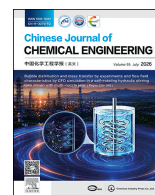




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Full Length Article

CFD analysis of particle deposition characteristics in the human upper respiratory tract: A study on multifactorial regulation laws under steady-state/cyclic breathing conditions

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ABSTRACT

Particle deposition in the respiratory tract involves interdisciplinary dynamic processes such as fluid mechanics, biomedicine, and materials science, and is of great significance for disease transmission (e.g., SARS-CoV-2 aerosol infection), toxicant exposure (e.g., cigarette carcinogens), and pulmonary drug delivery (e.g., asthma therapeutics). In this study, the geometric structure of the upper respiratory tract from the nasal vestibule to the tracheal bifurcation was reconstructed using clinical computed tomography scan data and the structural repair was completed. Then, we adopted a computational fluid dynamics framework based on the Eulerian–Lagrangian approach to simulate the transport and deposition processes of aerosols. The results show that the simulation results are basically consistent with the experimental data, which confirms the reliability of the proposed model. The positions of deposition hotspots mainly depend on structural features. For example, areas with abrupt changes in the shape and direction of the flow channel, such as the nasal vestibule, piriform fossae, and laryngeal constriction, are prone to form deposition hotspots, which are related to the vortex intensity. The particle deposition rules under steady-state and cyclic breathing conditions are obtained through the analysis using multifactorial design of experiments and response surface methodology. Under steady-state breathing conditions, the particle size dominates the influence on deposition efficiency (order of influencing factors: particle size > flow rate > particle density), and there is a significant synergistic effect between particle size and flow rate. Under cyclic breathing conditions, respiratory frequency and inspiration-to-expiration ratio have equivalent effects on regulating inspiratory time, with a strong coupling effect between them, while post-inspiration breath-hold has a limited effect on improving deposition efficiency. The results of this study have laid a solid theoretical foundation for aspects such as precise drug delivery and respiratory protection.

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1. Introduction

The deposition of particulate matter in the respiratory tract is a multi-stage dynamic process that involves interdisciplinary mechanisms spanning fluid dynamics, biomedical science, and materials science. Specifically, this process holds significant

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research value in the following domains: in the context of disease transmission, the deposition behavior of bacteria or viruses (such as SARS-CoV-2), which is inhaled through respiratory droplets and aerosol carriers, directly results in infection risk [1]; regarding exposure to harmful substances, particles with diameters ranging from 0.01 to 1 μm in cigarette smoke, which carry carcinogens such as polycyclic aromatic hydrocarbons, can induce diseases like lung cancer after depositing in the respiratory tract [2,3]; in terms of drug delivery, the deposition efficiency and distribution patterns of micron-sized therapeutic particles in inhalation therapy are critical determinants of treatment efficacy for conditions such as asthma

and chronic obstructive pulmonary disease [4]. Given the profound implications of these mechanisms for public health, disease treatment, and environmental toxicology, research in this field has garnered sustained interdisciplinary attention in recent years.

The study of respiratory particle deposition has evolved through three primary stages.

- (1) *In vitro* experimental stage. This stage utilized fresh excised respiratory tract tissues to construct experimental models and employed radioactively labeled particle tracking techniques to study deposition patterns. While this approach preserved the characteristics of biological tissue, it had limitations such as difficulty in obtaining samples and poor experimental repeatability [5], making it unable to meet statistical requirements.
- (2) Human experimental stage. This stage primarily used γ -scintigraphy technology to monitor the dynamic distribution of radiolabeled aerosols in the human body and acquire deposition data. However, this method faced significant challenges in obtaining ethical approval for human experimentation, and the statistical methods applied to imaging data had substantial errors [6–9].
- (3) Modern research stage. Considering the ethical aspects and barriers in the approval process of human experimentation, researchers progressively shifted toward a hybrid research strategy that integrated the construction of airway models and numerical simulation: Initially, researchers primarily utilized relatively idealized airway models for exploratory studies. Subsequently, with the iterative advancement of testing technologies, researchers began to reconstruct personalized airway models based on medical images (e.g., computed tomography, CT), and on this basis, performed experiments with greater physiological realism. Concurrently, researchers complemented these experiments using computational fluid dynamics (CFD) simulations, which were employed to elucidate mechanisms and analyze flow fields.

Jin *et al.* [10] nebulized a fluorescein-labeled normal saline solution, allowing the nebulized droplets to deposit in an idealized oropharyngeal model. Subsequently, the deposited droplets were eluted, and the absorbance of the eluate was measured, thereby achieving quantitative analysis of the deposition fraction. Due to their accessibility, idealized models are often employed in experiments where the association with respiratory tract structure is weak. Zhang *et al.* [11], who used a model constructed with tubes of unequal diameters to replace the real oropharynx, found that it was necessary to modify key structural parameters of the model to align with human experimental data under different breathing intensities. Weibel [12] proposed approximating the airways as a symmetric tree-like bifurcating network; however, their study revealed that such symmetric models exhibited significant distortion due to the highly asymmetric nature of the actual bronchial tree. These findings indicated that although idealized models had the advantage of accessibility, the accuracy of corresponding respiratory experiments was limited by structural distortions between ideal and realistic geometries. CFD simulations can obtain detailed local quantitative information on gas flow and particle deposition [13], supplementing the deficiencies of physical experiments. Researchers also reached conclusions similar to those from physical experiments when conducting CFD simulations, namely that the differences between idealized models and realistic models could not be ignored, and that the latter better reflected actual conditions [14,15].

Subsequently, based on CT scans, airway geometries were reconstructed using Mimics software, and transparent resin models of the respiratory tract were obtained via 3D-printed and PolyJet technology. The greatest advantage of this method is that it preserves the authenticity of physiological structural. Although the experimental data obtained through this method remain limited and do not account for human activities, it significantly improves experimental repeatability and reduces errors, thus establishing itself as one of the mainstream research approaches in this field [16–18]. Combining CT technology with CFD calculations not only acquires reliable batches of data, but also obtains precise details of internal flow and deposition within the human respiratory tract. Meanwhile, it facilitates in-depth exploration of the impacts of breathing patterns, individual differences, and special environments on particle deposition, thereby promoting the continuous refinement of research on the mechanisms of respiratory particle transport and deposition.

Not only are there differences between ideal geometric models and realistic geometric models, but the airway geometries of different individuals [19] also exhibit significant differences influenced by factors such as age [20,21], disease type and severity [22,23], and body size [24], which consequently lead to variations in particle deposition and distribution. In addition, to improve the convergence of numerical simulations, smoothing treatment was usually applied to the rough surfaces of airway [25], and hybrid modeling approaches that combined realistic and idealized model components were adopted. For example, Dong *et al.* [26] combined an idealized main trachea inlet with both an approximate airway model and a realistic human model, to evaluate and compare airflow patterns and particle transport/deposition under different gas flow rates. Their study showed that surface roughness increased the complexity of flow patterns; the deposition amount in the first-generation airways was the highest compared to subsequent bronchi; and for ultrafine particles smaller than 10 nm, Brownian diffusion remained the dominant deposition mechanism.

Airflow in the upper respiratory tract simultaneously exhibits laminar, transitional, and turbulent flow regimes. While large eddy simulation (LES) could predict detailed flow characteristics and particle deposition [27], it requires high grid resolution and incurs substantial computational cost. The $k-\omega$ SST (shear stress transport) model, which combines the Reynolds-averaged Navier–Stokes (RANS) methodology with a transition-sensitive SST formulation, was more widely applied [28–30]. Enabling the low-Reynolds-number (LRN) correction allows the $k-\omega$ SST model to accurately predict transitional flows while maintaining relatively lower computational costs.

Previous research results showed that under steady breathing conditions, particle diameter and breathing intensity were dominant factors. Peng *et al.* [31] used a model spanning the nasal cavity to the third-generation bronchi, and concluded that larger particles are more significantly affected by airflow conditions, and that the deposition rate of $7.07\text{ }\mu\text{m}$ particles at $90\text{ L}\cdot\text{min}^{-1}$ was 50.4% higher than that at $15\text{ L}\cdot\text{min}^{-1}$. Liu *et al.* [32] employed an upper airway model reconstructed from computed tomography and a Eulerian–Lagrangian gas–solid flow model, and found that at the same inhalation flow rate, smaller particles dispersed more widely, while larger particles aggregated more locally. Nearly all “large particles” aggregated in the anterior nasal region, and increasing inhalation velocity intensified particle accumulation.

Although in-depth findings have been achieved in studies related to aerosol deposition under steady-state breathing conditions [31,32], realistic respiration is intrinsically cyclic, consisting of three phases: inhalation, breath-hold, and exhalation. Accordingly, relevant computational studies have been gradually advanced, and the physiological fidelity of the modeling for the

aforementioned breathing phases has been continuously improved [33]. Previous studies mainly focused on the individual effects of key cyclic parameters: the inspiration-to-expiration (I:E) ratio modulated the peak flow velocity and inertial impaction [34], respiratory frequency governed the dynamics of the breathing cycle [35], and post-inspiratory breath-holding promoted particle deposition in the distal respiratory tract via gravitational settling and diffusion [36,37]. However, most of these studies adopted a univariate approach, analyzing a single parameter in isolation. This paradigm failed to capture the potential interactions among these coupled variables, such as how the effect of breath-hold duration may be influenced by the preceding I:E ratio or respiratory frequency, which limits its ability to predict particle deposition under the conditions of multifactorial and realistic breathing variations.

