Trajectories and Deposition Sites of Spherical Particles Moving Inside Rhythmically Expanding Alveoli under Gravity-Free Conditions

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Abstract

Background: Do fine particles (0.5–2 μm in diameter) deposit inside lung alveoli? This question is of particular interest in space flights where almost gravity-free conditions exist. Under such conditions, inhaled particles smaller than 0.5 μm in diameter or larger than 2 μm may deposit inside the alveoli due to Brownian motion or particle inertia, respectively. However, fine particles hardly affected by Brownian motion and of small mass can (wrongly) be perceived harmless, following closely fluid pathlines.

Methods: The interplay between alveoli rhythmical expansion and the largely, previously disregarded geometrical interception mechanism was explored vis-à-vis predictions based on nonexpanding alveoli models. To this end, we employed a three-dimensional flow model that accounts for the rhythmical expansion of alveoli, and the trajectories of fine particles embedded in this flow were numerically calculated.

Results: Stochastic trajectories and deposition sites that are substantially different than those obtained for reversible Poiseuille-like flow models were widely used in the past. Indeed, small, inertialess, non-Brownian particles can hardly enter rigid alveoli in microgravity circumstances because the flow field consists of isolated closed streamlines that separate the cavities from the airways. However, for expanding alveoli, the streamline map is significantly altered, allowing diversion of particles from the airways toward the alveoli walls. As a result, collision with the alveoli wall due to geometrical interception may occur, revealing an additional mechanism that may control particle deposition inside alveoli.

Conclusions: Fine particles 0.5–2 μm in diameter under zero gravity conditions may enter expanding alveoli and deposit due to the stochastic nature of the flow and the mechanism of geometrical interception. Their fate is very sensitive to their initial position. The majority of the particles tend to deposit inside alveoli located up the acinar tree, at the distal area of the alveoli and near its rim.

Key words: particle distribution, lung alveoli, zero gravity

Introduction

BREATHING IN A POLLUTED ENVIRONMENT under microgravity circumstances has gained significance with the onset of space programs in which astronauts were haphazardly exposed to aerosolized particles floating in the space cabin. Beeckmans⁽¹⁾ studied the effect of reduced gravity that exists on the Moon on particle deposition inside the lung. He concluded that more particles 7 μm in diameter and smaller tend to settle inside the alveoli on Earth than on the Moon and vice versa for particles larger than 7 μm . Darquenne et al.^(2–6)

examined the effect of high gravity and microgravity upon particles 0.5–3 μm in diameter. Darquenne et al.⁽²⁾ demonstrated (see Fig. 1) that the number of deposited particles increases with concomitant increase in gravity and particles size.

However, in a microgravity case deposition is only slightly affected by particle diameter. Darquenne et al.⁽³⁾ indicated that deep penetration of a bolus of particles results in higher deposition and dispersion. Similarly, Darquenne et al.⁽⁴⁾ illustrated that particle deposition is higher with increased penetration and is only slightly dependent upon particle

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FIG. 1. Efficiency of spherical particles deposition inside the lung alveoli subjected to various gravity accelerations (from Darquenne et al.⁽²⁾).

diameter. In all these articles the singular effect of particle deposition in the *acinar* region was not attempted, and the results pertain to the combined effect of particle deposition in the lung upper airways and the acinus. At best, the increased dispersion and deposition with penetration depths hints that the acinar region may have a profound effect on particle deposition. However, there are no conclusive or rigorous results demonstrating how deposition depends upon acinar airway generation or particle size. Generally, particle inertia is considered as the main mechanism that may cause particles of diameter larger than $3\mu\text{m}$ to cross streamlines and impact the alveolar walls in microgravity circumstance,

while finer particles of diameter lower than $0.5\mu\text{m}$ are mainly affected by Brownian motion. Such particles will be affected by the combination of diffusion and chaos, termed the "carousel effect," recently investigated by Laine-Pearson et al.⁽⁷⁾ Particles of about $1\mu\text{m}$ in diameter would follow fluid streamlines closely in the absence of gravity.

Previous flow models, that assumed rigid configuration of the acinus, predicted that isolated closed streamlines exist inside the lung alveoli, separating the cavities from the adjacent airways (e.g., Fig. 2 from Pozrikidis⁽⁸⁾).

