Three-dimensional Flow in Subject-specific Human Airways
From the Mouth to the Bronchial Tree

Andrew Banko¹, Filippo Coletti²*, Chris Elkins¹, John Eaton¹

1: Department of Mechanical Engineering, Stanford University, Stanford, USA
2: Department of Aerospace Engineering and Mechanics, University of Minnesota, Minneapolis, USA
* correspondent author: fcoletti@umn.edu

Abstract The three-dimensional flow through an in vitro model of the human airways was studied experimentally. Oral respiration was considered at a regime relevant to moderate exertion and deep inspiration for aerosol drug delivery. The model was based on the high-resolution scan of a healthy adult subject, from the mouth to the several generation of bronchial branching. Magnetic Resonance Velocimetry was used to obtain the three-component velocity throughout the entire volume. The Reynolds number in the trachea at steady inspiration was approximately 4200, which corresponds to 60 L/min of air flow rate. This value is representative of the mean flow during inspiration for a subject performing light activity, and is also typical for inhalation of aerosolized therapeutic drugs. The deep inhalation associated with aerosol drug delivery are typically considered quasi-steady: the present results are directly relevant to this regime. For the oscillatory case, a sinusoidal waveform with the same peak Reynolds number as in the steady case was used. The Womersley number was 6; this regime is relevant for moderate exertion. For both steady and oscillatory flow, a strong single-sided streamwise swirl is present in the trachea. Its origin is identified in the complex three-dimensional flow in the area above the glottis and in the esophageal space. At the first bifurcation, the combination of the swirl and the asymmetric alignment of the trachea impact both the streamwise momentum distribution and the secondary flows in the main bronchi. The latter are not of Dean-type, and indeed their sense of rotation and position are largely different from what is found in idealized branching tubes. In further generations, the streamwise velocity never recovers a symmetric profile and the intensity of the secondary flows remains strong, even in the more distal bronchi. The results indicate that, in real human airways, both axial dispersion (due to uneven streamwise velocity within the cross-section of each bronchus) and augmented dispersion (due to secondary flows within the cross-section) are very effective transport mechanisms. Moreover the oscillatory flow measurements show that axial and augmented dispersion are further increased during inversion phases of the secondary flows. Also, the temporal acceleration in the first part of inspiration/expiration increases the inertia effect, fostering separation at the sharp turns in the bronchial tree. Therefore the oscillatory dynamics augments the mixing with respect to steady flow.

1. Introduction

The fluid mechanics and airway mechanics during respiration is extremely complex: depending on the respiration pattern, the flow may be laminar in the nasal and oral cavities, it becomes transitional and turbulent after constrictions in the throat and at the larynx (with Reynolds numbers in the 1000-5000 range), and eventually turns laminar again after a few generations in the bronchial tree, as the total cross-section increases and the air velocity decays quickly. As a consequence, more than 90% of the total airway flow resistance is produced by the first ten branching generations (Pedley, 1977). The inhalation-exhalation cycle results in a Womersley number (the ratio of unsteady inertial forces to viscous forces) typically around 3, but that can vary by an order of magnitude from rest to exercise (Kleinstreuer and Zhang, 2010). Skewed velocity profiles are present in the curved portion of the oral cavity, and strong secondary motions are set up when the flow turns from the mouth to the pharynx (Heenan et al. 2003), and in the bronchial bifurcations (Fresconi and Prasad, 2007). Various levels of idealization have been accepted in previous studies. In early studies the most common type of simplification has been to represent the airways by assembling simple tubular passages, or other canonical geometries for the mouth-trachea. This approach has been applied broadly to both the bronchial tree (Jan et al., 1989) and the extra-thoracic region (Stapleton et al. 2000). These type of studies have provided fundamental insight into the flow patterns in branching networks and curved/tapered passages. Realistic features such as asymmetric branching and larger than average branching angles are often omitted from idealized representations. In fact specific anatomical features can play a major
role in the flow pattern, as suggested by the large inter-patient variability of deposition efficiency in aerosol drug delivery. Diseases as asthma and cystic fibrosis alter dramatically the size and shape of the central airways, therefore altering the flow topology and regime, which at the typical Reynolds numbers of the first few generations, can easily transition from laminar to turbulent due to a constriction or change in curvature.

