study emphasized the behaviour of ultra-fine particles (<100 nm), which are increasingly relevant in both environmental pollution and targeted drug delivery. The authors found that Brownian motion dominates nanoparticle transport, leading to high deposition efficiency in alveolar regions. The study also highlighted that nanoparticle aggregation can significantly alter transport behaviour, affecting deposition patterns. Furthermore, the authors demonstrated that traditional models may underestimate nanoparticle deposition due to simplified assumptions, emphasizing the need for refined modelling approaches for nano-scale aerosols.

Zhang and Kleinstreuer (2022) developed a CFD-based optimization framework for aerosol drug delivery, integrating fluid mechanics with optimization algorithms. The study focused on identifying optimal particle size distributions, inhalation flow rates, and device configurations to maximize drug deposition in targeted lung regions. The authors employed multi-objective optimization techniques, balancing efficiency and uniformity of deposition. Their findings showed that tailored particle size ranges (typically 1–5 μm) yield optimal deposition for therapeutic purposes. This work demonstrated the potential of combining fluid mechanical modelling with optimization strategies to enhance the effectiveness of inhalation therapies.

Ge et al. (2023) introduced a coupled fluid–structure interaction (FSI) model for respiratory aerosol transport, accounting for airway wall deformation during breathing. Unlike rigid-wall assumptions used in many CFD studies, this model incorporated the elasticity of airway tissues, enabling more realistic simulations of airflow dynamics. The results showed that airway deformation significantly influences airflow distribution and particle trajectories, particularly in lower airway regions. The study also revealed that FSI effects can alter deposition efficiency by modifying local flow velocities and pressure gradients. This research represents a significant advancement in incorporating biomechanical factors into fluid mechanical models.

Chen et al. (2023) proposed a real-time aerosol transport prediction framework using machine learning integrated with CFD-generated datasets. The study utilized deep neural networks trained on large simulation datasets to predict aerosol deposition patterns rapidly without performing full CFD simulations. The authors demonstrated that the model achieved high accuracy while significantly reducing computational time, making it suitable for clinical applications. This approach enables real-time decision-making in personalized medicine, such as optimizing inhaler usage or assessing exposure risks. The study highlights the growing role of artificial intelligence in transforming traditional fluid mechanical modelling into fast, scalable, and practical solutions.

Comparative Table

Study	Author (Year)	Method/Model	Focus Area	Key Findings	Limitations
1	Koullapis et al. (2018)	CFD + Lagrangian	Deposition patterns	Size-dependent deposition	High computational cost
2	Poorbahrami et al. (2019)	RANS	Turbulence effects	Enhanced mixing	Limited turbulence resolution
3	Elghobashi (2019)	Multiphase theory	Particle–fluid interaction	Coupling regimes defined	Theoretical limitations
4	Kolanjiyil & Kleinstreuer (2019)	CFD	Hygroscopic growth	Particle size evolution	Complex modelling
5	Lambert et al. (2020)	Patient-specific CFD	Clinical validation	Accurate deposition prediction	Data-intensive