More recently, the effect of alveolar rhythmical expansion was incorporated into the alveoli flow model⁽⁹⁻¹⁴⁾ that exhibit streamlines entering the alveolus (e.g., Fig. 3 from Haber et al.⁽⁹⁾ In Haber et al.,⁽¹⁵⁾ henceforth referred to as HYT, we have demonstrated the important effect of alveolar expansion on trajectories of particles moving under gravity.

Indeed, in many cases, a flow model of rigid alveoli predicts that particles would skip the alveolus and move along the airway during inhalation,⁽¹⁵⁾ whereas in an expanding/contracting alveoli model the particle would enter the alveolus, obviously, due to flow generated by the expanding alveolus and exhibit chaotic pathlines.

A broader discussion on aerodynamic models used in the past to describe the flow field inside lung alveoli and a comprehensive discussion on the forces exerted on a particle is presented in HYT and is not repeated.

The main goal of this article is to explore the effect of alveoli expansion on particle's fate and to elucidate that a new mechanism of "geometrical interception" is the sole mechanism responsible for deposition of inertialess non-Brownian particles inside alveoli. By "geometrical interception" we mean that a particle is trapped and physically deposited if the distance between its center and the wall is equal to the particle radius while moving inside the alveolus.

In the Methods section we provide a brief depiction of the aerodynamic model used in this article to describe the flow field inside a rhythmical expanding alveolus and the equations that govern the motion of a particle in a gravity-free

FIG. 2. Streamline map of shear flow over a hemispherical cavity (from Pozrikidis⁽⁸⁾).

FIG. 3. Streamline map for $\gamma=200$ of the combined flow generated by expanding alveoli and ductal shear flow over a hemispherical cavity (from Haber et al.⁽⁹⁾).

environment. Then particle fate is addressed and the results are discussed, underlying the difference between the current flow model and rigid wall alveoli models. Last, we present the main conclusions.

Methods

The aerodynamic model employed in this article to describe the creeping flow field inside rhythmical expanding alveoli was suggested by Haber et al.,⁽⁹⁾ and its main characteristics are recapitulated in HYT. The geometrical model of an alveolus and its neighboring duct is shown in Figure 4.

It consists of a hemisphere attached at its rim to a plane wherein both undergo cyclic expansion and contraction

motions. The radius of the alveolus depends on time, and is approximately given by the following expression,

$$R = R_0(1 + \beta \cos(\omega t)) \quad (1)$$

characterized by a single dimensionless parameter β , that is determined by the breathing flow rate.

We shall, henceforth, assume common values⁽¹⁶⁾ for the mean alveolus radius, $R_0 = 100 \mu\text{m}$, the dimensionless amplitude, $\beta = 0.1$ and the breathing frequency, $\omega = 2\pi/5 \text{ (sec}^{-1}\text{)}$ to reduce the number of parameters examined. [The maximum increase of lung volume from its mean value during breathing is given by $(1 + \beta)^3$]. We also assume that the far upstream or downstream flow inside the duct adjacent to the alveolus is given by a cyclic shear flow (Fig. 4).

$$v_y^\infty = -G_0 R_0 \frac{z}{R} \sin(\omega t + \delta) \quad (2)$$

that is slightly out of phase (observed in alive rabbit lungs⁽¹⁷⁾) with that of the radial velocity of the alveolus wall $\dot{R} = -R_0 \beta \omega \sin(\omega t)$. The parameter G_0 stands for the amplitude of the flow shear rate approaching the alveolus mouth.

As in HYT we assume that $\delta = 10^0$ for the phase angle. The alveolus expansion velocity (1) and the shear flow (2) induce a very complex flow field $\mathbf{v}$ inside the alveolus (e.g., Fig. 3) that is wholly dependent on a single dimensionless shear parameter γ ,

$$\gamma = G_0 / \beta \omega. \quad (3)$$

FIG. 4. The geometrical and kinematical model of a lung alveolus.

In essence, the γ parameter reflects alveolus placement along the acinar tree (see Fig. 2 in HYT for a distinctive

correlation that exists between γ and the generation number of lung airways). For rigid alveoli $\beta = 0$ and $\gamma \rightarrow \infty$, while for stretching alveoli β is nonzero and the value of γ varies according to changes in the shear rate G_0 along the acinar tree. Generally, the value of γ decreases with increasing generation number because the flow rate inside the airways diminishes with each successive bifurcation.