Recent advancements in manufacturing technology, measurement techniques and numerical methods have stimulated flow studies in anatomically accurate models, typically obtained by CT or MRI. Examples include Particle Image Velocimetry (PIV) measurements of oscillating flow in the first bifurcation (Grosse et al. 2007), MRI measurements of steady flow in proximal thoracic airways (de Rochefort et al. 2007), Reynolds-Averaged Navier-Stokes (RANS) simulation of upper airways and Large Eddy Simulation (LES) of steady flow from the mouth to the sixth generation. These studies highlight the limitations of idealized models. For example, in a recent LES study of a CT-based airway model, Lambert et al. (2011) found high left-to-right asymmetry in lung ventilation and particle deposition patterns, in agreement with in vivo studies.

Dispersion mechanisms in airway trees are of interest because they relate to the transport of micro- and nano-particles, and because they allow to interpret bolus inhalation tests, in which the patients inhale a detectable gas during a well-defined phase of the breathing cycle. Various transport mechanisms concur: bulk convection due to mean air flow, longitudinal (or axial) dispersion due to in-plane variation of streamwise velocities, augmented dispersion due to secondary flows, molecular diffusion, and turbulent dispersion. Longitudinal and augmented dispersion are especially important due to the airway architecture, that promotes skewed velocity profiles and secondary circulation. Both mechanism are typically considered antagonists, since a cross-plane exchange of momentum result in flatter velocity profiles. Moreover, during ventilation, the so-called convective exchange cause a drift of species because of differences of velocity profiles during inspiration and expiration.

In the present paper we investigate the three-dimensional, time-averaged flow field from the mouth to the eighth bronchial generation in a subject-specific geometry at steady inspiration and during the inspiration/expiration cycle. The specific objective of this contribution is to characterize the major flow features in an anatomically accurate model, in comparison with the established knowledge derived from idealized models, and with the few subject-specific cases reported in the literature.

2. Material and Methods

A subject-specific geometry of the airways was provided by Prof. C. Kleinstreuer (North Carolina State University, NC). The subject is a 47-year old healthy male volunteer, 174 cm for 78 kg. GE 64-slice CT scanner was used to image sections of 500 by 500 mm² at a resolution of 512 by 512 pixels² on the transverse plane. The data were segmented by the image processing software ScanIP (Simpleware Inc.), resulting in the geometry shown in Fig. 1. The most distal bronchi in the model correspond to the eighth generation of branching (Fig. 1b). The geometry was used without any scaling to manufacture the solid model depicted in Fig. 2, which was fabricated by stereolithography at the University of Texas El Paso, TX. It consists of three parts, hermetically flanged together: an inlet piece, an extrathoracic piece, and a thoracic piece. The inlet piece expands the circular inlet (19.85 mm in diameter) into a 20 mm by 60 mm rectangular cross-section, turns the flow by 90 degrees into a 40 mm by 60 mm rectangular cross-section, and smoothly connects to the inlet of the extrathoracic piece. Multiple screens in the expanding section prevent flow separation, and a honeycomb limits secondary flows after the turn. With respect to the original model, the terminal portion of the oral cavity was truncated near the point of largest cross-section (Fig. 1c). This was done to minimize the influence of a specific positioning of the lips and teeth. The bronchi discharge into five separate plena built in the thoracic piece, one for each lobe (see Fig. 2): right upper lobe (RUL), right middle lobe (RML), right lower lobe (RLL), left upper lobe (LUL), and left lower lobe (LLL). In order to avoid mutual interference, the plena have slightly different sizes and shape. Each of them, however, has characteristic dimensions at least 20 times larger than the distal bronchi, and therefore it is deemed that the specific lobe geometry does not affect the bronchial flow. Each plenum is connected to a separate circular outlet (10 mm in diameter).

Water was used as the working fluid, with the addition of copper sulfate at 0.06 mol/L in order to maximize the signal without appreciably changing the fluid properties. At steady inspiration, the inlet flow was 3.78 L/min, which is equivalent to ~60 L/min of air, for a Reynolds number based on the trachea
diameter of \( \text{Re} = 4200 \). This regime is relevant to deep inhalation during aerosol drug delivery. Periodic flow following a sinusoidal waveform was also studied at Womersley number of \( \text{Wo} = 6 \) and same peak Reynolds number as in the steady inspiration case, corresponding to moderate exertion.

