Human Respiration
Anatomy and Physiology, Mathematical Modeling, Numerical Simulation and Applications
Human Respiration
Anatomy and Physiology, Mathematical
Modeling, Numerical Simulation and
Applications

V. Kulish
Nanyang Technological University, Singapore
V. Kulish
Nanyang Technological University, Singapore

Published by

WIT Press
Ashurst Lodge, Ashurst, Southampton, SO40 7AA, UK
Tel: 44 (0) 238 029 3223; Fax: 44 (0) 238 029 2853
E-Mail: witpress@witpress.com
http://www.witpress.com

For USA, Canada and Mexico

WIT Press
25 Bridge Street, Billerica, MA 01821, USA
Tel: 978 667 5841; Fax: 978 667 7582
E-Mail: infousa@witpress.com
http://www.witpress.com

British Library Cataloguing-in-Publication Data

A Catalogue record for this book is available
from the British Library

ISSN: 1464-9292

Library of Congress Catalog Card Number: 2004116359

No responsibility is assumed by the Publisher, the Editors and Authors for any injury and/or
damage to persons or property as a matter of products liability, negligence or otherwise, or
from any use or operation of any methods, products, instructions or ideas contained in the
material herein.

© WIT Press 2006

Printed in Great Britain by Athenaeum Press Ltd.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval
system, or transmitted in any form or by any means, electronic, mechanical, photocopying,
recording, or otherwise, without the prior written permission of the Publisher.
Contents

Preface x

Chapter 1
Anatomy and physiology of the human respiratory system 1
R.L. Johnson, Jr. & C.C.W. Hsia

1
Postnatal growth and development 1
1.1 Anatomy of the adult lung 1
1.2 Postnatal development 2

2
Conducting airways structure and function 3
2.1 Functional anatomy 3
2.1.1 Distribution of inspired air 3
2.1.2 Air conditioning and filtering inspired air 4
2.2 Viscous resistance to flow in upper airways, lungs and thorax 4
2.3 Alveolar ventilation is not uniform even in the normal lung 5
2.4 Elastic properties of the lungs and thorax 6
2.5 Work of breathing 7

3
Mechanisms of gas exchange 9
3.1 Convective and diffusive distribution and mixing in airways 9
3.1.1 Relative importance of laminar and turbulent flow 9
3.1.2 Relative importance of convection and diffusion in transport 9
3.2 Alveolar gas exchange at equilibrium 11
3.2.1 CO₂ equilibrium 11
3.2.2 O₂ equilibrium 11
3.2.3 Effect of uneven $\dot{V}_A/\dot{Q}$ ratios in the lung 13
3.3 Alveolar capillary gas exchange and physiologic laws of diffusion 13
3.3.1 Diffusing capacity of the lung ($D_L$) 13
3.3.2 Fick’s law of diffusion defines how diffusive transport moves down a concentration gradient ........................................ 14
3.3.3 Krogh’s diffusion constant defines how a concentration gradient is translated into a more convenient pressure gradient .................................................................................. 15
3.3.4 Diffusing capacity of the pulmonary membrane ($D_M$) and its relationship to the Krogh constant .......................... 15
3.3.5 Rate of uptake of respired gases by red cells involving diffusion and chemical binding ........................................ 15
3.3.6 The Roughton–Forster method for estimating membrane-diffusing capacity ($D_{m0}$) and pulmonary capillary blood volume ($V_c$) ................................................................. 16
3.3.7 Recruitment of diffusing capacity during exercise .......... 17
3.3.8 The importance of the relationship between $D_{m0}$ and cardiac output [20]..................................................... 17

4 Pulmonary circulation................................................................. 19
4.1 A low-pressure system............................................................. 19
4.2 The pulmonary vascular waterfall and lung zones ............... 20

5 Respiratory muscles..................................................................... 21
5.1 Innervation and muscle mass of respiratory muscles ............ 21
5.2 Oxygen requirements of breathing .......................................... 22
5.3 Possible limits imposed by respiratory muscles in Olympic athletes ................................................................. 23
5.4 Possible limits imposed by respiratory muscles in a patient with asthma ............................................................ 23