The transport and deposition of inhalation particles play a pivotal role in pulmonary drug delivery and respiratory health risk assessment. However, the systematic quantification of the coupled effects of multiple influencing factors under physiologically representative breathing patterns remains insufficient. To fill this gap, this study introduces an integrated framework combining CFD, multifactorial design of experiments (DOE), and response surface methodology (RSM), aiming to elucidate the individual and interactive effects of key parameters. The methodology includes: (1) reconstructing a patient-specific upper airway model based on clinical CT images; (2) developing and validating of a transient Eulerian–Lagrangian CFD model based on published experimental deposition data [38]; (3) conducting a DOE to identify the dominant factors affecting deposition efficiency under steady-state and cyclic breathing conditions; (4) applying the RSM to quantify the interactions of multiple parameters. This structured approach advances the existing research paradigm from isolated parameter analysis to a predictive, interaction-aware understanding of aerosol deposition under realistic respiratory dynamics.

2. Numerical Simulation Method

2.1. Geometric and mesh models

The upper airway model used in this study was reconstructed from a series of CT images of a 31-year-old healthy Chinese female provided by the China–Japan Friendship Hospital, with the

CT scan having a slice interval of 1 mm. The employed CT scanner operated at a tube voltage of 120 kV and a tube current of 352 mA. Images were acquired with a slice thickness and reconstruction increment of 1 mm. The reconstruction field of view (FOV) was 479 mm, resulting in an in-plane pixel resolution of 512×512 and a corresponding pixel size of 0.936 mm. This set of parameters ensured the geometric accuracy required for the subsequent three-dimensional reconstruction of the airway model. To improve mesh quality and the convergence of numerical simulation, we repaired the core geometric defects existing the original model reconstructed from CT scans, including three types of problems: microscopic surface irregularities, unreasonable physiological structures, and incomplete topological structures. The respiratory airway model was constructed and processed in the following sequence. First, based on anatomical data of the upper respiratory tract from healthy individuals, the initial model was created and modified in Mimics software. The cross-sectional dimensions of constricted areas (e.g., the nasal vestibule) were adjusted to a physiologically reasonable range. Subsequently, microscopic defects such as sharp edges and protrusions were smoothed using Geomagic Studio software to reduce surface roughness. Finally, topological regularization was performed in ANSYS SpaceClaim to merge redundant small facets (area $\leq 0.01 \text{ mm}^2$), fill minor gaps ($\leq 0.05 \text{ mm}$), and eliminate overlapping facets, yielding a high-quality geometry ready for simulation. After optimization, the facets are evenly distributed, the topological structure of the model is continuous and complete, which meets the high-quality requirements for polyhedral meshing (mesh quality ≥ 0.4). The refined structural configuration is comprehensively illustrated in Fig. 1. The fluid inlets were located on the left and right nostrils.

The mesh was generated using Fluent Meshing. As shown in Fig. 2(a) and (b), a polyhedral mesh was adopted with the maximum grid size of 0.0005 m. A 5-layer boundary was used, with the first layer grid thickness of 0.00005 m and a growth rate of 1.05, as illustrated in Fig. 2(c).

2.2. Governing equations

In this work, the fluid in the nasal cavity was treated as an incompressible fluid, and the effects of heat transfer and variations

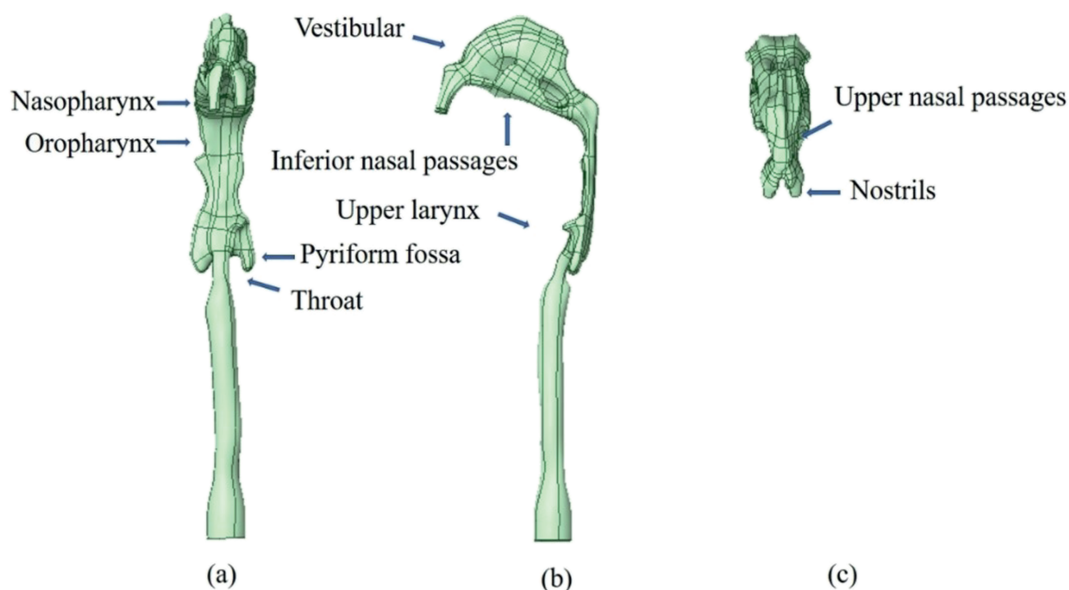


Fig. 1. Geometric structure of the upper respiratory tract: (a) main view; (b) side view; (c) top view.

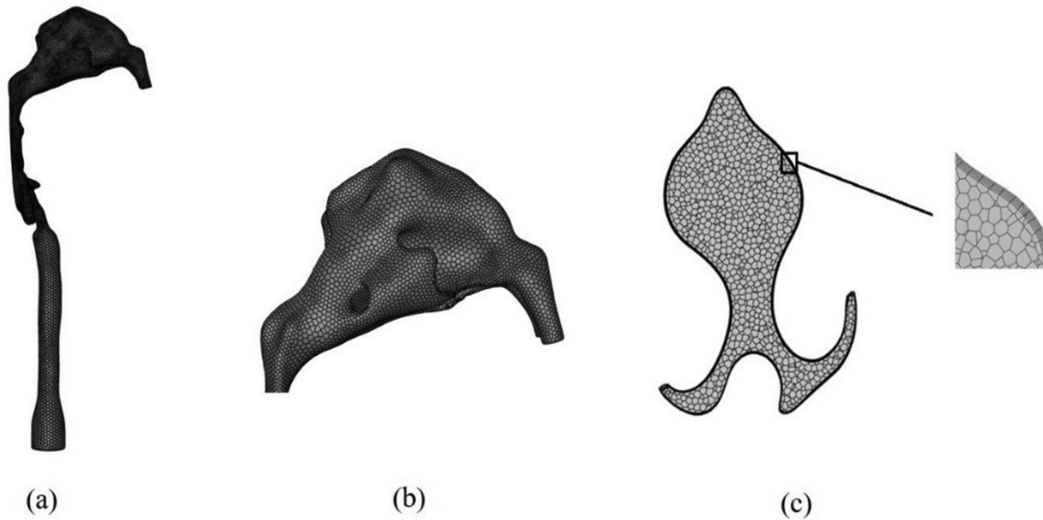


Fig. 2. Mesh models of the upper respiratory tract: (a) external surface of the upper respiratory tract polyhedral mesh model; (b) external surface of the nasal cavity polyhedral mesh model; (c) mesh model and boundary layer at a representative nasal cross-section.

in air humidity and particle movement were not considered. The governing equations of the fluid are as follows.

Mass conservation equation [39]:

$$\frac{\partial}{\partial t}(\rho) + \nabla \cdot (\rho \mathbf{v}) = S_m \quad (1)$$

where ρ denotes fluid density; $\mathbf{v}$ represents the velocity field of fluid; S_m is a user-defined mass source term. Under the physical conditions of this study, no external mass source is introduced, hence $S_m = 0$. To simulate turbulence at low Reynolds numbers in the nasal cavity, the k – ω SST turbulence model was used [28,30]. The equations for the turbulent model are as follows.

k equation:

$$\frac{\partial}{\partial t}(\rho k) + \frac{\partial}{\partial x_i}(\rho k u_i) = \frac{\partial}{\partial x_j} \left(\Gamma_k \frac{\partial k}{\partial x_j} \right) + G_k - Y_k + S_k \quad (2)$$

ω equation:

$$\frac{\partial}{\partial t}(\rho \omega) + \frac{\partial}{\partial x_j}(\rho \omega u_j) = \frac{\partial}{\partial x_j} \left(\Gamma_\omega \frac{\partial \omega}{\partial x_j} \right) + G_\omega - Y_\omega + D_\omega + S_\omega \quad (3)$$

where G_k , G_ω represent the turbulent kinetic energy and the specific dissipation rate generated by the mean velocity gradient, respectively; Γ_k , Γ_ω represent the effective diffusion coefficients; S_k , S_ω are the user-defined source terms. In this study, no additional source terms for turbulence are specified, hence $S_k = S_\omega = 0$; D_ω denotes the cross-diffusion coefficient.

Eq. (4) is the turbulent viscosity formula of the k – ω SST turbulence model.

$$\mu_t = \frac{\rho k}{\omega} \frac{1}{\max \left[\frac{1}{\alpha^*}, \frac{SF_2}{a_1 \omega} \right]} \quad (4)$$

where S denotes the amplitude of the strain rate; $a_1 = 0.31$; F_2 is defined by Eq. (5).

$$F_2 = \tanh \left(\max^2 \left[2 \frac{\sqrt{k}}{0.09 \omega y}, \frac{500 \mu}{\rho y^2 \omega} \right] \right) \quad (5)$$

Aerosol atomization was simulated using the Lagrangian method, which tracks the changes and deposition of droplets through a discrete phase model (DPM). During the calculation of

the continuous phase, the trajectories of particulate phases (such as bubbles, solid particles, or droplets) are individually computed at specified time intervals. The governing equations for this process are as follows.