6	Zhang et al. (2020)	LES	Turbulent transport	High accuracy in dispersion	Expensive computation
7	Feng et al. (2020)	Transient CFD	Breathing cycles	Unsteady flow impact	Model complexity
8	Longest & Holbrook (2020)	Hybrid CFD	Drug delivery	Improved inhaler design	Device dependency
9	Islam et al. (2021)	CFD	Disease modelling	Altered deposition	Limited datasets
10	Choi et al. (2021)	CFD–DEM	Multiphase interaction	Particle collision effects	High cost
11	Koullapis et al. (2021)	Multi-scale (1D+3D)	Whole lung modelling	Efficient simulation	Simplified distal lung
12	Dong et al. (2021)	CFD	Breathing patterns	Flow-dependent deposition	Behavioural variability
13	Li et al. (2022)	CFD	Alveolar transport	Diffusion-dominated	Limited validation
14	Wang et al. (2022)	CFD + ML	Fast prediction	Reduced computation	Approximation errors
15	Talaat & Xi (2022)	Multiphysics CFD	Thermal effects	Hygroscopic growth impact	Complex coupling
16	Xi et al. (2022)	CFD	Subject variability	Personalized modelling	Data requirement
17	Koullapis et al. (2022)	Stochastic CFD	Population modelling	Variability captured	Statistical uncertainty
18	Kleinstreuer et al. (2023)	CFD	Drug delivery	Device optimization	Model assumptions
19	Wei et al. (2023)	Multiphysics CFD	Environmental effects	Real-world modelling	High complexity
20	Sznitman (2023)	Analytical + CFD	Acinar flow	Diffusion dominance	Simplified geometry
21	Hofemeier et al. (2020)	CFD	Alveolar deposition	Brownian diffusion	Limited scale
22	Yin et al. (2021)	CFD	Airway bifurcation	Vortex effects	Local focus
23	Darquenne (2020)	Theoretical + CFD	Deposition mechanisms	Mechanism classification	Generalization limits
24	Miyawaki et al. (2022)	CFD	Diseased lungs	Constriction effects	Model assumptions
25	Koullapis et al. (2023)	CFD + AI	Population modelling	Fast prediction	Training dependency
26	Tian et al. (2021)	Transient CFD	Cough dynamics	High turbulence spread	Event variability
27	Liu et al. (2022)	Multiscale CFD	Nanoparticles	Diffusion dominance	Limited validation
28	Zhang & Kleinstreuer (2022)	CFD + Optimization	Drug delivery	Optimal particle size	Complexity
29	Ge et al. (2023)	FSI + CFD	Airway deformation	Realistic airflow	High computation
30	Chen et al. (2023)	AI + CFD	Real-time prediction	Fast simulation	Data dependency

Comparative Analysis

The comparative evaluation of the 30 studies reveals a clear evolution in fluid mechanical modelling of respiratory aerosol transport, transitioning from traditional deterministic models to advanced hybrid, multiscale, and data-driven approaches. Early studies (2018–2019) primarily relied on conventional CFD

frameworks and RANS turbulence models, which provided reasonable approximations of airflow and particle transport but were limited in capturing fine-scale turbulent structures and transient behaviours. These models were computationally efficient but often lacked the resolution required to accurately predict localized deposition patterns, particularly in complex airway geometries. As the field progressed into 2020–2021, there was a significant shift toward high-fidelity modelling techniques such as LES and transient CFD simulations. These approaches enabled detailed representation of turbulent airflow and unsteady breathing cycles, leading to improved prediction accuracy for aerosol dispersion and deposition. Additionally, hybrid models combining Eulerian airflow with Lagrangian particle tracking became increasingly common, allowing for more precise modelling of particle dynamics. During this period, there was also a growing emphasis on application-driven research, particularly in optimizing inhalation drug delivery systems and understanding disease-specific airflow alterations.

Between 2021 and 2023, the research landscape further evolved with the introduction of multi-scale, stochastic, and Multiphysics modelling frameworks. Studies began integrating 1D and 3D models to simulate the entire respiratory system efficiently, addressing the challenge of computational cost while maintaining accuracy. The incorporation of thermal effects, humidity, and particle hygroscopic growth marked a significant advancement in capturing realistic physiological conditions. Furthermore, fluid–structure interaction (FSI) models introduced the influence of airway deformation, providing a more accurate representation of breathing mechanics. A notable trend in recent years is the integration of artificial intelligence and machine learning with CFD. AI-assisted models have demonstrated the ability to significantly reduce computational time while maintaining acceptable prediction accuracy, enabling real-time simulations and personalized medical applications. These models are particularly useful in population-scale studies and clinical decision-making, where rapid predictions are essential. However, they also introduce new challenges related to data dependency, model generalization, and interpretability.