Haber et al.⁽⁹⁾ obtained a generic solution $\mathbf{v}^H$ describing the flow field inside an alveolus of radius *unity* that its wall expands with a *unit* radial velocity. Pozrikidis⁽⁸⁾ derived a generic solution $\mathbf{v}^P$ depicting the flow field induced inside a hemispherical cavity of radius *unity* that is affected by a *unit* downstream shear rate flow. Thus, the combined Stokes flow field is given by,

$$\mathbf{v} = -\beta\omega R_0[\mathbf{v}^H \sin(\omega t) + \gamma\mathbf{v}^P \sin(\omega t + \delta)]. \quad (4)$$

The dimensionless equation that governs the motion of a particle of diameter D_p in a gravity-free environment and neglecting particle inertia, possesses the simplified form,

$$\frac{d\hat{\mathbf{r}}_p}{d\hat{t}} = -\beta[\sin \hat{t}\mathbf{v}^H(\hat{\mathbf{r}}_p/\hat{R}) + \gamma \sin(\hat{t} + \delta)\mathbf{v}^P(\hat{\mathbf{r}}_p/\hat{R})], \quad (5)$$

because particles 0.5–2 μm in diameter are strongly affected by aerodynamic forces while inertia forces and Brownian displacements are negligibly small (see HYT).

The caret symbol in (5) is used to define the dimensionless variables,

$$\hat{\mathbf{r}}_p = \mathbf{r}_p/R_0, \quad \hat{t} = \omega t, \quad \hat{R} = R/R_0 = 1 + \beta \cos \hat{t}. \quad (6)$$

where $\mathbf{r}_p$ is the instantaneous location of the particle center.

The solution of (5) depends upon seven dimensionless parameters: three parameters stand for the particle initial position ($\hat{x}_{p0}, \hat{y}_{p0}, \hat{z}_{p0}$); an additional three characterize the flow field, namely, the dimensionless expansion amplitude β , the shear parameter γ , and the phase angle δ . The seventh parameter stands for dimensionless particle diameter $\alpha = D_p/R_0$. This last parameter is introduced via the condition that finite size particles may not penetrate the alveoli walls.

It is interesting to note that the respiratory frequency ω has no direct impact on the solution under gravity-free conditions. It merely serves to scale the time. Also note that particle and alveoli sizes affect the solution through the value of α only.

Notwithstanding, we shall use the physical particle diameters instead of α with $R_0 = 100 \mu\text{m}$. However, the solution would be similar for various values of R_0 and D_p as long as the value of α is preserved.

Equation (5) is solved using Matlab's ODE45 procedure, a self-starting Runge-Kutta method, and the desired accuracy is obtained with 1000×1000 grid-points for the velocity fields $\mathbf{v}^H$ and $\mathbf{v}^P$ (the third spatial dimension is represented analytically) and relative and absolute tolerances of 10^{-8} and 10^{-16} , respectively (see HYT for in-depth investigation).

Results and Discussion

Particle motion within the lung in a microgravity environment is distinctly different from that obtained in HYT that addressed gravity effects on particle trajectories and

deposition. In a gravity-free environment 0.5–2- μm particles closely move along pathlines, namely, their center of volume follows closely the trajectories of fluid particles. Neglecting effects of inertia and diffusion, it seems that no deposition can occur in this case. Notwithstanding, because particles are of finite size, their external surface may contact the alveoli walls and be captured. This geometrical interception mechanism must obviously depend upon the particle diameter—for a given alveolus radius—and on the alveoli expansion mechanism (or, more precisely, upon the dimensionless parameters α and γ).