The equilibrium equation of forces acting on particles:

$$m_p \frac{d\mathbf{u}_p}{dt} = m_p \frac{\mathbf{u} - \mathbf{u}_p}{\tau_r} + m_p \frac{\mathbf{g}(\rho_p - \rho)}{\rho_p} + \mathbf{F} \quad (6)$$

where m_p represents the mass of the particles; $\mathbf{u}$ represents the velocity of the continuous phase; $\mathbf{u}_p$ represents the velocity of the particles; ρ represents the density of the continuous phase; ρ_p represents the density of the particles; $\mathbf{F}$ represents the additional force. In our simulation experiments, the additional forces acting on aerosol particles include the Saffman lift force and the virtual mass force. The first term on the right side represents the particle drag force, while τ_r stands for the particle relaxation time. Particulate matter was introduced into the human respiratory tract along with the airflow. A velocity differential between the particles and the fluid is inevitable. When the fluid's velocity gradient is perpendicular to the direction of particle movement, the particles deviate from their initial trajectory, influencing their deposition within the tract. To address this phenomenon, we took the Saffman force into account. The Saffman lift force is expressed as [31,40]:

$$\mathbf{F}_{\text{saf}} = \frac{2Kv^{1/2}\rho d_{ij}}{\rho_p d_p (d_{lk} d_{kl})^{1/4}} (\mathbf{u} - \mathbf{u}_p) \quad (7)$$

where K represents the strain tensor, and its value is 2.594.

The virtual mass force was also included in this study. Although its magnitude is generally small in gas–solid flows, it was retained for reasons of theoretical completeness. The virtual mass force is expressed as [41]:

$$\mathbf{F}_{\text{vm}} = C_{\text{vm}} \frac{\rho}{\rho_p} \left(\mathbf{u}_p \nabla \mathbf{u} - \frac{d\mathbf{u}_p}{dt} \right) \quad (8)$$

where C_{vm} is the virtual mass coefficient with a value of 0.5.

The particle relaxation time τ_r scales its dynamic response and is expressed as:

$$\tau_r = \frac{\rho_p d_p^2}{18\mu} \frac{24}{C_d Re} \quad (9)$$

where μ represents the viscosity of the continuous phase; d_p represents the particle diameter; and Re is the relative Reynolds number, defined as [28,30]:

$$Re = \frac{\rho d_p |\mathbf{u}_p - \mathbf{u}|}{\mu} \quad (10)$$

By substituting the formulas for the particle Re and relaxation time into the drag force calculation formula, it can be derived that [38]:

$$\mathbf{F}_{\text{drag}} = \frac{\pi}{8} \rho C_d d_p^2 |\mathbf{u}_p - \mathbf{u}| (\mathbf{u} - \mathbf{u}_p) \quad (11)$$

From this equation, it can be seen that the drag force is affected by the drag coefficient under specific flow field and particle characteristics conditions. Assuming the particles are spherical, we adopt the spherical drag force model, and select the random trajectory model and the random eddy lifetime model. The spherical drag coefficient model is defined as follows [28,30]:

$$C_d = a_1 + \frac{a_2}{Re} + \frac{a_3}{Re^2} \quad (12)$$

where a_1 , a_2 and a_3 are constants divided according to the Re .

In this study, submicron/micron-sized particles are primarily influenced by the combined action of inertial force and gravity (with the latter governing settling behavior).

To quantify the deposition of particles in the respiratory tract, a wall deposition efficiency parameter was computationally incorporated and defined as:

$$R_{\text{accretion}} = \sum_{p=1}^{N_{\text{particles}}} \frac{m_{\text{part}}}{A_{\text{face}}} \quad (13)$$

where m_{part} represents the deposited particle mass per unit area and A_{face} denotes the surface area per unit region.

The deposition efficiency (DE) is used to quantify the deposition of particles in the airways [28], and it is defined as follows:

$$DE_i = \frac{m_{i,p}}{m_i} \quad (14)$$

where m_i represents the mass of particles entering region i and $m_{i,p}$ signifies the mass of particles depositing in region i .

The deposition enhancement factor (DEF), a dimensionless metric, is expressed as:

$$DEF_i = \frac{DE_i/A_i}{\sum_{i=1}^n DE_i / \sum_{i=1}^n A_i} \quad (15)$$

where DE_i represents the deposition efficiency of region i and A_i denotes the surface area of region i . This ratio can intuitively reflect the characteristics of deposition distribution. Regions with higher deposition concentrations have higher DEF values, which can effectively identify deposition “hotspots”. During post-processing, wall deposition efficiency's $R_{\text{accretion}}$ can be systematically converted into DEF values to facilitate enhanced spatial analysis of deposition characteristics.

2.3. Boundary conditions and calculation method

Gas enters through the bilateral nostril planes, with the inlet velocity defined as the ratio of breathing intensity to the inlet

cross-sectional area, and the inlet velocity remains constant during steady-state breathing. Particles are set as an escape boundary at the inlet and outlet boundaries. The wall condition is set to the trap mode, without considering particle rebound, suspension, or resuspension [30,42]. Particles are emitted at the inlet surface using a discrete particle model, with the surface injection mode adopted. Specifically, a single particle is injected at the center of each grid on the surface at each time step. Based on the physical principle that aerosol particles will quickly achieve momentum balance with the surrounding airflow after entering, the initial particle velocity is set to be equal to the gas inlet velocity. This simplification method is widely used in CFD studies in the field of respiration [42]. The outlet boundary condition is set as pressure outlet at 1 standard atmosphere, while the boundary condition of the nasal wall is set as the trapping boundary condition.

This study employs the SIMPLEC algorithm along with a second-order upwind discretization scheme, combined with a modified flux correction method, to improve the convergence and stability. The pressure and momentum equations are discretized using second-order upwind schemes. The temporal independence was validated by examining different time steps of 0.05, 0.01, 0.005, 0.001 and 0.0005 s. The results showed that the deposition efficiency at a time step of 0.005 s exhibited an error within 5% relative to the adjacent data points; therefore, a time step of 0.005 s was adopted in this study. All simulations employed a transient solver, with convergence criteria for the governing equations were set to 10^{-3} for all the cases.

2.4. Grid independence verification

In this section, grid independence verification was performed under inlet air velocity of $6 \text{ m} \cdot \text{s}^{-1}$, time step of 0.005 s, 200 time steps, thickness of a first layer grid boundary of 0.00005 m, growth rate of 1.05, and spanning 5 layers. To ensure the reliability of the numerical results, a grid independence study was carried out. A series of systematically refined grids, ranging from 0.1 to 2.0 million cells, were simulated. The 1.2-million-cell grid (1.2 M grid) was selected for the final analysis as it provided the optimal balance between computational cost and solution accuracy, as shown in Fig. 3. The grid convergence index (GCI) method [43] was used to quantitatively evaluated the numerical uncertainty. The GCI was calculated using three grid levels: 1.0 million, 1.2 million, and 1.4 million cells. The order of convergence was set as $p = 2.0$, which was consistent with the second-order discretization scheme used in this study. The safety factor was determined according to the data convergence quality. The GCI results in Table 1 show that the solutions at monitoring locations A, B, C, and D are all grid-independent, and all GCI values below the 5% engineering threshold.

3. Results and Discussion

3.1. Model validation

The experimental results of Kelly *et al.* [38] were used to validate the CFD model in this work. Considering their experiments, the statistical analysis of deposition efficiency was exclusively confined to the nasal cavity. Accordingly, the model validation has correspondingly focused on quantifying deposition outcomes in the identical anatomical regions. Six particle sizes ranging from 0.5 to $11 \mu\text{m}$ were used in the simulation with a uniform particle size distribution. The direction of gravity was vertically downward and the acceleration was $9.81 \text{ m} \cdot \text{s}^{-2}$. This calculation consisted of 200 steps, tracking a total of 140800 particles, with the flow field was simulation duration of 1 s.

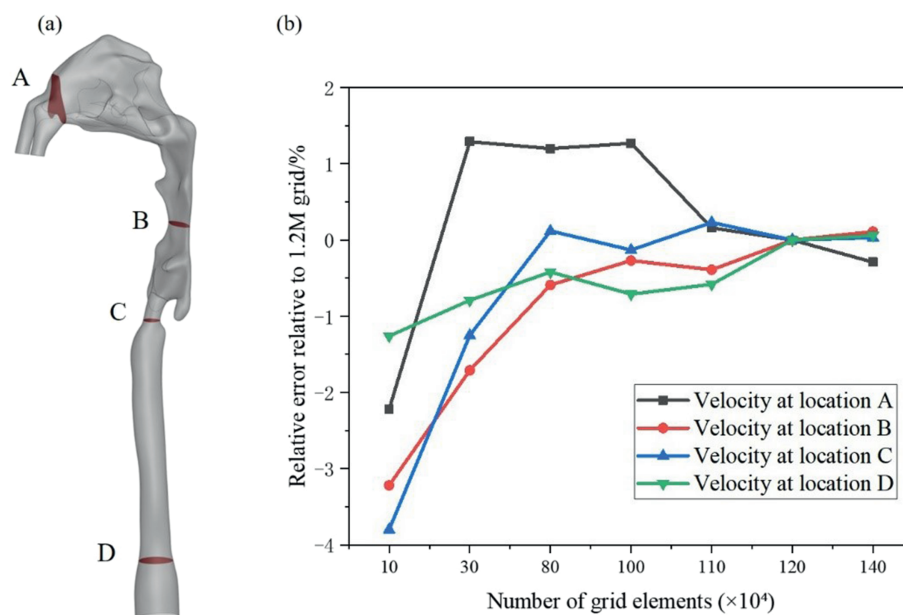


Fig. 3. Schematic diagram and grid independence verification: (a) four monitored locations (A, B, C, D); (b) verification results.