**Fig. 1.** Overview of the patient-specific anatomy displaying a global isometric view (a), bronchial path from G1-G8 in the Right Lower Lobe (b), location of STL truncation in the oropharynx (c), and upper airways from mouth to trachea (c, d).

All mean velocity measurements are normalized by the mean velocity in the trachea \( V_T = 0.2 \) m/s, and by the diameter at the trachea \( D_T = 18 \) mm. For the steady inspiration case, the flow is provided by a 1/2 HP magnetic drive centrifugal pump (Little Giant, TE-5.5-MD-HC), that circulates the fluid from a reservoir through the test section located in the magnet bore and back to the reservoir. The mass flow rate of is measured by a paddle wheel flow meter (Blue-White, F-1000). The uncertainty in the mass flow rate is
estimated to be about 2%. Plastic tubes connect the pump to the inlet, and the five plena to the holding tank. The pressure drop through the outlet tubes (about 10 meters long) is much larger than the head loss in any bronchial path. Therefore, because each outlet tube has the same length, each plenum (and therefore each lobe) outputs the same flow rate, i.e. 20% of the total inflow. This was verified by measurements of the flow rate through each outlet tube via an ultrasonic flow meter (Transonic Systems Inc. TS410). The measured outflow rates were found to differ from each other by less than 2.8%, and their sum matched the inflow rate to within 1.1%. This flow partitioning was chosen for simplicity, and is not representative of a specific physiological condition. The effect of different flow distributions among the five lobes can be investigated by regulating valves placed at each plenum outlet, but this was beyond the scope of the present study. For the oscillatory flow case, a custom made pump was used. It consisted of a 500 mL cylinder where a 60mm diameter piston slides. The piston is driven by a threaded rod, actuated by a stepper motor (7.5 W, 200 steps per revolution). The motor is controlled by a programmable voltage input, so that the piston pump produces a sinusoidal flow rate. At the present Womersley number, the oscillation period was 10 seconds.

Velocity data are obtained using the method of Magnetic Resonance Velocimetry (MRV) described by Elkins et al. (2007). The procedure for the data acquisition technique is described by Pelc et al. (1991). The acquisition process lasts several minutes, and the velocity fields acquired are time-averaged. Experiments are performed at the Richard M. Lucas Center for Imaging. A 3 Tesla General Electric whole body scanner is utilized, with a standard transmit-and-receive radio-frequency coil commonly used for imaging human heads. For both steady and oscillatory flow the volume was divided in two, slightly overlapping region of interest, one containing the mouth-throat portion, and the other containing the bronchial tree. Three-component velocity measurements are obtained on a uniform Cartesian grid at a resolution of 0.7 mm in each direction. As a point of comparison, the trachea diameter is about 18 mm, and bronchial airways taper down to 3.7 mm by the sixth/eighth generation. The scanned volume includes both the fluid and the solid walls of the test section. The wall identification is performed via thresholding based on the signal magnitude: voxels with signal magnitude smaller than 10 times the magnitude of the average noise are identified as solid material. In MRV the velocity encoding values \( V_{enc} \) control the maximum measurable velocity that is free of aliasing. The expected uncertainty in the MRV measurements can be calculated from the formula (Pelc et al., 1991):

\[
δ_V = \frac{\sqrt{2} V_{enc}}{π \text{ SNR}}
\]  

(2)

where the signal-to-noise ratio, \( \text{SNR} \), is given by the ratio of the signal in the flow region to the signal in the solid wall. Having fixed the \( V_{enc} \) at 0.7 m/s, this yields an uncertainty of about 2%. The velocity fields acquired are time-average.

For the oscillatory flow it was \( V_{enc} = 0.4 \) m/s. Accelerated sampling was used when scanning the downstream section. The coil was an 8 channel cardiac array, and the acceleration was in the in plane direction for this coronal scan. The phases were triggered by a digital pulse which passed through an ECG converter, and into the ECG trigger on the MRI system. Four triggers per period were sent to the ECG monitor so that the automatic gain in the system would not ramp up. However three out of four triggers were deliberately ignored, in order to effectively sample bins in the 10 second period of the flow oscillation. The acquired velocity was a phase-average of 12 bins within the period. A total of 20 bins were reconstructed using linear interpolation.