The dependence of particle trajectories upon alveoli shear to expansion ratio γ

Figure 5a, b, and c illustrates the trajectories of a 2- μm particle during five breathing cycles for three different values of the alveolus shear to expansion ratio parameter $\gamma = 20, 100$, and 200, which correlate to shear flow developed inside generations 23, 22, and 21, respectively, along the acinar tree. The particle is initially located at (0.3, 0.3, -0.7). For the smallest value tested $\gamma = 20$, the particle moves along almost periodic orbits mainly contained in the yz -plane and slowly drifts in the x -direction. The slow drift, per unit cycle, in the x direction (or $-x$ direction, for particles initially located at the $-x$ side of the alveolus) stems from the combined effect of expansion and shear flows and the asynchrony between the flows. For $\gamma = 100$ HYT predicts that the trajectory is quasi-periodic and remains almost exclusively in the original x -plane as can vividly be seen in Figure 5b. (Quasi-periodicity can best be observed by using a Poincare map, namely, sampling particle location after every period. If the trajectories are quasi-periodic, these locations never overlap but result in a closed line.) For $\gamma = 200$ HYT predicts the onset of chaos in some regions of the flow field. Figure 5c also shows the increasing number of orbits owing to the fact that shear flow becomes more dominant.

Had the phase angle δ been zero, the particle would have performed a periodic motion, never depositing or leaving the alveolar cavity.⁽⁹⁾ Similarly, in the absence of an expansion mode ($\gamma \rightarrow \infty$), a closed streamline region would be formed inside the cavity that is completely separated from the flow in the adjacent duct (Fig. 2⁽⁸⁾). Thus, a particle placed outside the alveolus can never enter the alveoli and its deposition inside the alveolus would have been impossible. However, according to our flow model, which accounts for expansion and contraction of the alveoli, slow motion of the particle toward the rim may eventually cause its interception or its escape from the alveolus.

Obviously, for very small values of γ the flow is periodic [see Eq. (5)], and particles trace the same locations repeatedly. Hence, for $\gamma = 20$ which is almost periodic, almost no geometrical interception occurs.

Figure 6b, d, and e addresses the fate of 2- μm particles after 10 breathing cycles for various γ values and for particles evenly distributed inside the alveolus. Here, we tacitly assume that particles can indeed reach all these initial locations either by convection, inertia, or diffusion effects. It is extremely difficult to determine, at this stage, what is the probability that a particle reached the assumed initial location due to the foregoing mechanisms. The symbol attached to a point signifies whether after the noted number of

breathing cycles a particle, initially located at that point, is still moving inside the alveolus (*), has left the alveolus and moves down- or upstream inside the adjacent alveolar duct (.) or has deposited (+). Figure 6b indicates that for a $\gamma = 20$ only a single particle has deposited for the given initial distribution of particles, while for $\gamma = (100, 200)$ the number of deposited particles is (43, 33) according to Figure 6d and e, respectively. Note that the number of deposited particles increases from $\gamma = 20$ to $\gamma = 100$ but decrease for $\gamma = 200$, a quite counterintuitive result. The onset of chaos occurs at about $\gamma = 200$. (See Haber et al.⁽⁹⁾ and Fig. 3, which indicates that at $\gamma = 200$; a saddle point and a homoclinic orbit are formed, a pattern intimately related with chaotic trajectories.) (A saddle point is a point of equilibrium in the streamline map that includes four branches: two leaving and two entering it. A homoclinic orbit is created if a branch leaving the saddle point also returns to it.) Thus, one might expect that chaos would increase the probability of particles getting close to the alveolus wall and increase geometrical interception monotonously with γ . In a previous article Haber and Tsuda⁽¹⁸⁾ addressing the amount of mixing in a comparable flow system encountered a similar dilemma in which mixing has a local maximum at about $\gamma = 100$ than it reduces and reaches a local minimum at about $\gamma = 200$ and increases again for increasing values of γ . A possible explanation is somewhat similar to that offered by Haber and Tsuda.⁽¹⁸⁾ There are two competing mechanisms that may affect geometrical interception: flow periodicity and chaos. The former would cause diminished geometrical interception, while the latter enhances it. Thus, for $\gamma = 20$, periodicity is the major mechanism controlling particle trajectories and geometrical interception is exceedingly small. The orbits are quasi-periodic for the intermediate value of $\gamma = 100$ and chaotic at $\gamma = 200$. For $\gamma = 100$, a particle would sample many nonrepeating locations near the wall and thus has a higher probability to be trapped. For $\gamma = 200$, just as chaos kicks in, the flow becomes more periodic (for $\gamma \rightarrow \infty$ the flow is periodic again) and geometrical interception decreases by a small amount. Thus, the geometrical interception mechanism is the least effective in alveoli of ingeneration 23 increases at generation 22 and decreases only slightly at generation 21. (This result by no means states that the *total* number of particles trapped in the distal region of the acinus is smaller, because this region comprises of an increasing number of alveoli.) Figure 7 illustrates the effect of γ on the deposition sites inside the alveolus. Particles, $0.5 \mu\text{m}$ in diameter, are initially placed according to Figure 6. It is shown that most particles tend to deposit at the distal end of the alveolus and close to the rim. However, for $\gamma = 200$, a wider spread is observed, probably, due to the onset of chaos.