Table 1
Grid convergence index (GCI) results.

Location	Value-1.2 M grid/m·s ⁻¹	GCI/%	Remark
A	2.518	3.40	Converged
B	4.690	1.32	Converged
C	8.921	0.30	Converged
D	2.208	0.72	Converged

Fig. 4 compares the simulated deposition efficiencies with the experimental results from the literature [38] at two respiration intensities. The impaction parameter $d_a^2 Q$ is used to relate the deposition efficiency, where d_a is the aerodynamic particle diameter and Q is the inhalation airflow rate. It can be seen that the larger the particle size, the higher the deposition efficiency, and the deviation between experimental values and simulated results decreases. However, for smaller particles, the simulated values of deposition efficiency notably exceed the experimental results.

There are several possible reasons for this discrepancy. Firstly, the nasal models are different. The nasal model of Kelly *et al.* [38] was a 53-year-old Caucasian male, whereas the model in this study was a 30-year-old Chinese female, which may be the main factor contributing to the error, as demonstrated by Vachhani and Kleinstreuer [44] where geometric variations were identified as a key source of discrepancy between simulation and experimental deposition results. The airways of young East Asian females tend to be more compact and regular, which may amplify the deposition of small particles dominated by diffusion and settling, while exerting a smaller effect on large particles dominated by inertial impaction. Additionally, the isotropy of pulsatile velocity in the stochastic tracking model led to an overestimation of deposition efficiency, especially for small particles with the significant inertia effects. Finally, the particle size distribution of aerosols used in the experiment was not uniform, and physical phenomena such as collision and aggregation, vaporization might occur during their motion. It should be noted that the current model is more suitable for predicting the characteristics of particle deposition in young East Asian females. For applications to other populations, it is necessary to conduct calibration based on specific airway geometries or adjust key parameters.

Nevertheless, the similarity between the deposition efficiency curves in this study and the experimental results demonstrates the validity and reasonableness of the constructed CFD model, and therefore we use it in the subsequent simulation study.

3.2. Analysis of flow field characteristics and deposition hotspots

Fig. 5 shows the upper respiratory tract streamlines during inhalation and exhalation at the respiratory intensity of 20 L·min⁻¹.

During the inhalation phase (Fig. 5(a)), the overall flow field in the upper respiratory tract exhibits a J-shaped distribution. The streamlines are generally clear but accompanied by complex phenomena such as vortices, secondary flows, and contracted jets. Due to the structural dislocation between the lower part of the laryngeal cavity and the laryngeal tube, obvious boundary layer separation occurs when airflow passes through the laryngeal tube. Additionally, the streamlines in the low-velocity region of the trachea are more disordered, which is directly related to airflow disturbance caused by abrupt airway geometric changes.

During the exhalation phase (Fig. 5(b)), the streamline distribution in the trachea and nasal cavity is more uniform compared to the inhalation phase. When exhaling, airflow is discharged from the airway to the outside, and the interference from abrupt airway structural changes is significantly weakened. No obvious boundary layer separation is observed, and the overall flow field is more stable.

Fig. 6 shows the streamlines and deposition enhancement coefficients of each region in the respiratory tract. As shown in Fig. 6(i)(a) and (iii)(a), vortices exist in the nasal vestibular area during inhalation, and deposition hotspots are present at the corresponding positions in Fig. 6(ii) (a). It can be observed from Fig. 6(i)(d) and (iii)(d) that during exhalation, the gas does not strongly impact the nasal vestibule and hardly any vortices are generated, with all deposition enhancement coefficients in Fig. 6 (ii) (d) being lower than 0.035%.

This phenomenon indicates that the weak vortices formed by airflow reflux in the pharyngeal region during inhalation do not significantly promote deposition. Such vortices originate from

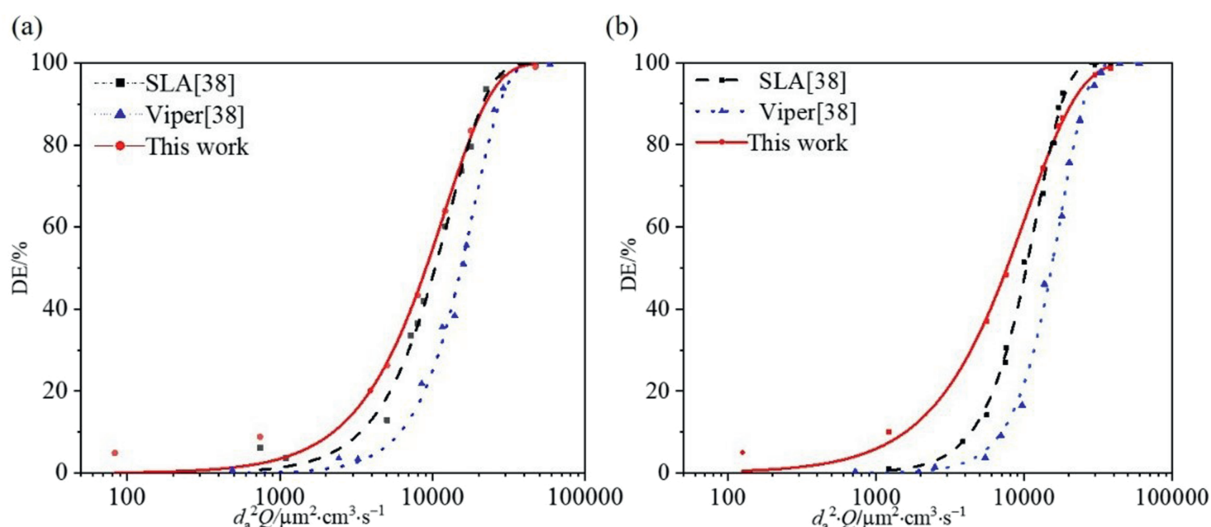


Fig. 4. Comparisons of simulated sedimentation rates with experimental results at different respiration intensities: (a) 20 L·min⁻¹; (b) 30 L·min⁻¹.

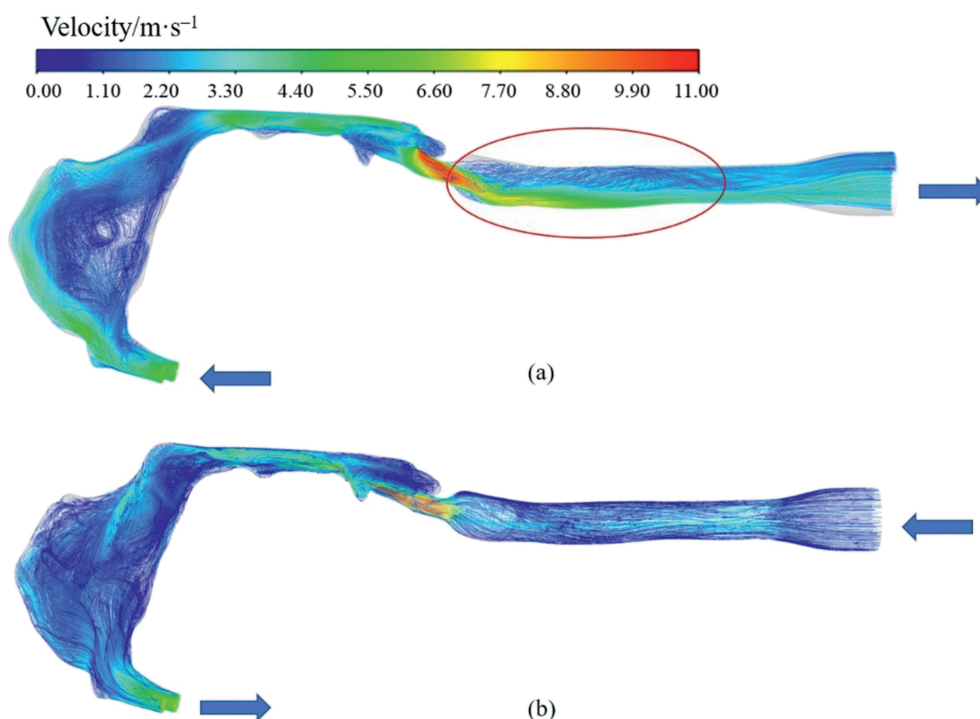


Fig. 5. Upper airway streamlines: (a) inhalation; (b) exhalation.

local airflow reflux, with low intensity and limited coverage, and are not accompanied by obvious airflow acceleration effects, thus making it difficult to effectively drive particles away from the streamlines and collide with the airway wall. This is in sharp contrast to the strong vortices formed by abrupt airway structural changes (*e.g.*, tube diameter contraction, direction turning) in regions such as the nasal vestibule and laryngeal constriction. The latter can significantly enhance local deposition efficiency by remarkably increasing airflow disturbance and the probability of particle inertial impaction, which is also consistent with the deposition hotspot characteristics observed earlier.