6 Interactions of heart and lungs....................................................... 26

Chapter 2
Fundamentals of alveolar gas diffusion: mathematical modeling and visualization ............................................................ 31
V.V. Kulish, J.L. Lage & A.I. Sourin
1 Human respiratory system ........................................................... 32
1.1 Convection versus diffusion ..................................................... 34
1.2 Alveolar gas exchange: the balance of mass ......................... 36
1.3 Effective diffusion coefficient .................................................. 38
1.4 Lung-diffusing capacity: single-breath test .............................. 40
1.5 Relationship between effective diffusion coefficient and lung-diffusing capacity ......................................................... 41
1.6 Numerical simulation of alveolar diffusion ............................. 43
1.6.1 Steady-state case .............................................................. 43
1.6.2 Transient case ................................................................. 48
1.7 Red blood cell clustering and chain effects ......................... 52
2 Impact of microscopic solid particles on the alveolar diffusion .... 57
3 Visualization of the results ......................................................... 61
Chapter 3
Lung-gas composition and transfer analysis: O₂ and CO₂ diffusion coefficients and metabolic rates ................................................................. 77
D.N. Ghista, K.M. Loh & D. Ng

1 Introduction ........................................................................................... 77
2 Lung-air composition analysis (and O₂ consumption and CO₂ production rates).................................................................................... 78
   2.1 Calculation of O₂ consumption rate and CO₂ production rate ...... 78
   2.2 Dead-space air composition.......................................................... 79
   2.3 Alveolar-air composition and partial pressures ............................ 80
3 Lung gas-exchange model and parametric analysis .............................. 81
   3.1 Expressions for $D_{O₂}$ and $D_{CO₂}$ .................................................... 81
   3.2 Alveolar O₂ and CO₂ partial-pressure expressions ....................... 85
   3.3 Arterial and venous O₂ and CO₂ partial-pressure expressions .......... 86
   3.4 Sequential procedure to compute $D_{O₂}$ and $D_{CO₂}$ ..................... 88
   3.5 Determining $D_{O₂}$ and $D_{CO₂}$ ......................................................... 89
4 Case studies ........................................................................................... 90

Chapter 4
Lung ventilation modeling and assessment ...................................................... 95
D.N. Ghista, K.M. Loh & M. Damodaran

1 Introduction ........................................................................................... 95
1.1 Role of lung ventilation ................................................................ 95
2 Lung ventilation performance using a linear first-order model ............ 96
3 Ventilatory Index ................................................................................... 101
   3.1 Noninvasively determinable ventilatory index ............................. 101
4 Variations in R and C during a respiratory cycle (towards nonlinear) ................................................................. 103
   4.1 Nonlinear compliance ................................................................. 104
5 Work of breathing (WOB)................................................................. 106
6 Second-order model for single-compartment lung model ..................... 108
7 Two-compartmental linear model .......................................................... 110
   7.1 Two compartmental model using first order ventilatory model ......... 112
      7.1.1 Stiff right lung (with compliance problems) ......................... 115
      7.1.2 Right lung with R problems .................................................... 115

Chapter 5
Modeling of two-phase flow in the human respiratory system .................. 117
V.V. Kulish, B. Wijayanto & C.S. Lim

1 Introduction .......................................................................................... 117
2 Methodology ........................................................................................ 118
   2.1 Geometry of the human respiratory duct ...................................... 118
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2</td>
<td>Self-similarity of the flow through the human respiratory duct</td>
<td>120</td>
</tr>
<tr>
<td>2.3</td>
<td>Transformation of the Navier-Stokes equation</td>
<td>121</td>
</tr>
<tr>
<td>2.4</td>
<td>The initial and boundary conditions</td>
<td>121</td>
</tr>
<tr>
<td>2.5</td>
<td>Computation of the velocity field</td>
<td>122</td>
</tr>
<tr>
<td>2.6</td>
<td>Computation of the concentration field</td>
<td>123</td>
</tr>
<tr>
<td>2.7</td>
<td>Fractal (Fractional) approach to the problem</td>
<td>123</td>
</tr>
<tr>
<td>3</td>
<td>Results</td>
<td>125</td>
</tr>
<tr>
<td>4</td>
<td>Discussion</td>
<td>127</td>
</tr>
<tr>
<td>5</td>
<td>Conclusions</td>
<td>127</td>
</tr>
</tbody>
</table>