3. Results

3.1. Steady inspiration

The extrathoracic airways were found to have significant impact on the flow structures in the trachea and the first bifurcation. A complex three-dimensional flow develops in the above the glottis. Figure 3 shows isosurfaces of \( λ_2 \) (colored by helicity) in the mouth-throat region. This highlights a strong streamwise vortex is generated between the esophageal space and larynx, and squeezes into the glottal constriction. The swirl persists into the trachea, and produce a strong, single-sided swirl. This is apparent in Fig. 4, that shows cross-sections one and two tracheal diameters downstream of the glottis. Color contours of out of plane velocity...
are superposed to in-plane velocity vectors. Evidently this type of inflow cannot be satisfactorily modeled as a fully-developed laminar or turbulent pipe flow (inlet conditions which are often assumed in simulations and experiments reproducing the main bronchial bifurcation).

**Fig. 3.** Isosurfaces of $\lambda_2$ in the oropharynx and larynx colored by helicity, $\bar{u} \cdot \bar{\omega}$, where $\bar{u}$ is the velocity and $\bar{\omega}$ is the vorticity.

**Fig. 4.** Contours of out of plane velocity and in plane velocity vectors along two transverse sections of the flow in the trachea, highlighting the strong streamwise swirl.

The impact on the swirling motion persists down the trachea, as illustrated by the streamtube depicted in Fig. 5. This is initiated from a rectangular profile right below the glottis, and is immediately distorted to a crescent shape, that rotates around the streamwise vertical axis by more than 90 degrees before reaching the first bifurcation. This effect combines with the orientation of the trachea (in this case better aligned with the right main bronchus) and with the streamwise swirl, to modify the momentum and vorticity distribution in the main bronchi. Of particular relevance is the strong shear and the separation region at the entrance of the left main bronchus (Fig. 6). The resulting pattern is largely different from the Dean vortex configuration commonly observed in the literature.
**Fig. 5.** Streamtube emanating from a rectangular closed curve in the trachea, downstream of the glottis. The effect of the streamwise swirl distorting the streamtube is apparent.

**Fig. 6.** Section A-A’ shows contours of velocity magnitude normalized by the mean speed in the trachea, $V_T$, with in-plane velocity vectors at several streamwise locations. B-B’ through E-E’ show contours of the plane-normal velocity component normalized by the mean speed in the trachea, with superimposed in-plane velocity vectors.
The strong shear layers produced by the relatively sharp turnings in the first bifurcations are best illustrated by the distribution of vorticity magnitude. This is shown in Fig. 7, where color contour of vorticity magnitude (normalized by $V_f/D_f$) are plotted along the same coronal section as in Fig. 6 (A-A’). Free shear layers are evident in correspondence of the separation at the entrance of both the right main bronchus and the left main bronchus, as well as in the bronchus leading to the right upper lobe. It is worth reminding that these are time-averaged data. The potential for instantaneous separation and recirculation in these region is very high, as it was pointed out by Grosse et al. (2007)

![Fig. 7. Contours of vorticity magnitude along a coronal section at the main bifurcation (section A-A’ in Fig. 6).](image)

In the bronchial generations the anatomically accurate geometry was found to produce very dissimilar flow structures when compared to idealized representations of the airway network (Fig. 8). The short generation length and the large branching angles reduce the flow development, increase local secondary flow strength, and lead to multiple regions of flow separation. The symmetric arrangement of vortices is also disrupted by the asymmetric branching configuration and by triple bifurcations of the patient-specific anatomy.

To quantitatively assess streamwise velocity profile uniformity and secondary flow strength, the momentum distortion parameter $D$, and the secondary flow energy parameter, $E$, are introduced:

$$D = \frac{\int_A (\bar{u} \cdot \hat{n})^2 dA}{Q^2 / A} - 1$$

$$E = \left( \frac{\int_A (\bar{u} \cdot \hat{t})^2 dA}{\int_A (\bar{u} \cdot \hat{n})^2 dA} \right)^{1/2}$$