Despite these advancements, several limitations persist across the studies. High computational cost remains a major barrier for high-fidelity models such as LES and FSI-based simulations. Additionally, many models rely on simplified assumptions regarding airway geometry, particle properties, and boundary conditions, which can affect accuracy. Validation against experimental or clinical data is still limited in many cases, highlighting the need for more comprehensive validation frameworks. Moreover, the integration of multi-scale and multi-physics phenomena remains an ongoing challenge, particularly in bridging the gap between micro-scale particle dynamics and macro-scale airflow behaviour. Overall, the comparative analysis indicates that while significant progress has been made in fluid mechanical modelling of respiratory aerosols, future research must focus on developing efficient, accurate, and clinically applicable models. This includes the integration of AI with physics-based models, improved patient-specific modelling techniques, and enhanced validation using real-world data.

Discussion

The analysis of fluid mechanical models for respiratory aerosol transport reveals a rapidly evolving research landscape characterized by increasing model sophistication, integration of Multiphysics phenomena, and a shift toward clinically relevant applications. The reviewed studies collectively demonstrate that aerosol transport in the respiratory system is governed by a complex interplay of airflow dynamics, particle properties, airway geometry, and physiological conditions. These factors interact across multiple spatial and temporal scales, making accurate modelling a challenging yet essential task. One of the most significant findings across the literature is the dominant role of particle size in determining deposition mechanisms. Larger particles (typically >5 μm) are primarily influenced by inertial impaction, leading to deposition in the upper airways such as the nasal cavity and trachea. In contrast, intermediate particles (1–5 μm) are affected by gravitational sedimentation, enabling deposition in bronchial regions. Ultrafine particles (<1 μm), however, are governed by Brownian diffusion and tend to penetrate deeper into alveolar regions. This size-dependent behaviour is consistently observed across CFD, LES, and multiscale models, forming a foundational principle in aerosol transport theory.

Another critical aspect highlighted in the studies is the influence of airflow regimes and turbulence. Under normal breathing conditions, airflow in smaller airways tends to remain laminar, whereas upper airways and high-flow conditions (e.g., coughing, exercise) induce turbulence. Advanced modelling techniques such as LES have shown superior capability in capturing transient turbulent structures, which significantly affect aerosol dispersion and deposition patterns. However, these models

come with high computational costs, limiting their widespread use in real-time or clinical applications. The importance of airway geometry and patient-specific modelling is also strongly emphasized. Variations in airway structure—whether due to natural anatomical differences or pathological conditions such as asthma or COPD—can significantly alter airflow distribution and particle trajectories. Studies using CT-based reconstructions have demonstrated that personalized CFD models can provide highly accurate predictions of aerosol deposition, paving the way for precision medicine. Nevertheless, such approaches require high-quality imaging data and substantial computational resources, posing challenges for routine clinical implementation.

In recent years, the integration of Multiphysics effects—including heat transfer, humidity, particle hygroscopic growth, and fluid–structure interaction—has improved the realism of aerosol transport models. These factors are particularly important in simulating real-world conditions, where inhaled air interacts with warm, moist airway environments. For instance, hygroscopic growth can increase particle size during transport, altering deposition locations and enhancing drug delivery efficiency in certain regions. A transformative development in this field is the incorporation of artificial intelligence and machine learning. AI-driven surrogate models trained on CFD datasets have shown the ability to predict aerosol transport behaviour with significantly reduced computational time. This advancement opens new possibilities for real-time simulation, personalized treatment planning, and large-scale exposure assessment. However, these models depend heavily on training data quality and may lack interpretability compared to physics-based approaches.

Despite the progress made, several research gaps remain. There is a need for improved model validation using experimental and clinical data, as well as better integration of multi-scale phenomena spanning from airway-level flows to cellular-level interactions. Additionally, balancing model accuracy with computational efficiency remains a critical challenge. In conclusion, fluid mechanical modelling of respiratory aerosol transport has advanced significantly, but future research must focus on developing hybrid, scalable, and validated models that can bridge the gap between theoretical simulations and real-world clinical applications.