**Chapter 6**

Quantification of human physiological response to toxic substances

V. Kulish & V. Novozhilov

1. Introduction | 129
2. Preliminary considerations | 130
3. Basic definitions and the scale of capability | 131
4. Conclusions | 133

**Chapter 7**

Anatomically based modeling of pulmonary structure

M.H. Tawhai

1. Introduction | 136
2. Finite-element models of the human lung lobes | 137
   2.1 High-order elements | 137
   2.2 Geometry-fitting | 138
   2.3 Mesh customization | 140
3. Finite-element models of the conducting airways | 141
   3.1 Modeling the central conducting airways | 143
   3.2 Modeling the conducting airway tree | 144
4. Modeling the respiratory airways as a volume-filling mesh | 147
   4.1 3D Voronoi meshing technique | 147
5. Modeling the microcirculation as a segmented network | 149
   5.1 2D Voronoi meshing technique | 150
6. Summary | 152

**Chapter 8**

Applied chest-wall vibration therapy for patients with obstructive lung disease

J.H. Ong & D.N. Ghista

1. Introduction | 157
2. Experimental methodology | 159
3. Theoretical considerations based on guidelines for HFCCT | 161
4. Results and discussions | 162
5. Concluding remarks | 165
Chapter 9
Indicator for lung status in a mechanically ventilated COPD patient using lung-ventilation modeling and assessment
D.N. Ghista, R. Pasam, S.B. Vasudev, P. Bandi & R.V. Kumar

1. Introduction ........................................................................................... 170
2. Methodology .......................................................................................... 171
3. Lung-ventilation model ......................................................................... 171
4. Determining lung compliance ($C_a$) and air-flow resistance ($R_a$) ....... 175
5. Formulating a lung-ventilatory index ($LVI$) incorporating $R_a$ and $C_a$ .......................................................................... 176
6. Evaluating lung-ventilatory index ($LVI$)................................................ 178
   6.1 $LVI$ characteristics ........................................................................ 178
   6.2 Comparing the efficacies of $R_a$ and $C_a$ with $LVI$ ....................... 178
   6.3 $LVI$ as a reliable predictor of ventilator discontinuation............. 181
7. Assessing lung-improvement index ($LII$) and rate of lung improvement ($\kappa$) ................................................................. 182
8. Conclusion ............................................................................................. 184

Chapter 10
Mechanics of proportional-assist ventilation ................................................. 187
A.C. Lua & K.C. Shi

1. Introduction ........................................................................................... 188
2. Development of proportional-assist ventilation..................................... 190
3. Theory of proportional-assist ventilation............................................... 192
4. Proportional solenoid valve PAV system.............................................. 194
5. Experimental results and discussion....................................................... 199
   5.1 Spontaneous breathing tests on breathing simulator ................. 199
   5.2 Performance tests on PAV system using breathing simulator .... 202
      5.2.1 PAV tests on breathing simulator with high resistance ... 202
      5.2.2 PAV tests on breathing simulator with high elastance .... 205
      5.2.3 PAV tests on breathing simulator with weak effort ........ 207
   5.3 Simulated tests on healthy human subjects................................. 210
      5.3.1 In-vivo PAV tests to overcome high resistance .......... 212
      5.3.2 In-vivo PAV tests to overcome high elastance .......... 214
6. Conclusions ........................................................................................... 215
Since ancient times breathing was believed to be the most important feature of life itself. The very Universe was viewed as a huge breathing organism, within which every part was related to everything else through a process of vibration – breath. Nowadays, our understanding of the laws governing the Universe and life has grown tremendously. Yet this has not changed our perception of breathing as one of the most important mechanisms of life support. In the human body, everything depends on the delivery of oxygen. Just think how long we can survive without eating and drinking in comparison to our ability to survive without breathing!

Therefore, the scientific study of the respiratory function becomes of paramount importance. Recent advances in applied mathematics, physics, engineering and other natural sciences make such a study quite feasible.

The book became possible as a result of a ten-year research collaboration of physicians, engineers, physicists and applied mathematicians. Hence, the material presented in this book covers a wide range of phenomena related to human respiration. Beginning with physiological and anatomical aspects of the respiratory system, the study goes into macro- and micro-scale modeling of the gas exchange processes that take place in the course of breathing. Such models allow in vitro simulations and even computer visualization of the processes involved. This is possible due to the recent advances in computational techniques and computer graphics, in particular.