When the gas enters the larynx during inhaling, the airway shrinks sharply and the velocity increases rapidly, creating a jet

and forming vortices (Fig. 6(i)(c) and (iii)(c)). Due to the angle between the laryngeal airway and the trachea, this jet impacts the tracheal wall, forming a deposition hotspot (Fig. 6(ii)(c)). As the airflow moves from the trachea to the larynx during exhaling, a jet is also formed due to the narrow channel. The key difference is that the vortices formed during exhalation are located lower (as shown in Fig. 6(iii)(c) and (f)), and since the laryngeal airflow is steady, the streamlines are more uniform. Fig. 6(ii)(f) shows a laryngeal deposition hotspot during exhalation, confirming the deposition-enhancing effect of the laryngeal jet. This finding aligns with that of Huang *et al.* [45], who reported that geometric constrictions in the larynx generate vortices which concentrate aerosol deposition.

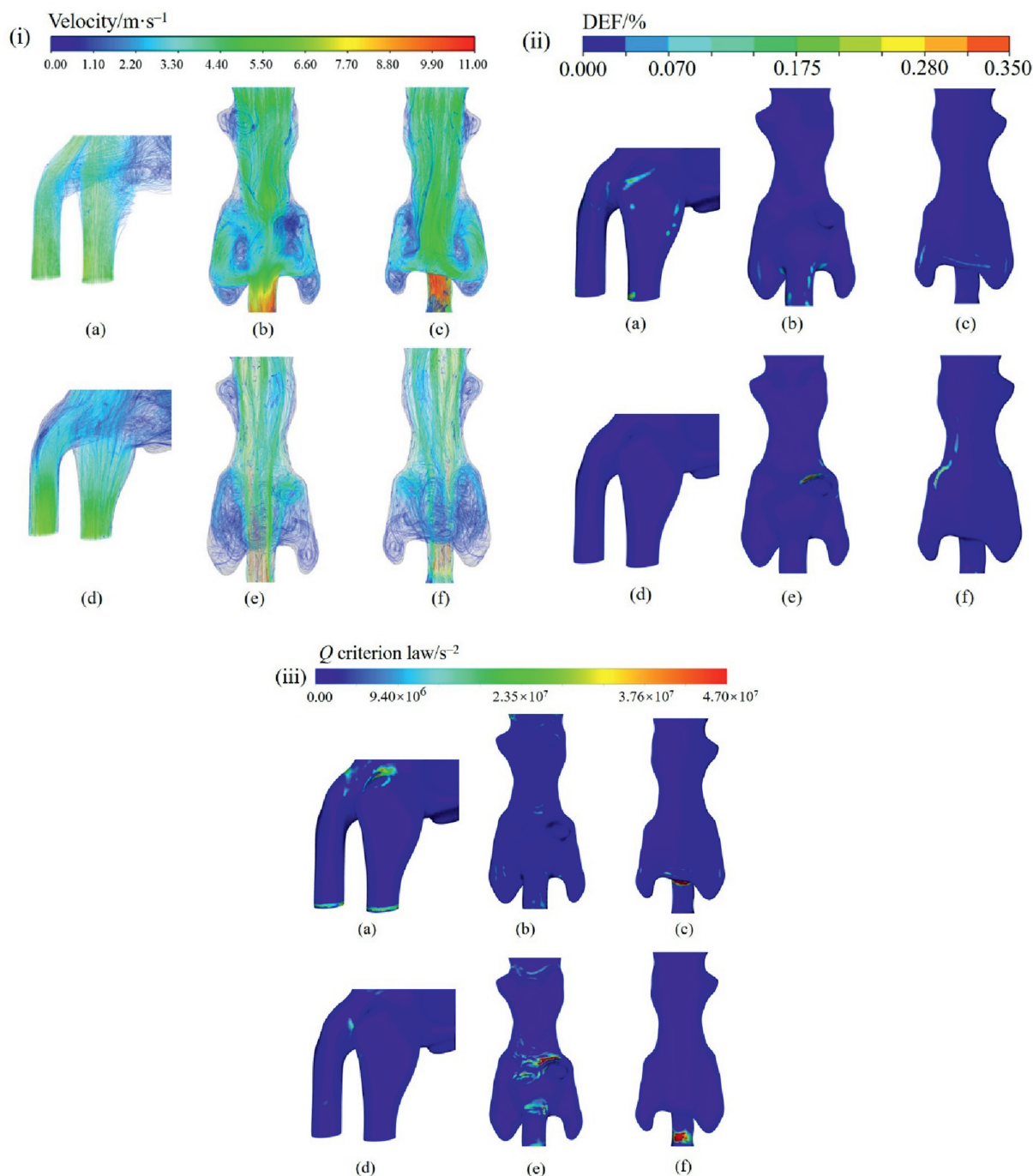


Fig. 6. Flow and deposition characteristics across the respiratory tract: (i) streamlines; (ii) deposition enhancement coefficient; (iii) Q -criterion. Subfigures correspond to: (a) inhalation in the vestibular area; (b) inhalation through the pharynx; (c) inhalation through the larynx; (d) exhalation in the vestibular area; (e) exhalation from the pharynx; (f) exhalation through the larynx.

3.3. Factors analysis of steady-state breathing

3.3.1. Simulation experiments under steady-state breathing

Under steady-state breathing conditions, several key parameters were selected for factor analysis, including respiratory strength, tidal volume, particle size, particle density, aerosol mass flow rate, and gravity direction. Each variable was assigned two values and a lot of 64 cases was simulated, and some of the results are shown in Table 2, and the full experimental data is presented in Table S1 (in Supplementary

Material). Continuous variables tended to adopt theoretical maximum and minimum values to maximize the effect of each parameter, thereby avoiding the risk that certain factors might be screened out due to inappropriate choice of values, as showed in Fig. 7.

Fig. 7 indicates that the effect of particle size is the most significant, while the effect of other factors is relatively minor. Since inhalation time is determined by the ratio of tidal volume to respiratory intensity, tidal volume determines the inhalation time in this simulation.

3.3.2. Response surface analysis based on respiratory intensity, particle density and particle size

Based on the results of factorial experiments, response surface analysis experiments including three factors, namely respiratory intensity, particle density and particle size, were designed. This study adopted Box–Behnken design (BBD) as the response surface analysis method, with five repetitions set at the center point in the experimental design to ensure the accuracy and statistical reliability of the established mathematical model. The ranges, variations, and design types of all factors in the steady-state breathing experiments are detailed in Table S2. The values of three factors and the deposition efficiency obtained by CFD simulation are shown in Table 3.

A regression curve equation with respiratory intensity as A , particle density as B , particle diameter as C , and particle deposition efficiency as Y is established as follows:

$$Y = -17.95951 + 1.71063A - 0.020208B - 5.25547C + 0.000729AB + 0.264933AC + 0.003958BC - 0.034983A^2 + 0.504798C^2 \quad (16)$$

The obtained regression model was subjected to analysis of variance (ANOVA) and the relevant parameters were tested, and the results are presented in Table 4. The p -value of this model is less than 0.0001, indicating that the obtained regression model is valid and authentic. The R^2 value of the model is 0.977, which suggests that the model is in good agreement with the CFD simulation results. The lack-of-fit term of the regression model is greater than 0.05, which indicates that the model can serve as an alternative to numerical simulation methods for exploring and predicting the deposition characteristics of particles in the upper respiratory tract.

It can be inferred from Table 4 that the particle diameter has a far impact than respiratory intensity, and the effect of respiratory intensity is significantly greater than that of particle density. Since tidal volume is proportional to respiratory intensity, the contribution of particle diameter to deposition is far greater than that of tidal volume. The three-dimensional plots from the simulation experiments illustrate the response surface analysis of the interaction among three factors in, as shown in Figs. 8–10. In these plots, when two influencing factors increase simultaneously,

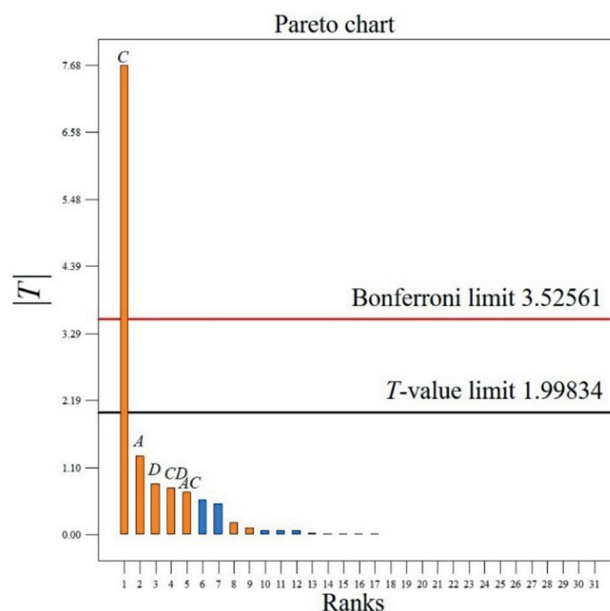


Fig. 7. Pareto diagram for calculating factorization under steady-state breathing.

additive effects occur, leading to a faster growth rate of deposition efficiency.

Fig. 8 illustrates the relationship among breathing intensity, particle density, and deposition efficiency under fixed particle size conditions. When the breathing intensities are 20, 30, and 40 $L \cdot min^{-1}$, the increases in deposition efficiency caused by increased particle density are 5.85%, 10.46%, and 14.87%, respectively. Conversely, when the particle densities are 900, 1200, and 1500 $kg \cdot m^{-3}$, the increases in deposition efficiency attributed to increased breathing intensity are 26.28%, 30.81%, and 35.30%, respectively. The changes in deposition efficiency associated with breathing intensity are greater than those related to particle density, indicating that breathing intensity has a more significant effect on deposition efficiency than particle density.

As breathing intensity increases, the airflow velocity increases accordingly, resulting in enhanced particle inertia. This results in more particles colliding with airway walls, thereby increasing deposition efficiency. In contrast, particle density has a limited

Table 2
Partial simulated results of factors analysis under steady-state breathing.

