Journal of Biomechanics 46 (2013) 284–298

Contents lists available at SciVerse ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

Review

Respiratory microflows in the pulmonary acinus

Josué Sznitman*

Department of Biomedical Engineering, Technion-Israel Institute of Technology, 32000 Haifa, Israel

ARTICLE INFO

Article history:
Accepted 23 October 2012

Keywords:
Biofluids
Respiratory flows
Pulmonary acinus
Alveoli
Particle transport
Aerosol deposition

ABSTRACT

Over the past few decades, our understanding of the fluid mechanics characterizing the pulmonary acinus of the lungs has been fundamentally revisited. In the present paper, we review the current knowledge of acinar convective airflows and their role in determining the fate of inhaled aerosols in the distal regions of the lungs. We discuss the influential body of computational and experimental efforts following the revealing bolus studies initiated by Heyder et al. (1988) that have dramatically advanced our description of acinar flow phenomena. In particular, we characterize the range of complex flow topologies that exist locally in alveolar cavities and describe the ensuing convective mechanisms known to generate kinematic irreversibility in the acinus, despite low-Reynolds-number flows. By using dimensional analysis, we shed some light on the intimate coupling that arises in the pulmonary acinus between diffusive, convective and sedimentation mechanisms for aerosol deposition. Finally, we evoke some of the critical challenges that lie ahead in predicting accurately the deposition of inhaled particles across the acinar region and give a brief outlook toward novel approaches for resolving acinar flow dynamics at the real scale.

1. Introduction: a historical perspective

The past 25 years have witnessed a profound reshaping of our understanding of the respiratory fluid mechanics describing the acinar region of the lung. This region is made of hundreds of millions of sub-millimeter gas-exchange units (alveoli) characterized by low-Reynolds-number airflows. Historically, convective acinar flows first drew little attention since research was mostly driven by studies on gas mixing and diffusion (Engel, 1983; Paiva and Engel, 1987). This trend may have resulted from the fact that the principal role of alveoli is to guarantee gas exchange with blood (i.e., oxygen and carbon-dioxide). In particular, in the acinus the role of convective airflows for oxygen transport is effectively negligible under normal circumstances compared to molecular diffusion (Asgharian and Yu, 1988; Hammersley and Olson, 1992; Sapoval et al., 2002; Weibel et al., 2005; Sznitman, 2009). This is best illustrated by the small values of the dimensionless Peclet number comparing convective to diffusive transport; namely, $Pe = UL/D_{mol} \ll 1$ in the acinar region where U is a characteristic velocity, L a characteristic length scale (e.g., airway diameter), and D_{mol} is the molecular diffusivity of the gas.

Until the 1980s, low-Reynolds-number airflows in the distal regions of the lung were widely thought to be kinematically reversible with little flow-induced mixing (Cinkotai, 1974; Davidson and Fitz-Gerald, 1972; Pedley, 1977). In turn, for fine aerosols with little intrinsic motion (e.g., sedimentation, diffusion), the adopted view was that most inhaled particles would be exhaled without mixing with residual gas, leading to negligible deposition within the acinus (Davies, 1972; Ultman, 1985). This classic interpretation was, however, revisited after the seminal work of Heyder et al. (1988) who demonstrated with bolus studies in subjects that non-diffusing inhaled particles do in fact mix significantly with residual alveolar gas. Namely, the deeper the inhaled bolus penetrated into the lungs, the more it became dispersed upon exhalation; the half-width of the expired bolus was observed to be a linear function of the volume to which the bolus initially penetrated, suggesting that convective mixing can occur in the lung periphery and is not confined to central airways only. This shift of paradigm combined with a rising concern to determine the fate of inhaled aerosols given their potential health risks or value as a therapeutic tool, has led to a resurgence of interest to unveil the complex nature of respiratory airflows in the pulmonary acinus.

In the present paper, we review the influential body of work following the series of revealing bolus studies (Darquenne et al., 1998, 1999; Rosenthal et al., 1992; Schulz et al., 1992) that has addressed acinar airflows and their role in determining inhaled aerosol transport. We begin with a short overview of anatomical aspects of the lungs and the pulmonary acinus pertinent to our discussion of fluid mechanics. By assessing through dimensional analysis the governing equations of fluid motion and particle transport, we shed some light on the intimate coupling that arises in the acinus between diffusive, convective and sedimentation

* Tel.: +972 4 8295678.
E-mail address: sznitman@bm.technion.ac.il

0021-9290/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jbiomech.2012.10.028

mechanisms for aerosol deposition. Next, we describe topologies of local alveolar flows and characteristics of kinematic irreversibility. In particular, we discuss existing efforts, both computational and experimental, that have advanced our understanding of acinar flow phenomena. Finally, we highlight some of the critical challenges that still lie ahead in predicting accurately the fate of inhaled particles across the acinar region and give an outlook on promising approaches to unveil acinar flow dynamics at the real scale.

2. Respiratory airways and the acinar morphology

In the human lung, air and blood must be brought into close contact over a large surface area to exchange necessary gases. For this to happen in an orderly fashion, a system of branched airways connects a vast network of airspaces with the external environment (Fig. 1). Alveoli, with a characteristic length scale of $\mathcal{O}(10^{-4})$ m, constitute the basic structural units of the lungs. In an average adult, recent estimates place the number of alveolar spaces at $\sim$480 million (Ochs et al., 2004), providing a total surface area available for gas exchange comparable to the size of a tennis court—on the order of 100 m^2 (Gehr et al., 1978).