Conclusion

The systematic review of fluid mechanical models for respiratory aerosol transport in human airways highlights the significant progress made between 2018 and 2023 in understanding, simulating, and optimizing aerosol behaviour within complex respiratory systems. The integration of advanced computational techniques, realistic airway geometries, and Multiphysics modelling has transformed this field into a highly interdisciplinary domain with direct applications in healthcare, environmental science, and public safety. One of the most important conclusions drawn from this review is the central role of computational fluid dynamics (CFD) as the foundational modelling approach for respiratory aerosol transport. Over the years, CFD has evolved from simplified steady-state simulations to highly detailed, transient, and patient-specific models capable of capturing complex airflow patterns and particle dynamics. The incorporation of advanced turbulence models such as Large Eddy Simulation (LES) and hybrid approaches has significantly improved prediction accuracy, particularly in capturing localized deposition patterns and transient flow behaviours. However, these improvements come at the cost of increased computational complexity, which remains a major limitation for large-scale or real-time applications.

Another key insight is the strong dependence of aerosol transport and deposition on particle characteristics, particularly size, shape, and hygroscopic properties. The reviewed studies consistently demonstrate that particle size determines the dominant deposition mechanism—ranging from inertial impaction in upper airways to diffusion-driven deposition in alveolar regions. The inclusion of particle growth due to humidity and temperature variations further enhances the realism of modern models, especially in applications involving pharmaceutical aerosols and environmental pollutants. These findings are critical for optimizing inhalation therapies and designing effective drug delivery systems. The review also underscores the importance of airway geometry and physiological variability. Patient-specific modelling, enabled by medical imaging techniques such as CT scans, has shown that anatomical differences can significantly influence airflow distribution and aerosol deposition. This has important implications for personalized medicine, حـ بث treatments can be tailored based on individual respiratory structures and breathing patterns. Additionally, the inclusion of pathological conditions such as airway constriction and mucus accumulation provides

deeper insights into disease-specific aerosol behaviour, which is essential for improving therapeutic outcomes in conditions like asthma and chronic obstructive pulmonary disease (COPD).

A major advancement in recent years is the incorporation of Multiphysics and multi-scale modelling frameworks. These models integrate various physical phenomena—including turbulence, heat transfer, humidity effects, and fluid–structure interaction—to provide a more comprehensive representation of respiratory processes. Multi-scale approaches that combine 1D and 3D models have also addressed the challenge of simulating the entire respiratory system efficiently, bridging the gap between detailed local simulations and whole-lung predictions. The emergence of artificial intelligence (AI) and machine learning (ML) represents a transformative shift in the field. AI-driven surrogate models have demonstrated the ability to replicate CFD predictions with significantly reduced computational time, enabling real-time simulations and large-scale population studies. These models hold great promise for clinical applications, such as optimizing inhaler usage, predicting disease progression, and assessing exposure risks. However, challenges related to data dependency, model generalization, and interpretability must be addressed to ensure their reliability and adoption in practice.

Despite these advancements, several challenges and research gaps persist. One of the primary limitations is the lack of comprehensive validation of computational models against experimental and clinical data. While some studies have achieved good agreement with imaging techniques, many models still rely on assumptions that may not fully capture real-world conditions. Additionally, the high computational cost associated with high-fidelity simulations limits their accessibility and scalability. The integration of multi-scale and multi-physics phenomena also remains an ongoing challenge, particularly in accurately linking micro-scale particle interactions with macro-scale airflow dynamics. Looking forward, future research should focus on developing hybrid modelling frameworks that combine the strengths of physics-based simulations and data-driven approaches. The use of AI to accelerate CFD simulations, coupled with improved experimental validation techniques, can significantly enhance model accuracy and applicability. Furthermore, advancements in medical imaging and computational resources will facilitate the development of fully personalized respiratory models, enabling precision medicine in aerosol-based therapies. In conclusion, fluid mechanical modelling of respiratory aerosol transport has reached a level of maturity that allows for detailed and accurate simulations of complex respiratory processes. However, continued innovation is required to overcome existing limitations and translate these models into practical, real-world applications. The integration of advanced computational techniques, experimental validation, and clinical insights will be key to advancing this field and improving outcomes in respiratory health and disease management.

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