FIG. 5. Particle trajectories under gravity-free conditions during five breathing cycles. The particle is initially located at $(0.3, 0.3, -0.7)$ and $\delta = 10^\circ$. In case (a) $\gamma = 20$, the particle moves along almost periodic orbits mainly contained in the yz -plane as it slowly drifts in the x -direction. In case (b) $\gamma = 100$ the trajectory is quasi-periodic and remains almost exclusively in the original x -plane. In case (c) $\gamma = 200$, HYT predicts the onset of chaos in some regions of the flow field and the number of orbits increases owing to the fact that shear flow becomes more dominant.

FIG. 6. The effect of various particle initial positions and γ on particle fate for particle size $D_b = 2 \mu\text{m}$ and $\delta = 10^\circ$ under gravity-free conditions. The symbol attached to a point signifies whether a particle, initially located at that point, is still moving inside the alveolus (*), has left the alveolus and moves down- or upstream inside the adjacent alveolar duct (.), or has deposited (+). (a) $\gamma = 20$, 5 breathing cycles; (b) $\gamma = 20$, 10 breathing cycles; (c) $\gamma = 20$, 20 breathing cycles; (d) $\gamma = 100$, 10 breathing cycles; (e) $\gamma = 200$, 10 breathing cycles; (f) a blowup of a small area of Figure 6e illustrates the sensitivity of the results to particle initial positioning.

FIG. 7. Deposition sites of $0.5\text{-}\mu\text{m}$ particles, initially positioned according to Figure 6, under gravity-free conditions, 10 breathing cycles, and $\delta = 10^\circ$. for (a) $\gamma = 20$, (b) $\gamma = 100$, (c) $\gamma = 200$.

In the next section particle fate is discussed vis-à-vis its initial location, size, number of breathing cycles, and the phase lag δ between the shear velocity and alveoli expansion.

The dependence of particle fate upon, number of breathing cycles, initial position, particle size, and phase lag

Number of breathing cycles. Figure 6a, b, and c addresses the fate of $2\text{-}\mu\text{m}$ particles vis-à-vis the number of breathing cycles. The particles are evenly placed initially inside the alveolus at the $x = 0.2$ plane and calculations are terminated after 5, 10, and 20 breathing cycles. One easily observes that increasing the number of breathing cycles hardly changes the number of deposited particles. Its sole effect is to decrease the number of particles still moving inside the alveoli. This effect may be important if the diffusion

FIG. 8. The effect of particle initial positions and sizes on its fate under gravity-free conditions ($\gamma = 100$) and $\delta = 10^\circ$. The symbol attached to a point signifies whether a particle, initially located at that point, is still moving inside the alveolus (*), has left the alveolus and moves down- or upstream inside the adjacent alveolar duct (.), or has deposited (+). (a) Particle diameter $D_b = 2\text{ }\mu\text{m}$; (b) particle diameter $D_b = 1\text{ }\mu\text{m}$.

mechanism is accounted for, leaving more time for particles to diffuse and reach the alveolar walls.

Initial position. Figure 6a, b, and c also reveals very complex and rich maps. In some regions, particles behave uniformly. For instance, particles located initially near the cavity opening are more likely to leave and many located near its bottom are likely to stay on or deposit. However, in a region near the saddle point (shown in Fig. 3), particles placed at close proximity to each other may behave in a completely nonuniform manner. This sensitivity to initial conditions is the hallmark of chaotic flows. Indeed, Figure 6f shows a blowup of a small region near the saddle point. It manifests the entanglement and the totally unpredictable behavior of very close points.