Early morphometric studies have characterized the anatomical arrangement of airways using lung casts (Horsfield and Cumming, 1968; Horsfield et al., 1971; Phillips et al., 1994; Weibel, 1963). In its simplest description, lung airways are arranged into a nearly dichotomous tree extending over about $z=23$ generations. Since the number of branches in a symmetric tree doubles with each generation, there are approximately 2^{23} (or 8×10^8) end branches known as terminal alveolar sacs (Fig. 1). This, of course, remains an average value as the number of generations needed to reach the alveolar sacs varies considerably, ranging from about 18 to 30 (Weibel et al., 2005). The observed variability results amongst other from the fact that the lungs form approximately a space-filling tree whose end branches must be homogenously distributed in space and reach into every corner and gap that exist inside the volume formed by the chest cavity. While some spaces are rapidly filled and airways cannot continue to divide, other regions require more bifurcating generations to fill the available space (Weibel, 1984). To this end, a number of morphometric studies have addressed the asymmetric nature of the lungs (Horsfield et al., 1982; Hammersley and Olson, 1992).

Airway variability is also contingent upon the specificities of the acinar space; noticeably, alveolar ducts exhibit irregular branching patterns (Hansen et al., 1975), where the shapes of alveoli are captured by a range of geometries including spheroids, ellipsoids and cylindroids (Hansen and Ampaya, 1975). In turn, significant uneven alveolar ventilation can take place due to variations in shape, size, and location of the alveoli (Berg et al., 2010). Alveolar geometry is also dynamic during breathing as described by the ratio of the alveolar depth to mouth diameter (D/MD), an index first introduced by Klingele and Staub (1970). During normal breathing alveolar shape remains nearly constant (D/MD=0.85–0.9) for lung volumes spanning functional residual capacity (FRC) to total lung capacity (TLC). However, alveoli become narrower (D/MD=0.95–1.5) and ultimately collapse at lung volumes lower than FRC (Klingele and Staub, 1970).

Despite intrinsic asymmetry and acinar irregularity, the lungs may be partitioned into two broad regions. The first 14 or so proximal airways are built as purely conducting smooth-walled "pipes" to distribute convective airflow into the lung (Weibel, 1963). Beyond this point begins the respiratory region. As one enters into the first generations of the acinar tree, individual isolated alveoli start to populate the airway surface; there, respiratory bronchioles are only partly alveolated (Fig. 1). In the more distal airways acinar ducts are gradually surrounded with alveoli of increasing size (Haefeli-Bleuer and Weibel, 1988), until they become entirely covered. This trend is schematically illustrated in acinar airway models (Fig. 2). In the lung parenchyma alveoli are arranged tightly as a foam-like sleeve around the surface of peripheral airways, where each alveolus opens onto a single duct (Weibel, 1984; Weibel et al., 2005). In particular, adjacent alveoli are separated by dividing interalveolar septa that contain dense networks of microvascular capillaries (Mead et al., 1970; Ryan et al., 1969; Reifenrath, 1975). This arrangement allows for an effective alveolar surface area available for gas exchange about five times larger than the duct surface alone.

The pulmonary acinus refers to the terminal unit of the respiratory airways that are directly associated with the gas-exchanging surface (Fig. 1). The most precise definition is that the pulmonary acinus comprises the branched complex of alveolated airways that are connected to the same first order respiratory bronchiole (Haefeli-Bleuer and Weibel, 1988). Since the acinus is a tree-like structure, this description would identify the transitional bronchioles as the stem of the acinus. Estimates place the total number of acini at approximately 30,000 in an average adult. This space accounts for well over 90% of the total lung volume (about 6 L at total lung capacity), while the conducting region holds a mere 150 mL of air known as the "dead space", as it does

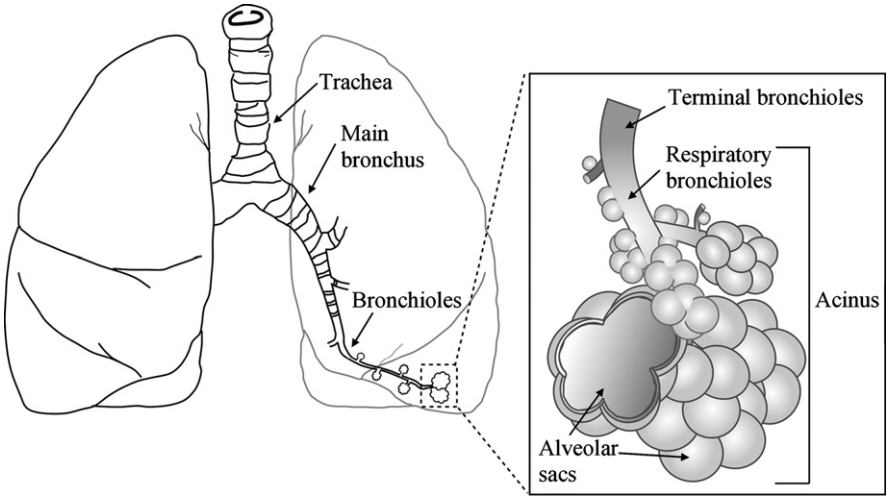

Fig. 1. Schematic of the lungs detailing the pulmonary acinus (*inset*).