It is worth mentioning here that the application of mathematical methods immediately yielded several very important results. To provide just one example: it became possible to explain the appearance of respiratory spaces on the walls of higher respiratory ways starting from the mass conservation principle applied to the system of respiratory ways. Another very important achievement from applying seemingly pure mathematical concepts was the possibility of modeling air flow through all the scales of the respiratory ways if these ways are viewed as a fractal structure.

A special chapter is devoted to the anatomically based computer modeling of the pulmonary structure. This modeling is essential if one wishes to obtain realistic results of computer simulations within the respiratory system. This modeling, therefore, may be of great help to those who concern themselves with numerical simulations within the lungs.

From these quite general models, the study evolves into more detailed investigations of such aspects as the impact that microscopic particles present in
the air have on the respiratory performance – both on their way downstream the respiratory duct and within the alveolar region. The breathing in an environment polluted by toxic substances has been as well considered: it becomes possible to quantify the physiological response of humans in such environments.

The lung ventilatory function is also investigated. As a result, some integral criteria (indices) for characterizing the lung performance have been proposed. In addition, the lung performance has been related to the cardiac function.

Consideration of therapeutic techniques employed for treatment of respiratory diseases was not left aside from the text either. Thus, mechanics of proportional assist ventilation is studied in detail. Some aspects of applied chest-wall vibration therapy are also considered.

It is our hope that the present book will help many researchers and students to keep abreast of the most recent developments in the area and will serve as a starting point to those who will carry out further investigations.

The editor is particularly grateful to all the contributing authors for their strong dedication to the project, continuous help and patience in the course of preparing this book.

The Editor
Singapore, March 2006
# Nomenclature

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$A$</td>
<td>area, m$^2$</td>
</tr>
<tr>
<td>$B$</td>
<td>amplitude of the net pressure wave form applied by the ventilator, m</td>
</tr>
<tr>
<td>$C$</td>
<td>compliance, (cmH$_2$O)$^{-1}$</td>
</tr>
<tr>
<td>$c$</td>
<td>concentration, kg/m$^3$</td>
</tr>
<tr>
<td>$d$</td>
<td>distance from RBC distribution center to center of domain, m</td>
</tr>
<tr>
<td>$D_{\text{eff}}$</td>
<td>effective diffusivity, m$^2$/s</td>
</tr>
<tr>
<td>$D_l$</td>
<td>lung-diffusing capacity, m$^3$/(Pa s)</td>
</tr>
<tr>
<td>$G$</td>
<td>control gain</td>
</tr>
<tr>
<td>$E$</td>
<td>elastance of respiratory system, cmH$_2$O/l</td>
</tr>
<tr>
<td>$H$</td>
<td>integration constant in the solution for the dynamic-equilibrium differential equation governing lung dynamics</td>
</tr>
<tr>
<td>$K_1$</td>
<td>proportionality between airway pressure and inspired volume, cmH$_2$O/l</td>
</tr>
<tr>
<td>$K_2$</td>
<td>proportionality between airway pressure and inspired flow rate, cmH$_2$O/l/s</td>
</tr>
<tr>
<td>$k_a$</td>
<td>averaged time constant of the respiratory cycle, s</td>
</tr>
<tr>
<td>$K_3$</td>
<td>control parameter</td>
</tr>
<tr>
<td>$M$</td>
<td>gas molecular mass, kg/kg-mol</td>
</tr>
<tr>
<td>$N$</td>
<td>total number of RBC</td>
</tr>
<tr>
<td>$P$</td>
<td>gas partial pressure, Pa</td>
</tr>
<tr>
<td>$P_a$</td>
<td>alveolar pressure, cmH$_2$O</td>
</tr>
<tr>
<td>$P_{\text{app}}$</td>
<td>total applied pressure to respiratory system, cmH$_2$O</td>
</tr>
<tr>
<td>$P_{\text{aw}}$</td>
<td>airway pressure, cmH$_2$O</td>
</tr>
<tr>
<td>$P_k$</td>
<td>peak pressure: maximum lung pressure, cmH$_2$O</td>
</tr>
<tr>
<td>$P_d$</td>
<td>pressure generated by elastic recoil of respiratory system, cmH$_2$O</td>
</tr>
<tr>
<td>$P_L$</td>
<td>lung airflow driving pressure, cmH$_2$O</td>
</tr>
<tr>
<td>$P_m$</td>
<td>mouth pressure, cmH$_2$O</td>
</tr>
<tr>
<td>$P_{\text{max}}$</td>
<td>pressure produced by respiratory muscles, cmH$_2$O</td>
</tr>
<tr>
<td>$P_N$</td>
<td>net lung pressure, cmH$_2$O</td>
</tr>
<tr>
<td>$P_p$</td>
<td>pleural pressure, cmH$_2$O</td>
</tr>
<tr>
<td>$P_{\text{ref}}$</td>
<td>reference gas partial pressure, Pa</td>
</tr>
<tr>
<td>$P_{\text{res}}$</td>
<td>dissipated pressure due to resistance of respiratory system, cmH$_2$O</td>
</tr>
</tbody>
</table>
$P_1$  
pause pressure: lung pressure at which the lung volume is maximal, cmH$_2$O