Serial number	A: respiratory intensity/ $L \cdot min^{-1}$	B: tidal volume/ ml	C: particle size/ μm	D: particle density/ $kg \cdot m^{-3}$	E: mass flow rate/ $kg \cdot s^{-1}$	F: gravity direction	Deposition efficiency/%
1	20	200	1	2000	2.0	Vertical	4.03203
2	50	800	9	2000	0.9	Horizontal	99.71380
3	20	800	1	2000	2.0	Horizontal	4.51527
4	20	800	1	900	2.0	Vertical	4.48132
5	50	200	9	2000	0.9	Vertical	98.94420
6	50	200	1	2000	0.9	Vertical	10.37370
7	50	800	9	900	0.9	Horizontal	95.49040
8	50	800	1	900	0.9	Horizontal	10.39260
9	50	200	1	900	0.9	Horizontal	9.03321
10	50	800	1	900	2.0	Horizontal	10.39260
11	20	200	1	900	2.0	Horizontal	4.00119
12	20	800	9	2000	0.9	Vertical	90.82410
13	20	800	9	2000	2.0	Vertical	90.82410
14	20	200	9	2000	2.0	Horizontal	89.08660
15	20	200	9	2000	0.9	Vertical	88.05870
–	–	–	–	–	–	–	–
62	20	200	9	900	2.0	Horizontal	59.45200
63	50	200	9	900	0.9	Vertical	92.00620
64	20	800	1	900	2.0	Horizontal	4.36670

Table 3

The simulated deposition efficiency based on response surface analysis under steady-state breathing.

Serial number	A: respiratory intensity/L·min ⁻¹	B: particle density/kg·m ⁻³	C: particle size/μm	Deposition efficiency/%
1	30	1500	1	11.625
2	40	900	4	50.417
3	20	900	4	13.708
4	20	1200	7	57.500
5	40	1200	7	94.167
6	30	1500	7	89.583
7	20	1200	1	6.458
8	40	1500	4	67.917
9	20	1500	4	22.458
10	30	1200	4	39.000
11	30	900	1	10.875
12	40	1200	1	11.333
13	30	900	7	74.583
14	30	1200	4	37.000
15	30	1200	4	41.000
16	30	1200	4	46.000
17	30	1200	4	44.000

Table 4

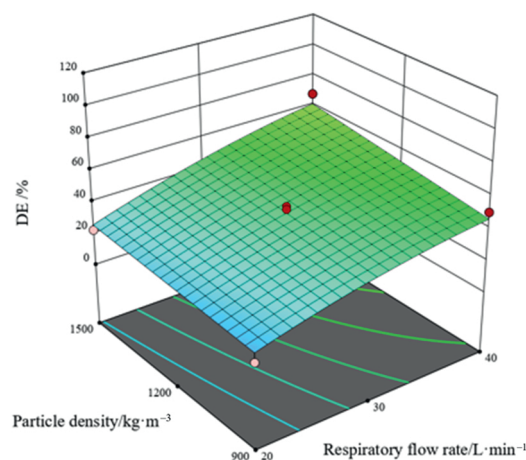
Significance and ANOVA of the coefficients of the regression equation.

Type	Variance	Degrees of freedom	Mean square	F-value	p-value
Model	12059.17	7	1722.74	51.26	<0.0001
A-respiration intensity	1913.02	1	1913.02	56.92	<0.0001
B-particle density	220.50	1	220.50	6.56	0.0306
C-particle size	9490.42	1	9490.42	282.39	<0.0001
AC	252.68	1	252.68	7.52	0.0228
AB	19.14	1	19.14	0.54	0.4832
BC	50.77	1	50.77	1.51	0.2502
A ²	51.67	1	51.67	1.54	0.2463
C ²	87.15	1	87.15	2.59	0.1418
Error	302.47	9	33.61	—	—
Bias	249.27	5	49.85	3.75	0.1123
Pure error	53.20	4	13.30	—	—
Total	12361.64	16	—	—	—

impact on gravitational and inertial forces, so its increase exerts only a weak effect on deposition efficiency. The gradual increase in deposition efficiency reflects the additive effect between breathing intensity and particle density.

Under higher breathing intensity conditions, the effect of increased particle density on deposition efficiency becomes more pronounced. On the one hand, higher particle density increases gravitational settling velocity, making particles more likely to deviate from airflow lines under airflow interference and thereby promoting deposition. On the other hand, airflow perturbations caused by increased breathing intensity enhance fluid turbulence, which further affects particle distribution and deposition and in turn highlights the differences in deposition efficiency induced by density variations. Theoretically, under lower breathing intensity conditions, although increased particle density can enhance particle inertia and promote deposition, the smooth airflow weakens this effect. As a result, under lower breathing intensity conditions, the increase in particle density has no significant impact on improving deposition efficiency.

Fig. 9 presents the relationship among particle density, particle diameter, and deposition efficiency under fixed breathing intensity conditions. When particle diameters are 1, 4, and 7 μm, the increases in deposition efficiency caused by increased particle density are 3.38%, 10.55%, and 17.63%, respectively. Conversely, when the particle densities are 900, 1200, and 1500 kg·m⁻³, the increases in deposition efficiency attributed to increased particle diameter are 61.76%, 68.48%, and 76.01%, respectively. It can be inferred that the effect of particle diameter on deposition

**Fig. 8.** Relationships among respiration intensity, particle density and deposition efficiency for a particle size of 4 μm.

efficiency is greater than that of particle density, and both factors exhibit an additive effect on deposition efficiency.

Particles with higher density are more prone to deviate from streamlines due to inertia effects, leading to a higher probability of contacting the wall at airway bends or bifurcations and thereby promoting deposition. Under higher density conditions, larger particles with greater mass and kinetic energy have more difficult moving with the airflow. Thus, the effect of particle diameter on

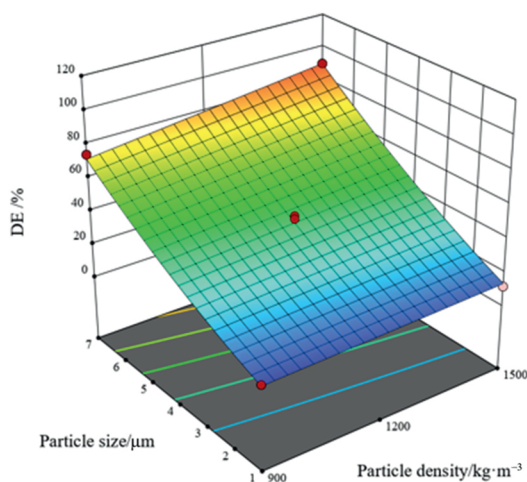


Fig. 9. Relationships among particle density, particle size and deposition efficiency at respiration intensity of $30 \text{ L} \cdot \text{min}^{-1}$.

deposition efficiency may be amplified, which in turn increases the deposition probability. Conversely, under lower density conditions, the effect of smaller particles with lower mass may be weakened, and their sensitivity to airflow changes is also reduced.

Fig. 10 illustrates the relationship among breathing intensity, particle diameter, and deposition efficiency under fixed particle density conditions. When the particle diameters are 1, 4, and $7 \mu\text{m}$, the increases in deposition efficiency attributed to breathing intensity are 15.03%, 31.24%, and 46.2%, respectively. Conversely, when breathing intensities are 20, 30, and $40 \text{ L} \cdot \text{min}^{-1}$, the increases in deposition efficiency caused by increased particle diameter are 52.99%, 68.74%, and 84.16%, respectively. The above changes in deposition efficiency indicate that particle diameter has a more significant effect on deposition efficiency than breathing intensity. The gradual increase in deposition efficiency reflects the additive effect between particle diameter and breathing intensity.

Under higher breathing intensities, the increased respiratory frequency elevates the flow velocity, resulting in higher collision frequency between particles (especially larger ones) and airway walls. This enhances the inertial impaction effect, thereby significantly increasing the deposition efficiency of larger diameter particles. In contrast, under lower breathing intensities, lower

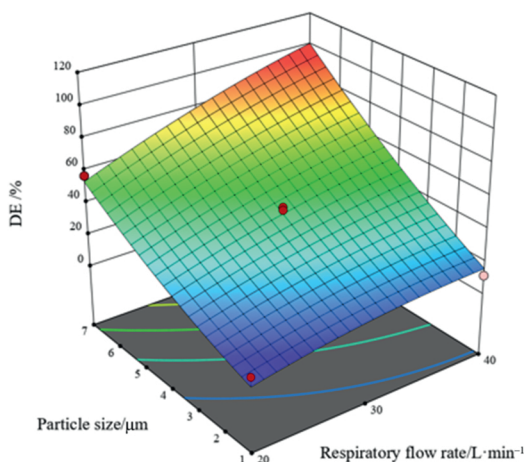


Fig. 10. Relationships among respiration intensity, particle size and deposition efficiency for particle density of $1200 \text{ kg} \cdot \text{m}^{-3}$.

airflow velocity weakens the inertial effects, resulting in less pronounced increases in deposition efficiency even for larger diameter particles. This is because the relatively stable airflow in the airway causes particle deposition to be primarily influenced by Brownian diffusion and gravity, thus diminishing the impact of particles diameter. This aligns with Vachhani and Kleinstreuer [44], who confirmed particle size as the primary factor and inhalation flow rate as the secondary factor affecting deposition, and demonstrated their synergistic effect through the impaction parameter $d_a^2 Q$.