where $A$ is the cross-sectional area, $\bar{u}$ is the velocity vector, $\hat{n}$ is a unit normal to the cross-section, $\hat{t}$ is any unit vector tangential to the cross-section, and $Q$ is the volumetric flow rate. $D$ represents the ratio of the streamwise momentum flux of the actual flow to that of a plug flow carrying the same mass flow rate, shifted such that $D \geq 0$. This is a measure of the velocity profile distortion, because a uniform profile carries the minimal momentum for a given flow rate. As a point of comparison, fully developed laminar (parabolic) and turbulent ($1/7^{th}$ power law) profiles have values of $D=1/3$ and $D=0.02$, respectively. The parameter $E$ gives the square root of the ratio of kinetic energy associated with the secondary flows to the streamwise kinetic energy. By taking the square root, $E$ represents the magnitude of a velocity vector carrying the same energy as the secondary flows to that of a velocity vector carrying the same energy as the streamwise components, and thereby measures the strength of secondary flows. As an example, if $E$ is 0.1, then an average velocity vector carrying the same energy as the total flow through the cross-section would have a secondary flow component that is 10 percent of the streamwise component. $D$ and $E$ can be regarded as indicators of axial and augmented dispersion, respectively.
Fig. 8 Contours of plane-normal velocity component with superimposed in-plane velocity vectors for G2-G8 along a bronchial path into the right lower lobe. The velocity has been normalized by the mean speed in the trachea, $V_T = 0.2 \text{ m/s}$. The vectors are shown at the full experimental resolution. Note the change in color scale from slices A-A’ and B-B’ to C-C’ through G-G’.

In Tab. 1 the values of D and E at steady inspiration are reported for the transverse sections depicted in Fig.4 and 6. Both indicators have relatively high values, which is noteworthy because usually axial and augmented dispersion are considered counteracting mechanisms.

<table>
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<td>E-E'</td>
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Tab. 1. Values of the integral parameter D and E along various cross-sections.
### 3.2. Oscillatory flow

In this section the main outcomes of the oscillatory flow measurements are presented. In Fig. 9 the flow rate as a function of time is plotted, as measure by integrating the velocity from phase-resolved MRV at the trachea (section G-G’ in Fig. 4). The very close match with the ideal sinusoidal waveform give confidence on the robustness of the method.

![Graph](image)

**Fig. 9.** Flow rate across the trachea at various phases in the oscillatory flow

Figure 10, 11 and 12 present transverse sections of the trachea at one, two and five diameters downstream of the glottal constriction (i.e. sections G-G’ and H-H’ in Fig. 4, and section B-B’ in Fig. 6), for various phases in the breathing cycle (phases 3, 6, 9, 13, 16 and 19 in Fig. 9). As in previous illustrations, the color contours represent out of plane velocity, overlaid to in plane velocity vectors. It is evident that the single-sided axial swirl is a major feature also during dynamic inspiration, and not only during steady inspiration. The structure actually starts off as two counter-rotating vortices (Fig. 10, phase 3), but one soon takes over and dominates the inspiratory part (phases 6 and 9). During expiration the flow in the upper part of the trachea (Fig. 10 and 11) shows some residue of vortical motion however not much survives in terms of coherent structures (at least in the phase-average sense). Close to the bifurcation instead multiple streamwise vortices generated in the bronchi are seen to merge, especially at peak expiration (Fig. 12, phase 16). However, due to the asymmetry and complexity of the geometry, the picture is much different from the four vortex configuration found in idealized geometries (Fresconi and Prasad, 2007).

![Contour Images](image)

**Fig. 10.** Contours of out of plane velocity and in plane velocity vectors, at a tracheal section one diameter downstream of the glottis. Phases 3 (a), 6 (b), 9 (c), 13 (d), 16 (e), and 19 (f) are shown.
Fig. 11. Contours of out of plane velocity and in plane velocity vectors, at a tracheal section two diameters downstream of the glottis. Phases 3 (a), 6 (b), 9 (c), 13 (d), 16 (e), and 19 (f) are shown.

Fig. 12. Contours of out of plane velocity and in plane velocity vectors, at a tracheal section five diameters downstream of the glottis. Phases 3 (a), 6 (b), 9 (c), 13 (d), 16 (e), and 19 (f) are shown.

Figure 13 illustrates the phase variation of vorticity magnitude along a coronal section of the main bifurcation (section A-A’ in Fig. 6). As one would expect, the phases close to peak inspiration present similar features to the steady inflow. However, phase 7 (Fig. 13c) shows a closer resemblance to the steady inspiratory phase than phase 5 (Fig. 13b), although they have both an instantaneous flow close to the maximum (and so matching the steady inflow case). Indeed in phase 5 the temporal acceleration is still significant. This results in higher inertia, and in turn in larger separation at the entrance of the left main bronchus (as clear from the more pronounced shear layer). During expiration strong shear layers also indicate a tendency to separation, especially on the right main bronchus and the bronchus connected to the right upper lobe.