$P_{al}^{O_2}$  
alveolar O$_2$ partial pressure, mmH$_2$O

$P_{cap}^{O_2}$  
capillary O$_2$ partial pressure, mmH$_2$O

$P_{al}^{CO_2}$  
alveolar CO$_2$ partial pressure, mmH$_2$O

$P_{cap}^{CO_2}$  
capillary CO$_2$ partial pressure, mmH$_2$O

$Q_{ah}$  
arrest blood flow rate, l/min

$Q_{ae}$  
arrest blood flow rates at arrest end, l/min

$Q_{vb}$  
vessell blood flow rate, l/min

$Q_{ve}$  
vessell blood flow rate at vessell end, l/min

$R$  
resistance of respiratory system, cmH$_2$O/l/s

$R$  
distribution radius or effective radius, m

$S$  
diagonal half-length, m

$T$  
temperature, K

$t$  
time, s

$V$  
volume, m$^3$

$V'$  
volumetric flow rate, m$^3$/s

$x, y, z$  
Cartesian coordinates

$X, Y, Z$  
coordinates

Greek symbols

$\gamma$  
dimensionless gas partial pressure

$\theta$  
phase of oscillating pressure profile applied by the ventilator, rad

$\kappa$  
coefficient corresponding to the rate of improvement or deterioration in lung status

$\omega$  
frequency of the oscillating pressure profile applied by the ventilator, Hz

Mixed and other symbols

$\Delta t$  
time lag between the peak and pause pressures, s

$\nabla$  
gradient

$\nabla^2$  
the Laplace operator

Abbreviations

BMI  
body-mass index

CF  
cystic fibrosis

COH  
coherence function

COPD  
chronic obstructive pulmonary disease
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>chest physiotherapy</td>
</tr>
<tr>
<td>CRF</td>
<td>chest-resonance frequency</td>
</tr>
<tr>
<td>FRF</td>
<td>frequency-response function</td>
</tr>
<tr>
<td>HFCCT</td>
<td>high-frequency chest-compression therapy</td>
</tr>
<tr>
<td>HFWCO</td>
<td>high-frequency chest-wall oscillation</td>
</tr>
<tr>
<td>LII</td>
<td>lung-improvement index</td>
</tr>
<tr>
<td>LVI</td>
<td>lung-ventilatory index</td>
</tr>
<tr>
<td>PSV</td>
<td>pressure-support ventilation</td>
</tr>
<tr>
<td>RBC</td>
<td>red blood cell</td>
</tr>
<tr>
<td>RF</td>
<td>respiratory rate or frequency</td>
</tr>
<tr>
<td>RSBI</td>
<td>rapid shallow breathing index</td>
</tr>
<tr>
<td>SBT</td>
<td>spontaneous breathing trial</td>
</tr>
<tr>
<td>SIMV</td>
<td>synchronized intermittent mandatory ventilation</td>
</tr>
<tr>
<td>TV</td>
<td>tidal volume</td>
</tr>
<tr>
<td>WOB</td>
<td>work of breathing</td>
</tr>
<tr>
<td>CABG</td>
<td>coronary-artery-bypass-graft</td>
</tr>
<tr>
<td>SEPs</td>
<td>successfully extubated patients</td>
</tr>
<tr>
<td>UEPs</td>
<td>unsuccessfully extubated patients</td>
</tr>
</tbody>
</table>