3.4. Factor analysis of circulatory respiration

3.4.1. Simulation experiments under circulatory respiration

The actual human respiratory process occurs as cyclic breathing, and thus special attention should be given to the effect of cyclic breathing conditions on particle deposition. In this section, the main factors selected for the factorial experiments include respiratory frequency, breath-holding time, breathing ratio, aerosol mass flow rate, and gravity direction. These experiments aim to examine whether a superimposed effect exists among factors with relatively minor influences. The simulation results are presented in Table 5 and the full experimental data is presented in Table S3.

3.4.2. Response surface analysis based on respiration ratio, respiratory frequency and breath-holding time

Fig. 11 shows the Pareto chart of factorial analysis under cyclic breathing conditions. As seen from this figure, the most influential factors are respiratory frequency, respiration ratio, and breath-holding time. Therefore, these three factors are selected for the subsequent analysis.

The real breathing curve is a physiologically driven asymmetric and non-smooth periodic motion, while the sine wave is a symmetric and smooth ideal mathematical simplified model. The real breathing curve has a higher inspiratory flow velocity peak and a longer inspiratory time, while the symmetric flow velocity of sine wave averages out the deposition contributions of inspiration and expiration, which might lead to the underestimation of deposition rate of large particles and the overestimation of that of small particles. On the premise of retaining key parameters such as periodicity and flow velocity range, the sine wave can greatly simplify calculations, improve efficiency, and meet the accuracy requirements of engineering design [46]. For example, studies by Naftali *et al.* [47] and Naseri *et al.* [48] adopted sine waves to replace breathing curves. In this study, a sine wave replaced the respiratory curve, with tidal volume constant of 400 ml , particle size of $4 \mu\text{m}$, and the particle density of $900 \text{ kg} \cdot \text{m}^{-3}$. The ranges, variations, and design types of all factors in the cyclic breathing experiments are detailed in Table S4. The simulated parameters and results for response surface analysis are presented in Table 6. The inlet velocity varies with time, following a sinusoidal velocity–time relationship. The particle incident velocity is identical to the inlet velocity of air, and all the inhaled gas is expelled. All experiments include three stages: inhalation, breath-holding, and exhalation. The core parameter calculation and waveform construction follow the general rules below:

Key parameter calculation formulas (based on respiratory frequency f , I:E ratio, and breath-hold time T_{hold}):

Total breathing cycle duration: $T_{\text{total}} = 60/f$

Effective inspiration–expiration duration: $T_{\text{breath}} = T_{\text{total}} - T_{\text{hold}}$

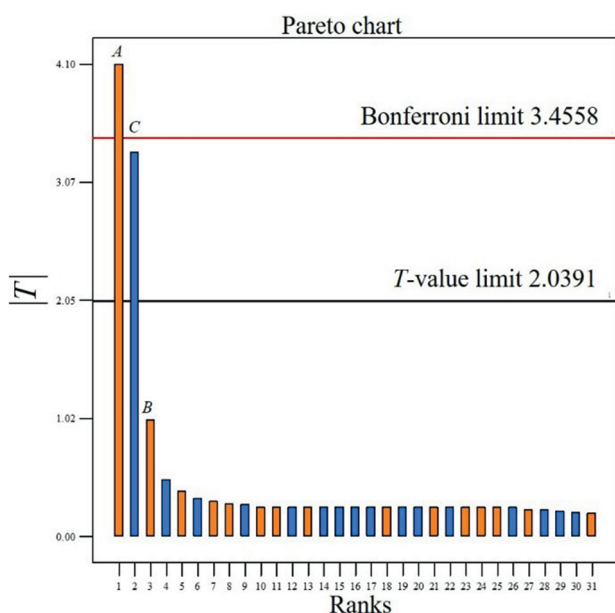
Inspiration duration: $T_{\text{insp}} = T_{\text{breath}} / (1 + n)$ (where I : E = 1 : n)

Expiration duration: $T_{\text{exp}} = T_{\text{breath}} - T_{\text{insp}} = n \times T_{\text{insp}}$

Table 5

The simulated results of factor analysis under circulating respiratory.

Type	A: respiratory frequency/times·min ⁻¹	B: breath-holding time/s	C: respiration ratio	D: mass flow rate/kg·s ⁻¹	E: gravity direction	Deposition efficiency/%
1	20	1.5	0.5	0.9	Horizontal	38.690390
2	20	1.5	1.0	0.9	Horizontal	21.206170
3	20	1.5	1.0	2.0	Vertical	20.815180
4	20	0	1.0	0.9	Vertical	19.416370
5	12	0	1.0	2.0	Vertical	9.845409
6	12	0	0.5	2.0	Vertical	17.676300
7	12	0	1.0	0.9	Horizontal	9.800996
8	20	1.5	0.5	2.0	Horizontal	28.807120
9	12	0	1.0	2.0	Horizontal	9.800996
10	20	0	0.5	0.9	Vertical	26.506760
11	20	0	1.0	2.0	Horizontal	18.808070
12	12	1.5	1.0	0.9	Vertical	10.739360
13	12	1.5	0.5	2.0	Vertical	18.936940
14	12	1.5	1.0	0.9	Horizontal	12.223770
15	20	1.5	1.0	0.9	Vertical	20.815180
16	20	0	1.0	2.0	Vertical	19.416370
17	20	1.5	0.5	2.0	Vertical	27.971530
18	12	0	0.5	0.9	Vertical	17.676300
–	–	–	–	–	–	–
30	20	0	0.5	2.0	Horizontal	26.270460
31	20	0	0.5	2.0	Vertical	26.506760
32	20	1.5	1.0	2.0	Horizontal	21.206170

**Fig. 11.** Pareto diagram for calculating factorization under circulating breathing.

Velocity waveform construction: the velocity during inspiration follows a sinusoidal half-wave starting from 0 (amplitude determined by the fixed tidal volume of 400 ml and T_{insp}); the velocity remains 0 during the breath-hold phase (if $T_{\text{hold}} > 0$); the expiration phase is a reverse sinusoidal half-wave to ensure the exhaled gas volume equals the inhaled volume. Particle are delivered only during inhalation, with none during breath-holding and exhalation phases. For example, the gas inlet velocity in experiment No. 1 is expressed as:

$$\begin{cases} 0 - 1.5 \text{ s} \rightarrow v = 7.2055 \sin(2.0944t) \\ 1.5 - 2.5 \text{ s} \rightarrow v = 0 \\ 2.5 - 4.75 \text{ s} \rightarrow v = 0.9504 \sin(1.3963t - 3.4908) \end{cases} \quad (17)$$

With respiration ratio as A, frequency as B, breath-holding time as C, and particle deposition efficiency as Y, a regression curve equation is established as follows:

$$\begin{aligned} Y = & 22.30390 - 74.32290A + 2.15679B + 1.16159C \\ & - 2.10995AB + 0.085189AC - 0.045500BC + 54.16464A^2 \\ & + 0.040275B^2 + 0.391400C^2 \end{aligned} \quad (18)$$

The test results of the regressed model are presented in Table 7. The model has a p -value less than 0.0001, the R^2 value of 0.991, and a lack-of-fit term greater than 0.05. The results indicate that this regression model can serve as an alternative to CFD simulations for exploring and predicting the particles deposition in the upper respiratory tract. According to the F -values of the three influencing factors, the effect of respiration ratio on the deposition efficiency is similar to that of respiratory frequency, with both being significantly greater than the effect of breath-holding time. Furthermore, by comparing the deposition efficiency of the inhalation and breath-hold phases with that of the entire process, it was found that the contribution of the exhalation phase to the deposition efficiency is only 0.94%. Although this might be related to the assumption that exhaled particles no longer participate in subsequent inhalation, it does not alter the fact that the exhalation phase has a negligible impact on the deposition efficiency. The three-dimensional response surface analysis diagrams of the interactions among three factors considered in the simulation experiments are shown in Figs. 12–14.

Fig. 12 illustrates the relationship among breathing ratio, breath-holding time, and deposition efficiency under fixed breathing frequency conditions. When the breathing ratios are 0.5, 0.75, and 1, the increases in deposition efficiency caused by extended breath-holding time are 2.17%, 2.46%, and 2.56%, respectively. Conversely, when the breath-holding times are 0, 1, and 2 s, the increases in deposition efficiency attributed to decreased breathing ratio are 13.37%, 13.26%, and 12.98%, respectively.

When breath-holding time remains constant and the breathing ratio decreases, the inhalation time decreases, the gas flow rate increases, turbulence intensity increases, and the deposition efficiency increases accordingly. Extending breath-holding time has almost no effect on the deposition efficiency of particles in the nasal cavity, and this is primarily because inertial impact serves as the main mechanism for particle deposition in the nasal cavity—such a mechanism means that particle deposition here is

Table 6

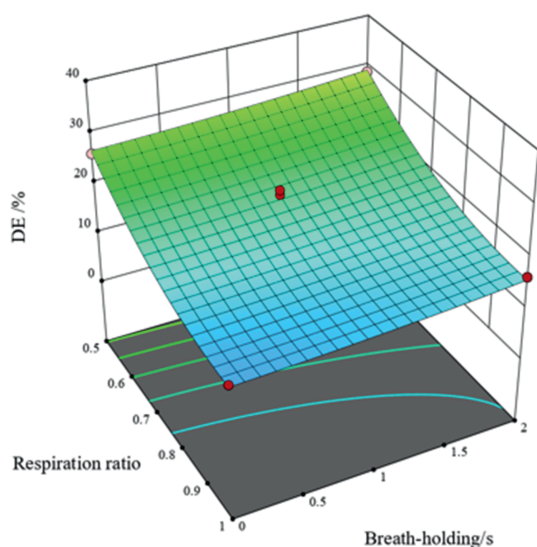
The simulated deposition efficiency based on response surface analysis under circulating breathing.