Figures 14 and 15 presents plots of the variation of the integral parameters D and E at two tracheal sections during the breathing cycle, an upper section (G-G’ in Fig. 4), and a lower section (C-C’ in Fig. 6). Their values close to peak inspiration (phases 5 and 6) are comparable to those found at steady inspiration. During expiration, both D and E are relatively low in the upper tracheal section, because most of the flow structures converging from the bronchi have dissipated along the trachea. On the other hand, at the lower tracheal section the augmented dispersion is much higher during inspiration, due to the strong secondary flow merging from the bronchi. Both D and E reach much larger values close to the inversion points in the
cycle. While the very pronounced peaks at phases 11 and 20 are likely influenced by the streamwise velocities going to zero, the trend across the whole cycle clearly indicates that both D and E greatly increase as the inversion is approached. In terms of mixing mechanisms this means that, in the transient flow in the trachea, axial dispersion and augmented dispersion are slower to decay and quicker to build up than the bulk convection.

![Fig. 13. Contours of vorticity magnitude along a coronal section at the main bronchial bifurcation. Phases 3 (a), 5 (b), 7 (c), 9 (d), 11 (e), 13 (f), 15 (g), 17 (h), and 19 (i) are shown.](image)

![Fig. 14. Integral parameter related to the axial dispersion measured at the upper and lower tracheal section for various phases during the breathing cycle. The continuous line marks the value for steady inspiratory flow.](image)
Figure 16 and 17 display similar plots for parameter D and E at the right and left main bronchi (sections D-D’ and E-E’ in Fig. 6). During inspiration the levels are comparable to the steady case. During expiration the shear layers and the vortical structures from the further generation bronchi, converging into the main bronchi, greatly elevates the level of both axial and augmented dispersion. This is especially true for the right main bronchus. As in the trachea, both D and E are at their maximum.

**Fig. 15.** Integral parameter related to the augmented dispersion measured at the upper and lower tracheal section for various phases during the breathing cycle. The continuous line marks the value for steady inspiratory flow.

**Fig. 16.** Integral parameter related to the axial dispersion measured at the right and left main bronchi for various phases during the breathing cycle. The continuous line marks the value for steady inspiratory flow.

### 4. Conclusions

We have described the three-dimensional, time-averaged velocity field in an anatomically accurate model of the human airways, both at steady inspiration and in oscillatory regime. The Reynolds number in the trachea at steady inspiration was approximately 4200, which corresponds to 60 L/min of air flow rate. This value is representative of the mean flow during inspiration for a subject performing light activity, and is also typical for inhalation of aerosolized therapeutic drugs. The deep inhalation associated with aerosol drug delivery are typically considered quasi-steady: the present results are directly relevant to this regime. For the oscillatory case, the a sinusoidal waveform with the same peak Reynolds number as in the steady case was used. The Womersley number was 6, and the regime is relevant for moderate exertion. The use of a rigid model limits the realism of the study, because airway deformation during breathing can be significant, especially in the
distal bronchi. While the previous results suggest that the effect on the primary and secondary flows in the first four bronchial generations is small, the fluid structure interaction is complex and remains a current topic of research. Further research in a compliant model is warranted in this sense.

The present results suggest that, in real human airways, both streamwise dispersion (due to uneven streamwise velocity within the cross-section of each bronchus) and augmented dispersion (due to secondary flows within the cross-section) are very effective transport mechanisms. Although the subject-specific nature of the present study does not allow for a straightforward generalization, it is demonstrated that neglecting the extra-thoracic airways and idealizing the bronchial tree may lead to qualitatively different conclusions on the inspiratory flow field, with respect to more complete and anatomically accurate representations. The oscillatory flow measurements show that integral indicators for axial and augmented dispersion are increased during inversion phases of the secondary flows. Moreover, the temporal acceleration in the first part of inspiration/expiration increases the inertia effect, and the flow is more prone to separation at the sharp turns in the bronchial tree. All these indicate that, for the considered regime, the oscillatory flow augments the mixing with respect to steady flow, and not only because of the difference between inspiratory and expiratory flow pattern (steady streaming).

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