Particle size. The effect of particle size on its fate and the deposition sites is addressed in Figures 8 and 9 where particles, 1 and $2\text{ }\mu\text{m}$ in diameter, are examined for $\gamma = 100$. They manifest that smaller size particles are less inclined to deposit

FIG. 9. Deposition sites for $\gamma = 100$, $\delta = 10^\circ$ and (a) $D_b = 1 \mu\text{m}$, (b) $D_b = 1 \mu\text{m}$ under gravity-free conditions.

due to the geometrical interception mechanism, and that deposition sites occur mainly near the distal side of the alveolus. Darquenne et al.⁽³⁻⁵⁾ observed that particle size has only a slight effect on particle deposition in a microgravity environment. However, one should notice that Darquenne et al.⁽³⁻⁵⁾ have monitored the total number of particles deposited inside the lung as a whole, namely, interception at the upper airways, bifurcation regions, and the acinus, whereas our prediction pertains to the alveolar region only. Thus, alas, no rigorous or meaningful comparison can be made with their experiments.

Phase lag. The effect of and phase lag $\delta = 5^\circ$ shown in Figure 10 is examined versus those illustrated in Figures 8b and 9b in which the phase lag is $\delta = 10^\circ$. In all foregoing figures particles are $1 \mu\text{m}$ in diameter and $\gamma = 100$. They support our contention that periodicity of the flow reduces the number of deposited particles. The smaller phase lag angle is, the "more" periodic the flow field tends to be. In the limiting case of $\delta = 0$ the flow is completely periodic and no deposition would occur. The foregoing results manifest the importance of alveolar expansion that combined with the geometrical interception mechanism yield nonzero deposition of particles inside lung alveoli. Had the flow model disregarded the off-phase acinar expansion, zero deposition due to geometrical interception would have been predicted.

FIG. 10. The effect of phase lag on particle fate and the deposition where the particle $1 \mu\text{m}$ in diameter is examined for $\gamma = 100$ and phase lag of $\delta = 5^\circ$.

Conclusions

With the onset of space programs, astronauts were hap-hazardly exposed to aerosolized particles floating in the space cabin. Particle deposition inside the lung alveoli due to the geometrical interception mechanism has not been studied widely, and may affect astronauts' health. This article focuses on this mechanism. This mechanism of geometrical interception may also be important to consider when one predicts the deposition of porous particles (D.A. Edwards type drug particles), which are mainly affected by convection due to their large diameter and low density.

Under gravity-free conditions, particles in the $0.5\text{--}2\text{-}\mu\text{m}$ size range are strongly affected by aerodynamic drag forces and to a much lesser extent by their inertia (the Stokes number is of the order of 10^{-4} ; see Haber et al.⁽¹⁵⁾ and Brownian motion. Consequently, particle trajectories follow fluid pathlines closely and geometrical impaction is the governing mechanism that may affect their deposition. If no expansion of the alveolus is considered, particles initially located inside the airways would travel back and forth along the alveolar ducts, performing a cyclic reversible motion during the breathing cycle, never penetrating the alveoli during the breathing process because the flow streamlines inside the alveolus, are known to be completely separated from that inside the duct.

Thus, no deposition can be predicted by rigid wall alveoli models.

However, if alveoli expansion is accounted for, particles may be diverted toward the cavity region. Because chaotic particle motion may ensue, the fate of the particles is very sensitive to their initial location. Particle deposition due to geometrical impaction may occur with their majority entrapped at the distal area of the alveoli and close to the rim. More particles are deposited in an alveolus located at generation 21 and 22 of the acinar tree compared with that of generation 23, and larger particles are more likely to deposit due geometrical interception. We reiterate that the foregoing conclusions were reached disregarding diffusion, gravity, and inertia effects while focusing on the mechanism of "geometrical interception" only.

We would like to emphasize that this work is just one step of a comprehensive investigation on particle deposition in lung alveoli. We believe that better understanding is acquired if one investigates separately the various mechanisms that may affect particle deposition, such as gravity, inertia, and diffusion, all of which result from interaction of particle properties and flow field patterns.

In this article we focus on geometrical interception many times a neglected mechanism.

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Author Disclosure Statement

No conflict of interest exists.

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