Critical Reviews™ in Biomedical Engineering, 39(4):261–262 (2011)

Preface

The development of an oxygen-containing atmosphere on our planet by photosynthetic bacteria billions of years ago resulted in the formation of microorganisms that rely on oxidative phosphorylation for energy. As these life forms grew in size from single cells to multicellular organisms, the ratio of surface area to body volume decreased such that oxygen requirements could no longer be fulfilled via direct molecular diffusion. Nature's solution to this problem was the development and evolution of the cardiopulmonary system, the principle function of which is to bring air from the environment (ventilation) into close juxtaposition with flowing blood (perfusion) over an enormous internal surface area. The lung is the organ that achieves this remarkable feat, and it does so using two systems of branching networks. In direct communication with the atmosphere, a system of sequentially branching airways takes the cross-sectional area of the trachea (a few square centimeters in humans) to the area of the alveolar surface (tens of square meters). Oxygen and carbon dioxide are transported along this airway tree through a combination of convection and diffusion, driven in most species by a mechanically reciprocating process known as breathing. Similarly, the pulmonary vasculature proceeds through multiple divisions, starting from the heart and giving rise to a network of capillaries, that achieves a corresponding increase in surface area for the circulation.

Despite the structural complexity of the mammalian lung, ventilation and perfusion are normally closely matched throughout the entire organ, allowing for the optimal exchange of oxygen and carbon dioxide between air and blood. This relies on specific structure–function relationships in the lung that are essential to its normal operation. Alterations in these relationships are characteristic of many respiratory diseases, and they are often associated with clinical symptoms. Thus, understanding the link between structure and function in the lung is central to clinical diagnoses and to the elucidation of pathogenesis. Moreover, structure–function relationships often yield unique constraints on the development of treatment protocols or therapeutic interventions for diseases that currently constitute a substantial public health burden in all parts of the world.

Despite its complexities, the lung is amenable to detailed quantitative investigation in many ways. The measurement of pressures, flows, and gas concentrations associated with respiration can be achieved with high precision and temporal resolution. Modern imaging modalities provide exquisite anatomic detail about the structure of the airways and vasculature, as both air and blood can easily be differentiated from adjacent structures. Because of these various factors, it is now possible to construct computational models of the respiratory system that possess considerable anatomic fidelity and physiologic relevance. This makes the lung an organ of particular interest to quantitative scientists such as physicists, mathematicians and engineers. Moreover, the application of engineering principles and practices to the study of the respiratory system has now reached a high degree of sophistication. Indeed, much of the forefront of research into pulmonary physiology has become the domain of the biomedical engineer, as is amply demonstrated in this special issue of *Critical Reviews in Biomedical Engineering*.

The issue begins with an article by Winkler and Suki that discusses how the application of network theory and nonlinear interactions within the unique architectural environment of the lung result in the emergence of self-organized pathologic characteristics of two common lung diseases, asthma and emphysema. This illustrates the role that complex systems theory is beginning to play in our understanding of what is, in reality, a very complex organ, and how this may impact the development of disease treatment protocols. Next, Bates and Maksym examine the various specific mechanical factors that contribute to the characteristic hyperresponsiveness of the asthmatic airway. Here we see how the lung must be viewed as a multiscale system in which the laws of classical physics give rise to different types of dynamic mechanical behaviors over a wide range of length and time scales. The article by Ghadiali and Huang then highlights recent developments in computational modeling of the mechanisms responsible for cellular injury during the processes of recruitment and derecruitment that take place during positive pressure ventilation. This illustrates how computational models can help in the design of novel treatment strategies for making respiratory epithelium more resistant to mechanical injury. Tawhai et al. return to the issue of multiscale lung modeling, this time applying it to the airway and pulmonary vascular systems. Just as these systems themselves span huge ranges of surface area, computational modeling bridges our knowledge base of structure and function over many spatial scales, from the molecule to the whole organ. Finally in the review by Kaczka and Dellacá, we see how the classical engineering methodology known as system identification has become the central investigative paradigm for probing the mechanical properties of the respiratory system. Combined with the use of physiologically relevant inverse mathematical models, this approach is beginning to provide clinicians with unparalleled diagnostic information about altered structure–function relationships in pulmonary disease.

The articles in this special issue have been assembled based on a wide range of research interests and expertise from their respective authors. Nonetheless, all share a common thread related to how quantitative engineering tools can be used to elucidate the way in which a remarkably efficient and well-designed complex physiologic system behaves, both in health and disease, as well as over tremendous ranges of length and time scales. We hope that this issue will provide researchers, educators, and clinicians with a compelling introduction to some of the most recent developments in respiratory bioengineering, and that it will help to identify likely future trends in this rapidly emerging field.

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