Type	A: respiration ratio	B: respiratory frequency/times·min ⁻¹	C: breath-holding time/s	Deposition efficiency/%
1	1:1.5	16	1	20.056
2	1:2	12	1	18.250
3	1:1.5	12	0	12.417
4	1:1.5	20	2	29.313
5	1:2	16	2	28.800
6	1:1.5	12	2	15.166
7	1:1.5	16	1	19.000
8	1:1	16	0	13.600
9	1:1	16	2	16.311
10	1:1.5	16	1	21.000
11	1:1.5	20	0	27.292
12	1:2	16	0	26.067
13	1:2	20	1	38.917
14	1:1.5	16	1	20.000
15	1:1	12	1	8.673
16	1:1.5	16	1	20.000
17	1:1	20	1	19.950

Table 7

Significance and ANOVA of the coefficients of the regression equation under circulating breathing.

Type	Variance	Degrees of freedom	Mean square	F-value	p-value
Model	859.9200	9	95.5500	83.7300	<0.0001
A- respiration ratio	357.7800	1	357.7800	313.5300	<0.0001
B- respiratory frequency	401.8900	1	401.8900	352.1800	<0.0001
C- breath-holding time	12.4600	1	12.4600	10.9200	0.0130
AB	18.7900	1	18.7900	16.4700	0.0048
AC	0.0019	1	0.0019	0.0017	0.9685
BC	0.1325	1	0.1325	0.1161	0.7433
A ²	36.1100	1	36.1100	31.6400	0.0008
B ²	1.7500	1	1.7500	1.5300	0.2557
C ²	0.6450	1	0.6450	0.5652	0.4767
Error	7.9900	7	1.1400	—	—
Bias	5.9900	3	2.0000	3.9900	0.1075
Pure error	2.0000	4	0.5006	—	—
Total	867.9100	16	—	—	—

**Fig. 12.** Relationships among respiration ratio, breath-holding time and particle deposition efficiency at respiratory frequency of 16 times per min.

less dependent on the duration of breath holding. However, extending breath-holding time slightly increases the retention time of particles in the main trachea; and since gravity settling is the primary mechanism for particle deposition in the main trachea, the prolonged particle retention time allows gravity settling

to act more fully, which in turn slightly improves the deposition efficiency of particles in this region.

Fig. 13 illustrates the relationship among breathing frequency, breath-holding time, and deposition efficiency under fixed breathing ratio conditions. When the breathing frequencies are 12, 16, and 20 breaths per minute, the increases in deposition efficiency due to extended breath-holding time are 2.92%, 2.78%, and 2.02%, respectively. Conversely, when the breath-holding times are 0, 1, and 2 s, the increases in deposition efficiency attributable to increased breathing frequency are 14.78%, 14.46%, and 13.88%, respectively. The results indicate that the influence of breathing frequency on deposition efficiency is greater than that of breath-holding time. Like respiratory ratio, respiratory frequency is a significant factor affecting deposition efficiency. The improvement of deposition efficiency by increasing respiratory frequency is achieved in the same manner as reducing the respiratory ratio by shortening inhalation time and increasing airflow velocity.

Fig. 14 presents the relationship among breathing ratio, breathing frequency, and deposition efficiency under fixed breath-holding time conditions. It can be seen that both breathing ratio and breathing frequency are significant influencing factors. When the tidal volume is fixed, increasing breathing frequency or decreasing breathing ratio shortens inhalation time, leading to higher airflow velocity, which are more conducive to deposition process. When the breathing ratios are 0.5, 0.75, and 1, the increases in deposition efficiency caused by elevated breathing frequency are 18.51%, 14.39%, and 10.33%, respectively. Conversely, when the breathing frequencies are 12, 16, and 20 breaths per minute, the increases in deposition efficiency

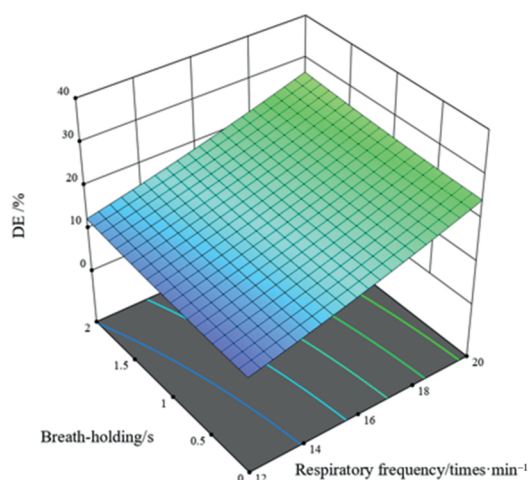


Fig. 13. Relationships among respiratory frequency, breath-holding time and particle deposition efficiency at respiration ratio of 1:1.5.

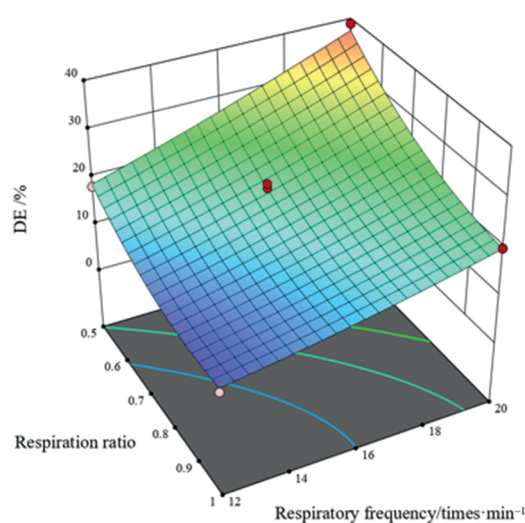


Fig. 14. Relationships among respiration ratio, respiratory frequency and particle deposition efficiency at breath-holding time of 1 s.

attributed to breathing ratio are 9.21%, 12.95%, and 17.39%, respectively. The results indicate that the changes in deposition efficiency induced by increased breathing frequency are slightly greater than those caused by the decrease in breathing ratio. This may be attributed to the fact that increasing breathing frequency not only enhances fluid turbulence but also results in rapid changes in airflow direction, thereby more effectively improving the deposition efficiency. Simultaneously reducing the respiratory ratio and increasing the respiratory frequency will significantly enhance particle deposition efficiency.

The results of this study indicate that during cyclic breathing, respiratory frequency and the inspiration–expiration (I:E) ratio exert similar effects on deposition efficiency, and both primarily function by jointly regulating inspiratory time. This aligns with the research conclusion of Kuga *et al.* [49], who proposed that the breathing cycle duration is a key influencing factor. Our work further quantifies the strong synergistic effect between these two parameters. In contrast to studies of alveolar deposition [50,51], breath-holding time has a limited effect on deposition in the upper airways, because deposition here is mainly dominated by inertial impaction, rather than the mechanisms (gravitational settling,

diffusion) that benefit from prolonged breath-holding in the distal regions of the respiratory tract.

4. Conclusions

In this study, a three-dimensional CFD model of particle deposition in the nasal cavity was constructed using CT scanning, and verified by comparison with physical experiment data. Subsequently, RSM was adopted to explore the interaction among various influencing factors during steady-state and cyclic breathing. The main research results are as follows.

- (1) Compared with the experimental data in the literature, the numerical model of nasal deposition tends to overestimate the deposition efficiency of smaller particles under higher respiratory strength. This is mainly due to the differences between the two nasal cavity models. Additionally, the isotropy of the pulsating velocity in the random tracking model also contributes to these errors. During the inhalation stage, due to changes in airway structure, vortexes form in the nasal vestibule and piriform fossa, which become deposition hotspots. Significant enhancement of respiratory tract particle deposition is induced by strong vortexes from abrupt airway structural variations during both inhalation and exhalation, with higher-positioned laryngeal vortexes formed during inhalation and lower-positioned ones during exhalation, whereas weak vortexes induced by pharyngeal airflow reflux during inhalation exert negligible effects on promoting particle deposition.
- (2) Under steady-state breathing conditions, particle size is the most critical factor affecting deposition efficiency, followed by respiration intensity, while particle density has the least influence. Simultaneously, increasing any two of three factors produces a synergistic effect, further improving deposition efficiency. Among these, increasing the particle size and the strength of the respiratory has the most significant effect on improving deposition efficiency.
- (3) During cyclic breathing, this study focused on the effects of respiration conditions on deposition efficiency. Whether adjusting the respiratory ratio and respiratory frequency, it essentially changes the inspiratory time, thus exhibiting a similar pattern of effect on deposition efficiency. The results indicate that increasing the respiratory frequency while reducing the respiratory ratio has the most significant effect on enhancing the deposition efficiency during cyclic breathing, but breath-holding time has a relatively small effect.

The results of this study have laid a solid theoretical foundation for the following aspects: in terms of drug delivery, particle size and breathing parameters can be accurately matched according to the target site; in terms of respiratory protection, local protection can be strengthened for deposition hotspots such as the nasal vestibule and piriform fossae. Although this study clarifies the key laws governing the deposition of respiratory particles under different breathing patterns, it still has limitations such as limited model representativeness. In the next step, we will carry out follow-up research in aspects including expanding population representativeness and improving physical field coupling.

CRedit Authorship Contribution Statement

Haiyun Jing: Writing – original draft, Visualization, Validation, Data curation. Zhuangzhuang Yu: Software, Formal analysis,

Conceptualization. Shiyu Hu: Writing – review & editing, Supervision. Jingen Xia: Resources, Project administration. Yang Xiang: Writing – review & editing, Validation, Supervision, Resources.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Supplementary Material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cjche.2026.01.023>.

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